A longitudinal study exploring the use of analgesic medication in English care home residents with dementia

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Declaration

I, Francesca La Frenais, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the text.

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Abstract

Background: Analgesic medication is widely used in care homes but little is known about how often this medication is prescribed or administered, or what factors influence its use.

Aim: To describe the prescription and administration of regular and PRN analgesic medication in care homes; to investigate whether individual or care home differences are associated with analgesic use; and to compare analgesic prescribing in English care homes to international prescriptions.

Methods: This study is embedded in a longitudinal study of 86 care homes in England. Data were collected at 0-, 4-, and 12-months. Residents were eligible if they had diagnosed or probable dementia. Analgesic prescriptions are presented by drug and class. Administration of PRN analgesics is described. Individual differences (sociodemographic; agitation [Cohen-Mansfield Agitation Inventory]; dementia severity [Clinical Dementia Rating]; psychotropic drug prescriptions) and care home differences (type; ownership; number of beds; dementia-registered/specialist; CQC rating) are explored using multilevel models.

Results: Data were available for 1483 residents. Around 70% of residents were prescribed analgesics at all study visits, predominantly PRN paracetamol. Overall, PRN analgesics were not administered frequently. There were differences between care homes in administration but these differences were not accounted for by the modelled care home-level variables. Residents with more severe dementia, and males, appear to be more at risk of untreated pain.

Conclusion: This is the largest study to date exploring analgesic administration in care homes. Prescription levels of regular analgesics are lower in England compared to other countries, however it is unclear why. Pain management in care homes is largely reliant on PRN paracetamol that is frequently prescribed but infrequently administered. Care homes differ in how often they administer PRN analgesics and

this is likely due to internal factors. Therefore care home residents are likely to have untreated pain, and some groups are more at risk than others.

Impact statement

There has been a growth in care home research over the last two decades, with increasing focus on dementia, pain, how medication is used, and whether pain is undertreated in care home residents with dementia. While we have some data on regular prescribing, 'as required' (PRN) pain relief is frequently used in care homes and currently little is known about how often it is administered and what factors influence its use. Thus, the data presented in this PhD regarding analgesic prescriptions and PRN administration are not only a significant contribution to the literature, but also demonstrate why it is important for PRN medication data to be collected in future studies and why it should be of interest to care home prescribers.

The findings regarding analgesic prescribing and administration, and factors related to analgesic use, will be disseminated through scholarly journals and will include international collaborations. Cross-country comparisons mean that researchers can explore how the economic, political, and social care landscape impacts medication use. Those intending to collect similar data in future studies can learn from the methodology used here and the associated advantages and limitations.

Outside academia, the clinical and financial implications described in this thesis will be of interest to those working in health care (GPs and other clinicians; pharmacists), social care (care home managers, nurses, and carers), and policy makers (clinical commissioning groups; NICE). There are currently no existing guidelines for treating pain in care home residents and these findings provide a deeper understanding of current medication use in care homes.

The systematic review presented here has already been published in an international peer-reviewed journal, and further papers of the findings are planned, following thesis submission. Oral and poster presentations of the results have been presented at national and international conferences (see 11.2 for details). Further avenues for dissemination and feedback include meetings, presentations, blogs, podcasts (NIHR), and social media (Twitter).

Abbreviations

ADL	Activities of daily living
BNF	British National Formulary
BPSD	Behavioural and psychological symptoms of dementia
CA	Care assistant
CDR	Clinical Dementia Rating
CI	Confidence interval
CMAI	Cohen-Mansfield Agitation Inventory
Coef.	Regression coefficient
ESRC	Economic and Social Research Council
GP	General practitioner
IQR	Interquartile range
MARQUE	Managing Agitation and Raising QUality of LifE
MDS	Minimum Data Set
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute of Health Research
NPC	Noticeable Problems Checklist
NSAID	Nonsteroidal anti-inflammatory drug
OR	Odds ratio
PRN	*pro re nata*; 'as required'
RCT	Randomised controlled trial
UCL	University College London
UK	United Kingdom
US	United States
vs	versus
WHO	World Health Organisation
WS2	Work stream 2 (of the MARQUE project)

Table of contents

Table of figures

Table of tables

Outline of research and statement of personal contribution

This thesis has two overarching aims: first, to comprehensively understand how analgesic medications are used in care homes; second, to explore factors associated with medication use. I was enabled to do this through the MARQUE (Managing Agitation and Raising QUality of LifE in dementia) programme, a longitudinal cohort study exploring, among other areas, symptoms and health resource use including medication, in English care home residents with dementia. I started working full-time for MARQUE as a research assistant in August 2014 and commenced a part-time PhD (one day per week) in November 2014.

Prescription data was already being collected as part of MARQUE, and I amended the case report forms to include data on 'as required' medication, which I had identified as a gap in current knowledge through literature review. These data were collected by myself and a team of researchers based in UCL and clinical research networks across England. Of the 86 care homes included, I personally recruited and collected data from 16 care homes. The systematic review and data analysis was conducted independently of the MARQUE study programme. Throughout this thesis I will be explicit about my contribution.

The first part of the thesis (chapters 1–3) introduces existing knowledge of medication use and behavioural symptoms in care home residents, and comprises a systematic review summarising temporal trends in analgesics. The main body of the thesis (chapters 4–8) describes an empirical study (embedded in the MARQUE programme) observing the prescribing patterns and administration of medication in English care home residents. Throughout the thesis I will refer to the care home participants as residents. Medication use is analysed with regards to resident factors, such as agitation and dementia severity, and care home factors. The thesis concludes (chapters 9-10) with a discussion of the findings in relation to previous literature, a critical appraisal of the research, an exploration of the clinical and policy implications, and directions for future research.

Chapter 1 Introduction

1.1 Summary

This chapter will explore the context for my empirical work. I will describe the setting (care homes), the population (cognitively impaired residents) and the main focus of the thesis (analgesics). I will discuss pain and pain management in the context of these three areas, and factors that may influence pain assessment and treatment.

1.2 Ageing population and dementia

People are now living longer than they have ever done and as a result the age structure of the current population has changed, with over 65s the fastest growing demographic group (Office for National Statistics, 2017). Although advances in medical research, safety, public health, and life expectancy are to be celebrated, age remains the greatest risk factor for developing dementia.

Dementia is a syndrome that includes problems with memory, thinking, communication, changes in behaviour, emotions, and activities of daily living (ADLs) (World Health Organization, 1992). Dementia is used as an umbrella term for different diseases that cause changes in the structure and chemistry of the brain. The most common types of dementia are Alzheimer's disease, vascular dementia, and Lewy body dementia, all of which cause the degeneration of brain cells. The rate of progression and the brain areas affected depends on the type of dementia and the individual. It is estimated that over 700,000 people in England have dementia (Dowrick and Southern, 2014).

1.3 Care homes

There are approximately 405,000 people aged 65 years and over living in care homes in the United Kingdom (UK) (Laing and Buisson, 2014) because they are unable to live independently. A care home is an institution providing accommodation, meals, and 24 hour staffing. They range in size from a few beds to larger facilities with different units. There are two types of care home in the UK: residential homes, also known as care homes without nursing, where people live and can be assisted with personal

care, for example washing, dressing, and eating; nursing homes, also known as care homes with nursing, which are similar to residential homes but also employ registered nurses to provide round-the-clock care for those with a higher level of health needs. Both residential and nursing homes employ care assistants (CAs), also known as nursing assistants, to provide frontline care.

All care home residents should be registered with a GP, and GPs are often central to the care, care co-ordination, and prescribing, for a resident. Some care homes will be served by multiple GPs whereas others may be served by a single GP on a block contract. There are often financial incentives in place for local GP practices, including the capacity to organise private arrangements for providing extra administrative services. Care homes will have different agreements in place regarding level of contact. Thus, models of clinical and multidisciplinary input to care homes can vary across the country and between homes, including pharmacy input (NHS England, 2015, Gordon et al., 2018). There is a drive to increase the number of pharmacists involved in care homes, and local projects that have increased pharmacy input have led to more optimised prescriptions, reductions in hospital admissions, and financial savings (Royal Pharmaceutical Company, 2016).

A survey conducted by the Alzheimer's Society explored the reasons behind care home admission for UK residents with dementia, and found that the main reasons were a lack of community support, and carers being unable to look after the person with dementia (Quince, 2011). Many care home admissions occur following a crisis, such as a hospital admission (Stillwell and Kerslake, 2004). Another common cause for care home admission is agitation (Yaffe et al., 2002, Balestreri et al., 2000), which will be discussed in further detail in 1.4.5.

Care homes come under the remit of social care (as opposed to the health system), because the support provided for the person with dementia is often assistance with ADLs, which is considered to be a social problem. The health care provision for care home residents is different and community medical services are often inadequate compared to people who live outside of care homes (Gordon et al., 2013, Sampson

et al., 2018). Medical care for UK care home residents is provided and co-ordinated by GPs. Normally medication is prescribed by the GP and administered by care home staff.

1.4 Pain and analgesics

1.4.1 Definition of pain, and treatment options

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey and Bogduk, 1994). Pain is considered chronic if it lasts three months or longer, whereas acute pain has sudden onset and is provoked and limited by an underlying cause. Pain can be nociceptive, resulting from damage to tissue, or neuropathic, caused by nerve damage. The two types of pain cause different sensations and are treated with different types of painkillers (analgesics). Analgesics can be divided into non-opioids, opioids, compound analgesics, and adjuvants.

Nociceptive pain is often described as a sharp, aching or throbbing, for example tissue damage, and is treated with non-opioids or opioids.

Non-opioid drugs (some of which are available over the counter) are the most common class, and include paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDS) like ibuprofen. Paracetamol is indicated as first-line therapy for mild to moderate pain in older adults. It has few side effects, but over-dosage can cause hepatic damage; there is also concern over the long-term use of the maximum dosage especially when given to malnourished patients (Abdulla et al., 2013, AGS Panel, 2009). NSAIDs have both analgesic and anti-inflammatory properties, are effective in relieving musculoskeletal pain, and are more appropriate than paracetamol in inflammatory arthritis (Bradley et al., 1991). However, NSAIDs should be used with caution in older adults due to risks including gastrointestinal bleeding and effects on the renal system, and have been implicated in cases of hospitalisations resulting from adverse drug reactions (Franceschi et al., 2008). Of the NSAIDs tested

in this population, ibuprofen is preferred as it has the lowest risk of serious side effects (Ong et al., 2007). Ibuprofen has both analgesic and inflammatory properties, and is indicated for use in mild to moderate pain in migraine, dental pain, and rheumatic disease (Joint Formulary Committee, 2016). Topical NSAIDs have also been shown to be efficacious in the treatment of musculoskeletal pain (Mason et al., 2004). NSAIDs can also be bought over the counter.

Opioids are the strongest class of analgesic, and most are prescription only. Opioids are used to treat moderate to severe pain, particularly visceral pain (Joint Formulary Committee, 2016), and have shown efficacy in controlled trials in providing relief for persistent nociceptive and neuropathic pain (Dworkin et al., 2007). NICE (National Institute for Health and Care Excellence) recommend that, when oral opioids are appropriate (and oral drugs should always be prescribed if possible), the first-line maintenance treatment should be morphine, with immediate-release morphine prescribed 'as required' (*pro re nata*; PRN) in case of breakthrough pain (National Institute for Health and Clinical Excellence, 2012a). Adverse effects of opioids include gastrointestinal effects, constipation, headache, somnolence, lethargy, urinary complications, and respiratory depression (Noble et al., 2008, AGS Panel, 2009). Opioids are often used long-term to treat chronic musculoskeletal pain, however there are questions around the efficacy of opioids versus non-opioids, especially considering the risk of harm from opioids (Krebs et al., 2018, Chou et al., 2015). Compound analgesics are a combination of drugs, typically an opioid and a non-opioid (for example codeine and paracetamol), and weaker combinations can be bought over the counter.

Neuropathic pain is usually described as shooting, tingling or burning, for example diabetic neuropathy, and is often treated with medication primarily associated with remedying other conditions (adjuvant drugs) like antidepressants.

Although adjuvant analgesics are used for treating this type of pain, there are no primary studies relating to their use in pain management in older adults (Abdulla et al., 2013). Anticonvulsants, such as gabapentin and pregabalin, and antidepressants,

such as amitriptyline or duloxetine, have demonstrated efficacy, but have been associated with adverse effects. Anticonvulsants can cause drowsiness and sedation, and their excretion is affected by renal function. Antidepressants can cause urinary retention, cardiovascular effects, and postural hypotension.

1.4.2 Pain management

Drugs can be prescribed on a regular basis or PRN, which means that they are only given when necessary. PRN prescriptions are widely used in care homes and reflect how analgesics are typically used by the general population for episodic, acute pain (such as headaches). In chronic pain it is best, generally, for analgesics to be prescribed regularly.

There are no specific pain management guidelines for people with cognitive impairment or care home residents. Current guidelines that could be applied to this population include STOPP/START criteria, British Geriatrics Society/British Pain Society guidelines for older people, national palliative care guidelines, or guidelines specific to NHS trusts (O'Mahony et al., 2015, Abdulla et al., 2013, National Institute for Health and Clinical Excellence, 2012b, Denison Davies et al., 2011, Department of Health, 2001, AGS Panel, 2009). Existing guidelines recommend that analgesics should be titrated from low starting doses (Abdulla et al., 2013, Scherder and Plooij, 2012, AGS Panel, 2009), and a stepwise approach to prescribing pain relief is recommended, balancing adequate pain management and potential adverse effects (Abdulla et al., 2013, Corbett et al., 2012, AGS Panel, 2009, National Institute for Health and Care Excellence, 2018b). The World Health Organisation (WHO) developed a tool (see Figure 1) called the WHO pain relief ladder that was originally intended for use in prescribing analgesics to adults with cancer pain (World Health Organization, 1987). Clinicians are advised to start at the first step with non-opioid analgesics for mild to moderate pain. If this proves insufficient (i.e. the patient has moderate to severe pain) weak opioids can be added and adjuvant therapy can be considered. The third step introduces the prescription of strong opioids for severe pain. The WHO pain relief ladder is a useful and valid tool, and adaptations have been

suggested for use in acute pain, and persistent non-cancer pain (Schaffer, 2010). It has been suggested that people with dementia may benefit from a higher dose of analgesic medication due to diminished placebo effect (Achterberg et al., 2013).

The SHELTER study, a large-scale study in European care homes, found that 47.7% of residents were prescribed analgesics at WHO step 1, 5.9% at WHO step 2, and 7.4% at WHO step 3. Combination therapy (step 1, and 2 or 3) was prescribed to 15.3% of care home residents (Lukas et al., 2013a).

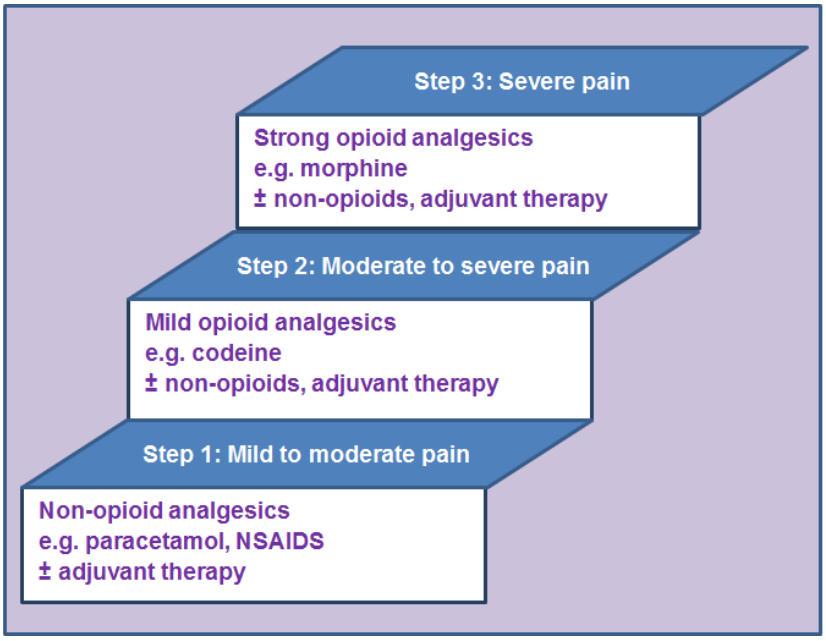

Figure 1. Adaptation of WHO pain relief ladder

1.4.3 Pain prevalence

The most common morbidities within the care home population are reported to be dementia, musculoskeletal disorders, diabetes, cerebrovascular disease, and depression (Gordon et al., 2013, Jensen-Dahm, 2013). These conditions are often painful, for example osteoarthritis (from musculoskeletal disorders) or diabetic neuropathy (Hunter et al., 2008, Davies et al., 2006). It can be difficult to determine the absolute prevalence of pain due to differences in reporting or study methodology, such as different definitions of pain or assessment tools. A recent study

in Europe reported that 48.4% of nursing home residents experienced pain, where a diagnosis of pain was given based on resident interview, observation, or if the resident was receiving a prescription of analgesic medication (Lukas et al., 2013b). Pain was reported as highest in Finland (73.0%) and lowest in Israel (19.8%). In the Netherlands, from a longitudinal care home study, 18-25% of residents experienced pain rarely, 12-25% experienced pain sometimes, 3-10% experienced pain often, and 7-17% experienced pain almost daily (Hendriks et al., 2015).

In England, pain prevalence was reported to be 54.5%, with 8.1% of all residents in constant pain (comparatively low against other European countries), 57.4% experiencing intermittent pain, 6.2% who had experienced a single episode of pain, and 10.9% who had experienced breakthrough pain. Interestingly, England had the highest levels of residents with most or total dependence on assistance with ADLs (Lukas et al., 2013b). Of those in pain, 53.8% received regular analgesic medication only, 16.3% were prescribed PRN analgesics only, and 4.3% received regular and PRN (Lukas et al., 2013a). A study based in Greater London (England) used an observational scale and found that 11% of residents with severe dementia were in pain at rest and 61% were in pain at movement, and prevalence was largely unchanged 9 months later (Sampson et al., 2018). The WHELD study was also conducted in and near London and found that 35.3% of residents with dementia (of any severity) had clinically relevant pain, predominantly mild chronic pain. WHELD authors acknowledged that the lower prevalence of pain compared to other studies could have been related to the use of analgesics in 39.0% of their population which may have reduced pain behaviours. There was still evidence of under-treatment of pain, as 41.9% of residents with pain were not prescribed regular analgesics (Rajkumar et al., 2017).

A literature review conducted in 2010 reported that approximately 40-60% care home residents were in pain currently or had experienced pain in the last three months (Takai et al., 2010). Takai and colleagues found that the prevalence was dependent upon the methods and time frame used to detect pain. Prevalence was highest when based on interviews with residents, compared to those whose pain was

assessed using observation or chart review. However figures obtained from interview data may not be representative of the care home population as most residents able to complete interviews had mild or no cognitive impairment (and were presumably more able to remember and communicate their pain than residents with moderate or severe dementia) and higher levels of ADL (whereas nursing patients may be in more pain from physical difficulties that require nursing care). Chart review (which assumes that all residents in pain are receiving analgesia) and use of Minimum Data Set (MDS) reported lower levels (Takai et al., 2010). The limitations of observational assessment tools are discussed in 1.4.4.1.

Between the years of 2001 and 2011, there has been an 11% growth in UK citizens aged 65 years and over. However there has only been an increase of 0.3% in care home beds, and higher levels of community support. As a result there has been a change in the health profile of care home residents; they are older and have increased levels of dependency and morbidity (Office for National Statistics, 2014, Pitkala et al., 2015, Robbins et al., 2013) therefore it can be assumed that pain prevalence in care homes will remain high and is likely to increase.

1.4.4 Barriers to recognising and treating pain

Barriers and challenges in identifying and appropriately treating pain include pain assessment, personal beliefs of residents, clinicians, and carers, and institutional barriers relating to care homes.

1.4.4.1 Pain assessment in dementia

Pain has been described as “whatever the experiencing person says it is, existing whenever the experiencing person says it does” (McCaffery, 1968). However, this definition assumes that the patient is able to self-report, and for many residents this is impossible due to physical or cognitive impairment.

It is estimated that around 80% of care home residents have some form of dementia or severe memory problem (Quince, 2013, Selbæk et al., 2016). In England this

equates to around 322,000 people, with roughly 91,000 of these residents cared for in registered 'dementia' beds (Quince, 2013). Dementia is often underdiagnosed and prevalence rates of dementia diagnoses tend to give a more conservative figure (Gordon et al., 2013, Lukas et al., 2013b); an Irish hospital study found that 22.9% of patients admitted from nursing homes did not have a clinical diagnosis but did have dementia (Walsh et al., 2016). If dementia is underdiagnosed and not recognised by care home staff then they may not consider impaired cognition or communication when assessing pain or discussing pain with residents.

Self-reporting pain can be difficult for people with dementia for a number of reasons. First, they may not be able to understand or remember the question. Second, the person needs both a semantic understanding of the construct of pain, and the episodic memory of the pain, for the abstract thinking required to report an episode of pain (Oosterman et al., 2014, Herr, 2011, Ferrell et al., 1995). Third, the person must also be able to translate a subjective experience of pain and communicate this to the carer. Fourth, pain assessment tools often ask that the patient quantifies their pain in terms of severity or frequency which requires further skills that may be impaired as a result of dementia (Gagliese et al., 2017). As self-report can be complex, and because the ability of each person with dementia can be compromised in a different way and can fluctuate, it can be very difficult for carers to assess pain in this way. In a study comparing the correlation between staff proxy and resident pain reports for residents without dementia compared to residents with dementia, the correlations were, respectively, 0.88 and 0.41 (Lövheim, 2008).

Conversely, the presence of a dementia diagnosis may lead nurses to assume that these residents are unable to report their own pain and therefore staff may not routinely ask them. A study in a single care home found that, despite being able to verbally communicate, residents with mild or moderate dementia were significantly less likely to have an opioid prescription, and reported greater pain intensity, than residents without dementia (Monroe et al., 2014).

In place of self-report, observational tools are widely (but not necessarily consistently) used in care homes. These tools consider pain indicators such as facial expression and distress behaviours. They are reliant on the ability of the carer to appropriately recognise pain, as well as have adequate training and time to complete the observation, interpret the results, and take further appropriate action (Sawyer et al., 2007, Kaasalainen et al., 2010, Zwakhalen et al., 2018). There is evidence to suggest that judgements of observed pain may be influenced by resident factors (to be discussed in 1.6) and observer factors. For example, observers with higher levels of empathy and who are female tend to rate pain more frequently (Green et al., 2009, Robinson and Wise, 2003).

Another concern is that pain behaviours may not have enough discriminant validity to distinguish from other behaviours typically seen in older age, for example, difficulty moving may be related to frailty and not arthritic pain, and care home staff may become desensitised to this, especially in chronic pain where a resident's behaviour is not vastly, or at all, different from their baseline (Weiner et al., 1999). However there is also a risk of false positives, whereby pain is mistakenly identified using observational scales, but the behaviours are actually caused by other reasons such as psychosocial distress (Jordan et al., 2010).

1.4.4.2 Personal beliefs

It has been questioned whether people with dementia experience pain in the same way as people without dementia, which may lead to under-treatment of pain. There does not appear to be a difference in number or type of painful conditions between people with Alzheimer's disease and people without dementia (Pickering et al., 2006). As verbal self-report becomes more difficult for the person with dementia, researchers have investigated response to pain using a variety of assessment tools including facial response, motor reflexes, neuroimaging, and autonomic responses. The differences, and direction of difference, is dependent upon the type of assessment (Scherder et al., 2009, Kunz et al., 2009), but in summary, it appears that pain processing is not reduced for those with cognitive impairment, nor pain threshold (the lowest level of stimuli perceived as painful), but there may be an

increase in pain tolerance (the greatest acceptable stimulation of pain) (Achterberg et al., 2013, Defrin et al., 2015, Gagliese et al., 2017). A limitation of the literature is that the majority of experimental research in this field has focused on Alzheimer's disease over other dementias (Achterberg et al., 2013). However current evidence suggests that there is no difference in pain prevalence between dementia subtypes (Gagliese et al., 2017).

Residents may be reluctant to report their own pain for a number of reasons. First, there can be an inclination to believe that pain is a natural part of ageing (de Souto Barreto et al., 2013, Vaismoradi et al., 2016). Second, residents may be stoical about their pain and not report it for a number of reasons: because they do not want to bother staff, they do not want to be labelled as a 'complainer', they do not have any hope of relief, or they lack confidence in their own value (Achterberg, 2016, Mentes et al., 2004, Kaasalainen et al., 2010, Vaismoradi et al., 2016). Third, pain may signify their own frailty including impending death or loss of independence so they may be reluctant to admit or publicise their pain (Kaasalainen et al., 2010). Fourth, residents may become desensitised to their own chronic pain (Weiner et al., 1999).

Clinicians also have differing perceptions about opioids, and may refrain from prescribing opioids due to fears regarding addiction or side effects, occasionally referred to as 'opiophobia'. Family members and nurses may also be reluctant to agree to the use of stronger pain medication for this reason (Kaasalainen et al., 2010). However these concerns may be unfounded (Noble et al., 2008, Rainov et al., 2001, Morley-Forster et al., 2003), and nonetheless are less risky for care home residents who do not have autonomy over their medication.

1.4.4.3 Institutional barriers and communication

Medical care and prescribing is typically managed by a resident's GP. This can be a resident's own GP but is often a GP associated with the care home, and so prescribing practice in a home may be subject to their own clinical preference. Care homes need a close relationship with primary care (Corbett et al., 2016) and GPs are often the 'gatekeepers' to accessing secondary care services that could aid pain management

such as palliative care services or physiotherapy or more specialist hospital care. A study in Germany (where the primary clinician also tends to be a GP) found that the number of clinician contacts correlated with appropriateness of pain medication, but only when combining primary care clinician visits and specialist visits. The authors suggested that good pain management may be somewhat dependent on a multidisciplinary approach due to the complexity of this population. It is of interest that the positive correlation was identified only after combining visits, as the authors found low levels of input from specialists for care home residents, which could indicate a lack of training for primary care clinicians or poor quality visits, however evidence is sparse in this area (Flaig et al., 2016). Similarly, community medical service provision in England is low for nursing home residents (Sampson et al., 2018).

Carers (with the exception of those with nursing qualifications) may not receive training in pain (Corbett et al., 2016) and do not necessarily relate the presence of a chronic painful diagnosis with the need for analgesia (Mezinskis et al., 2004). Pain assessment is variable between care homes. In some homes formal tools for pain assessment in dementia were used, and in others they relied on observations of body language (Care Quality Commission UK, 2014). Carers may already believe that the residents are receiving analgesia; care assistants may overestimate the total number of residents prescribed analgesics, or incorrectly believe that residents assessed as in pain are prescribed pain relief. In these cases CAs will be less likely to hand over concerns about pain and advocate for analgesia (Lövheim et al., 2006, Hemmingsson et al., 2017).

Communication within care homes can also be lacking. First, shift work and handovers can hinder clear and consistent channels of communication, and residents are likely to see multiple carers in a day (Lukas et al., 2013a). Second, the main channel of communication between nurses and CAs tends to be unidirectional: CAs report pain to nurses, at which point they devolve responsibility. Gaps in responsibility for follow-up assessments have been described, as well as a lack of confidence from junior staff in taking a proactive role in pain management (Corbett et al., 2016). Therefore it may not be an issue of lack of understanding of pain

assessments but a lack of communication between front-line staff and those with responsibility for prescribing pain medication, for example GPs, or nurses who advise GPs (Mezinskis et al., 2004, Mentes et al., 2004, Lövheim et al., 2006).

Similar factors were implicated in inadequate pain management in a large study of European care homes: heavy workload including staff shortages, team instability, professional staff mix, high staff turnover, and lack of time (Lukas et al., 2013a). These factors can undermine the motivated and well-trained workforce that is needed to implement evidence-based care (Corbett et al., 2016).

Family members may be an under-utilised source of information; knowing residents well is often raised as a means of improving pain assessment and family members can increase this knowledge by relaying how the resident used to be, including behaviours (especially non-verbal) indicative of pain that can be particularly helpful when assessing residents with cognitive impairment (Mentes et al., 2004). However discussions with family carers can be challenging if relationships are not good, and miscommunication can lead to more confusion (Corbett et al., 2016).

1.4.5 Pain and behavioural and psychological symptoms of dementia

If pain is not recognised then residents are at risk of under-treatment which can, aside from discomfort, distress, and decreased quality of life, have more pervasive consequences for the resident, for instance pain can lead to the development of, or contribute to, existing behavioural and psychological symptoms of dementia (BPSD) (Corbett et al., 2014b, Algase et al., 1996, Katz, 2002). BPSD is an umbrella term used to describe a heterogeneous range of symptoms of disturbed behaviour, mood, thought content, or perception, that often occur in people with dementia of any type (Lawlor, 2002, Finkel and Burns, 2000, Cilag, 2002). Common BPSD include psychosis, depression, anxiety, and agitation behaviours (Cilag, 2002). Agitation and depression have been linked to pain (Sampson et al., 2015, Fishbain et al., 1997).

1.4.5.1 Agitation

Agitated behaviour has been defined as behaviour that is socially inappropriate: abusive or aggressive; appropriate behaviour at an inappropriate frequency; inappropriate for the social situation (Cohen-Mansfield et al., 1989). A study conducted in England estimated that 79% of care home residents had clinically significant BPSD, and the most common symptoms were agitation, irritability, and aberrant motor behaviour (Margallo-Lana et al., 2001). This is similar to a Norwegian study that found 72% of nursing home residents with dementia had clinically significant BPSD, and furthermore, that frequency of symptoms increased with severity of dementia (Selbæk et al., 2007). A study exploring the association between agitation behaviours and dementia severity found that physically aggressive behaviours were more common in severe dementia and physically non-aggressive and verbally aggressive behaviours were more common in moderate dementia. The study also reported that female gender was associated with more verbally agitated behaviours and male gender with physically aggressive behaviours (Zuidema et al., 2009). There is mixed evidence with regard to agitation prevalence and gender. Mega and colleagues found that agitation was more common in males (Mega et al., 1996). However the participants were community-dwelling and may present differently to care home populations. In contrast, a Norwegian care home study found that female residents had more severe symptoms of agitation (Helvik et al., 2016).

There is an overlap between behaviours associated with pain and agitation (Sampson et al., 2015, Cipher and Clifford, 2004, Ahn and Horgas, 2013). Pain is associated with aggression, increased pacing, socially inappropriate behaviour and resistance to care (Herr et al., 2006, AGS Panel, 2009, Tosato et al., 2012). A US database study found that residents with more severe pain were more likely to display agitation behaviours that involved less movement (controlling for ADL impairment) and were less likely to have wandering behaviours (Ahn and Horgas, 2013). An inverse association between wandering and pain was also found in European care homes (Tosato et al., 2012).

1.4.5.2 Antipsychotics and anxiolytics/hypnotics to treat BPSD

Psychotropic drugs (drugs that affect the mind, behaviour, and mood), predominantly antipsychotics and anxiolytic/hypnotic drugs, are often used in care homes to treat BPSD (including agitation) and for their sedative effects. Currently risperidone and haloperidol are the only antipsychotics licensed in the UK to treat BPSD in dementia (National Institute for Health and Care Excellence, 2018b) however other antipsychotics are used 'off-label' for this purpose. In English care homes antipsychotic prevalence is 17.7% (Ballard et al., 2015). This is lower than other countries such as the US (25% in nursing homes), Canada (34%, atypical antipsychotics only), Finland (39-42%), and Australia (25.1%) (Szczepura et al., 2016, Vasudev et al., 2015). Overall, there is limited and conflicting evidence regarding the efficacy of antipsychotics, especially as the benefit may not justify the side effect profile that includes sedation, extrapyramidal symptoms, and associations with cardiovascular events (Banerjee, 2009, Medicines and Healthcare products Regulatory Agency, 2005, Ballard et al., 2014, Sink et al., 2005).

Anxiolytics and hypnotics are drugs that are used to relieve anxiety, sedate, or as a sleep aid. NICE does not recommend the use of benzodiazepines or Z-drugs (zopiclone and zolpidem; drugs that aid sleep) in the older population due to higher risk of adverse effects (National Institute for Health and Care Excellence, 2018c) including falls, confusion, impaired balance, over-sedation, and because there is no indication for prolonged use (O'Mahony et al., 2015). Anxiolytics and hypnotics are frequently used in care homes for long periods of time to treat BPSD including agitation despite evidence that does not support routine use (Margallo-Lana et al., 2001, Olsson et al., 2010, Tampi and Tampi, 2014). In England and Wales, care home residents are over twice as likely to be prescribed benzodiazepines than older people who live in the community (Shah et al., 2012) which may be due to a higher proportion of BPSD in care homes (Margallo-Lana et al., 2001, Sørensen et al., 2001).

1.4.5.3 Depression and antidepressants

Pain can also affect cognition and mood, and correlations have been found between pain and depression (Parmelee et al., 1991, Fishbain et al., 1997). One study found

that while pain did not directly affect ADL, it did influence depression and behavioural symptoms which in turn affected ADL (Cipher and Clifford, 2004). Pain and depression commonly occur together, and there is a body of evidence to suggest an interaction between symptoms of depression and pain, including exacerbating one another and overlapping symptoms. A literature review (including all settings) exploring this comorbidity found an association between depression and negative pain outcomes and worse prognosis, including increased pain complaints, pain that lasted longer, and pain that was more severe (Bair et al., 2003). A US study found that higher levels of self-reported pain of people with dementia predicted an increase in depression over the following four months but there is evidence that this relationship is multidirectional (Snow et al., 2009). An English study in care homes reported a prevalence of depression of 26.3% (Stewart et al., 2014).

Antidepressants are another class of psychotropic drug. They are used to treat moderate to severe depression, have adjuvant uses that include treating neuropathic pain, and can have a sedating effect so may be prescribed for insomnia or agitation rather than depression. A study from 2010 reported that 37.5% of care home residents in England and Wales were prescribed antidepressants (Shah et al., 2012). Treating pain can improve symptoms of depression (Husebø et al., 2014a). In a care home study conducted by Mezinskis et al. (2004) where antidepressants were the most commonly prescribed type of regular medication, it was posited that care home staff were missing the link between chronic pain and depression.

1.5 BPSD and analgesics

Pain may be falsely identified as distress or agitation, and it can be impossible to confidently assess concordance between dyads (person with dementia and proxy reporter), so staff cannot definitively know whether their assessment was accurate (Gagliese et al., 2017). In clinical practice there is no standard guidance to accurately distinguish agitation caused by pain from other causes. Some studies have explored whether treating agitation with a trial of analgesic medication can result in an improvement in symptoms. When assessing the effect of paracetamol in a randomised placebo-controlled cross-over trial, during treatment there was no effect

on agitation or PRN psychotropic use, but there was increased activity through social interaction, engagement with media, and work-like activities (Chibnall et al., 2005). Husebø and colleagues tested the efficacy of analgesia for treating agitation using a systematic stepwise protocol, and found significant improvements in agitation (particularly verbal) and aggression and severity of neuropsychiatric symptoms, but no difference in ADL or cognition (Husebø et al., 2011, Husebø et al., 2014b). From these results it was inferred that pain relief could contribute to a reduction in agitation.

As previously mentioned, there is also a risk of falsely identifying pain through observational pain assessments. However in one study where this was the case, the identification of psychosocial distress via the pain assessment tool led to carers developing strategies to reduce the distress (Jordan et al., 2010).

Dementia costs the UK economy £26.3 billion per year and the average cost of a person with dementia living in a care home is £36,738 (Prince et al., 2014). Agitation has been implicated in increasing costs for care home residents. A cross-sectional study using data from eight European countries found that care home residents who were agitated used more healthcare resources; primarily through increased outpatient visits but also inpatient admissions and medication, and on average cost €261 more per month than residents that were not agitated (Costa et al., 2015). Therefore, besides the distress that untreated agitation can cause (for the person with dementia, family members, and paid carers), there is an economic imperative to reduce these symptoms too.

1.6 Individual differences in analgesic prescribing in care home residents

There is limited research exploring whether analgesic prescriptions and administration are associated with individual differences in care home residents, however several studies have highlighted influencing factors. These include age, gender, dementia diagnosis, and dementia severity.

1.6.1 Age

There is no evidence to suggest that pain lessens with age (Rajkumar et al., 2017, Hemmingsson et al., 2017) but differences have been found in analgesic prescribing. A Danish population study reported that prescriptions of opioids increased with age, although this was less pronounced for care home residents than those living in the community (Jensen-Dahm et al., 2015). Age as an influencing factor is supported in a Norwegian study as care home residents above the age of 81 years received significantly more analgesics than residents younger than 80 years (Sandvik et al., 2016). On the contrary, other studies have found no association between analgesic prescribing or administration and age (Stokes et al., 2004, Rigler et al., 2007).

1.6.2 Gender

Gender differences with regards to both pain and pain relief have been identified in several studies. In the community, females were more likely to use analgesics (prescription and non-prescription) (Kung et al., 1999, Jacob and Kostev, 2018), and this association was also found in European care homes (Lukas et al., 2013a, Sandvik et al., 2016). In a recent study female care home residents were more likely to receive a prescription of paracetamol than men (Sandvik et al., 2016), and a US study found higher use of opioids in female residents compared to males, however this study excluded residents with moderate to severe dementia and is therefore less generalisable to most care home populations (Won et al., 2004). Conversely, several studies have found no gender difference in analgesic prescribing or administration (Hemmingsson et al., 2017, Stokes et al., 2004, Rigler et al., 2007). The gender difference may be explained by results from clinical studies that indicate that females are at increased risk of painful conditions, but are also likely to report pain more frequently, have higher pain intensity levels, and have a greater amount of painful body areas than males (Fillingim et al., 2009, Racine et al., 2012).

1.6.3 Diagnosis of dementia

Many researchers have investigated whether care home residents with dementia are at risk of under-detected and under-treated pain. Earlier studies (data collected pre-2000) exploring the risk of under-treatment of pain consistently reported that people with dementia were less likely to receive analgesic medication (Horgas and Tsai, 1998, Mantyselka et al., 2004, Won et al., 2004). In one study, despite non-verbal cues (for example increased irritability, change in behaviours, not moving a body part, grimacing, crying) that were interpreted by care assistants and nurses as pain, nurses were still not administering pain medication to the majority of cognitively impaired patients (Mezinskis et al., 2004).

Recent findings, predominantly from the Nordic countries, present a mixed picture. Several studies show that people with dementia are more likely to receive paracetamol than people without dementia (Lövheim et al., 2008, Haasum et al., 2011). Care home residents with dementia appear less likely to receive opioid medication than residents without dementia (Jensen-Dahm et al., 2015). These results are supported by the findings of a recent international systematic review: Griffioen et al. (2017b) reported that opioid use ranged from 4-41% and that people without cognitive impairment were prescribed the same amount or more opioids than cognitively impaired residents. A recent Norwegian study investigating trends over time found that in 2000, 2004, and 2009, care home residents with dementia received significantly fewer opioids (and analgesics) than care home residents without dementia, but in 2011 there was no significant difference (Sandvik et al., 2016), which was also found in 2013 in Sweden (Hemmingsson et al., 2017). This review also found that care home residents were prescribed more opioids than those living in the community.

1.6.4 Dementia severity

A US study using the MDS found that people with moderate or severe cognitive impairment experienced less pain but, even accounting for that, cognitive

impairment was found to be strongly associated with untreated pain (Hunnicutt et al., 2017). In a study of Norwegian care home residents with severe dementia, 38.4% of residents who were in pain were not prescribed analgesics (Griffioen et al., 2017a). A recent study in England found a positive association between pain and dementia severity; 37.1% of people with severe dementia had mild pain compared to 26.1% residents with mild dementia, and at follow-up residents with severe dementia were more likely to still be experiencing mild pain compared to those with mild dementia (29.5% versus [vs] 7.7%) (Rajkumar et al., 2017).

Considering analgesic use, a UK study reported that as dementia severity increased, prescription and administration decreased, despite no differences in pain scores across the levels of severity (Closs et al., 2004). Several studies have found that residents with greater communication impairments were prescribed fewer regular analgesics, or administered less PRN analgesia, thus supporting the idea that those less able to communicate are less able to report their own pain and advocate for their own pain relief (Mezinskis et al., 2004, Bauer et al., 2016, Stokes et al., 2004). Disorientation, withdrawal, functional impairment, and needing help to eat (and thus find taking medication more difficult) have also been identified as predictors of whether analgesics were administered, with more cognitively impaired residents given fewer analgesics (Horgas and Tsai, 1998, Stokes et al., 2004). A Dutch study found under-treatment for those people with dementia in pain but no difference in treatment when looking at dementia severity (Plooij et al., 2012), however another Dutch study found that residents with high cognitive performance were administered more analgesics than residents with low cognitive performance (60.9% received medication versus 55.8%) (Achterberg et al., 2007).

Overall it appears that analgesic prescribing is improving in care homes, and fewer residents are at risk of under-treatment for their pain. However while individual studies provide a snapshot of analgesic prescribing, it would be useful to have a global picture of prescribing prevalence in care homes, and furthermore, if and how prescribing has changed in this population. I conducted a systematic review to answer these questions. Due to under-diagnosis of dementia in care homes I did not

conduct separate analyses comparing residents diagnosed with dementia versus those without a diagnosis.

Chapter 2 Temporal trends in analgesic use in care homes: a systematic review of international prescribing

The following systematic review is an edited version of a published paper:

LA FRENAIS, F. L., BEDDER, R., VICKERSTAFF, V., STONE, P. & SAMPSON, E. L. 2017. Temporal Trends in Analgesic Use in Long-Term Care Facilities: A Systematic Review of International Prescribing. *Journal of the American Geriatrics Society*.

Please see Appendix 1 for the full article.

2.1 Review aims

The aim of this systematic review was to investigate whether, and how, international prescribing patterns of analgesic medication for care home residents have changed over time. Specific objectives were to explore changes in the prescription of analgesic drugs, explore changes in prescribing of opioids and paracetamol; and examine changes in regular medications and regular plus as-needed (pro re nata (PRN)) medications.

2.2 Methods

2.2.1 Search Strategy

A three-step search strategy was used. To refine the search terms, an initial limited search of PubMed was run, followed by analysis of the text words and Medical Subject Heading terms contained in the title, abstract, and index of identified papers. Then a search was run using identified key words and index terms (for long-term care facilities and analgesics; see Appendix 2) across included databases (PubMed (including Medline, 1966–present), EMBASE (1947–present), CINAHL (1937–present), International Pharmaceutical Abstracts (1970–present), PsycINFO (1880s–present), Cochrane (1898–present), Web of Science (1900–present) and Google Scholar). There were no restrictions on country. Finally, references of included articles were hand searched. The original (published) search was run until December 2016. The updated search (analgesics only) was run in May 2018.

2.2.2 Eligibility Criteria

Original research articles reporting prescribing of analgesics in care homes were included. Single case studies and studies not published in English were excluded.

2.2.3 Setting

Care homes (residential homes (institution with board, meals, 24-hour staffing), nursing homes (as before plus 24-hour nurse coverage), and group dwellings (if deemed suitable based on description)) were included. Assisted living accommodations, sheltered accommodations, retirement apartments, and hospitals, were excluded.

2.2.4 Study population

Included participants were residents in an eligible setting where the majority of residents were aged 55 and older in studies that did not focus on a specific illness or condition. A study population was ineligible if it consisted of newly admitted (admission <3 months) residents; those diagnosed with a specific illness, those receiving palliative care, individuals who were included only if they were deemed to be in pain; individuals who were included only because of polypharmacy; incidence of adverse drug event; incidence of fall or recent hospital admission; if dementia or cognitive impairment were excluded; mild cognitive impairment or severe cognitive impairment only; or where residents with severe impairment were excluded, and the number of residents in the excluded population exceeded the number of included residents.

2.2.5 Data

One reviewer (FL) independently screened titles, abstracts, and full-text articles and extracted the number or percentage of residents prescribed analgesics (including analgesic-antipyretics), opioids, or paracetamol; the total number of residents; if available the number of care homes; and year and country of data collection. Data

were ineligible if prescriptions included drugs that were potentially not for analgesia or analgesics combined with other medications, such as disease modifying antirheumatic products; only PRN data were available; medication was recorded only if the drug was administered within a specific time window (unless daily, when it was counted as regular only); or only weighted percentages were given. If authors indicated that they had collected relevant but unpublished information, they were contacted. There was no restriction on study design. Randomized controlled trials were included if baseline data were published. For longitudinal studies, data were analysed from the first time point that was at least 3 months after admission to the care home to avoid confounding variables associated with newly admitted residents.

2.2.6 Data extraction and quality checking (original search only)

Two researchers independently extracted and reviewed data (FL, RB). Eligible studies were assessed for methodological validity using a 5-point scale (Appendix 3) adapted from the Newcastle-Ottawa scale (Wells et al., 2000) and Boyle scale (Boyle, 1998). Studies were deemed strong, moderate, or weak (adapted from (Boyle, 1998)) by rating representativeness of the target cohort, adequacy and standardization of data collection tools, participation rate, and inclusion of cluster sampling in analysis. If a study did not account for cluster sampling, it was demoted by 1 quality rating. If answers were unclear, the authors were contacted. If they could not be reached, lowest score for that item was used. Final scores were resolved through discussion and with a third independent author (ELS).

2.2.7 Analysis

The percentage of residents prescribed analgesics was calculated to one decimal place. Data were specified as regular drugs only or regular plus PRN; if not explicitly mentioned, they were deemed to be regular plus PRN. Articles that included regular medications and regular plus PRN medications or published data from 2 time points were divided into “cohorts” for separate analysis. Analgesic medications were coded

using the Anatomical Therapeutic Chemical classification system (World Health Organization, 2015) (Appendix 4).

Study heterogeneity was quantified (I^2 > 75% is considerable heterogeneity) (original search only). If the data were statistically viable it would be meta-analysed, but if that was not possible, then correlation coefficients would be generated using the Pearson correlation. The Pearson correlation is sensitive to outliers. Extreme outliers would be identified from the scatter plot, and if there was sufficient clinical justification to do so based on the original article's discussion, would be excluded from the analysis. Stata version 14 (StataCorp, 2015) was used.

2.3 Results

In the original search 14,323 citations were reviewed, and 40 studies were included (Figure 2). From the 40 studies, 50 cohorts were eligible. Appendix 5 describes study characteristics and quality ratings. The updated search added four new studies.

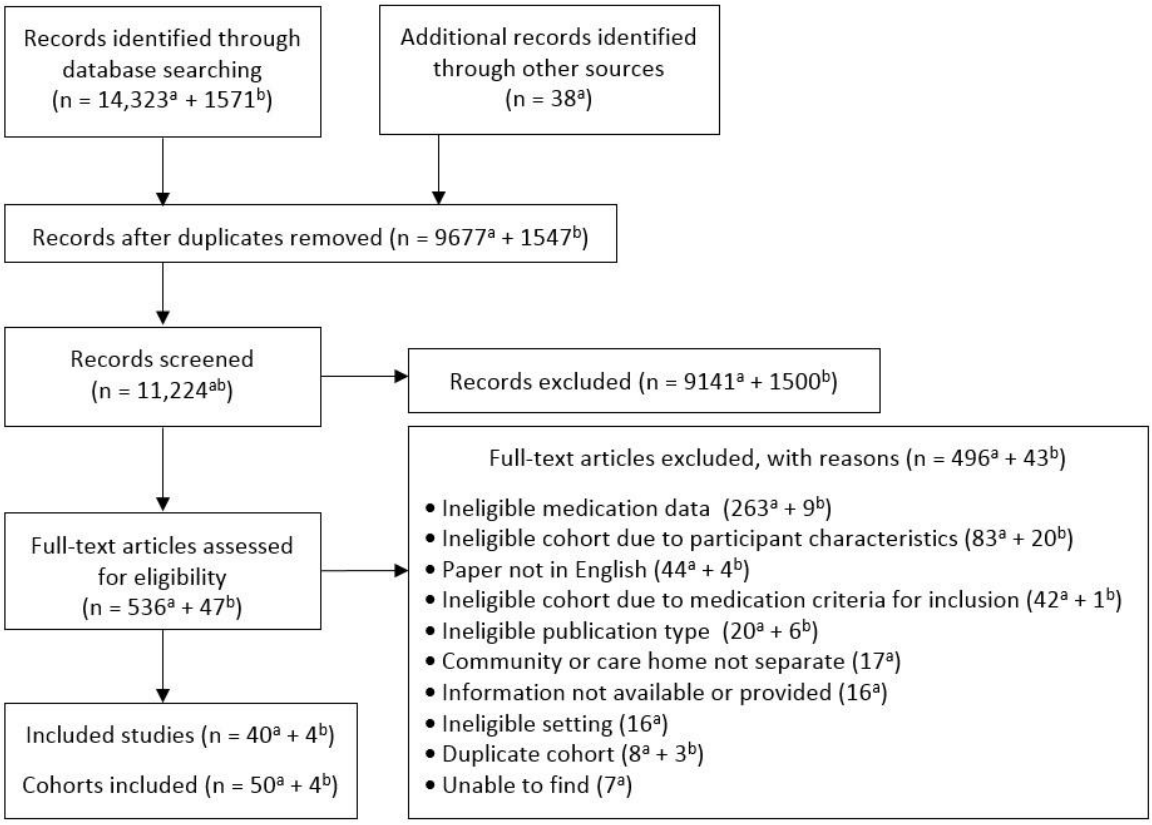

Figure 2. Flow diagram of study selection.

Data were divided according to prescription type: regular only (n = 17) or regular plus PRN (n = 37). For regular only, the median number of residents per study was 705 (range 215–1,387,405). For regular plus PRN prescriptions, the median was 818 (range 13–16,126). Data were available from 17 countries. One study included data from across Europe (excluding Italy). The countries with the most cohorts were Australia (n = 8), Norway (n = 10), and the United States (n = 7). All other cohorts were from Europe, North America, and Australia. It was not possible to meta-analyse the data because of heterogeneity (prescriptions of regular analgesics, I^2 = 99.1, regular plus PRN analgesics, I^2 = 99.8).

2.3.1 Quality Rating

Six cohorts were scored as being of strong quality, 20 as moderate, and 24 as weak. The main reasons for low scores were authors not using cluster sampling and lack of detail about data collection methods.

2.3.2 Analgesics

2.3.2.1 Temporal changes in prescriptions of regular analgesics

There were 17 cohorts eligible (Table 1) (data drawn from 1,406,006 residents and at least 555 care homes in 8 countries). Two studies (Veal et al., 2014, Lövheim et al., 2008) accounting for 1,394,950 residents, did not provide the number of included care homes. Figure 3 suggests that, between 1996 and 2015, analgesic prescribing increased in care homes. Data from Norwegian studies show that 23% of residents were prescribed regular analgesics in 1996, compared with 57.6% in 2011 (Nygaard and Naik, 1999, Sandvik et al., 2016) and 47.8% in 2015 (Erdal et al., 2017). Two studies, both from Germany, reported lower levels: one (Hoffmann and Schmiemann, 2016) reported that 33.7% of residents were prescribed regular analgesics in 2014, and another (Kölzsch et al., 2012) reported a 32% prescription rate in 2010. In the original review the correlation between prescription prevalence and final year of data collection was 0.59, showing a moderate positive trend. In the updated review, the correlation was 0.54.

2.3.2.2 Temporal changes in prescriptions of regular opioids and paracetamol

Ten studies included data on opioid prescriptions (correlation coefficients (Rs) = 0.94), and eight on paracetamol prescriptions (Rs = 0.93, excluding one outlier that reported very low paracetamol use (2.5%)). The number of regular prescriptions of opioids and paracetamol has increased over time (see Figure 4).

Table 1. Cohorts included in analysis of regular analgesic prescribing rates

Study	Year data collection ended	Country	% of residents prescribed regular analgesics
Erdal et al. (2017)	2015	Norway	47.8
Hoffmann and Schmiemann (2016) [2]	2015	Germany	33.7
Tan et al. (2015) [1,2]	2014	Australia	75.2
Bauer et al. (2016) [1]	2012	Austria	52
(Hunnicutt et al., 2017)	2012	US	39.7
Veal et al. (2014) [1]	2012	Australia	62.8
Sandvik et al. (2016) [1,2]	2011	Norway	57.6
Kölzsch et al. (2012)	2010	Germany	32
Krüger et al. (2012) [1]	2008	Norway	54.8
Lövheim et al. (2008) [1,2]	2006	Sweden, Finland	60.6
Reynolds et al. (2008)	2004	US	32
Sandvik et al. (2016) [1,2]	2004	Norway	45
Decker et al. (2009)	2003	US	45.6
Smalbrugge et al. (2007) [1,2]	2001	Netherlands	45.9
Sandvik et al. (2016) [1,2]	2000	Norway	34.9
Nygaard et al. (2003) [1,2]	1997	Norway	29.9
Nygaard and Naik (1999)	1996	Norway	23

[1] Opioid data available

[2] Paracetamol data available

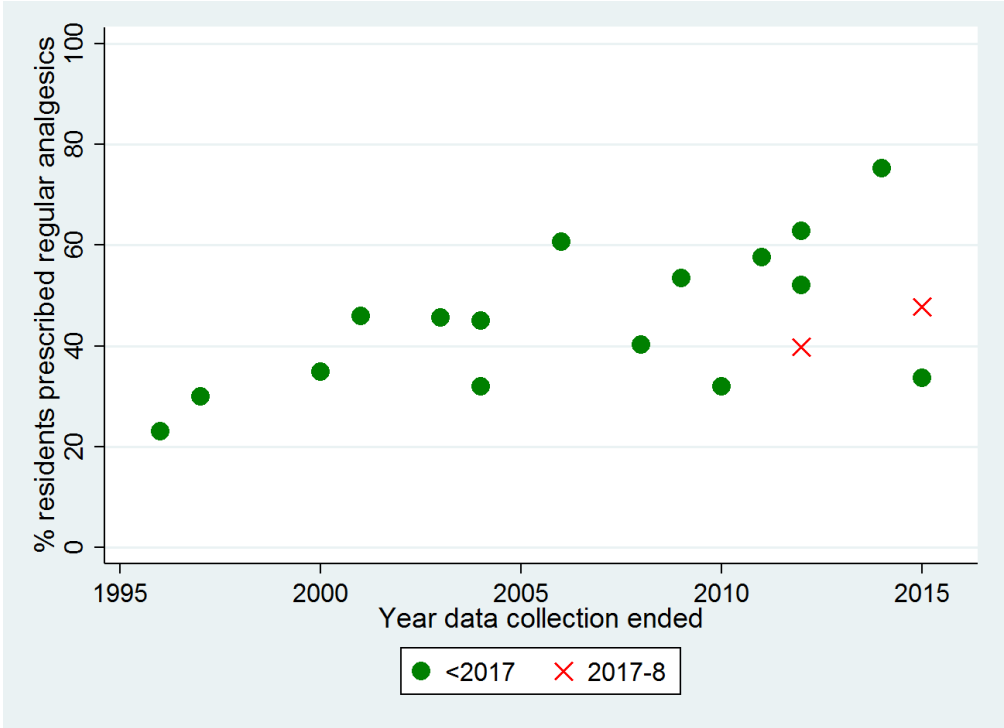

Figure 3. Percentage of residents prescribed regular analgesics over time

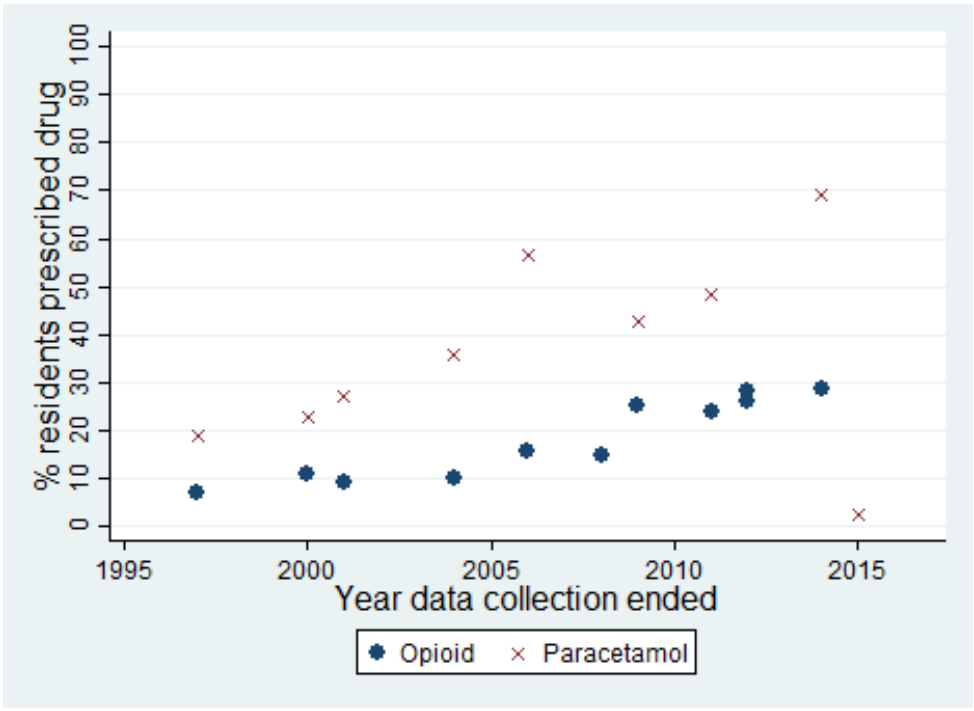

Figure 4. Percentage of residents prescribed regular opioids and paracetamol over time

2.3.2.3 Temporal changes in prescriptions of regular plus PRN analgesics

There were 33 eligible cohorts (87,450 residents, at least 590 care homes in 17 countries plus Europe, excluding Italy; see Table 2). There were 11 cohorts, accounting for 57,898 residents, which did not provide the number of care homes included. Because the scatter plot did not suggest a trend, it was not appropriate to run a correlation. Regular plus PRN prescriptions have not changed since 1984. Several studies (Lövheim et al., 2008, Jervis et al., 2007, Kaasalainen et al., 1998) show very high prescribing rates (>90%). One of the most recent studies (from 2013) reported the lowest prescribing rate (16%) (Onder et al., 2014). Of the four U.S. studies, the earliest (1990) reported that 38.3% of residents were prescribed analgesics (Williams et al., 1999), compared with 68.6% in 2004 (Reynolds et al., 2008).

Table 2. Cohorts Included in analysis of regular plus PRN analgesic prescribing rates

Study	Year data collection ended	Country	% of residents prescribed regular plus PRN analgesics
Hoffmann and Schmiemann (2016) [2]	2015	Germany	73.8
Hemmingsson et al. (2017) [1,2]	2013	Sweden	66.6
Atramont et al. (2018)	2013	France	61.2
Onder et al. (2014) [1]	2013	Europe not including Italy	28
Onder et al. (2014) [1]	2013	Italy	16
Bauer et al. (2016)	2012	Austria	83
Kaasalainen et al. (2016)	2012	Canada	90
Veal et al. (2014)	2012	Australia	90.8
Blytt et al. (2018)	2011	Norway	55

Study	Year data collection ended	Country	% of residents prescribed regular plus PRN analgesics
Taxis et al. (2016)[1]	2009	Australia, Netherlands	80.8
Boerlage et al. (2013)[1]	2008	Netherlands	45.8
Hemmingsson et al. (2017) [1,2]	2007	Sweden	62.8
Stafford et al. (2011)	2007	Australia	56.8
Torvik et al. (2009)[1]	2006	Norway	54.7
Carey et al. (2008)	2005	UK	60.6
Elseviers et al. (2010)	2005	Belgium	41.5
Roughead et al. (2008) [2]	2005	Australia	53.8
Reynolds et al. (2008)	2004	US	68.6
Bergman et al. (2007)[1]	2003	Sweden	61.5
Snowdon et al. (2006)	2003	Australia	63.6
Jervis et al. (2007)	2002	US	95
Smalbrugge et al. (2007)	2001	Netherlands	54.5
Jyrkka et al. (2006)	1998	Finland	54
King (2003) [1,2]	1997	Australia	74
O'Grady and Weedle (1997)	1997	Ireland	20
Kaasalainen et al. (1998)	1996	Canada	95
Neutel et al. (2002)	1996	Canada	33.5
van Dijk et al. (2000)[1]	1995	Netherlands	53
King (2003) [1,2]	1994	Australia	60.9
Ferrell et al. (1990)	1990	US	78
Vander Stichele et al. (1992)	1990	Belgium	26

Study	Year data collection ended	Country	% of residents prescribed regular plus PRN analgesics
Williams et al. (1999)	1990	US	38.3
Passmore et al. (1995)	1989	N. Ireland	24.8
Hatton (1990)	1987	England	43
Nolan and O'Malley (1989)	1987	Ireland	27
Yakabowich et al. (1994)	1987	Canada	58.5
Primrose et al. (1987)	1984	Scotland	32

[1]Opioid data available
[2] Paracetamol data available

2.3.2.4 Temporal changes in prescriptions of regular plus PRN opioids and paracetamol

For regular plus PRN prescriptions for opioids and paracetamol over time, there was a positive linear trend for opioids over time, with a moderate correlation coefficient (0.48). It appears that regular prescriptions for opioids have increased. Opioids were prescribed less frequently than paracetamol.

2.4 Discussion

2.4.1 Prescribing Patterns

There is a multinational trend of increased prescription of regular analgesics, with corroborative findings for paracetamol and opioids. Intra-country longitudinal studies (e.g., increases in Norway between 2000 and 2011) and intercountry comparisons (in 2000–01, 34.9% of Norwegian residents and 45.9% of Dutch residents were prescribed analgesics, and in 2011–12, 57.6% of Norwegian residents

and 62.8% Australian residents were prescribed analgesics) support this finding (Sandvik et al., 2016, Veal et al., 2014, Smalbrugge et al., 2007).

There does not appear to be a temporal trend for regular plus PRN prescribing. This may be because there is no explicit guidance regarding assessment before giving PRN medication (Barry et al., 2014) and individual clinical preference continues to influence prescribing.

As expected, paracetamol remained the most commonly prescribed analgesic (Lukas et al., 2013a, Veal et al., 2014, Miu and Chan, 2014), and prescriptions have increased. The exception is Germany, probably because of the frequent use of dipyrone, a drug banned in several other countries because of risk of agranulocytosis (Hoffmann and Schmiemann, 2016).

Several factors may have influenced increases in opioid prescriptions. Clinicians are more cautious about nonsteroidal anti-inflammatory drugs (NSAIDS) and may prescribe opioids as an alternative. A Finnish study saw a reduction in NSAID use in care homes from 13.0% in 2003 to 2.6% in 2011 (Pitkala et al., 2015), as did a Norwegian study (6.8% in 2000 to 3.2% in 2011), alongside increases in opioids and paracetamol (Sandvik et al., 2016). Concerns have been expressed that opioids are used for their sedative effect, not just pain (Jensen-Dahm et al., 2015, Pitkala et al., 2015). Another concern is that opioids may be wrongly prescribed for neuropathic pain, for which an adjuvant drug may be more effective; the prevalence of adjuvant drugs does not match the prevalence of neuropathic pain (Pitkala et al., 2015, Sandvik et al., 2016).

More detailed studies have identified that strong opioids are used more than weak opioids (Sandvik et al., 2016, Lukas et al., 2013a, Ruscitto et al., 2015). The introduction of buprenorphine and fentanyl patches may have contributed to use of strong opioids (Achterberg, 2016). A Danish study reported that nursing home residents were more likely to receive transdermal opioids (Jensen-Dahm et al., 2015). Their use may be appealing because of ease of administration (Vadivelu and Hines,

2008), but U.S. and U.K. guidelines advise that extended-release opioids should not be the first choice because of negative side effects (Vadivelu and Hines, 2008, Abdulla et al., 2013, National Institute for Health and Clinical Excellence, 2012a, Dowell et al., 2016).

2.4.2 Quality Rating

The ranges of prescribing prevalence were similar for high and low-quality studies. It is troubling that there were so few high-quality studies (6 out of 50 cohorts). There was no clear indication that higher-quality studies produced mutually consistent results in terms of prescribing prevalence, which may be because of the heterogeneity of samples and settings.

2.4.3 Systemic and organisational factors

Several studies found a low prevalence of analgesic use. In Italy, 24% of residents reporting pain did not receive analgesics, and authors commented that medication was neither appropriately nor effectively managing pain (Onder et al., 2014). A Dutch study reported that 38% of residents in "substantial" pain received no analgesics, noting that pain was not included in national nursing home performance indicators (Boerlage et al., 2013). Another study reported remarkably low analgesic use in Poland. Only 28.8% of residents received analgesics, and only 21.4% of these received regular pain relief. Authors commented that pain is not routinely assessed in nursing homes (Neumann-Podczaska et al., 2016). Where low analgesic use is reported, authors often describe a climate that does not prioritize pain assessment. In Italy, where low rates of analgesic prescriptions are reported, nonpharmacological analgesia is used more frequently, as it is in Finland (Lukas et al., 2013a). Long-term care is organised differently between countries, and is impacted by healthcare systems, the economy, care service provision from the state, and sociocultural factors. These factors can influence analgesic prescribing, and lead to variability in resident factors. For example, there are differences between countries in family responsibilities towards care, place of death for older adults, organisational access to

multidisciplinary and dementia care, and medical training for clinicians in this sector (Van den Block et al., 2016, Verbeek et al., 2015, Froggatt et al., 2010).

2.4.4 Limitations

In this review, findings from different countries were compiled and analysed over time. However studies from different countries were not evenly spread over time. For example, data from Australia (Veal et al., 2014, Tan et al., 2015) which is a particularly high prescribing country, appears towards the end. Further, an increase in analgesic prescribing is not always seen within countries, such as the US and Germany where prescribing prevalence is largely static. Therefore increases seen may be a reflection of different practices between countries instead of a universal increase. Future studies should consider controlling for the effect of country.

The cohorts included in this review are heterogeneous. Sample sizes varied greatly, from primary data collection studies involving one care home to databases of thousands. One doctor or practice typically manages care home prescribing, which is thus subject to individual preferences. Data from a small number of facilities may indicate less typical prescribing patterns than a larger sample and contribute to the high levels of observed heterogeneity. Conversely, it can be more difficult to ensure reliability of database records because they depend on accurate input from the care home (Lix et al., 2015). While authors did their best to ensure that the cohorts included in the review were drawn from care home populations that were as homogenous as possible, the long-term care sector does vary between countries. There are likely to be factors, such as medical and pharmacist input into care homes, that influence prescribing rates, and these are not measured. There were no studies from South America, Africa, or Asia, and conclusions are not generalizable outside Western Europe, North America, and Australia. Lastly, it has been suggested that neuropathic pain, estimated to be present in 8% to 11% of elderly and nursing home populations (Kollenburg et al., 2012, Torrance et al., 2006) is often treated inappropriately. This review has not explored prescriptions of neuropathic analgesics

because they may be prescribed for other conditions, and most studies do not collect information on prescribing indications.

2.4.5 Clinical and policy implications

Many countries have shifted from NSAID use, and in their place other analgesics may be prescribed. In Australia, 2005 national prescribing guidelines, which highlighted good practice in pain management in residential care (Veal et al., 2014, The Australian Pain Society, 2005) may be influencing increasing analgesic use, and a UK increase in fentanyl use may have occurred after its licensing for non-cancer pain in 2002. There has been growing interest in pain in individuals with dementia and care homes highlighting under-treatment (Lukas et al., 2013b, Barry et al., 2014), leading to greater use of assessment tools and treatment guidelines (AGS Panel, 2009, Abdulla et al., 2013, Corbett et al., 2014a). Furthermore, there has been more research into behavioural and psychological symptoms of dementia and pain (Sampson et al., 2015, Tosato et al., 2012). These studies, combined with policy pressure to limit use of psychotropics, such as the Omnibus Budget Reconciliation Act of 1987, may have contributed to the increase in analgesic prescriptions, particularly opioids (Banerjee, 2009, Hawes et al., 1997).

2.4.6 Future research needed

An increase in analgesic prescribing does not necessarily mean that residents are receiving the most appropriate treatment (Ruscitto et al., 2015), and more frequent pain assessment does not necessarily equate to more analgesia (Petyaeva et al., 2018). Medication is often prescribed as needed, and administration depends upon staff and their ability to assess pain accurately. This is particularly relevant for cognitively impaired residents who cannot communicate their pain; regular prescriptions may ensure that this population is at less risk of under-treatment (Veal et al., 2015). Research into using clinical decision-making algorithms (with stepped treatment approaches), greater collaboration between professionals such as pharmacists and palliative care nurses, and developing interventions to empower

and engage the whole care team involved in regularly assessing pain and evaluating pain management strategies could address the disconnect between recognizing and treating pain (Achterberg, 2016).

Chapter 3 **Review conclusion and future directions**

This is the first systematic review to investigate temporal changes in prescribing patterns of analgesics in the international care home population. We included data from all studies reporting analgesic use and demonstrated that increases in prescribing seen in smaller studies are representative of an international upward trend, providing a context for current prescribing practices in care homes and insight into the influence of research focus and policy changes.

This upward trend may be attributed to improvements in pain recognition and pain management in care homes since early studies focused on under-treatment of people with dementia (for example, Ferrell et al. (1995), Horgas and Tsai (1998)), which is undoubtedly in part thanks to the priority that this field has been given within the international research community, and new and improved pain management guidelines. Increases may also be a result of changes in the care home population, namely an older and frailer group of residents with more painful conditions (Pitkala et al., 2015). It is important to note that the analysis included data from different countries and there is variability between care home populations and analgesic prescribing that is not accounted for this in this review. Therefore the conclusions drawn may not be universally representative.

We have not yet achieved a consistent approach to analgesic prescribing, even where pain is recognised (de Souto Barreto et al., 2013), and this was seen very clearly when analysing regular and PRN prescriptions. The findings from the review further reinforce that there is a huge gap in our knowledge of the use of PRN medication. A commercially-funded report (Napp Pharmaceuticals Limited, 2014) recommended a national study to be initiated into the administration of analgesics (as opposed to prescribing prevalence) and many studies have reiterated the need for data regarding PRN use (Achterberg, 2016, Dörks et al., 2016, Hoffmann and Schmiemann, 2016, Bauer et al., 2016).

Care home residents with dementia are a vulnerable population, with limited or no autonomy concerning their own medication use. They are largely unable to advocate for themselves and are entirely reliant on the medical care services provided by the home that they reside in. Analgesics are often prescribed as PRN, but currently there are no large-scale studies that report how PRN drugs are used in care homes. Fortunately the MARQUE programme (detailed on page 57) had access to a large number of care homes with the benefit of detailed data that previously has only been achievable in small-scale studies. MARQUE offers a large dataset to test the association between resident factors but also care home factors. Little work has been conducted analysing care home characteristics and analgesic use; a positive association has been found between nursing home size and PRN prescribing (but not administration) (Stokes et al., 2004).

Pain treatment estimates may be misleading if the presence of PRN analgesia is treated with equal weight compared to regular analgesia and influencing factors may be missed. Analgesics prescribed on a PRN basis may lead to under-treatment, even when patients do not have cognitive impairment and are able to self-report pain (Short et al., 1990). There is evidence of under-treatment with PRN analgesics in care homes. Despite significant pain, nearly 21% of residents did not receive any analgesics (Lukas et al., 2013a). In a study where the majority of cognitively impaired residents had a prescription for PRN analgesia, less than a third received any, despite the presence of chronic painful diagnoses (Mezinskis et al., 2004). Pickering et al. (2006) found that residents with Alzheimer's disease were administered significantly fewer dosages for chronic pain compared to residents without dementia. A French study found that, of the residents who complained of pain, 65.8% of those with diagnosed dementia were administered an analgesic in the prior week compared to 77.0% of residents without dementia (de Souto Barreto et al., 2013). Given the relationships that exist between pain, analgesics, BPSD, and psychotropics, it is vital that we understand how often these drugs are used. These data will also increase our ability to interpret previous studies where PRN prescriptions are reported without administration data.

Chapter 4 **The MARQUE programme and my contribution**

The MARQUE (Managing Agitation and Raising QUality of LifE in dementia) programme consists of six work streams exploring dementia and agitation. It is funded by the Economic and Social Research Council (ESRC) and National Institute of Health Research (NIHR), as part of their Improving Dementia Care initiative. The data used in this study were collected as part of work stream 2 (WS2): *A Naturalistic Two-Year Cohort study of Agitation and Quality of Life in Care Homes*. Stream 2 was a longitudinal study that recruited residents, relatives, and staff members from care homes across England. Research assistants interviewed residents and relatives about the resident's quality of life, and interviewed staff members about residents' quality of life, health, BPSD, and health resource use. Staff were also able to complete questionnaires about their own levels of coping and stress.

The MARQUE programme commenced in March 2014, and recruitment for Stream 2 started in April 2014. The Chief Investigator of MARQUE is Professor Gill Livingston and Principal Investigator for Stream 2 was Dr Claudia Cooper, both based in the Division of Psychiatry at UCL.

I have been working as a MARQUE research assistant full-time since August 2014 and completing my PhD part-time since November 2014. My primary responsibilities were recruiting participants and collecting data, and as such where I write 'research assistants' or 'we', I refer to the team of research assistants, within which I had an active role. The London-based team of eight research assistants collected data in London, Cambridge, Kent, and Sussex, and NHS researchers collected the data elsewhere.

Table 3 details the data collected as part of the MARQUE study analysis and additional data collected for the purpose of my PhD.

Table 3. Measures collected and whether it was relevant for the MARQUE Stream 2 study only, PhD only (in bold), or both (in bold)

	Name of measure	Subject	Analysis
Home measures	**Home census**	**Home demographics**	**PhD + MARQUE**
	TESS-NH/RC (Therapeutic Environment Screening Survey for Nursing Homes and Residential Care) (Lawton et al., 2000)	Physical environment	MARQUE only
Staff measures	Brief COPE (Coping Orientations to Problems Experienced) (Burgess et al., 2010)	Coping	MARQUE only
	MBI (Maslach Burnout Inventory) (Maslach and Jackson, 1981)	Burnout	MARQUE only
	MCTS (Modified Conflicts Tactics Scale) (Beach et al., 2005) (adapted for use in care homes, as it was in a previous UCL study: SILQ IRAS ID 84034)	Possible abusive behaviour	MARQUE only
Resident measures	DEMQOL (Dementia quality of life) (Smith et al., 2007)	Quality of life	MARQUE only
	EQ-5D (EuroQoL Five Dimensions) (Brooks and Group, 1996)	Health status	MARQUE only
	CMAI (Cohen-Mansfield Agitation Inventory) (Cohen-Mansfield and Billig, 1986)	**Agitation**	**PhD + MARQUE**
	NPI (Neuropsychiatric Inventory) (Cummings et al., 1994)	Neuropsychiatric symptoms	MARQUE only
	CDR (Clinical Dementia Rating) (Hughes et al., 1982)	**Dementia severity**	**PhD + MARQUE**
	CSRI (Client Service Receipt Inventory) (Beecham and Knapp, 2001)	Use of health and social care resources	MARQUE only
	Medication – prescriptions (preceding 30 days)	**Drug, dosage, frequency, length of prescription**	**PhD + MARQUE**
	Medication – PRN administration (preceding 14 days)	**Route; indication; how many times the drug was offered/administered**	**PhD only**

The additional data for PRN medication were solely collected for the purpose of my PhD. To improve the quality of data collection I provided further training to research assistants (face-to-face and telephone), and wrote and disseminated detailed instructions (see Appendix 6). Furthermore, I was the named contact for queries relating to the PRN data and more often than not, all medication queries that were sent to the London team.

4.1 Ethical approval

The Principal Investigator submitted the application for ethical approval of this study on 2nd December 2012 to Harrow Research Ethics Committee. Ethical approval was granted on 6th March 2014 (REC reference 14/LO/0034; see Appendix 7). No further ethical approval was required for my PhD data.

Chapter 5 Research aims and objectives

5.1 Aims

The primary aim of my thesis was to describe prescribing patterns and administration of analgesics for residents with dementia in a representative sample of English care homes.

The secondary aim was to explore associations between analgesic medication use and care home factors and resident factors, including psychotropic use.

5.2 Primary objective

1. To describe at three study visits (baseline; four-month; twelve-month) the prescription of analgesic medication (overall, and analgesic drug classes [non-opioids, opioids], and prescription type [regular or PRN])

2. To describe at three study visits the administration of PRN analgesic medication.

5.3 Secondary objectives: analgesics

1. To identify whether care home factors (care provision; ownership; dementia registered; dementia specialist; number of beds; overall CQC rating) are associated with the prescription and/or PRN administration of analgesic medication.

2. To identify differences in prescribing and PRN administration of analgesic medication according to different resident factors, specifically age, gender, and dementia severity.

3. To identify associations between agitation (as measured on the CMAI) and the prescription and PRN administration of analgesic medication, and specifically the associations with clinically significant agitation, and with agitation subtypes.

4. To compare analgesic prescribing in this cohort to international prescribing prevalence.

5.4 Secondary objectives: psychotropics and analgesics

1. To describe at three study visits (baseline; four-month; twelve-month) the prescription of psychotropic medication.
2. To identify whether there is an association between the number of analgesic prescriptions and the number of psychotropic prescriptions prescribed to a resident.

Chapter 6 **Methods**

6.1 Setting and Sampling

MARQUE WS2 was an observational cohort study that collected data from care homes across England. Care homes were eligible for participation if they had residents with dementia. Recruitment of care homes was intended to be representative of care provision (nursing or residential), ownership (state, private, or third sector), and location (urban, suburban, or rural), to ensure external validity and generalisability.

The sample size is based upon the multivariable logistic regressions exploring the prescribing rates. Various variables, including agitation and dementia severity, will be examined to explore the associations with prescribing rates. The regression with the most variables includes agitation subtypes (four groups), gender (two groups) and age (continuous), and thus has five covariates included in the model (number of groups minus 1 for each variable, where continuous equals 1 covariate). Consequently, using the rule of 10 events per variable, 50 events will be required. We estimate that 8.1% of people with dementia will be prescribed opioids (Lukas et al., 2013a), consequently 618 people with dementia will be required. Inflating for clustering effects, assuming 16 participants on average per care home (Whitaker et al., 2014) and an intra cluster correlation of 0.075 (Fossey et al., 2006), as used in the main WS2 study, the sample size needed for this PhD was calculated as 1313 participants from 82 care homes. This was achieved.

6.2 Procedures

6.2.1 *Care home consent*

Care homes were recruited through local clinicians, the NIHR (National Institute of Health Research) Clinical Research Network, study links in the private and voluntary sector, and cold calling. Study managers approached the care home manager (or most appropriate individual) for an initial meeting or phone call to introduce the

study. If they were interested in proceeding, a 'set-up' meeting was held, with a study manager and a research assistant, to explain the study procedures and complete consent. It was typical that in this meeting potential participants within the home were identified.

6.2.2 *Resident consent*

Care home residents were eligible for inclusion if they had a known dementia diagnosis, or screened positively using the Noticeable Problems Checklist (NPC) (Levin, 1989) (see Appendix 8), a checklist where scoring two or more out of five indicates probable dementia. This screening measure is completed by care home staff and so does not cause distress to the resident, it is independent of culture and education, and has been validated against clinical diagnosis (Moriarty and Webb, 2000). Henceforth all eligible residents, whether identified through clinical diagnosis or NPC, will be referred to as having dementia.

All residents with dementia were invited to take part. We worked in line with the Mental Capacity Act (Department of Health, 2005) to assess residents' capacity and obtain consent. During the set-up meeting we asked staff if they thought that the resident would potentially have the capacity to consent themselves into the study. When it was indicated that the resident may have capacity, to gain informed consent from the resident. Where the resident did not have capacity, we sought consent from a personal consultee. If there was no appropriate personal consultee, we spoke to the care home manager and sought consent from a professional consultee: either a care home staff member who worked closely with the resident or a social worker. Appendices 9 to 12 comprise information sheets and consent forms used for residents and consultees.

6.3 Care home measures

We used a home census (Appendix 13) to record characteristics of each care home: number of beds; number of staff; whether it was residential or nursing; whether it was dementia–registered or dementia-specialist; staff turnover; current Care Quality

Commission rating (CQC) rating. A care home can receive one of four CQC ratings: 'Outstanding', 'Good', 'Requires improvement', or 'Inadequate'.

6.4 Resident measures

The MARQUE study collected data at baseline (0-month) and four further study visits (at 4-month, 8-month, 12-month, and 16-month). Due to time and resource constraints, this PhD used data from baseline, 4-month, and 12-month study visits. These data were collected from May 2014 – December 2016.

At the baseline visit, demographics were recorded for each resident, comprising date of birth, gender, ethnicity, and whether English was their first language. At every study visit interviews were conducted with a care home staff member who knew the resident well, to collect data regarding medication, agitation, and dementia severity. Residents were eligible for inclusion in analysis for this PhD if both medication data and agitation data were available.

6.4.1 *Medication*

Prescriptions of all medication were taken from Medication Administration Records (MAR) and transcribed to study case report forms (CRF; see Appendix 14). These data were collected: drug; dosage; frequency; length of prescription (up to 28 days); whether it was regular or PRN. If the drug was prescribed PRN, additional data were collected from the previous two-week period (ending the day before the interview): how many times the drug was offered (if there were initials or a code recorded for the dose on the MAR); of the doses offered, how many days it was not given (it was not possible to accurately record reasons why it was not given due to a number of reasons, for example absence of reason, illegible, or unclear records); the indication (if available on the MAR). The two-week period was chosen to coincide with the agitation data.

Analgesic and psychotropic drugs were considered relevant for this thesis (see Appendix 15 for list of relevant drugs), categorised as per the British National Formulary (BNF) (Joint Formulary Committee, 2016).

Table 4. Drug categories relevant to this thesis

Analgesics	**Psychotropics**
Simple non-opioids	Anxiolytics and hypnotics
Opioids	Antidepressants
NSAIDs (oral)	Antipsychotics

6.4.2 *Agitation*

The Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield et al., 1989) is a 29-item questionnaire measuring agitation in people with dementia retrospectively over a two-week period (see Appendix 16), assessing average frequency as: 1, 'Never'; 2, 'Less than once a week'; 3, 'Once or twice a week'; 4, 'Several times a week'; 5, 'Once or twice a day'; 6, 'Several times a day'; 7, 'Several times an hour'. CMAI data were collected during interview with a care home staff member who knew the resident well. The score range is 29-203, where 29 indicates no agitation. A total sum score of 45 and greater indicates clinically significant agitation (Cohen-Mansfield et al., 1989).

There are four syndromes of agitation identified, described in Table 5 below: aggressive behaviour, physically nonaggressive behaviour, verbally agitated behaviour, and hiding/hoarding behaviour (Cohen-Mansfield et al., 1989, Schreiner et al., 2001, Choy et al., 2001, Jonghe and Kat, 1996). Some items are excluded due to low occurrence, or they did not load onto any factor. The CMAI and factor structure have demonstrated acceptable reliability and validity, including good construct validity and inter-rater and test-retest reliability (Husebø et al., 2014b, Rabinowitz et al., 2005, Zuidema et al., 2011).

Table 5. CMAI factor structure

Factor	Behaviours
Aggressive behaviour	Hitting, kicking, pushing, scratching, grabbing, cursing or verbal aggression, hurting self or other, biting, spitting, throwing things, tearing things or destroying property, screaming
Physically nonaggressive behaviour	Pacing or aimless wandering, inappropriate undressing or disrobing, performing repetitive mannerisms, trying to get to a different place, handling things inappropriately, general restlessness
Verbally agitated behaviour	Constant requests for attention, repetitive sentences or questions, complaining, negativism
Hiding/hoarding	Hiding, hoarding
Excluded factors	Low occurrence: intentional falling, verbal sexual advances, physical sexual advances Did not load: strange noises, eating or drinking inappropriate substances

6.4.3 *Dementia severity*

The Clinical Dementia Rating (CDR) (Hughes et al., 1982, Berg, 1988) is a measure that assesses dementia severity in six domains of cognition and function: memory; orientation; judgement; problem solving; community affairs; home and hobbies; personal care. Each domain is rated according to impairment: 0, 'None'; 0.5, 'Questionable'; 1, 'Mild'; 2, 'Moderate'; 3, 'Severe'. A global impairment score is generated via an algorithm (score range 0-3, also from None to Severe) (Baty and Morris, 2011). The CDR was completed during interview with a care home staff member who knew the resident well. The global score, and internal factors, are widely accepted as a valid and reliable assessment measure of dementia severity, including acceptable content and convergent validity, and inter-rater and test-retest reliability (Morris, 1997, Cedarbaum et al., 2013). An adapted version that did not

involve interviewing the resident (see Appendix 17) was used. For analysis purposes, residents with questionable dementia were subsumed into the mild dementia group.

6.5 Data quality checking, input and cleaning

I requested a random sample of one in ten MAR charts from each research assistant at each visit to audit against the case report form (CRF) regarding the transcription of relevant drugs. Where persistent errors were identified, I contacted the researcher to clarify data collection procedures.

All data were entered by research assistants into an online database ('MACRO'), with the exception of the additional PRN data as the MACRO database creation pre-dated my PhD.

I initially intended to check ten per cent of all CRFs against the MACRO database. However due to the high levels of inaccuracy I decided to check every CRF against the MACRO entry for all relevant drugs. I did this at each study visit.

The data sets required for my analysis were extracted from MACRO by the MARQUE statisticians at the request of the study manager. Two data sets were extracted per study visit; one for resident measures and one for care home measures. The extracted data sets were in Microsoft Excel 2013 version. I added the additional PRN data from the CRF, the number of days that PRN data were available (out of a possible 14), and whether I had audited the CRF against the MAR chart.

Regarding dementia diagnosis, demographic, agitation, and dementia severity data, study managers checked ten per cent of all CRFs against the MACRO entry.

6.6 Data analysis

I developed the analysis plan after discussion with my primary and secondary supervisor, and a statistician based in the Marie Curie Palliative Care Research Department, Division of Psychiatry at UCL.

I independently imported and merged datasets in StataSE 14 (StataCorp, 2015), generated new variables, and recoded missing variables. I conducted my analysis independently, however for more complex analyses I consulted the statistician before proceeding.

6.6.1 Missing data

All instances of missing data were described. Residents for whom we had no data were identified by selecting those without a caregiver interview date, and checked to confirm that there was no data available.

In the case of missing items in the CMAI (and thus unable to generate a total sum score) I assessed the data to see whether missingness was random or not. If deemed random, I used person mean imputation, whereby the mean response of the available items is calculated and replaces the missing items (Shrive et al., 2006). This imputation method was only employed where less than 50% of the questionnaire was missing.

6.7 Analysis plan

6.7.1 Description of sample

The study population was explored using descriptive analyses. For care homes I have described these characteristics at baseline: number of beds; whether it is residential or nursing; dementia registration; dementia specialism (if any); current CQC rating. For residents I have described these characteristics at baseline: age, gender, ethnicity, marital status, first language (English or other), dementia diagnosis, and dementia severity.

Simple analyses are used to describe the variables of dementia severity and agitation, including the four subtypes: physically aggressive agitation; physically non-aggressive agitation; verbally agitated agitation; hiding/hoarding behaviour.

Mean and standard deviations are used for continuous, symmetric variables. Medians and inter-quartile ranges (IQR) are used for continuous, skewed variables. Frequencies and percentages are used for categorical variables. Descriptive statistics are presented as cross-sectional data from each study visit.

6.7.2 Primary objective: analgesics

1. The primary objective was to describe prescribing patterns and administration of analgesic drugs and analgesic classes. These data are presented as cross-sectional data from each study visit.

Analgesics were categorised into five classes: simple non-opioids; weak opioids; strong opioids; compound drugs; oral NSAIDs. Compound drugs were divided into their constituent parts and incorporated into the relevant drug type, for instance co-codamol was divided into paracetamol (simple non-opioid) and codeine (weak opioid).

For each drug and class: the total number (n) and percentage (with 95% confidence intervals) of residents who were prescribed each drug at each study visit was recorded, and the total number (n) and percentage (with 95% confidence intervals) of residents who were prescribed a regular prescription, PRN prescription, or both. The median daily dose (and IQR) was recorded. The median number (and IQR) of study visits that residents were prescribed each drug was recorded, both including and excluding those who were withdrawn from the study (as inclusion would increase the number of false negatives of prescription cessation).

Daily doses were calculated for each drug. Doses of non-oral non-morphine opioids were converted to an equianalgesic dose of oral morphine (cross-tolerance set at 0%). The BNF was used for calculating opioid conversion ratios (BMJ Group and the Royal Pharmaceutical Society of Great Britain, 2017). The tables below describe conversion information. Total opioid daily doses were generated from oral and non-oral opioid medications.

Table 6. Equivalent opioid doses (National Institute for Health and Care Excellence, 2017)

Analgesic (route) *Reference: Morphine (oral)*	Dose (mg) *Reference: 10mg*
Codeine (oral)	100
Diamorphine (intramuscular, intravenous, subcutaneous)	3
Morphine (intramuscular, intravenous, subcutaneous)	5
Oxycodone (oral)	6.6
Tramadol (oral)	100
Buprenorphine 5mcg/hour (patch)	12
Buprenorphine 10mcg/hour (patch)	24
Buprenorphine 20mcg/hour (patch)	48
Buprenorphine 35mcg/hour (patch)	84
Buprenorphine 70mcg/hour (patch)	168
Fentanyl 12mcg/hour (patch)	30
Fentanyl 25mcg/hour (patch)	60
Fentanyl 50mcg/hour (patch)	120
Fentanyl 100mcg/hour (patch)	240

For PRN prescriptions (where 14 days' worth of PRN prescriptions were available) the median and IQR of the percentage of times the drug was offered and administered was recorded, and compared to the amount prescribed. A flowchart was created, for simple non-opioids, weak opioids, and strong opioids, to describe at each study visit the number of residents that were offered and administered a PRN analgesic, and the median and IQR of the number of doses offered and administered per week. A graph was generated to show the mean PRN administration across study visits for residents who were prescribed a PRN analgesic.

Analgesic levels were compared to the WHO pain ladder (World Health Organization, 2015) and data are analysed with the whole cohort, and including only those who remained in the study for all three study visits, to examine attrition bias.

6.7.3 Secondary objectives: analgesics

A multi-level linear regression model was used to explore the effects of care home factors (demographics; CQC ratings) on prescribing patterns and administration of analgesics at baseline. Prior to this I conducted univariate analysis to identify potential confounders, which were included in the final model. If no care home factors had a relationship with prescribing or administration, then heterogeneity between care homes was quantified by calculating I^2 (I^2 > 75% is considerable heterogeneity) and forest plots were generated.

Analgesic prescriptions and administration (as binary [yes/no] variables) were compared between different groups. Prior to running these tests, a sensitivity analysis was run to determine any differences in baseline factors between residents who had died compared to those who were still alive. To do this, a chi-square test was run for binary variables, or a t-test for continuous baseline factors, with missingness due to death at each study visit as an outcome. The distribution of the data was tested to determine the most appropriate test; Mann-Whitney U tests were used to analyse nonparametric data. If any baseline variables predicted missingness they were incorporated as independent variables in the models. Factors were also included in the model if there was a clinical reason to do so. The following regression models were run as longitudinal data, clustered at the study visit and care home level.

A multi-level logistic regression model was used to explore the effects of age and gender on prescribing patterns and administration over the three study visits. When exploring age, data were analysed as a continuous variable and also as a binary variable, divided into two groups: 65-80 years; 81 years and over. Where appropriate, odds ratios were calculated.

A multi-level logistic regression model was used to explore whether residents with more severe dementia were prescribed and/or administered fewer doses of analgesic medication than those with mild dementia (using three levels of severity: mild; moderate; severe).

To explore associations between agitation behaviours and the prescription of analgesic medication, subscales for the CMAI were generated (verbally agitated; verbally non-aggressive; physically aggressive; hiding/hoarding). Multi-level logistic regression models were run to explore associations between clinically significant agitation, total CMAI score, and agitation subtypes, and prescription and administration of analgesic medication.

Analgesic prescribing prevalence in this cohort versus international prescribing prevalence were visually compared using a scatter plot, utilising the studies included in the systematic review.

6.7.4 Secondary objective: psychotropics and analgesics

A secondary objective was to describe prescribing patterns of psychotropic drugs.

Psychotropics were categorised into three classes: anxiolytics and hypnotics; antidepressants; antipsychotics (see Appendix 15 for full list of relevant drugs). These categorisations are based on the first indication for these drugs according to the BNF (Joint Formulary Committee, 2016).

For each drug and drug class: the total number (n) and percentage (with 95% confidence intervals) of residents who were prescribed each drug at each study visit was recorded, and the total number (n) and percentage (with 95% confidence intervals) of residents who were prescribed a regular prescription, PRN prescription, or both. The median number of study visits (and IQR) that residents were prescribed each drug was recorded, both including and excluding those who were withdrawn from the study (as inclusion would increase the number of false negatives of

prescription cessation). Median daily doses (and IQR) were also calculated for each drug.

To explore the association between analgesic and psychotropic medication, a simple multi-level Poisson regression model was used to test by how many the number of psychotropic medication drug prescriptions increased or decreased for every increase in analgesic medication drug prescriptions. Multi-level logistic regression models were run to explore associations between analgesic prescriptions and prescriptions of each psychotropic class. The models were clustered at the care home and study visit level.

6.7.5 Clustering

Where appropriate, the analysis was clustered at two levels (see Table 7), at the level of study visit (baseline; 4-month; 12-month) to account for the longitudinal nature of the data, and at the care home level, so the model will recognise all residents who reside in the same care home. This is important because residents of the same care home may be more alike than residents chosen at random from the population, and unobserved variables that may result from this shared context can be accounted for within the analysis. Adjustments are made for standard errors and different degrees of freedom, and furthermore it allows you to explore cross-level interactions (Robson and Pevalin, 2015).

Table 7. Hierarchical structure of my analysis

Level 1	Care home		
Level 2	Resident		
Level 3	Study visit 1	Study visit 2	Study visit 3

Chapter 7 Results: Description of cohort and data

7.1 Care homes

Of the 114 care homes approached, 86 care homes participated (75.4%). Of those that did not participate, 21 were nursing homes and 7 were residential homes. Figure 5 describes reasons for non-participation and Table 8 describes the recruited care homes.

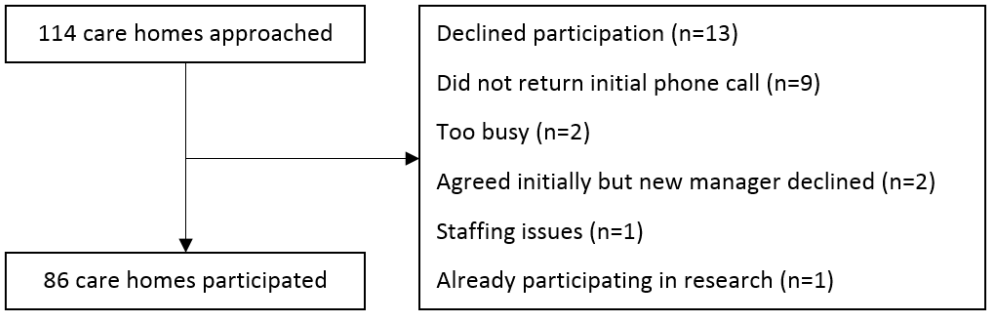

Figure 5. Flow diagram of care home participation

A total of 3859 staff members worked across the recruited homes (median 30, IQR 20, 48). Two care homes dropped out at the 4-month study visit (one private dementia-specific nursing home, and one voluntary residential home). A further two homes had withdrawn by the 12-month study visit (one private dementia-registered nursing home, and one private dementia-specific residential home). Figure 6 shows the spread of recruited care homes across England.

The MARQUE study recruited a higher proportion of dementia-registered and dementia-specialist care homes compared to the national average. The study also recruited more homes with 'Outstanding' and 'Good' CQC ratings, and fewer homes with 'Requires improvement' and 'Inadequate' CQC ratings compared to national distribution.

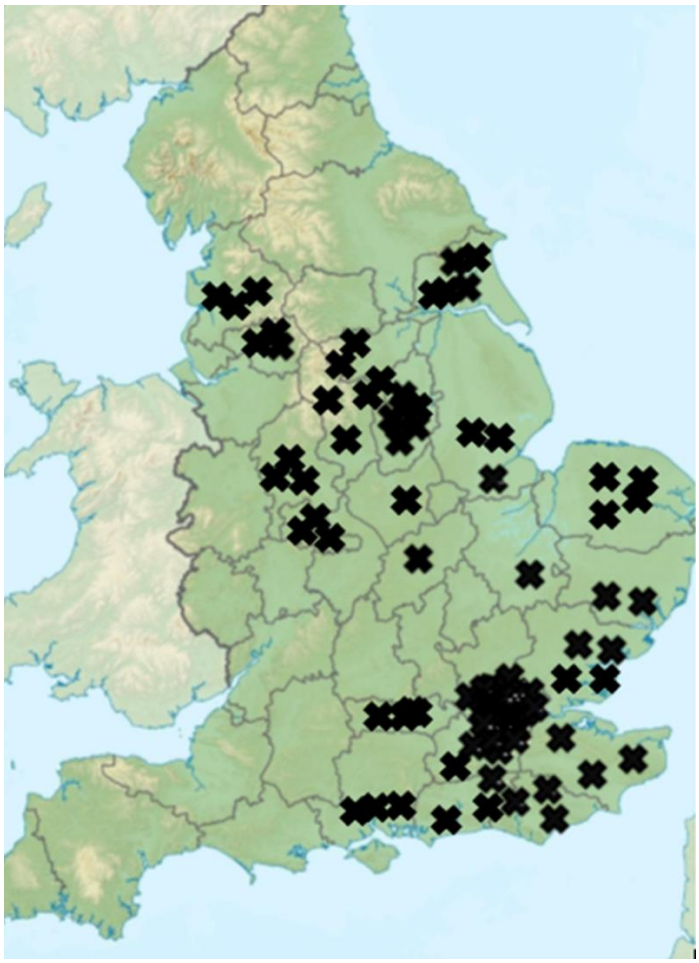

Figure 6. Geographical spread of recruited care homes in MARQUE study (Robertson, 2017)

7.2 Residents

At baseline, there were 4186 beds in the recruited care homes, and the median number of residents per care home was 44 (IQR 32, 62). We screened 3542 residents for eligibility. Of those, 3053 (86.2%) were identified as having dementia and therefore eligible for participation. We approached 2825 residents for consent and 1489 (52.7%) participated in MARQUE. There were 300 residents (20.1%) who consented themselves, and for the remaining residents, consultee agreement was sought from next of kin, or care home staff members. The STROBE diagram below (Figure 7) describes reasons for non-participation and missing data.

Table 8. Type and provider of recruited care homes compared to national average

Type	N	%	National average[1], %
Nursing	50	58.1	26.0[1]
Residential	36	41.9	74.0[1]
Provider			
Charity/Voluntary	15	17.4	20.7
Council/Local authority	2	2.3	4.0
Independent/Private	68	79.1	75.0
NHS	1	1.2	0.3
Registration			
Dementia specialist	76	87.4	46.1
Dementia registered	29	33.3	15.0
CQC rating			
Outstanding	6	7.1	0.6
Good	59	69.4	49.6
Requires improvement	18	21.2	45.1
Inadequate	2	2.4	4.8

[1](Care Quality Commission, 2016)

The median number of participating residents per care home was 17. Baseline data were collected for 1483 residents. Of these, 1281 (86.4%) had a clinical diagnosis of dementia and the remaining 202 residents (13.6%) were identified as eligible using the Noticeable Problems Checklist (Levin, 1989). At baseline, there were staff proxy data available for 1465 residents, and 1425 residents had CMAI and medication data (and were therefore eligible for the analysis in my thesis). Of these 1425 residents, 1231 (86.4%) had a diagnosis of dementia and 194 (13.6%) scored positively on the NPC.

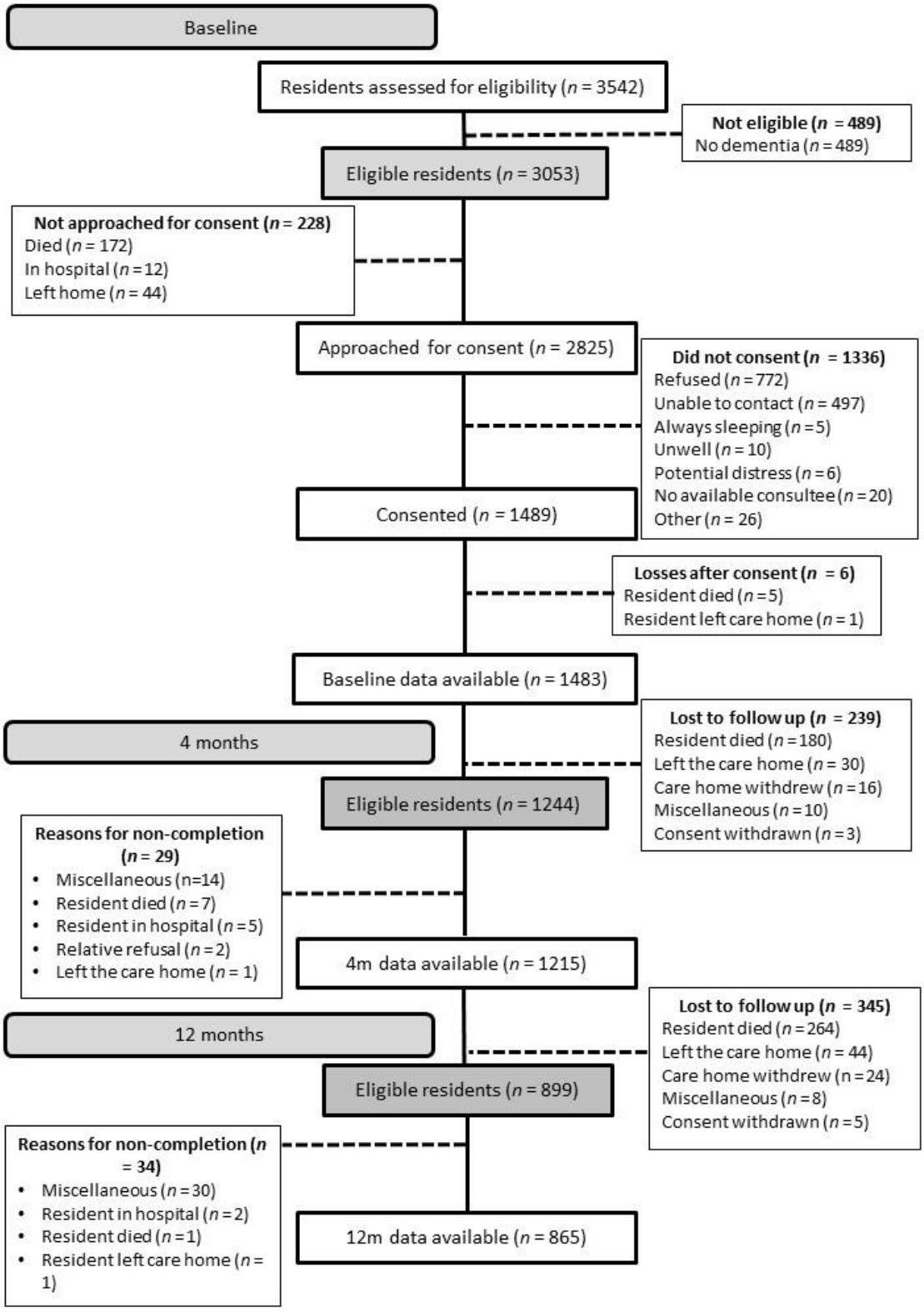

Figure 7. STROBE diagram describing eligible residents at each study visit and number of residents with medication and agitation data, with reasons for withdrawal and missing data

At the 4-month study visit, 1244 residents were eligible, and proxy data including CMAI and medication data were available for 1215 residents. At the 12-month study visit there were 899 eligible residents, with proxy data available for 865 residents. CMAI and medication data were collected for 856 residents. Table 9 describes the resident characteristics at each study visit.

Table 9. Resident characteristics at each study visit: baseline (n=1425), 4-month (n=1215), and 12-month (n=856)

Characteristic	**Study visit**	**N**	**%**
Gender (baseline only)			
Female		985	69.1
Male		440	30.9
Marital status (baseline only)			
Single/unmarried		201	14.1
Married		331	23.2
Separated		10	0.7
Divorced		3	5.1
Widowed		769	53.7
Common law couple		4	0.3
Ethnicity (baseline only)			
White British		1251	87.8
White Irish		43	3.0
White Other		46	3.2
Chinese		2	0.1
Black or Black British Caribbean		22	1.5
Black or Black British African		11	0.8

Characteristic	Study visit	N	%
Asian or Asian British: Indian		7	0.5
Asian or Asian British: Pakistani		3	0.2
Asian or Asian British: Bangladeshi		3	0.2
Mixed: White and Black Caribbean		1	0.1
Other		26	1.9
Dementia diagnosis[1]			
Dementia diagnosis		1231	86.4
NPC		194	13.6
First language English (baseline only)			
Yes		1318	92.5
No		67	4.7
Dementia severity (based on Clinical Dementia Rating assessment)			
Very mild or Mild	*Baseline*	419	29.4
	4-month	289	23.8
	12-month	160	18.7
Moderate	*Baseline*	464	32.6
	4-month	358	29.5
	12-month	264	30.8
Severe	*Baseline*	534	37.5
	4-month	568	46.8
	12-month	431	50.4

[1] Data only collected at baseline

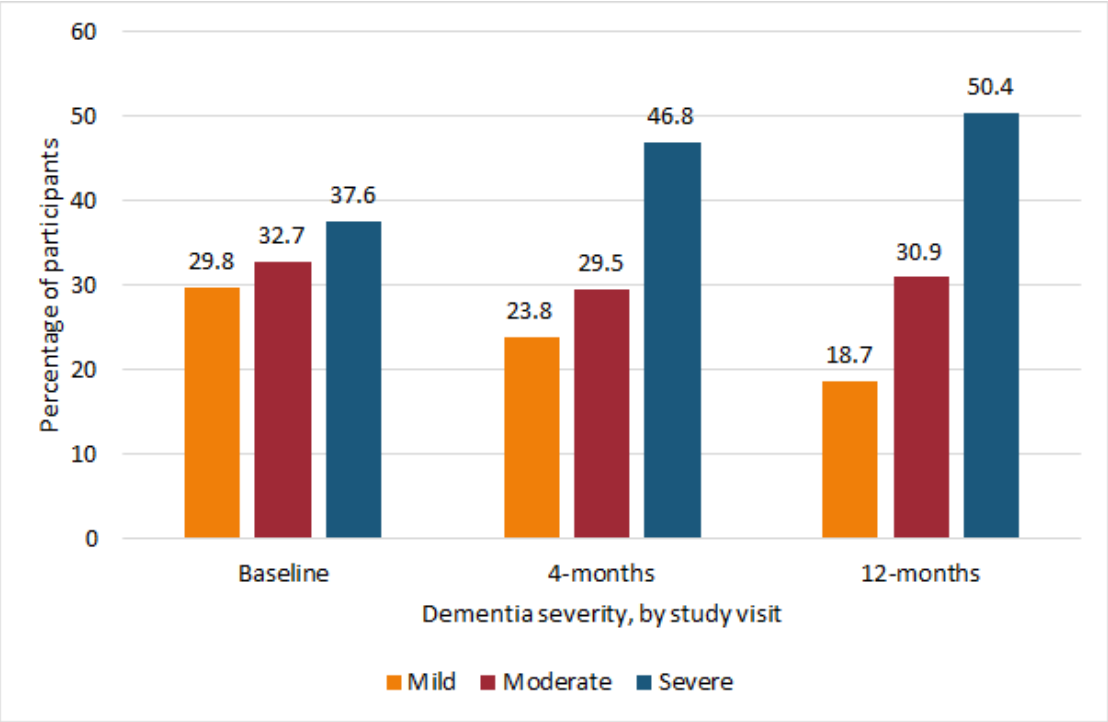

Figure 8. Percentage of residents at each study visit with mild, moderate, and severe dementia

Table 10. Missing demographic data at baseline

Characteristic	N	%
Gender	0	0
Marital status	32	2.2
Ethnicity	10	0.7
Dementia diagnosis	0	0
First language	40	2.8

At baseline, the mean age of the group was 84.9 years (range 40-105 years, SD 8.6). The majority of residents (69.1%, n=985) were female. There were 889 females (87.8%) and 377 males (83.4%) with a diagnosis of dementia. More males than females (16.6% vs 12.2%) were deemed eligible via the NPC. Table 10 and Table 11 describe the missing demographic and dementia rating data. Figure 8 describes the

proportion of residents at each study visit with mild (and very mild), moderate, and severe dementia.

Table 11. Missingness of CDR, by study visit

Characteristic	Study visit	N	%
Dementia severity (CDR)	*Baseline*	2	0.1
	4-month	0	0
	12-month	1	0.1

7.3 Medication data

At baseline, medication data were available for 1425 residents and a full 14 days' worth of PRN data were available for 641 residents. At the 4-month study visit, medication data were available for 1215 residents. A full 14 days' worth of PRN data were available for 587 residents. At 12-month, medication data were available for 856 residents. A full 14 days' worth of PRN data were available for 390 residents. At each study visit, there were four residents who were not prescribed any medication. One resident was not prescribed any medication for all three study visits, and one resident was not prescribed any medication for two study visits (4-month and 12-month).

7.4 Cohen-Mansfield Agitation Inventory

At baseline, CMAI data were available for 1426 residents, but one resident did not have any medication data and was excluded from this analysis. Table 12 shows the spread of missing data of the CMAI across all three study visits.

Table 12. Missingness of CMAI by item, at each study visit

CMAI item	**Missing items**		
	Baseline	4-month	12-month
Pacing and aimless wandering	0	0	2
Inappropriate dressing or disrobing	1	0	0
Spitting (including while feeding)	0	0	0
Cursing or verbal aggression	1	0	0
Constant unwarranted request for attention or help	1	0	0
Repetitive sentences or questions	1	0	0
Hitting (including self)	0	1	1
Kicking	3	3	1
Grabbing onto people or things inappropriately	0	0	0
Pushing	0	3	3
Throwing things	1	1	0
Making strange noises	1	3	0
Screaming	2	1	1
Biting	3	0	0
Scratching	3	1	1
Trying to get to a different place	2	1	2
Intentional falling	2	0	2
Complaining	1	2	1
Negativism	1	0	0
Eating or drinking inappropriate substances	1	1	1

CMAI item	Missing items		
	Baseline	4-month	12-month
Hurting self or others	6	1	0
Handling things inappropriately	4	1	0
Hiding things	1	1	2
Hoarding things	3	0	0
Tearing things or destroying property	1	0	0
Performing repetitive mannerisms	1	1	1
Making verbal sexual advances	2	0	1
Making physical sexual advances or exposing genitals	1	2	0
General restlessness	3	1	0

The range of missing data was 0-6. The item with the most missing responses ('hurting self or others') accounted for 0.4% of data. Given that the level of missingness was low, it was assumed to be random, and person mean imputation was used.

At baseline, the median CMAI score was 41 (IQR 33, 55). It was reported that 574 (40.0%) residents had clinically significant agitation (CMAI>45). 208 (14.6%) residents did not have any agitated behaviours on the CMAI. Table 13 describes how many residents displayed behaviours relating to different factors of the CMAI, including those who displayed clinically significant agitation in the previous two weeks.

At the 4-month study visit, the median CMAI score was 40 (IQR 32, 55). It was reported that 190 (15.6%) residents had not been agitated in the two weeks prior to data collection. There were 474 (39.0%) residents with clinically significant agitation.

At the 12-month study visit, 329 (38.4%) residents had clinically significant agitation. The median CMAI score was 40 (IQR 32, 55) and 149 (17.4%) residents were not reported to have shown any agitated behaviours in the preceding 2 weeks.

Table 13. Number of residents (all, and those with clinically significant agitation) who had agitated behaviours, relating to CMAI factors, and divided by gender

	All residents (n, %)			**Residents with clinically significant agitation (n, %)**		
CMAI factor	**Baseline**	**4-month**	**12-month**	**Baseline**	**4-month**	**12-month**
Aggressive	855 (60.0)	714 (58.8)	513 (59.9)	528 (37.1)	438 (36.0)	304 (35.5)
Females	*564 (57.3)*	472 (55.6)	351 (57.4)	*342 (34.7)*	298 (35.1)	205 (33.5)
Males	*291 (66.1)*	242 (66.1)	162 (66.4)	*184 (41.8)*	140 (38.3)	99 (40.6)
Physically non-aggressive	894 (62.7)	737 (60.7)	488 (57.0)	527 (37.0)	441 (36.3)	295 (34.5)
Females	*608 (61.7)*	501 (59.0)	346 (56.5)	*349(35.4)*	304 (35.8)	202 (33.0)
Males	*286(65.0)*	236 (64.5)	142 (58.2)	*176 (40.0)*	137 (37.4)	93 (38.1)
Verbally agitated	857 (60.1)	691 (56.9)	473 (55.3)	481 (33.8)	385 (31.7)	268 (31.3)
Females	*609 (61.8)*	503 (59.2)	348 (56.8)	*324 (32.9)*	274 (32.3)	190 (31.0)
Males	*248 (56.4)*	188 (51.4)	125 (51.2)	*155 (35.2)*	111 (30.3)	78 (32.0)
Hiding/ hoarding	233 (16.6)	195 (16.0)	119 (13.9)	169 (11.9)	132 (10.9)	84 (9.8)
Females	*168 (17.1)*	136 (16.0)	87 (14.2)	*117 (11.9)*	91 (10.7)	58 (9.4)
Males	*65 (14.8)*	59 (16.1)	32 (13.1)	*52 (11.8)*	41 (11.2)	26 (10.7)

Table 13 describes the prevalence of agitation related to each of the CMAI factors. There was a similar prevalence between aggressive, physically non-aggressive, and verbally agitated behaviours; hiding/hoarding was the least prevalent. For each factor and overall, agitation prevalence appeared to remain stable with a small decline over the three study visits.

Prevalence was similar when comparing genders but males were more agitated than females on each factor except verbally agitated behaviours. The biggest difference was seen for aggressive behaviours (males, 66.1% vs females, 57.3%). This pattern was consistent when including only those with clinically significant agitation.

Chapter 8 Results: Aims and objectives

8.1 Primary aim and objective: analgesics

8.1.1 Description of the prescription of analgesic medication

At baseline, 968 (67.9%) residents were prescribed analgesics, and at the final study visit, analgesics were prescribed to 70.4% of residents. More residents were prescribed analgesics as PRN (46.9-50.5% across study visits) rather than regular (29.9-28.3%), and at each study visit, 38.0-42.2% of residents were prescribed analgesia PRN only.

Paracetamol was the most widely used analgesic drug, prescribed to 56.7-59.4% residents and as such, the most commonly prescribed class of analgesics were simple non-opioids (paracetamol or nefopam), received by 63.3-65.2% of residents. More non-opioids were prescribed as PRN rather than regular prescriptions, with 43.8-48.1% of residents receiving PRN prescriptions compared to 17.7-20.5% of residents with regular prescriptions. There was a low prevalence of NSAID prescribing in this cohort, with around 1% of residents prescribed these drugs at each study visit. Ibuprofen was the most commonly prescribed NSAID.

Opioids were prescribed to 22.8-23.6% of residents. At baseline more residents were prescribed weak opioids compared to strong opioids (13.4% vs 11.4%) however at the 12-month study visit, strong opioids were more prevalent (12.4% vs 14.1%). Residents were more likely to be prescribed regular strong opioids than PRN (9.8% vs 2.8%). More weak opioids were prescribed as PRN rather than regular (7.8% vs 5.7%). Overall, opioids were more likely to be prescribed regularly than PRN (14.3-15.8% vs 10.3-10.7%). Approximately 2% of residents were prescribed both regular and PRN opioids. Table 14 describes the prescribing prevalence of analgesic drugs and classes at each study visit.

Table 14. Prescribing prevalence of analgesic drugs and classes at baseline (n=1425), 4-month study visit (n=1215) and 12-month study visit (n=856), by prescription schedule

	Study visit	**Total** N (%) [95% CI]	**Regular only** N (%) [95% CI]	**PRN only** N (%) [95% CI]	**Both regular + PRN** N (%) [95% CI]	**Daily dose (mg)** Mean (SD) range
Analgesics	Baseline	967 (67.9%) [65.4-70.2]	298 (20.9%) [18.9-23.1]	542 (38.0%) [35.5-40.6]	128 (9.0%) [7.6-10.6]	na
	4-month	851 (70.0%) [67.4-72.6]	232 (19.1%) [17.0-21.4]	513 (42.2%) [39.5-45.0]	100 (8.2%) [6.8-9.9]	na
	12-month	604 (70.6%) [67.4-73.5]	172 (20.1%) [17.5-22.9]	361 (42.2%) [38.9-45.5]	71 (8.3%) [6.6-10.3]	na
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Simple non-opioids[1]	Baseline	902 (63.3) [60.8-65.8]	277 (19.4) [17.4-21.6]	609 (42.7) [40.2-45.3]	16 (1.1) [0.7-1.8]	na
	4-month	793 (65.3%) [62.5-67.9]	196 (16.1%) [14.2-18.3]	559 (46.0%) [43.2-48.8]	20 (1.6%) [1.1-2.5]	na

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	558 (65.2%) [61.9-68.3]	146 (17.1%) [14.7-19.7]	405 (47.3%) [44.0-50.7]	7 (0.8%) [0.4-1.7]	na
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Paracetamol	Baseline	809 (56.7%) [54.2-59.3]	237 (16.6%) [14.8-18.7]	566 (39.7%) [37.2-42.3]	6 (0.4%) [0.2-0.9]	3430.0[1] (975.7) 500-5000
	4-month	722 (59.4%) [56.6-62.2]	178 (14.7%) [12.8-16.8]	538 (44.3%) [41.5-47.1]	6 (0.5%) [0.2-1.1]	3624.0[1] (833.2) 500-4000
	12-month	504 (58.9%) [55.5-62.1]	122 (14.3%) [12.1-16.8]	378 (44.2%) [40.9-47.5]	4 (0.5%) [0.2-1.2]	3483.3[1] (920.9) 500-4000
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Nefopam	Baseline	4 (0.3%) [0.1-0.7]	3 (0.2%) [0.1-0.7]	1 (0.1%) [0.0-0.5]	0 (0%)	90.0 (0)
	4-month	2 (0.2%) [0.0-0.6]	2 (0.2%) [0.0-0.6]	0 (0%)	0 (0%)	135 (63.6) 90-180

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 2 (1.5, 2.5) (inc. withdrawn residents), 1.5 (1, 2) (exc. withdrawn residents)					
Opioids	Baseline	332 (23.3%) [21.2-25.6]	185 (13.0%) [11.3-14.8]	121 (8.5%) [7.1-10.1]	26 (1.8%) [1.2-2.7]	7.5[2] (6.8) 0-27
	4-month	277 (22.8%) [20.5-25.2]	147 (12.1%) [10.4-14.1]	103 (8.5%) [7.0-10.2]	27 (2.2%) [1.5-3.2]	7.0[2] (6.0) 0-25
	12-month	202 (23.6%) [20.9-26.6]	111 (13.0%) [10.9-15.4]	67 (7.8%) [6.2-9.8]	24 (2.8%) [1.9-4.2]	9.1[2] (7.7) 0-46
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Weak opioids[1]	Baseline	191 (13.4%) [11.7-15.3]	80 (5.6%) [4.5-6.9]	110 (7.7%) [6.4-9.2]	1 (0.1%) [0.0-0.4]	na
	4-month	153 (12.6%) [10.8-14.6]	55 (4.5%) [3.5-5.9]	97 (8.0%) [6.6-9.6]	1 (0.1%) [0.0-0.6]	na

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	106 (12.4%) [10.3-14.8]	43 (5.0%) [3.7-6.7]	62 (7.2%) [5.7-9.2]	1 (0.1%) [0.0-0.8]	na
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Codeine	Baseline	77 (5.4%) [4.3-6.7]	28 (2.0%) [1.4-2.8]	49 (3.4%) [2.6-4.5]	0 (0%)	108.3[1] (75.1) 15-480
	4-month	64 (5.3%) [4.1-6.7]	24 (2.0%) [1.3-2.9]	40 (3.3%) [2.4-4.5]	0 (0%)	100.8[1] (58.8) 15-240
	12-month	40 (4.7%) [3.4-6.3]	12 (1.4%) [0.8-2.5]	27 (3.2%) [2.2-4.6]	1 (0.1%) [0.0-0.6]	101.9[1] (67.0) 15-360
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 2.8 (1, 3) (exc. withdrawn residents)					
Dihydrocodeine	Baseline	7 (0.5%) [0.2-1.0]	4 (0.3%) [0.1-0.7]	3 (0.2%) [0.1-0.7]	0 (0%)	137.1[1] (45.4) 120-240
	4-month	4 (0.3%) [0.1-0.8]	1 (0.1%) [0.0-0.5]	3 (0.2%) [0.1-0.7]	0 (0%)	90[1] (52.0) 30-120

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	2 (0.2%) [0.1-0.9]	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	0 (0%)	180[1] (84.9) 120-240
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Meptazinol	Baseline	1 (0.1%) [0.0-0.5]	0 (0%)	1 (0.1%) [0.0-0.5]	0 (0%)	200 (0.0)
	4-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 2 (N/A) (inc. withdrawn residents), 2 (N/A) (exc. withdrawn residents)					
Strong opioids	Baseline	163 (11.4%) [9.9-13.2]	125 (8.8%) [7.4-10.4]	24 (1.7%) [1.1-2.5]	14 (1.0%) [0.6-1.7]	na
	4-month	147 (12.1%) [10.4-14.1]	113 (9.3%) [7.8-11.1]	23 (1.9%) [1.3-2.8]	11 (0.9%) [0.5-1.6]	na
	12-month	121 (14.1%)	88 (10.3%)	22 (2.6%)	11 (1.3%)	na

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[12.0-16.6]	[8.4-12.5]	[1.7-3.9]	[0.7-2.3]	
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Buprenorphine	Baseline	100 (7.0%) [5.8-8.5]	99 (6.9%) [5.7-8.4]	1 (0.1%) [0.0-0.5]	0 (0%)	21.7 (19.9) 12-168[2]
	4-month	93 (7.7%) [6.3-9.1]	89 (7.3%) [6.0-8.9]	4 (0.3%) [0.1-0.9]	0 (0%)	20.7 (19.3) 12-168[2]
	12-month	71 (8.3%) [6.6-10.3]	71 (8.3%) [6.6-10.3]	0 (0%)	0 (0%)	21.9 (20.0) 12-168[2]
	Median (IQR) study visits that drug is prescribed: 1.5 (1, 2) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Diamorphine	Baseline	7 (0.5%) [0.2-1.0]	0 (0%)	7 (0.5%) [0.2-1.0]	0 (0%)	25.0 (7.1) 20-30
	4-month	8 (0.7%) [0.3-1.3]	2 (0.2%) [0.0-0.8]	6 (0.7%) [0.3-1.5]	0 (0%)	30.0 (0.0)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	7 (0.8%) [0.4-1.7]	1 (0.1%) [0.0-0.6]	6 (0.7%) [0.3-1.5]	0 (0%)	30.0 (15.5) 20-60
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Fentanyl	Baseline	24 (1.7%) [1.1-2.5]	22 (1.5%) [1.0-2.3]	2 (0.1%) [0.0-0.6]	0 (0%)	21.2 (19.2) 4-79
	4-month	25 (2.1%) [1.4-3.0]	25 (2.1%) [1.4-3.0]	0 (0%)	0 (0%)	9.2 (5.9) 4-24
	12-month	21 (2.5%) [1.6-3.7]	21 (2.5%) [1.6-3.7]	0 (0%)	0 (0%)	12.3 (8.1) 4-33
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 2 (2, 3) (exc. withdrawn residents)					
Morphine	Baseline	32 (2.2) [1.6-3.2]	10 (0.7) [0.4-1.3]	22 (1.5%) [1.0-2.3]	0 (0%)	39.8[1] (61.1) 5-240
	4-month	21 (1.7%) [1.1-2.6]	3 (0.2%) [0.1-0.8]	15 (1.2%) [0.7-2.0]	3 (0.2%) [0.1-0.8]	48.6[1] (58.1) 10-240

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	25 (2.9%) [2.0-4.3]	5 (0.6%) [0.2-1.4]	19 (2.2%) [1.4-3.5]	1 (0.1%) [0.0-0.6]	48.0 (51.2) 10-200
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Oxycodone	Baseline	6 (0.4) [0.2-0.9]	2 (0.1%) [0.0-0.6]	3 (0.2%) [0.1-0.7]	1 (0.1%) [0.0-0.5]	31 (24.3) 4-60
	4-month	5 (0.4%) [0.2-1.0]	2 (0.2%) [0.0-0.7]	3 (0.2%) [0.1-0.8]	0 (0%)	28.8 (21.0) 15-60
	12-month	4 (0.5%) [0.2-1.2]	3 (0.4%) [0.1-1.1]	1 (0.1%) [0.0-0.6]	0 (0%)	33.5 (21.5) 10-60
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Tramadol	Baseline	13 (0.9) [0.5-1.6]	10 (0.7) [0.4-1.3]	2 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.5]	219.3 (117.8) 100-400
	4-month	8 (0.7%) [0.3-1.3]	4 (0.3%) [0.1-0.9]	4 (0.3%) [0.1-0.9]	0 (0%)	243.8 (134.8) 100-400

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	7 (0.8%) [0.4-1.7]	1 (0.1%) [0.0-0.6]	6 (0.7%) [0.3-1.4]	0 (0%)	233.3 (136.6) 100-400
	Median (IQR) study visits that drug is prescribed: 1 (1, 2) (inc. withdrawn residents), 2 (1, 3) (exc. withdrawn residents)					
Compound analgesics	Baseline	108 (7.6) [6.3-9.1]	49 (3.4) [2.6-4.5]	58 (4.1) [3.2-5.2]	1 (0.1) [0.0-0.4]	na
	4-month	86 (7.1%) [5.8-8.7]	31 (2.6%) [1.8-3.6]	64 (5.3%) [4.1-6.7]	0 (0%)	na
	12-month	64 (7.5%) [5.9-9.4]	30 (3.5%) [2.5-5.0]	34 (4.0%) [2.8-5.5]	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Co-codamol						Paracetamol + codeine
	Baseline	86 (6.0) [4.9-7.4]	37 (2.6) [1.8-3.6]	48 (3.4) [2.5-4.4]	0 (0%)	2613.3 + 87.8 (1478.6) + (69.9) 500-4000 + 16-24

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	4-month	71 (5.8%) [4.7-7.3]	24 (2.0%) [1.3-2.9]	47 (3.9%) [2.9-5.1]	0 (0%)	2608.3 + 85.9 (1476.1) + (64.9) 500-1000 + 16-240
	12-month	55 (6.4%) [5.0-8.3]	24 (2.8%) [1.9-4.2]	31 (3.6%) [2.6-5.1]	0 (0%)	2659.6 + 86.8 (1496.8) + (73.6) 500-4000 + 8-240
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Co-dydramol						Paracetamol + dihydrocodeine
	Baseline	22 (1.5) [1.0-2.3]	12 (0.8) [0.4-1.5]	0 (0%)	0 (0%)	3026.3 + 60.6 (1060.3) + (21.8) 1000-4000 + 20-80
	4-month	16 (1.3%) [0.8-2.1]	7 (0.6%) [0.2-1.2]	9 (0.7%) [0.3-1.4]	0 (0%)	3033.3 + 62.3 (1342.5) + (28.3) 500-4000 + 10-80

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	9 (1.1%) 0.5-2.0]	6 (0.7%) [0.3-1.6]	1 (0.1%) [0.0-0.6]	0 (0%)	3111.1 + 62.5 (928.0) + (19.8) 2000-4000 + 40-80
	Median (IQR) study visits that drug is prescribed: 2.5 (1, 3) (inc. withdrawn residents), 2.5 (1, 3) (exc. withdrawn residents)					
NSAIDs	Baseline	15 (1.1) [0.7-1.8]	10 (0.7) [0.4-1.3]	5 (0.4) [0.1-0.8]	0 (0.0) [0.0-0.0]	na
	4-month	16 (1.3%) [0.8-2.1]	11 (0.9%) [0.5-1.6]	5 (0.4%) [0.2-1.0]	0 (0%)	na
	12-month	5 (0.6%) [0.2-1.4]	5 (0.6%) [0.2-1.4]	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 1.5 (1, 3) (inc. withdrawn residents), 1 (1, 3) (exc. withdrawn residents)					
Aspirin (>75mg)	Baseline	2 (0.1%) [0.0-0.6]	2 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	300 (0.0)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	4-month	4 (0.3%) [0.1-0.9]	4 (0.3%) [0.1-0.9]	0 (0%)	0 (0%)	262.5 (75.0) 150-300
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 1 (1, 2) (inc. withdrawn residents), 1 (1, 1) (exc. withdrawn residents)					
Ibuprofen	Baseline	7 (0.5) [0.2-1.0]	3 (0.2) [0.0-0.6]	4 (0.3) [0.1-0.7]	0 (0%)	885.7 (397.6) 400-1200
	4-month	5 (0.4%) [0.1-1.0]	2 (0.2%) [0.0-0.7]	3 (0.2) [0.0-0.6]	0 (0%)	940.0 (527.3) 200-1500
	12-month	1 (0.1%) [0.0-0.8]	1 (0.1%) [0.0-0.8]	0 (0%)	0 (0%)	1200 (0.0)
	Median (IQR) study visits that drug is prescribed: 1 (1, 3) (inc. withdrawn residents), 1 (1, 1) (exc. withdrawn residents)					
Meloxicam	Baseline	2 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	15 (0.0)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	4-month	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	0 (0%)	15 (0.0)
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 2.5 (2, 3) (inc. withdrawn residents), 2.5 (2, 3) (exc. withdrawn residents)					
Naproxen	Baseline	4 (0.3) [0.1-0.7]	4 (0.3) [0.1-0.7]	0 (0%)	0 (0%)	1187.5 (746.5) 500-2250
	4-month	6 (0.5%) [0.1-1.1]	4 (0.3%) [0.1-0.9]	2 (0.1%) [0.0-0.6]	0 (0%)	708.3 (245.8) 500-1000
	12-month	4 (0.5%) [0.2-1.2]	4 (0.5%) [0.2-1.2]	0 (0%)	0 (0%)	583.3 (144.3) 500-750
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					

[1]including compound analgesics
[2] Oral morphine equivalent

Table 14 identified several prescriptions that warranted further investigation. For example, some residents were prescribed both regular and PRN paracetamol. On closer inspection it was found that most residents had two concurrent prescriptions, for example a resident who was prescribed PRN paracetamol then received a prescription for regular paracetamol and the initial PRN prescription was ceased. A common prescribing error identified was that regular strong opioid prescriptions were not accompanied by PRN prescriptions (in case of breakthrough pain). There were also cases of residents with both regular and PRN opioid prescriptions, for example Tramadol and compound analgesics, and in these cases the regular prescription was for a dose lower than the BNF recommended maximum daily dose (Joint Formulary Committee, 2016).

Analgesics and analgesic classes were typically prescribed for at least two study visits. The exception to this was NSAIDs, with a median prescription duration of one study visit (IQR 1, 3) (excluding those who had withdrawn from the study).

8.1.1.1 WHO Ladder

The WHO ladder (World Health Organization, 2015) corresponds to the level of analgesia prescribed. Step 1 is non-opioids or NSAIDs only, step 2 is weak opioids (+/- non-opioids or NSAIDs), and step 3 is strong opioids (+/- non-opioids or NSAIDs). Figure 9 shows the percentage of residents at each study visit who were prescribed analgesics, corresponding to the WHO ladder. The highest proportion of residents (44.6-47.2%) received step 1 analgesics. At baseline, slightly more residents were prescribed step 2 analgesics (11.9%) than step 3 (11.4%) but at 4- and 12-months, there are more residents prescribed step 3 analgesics (12.1% and 14.0%, respectively) than those on step 2 (10.7% and 9.4%).

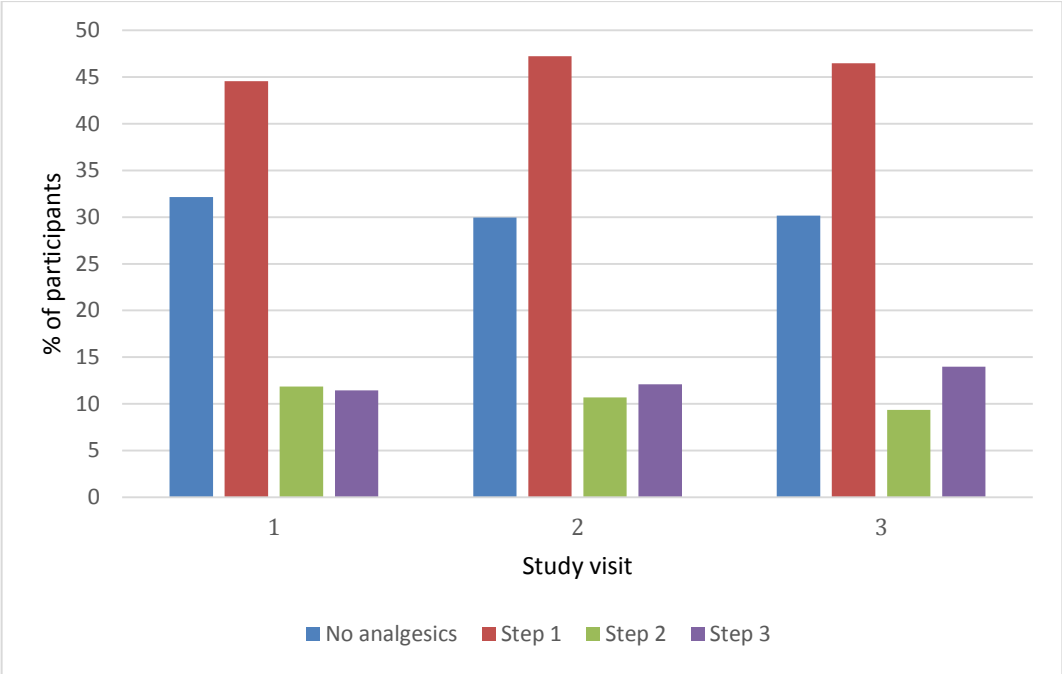

Figure 9. Percentage of residents at each study visit prescribed analgesics according to WHO analgesic ladder

Figure 10 shows the WHO ladder, but only includes residents who survived (or did not withdraw) until the 12-month study visit, thus eliminating attrition bias. The highest proportion of residents (43.7-53.0%) received step 1 analgesics. Overall prescribing prevalence does not differ largely between the whole cohort and the surviving cohort. Similar to above, at baseline, slightly more residents were prescribed step 2 analgesics (12.0%) than step 3 (10.0%) but at 4- and 12-months, there was a more marked difference in the surviving cohort, and more residents were prescribed step 3 analgesics (11.0% and 14.1%, respectively) than those on step 2 (4.4% and 3.5%).

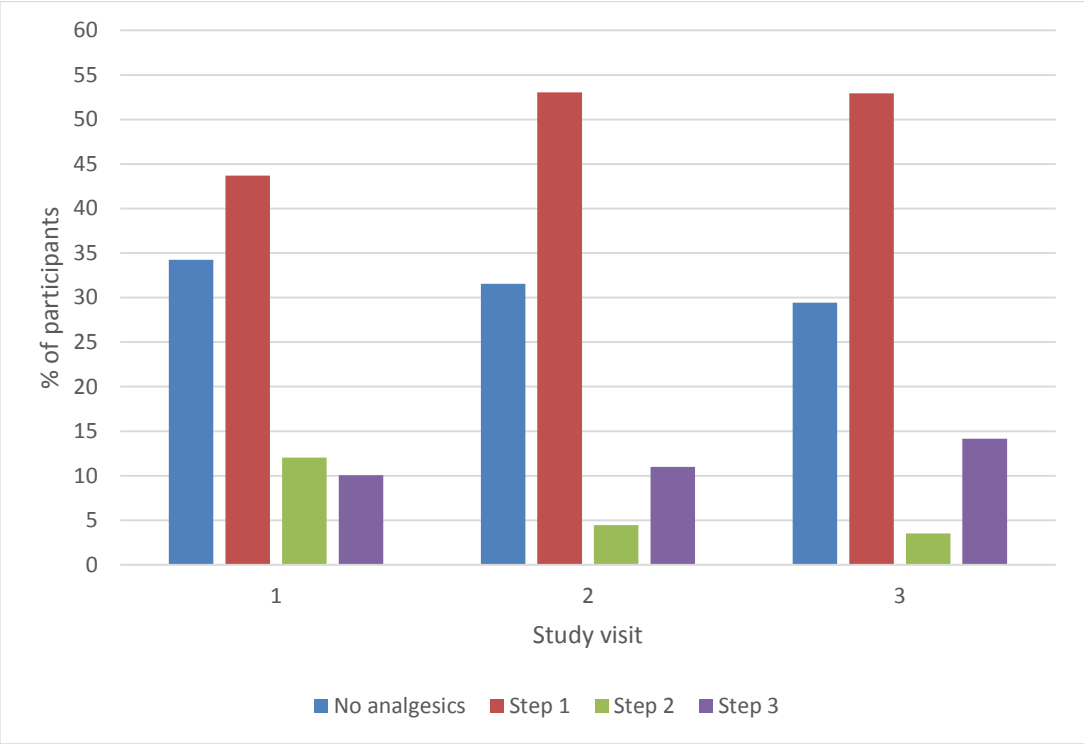

Figure 10. Percentage of residents at each study visit prescribed analgesics according to WHO analgesic ladder, excluding withdrawn residents

8.1.2 Description of the administration of analgesic medication

At baseline, there were 641 residents (44.9%) with 14 days' worth of PRN prescription data. At 4-months, there were data for 587 residents (48.3%) and at 12-months there were data for 390 residents (45.6%).

Figure 11 shows the percentage of pain relief, of the total amount prescribed, that was administered to the residents. Many residents did not receive any of their potential PRN analgesia: at baseline 32.8% of residents who were prescribed PRN analgesics were not administered any; at 4-months, 55.2%; at 12-months, 55.9%. Looking at all study visits, 41.9% residents did not receive any analgesic medication during the three two-week periods of data collection. One resident was prescribed 500mg of paracetamol once daily, but (during the three study visits) was administered 2.5 times (250%) the dose prescribed.

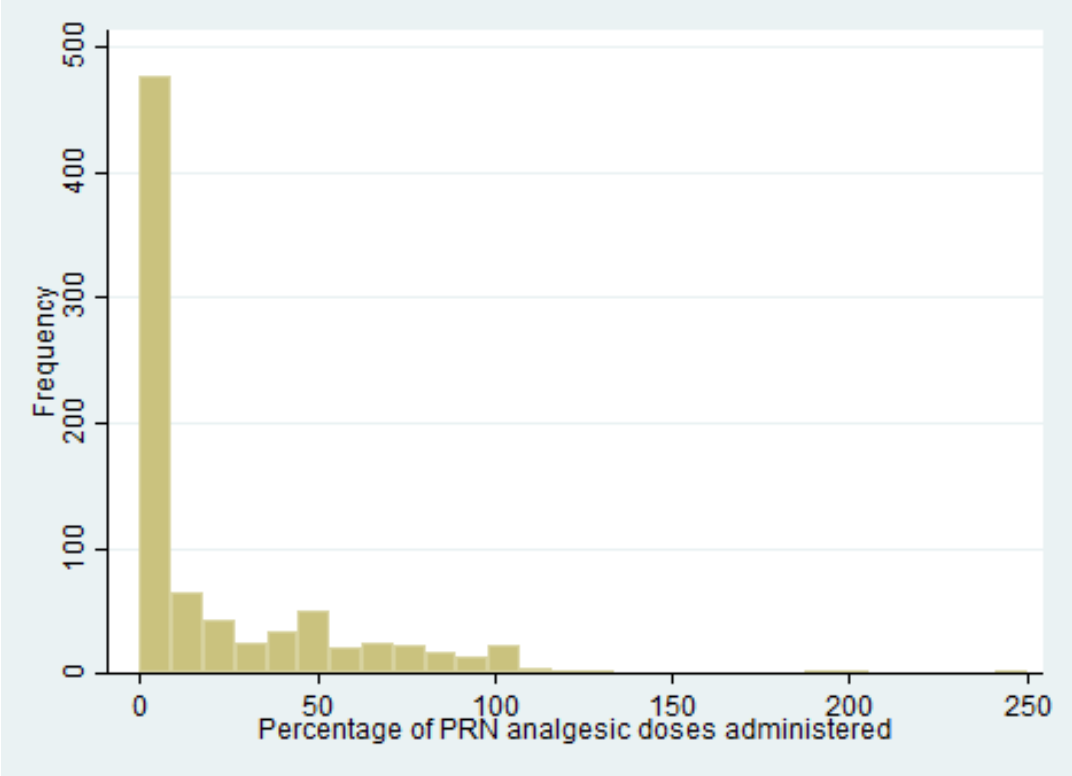

Figure 11. Frequency graph of number of residents prescribed PRN analgesics and the mean percentage (across all study visits) of potential analgesic doses administered (range 0%-250%)

8.1.2.1 Simple non-opioids

At all study visits, the only non-opioid drug with 14 days' worth of PRN records was paracetamol. At baseline, there were 500 residents with 14 days' worth of PRN dose records for paracetamol.

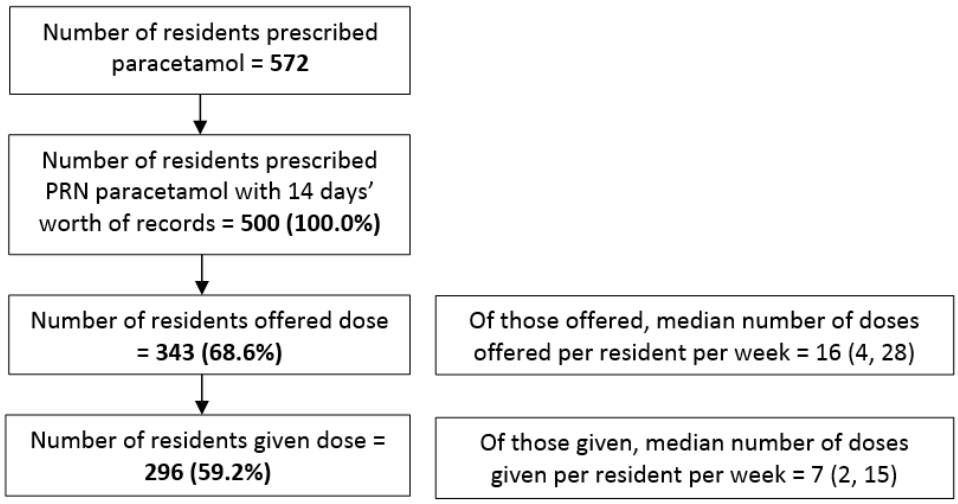

Figure 12. Flow diagram of number of residents prescribed, offered, and administered PRN paracetamol at baseline, plus median (and interquartile range) of doses offered and received

Figure 12 describes how many residents were offered and administered paracetamol, and the median number of doses offered and administered. For those residents who were not prescribed another type of analgesic (i.e. regular non-opioid, or regular or PRN opioid; N=302) 43.6% were offered paracetamol and 19.6% were administered paracetamol. In the previous 14 days: 157 (31.4%) residents were not offered any PRN paracetamol and 204 (40.8%) residents were not administered any PRN paracetamol.

At 4-months (see Figure 13, below), there were 466 residents with 14 days' worth of PRN dose records for paracetamol. In the previous 14 days: 127 (27.3%) residents were not offered any PRN paracetamol and 217 (46.6%) residents were not administered any PRN paracetamol. At 12-months, (Figure 14), 72 (23.4%) residents were not offered any PRN paracetamol and 142 (46.1%) residents were not administered any PRN paracetamol.

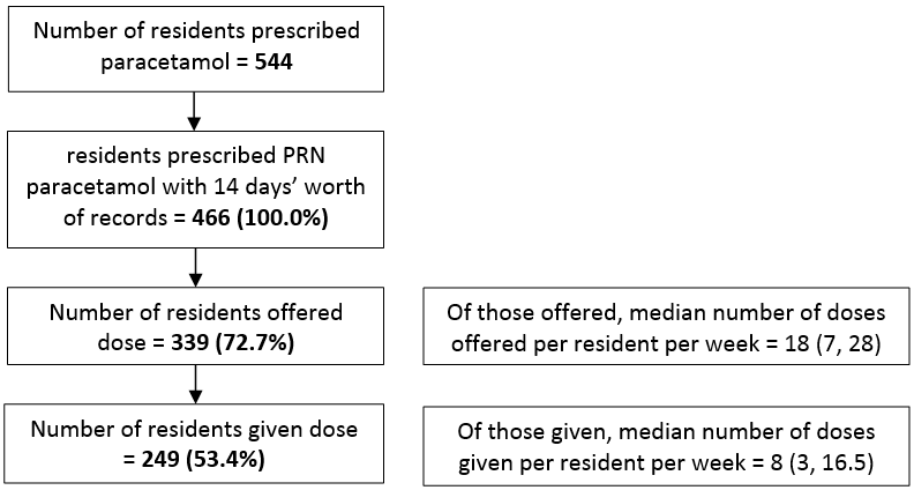

Figure 13. Flow diagram of number of residents prescribed, offered, and administered PRN paracetamol at 4-month study visit, plus median (and interquartile range) of doses offered and received

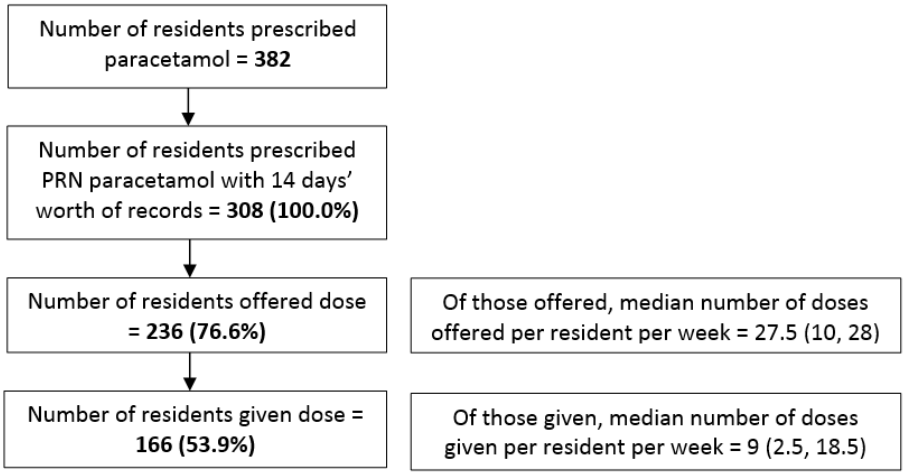

Figure 14. Flow diagram of number of residents prescribed, offered, and administered PRN paracetamol at 12-month study visit, plus median (and interquartile range) of doses offered and received

Looking at all three study visits, the mean number of residents who were offered paracetamol at least once was 72.6% and the mean percentage of residents who were given paracetamol at least once was 55.5%.

8.1.2.2 Weak opioids

At baseline, there were 77 residents with 14 days' worth of PRN dose records for weak opioids. In the previous 14 days: 46 (59.7%) residents were not offered any PRN weak opioids and 51 (72.7%) residents were not administered any PRN weak opioids. See Figure 15 for details. For residents whose only prescribed analgesic was a weak opioid (n=31), the median number of days that it was administered was 9 (IQR, 1, 12).

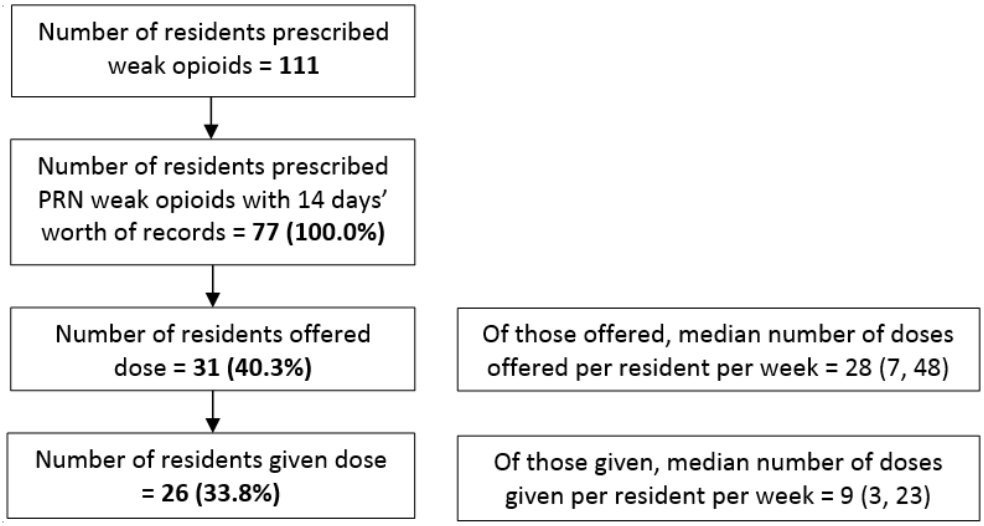

Figure 15. Flow diagram of number of residents prescribed, offered, and administered PRN weak opioids at baseline, plus median (and interquartile range) of doses offered and received

At 4-months, there were 69 residents with 14 days' worth of PRN dose records for weak opioids. In the previous 14 days: 19 (27.5%) residents were not offered any PRN weak opioids and 28 (40.6%) residents were not administered any PRN weak opioids (see Figure 16). The median number of days that weak opioids were administered was 2 (IQR, 0, 11). For residents whose only prescribed analgesic was a weak opioid (n=31), the median number of days that it was administered was 0 (IQR, 0, 9).

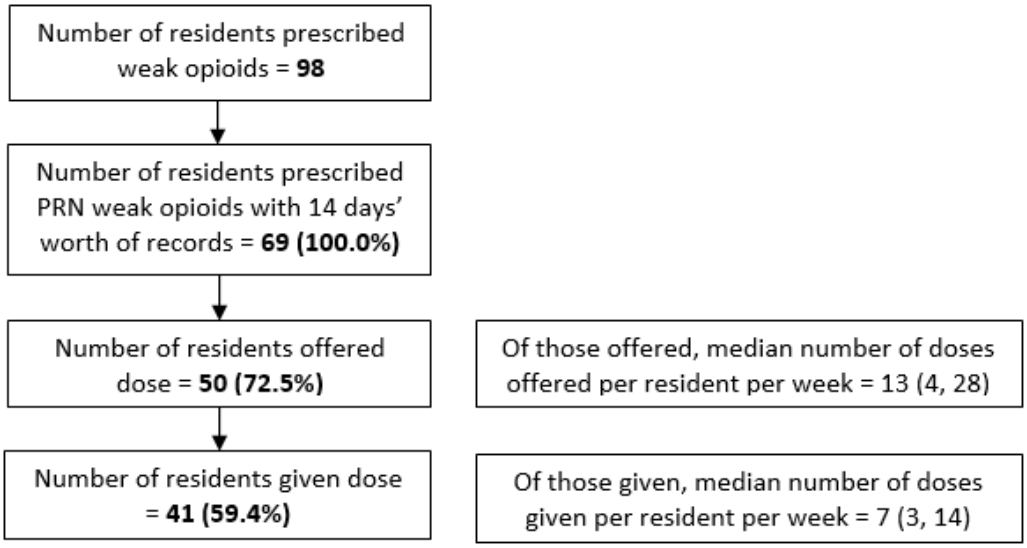

Figure 16. Flow diagram of number of residents prescribed, offered, and administered PRN weak opioids at 4-month study visit, plus median (and interquartile range) of doses offered and received

At 12-months, there were 40 residents with 14 days' worth of PRN dose records for weak opioids. In the previous 14 days: 4 (10.0%) residents were not offered any PRN weak opioids and 13 (32.5%) residents were not administered any PRN weak opioids. See Figure 17 for details.

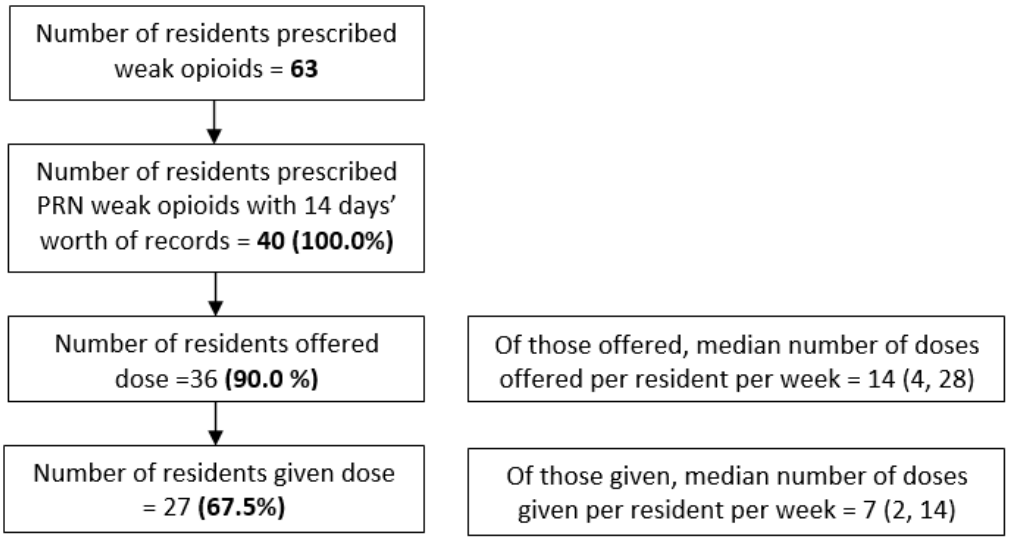

Figure 17. Flow diagram of number of residents prescribed, offered, and administered PRN weak opioids at 12-month study visit, plus median (and interquartile range) of doses offered and received

The median number of days that weak opioids were administered in the previous 2 weeks was 2 (IQR, 0, 13). For residents whose only prescribed analgesic was a weak opioid (n=20), the median number of days that it was administered was 1 (IQR, 0, 14).

Across all three study visits, the mean number of residents who were offered a weak opioid at least once was 67.5% and the mean percentage of residents who were given a weak opioid at least once was 52.3%.

8.1.2.3 Strong opioids

At baseline there were 20 residents with 14 days' worth of PRN dose records for strong opioids. In the previous 14 days: 12 (60.0%) residents were not offered any PRN strong opioids and 14 (70.0%) were not administered any (see Figure 18). At all study visits, there were no residents who were only prescribed PRN strong opioids.

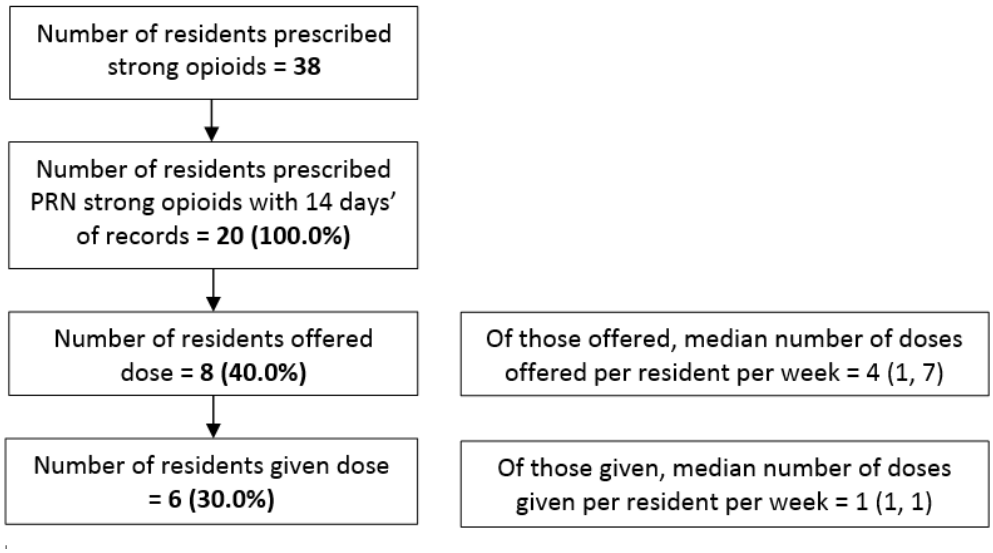

Figure 18. Flow diagram of number of residents prescribed, offered, and administered PRN strong opioids at baseline, plus median (and interquartile range) of doses offered and received

At 4-months there were 18 residents with 14 days' worth of PRN dose records. In the previous 14 days: 6 (33.3%) residents were not offered and 8 (44.4%) were not administered any PRN strong opioids (see Figure 19).

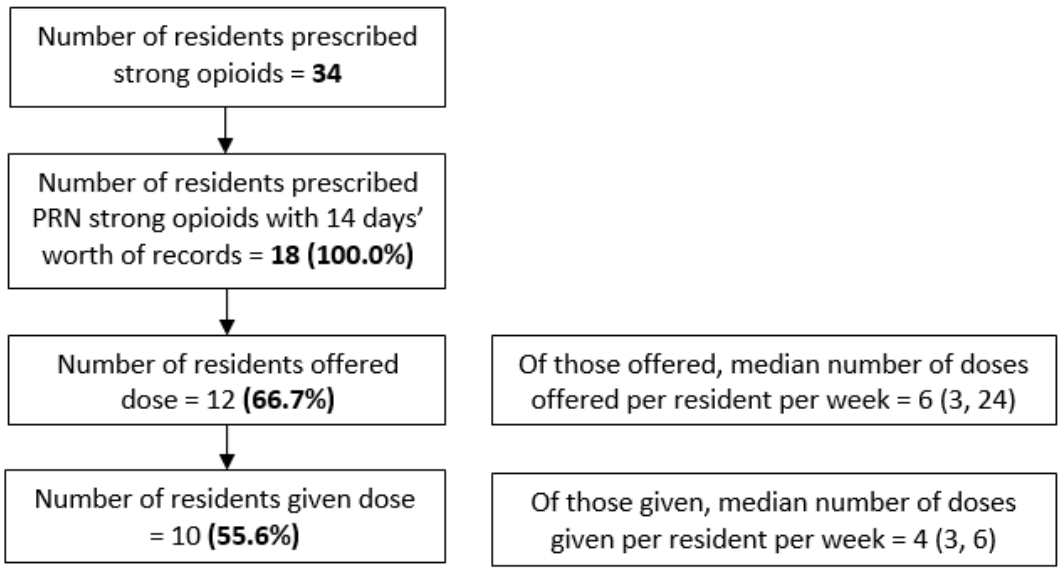

Figure 19. Flow diagram of number of residents prescribed, offered, and administered PRN strong opioids at 4-month study visit, plus median (and interquartile range) of doses offered and received

At 12-months there were 17 residents with 14 days' worth of PRN dose records. In the previous 14 days: 9 (52.9%) residents were not offered and 14 (82.4%) were not administered any PRN strong opioids (Figure 20 below).

At all study visits, there were no residents who were only prescribed PRN strong opioids. Looking at all three study visits, the mean number of residents who were offered a strong opioid at least once was 51.3% and the mean percentage of residents who were given a strong opioid at least once was 34.4%.

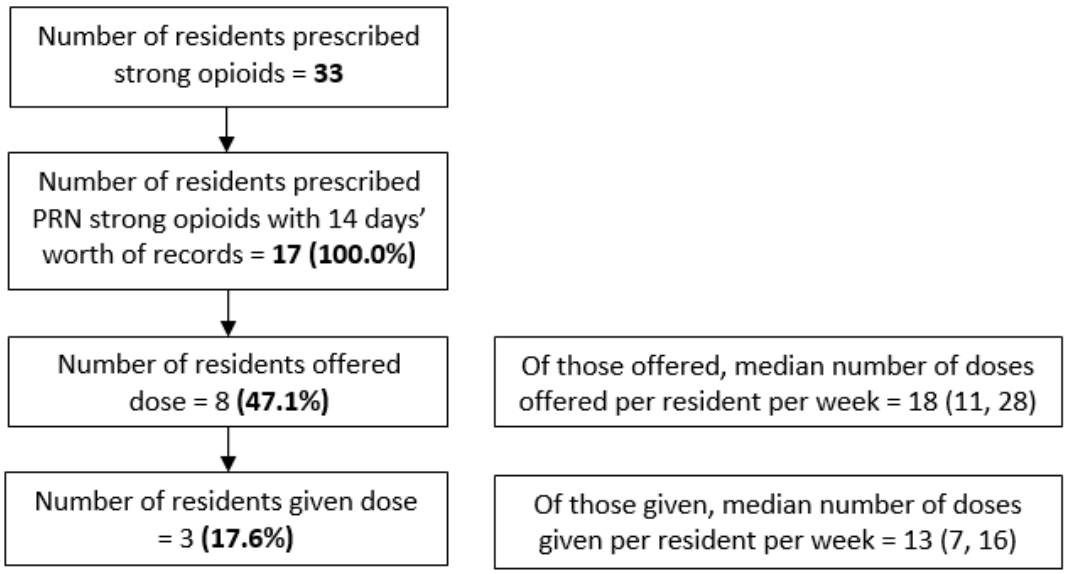

Figure 20. Flow diagram of number of residents prescribed, offered, and administered PRN strong opioids at 12-month study visit, plus median (and interquartile range) of doses offered and received

8.1.3 Key results from analgesic prescription and administration data, including care home factors

These data show that the majority of care home residents in this sample were prescribed analgesics but this was mostly prescribed as PRN. More detailed study illustrates that many residents did not receive their prescribed PRN analgesics in the previous two weeks of each study visit, and in comparison to the total number of analgesic doses available, very little was given. Across all study visits, 41.9% residents did not receive any analgesic medication during the three 2-week periods of data collection.

Paracetamol was the most commonly prescribed analgesic. Prescriptions of weak and strong opioids were even at baseline, and at the 4-month and 12-month visits, strong opioids were prescribed more frequently than weak opioids. A common prescribing error was that regular strong opioids were not accompanied by a prescription of PRN strong opioids (in case of breakthrough pain).

8.2 Secondary aims and objectives: analgesics

8.2.1 The effects of care home factors on analgesic use

8.2.1.1 Analgesic prescriptions

Before running a clustered regression model exploring the association between care home factors and analgesic prescriptions, univariable analyses were conducted (also clustered at care home level) of potential predictor variables (age, gender, dementia diagnosis and severity, agitation, ethnicity, and first language) (Jensen-Dahm et al., 2015, Sandvik et al., 2016, Kung et al., 1999, Horgas and Tsai, 1998, Closs et al., 2004). A mixed-effect univariate logistic regression analysis was run to explore the association between each potential predictor variable and whether or not the resident was prescribed an analgesic at baseline. The model accounted for clustering at the level of the care home. Table 15 displays the results of the analysis.

Table 15. Univariable analysis prior to investigation of the effect of care home factors on analgesic prescription

	Regression coefficient (Coef.)	95% conf. intervals
Age	0.00	-0.00, 0.01
Baseline CDR		
Mild	*Ref*	*Ref*
Moderate	*0.01*	*-0.07, 0.08*
Severe	***0.67***	***0.61, 0.74***
CMAI total	0.00	-0.00, 0.00
	Chi-squared	P value
Gender	0.83	0.36
Ethnicity (White or non-White)	0.35	0.55
English as first language	0.59	0.96
Dementia diagnosis	0.86	0.35
Clinically significant CMAI	0.27	0.60

The preliminary analysis identified dementia severity as a potential confounder ($p<0.05$): residents with severe dementia received more analgesic prescriptions than those with mild dementia. Thus dementia severity was included in the final model exploring care home factors as predictors of analgesic prescriptions (see Table 16).

Table 16. Results of multi-level model exploring effect of care home factors on whether or not a resident received a prescription of analgesic medication

	Odds ratio	95% conf. intervals
Nursing home	1.23	-0.74, 2.04
Ownership		
Private	*Ref*	*Ref*
Charity	*0.88*	*0.47, 1.67*
Council/local authority	*2.27*	*0.58, 8.94*
Dementia registered	0.91	0.36, 2.35
Dementia specialist	0.69	0.41, 1.16
Number of beds	1.00	0.99, 1.02
CQC rating		
Outstanding	*Ref*	*Ref*
Good	*0.39*	*0.14, 1.05*
Requires improvement	***0.26***	***0.09, 0.92***
Inadequate	1.06	0.13, 7.89

The only care home factor that significantly contributed to whether or not a resident was prescribed analgesics (at baseline) was if the care home was rated as 'requires improvement' by the CQC. The coefficient indicates that residents from these homes were 1.2 times less likely to receive a prescription for analgesics compared to residents in a home rated 'outstanding'. It is worth noting that there are sizeable group differences in CQC ratings, with 69.4% of care homes in the sample rated as 'good'. It did not appear to make a difference if the care home was a nursing home or residential home, whether it was owned by a charity, council/local authority or private owner, whether it was dementia-registered or dementia specialist, or number of beds.

To further explore the reasons why the majority of care home factors did not appear to influence analgesic prescribing, post-hoc tests of heterogeneity were run. A forest

plot identified that there was no difference between care homes and analgesic prescribing (I^2=0.0%). The homogeneity in the sample explains why no differences were highlighted in the regression models.

8.2.1.2 Analgesic administration

As before, univariable analyses were conducted to identify clinically relevant potential covariates before running a multi-level regression model. The dependent variable was whether or not the resident was administered a PRN analgesic at baseline.

Table 17. Univariable analyses of demographic and individual factors to identify potential confounders regarding baseline analgesic administration

	Coef.	95% conf. intervals
Age	-0.01	**-0.01, -0.00**
Baseline CDR		
Mild	*Ref*	*Ref*
Moderate	*-0.07*	*-0.19, 0.06*
Severe	*-0.13*	***-0.26, -0.00***
CMAI total	0.00	-0.00, 0.00
	Chi-squared	p-value
Gender	0.42	0.52
Ethnicity (White or non-White)	4.90	**0.03**
English as first language	3.31	0.07
Dementia diagnosis	0.41	0.52
Clinically significant CMAI	0.37	0.54

Univariable analyses (clustered at care home level) identified these baseline demographic variables as potential confounders (see Table 17):

- age (older residents were administered fewer PRN analgesics)
- dementia severity (those with severe dementia were administered fewer PRN analgesics)
- ethnicity (non-White residents were administered more PRN analgesics)

These variables were therefore included in the final model exploring the effects of care home factors on baseline analgesic administration (as a binary variable).

Table 18. Multi-level regression model exploring the effect of care home factors on PRN analgesic administration at baseline

	Odds ratio	95% conf. intervals
Nursing home	0.86	0.36, 1.94
Ownership		
Private	*Ref*	*Ref*
Charity	*1.46*	*0.53, 4.05*
Council/local authority	*2.46*	*0.36, 16.75*
Dementia registered	0.74	0.15. 3.61
Dementia specialist	0.70	0.32, 1.53
Number of beds	1.00	0.98, 1.01
CQC rating		
Outstanding	*Ref*	*Ref*
Good	*1.06*	*0.30, 3.70*
Requires improvement	*0.86*	*0.19, 3.86*
Inadequate	*2.80*	*0.10, 79.7*

Table 18 shows that no care home factors (care provision; ownership; dementia registered; dementia specialist; number of beds; overall CQC rating) were significant; that is, there was no difference in analgesic administration when comparing different types of care homes.

As before, post-hoc tests were run to explore whether the lack of effect of care home factors could be attributed to homogeneity between care homes. A forest plot showed that there was heterogeneity between all care homes, I^2=56.7% (over 50% indicates that the difference may be caused by something other than chance), but these differences were not associated with the factors identified above. For example, by comparing the groups above it was found that there was heterogeneity between: care provision (nursing home, I^2=56.3%, residential homes, I^2=55.3%); ownership (private, I^2=52.6%, charity, I^2=70.4%, council/local authority *n* too low); CQC rating (I^2 ranged from 44.8%-82.1%), and dementia-registered and dementia-specialist tests returned I^2 values>50%. This indicated that the differences between care homes cannot be defined by typical methods of classifying care homes but there were other factors involved.

8.2.2 Differences in analgesic prescribing between groups

Prior to investigating group differences in analgesic use, a sensitivity analysis was run that showed that age was the only demographic variable that significantly contributed to missingness resulting from death at any study visit (coef. = 0.01, 95% confidence interval (CI) = 0.01, 0.01, p<0.001). Therefore, where appropriate, age was included as a covariate in the final model.

8.2.2.1 Do females receive more analgesics than males?

Using a logistic regression clustered at the care home and study visit level, it was found that females received significantly more analgesic prescriptions than males (p=0.011), odds ratio (OR) = 1.27, therefore females were 27% more likely to be prescribed an analgesic compared to males. Females also received more prescriptions for regular analgesics compared to males (p=0.003, OR 1.33). There was

no difference in PRN prescriptions, nor a gender difference when considering PRN administration.

Females received significantly more prescriptions for opioid drugs than males (OR 1.39), including regular opioids (OR 1.67) so were 67% more likely to be prescribed a regular opioid. Females did not receive more PRN opioids than males. Table 19 displays the results of the regression analyses.

8.2.2.2 Is there an age difference in analgesic prescribing and administration, and do residents aged 81 years plus receive more analgesics than younger residents, aged 65-80 years?

There were no age differences in analgesic prescriptions (see Table 19) however there was a difference in analgesic administration (p=0.004). In this sample, for every year increase in age, the probability that a PRN analgesic was administered in the previous 2 weeks decreased by 0.04.

When analysing age group (65-80 years vs 81 years and over) age was not included as a covariate in the model, to avoid collinearity with the independent variable. Using a multi-level logistic regression, there was no significant difference in analgesic prescription (overall, regular, or PRN), or analgesic administration, when comparing residents aged 65-80 and residents aged 81 and above.

Looking at analgesic classes, residents aged 81 years and over were prescribed significantly fewer regular non-opioids (OR 0.77) and less PRN opioids than younger residents (OR 0.76) (see Table 19). To investigate whether the significant association of age and analgesic administration was related to dementia severity or gender, a post-hoc test was run (controlling for CDR and gender). Coef. = -0.04 (95% CI, -0.07, -0.01); thus age was independently associated with less administration of PRN analgesia.

8.2.2.3 Are residents with more severe dementia prescribed less analgesic medication than those with mild dementia?

Residents with moderate or severe dementia were not prescribed fewer analgesics than residents with mild dementia. This also applied to regular and PRN analgesics. There was also no difference in prescribing prevalence when looking at non-opioids and opioids overall, but residents with severe dementia were 47% more likely to be prescribed regular opioids than residents with mild dementia (OR 1.47). See Table 20 for details.

Table 19. Gender differences and age differences in prescriptions of analgesics and classes

	Gender (OR) (*reference* = female)	Age	Age group (OR) (*reference* = 65-80 years)
Analgesics (Odds ratio [OR]/Coef. (95% conf. intervals))			
Prescribed	**1.27 (1.06, 1.53)**	0.00 (-0.01, 0.01)	0.92 (0.76, 1.12)
Prescribed regular	**1.33 (1.10, 1.60)**	-0.01 (-0.02, 0.00)	0.84 (0.69, 1.01)
Prescribed PRN	1.09 (0.92, 1.31)	0.00 (-0.00, 0.01)	0.98 (0.82, 1.18)
Administered PRN	0.82 (0.49, 1.37)	**-0.04 (-0.07, -0.01)**	0.59 (0.33, 1.06)
Non-opioids			
Prescribed	1.19 (0.99, 1.42)	0.00 (-0.01, 0.01)	0.87 (0.73, 1.06)
Prescribed regular	1.20 (0.96, 1.49)	-0.01 (-0.02, 0.00)	**0.77 (0.62, 0.96)**
Prescribed PRN	1.08 (0.91, 1.29)	0.01 (-0.00, 0.02)	1.06 (0.88, 1.28)
Opioids			
Prescribed	**1.39 (1.14, 1.71)**	0.00 (-0.01, 0.01)	0.96 (0.79, 1.18)
Prescribed regular	**1.67 (1.31, 2.15)**	0.01 (-0.00, 0.02)	1.19 (0.92, 1.52)
Prescribed PRN	1.09 (0.84, 1.42)	-0.01 (-0.02, 0.01)	**0.76 (0.59, 0.99)**

Table 20. Relationship between dementia severity and analgesic use

	Dementia severity (*mild as reference*)	
	Moderate	Severe
Analgesics (Odds ratios (95% conf. intervals))		
Prescribed	1.05 (0.84, 1.31)	1.01 (0.81, 1.26)
Prescribed regular	0.95 (0.76, 1.19)	1.21 (0.97, 1.50)
Prescribed PRN	1.11 (0.90, 1.37)	0.95 (0.77, 1.16)
Administered PRN	0.72 (0.39, 1.34)	**0.50 (0.27, 0.93)**
Non-opioids		
Prescribed	0.96 (0.77, 1.19)	0.82 (0.66, 1.02)
Prescribed regular	0.78 (0.60, 1.00)	0.83 (0.65, 1.06)
Prescribed PRN	1.10 (0.89, 1.36)	0.93 (0.75, 1.14)
Opioids		
Prescribed	1.14 (0.90, 1.45)	1.23 (0.98, 1.55)
Prescribed regular	1.05 (0.79, 1.41)	**1.47 (1.12, 1.93)**
Prescribed PRN	1.14 (0.83, 1.56)	0.98 (0.72, 1.35)

8.2.2.4 Is severity of dementia negatively associated with the number of analgesic drugs administered?

Residents with severe dementia were administered significantly fewer analgesics (p=0.03, OR 0.50) than those with mild dementia. Those with moderate dementia also received less analgesia but not at a significant level. Figure 21 displays the administration of analgesics by dementia severity and study visit. At the second study visit residents with moderate dementia were administered fewer analgesics than residents with mild or severe dementia, and fewer analgesics than residents with moderate dementia at other study visits. Residents with severe dementia consistently received fewer analgesics than those with mild dementia. For residents

with moderate dementia there is greater variance; at 4-months it appears that those with moderate dementia were administered less pain relief than residents with severe dementia. In addition, fewer analgesics were administered, and therefore all residents appear to receive less pain relief, as the study progressed.

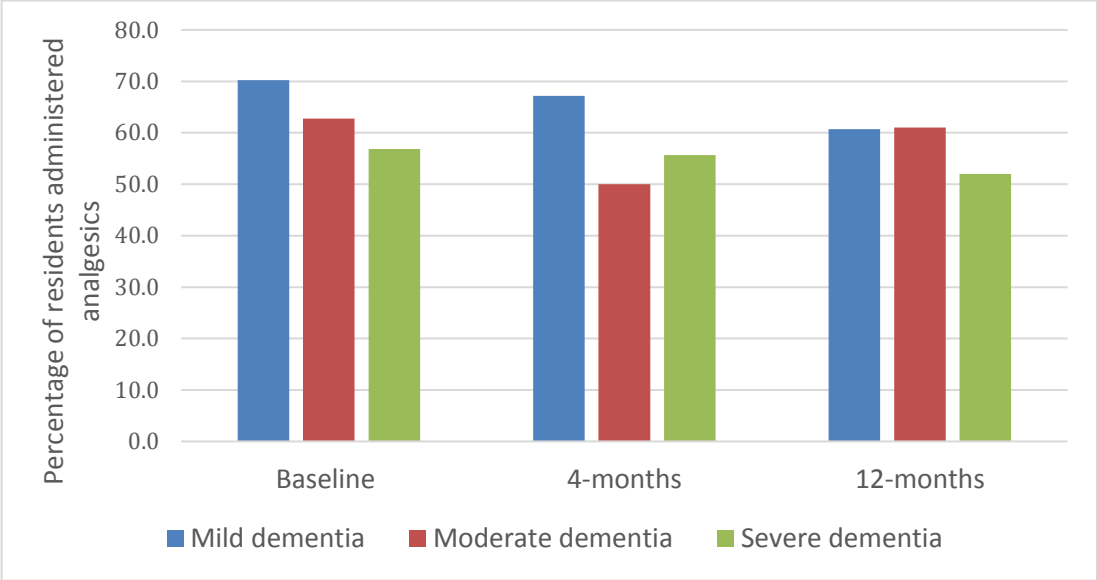

Figure 21. At each study visit, percentage of residents (of those prescribed analgesics) who were administered analgesics, by dementia severity

8.2.3 Association between agitation and prescription of analgesic medication

8.2.3.1 Is analgesic medication associated with different types of agitation (CMAI score)?

These models controlled for gender and excluded CMAI factors as well as age. There was no association between CMAI score and analgesic prescribing (coef. = 0.00, 95% CI = -0.00, 0.01), nor whether residents had clinically significant agitation or not (coef. = 0.16, 95% CI = -0.07, 0.38). Residents with clinically significant agitation were prescribed more opioids (coef. = 0.23, 95% CI = 0.05, 0.40) but there was no association between clinically significant agitation and non-opioids (coef. = 0.14, 95% CI = -0.03, 0.31). See Table 21 for details regarding agitation subtypes.

Table 21. Analgesic and subtype prescribing by agitation behaviours

	Aggressive	Physically nonaggressive	Verbally agitated	Hiding/hoarding
	(Odds ratio, (95% CI)			
Prescribed - analgesics	1.00 (0.99, 1.01)	1.00 (0.99, 1.02)	1.01 (0.96, 1.03)	**0.94 (0.90, 0.98)**
Prescribed regular analgesics	**1.01 (1.00, 1.03)**	1.00 (0.98, 1.01)	1.00 (0.99. 1.02)	**0.95 (0.91, 0.99)**
Prescribed PRN analgesics	0.99 (0.98, 1.00)	1.00 (0.99, 1.02)	1.01 (1.00, 1.03)	**0.95 (0.92, 0.99)**
Administered analgesics	**0.96 (0.93, 0.99)**	**1.05 (1.01, 1.10)**	1.02 (0.98, 1.07)	1.03 (0.90, 1.17)
Prescribed - opioids	1.01 (1.00, 1.02)	0.98 (0.97, 1.00)	**1.04 (1.03, 1.06)**	**0.94 (0.89, 0.98)**
Prescribed regular opioids	**1.02 (1.01, 1.03)**	0.98 (0.96, 1.00)	**1.03 (1.00, 1.05)**	**0.93 (0.88, 0.99)**
Prescribed PRN opioids	0.99 (0.98, 1.01)	1.00 (0.98, 1.02)	**1.05 (1.03, 1.08)**	0.94 (0.88, 1.00)
Prescribed – non opioids	0.99 (0.98, 1.00)	1.01 (1.00, 1.03)	1.02 (1.00, 1.03)	0.96 (0.92, 1.00)
Prescribed regular non-opioids	1.00 (0.99, 1.02)	1.00 (0.98, 1.02)	1.01 (0.99, 1.03)	0.99 (0.94, 1.04)
Prescribed PRN non-opioids	0.99 (0.98, 1.00)	1.01 (0.99, 1.02)	1.01 (0.99, 1.03)	**0.96 (0.92, 1.00)**

A multilevel regression model identified that there was a significant positive association between:

- aggressive behaviours and regular analgesics including regular opioids

- physically non-aggressive behaviours and administered PRN analgesics
- verbally agitated behaviours and opioids including regular and PRN opioids

There was a negative association between:

- aggressive behaviours and administered PRN analgesics
- hiding/hoarding behaviours and prescribed analgesics (regular and PRN), opioids including regular opioids, non-opioids including PRN non-opioids

8.2.4 Comparing analgesic prescribing prevalence in this cohort compared to international prescribing patterns

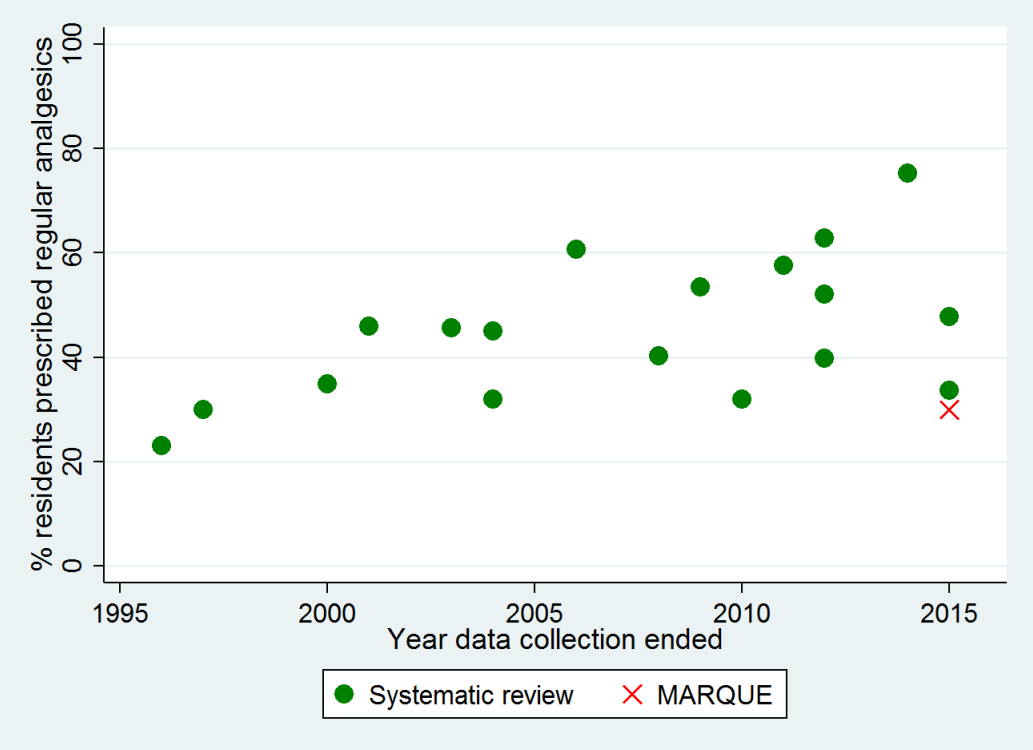

Figure 22. Scatter plot of prescription prevalence over time, comparing regular analgesic prescribing in this cohort compared to systematic review studies

Looking at Figure 22, prescriptions of regular analgesics in this cohort appear much lower than regular prescriptions in other countries. When incorporating PRN prescriptions, prescribing patterns of analgesics are similar to international prescribing prevalence (see Figure 23).

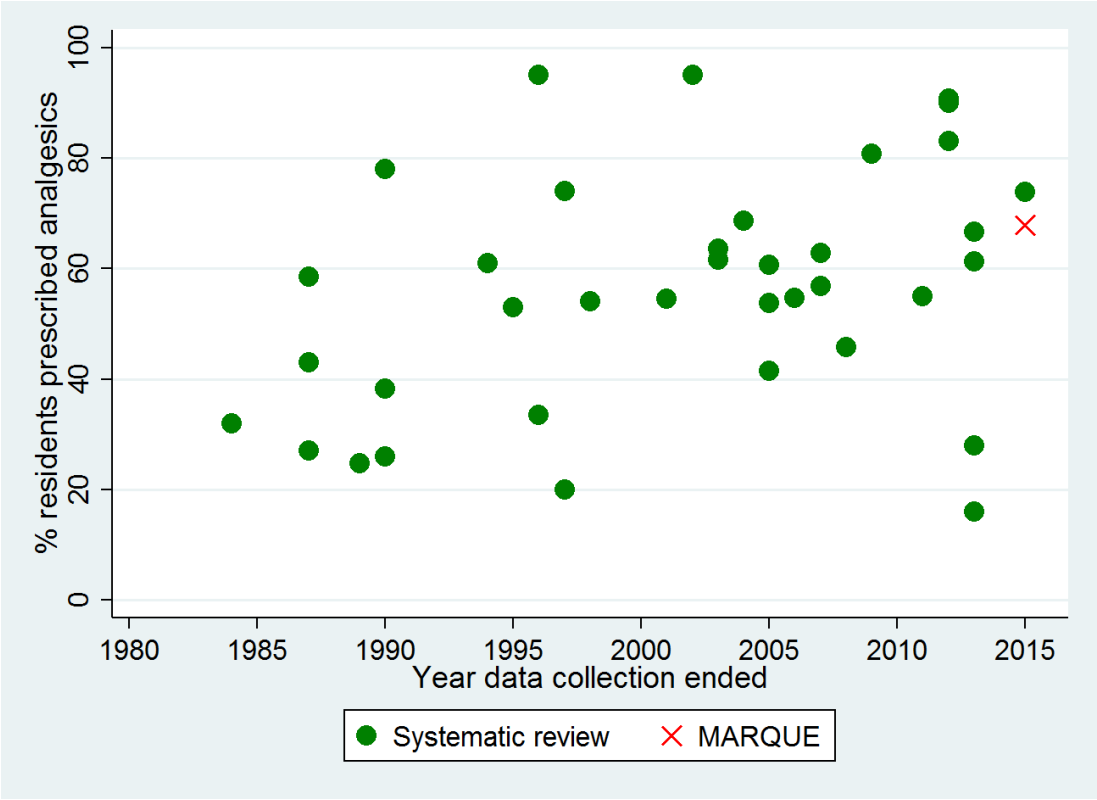

Figure 23. Scatter plot of prescription prevalence over time, comparing regular and PRN analgesic prescribing in this cohort compared to systematic review studies

8.2.5 Key results of factors associated with analgesic prescription and administration

Analyses of care home factors identified that care homes were homogeneous with regards to analgesic prescribing, and therefore no obvious categorisations of care homes (i.e. ownership, CQC rating, care provision, dementia-registration or dementia–specialism, number of beds) were predictive of higher prescription prevalence. However when looking at analgesic administration, care homes were heterogeneous to a level other than chance, and these differences appeared unrelated to aforementioned care home factors, indicating that there were ulterior factors contributing to analgesic administration.

Individual factors also played a role in analgesic use. There were no gender differences for PRN prescriptions or administration, but females were prescribed significantly more regular analgesics, and based on the administration data that

showed that PRN analgesics were not given to their full prescription potential, it appears females received more pain relief than males.

Residents with severe dementia were prescribed more regular opioids but were administered fewer PRN analgesics than residents with mild dementia (at a significant level) and moderate dementia, which was consistent across all study visits.

Comparing analgesic prescribing prevalence in this cohort compared to the international studies included in the systematic review, it appears that English care homes prescribe fewer regular analgesics and are more reliant on PRN prescriptions than other countries.

8.3 Secondary aims and objectives: psychotropics and analgesics

8.3.1 Description of the prescription of psychotropic medication

Psychotropic drugs were prescribed to 822 residents (57.7%) at baseline; prescribing levels were stable throughout the study (56.8% at 4-months, 57.4% at 12-months). Appendix 18 lists the prescribing prevalence of psychotropic drugs and drug classes at each study visit. The most commonly prescribed class of psychotropic drug was antidepressants, prescribed at baseline to 40.6% of residents, and 39.4% of residents at 12-months. Antidepressants were prescribed PRN to four residents, which is not common practice. In two cases, trazodone was prescribed with indications specified as anxiety and agitation, and in two cases amitriptyline was prescribed with no indication.

Anxiolytics and hypnotics were prescribed to around 22% of residents. At baseline, 18.4% of residents received regular prescriptions and 15.4% of residents were prescribed PRN anxiolytics/hypnotics. At 12-months, it was even: 12.6% were prescribed them regularly and 12.6% were prescribed them PRN. The most commonly prescribed drugs in this class were lorazepam (a benzodiazepine) and zopiclone (a hypnotic drug commonly used to treat insomnia).

Antipsychotic drugs were the least commonly prescribed class of psychotropics, prescribed to 17.3% of residents at baseline, rising to 18.5% at the 12-month study visit. The most commonly prescribed antipsychotic drug was risperidone (prescribed to 7.2% of residents at baseline). Antipsychotics were more likely to be prescribed regularly, not PRN (15.9% versus 1.9%, at baseline). Of the 246 residents prescribed antipsychotic medication, 232 residents were prescribed 1 antipsychotic (94.3% [95% CI, 90.6-96.6]), and 14 residents were prescribed 2 antipsychotics (5.7% [95% CI, 3.4-9.4]).

The median prescription duration (excluding residents who have withdrawn) of psychotropic drugs overall, and the three psychotropic classes, was three study visits i.e. at least one year.

8.3.2 Secondary aim and objective: association between analgesics and psychotropics

A multilevel Poisson regression model showed a significant positive relationship between number of analgesic prescriptions and number of psychotropic prescriptions (coef. = 0.07 [95% CI, 0.02, 0.11]) which means that residents who were prescribed a higher number of analgesic medications were also prescribed a higher number of psychotropic medications, compared to those who were prescribed fewer analgesics. This model included age and gender as possible confounding variables.

An association was also found between antidepressants and analgesics. A multi-level regression, including age and gender as possible confounding variables, was run and the odds of being prescribed an analgesic was larger for those also prescribed an antidepressant (OR 1.24 [95% CI, 1.04-1.47]).

A significant association was also found for anxiolytics/hypnotics (OR 1.33 [95% CI, 1.07-1.64]).

There was no association found between having a prescription of analgesics and a prescription of antipsychotics.

8.3.3 Key results from secondary aims and objectives: psychotropics and analgesics

The majority of residents were prescribed psychotropics and the most prevalent class of psychotropic was antidepressants, prescribed to approximately 40% of residents.

Residents in this cohort who were prescribed analgesics were more likely to also have been prescribed antidepressants and anxiolytic/hypnotics.

Chapter 9 **Discussion**

9.1 Outline

In this chapter I will describe the principal findings of the empirical study and draw comparisons with existing literature. I will discuss the strengths and limitations of the study, both inherent and in the context of other research. I will consider the possible explanations for the findings, and suggest clinical and policy implications. Finally I will propose avenues of future work that can build on this research.

9.2 Principal findings

This thesis describes how analgesic medication is used in English care homes. Across all study visits around 70% of residents were prescribed analgesics. The most commonly prescribed analgesic class was simple non-opioids, and paracetamol was the most widely used analgesic drug, prescribed to around 58% of residents. Non-opioids were over twice as likely to be prescribed as PRN prescriptions compared to regular prescriptions. There was a low prevalence of NSAID prescribing in this cohort, with around 1% of residents prescribed these drugs at each study visit. Opioids were prescribed to approximately 23% of residents.

There was little difference in prevalence between strong opioids and weak opioids at baseline (11.4% vs 11.5%) but by the final study visit more residents received strong opioids than weak opioids (14.1% vs 12.4%). Most strong opioids prescribed were transdermal patches, primarily buprenorphine. The median prescription duration (constrained by study duration of three study visits; one year) was two study visits (either at least 4 months, or at least 8 months) for strong opioids and three study visits (at least 1 year) for weak opioids.

It was rare that residents were prescribed both regular and PRN opioids. At baseline, 12.3% of residents prescribed a regular opioid were also prescribed a PRN opioid, at 4-months, 15.5%, and at 12-months, 17.8%. This represents a prescribing error: it is recommended that those on a regular strong opioid are also prescribed a PRN dose

for breakthrough pain (National Institute for Health and Clinical Excellence, 2012b, Denison Davies et al., 2011).

Care homes were homogeneous in terms of analgesic prescriptions but heterogeneous in administering PRN analgesics. Differences between care homes were not defined by the factors that were measured - and the factors that we may assume to influence administration - that is, care home quality, care provision, ownership, dementia- registration or dementia-specialism, or number of beds.

PRN prescriptions for analgesics are used ubiquitously in care homes but little is currently known about typical usage. In this study, 67.9-70.6% of residents were prescribed analgesics but the majority (56.0-60.3%) of those residents were prescribed them PRN only. PRN analgesics were, on the whole, not offered as many times as they could have been, and were administered on even fewer occasions. There were 23.5% (n=227) of residents who were prescribed pain relief that was not administered at all during the three study visits. Overall, 41.9% of residents did not receive any pain relief (either no prescribed analgesia or PRN analgesia never administered). Typically the indication was not given on the MAR chart so it was not possible to make a judgement regarding the appropriateness of the decision to give or not give pain relief. As the study progressed fewer analgesics were administered.

Individual differences were observed in both analgesic prescribing and administration. These differences were seen between age, gender, dementia severity, and type of agitation.

When comparing dementia severity (and controlling for age), the only significant difference in prescribing prevalence was that residents with severe dementia were prescribed more regular opioids than residents with mild dementia. Residents with mild dementia were administered more PRN analgesics than those with moderate dementia, and significantly more than those with severe dementia. This was consistent across all three study visits.

Females were prescribed more regular opioids than males, but there was no difference between males and females in relation to PRN administration. Thus, it appears that overall female residents received more pain relief than male residents.

Regarding age as a continuous variable there was no prescribing difference, but there was a negative association between age and administration of PRN medication (which was independent of both gender and dementia severity). Residents in the 81 years and over age group were prescribed fewer regular non-opioids and more regular opioids than residents aged 65-80 years.

Residents with more aggressive behaviours were prescribed more regular analgesics and regular opioids compared to other agitation types, but were administered fewer PRN analgesics. Residents with physically non-aggressive behaviours were administered more PRN analgesics. Residents with verbally agitated behaviours were prescribed more opioids.

9.3 Differences in results in my study versus other studies

Compared to the prescribing prevalence reported in the systematic review, regular analgesics are prescribed much less in England than in other countries. For example, approximately 30% of residents in this cohort were prescribed regular analgesics compared to 40-60% in other countries, and regular prescriptions of paracetamol were substantially lower than other countries: around 15% in this study versus around 50% in recent studies included in my review (La Frenais et al., 2017).

Opioid prevalence has not changed much in English care homes since 2010 (22.8-23.6% versus 22.4%) (Shah et al., 2012), but again, is lower than in other countries. International prescribing prevalence of regular opioids is around 20-30%, whereas in this cohort around 13% were prescribed regular opioids (La Frenais et al., 2017). The finding that strong opioids were increasingly prescribed over weak opioids, and patches were used more than oral opioids, is similar to other countries (Jensen-Dahm et al., 2015). A US study reported that nearly one quarter of long-term opioid users received transdermal prescriptions. The US prescriptions were primarily fentanyl

whereas in this study the most prevalent strong opioid was buprenorphine (Hunnicutt et al., 2018).

The finding that 1.8-2.8% of the population were prescribed both regular and PRN opioids was low compared to other countries (O'Mahony et al., 2015). A US study of MDS data from 1998-2000 reported that only 1.7% of residents were prescribed both long- and short-acting opioids (Won et al., 2004) but in a recent study this had risen to 21.8% (Hunnicutt et al., 2018).

In line with this study, previous research has also found that PRN medication is not often administered. One study looked at PRN use across the spectrum of drug classes and found that all types of PRN medications were infrequently administered, and only 9.0% of residents were administered at least one dose of PRN paracetamol (Stasinopoulos et al., 2017). Several studies have compared PRN analgesic use and pain, and there is evidence of under-treatment with PRN analgesics in care homes. Mezinskis et al. (2004) found that, in a study where the majority of cognitively impaired residents had a prescription for PRN analgesia, less than a third received any, despite the presence of chronic painful diagnoses. Lukas et al. (2013a) reported that nearly 21% of residents did not receive any analgesics despite significant pain.

Few studies have explored care home factors at the organisation level (for example care provision, ownership, registration, or specialism) and analgesic use. One study from Norway did not observe any difference between care homes with regards to strong opioid prescribing (Griffioen et al., 2017a). However, intrinsic factors have previously been implicated in influencing pain management, and the findings presented in this thesis contribute to this evidence. A large European study identified heavy workload, staff shortages, team instability, staff turnover, and lack of time, as contributing to poor pain management (Lukas et al., 2013a). Person-centred care, pain awareness, training, consistency of care, confidence and responsibility, good communication between staff and family carers, and good internal communication are important for good pain management (Corbett et al., 2016).

Prior to a study conducted by Rigler et al. (2007), no association had been identified between opioid prescribing and age in the US. Rigler et al. (2007) found that long-acting opioids were more likely to be prescribed to people aged 85 years and over (compared to those aged 60-75 years) and to people with dementia, instead of other non-transdermal opioids. The median age of the MARQUE population was 84.9 years at baseline, and all had dementia or probable dementia so the findings are comparable to this cohort. A more recent study found that in UK primary care between 2000 and 2010 the prescription of strong opioids had risen in people aged 66-80 (Zin et al., 2014), and a study of the entire elderly Danish population found a strong association between age and opioid use (Jensen-Dahm et al., 2015). Unfortunately there is a dearth of studies exploring age and analgesic PRN use. Two Australian studies explored associations with PRN medications generally and did not find any association with age (Stasinopoulos et al., 2017, Stokes et al., 2004) but the residents' ages in their populations were relatively homogenous. Thus, this study is the first to explore the specific relationship between PRN analgesic administration and age.

The findings regarding gender difference are in line with previous evidence that female care home residents receive more analgesia than male residents (Jacob and Kostev, 2018, Lukas et al., 2013a, Sandvik et al., 2016). A large US care home study found a positive relationship between female gender and regular analgesics (Won et al., 2004). Furthermore, in this study female residents were prescribed more regular opioids, which is also seen in UK primary care (Zin et al., 2014). A review of Norwegian prescribing practice in care homes (Sandvik et al., 2016) found a positive relationship between regular paracetamol prescriptions and females but in this study there was no difference. Conversely several other care home studies have found no gender difference in analgesic prescribing or administration (Hemmingsson et al., 2017, Stokes et al., 2004, Rigler et al., 2007). Interestingly, in Sweden there was an increase from 2007 to 2013 in analgesic use in male residents who were in pain, which may indicate that under-treatment in males is decreasing (Hemmingsson et al., 2017). There is a limited body of research exploring gender differences and PRN analgesic

administration; an Australian study did not find a relationship between gender and PRN drug use (not specifically analgesics) (Stokes et al., 2004).

In terms of dementia severity, existing data are mixed. In care homes (where there is a higher prevalence of dementia) there tends to be a higher prescribing prevalence of opioids compared to those who live in the community (Jensen-Dahm et al., 2015, Shah et al., 2012), and, as reported and discussed in my systematic review, use of opioids has increased in the care home population over time (La Frenais et al., 2017). These increases may be reflective of higher needs of the care home population (Pitkala et al., 2015). A Dutch study found no difference in prescriptions of analgesic class and dementia severity, but did report that despite receiving regular analgesics a significant number of residents were still in moderate to severe pain (van Kooten et al., 2017). A US care home study (Hunnicutt et al., 2018) reported that strong opioid use was lower in those with moderate to severe dementia, which is opposite to the findings in this study. Regarding PRN use, most studies appear to agree that residents with more severe dementia are administered these less (Closs et al., 2004, Mezinskis et al., 2004, Bauer et al., 2016).

A number of studies have explored the effect of analgesia on agitation, but there are few studies that report analgesic prescriptions and types of agitation. Hendriks et al. (2015) found no association between pain and agitation in a longitudinal care home study from admission to death, however they did not do any subgroup analyses on different agitation behaviours (Ahn and Horgas, 2013). Verbally agitated behaviour has been found to decrease following increased analgesia, as have physically non-aggressive behaviours, but no response was seen in aggressive behaviours (Husebø et al., 2014b).

9.4 Strengths and weaknesses

9.4.1 Strengths

This study presents new information. Many researchers have expressed the need for data regarding PRN use (Achterberg, 2016, Dörks et al., 2016, Hoffmann and Schmiemann, 2016, Bauer et al., 2016). It is the largest study to describe PRN medication use in care homes and presents the most comprehensive assessment of analgesic administration in care homes. Given that PRN prescriptions were infrequently administered, it appears that (at least in English care homes) the presence of a PRN prescription of analgesia is not an accurate measure of pain treatment and future studies reporting medication use in care homes should consider this.

Many studies have compared analgesic use in people with and without dementia, but the comparison between different dementia severities is an important aspect of this research as it includes potentially at-risk groups that may be missed in a broader population. The two weeks' worth of PRN administration data coincides with the CMAI data. As a result it is possible to compare PRN administration with agitated behaviours that have occurred over the same time period. Furthermore, the CMAI is described in terms of its factors, which has more clinical relevance than the global score.

The heterogeneity identified between care homes is a valuable addition to an ongoing discourse in the literature around analgesic prescribing and administration in care homes, and about identifying areas for improvement in pain assessment and management. Recent studies have also observed that factors associated with the care home team (for example, internal communication, training, high staff turnover, team culture, and leadership) appear to play a larger role than factors external to the team (such as care home size, GP, or ownership) (Kaasalainen et al., 2010, Bowers et al., 2003, Stokes et al., 2004, Griffioen et al., 2017b, Lukas et al., 2013a). These factors will be discussed in more detail in the context of clinical and policy implications.

This study is representative of the population that it aims to describe. The care homes were geographically diverse within England, and in terms of number of residents, the study is the largest prospective care home study to date. A large sample size is important because the needs of care home residents are so varied. As dementia is underdiagnosed in the care home population, using the NPC to identify those with probable dementia was a strength as it led to the inclusion of residents who would have been excluded if a clinical dementia diagnosis was a criterion (Gordon et al., 2013, Lukas et al., 2013b). Other than lack of cognitive impairment there were no other eligibility criteria, which increases external validity, and all eligible cognitively impaired residents (or next of kin) were contacted, thus reducing selection bias.

This study has reported prescribing patterns in terms of residents and not number of prescriptions. Quantifying medication use in this way is valuable because it accounts for multiple prescriptions for one individual, and it is easier to observe prescribing errors, such as a lack of PRN opioid prescriptions accompanying regular prescriptions for opioids.

The longitudinal nature of the study means that medication use could be observed over time. Care home residents can experience significant changes (such as increased cognitive impairment and agitation) over relatively short periods of time, and individuals can experience these changes at different rates. Longitudinal data allows us to capture medication prescribing and administration in relation to an individual resident's current status. These data have identified a prescribing dominance shift from weak opioids to strong opioids that in cross-sectional data may not have been observed.

Analyses controlled for clustering at the care home level thus accounting for unobserved variables that may result from this shared context. Clustering controls for the confounding effect of care homes for both independent and dependent variables, and thus increases the validity of the differences identified. As such, findings can be generalised with some confidence to the wider population and can also provide a good comparison of prescribing patterns in relation to other studies.

This study provides reliable data. Trained researchers conducted proxy interviews with raters who were familiar with the residents. Many large studies utilise databases, for example MDS data, where efforts may not be made to ensure familiarity and so documentation may be completed by a MDS coordinator who does not provide direct care to the resident (Won et al., 2004). MARQUE researchers collected prescription data directly from source data (i.e. MAR charts). Transcriptions from hard copy data to database were audited for every resident at all three study visits. These steps contribute to ensuring that data was reliable and therefore an accurate representation of current clinical practice.

9.4.2 Limitations

It is impossible to assess the appropriateness of prescriptions without pain data. Ideally study findings would include and triangulate prescription data, individual factors, and level of pain, to determine whether pain relief was appropriate. For example, the residents who were prescribed PRN pain relief and did not receive any may not have been in any pain during the study visits. Unfortunately given the scope of the research, principally the time limits and high recruitment target, pain assessments were not included. Conversely, observational pain assessments are a snapshot in time, and even if these data were collected they may not have presented a valid picture of the previous two weeks, because pain is likely to fluctuate (Rajkumar et al., 2017). As the medication forms did not routinely include the indications for the prescriptions, nor identify palliative drugs or adjuvants such as amitriptyline or pregabalin for pain, these data also could not have been utilised. This limitation (the omission of indication) is often found in larger scale studies and database studies. Therefore the findings presented in this thesis cannot directly contribute to the ongoing exploration of groups at risk of untreated or undertreated pain.

The sample lacks external validity to some groups of care home residents. Within the sociodemographic data typically one group was far more dominant. For example, 87.8% of residents were white British versus the next largest group, 3.2% white other,

or 53.7% widowed versus the next largest group, 23.2% married. While representative of the English care home population, the groups were likely underpowered for subgroup analyses. As a result differences in prescribing between groups, and consequently at-risk groups, were not identified. Furthermore, for the purposes of analysis, questionable dementia and mild dementia (according to the CDR) were merged as one group and so comparisons from these data and other studies reporting data regarding mild dementia cannot be directly compared. However there were only a few residents who were rated as having questionable dementia and so it is unlikely that this has affected the findings. The mean age of this population was 84.9 years (SD = 8.6) at baseline so relatively homogeneous and potentially less comparable to other studies.

Data were only collected in England versus other larger studies like SHELTER that reported from countries across Europe (Lukas et al., 2013b). National policies, social care provision, funding, and medical input vary considerably between countries and therefore these data may not be generalisable outside of England. The population oversampled dementia-registered and dementia-specialist homes, nursing homes, and better quality care homes (CQC ratings of 'outstanding' or 'good'). While most homes that were approached agreed to participate in the study, there may be selection bias: care homes that allow access to researchers and are open to research may be more confident about additional scrutiny (Livingston et al., 2017), be better placed to accommodate the extra burden of research participation, have more external healthcare support, or have a more proactive management team who may apply this approach to care improvement as well. These homes may also be less reliant on pharmacological management of BPSD (Sawan et al., 2016, Walsh et al., 2017).

There are limitations to the reliability of the data. The CMAI and the modified Clinical Dementia Rating scale are observational ratings. While every effort was made to ensure that proxy raters were sufficiently familiar with the resident and had not been on leave during the assessment period, it is not guaranteed that this was always the case. Therefore data may not be consistently reliable. It was also not possible to

ensure the same rater at each follow-up due to staff turnover, shift patterns, and competing priorities. However both measures have previously shown good inter-rater reliability (Zuidema et al., 2011, Cedarbaum et al., 2013). A further possible limitation of the CMAI is that more disruptive behaviours may be reported more frequently than less disruptive behaviours. Care home staff are busy and may not be as aware of behaviours that attract less attention, such as a resident who is restless in their bedroom. Furthermore, because interviews took place during the day, night-time behaviours may not have been recorded, or been recorded at a lower frequency. Hence, agitation may have been more prevalent than the data suggests.

It was difficult to record accurate data about whether PRN medication was actually offered or not, often due to indecipherable MAR charts. PRN analgesics were deemed to be offered if the relevant box on the MAR chart had a code entered. The codes typically represented 'PRN offered but not required' or occasionally reasons why it was not appropriate to give medication such as if the resident was unwell or sleeping. More unusually, there was a code that was not in the key; it was tentatively presumed that this was written by an agency nurse who was familiar with a different set of MAR chart codes. However 'PRN offered but not required' does not necessarily describe a situation where medication was actually offered to the resident and declined. Instead the decision may have been made by the nurse without any communication with the resident. It seemed that some care homes required every box on the MAR chart to be completed whereas other homes were content with empty boxes for PRN medication. If the care home policy requires a box to be filled, then codes for medication decisions may be entered by nurses 'automatically' without an assessment of need. As a result inferences could not be made about the rigour with which pain assessments were undertaken in care homes, as there may not have been any clinical difference in homes that 'offered' medications according to their MAR chart, and those that did not.

There are no data regarding GP input for each care home, or whether care home pharmacists were involved in medicines management. As prescribers, GPs and pharmacists can influence how analgesics are administered. For example in care

homes where PRN prescribing is more personalised (and where perhaps blanket PRN prescriptions are used less frequently), administration rates for PRN pain relief may be expected to be higher. Information regarding support arrangements between homes could have helped to explain some of the observed variation, and thus its omission limits our interpretation of these data.

The prescription duration data assume that three study visits equals one year of continuous prescription, however prescriptions may have been stopped and started between study visits. Therefore drug durations may be shorter than reported.

Finally, there is also no information on non-pharmacological treatments that may be used to manage pain. However it has been reported that in England non-pharmacological treatment is not part of normal practice (Corbett et al., 2016).

9.5 Meaning and possible explanations

In this section I will consider existing research and my own theories to explain the findings in terms of the following four themes. First, why prescribing levels of analgesics are lower in English care homes compared to other countries. Second, the increasing prevalence of strong opioid use. Third, the role that resident factors contribute to analgesic prescription and PRN administration. Fourth, the differences observed between care homes and PRN administration.

9.5.1 Prescribing levels in English care homes compared to other countries

Analgesic prescribing is lower in English care homes compared to other countries in Europe, for both regular and PRN medications (Lukas et al., 2013a, La Frenais et al., 2017). Comparing recent studies (data collected post-2010) reported in the systematic review, regular analgesic prescribing levels are considerably lower than in countries such as Australia (62.8-75.2%), Austria (52.0%), and Norway (57.6%), some of which have similar healthcare systems to the UK. As discussed in my review, authors who reported low analgesic use often also described a culture where pain

assessment was not a priority (Boerlage et al., 2013, Neumann-Podczaska et al., 2016, Onder et al., 2014, Lukas et al., 2013a).

Looking at 2010 UK prescribing data reported by Shah et al. (2012), paracetamol prescribing was almost twice as high in care homes as in the community (37.6% vs 20.4) and was considerably lower than in this cohort (56.7-59.4%). High levels of PRN paracetamol prescriptions may be a result of clinicians prescribing PRN analgesics in case of incidences of pain for residents who do not need a regular prescription, in order to limit unnecessary contact and delays in pain relief (Stasinopoulos et al., 2017, Carder, 2011). Opioid prescribing levels between care homes and the community were more similar in the 2010 data (22.4% vs 20.1%) (Shah et al., 2012), and in this cohort, prevalence was only slightly higher (22.8-23.6%). Therefore lower prescribing levels of opioids observed in English care homes compared to international levels appear to reflect the national healthcare system. It has been suggested that, following the murders by Harold Shipman, a GP who killed patients with lethal diamorphine doses, clinicians are more reserved in their prescribing of opioids and may avoid or minimise their use (BMA, 2017), which may translate to under-prescribing or low dose prescriptions.

It is important to note that the distinction between weak and strong opioids is somewhat arbitrary. For instance, a low dose of buprenorphine has a lower potency compared to a high dose of codeine. In this study, buprenorphine patches were the most commonly prescribed strong opioid, and the median dose was 21.4mg of morphine, equivalent to a buprenorphine dose between 5mcg/hour and 10mcg/hour, the two lowest available doses of transdermal buprenorphine. This may be indicative of misinterpretation of the 'start low, go slow' guidance as 'start low, stay low' (Hanlon et al., 2009), and residents may still be in pain despite regular analgesics (van Kooten et al., 2017).

A concern is that residents' pain may be undertreated. Without pain data it is impossible to infer appropriateness of medication use in this cohort, however existing data are a useful source of comparison. In the SHELTER study it was reported

that in English care homes 54.5% of residents experienced pain; specifically, 8.1% of all residents reported being in constant pain and 57.4% experienced intermittent pain (Lukas et al., 2013b). Overall, pain prevalence was similar to other countries but constant pain was lower in England. The WHELD study, which was conducted in and near London (UK), used an observational scale and found that 35.3% of residents had clinically relevant pain, predominantly mild chronic pain (Rajkumar et al., 2017). Given that around 20% of the residents in the MARQUE study were prescribed regular analgesics, and PRN analgesia was not given often (on average non-opioids were given 8 times a week and opioids were given 7 times a week, based on median prescribed doses), it appears that some residents may have untreated pain. The studies cited above reported similar findings. The SHELTER study identified that 25.6% of residents who were in pain were not prescribed pain medication and 16.3% of residents in pain were prescribed analgesia PRN only (Lukas et al., 2013a). The WHELD study found that 41.9% of residents in pain were not prescribed regular analgesics (Rajkumar et al., 2017).

Residents can be reticent to report their own pain for a number of reasons including the belief that pain is a normal part of ageing, reluctance to recognise or signpost their own frailty or dependence, stoicism, not wanting to bother staff or be seen as a 'complainer', or a lack of confidence in either their own value or hope for effective treatment (de Souto Barreto et al., 2013, Vaismoradi et al., 2016, Achterberg, 2016, Mentes et al., 2004, Kaasalainen et al., 2010). GPs and care home staff may not have the time or training to complete detailed assessments or regular reviews for complex residents with multiple morbidities including dementia. It is rare that other specialisms (such as physiotherapy) are involved (Gordon, 2015, Robbins et al., 2013, Sampson et al., 2018). As a result, care home residents may not receive adequate pain assessments.

Furthermore, there are no guidelines specific to this population. There are several guidelines that could be applied to this population, for example, STOPP/START criteria, British Geriatrics Society/British Pain Society guidelines for older people (O'Mahony et al., 2015, Abdulla et al., 2013), national palliative care guidelines

(National Institute for Health and Clinical Excellence, 2012b), or guidelines written for NHS trusts (Denison Davies et al., 2011). However there are none explicitly for care home residents and as a result clinicians working with this population may not refer to existing guidelines. It appears that care home residents and their pain are excluded as a result, either slipping through the gaps or viewed differently to those in hospitals or the community. This may in part explain the commonly observed prescribing error where regular opioid prescriptions were not accompanied by a PRN opioid prescription. The omission of a PRN opioid alongside a regular prescription could lead to undertreated chronic severe pain or untreated breakthrough pain (Hanlon et al., 2010).

9.5.2 Increasing prevalence of strong opioid use

Although opioid prescribing levels are lower than in other countries (La Frenais et al., 2017) there appear to be a global rise in the use of strong opioids, and inappropriate use or overuse of opioids is another concern. A study conducted in South London homes found that, following paracetamol, care home staff were most familiar with buprenorphine patches as the next treatment approach (Corbett et al., 2016). Pimentel et al. (2016) reported that many care home residents were opioid-naïve prior to their prescription of transdermal opioids. In the WHELD study, moderate pain was more prevalent than severe pain (Rajkumar et al., 2017). More than 90% of residents prescribed transdermal fentanyl did not have chronic pain (Fain et al., 2017). Potentially inappropriate use of strong opioids may be due to a number of reasons. First, use of patches has been attributed to ease of administration (Griffioen et al., 2017b). Second, as NSAID use has decreased, so has use of weak opioids (to a lesser extent) whereas strong opioid use has increased in people with and without dementia (Sandvik et al., 2016). It may be that strong opioids have replaced NSAIDs. Third, it has been suggested that strong opioids may be used for their sedative effects (Jensen-Dahm et al., 2015). Looking at antipsychotic use, and comparing this to worldwide data, perhaps the scrutiny of antipsychotics (Banerjee, 2009) has led to increases in other drugs compensating, such as strong opioids or other psychotropics.

Antipsychotic prescribing prevalence is lower compared to other countries; a systematic review of antipsychotic use in people with dementia in Europe, US, and Canada found a pooled prevalence of 27.5% (95% CI, 25.7-29.3%) (Kirkham et al., 2017). In this study lorazepam, a benzodiazepine commonly used in the management of BPSD, was prescribed to 8.4-9.3% of residents in this study, mostly PRN. Antidepressants can also be used to treat agitation. A Cochrane review saw a modest reduction in BPSD when comparing citalopram and sertraline to placebo, and antidepressants have been suggested as a safer alternative to antipsychotics (Seitz et al., 2011, Porsteinsson et al., 2014). Both citalopram and sertraline have a similar efficacy and safety profile, however sertraline does not have the additional caution regarding QT-interval prolongation (National Institute for Health and Care Excellence, 2018a). In a study published in 2011, sertraline was reported to be the most commonly prescribed antidepressant in the UK, in line with NICE guidelines (Banerjee et al., 2011, National Institute for Health and Care Excellence, 2018a), but citalopram appears to be the most prevalent antidepressant in care homes (Bergh et al., 2012, Bourgeois et al., 2012, Karkare et al., 2011). In this study citalopram (the most commonly prescribed antidepressant) was prescribed over twice as much as sertraline (13.7-15.2% vs 5.7-7.5%).

9.5.3 The associations between resident factors and analgesic use

Resident factors such as gender, dementia severity, and agitation behaviours, are associated with pain management. Even considering that pain has been found to be more prevalent in females compared to males (Fillingim et al., 2009), under-treatment of pain in males has also been identified by Won et al. (2004) and Hunnicutt et al. (2017), two care home studies from the US. Females may be prescribed more regular medication because they are more likely to report pain compared to males (including higher intensity pain levels, higher frequency pain, and an increased number of painful body areas) (Lukas et al., 2013a, Racine et al., 2012). A qualitative study in assisted-living residences found that resident request made it easier for carers to know when to administer PRN medication (Carder, 2011). In this study females were also prescribed more antidepressants, and there was a positive

association between antidepressants and analgesics. Chronic pain can cause depression, including in care home residents with dementia (Lukas et al., 2013b, Erdal et al., 2017).

Existing literature supports the idea that pain is of equal or increased prevalence in more severe dementia (Closs et al., 2004, Rajkumar et al., 2017). In terms of less administration of PRN analgesia for residents with severe dementia and older age, these residents may be administered fewer PRN drugs because their pain is better controlled by regular stronger drugs. Residents with severe dementia may be prescribed more regular opioids because they are perceived as more 'end of life'. A longitudinal Dutch study found that paracetamol was the primary treatment for pain, and reported that analgesic treatment was typically only stepped up towards end of life. The authors queried whether there was new or increased pain at this time, or whether clinicians were more accepting of side effects like sedation when patients were considered palliative (Hendriks et al., 2015).

There may still be under-treated pain in residents with severe dementia, in residents who are not prescribed any regular analgesia, or those who are prescribed a regular opioid but no PRN. Cognitive impairment and inability to verbalise pain has been shown to be strongly associated with untreated pain (Hunnicutt et al., 2017, Ahn et al., 2015). Underestimation of pain in dementia patients may be caused by an atypical presentation of pain, for example agitation or posture (Neumann-Podczaska et al., 2016). Carers may not notice a slow decline in impairment or realise that residents who were previously able to communicate their pain are now unable to do so, instead believing that cessation of pain complaints represents a lack of pain. Even if a resident is assessed to be in pain, there are institutional barriers that demote the likelihood that a positive assessment of pain will lead to increased analgesia, which have been discussed on page 25.

Aggressive and verbally agitated residents were prescribed more analgesics. Verbally agitated behaviour has been found to decrease following pain interventions (Husebø et al., 2014b). Additionally, verbally agitated behaviour may be perceived as a

symptom of pain because the behaviours, like crying or shouting, are similar to how people without dementia behave when they are in pain, which may be why verbally agitated residents were prescribed more opioids. Previous studies exploring an association between pain and aggression have produced mixed results. Resistance to care has been associated with pain previously (Hunnicutt et al., 2017) but in a trial of stepped pain management, there was no difference in prevalence of aggressive behaviours following increased analgesia (Husebø et al., 2014b). Residents with more aggressive behaviours may be administered fewer PRN analgesics (and possibly less PRN medication overall) because staff find it more difficult to administer these drugs to aggressive residents (where residents are resistive, or staff are fearful) and either fail to do so or do not attempt to do so (Barber et al., 2009). This idea is supported by the fact that residents with more physically aggressive agitation were prescribed more regular opioids, which were typically patches and thus easier to administer. Residents with physically non-aggressive behaviours may not encounter this problem because there may not be any issues regarding medication administration or staff avoidance, or because their behaviour may be more disruptive (such as wandering or trying to leave) and receive more attention from the care team and consequently more PRN medication. However, increased pain has been found to have a negative association with behaviours that require movement (as movement may be compromised by pain) (Ahn and Horgas, 2013, Tosato et al., 2012). In some of these cases, staff may be falsely identifying pain (Jordan et al., 2010).

9.5.4 Differences observed between care homes and PRN administration

The heterogeneity between care homes regarding PRN administration suggests internal factors. Even if a pain assessment is undertaken it does not necessarily result in administered pain relief; the process is non-sequential (Dowding et al., 2016). It is inevitable that there will be variability between care homes, as some will be better at translating a positive pain assessment to effective pain management, and there will be different reasons for this. A study conducted in Norway by Lövheim et al. (2006) found that carers overestimated how many residents were being treated for their pain. It seems logical that in these cases carers would be less likely to escalate

concerns about pain management. This study also posited that carers appeared to have a good understanding of pain and that poor communication was more relevant in under-treatment of pain. Fragmented lines of communication can result from processes inherent to care homes, such as multiple care staff working with an individual resident over a short period of time, shift work, and poor documentation practices (Lichtner et al., 2016, Dowding et al., 2016).

9.6 Clinical implications

Currently, care home residents in the UK receive limited external healthcare (and therefore multidisciplinary) support. In contrast to other countries, for example the Netherlands where there are on-site nursing home physicians, the majority of care home residents in the UK are only seen sporadically by their GPs (Sampson et al., 2018), and it is unclear how aware GPs are of each resident's pain status (de Souto Barreto et al., 2013). GPs have limited time and so support is needed both inside and outside the care home. A Canadian trial found that implementing an on-site pain team improved team collaboration and communication, increased autonomy in staff, and resulted in better pain management including individualised plans for residents. Barriers included lack of pain education, maintaining frequent meetings, lines of communication, and competing priorities for team members, so support from the care home management to provide protected time for meetings and related tasks is imperative (Kaasalainen et al., 2016). Pain management training could be provided to a care home staff member who can cascade this knowledge and create an in-house pain team comprising different disciplines. Alternatively, or additionally, care homes and clinicians could better utilise community pharmacists, care home liaison nurses, geriatricians, or enhanced care teams (Alsaeed et al., 2016, Sampson et al., 2018). In March 2018 the Royal Pharmaceutical Company stated that pharmacists should work with GPs to regularly review medicines in care homes and NHS England announced plans to start recruiting more pharmacists to meet this need (NHS England, 2018, Royal Pharmaceutical Company, 2018).

Prescribers such as GPs and pharmacists have a duty to provide residents with personalised schedules and ensure they write sufficiently detailed prescriptions. An

English study intervened with pain management strategies for 13 residents with severe dementia, and each resident received a different treatment plan. These ranged from pharmacological including regular paracetamol, topical NSAIDs, and changing the time of administration, to non-pharmacological including massage, dental treatment, and reduced time sitting on hard surfaces, and pain assessment scores were reduced one month later (Jordan et al., 2010). There is no one-size–fits-all approach to managing pain in this population, but careful assessment and reassessment is key. If there are barriers to administration then clinicians and nurses should work together to ameliorate this, such as de-prescribing other drugs or changing the route, for example an oral solution for residents averse to swallowing pills. Prescribers should ensure that they write the indication on the MAR to advise and remind nurses of the reason for the prescription, which could lead to more appropriate use of PRN analgesics.

There may be residents who are not in pain who are prescribed round-the-clock transdermal opioids. Potentially inappropriate use of strong opioids due to ease of administration or sedative effects is unethical because strong opioids can have negative side effects (Abdulla et al., 2013). A further ethical consideration is the lack of ongoing consent or assent given in the administration of transdermal opioids (Jensen-Dahm et al., 2015). Residents are typically not involved in their treatment plans and this further reinforces their lack of autonomy in these decisions. Patches are not recommended where oral opioids are suitable, and opioids should be prescribed on a trial basis with defined treatment goals. As such, weak opioids should usually be used prior to strong opioids. Clinicians and care home staff should monitor regular opioid use including adherence (residents may now be willing to take oral medications where previously they were not), effectiveness, and side effects.

It is important for GPs to understand and consider communication difficulties and potential biases within the care home team (and themselves) when prescribing PRN medication, and should review MAR charts retrospectively to find out whether analgesics are administered as intended. Family members are valuable sources of information regarding past pain behaviours such as stoicism and non-verbal cues that

would be useful for paid carers when assessing residents who are unable to communicate their own pain. Including families in these discussions will require more time as relatives often have concerns about the adverse effects of analgesic use (Kaasalainen et al., 2010). Furthermore family reports of behavioural response may not be accurate (Weiner et al., 1999) so it is best to supplement pain assessments with knowledge of diagnosed painful conditions and observational tools. This may, for example, decrease potential under-treatment of males who may verbalise their pain less. GPs should think very carefully before prescribing analgesics as PRN; these data show that these drugs may only rarely be administered to their patient.

There appears to be a gap between pain assessment and pain management and potentially a need for an algorithm to accompany assessments and trigger an action by the care team. There are existing examples of pragmatic pain pathway tools that could be adapted from NHS care to care homes (South Worcestershire Clinical Commissioning Group, 2017, Herefordshire Clinical Commissioning Group, 2015). Adaptation has been shown to be feasible in a care home setting (Petyaeva et al., 2018). Tools need to be simple so they can be used by new and junior care staff, as well as minimising the time burden (Kaasalainen et al., 2010).

Communication between CAs and nurses has been found to mostly be unidirectional, where CAs report pain to nurses but receive limited feedback in return (Corbett et al., 2016). A lack, or perceived lack, of response to reporting pain may lead to CAs not taking ownership of pain management, feeling dismissed or less motivated, or being less proactive in the future (Kaasalainen et al., 2010, Corbett et al., 2016, Mentes et al., 2004). CAs should be empowered within this pathway. First, by enabling CAs to report pain in a standardised manner that is consistent. Second, by ensuring that the 'conversation' does not end at the point that CAs report pain to nurses; the pathway should include feedback from nurses to CAs about action taken as a result (Kaasalainen et al., 2010). Third, a request for ongoing monitoring and supporting documentation regarding the effectiveness of the pain management plan for which CAs are responsible. A French study found that 72.8% of residents in pain were not receiving regular pain evaluations (de Souto Barreto et al., 2013).

Further efforts to improve communication include dedicated reporting between shifts to promote consistency of care (for example, the continuity of PRN administration if a resident is in pain that day), or encouragement from nurses for CAs to communicate expected episodes of pain (such as personal care or dressing changes) so that pain can be diminished by pre-emptive analgesia (Mentes et al., 2004, Kaasalainen et al., 2010). Efforts to improve communication can be low-cost but valuable (Lövheim et al., 2006).

9.6.1 Key points for clinicians

- Clinicians and care home staff need to better utilise community support, for example, pharmacists, geriatricians, or enhanced care teams.
- Pain management schedules should be personalised for each resident (including non-pharmacological treatments) with better documentation including indications.
- GPs need to mediate the risk that PRN analgesics may not be administered, and think carefully before deciding not to prescribe analgesia regularly.
- Clear and simple pain management algorithms should be used to trigger an action following pain assessment, including a further assessment of effectiveness.
- Communication between nurses and CAs should be bi-directional, continue throughout the day, and be used to empower junior staff.

9.7 Policy implications

This work has demonstrated that care home residents, and particularly certain groups, are at risk of untreated pain. Care for residents is provided by both health and social care, and therefore policies that can improve outcomes for this population need to be addressed by both sectors. For health care, improvements via policy can be provided by NICE. For social care, which is a mixed-economy sector with many providers, these improvements need to be driven by the regulators, CQC. Stakeholders such as the Alzheimer's Society, can also be influential in driving towards better standards in pain management.

There is a need for pain management guidelines to be written specifically for care home residents. They should be accessible and practical for non-specialists including care staff (Rajkumar et al., 2017, Kaasalainen et al., 2010), and have explicit and specific guidance for different stages of cognitive impairment, and residents with communication difficulties. The CQC reported that in 40% of care homes they found limited staff knowledge and use of available guidance, which translated into variable or poor care (Care Quality Commission UK, 2014). A comparison of prescribing patterns and recommendations by the American Geriatrics Society for prescribing for older adults in chronic pain identified that analgesic choices were mostly inconsistent with recommendations (Won et al., 2004) and specific guidelines may increase adherence. Where policies advocate for reduced use of a drug class, they should also attempt to predict substitutions and provide guidance for their use too (Maust et al., 2018, Soumerai et al., 1993). For example, reducing use of antipsychotics may have led to increased use of opioids, benzodiazepines, and antidepressants, but these drugs have side effects and risks as well. Increasingly, care homes are moving to electronic notes systems. These systems could be used to flag prescriptions that do not adhere to guidelines, such as regular opioid prescriptions without a prescription of a PRN opioid.

NICE have published a quality standard for care in people with dementia that stated that every patient in later stages of dementia should have an assessment from a palliative care service, including a review of pain (National Institute for Health and Clinical Excellence, 2010). However following admission to a care home residents may not undergo regular assessments of dementia severity, the term ‘later stages’ could be seen as vague, and as a consequence of these factors, and service capacity, uptake of this guidance is likely to be low. A multidisciplinary approach to medications management can work towards ensuring appropriate medication use (Walsh et al., 2017). Fortunately this sentiment has been echoed elsewhere and action has been taken to introduce more pharmacy support into care homes (Royal Pharmaceutical Company, 2018, NHS England, 2018). Commissioners and health care

providers need to ensure that gaps including care planning, and access to primary and specialist care services, are filled (Carter, 2011).

The CQC should include pain management in their assessments, and check MAR charts including PRN administration to ensure better documentation. In the US, where prescribing levels are often higher than other countries, pain assessment is part of the quality assessment procedure (La Frenais et al., 2017, Morris et al., 1990). Using pain assessment as a quality indicator has been explored in the Netherlands and found to be feasible (Zwakhalen et al., 2012, Boerlage et al., 2013). Despite availability of a number of pain assessment tools including the PAINAD and Abbey Pain Scale (Warden et al., 2003, Abbey et al., 2004) they are rarely consistently implemented in care home practice (Griffioen et al., 2017b) and policy changes could promote use. To support this, the CQC could include medication reviews as part of its quality standards, enforcing the need for clear documentation regarding decisions to commence, continue, or de-prescribe, and promoting family carer and CA involvement.

Finally, the financial implications of low administration rates and potential medicines waste can be vast. It is estimated that care homes discard £24 million worth of unused medicines each year, and a contributing factor is repeat dispensing of PRN medicines that are prescribed but not used (Trueman et al., 2010). Analgesics are one of the most prevalent PRN medications in care homes (Stasinopoulos et al., 2017). Reducing this unnecessary cost with more appropriate prescribing and dispensing can only be beneficial for our care system. An alternative to 'just in case' PRN prescriptions could be increased use of 'home remedies' where care home staff can offer over-the-counter products such as paracetamol to residents without a prescription.

9.7.1 Key points for policy makers

- It is imperative that guidelines are written that are specific for care home residents, and these should explicitly address cognitive and communication impairments.
- Pain assessment could be included as a CQC quality indicator, and used to promote regular use of pain assessment tools.
- Commissioners and health care providers need to ensure that care home residents are able to access primary and secondary care services.
- Money can be saved by avoiding routine dispensing of PRN drugs that are not administered and instead using 'home remedies'.

9.8 Future research

Pain assessment does not necessarily lead to pain management interventions (Zwakhalen et al., 2012) and there is a need for more research to understand this process within the care home context. Care homes are unique in their disciplinary isolation and hierarchical structure and studies from other settings may not be relevant (Wilson et al., 2012, Lichtner et al., 2016, Goodman et al., 2016). There is a need for qualitative work to understand the gap between personal beliefs and attitudes about the identified factors (such as age, and types of agitation) and how this impacts the pathway to analgesic prescription and PRN administration. In this study poor documentation was a limitation; a better way to assess whether or not PRN drugs are being offered may be to adopt a non-participant observation of practice. Additionally, mixed-methods research could explore whether increasing continuity of care (that is, ensuring that where possible the same CAs provide care for the same residents) can enhance pain management through increased knowledge of individual pain behaviours, increased familiarity with predictable pain episodes, and allowing CAs to be more empowered in the process of assessment, escalation, and reassessment.

Building on current efforts to produce a superior pain assessment tool for people with cognitive impairment (van der Steen et al., 2015), there needs to be a study that

ties in pain assessment, pain conditions experienced by the resident, type of dementia (for there is some evidence that this has an effect on the experience of pain), and the type, dosage, and administration of analgesics (Gagliese et al., 2017). As the population is so heterogeneous, future studies need to find a good balance of sampling a large population from many care homes but also collecting detailed data regarding (potentially painful) comorbidities and pain assessments (there are several well-validated observational measures). Where pain assessments may not be feasible, another option would be to collect data from residents' notes about diagnosed painful conditions, or a medication-based comorbidity index (for example the Rx-Risk model (Von Korff et al., 1992) or Medication-Based Disease Burden Index (George et al., 2006)). Where possible, indications should account for adjuvants to give a better picture of analgesic prescribing. That way, researchers can compare neuropathic pain prevalence and analgesic prescribing to ensure that residents who suffer this type of pain are not at risk of under-treatment.

Care home residents are very different from typical drug trial participants, with multiple morbidities and polypharmacy. More clinical trials are needed to explore the safety and efficacy of drugs that are commonly used in this population. This is particularly important for drugs used off-label such as antipsychotics and benzodiazepines for agitation, for longer durations than recommended such as zopiclone, or medications at risk of over-use like strong opioid patches.

With a population at increased risk of adverse effects from medication, further research into non-drug treatments, and how to ensure appropriate and consistent use, is necessary. It has been reported that in England non-pharmacological treatment is not seen as part of normal practice and family carers are more likely to suggest non-drug treatments than care staff (despite care staff recognising their value) (Corbett et al., 2016), however they can be an effective, and cheaper, alternative (Jordan et al., 2010).

9.8.1 Key points for researchers

- Qualitative work is needed to 1) compensate for care home documentation that may not be reliable, and 2) understand how personal beliefs and attitudes of clinicians and carers may influence analgesic prescribing and administration.
- Future research proposals should aim to collect data that can triangulate resident pain, care staff assessment of pain, and analgesic treatment.
- Long-term clinical trials are needed to explore the safety and efficacy of potentially risky drugs in the care home population.

Chapter 10 **Conclusion**

This thesis achieved its aims to describe how analgesic medication was prescribed and administered in English care homes and additionally, to explore resident and care home factors that may be related to analgesic use. This work has increased knowledge about current analgesic prescribing, and added new knowledge about PRN administration and factors associated with analgesic use. Prior to this thesis, little was known about how analgesics were used in English care homes, and thus it is a significant contribution to the field.

The three main findings from this research are 1) there is generally lower prescribing of regular analgesics in England compared to other countries, 2) care homes rely largely on PRN prescriptions of paracetamol that are not often administered, and 3) there is heterogeneity between care homes regarding PRN administration but this is not associated with care home quality.

It appears that, while overall analgesic prescribing is similar to other countries, clinicians in England are more reliant on prescribing PRN analgesics than other countries where regular pain relief is more commonly used. It is not possible to speculate on the appropriateness of prescriptions but assuming that care home populations in other countries are broadly similar, it appears English care home residents are receiving less pain relief than their international counterparts. Clinicians may be unaware of how often prescribed PRN analgesics are administered. There are disparities between care homes regarding PRN administration, implying that internal factors are influential in the administration of PRN analgesics. Prescribing clinicians may be delegating too much responsibility to a workforce that may not have the skills, time, experience, or internal culture to facilitate good and consistent pain management.

Policymakers may be interested in the financial implications of unused PRN medications, but should also consider how policy can influence good pain management. PRN administration data and resident factors associated with analgesic

use should be accounted for when creating pain management guidelines aimed at care home residents with dementia. There are examples from other countries about how quality indicators are used to improve pain management, and these could also be used to ensure better medication documentation. Clinicians and researchers should understand that a prescription for a PRN analgesic does not necessarily equate to adequate pain relief, and it is vital to collect PRN administration data in clinical practice and in future studies.

Chapter 11 **Other academic achievements**

11.1 Published papers

LA FRENAIS, F., STONE, P., SAMPSON, EL. 2016. Analgesic prescribing in care home residents: how epidemiological studies may inform clinical practice. *Pain Management.* (Appendix 19)

LA FRENAIS, F. L., BEDDER, R., VICKERSTAFF, V., STONE, P. & SAMPSON, E. L. 2017. Temporal Trends in Analgesic Use in Long-Term Care Facilities: A Systematic Review of International Prescribing. *Journal of the American Geriatrics Society*. (Appendix 1)

LIVINGSTON, G., BARBER, J., MARSTON, L., RAPAPORT, P., LIVINGSTON, D., COUSINS, S., ROBERTSON, S., LA FRENAIS, F. & COOPER, C. 2017. Prevalence of and associations with agitation in residents with dementia living in care homes: MARQUE cross-sectional study. *British Journal of Psychiatry Open,* 3**,** 171-178. (Appendix 20)

LAYBOURNE, A., LIVINGSTON, G., COUSINS, S., RAPAPORT, P., LAMBE, K., LA FRENAIS, F., SAVAGE, H., MANELA, M., STRINGER, A., MARSTON, L., BARBER, J. & COOPER, C. 2018. Carer coping and resident agitation as predictors of quality of life in care home residents living with dementia: Managing Agitation and Raising Quality of Life (MARQUE) English national care home prospective cohort study. *International journal of geriatric psychiatry.* (Appendix 21)

11.2 Presentations

LA FRENAIS, F. (2017, June). *Are care home residents with undiagnosed dementia more at risk of antipsychotic overuse?* Oral presentation at the Alzheimer's Association International Conference, London.

LA FRENAIS, F., LIVINGSTON, G., COOPER, C., MARSTON, L., BARBER, J., VICKERSTAFF, V., STONE, P., SAMPSON, EL. (2017, May). *Use of analgesic and psychotropic medication in UK care home residents living with dementia.* Poster session presented at the European Association of Palliative Care, Madrid.

LA FRENAIS, F., BEDDER, R., STONE, P., SAMPSON, EL. (2016, October). *Systematic review of prescribing patterns of analgesic medications for older people living in care*

homes over time. Poster session presented at the Annual Palliative Care Research Conference for Marie Curie.

11.3 Other

Podcast '*Discussing the MARQUE Study – Managing Agitation in Dementia',* for NIHR Dementia Researcher website - March, 2018.

Training school of the COST Action TD 1005 (Pain assessment in patients with impaired cognition, especially dementia) in Gent (Belgium) – March, 2015.

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ACHTERBERG, W. 2016. Pain management in long-term care: are we finally on the right track? *Age and Ageing* [Online], 45. Available: http://dx.doi.org/10.1093/ageing/afv182 [Accessed January 1, 2016].

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Appendices

Appendix 1 – Published systematic review

REVIEW ARTICLE

Temporal Trends in Analgesic Use in Long-Term Care Facilities: A Systematic Review of International Prescribing

Francesca L. La Frenais, BSc,†‡ Rachel Bedder, MSc,*‡ Victoria Vickerstaff, MSc,† Patrick Stone, MA, MD,† and Elizabeth L. Sampson, MD†§*

OBJECTIVES: To explore global changes in the prescription of analgesic drugs over time in the international long-term care (LTC) population.

DESIGN: Systematic review.

SETTING: We included original research articles in English, published and unpublished, that included number of participants, country and year(s) of data collection, and prescription of analgesics (analgesics not otherwise specified, opioids, acetaminophen; scheduled only, or scheduled plus as needed (PRN)).

PARTICIPANTS: LTC residents.

MEASUREMENTS: We searched PubMed, EMBASE, CINAHL, International Pharmaceutical Abstracts, PsycINFO, Cochrane, Web of Science, Google Scholar, using keywords for LTC facilities and analgesic medication; hand-searched references of eligible papers; correspondence. Studies were quality rated using an adapted Newcastle-Ottawa scale. Pearson correlation coefficients were generated between percentage of residents prescribed an analgesic and year of data collection. If available, we investigated changes in acetaminophen and opioid prescriptions.

RESULTS: Forty studies met inclusion criteria. A moderate correlation (0.59) suggested that scheduled prescription rates for analgesics have increased over time. Similar findings were reflected in scheduled prescriptions for acetaminophen and opioids. No increase was seen when analyzing scheduled plus PRN analgesics. Use of opioids (scheduled plus PRN) appears to have increased over time.

CONCLUSION: Worldwide, use of opioids and acetaminophen has increased in LTC residents. Research is needed to explore whether this reflects appropriate pain management for LTC residents and if PRN medication is used effectively. **J Am Geriatr Soc 2017.**

Key words: analgesics; pain; nursing home; dementia

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A long-term care (LTC) facility is an institution providing accommodation, meals, 24-hour staffing, and in some cases 24-hour nursing care. In 2011, in the United States, 3.9% of individuals aged 65 and older received LTC,[1] similar to other developed countries.[2,3]

It is suggested that LTC residents are undertreated for pain[4–6]; common painful diseases affecting LTC residents include musculoskeletal disorders, cancer, pressure sores, and neuropathies.[7,8] A large European study estimated that pain affected 48.4% of LTC residents, with 12.0% reporting uncontrolled pain,[9] consistent with other countries,[5,6] including a U.S. study that found that 23.0% of residents reporting persistent pain did not receive scheduled analgesics.[10] Dementia is often underdiagnosed in this population[11]; cognitively impaired residents may not remember, understand, or communicate their pain, presenting a complex challenge for care staff assessing pain.[12,13] Poorly managed pain can lead to distress, poor quality of life,[14,15] worsening cognition, and depression.[16,17]

Prescribers should take a stepwise approach from nonopioids, used for mild to moderate pain (e.g., acetaminophen, considered a first-line treatment because it is well tolerated) to opioids, generally used for severe acute pain or chronic pain but with risk of side effects such as sedation, constipation, nausea, and vomiting. In older adults multimorbidity and polypharmacy increase the likelihood of adverse events.[8,18,19]

Review Aims

Our aim was to investigate whether, and how, international prescribing patterns of analgesic medication for LTC residents have changed over time. Specific objectives were to explore changes in the prescription of analgesic drugs, explore changes in prescribing of opioids and

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acetaminophen; and examine changes in scheduled medications and scheduled plus as-needed (pro re nata (PRN)) medications.

METHOD

Search Strategy

We used a three-step search strategy. To refine the search terms, an initial limited search of PubMed was run, followed by analysis of the text words and Medical Subject Heading terms contained in the title, abstract, and index of identified papers. Then a search was run using identified key words and index terms (for LTC facilities and analgesics; see Appendix S1) across included databases until December 2016 (PubMed (including Medline, 1966–present), EMBASE (1947–present), CINAHL (1937–present), International Pharmaceutical Abstracts (1970–present), PsycINFO (1880s–present), Cochrane (1898–present), Web of Science (1900–present) and Google Scholar). There were no restrictions on country. Finally, references of included articles were hand searched.

Eligibility Criteria

Original research articles reporting prescribing of analgesics in LTC facilities were included. Single case studies and studies not published in English were excluded.

Setting

We included LTC facilities (residential homes (institution with board, meals, 24-hour staffing), nursing homes (as before plus 24-hour nurse coverage), group dwellings (if deemed suitable based on description)). We excluded assisted living accommodations, sheltered accommodations, retirement apartments, and hospitals.

Study Population

Included participants were residents in an eligible setting where the majority of participants were aged 55 and older in studies that did not focus on a specific illness or condition. A study population was ineligible if it consisted of newly admitted (admission <3 months) residents; those diagnosed with a specific illness, those receiving palliative care, individuals who were included only if they were deemed to be in pain; individuals who were included only because of polypharmacy; incidence of adverse drug event; incidence of fall or recent hospital admission; if dementia or cognitive impairment were excluded; mild cognitive impairment or severe cognitive impairment only; or where residents with severe impairment were excluded, and the number of residents in the excluded population exceeded the number of included participants.

Data

One reviewer (FL) independently screened titles, abstracts, and full-text articles and extracted the number or percentage of residents prescribed analgesics (including analgesic-antipyretics), opioids, or acetaminophen; the total number of participants; if available the number of LTC facilities; and year and country of data collection. Data were ineligible if prescriptions included drugs that were potentially not for analgesia (e.g., MO1 drug class) or analgesics combined with other medications, such as disease-modifying antirheumatic products; only PRN data were available; medication was recorded only if the drug was administered within a specific time window (unless daily, when it was counted as scheduled only); or only weighted percentages were given. If authors indicated that they had collected relevant but unpublished information, they were contacted. There was no restriction on study design. Randomized controlled trials were included if baseline data were published. For longitudinal studies, data were analyzed from the first time point that was at least 3 months after admission to the LTC facility to avoid confounding variables associated with newly admitted residents.

Data Extraction and Quality Checking

Two researchers independently extracted and reviewed data (FL, RB). Eligible studies were assessed for methodological validity using a 5-point scale (Appendix S2) adapted from the Newcastle-Ottawa scale[20] and Boyle scale.[21] Studies were deemed strong, moderate, or weak (adapted from Boyle[21]) by rating representativeness of the target cohort, adequacy and standardization of data collection tools, participation rate, and inclusion of cluster sampling in analysis. If a study did not account for cluster sampling, it was demoted by 1 quality rating. If answers were unclear, the authors were contacted. If they could not be reached, we used the lowest score for that item. Final scores were resolved through discussion and with a third independent author (ELS).

Analysis

The percentage of residents prescribed analgesics was calculated to one decimal place. Data were specified as scheduled drugs only or scheduled plus PRN; if not explicitly mentioned, they were deemed to be scheduled plus PRN. Articles that included scheduled medications and scheduled plus PRN medications or published data from 2 time points were divided into "cohorts" for separate analysis. Analgesic medications were coded using the Anatomical Therapeutic Chemical classification system[22] (Appendix S3).

We quantified study heterogeneity ($I^2 > 75\%$ is considerable heterogeneity). If the data were statistically viable, we planned to meta-analyze them, but if that was not possible, we planned to generate correlation coefficients using the Pearson correlation. The Pearson correlation is sensitive to outliers, so we planned to exclude extreme outliers, identified from the scatter plot, if there was sufficient clinical justification to do so based on the original article's discussion. Stata version 14 (Stata Corp., College Station, TX) was used.

RESULTS

Of 14,323 citations reviewed, 40 studies were included (Figure 1). From the 40 studies, 50 cohorts were eligible. Supplementary Appendix S4 describes study characteristics and quality ratings.

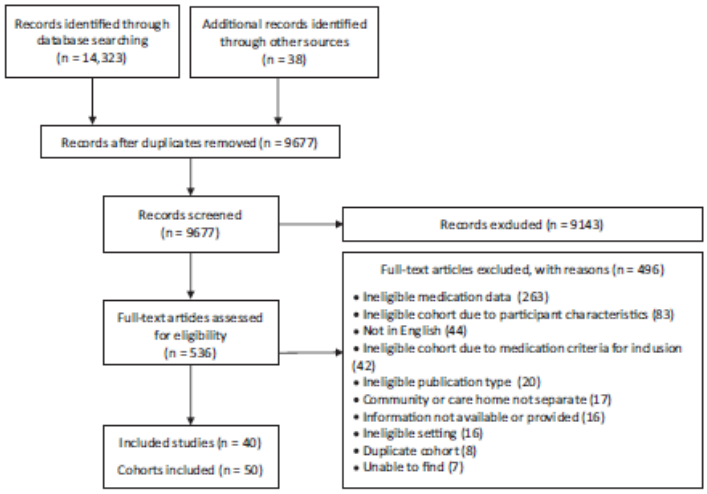

Figure 1. Flow diagram of study selection.

Data were divided according to prescription type: scheduled only (n = 15) or scheduled plus PRN (n = 35). For scheduled only, the median number of participants per study was 551 (range 215–7,309). For scheduled plus PRN prescriptions, the median was 595 (range 13–16,126).

Data were available from 16 countries. One study included data from across Europe (excluding Italy). The countries with the most cohorts were Australia (n = 8), Norway (n = 7), and the United States (n = 6). All other cohorts were from Europe, North America, and Australia. We were unable to meta-analyze because of heterogeneity (prescriptions of scheduled analgesics $I^2 = 99.1$, scheduled plus PRN analgesics, $I^2 = 99.8$).

Quality Rating

Six cohorts were scored as being of strong quality, 20 as moderate, and 24 as weak. The main reasons for low scores were authors not using cluster sampling and lack of detail about data collection methods.

Analgesics

Temporal Changes in Prescriptions of Scheduled Analgesics

Fifteen cohorts were eligible (Table 1) (data drawn from 17,670 residents and at least 490 LTC facilities in 8 countries). Two studies,[23,24] accounting for 7,545 residents, did not provide the number of included LTC facilities.

Figure 2 suggests that, between 1996 and 2015, analgesic prescribing increased in LTC facilities. Data from a Norwegian study show that 23% of residents were prescribed scheduled analgesics in 1996, compared with 57.6% in 2011.[19,25] Two studies, both from Germany, reported lower levels: one[26] reported that 33.7% of residents were prescribed scheduled analgesics in 2014, and another[27] reported a 32% prescription rate in 2010. The correlation between prescription prevalence and final year of data collection was 0.59, showing a moderate positive trend.

Table 1. Cohorts Included in Analysis of Scheduled Analgesic Prescribing Rates

Study	Year Data Collection Ended	Country	Residents Prescribed Regular Analgesics, % (n = 18,867)
Hoffmann and Schmiemann[26,a]	2015	Germany	33.7
Tan, Visvanathan[54,a,b]	2014	Australia	75.2
Bauer, Pitzer[55,b]	2012	Austria	52
Veal, Bereznicki[23,b]	2012	Australia	62.8
Sandvik, Selbaek[19,a,b]	2011	Norway	57.6
Kölzsch, Wulff[27]	2010	Germany	32
Krüger, Folkestad[56,b]	2008	Norway	54.8
Lövheim, Karlsson[24,a,b]	2006	Sweden, Finland	60.6
Reynolds, Hanson[32]	2004	United States	32
Sandvik, Selbaek[19,a,b]	2004	Norway	45
Decker, Culp[57]	2003	United States	45.6
Smalbrugge, Jongenelis[33,a,b]	2001	Netherlands	45.9
Sandvik, Selbaek[19,a,b]	2000	Norway	34.9
Nygaard, Naik[58,a,b]	1997	Norway	29.9
Nygaard and Naik[25]	1996	Norway	23

[a]Acetaminophen data available.
[b]Opioid data available.

Temporal Changes in Prescriptions of Scheduled Opioids and Acetaminophen

Ten studies included data on opioid prescriptions (correlation coefficients (Rs) = 0.94), and eight on acetaminophen prescriptions (Rs = 0.93, excluding one outlier that reported very low acetaminophen use (2.5%)). The

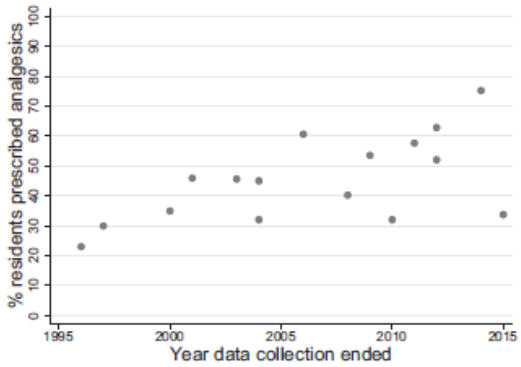

Figure 2. Percentage of residents prescribed scheduled analgesic medication over time.

number of scheduled prescriptions of opioids and acetaminophen has increased over time.

Temporal Changes in Prescriptions of Scheduled Plus PRN Analgesics

Thirty-one cohorts were eligible (73,938 residents, at least 526 LTC facilities in 16 countries plus Europe, excluding Italy; Table 2). There were 10 cohorts, accounting for 46,211 residents, that did not provide the number of LTC facilities included.

Because the scatter plot did not suggest a trend, it was not appropriate to run a correlation. Scheduled plus PRN prescriptions have not changed since 1984. Several studies[24,28,29] show very high prescribing rates (>90%). One of the most recent studies (from 2013) reported the lowest prescribing rate (16%).[30] Of the four U.S. studies, the earliest (1990) reported that 38.3% of residents were prescribed analgesics,[31] compared with 68.6% in 2004.[32]

Temporal Changes in Prescriptions of Scheduled Plus PRN Opioids and Acetaminophen

For scheduled plus PRN prescriptions for opioids and acetaminophen over time, there was a positive linear trend for opioids over time, with a moderate correlation coefficient (0.48). It appears that scheduled plus PRN prescriptions for opioids have increased. Opioids were prescribed less frequently than acetaminophen.

DISCUSSION

Prescribing Patterns

We have demonstrated a multinational trend of increased prescription of scheduled analgesics, with corroborative findings for acetaminophen and opioids. Intracountry longitudinal studies (e.g., increases in Norway between 2000 and 2011) and intercountry comparisons (in 2000–01, 34.9% of Norwegian residents and 45.9% of Dutch residents were prescribed analgesics, and in 2011–12, 57.6% of Norwegian residents and 62.8% Australian residents were prescribed analgesics) support this finding.[19,23,33]

There does not appear to be a temporal trend for scheduled plus PRN prescribing. This may be because there is no explicit guidance regarding assessment before giving PRN medication[12] and individual clinical preference continues to influence prescribing.

As expected, acetaminophen remained the most commonly prescribed analgesic,[4,23,34] and prescriptions have increased. The exception is Germany, probably because of the frequent use of dipyrone, a drug banned in several other countries because of risk of agranulocytosis.[26]

Several factors may have influenced increases in opioid prescriptions. Clinicians are more cautious about nonsteroidal antiinflammatory drugs (NSAIDS) and may prescribe opioids as an alternative. A Finnish study saw a reduction in NSAID use in LTC facilities from 13.0% in 2003 to 2.6% in 2011,[35] as did a Norwegian study (6.8% in 2000 to 3.2% in 2011), alongside increases in opioids and acetaminophen.[19] Concerns have been expressed that opioids are used for their sedative effect, not just pain.[13,35] Another concern is that opioids may be wrongly prescribed for neuropathic pain, for which an adjuvant drug may be more effective; the prevalence of adjuvant drugs does not match the prevalence of neuropathic pain.[19,35]

More detailed studies have identified that strong opioids are used more than weak opioids.[4,19,36] The introduction of buprenorphine and fentanyl patches may have contributed to use of strong opioids.[37] A Danish study reported that nursing home residents were more likely to receive transdermal opioids.[13] Their use may be appealing because of ease of administration,[38] but U.S. and U.K. guidelines advise that extended-release opioids should not be the first choice because of negative side effects.[18,38–40]

Quality Rating

The ranges of prescribing prevalence were similar for high- and low-quality studies. It is troubling that there were so few high-quality studies (6 out of 50 cohorts). There was no clear indication that higher-quality studies produced mutually consistent results in terms of prescribing prevalence, which may be because of the heterogeneity of samples and settings.

Cultural Factors

Several studies found a low prevalence of analgesic use. In Italy, 24% of residents reporting pain did not receive analgesics, and authors commented that medication was neither appropriately nor effectively managing pain.[30] A Dutch study reported that 38% of residents in "substantial" pain received no analgesics, noting that pain was not included in national nursing home performance indicators.[41] Another study reported remarkably low analgesic use in Poland. Only 28.8% of residents received analgesics, and only 21.4% of these received scheduled pain relief. Authors commented that pain is not routinely assessed in nursing homes.[42] Where low analgesic use is reported, authors often describe a cultural climate that does not prioritize pain assessment. In Italy, where low rates of analgesic prescriptions are reported,[4] nonpharmacological analgesia is used more frequently, as it is in Finland.

Table 2. Cohorts Included in Analysis of Scheduled Plus As-Needed Analgesic Prescribing Rates

Study	Year Data Collection Ended	Country	Residents Prescribed Regular Analgesics, % (n = 73,938)
Hoffmann and Schmiemann[26,a]	2015	Germany	73.8
Lövheim (2017, personal communication, 3 April)[a,b]	2013	Sweden	66.6
Onder, Vetrano[30,b]	2013	Europe, not including Italy	28
Onder, Vetrano[30,b]	2013	Italy	16
Bauer, Pitzer[55]	2012	Austria	83
Kaasalainen, Wickson-Griffiths[59]	2012	Canada	90
Veal, Bereznicki[23]	2012	Australia	90.8
Taxis, Kochen[60,b]	2009	Australia, Netherlands	80.8
Boerlage, Masman[41,b]	2008	Netherlands	45.8
Lövheim (2017, personal communication, 3 April)[a,b]	2007	Sweden	62.8
Stafford, Alswayan[61]	2007	Australia	56.8
Torvik, Kaasa[62,b]	2006	Norway	54.7
Carey, De Wilde[63]	2005	United Kingdom	60.6
Elseviers, Vander Stichele[64]	2005	Belgium	41.5
Roughead, Gilbert[65,a]	2005	Australia	53.8
Reynolds, Hanson[32]	2004	United States	68.6
Bergman, Olsson[66,b]	2003	Sweden	61.5
Snowdon, Day[67]	2003	Australia	63.6
Jervis, Shore[28]	2002	United States	95
Smalbrugge, Jongenelis[33]	2001	Netherlands	54.5
Jyrkka, Vartiainen[68]	1998	Finland	54
King[69,a,b]	1997	Australia	74
O'Grady and Weedle[70]	1997	Ireland	20
Kaasalainen, Middleton[29]	1996	Canada	95
Neutel, Perry[71]	1996	Canada	33.5
Van Dijk, de Vries[72,b]	1995	Netherlands	53
King[69,a,b]	1994	Australia	60.9
Ferrell, Ferrell[73]	1990	United States	78
Vander Stichele, Mestdagh[74]	1990	Belgium	26
Williams, Nichol[31]	1990	United States	38.3
Passmore, Crawford[75]	1989	Northern Ireland	24.8
Hatton[76]	1987	England	43
Nolan and O'Malley[77]	1987	Ireland	27
Yakabowich, Keeley[78]	1987	Canada	58.5
Primrose, Capewell[79]	1984	Scotland	32

[a]Acetaminophen data available.
[b]Opioid data available.

Limitations

Sample sizes varied greatly, from primary data collection studies involving 1 LTC facility to databases of thousands. One doctor or practice typically manages LTC prescribing, which is thus subject to individual preferences. Data from a small number of facilities may indicate less typical prescribing patterns than a larger sample and contribute to the high levels of observed heterogeneity. Conversely, it can be more difficult to ensure reliability of database records because they depend on accurate input from the LTC facility.[43] There were no studies from South America, Africa, or Asia, and conclusions are not generalizable outside Western Europe, North America, and Australia. Lastly, it has been suggested that neuropathic pain, estimated to be present in 8% to 11% of elderly and nursing home populations,[44,45] is often treated inappropriately. This review has not explored prescriptions of neuropathic analgesics because they may be prescribed for other conditions, and most studies do not collect information on prescribing indications.

Clinical and Policy Implications

Many countries have shifted from NSAID use, and in their place other analgesics may be prescribed. In Australia, 2005 national prescribing guidelines, which highlighted good practice in pain management in residential care,[23,46] may be influencing increasing analgesic use, and a UK increase in fentanyl use may have occurred after its licensing for noncancer pain in 2002. There has been growing interest in pain in individuals with dementia and LTC facilities highlighting undertreatment,[9,12] leading to greater use of assessment tools and treatment guidelines.[8,18,47] Furthermore, there has been more research into behavioral and psychological symptoms of dementia and pain.[48,49] These studies, combined with policy pressure to limit use of psychotropics, such as the Omnibus Budget Reconciliation Act of 1987, may have contributed to the increase in analgesic prescriptions, particularly opioids.[50,51]

Future Research Needed

An increase in analgesic prescribing does not necessarily mean that residents are receiving the most appropriate treatment,[36] and more frequent pain assessment does not necessarily equate to more analgesia.[52] Medication is often prescribed as needed, and administration depends upon staff and their ability to assess pain accurately. This is particularly relevant for cognitively impaired residents who cannot communicate their pain; regular prescriptions may ensure that this population is at less risk of undertreatment.[53] Research into using clinical decision-making algorithms (with stepped treatment approaches), greater collaboration between professionals such as pharmacists and palliative care nurses, and developing interventions to empower and engage the whole care team involved in regularly assessing pain and evaluating pain management strategies could address the disconnect between recognizing and treating pain.[37]

CONCLUSION

This is the first systematic review to investigate changes in prescribing patterns of analgesics in the international LTC population. We included data from all studies reporting analgesic use and demonstrated that increases in prescribing seen in smaller studies are representative of an international upward trend, providing a context for current prescribing practices in LTC facilities and insight into the influence of research focus and policy changes.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Search terms used in each database
Appendix S2. Adapted quality rating scale
Appendix S3. Anatomical Therapeutic Chemical codes used to describe analgesics included in cohorts
Appendix S4. Table of included cohorts: study characteristics and quality ratings

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Appendix 2 – Systematic review search terms

PubMed/Medline/International Pharmaceutical Abstracts

1. exp home for the aged/ or exp elderly care/ or exp institutional care/
2. home for the aged.mp. or exp home for the aged/
3. residential facilities.mp. or exp residential home/
4. ("care home" or "care homes").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
5. ("long term care" or "long-term care" or "longterm care").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
6. ("aged care" or "aged-care").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
7. ("residential home" or "residential homes").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
8. "assisted living".mp. or exp assisted living facility/
9. (convalescent or elderly or geriatric or aged or nursing or residential or care or healthcare).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
10. (home or facility or centre or center or facilities).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
11. ((convalescent or elderly or geriatric or aged or nursing or residential or care or healthcare) adj (home or facility or centre or center or facilities)).mp.
12. analgesic.mp. or exp analgesic agent/
13. pain management.mp. or exp analgesia/
14. 12 or 13
15. ("nursing home" or "nursing homes").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
16. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 11 or 15
17. 14 and 16

Embase

1. exp home for the aged/ or exp elderly care/ or exp institutional care/
2. home for the aged.mp. or exp home for the aged/
3. residential facilities.mp. or exp residential home/
4. ("aged care" or "aged-care").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
5. "assisted living".mp. or exp assisted living facility/

6. (convalescent or elderly or geriatric or aged or nursing or residential or care or healthcare).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

7. analgesic.mp. or exp analgesic agent/

8. pain management.mp. or exp analgesia/

9. 7 or 8

10. (home or homes or facility or centre or center or facilities).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

11. ((convalescent or elderly or geriatric or aged or nursing or residential or care or healthcare) adj (home or homes or facility or centre or center or facilities)).mp.

12. 1 or 2 or 3 or 4 or 5 or 11
13. 9 and 12

PsycINFO

1. nursing homes/ or exp residential care institutions/

2. residential care institutions/ or exp nursing homes/

3. institutional care.mp.

4. long term care.mp.

5. home for the aged.mp.

6. care home.mp.

7. (convalescent or elderly or geriatric or aged or nursing or residential).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

8. (home or homes or facility or facilities or centre or center).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

9. ((convalescent or elderly or geriatric or aged or nursing or residential) adj (home or homes or facility or facilities or centre or center)).mp.

10. 1 or 2 or 3 or 4 or 5 or 6 or 9

11. exp analgesic drugs/

12. exp pain management/

13. exp prescription drugs/

14. 11 or 12 or 13

15. 10 and 14

Cochrane

1. MeSH descriptor: [Analgesics] explode all trees
2. MeSH descriptor: [Pain Management] explode all trees
3. MeSH descriptor: [Prescription Drugs] explode all trees
4. #1 or #2 or #3
5. MeSH descriptor: [Homes for the Aged] explode all trees
6. MeSH descriptor: [Nursing Homes] explode all trees
7. MeSH descriptor: [Long-Term Care] explode all trees

8. MeSH descriptor: [Residential Facilities] explode all trees
9. "care home" or "care homes"
10. "longterm care" or "long term care"
11. "aged care" or "aged-care"
12. #12 "nursing home"
13. #13 "residential home" or "residential homes"
14. #14 "assisted living"
15. #15 convalescent or elderly or geriatric or aged or nursing or residential or care or healthcare
16. #16 home or facility or centre or center or facilities
17. #17 #15 adj #16
18. #18 #17 or #14 or #13 or #12 or #11 or #10 or #9 or #8 or #7 or #6 or #5
19. #19 #18 and #4

Web of Science

1. **TOPIC:** ("home for the aged" or "institutional care" or "care home") *OR*
2. **TOPIC:** ((convalescent or elderly or geriatric or aged or nursing or residential) AND (home or homes or facility or facilities)) *AND*
3. **TOPIC:** (analges* or "analgesic agent" or "pain management" or analgesic) *AND*
4. **TOPIC:** (resident)

CINAHL

1. MH nursing homes or residential care
2. nursing home
3. nursing homes or long-term facilities
4. MH nursing homes or nursing home patients
5. nursing homes or housing for the elderly or long term care
6. (MH "Nursing Homes+") OR (MH "Nursing Home Patients")
7. (MH "Long Term Care")
8. "home for the aged"
9. (MH "Institutionalization") OR "institutional care"
10. "aged-care"
11. convalescent or elderly or geriatric or aged or nursing or residential
12. "care home" or "care homes"
13. home or homes or facility or facilities or centre or center
14. S11 adj S13
15. S1 OR S2 OR S3 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S12 OR S14
16. (MH "Analgesics+")
17. "analgesic agent"
18. "pain management"
19. (MH "Drugs, Prescription")
20. (MH "Prescriptions, Drug")
21. S17 OR S18 OR S19 OR S20
22. S15 AND S21

Google Scholar

(prescription* or prescribing or drug* or medicine* or medication* or pharma* or polypharmacy) and (residential or care home* or care facilit* or nursing home*)

Appendix 3 – Systematic review quality scale

STUDY:

1) Representativeness of the target cohort

a) truly representative of the average care home resident / CH resident with dementia
b) somewhat representative of the average care home resident / CH resident with dementia
c) selected group of users e.g. nurses, volunteers
d) no description of the derivation of the cohort

2) Is the case definition adequate? (cognitively impaired vs non-cognitively impaired)

a) yes, with independent validation
Requires some independent validation (e.g. >1 person/record/time/process to extract information, or reference to primary record source such medical/hospital records) or (valid and reliable) cognitive assessment (conducted by study team or completed <3 months prior)
b) yes, e.g. record linkage or reports or (unvalidated or unreliable) cognitive assessment
(e.g. ICD codes in database) or nurse or self report with no reference to primary record, or cognitive assessment completed >3 months prior
c) no description
d) not applicable

3) Were data collection tools adequate? (analgesic prescription information)

a) Yes – *medical records, insurance data*
b) No – *nurse or self report*
c) Can't tell

4) Were data collection tools standardised? (case definition and analgesic prescription information)

a) Yes
b) No
c) Can't tell

5) What percentage of selected individuals agreed to participate?

a) 60-100% agreement
b) Less than 60% agreement
c) Can't tell

6) Were special features of the sampling design accounted for in the analysis?

a) Yes/not applicable
b) No

7) Conflict of interest

a) No clear conflict of interest
b) Conflict of interest acknowledged

STRONG: 1 = a and 2 = a/d and 3 = a and 4 = a and 5 = a and 6 = a

MODERATE: 1 = a/b; and 2 = a/b/d; and 3 = a; and 5 = c/d; or 4 = b/c and 6 = a/b

WEAK: 1 = c/d; or 2 = c; or 3 = b/c or 4 = c and 6 = a/b

RATER 1: **RATER 2:**

Is there a discrepancy?	**Yes**	**No**	**FINAL RATING:**
If yes, why?	Differences in interpretation of criteria		Oversight
	Differences in interpretation of study		Other

Appendix 4 – ATC codes according to WHO

N02	General analgesics and antipyretics
N02A	Opioids
N02B	Other analgesics and antipyretics
N02BE01	Acetaminophen
M01	Anti-inflammatory and anti-rheumatic products
M01A	Anti-inflammatory and anti-rheumatic products, non-steroids
M02A	Topical products for joint and muscular pain
B01AC06	Acetylsalicylic acid (aspirin)

Appendix 5 – Systematic review included study characteristics and quality ratings

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Atramont et al. (2018)[a]	France	2013	11687	nk	na	both
Bauer et al. (2016)	Austria	2012	425	12	weak	both
Bauer et al. (2016)	Austria	2012	425	12	weak	regular
Bergman et al. (2007)	Sweden	2003	7904	nk	moderate	both
Blytt et al. (2018)[a]	Norway	2011	1825	64	na	both
Boerlage et al. (2013)	Netherlands	2008	201	1	strong	both
Carey et al. (2008)	UK	2005	2864	nk	moderate	both

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Decker et al. (2009)	US	2003	215	13	weak	regular
Elseviers et al. (2010)	Belgium	2005	2510	76	weak	both
Erdal et al. (2017)[a]	Norway	2015	931	65	na	regular
Ferrell et al. (1990)	US	1990	92	1	moderate	both
Hatton (1990)	England	1987	449	25	weak	both
Hoffmann and Schmiemann (2016)	Germany	2015	852	21	strong	regular
Hoffmann and Schmiemann (2016)	Germany	2015	852	21	strong	both
Hunnicutt et al. (2017)[a]	US	2012	1,387,405	nk	na	regular

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Jervis et al. (2007)	US	2002	45	1	moderate	both
Jyrkka et al. (2006)	Finland	1998	13	nk	moderate	both
Kaasalainen et al. (1998)	Canada	1996	83	1	moderate	both
Kaasalainen et al. (2016)	Canada	2012	345	6	weak	both
King (2003)	Australia	1994	998	15	moderate	both
King (2003)	Australia	1997	414	11	weak	both
Kölzsch et al. (2012)	Germany	2010	560	40	weak	regular
Krüger et al. (2012)	Norway	2008	513	7	moderate	regular

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Hemmingsson et al. (2017)	Sweden	2013	1849	nk	weak	both
Hemmingsson et al. (2017)	Sweden	2007	2764	nk	weak	both
Lövheim et al. (2008)	Sweden, Finland	2006	236	nk	weak	regular
Neutel et al. (2002)	Canada	1996	227	1	strong	both
Nolan and O'Malley (1989)	Ireland	1987	301	11	moderate	both
Nygaard and Naik (1999)	Norway	1996	347	15	weak	regular
Nygaard et al. (2003)	Norway	1997	1042	15	moderate	regular

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
O'Grady and Weedle (1997)	Ireland	1997	115	1	weak	both
Onder et al. (2014)	Italy	2013	3179	nk	weak	both
Onder et al. (2014)	Europe not including Italy	2013	3608	nk	weak	both
Passmore et al. (1995)	N. Ireland	1989	595	nk	moderate	both
Primrose et al. (1987)	Scotland	1984	400	18	weak	both
Reynolds et al. (2008)	US	2004	551	6	weak	both
Reynolds et al. (2008)	US	2004	551	6	weak	regular

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Roughead et al. (2008)	Australia	2005	16126	nk	weak	both
Sandvik et al. (2016)	Norway	2004	1163	26	strong	regular
Sandvik et al. (2016)	Norway	2011	1858	64	strong	regular
Sandvik et al. (2016)	Norway	2000	1926	251	weak	regular
Smalbrugge et al. (2007)	Netherlands	2001	290	14	weak	regular
Smalbrugge et al. (2007)	Netherlands	2001	290	14	weak	both
Snowdon et al. (2006)	Australia	2003	3054	50	moderate	both
Stafford et al. (2011)	Australia	2007	2345	41	moderate	both

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Tan et al. (2015)	Australia	2014	383	6	moderate	regular
Taxis et al. (2016)	Australia, Netherlands	2009	3597	32	moderate	both
Torvik et al. (2009).	Norway	2006	214	7	moderate	both
van Dijk et al. (2000)	Netherlands	1995	2355	6	moderate	both
Vander Stichele et al. (1992)	Belgium	1990	198	20	weak	both
Veal et al. (2014)	Australia	2012	7309	nk	moderate	both
Veal et al. (2014)	Australia	2012	7309	nk	moderate	regular
Williams et al. (1999)	US	1990	818	61	weak	both

Included cohorts – Author and year of publication	Country	Year data collection ended	n	Number of care homes	Quality rating	Regular prescriptions only, or regular + PRN
Yakabowich et al. (1994)	Canada	1987	6848	88	moderate	Both

[a]2017- 2018 update

Appendix 6 – Medication instructions

- **Medication**
  - All medications prescribed in the last 4 weeks should be noted on the MARQUE medication data capture form.
  - For all medications (as prescribed and PRN/as required), the left hand side columns should be completed.
  - For PRN/as required medications only, please complete the ride hand side columns giving details for the last 2 weeks.
  - Care home MAR (Medication Administration Record) should be sent with approx. 10% of the residents. Please anonymise and attach to the (completed) MARQUE medication data capture form

1. **Common MACRO issues**

- If a medication is given in liquid form/oral suspension, e.g. Paracetamol 250mg/5ml, **please put strength on the hard copy and in the medication name box on MACRO** (i.e. 250mg/5ml) but **put the mg dosage (i.e. 250mg) in the Prescribed Dosage section on MACRO.**

Please note. i) If you only put the 'ml' or do not put a strength then we cannot tell how much of the drug the resident is being prescribed. ii) Please always put the full dose i.e. if it is 'up to 20ml' of the above drug, you should record it as 1000mg

- Please also record other strengths e.g. Codeine 8/500. If it is one tablet per dosage, put 508mg on MACRO, if 2, put 1016mg on MACRO

- Alendronic acid 70mg weekly should be recorded as: Alendronic acid – prescribed dosage - 70 –mg - How many times over 4 months* - 4 – (duration)

- Buprenorphine patch 5mcg/hour please record as: Buprenorphine patch 5mcg/hour – prescribed dosage – 1 – 777 – How many times over 4 months* - 4 – (duration)

- For any medications given less than daily, use the How many times over 4 months* frequency and then put the number of times per month.

- Dosages for creams etc should be put as Dose: 7777.77 Units of dose: 777

**this actually means How many times over 1 month, but we are unable to change it.*

2. **PRN specific** comments

- PRN is indicated by **'p.r.n'** or **'as required'** or **'up to'**

- On MACRO this should be recorded as Dosage type: **As required**

- **As directed is not PRN**, and should be recorded as a **Prescribed dosage on MACRO**

- MARQUE medication data capture form: Do not put PRN in the Prescribed frequency column, **always put the maximum frequency specified on the MAR chart (e.g. 'up to twice a day'), on the data capture form and on MACRO.** We will know it is PRN if there is a 'Yes' in the 'PRN?' column

- If no frequency is specified, put NA in the Prescribed frequency column/777 on MACRO

- If a PRN medication is never given to the resident, still put the maximum frequency on the data capture form and on MACRO, and then put zeros on the right hand side (the PRN section) of the data capture form.

- If frequency is not indicated sometimes medication charts will have dots/asterisks by the times on the MAR charts which indicates that it should be given/offered at that time – please check with care home staff if this is unclear

- Please try and **get the full 14 days of PRN medication data,** as it corresponds to the agitation inventory. Do not put days outside of the last 14 days as they do not correspond to the agitation inventory.

PRN column definitions on Medication Data Capture Form

- PRN? If yes please complete boxes to the right: please put yes or no, if on the MAR chart it says any of these: 'p.r.n' or 'as required' or 'up to'. Columns to the right of this only need to be completed for PRN medication
- Route of administration: tablet/caplet/oral suspension/soluble tablet/cream/injection/etc

- Total number of doses offered: In the last 14 days (ending on the day before the proxy) how many times did the nurse think about giving the resident medication – basically how many boxes have either initials or a letter in them?
- Total number of doses refused: Of the boxes with a letter or initial in, how many of those doses were refused? Either by the nurse or the resident, for whatever reason, including social leave and asleep.
- No. of days medication given: Out of the 14 days, on how many days did the resident actually ingest the medication?
- Indication: if it gives any reason on the MAR chart for why this drug is prescribed. If possible please ask a nurse, and put (verbal) after the reason.

If you are not sure about any medication, please anonymise the MAR chart and scan and send directly with your questions to Frankie, f.lafrenais@ucl.ac.uk or f.lafrenais@nhs.net (if you do not get a response on the nhs.net email please email my UCL account to let Frankie know).

Appendix 7 – MARQUE Stream 2 (WS2) ethical approval letter

NHS
Health Research Authority
NRES Committee London - Harrow
Bristol Research Ethics Committee Centre
Level 3, Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT
Telephone: 0117 342 1384

06 March 2014

Dr Claudia Cooper
Clinical senior lecturer in old age psychiatry
Mental health sciences unit, 2nd floor, Charles Bell House
Riding House street
London
W1W 7EJ

Dear Dr Cooper

Study title:	**A naturalistic 16 month cohort study of agitation and quality of life in care homes**
REC reference:	**14/LO/0034**
IRAS project ID:	**143438**

Thank you for your letter of 20 February 2014, responding to the Committee's request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, as revised, subject to the conditions specified below.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager, Libby Watson, at: nrescommittee.london-harrow@nhs.net.

Mental Capacity Act 2005

I confirm that the Committee has approved this research project for the purposes of the Mental Capacity Act 2005. The Committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Relevance of the research to impairing condition

The Committee agreed the research is connected with an impairing condition affecting persons lacking capacity or with the treatment of the condition.

Justification for including adults lacking capacity to meet the research objectives

The Committee agreed the research could not be carried out as effectively if it was confined to participants able to give consent.

Balance between benefit and risk, burden and intrusion

The REC noted that while the research would not benefit participants lacking capacity, it is intended to provide knowledge of the causes or the treatment or care of patients with dementia. After discussion, the REC agreed that the risk to participants is likely to be negligible and the research will not significantly interfere with their freedom of action or privacy or be unduly invasive or restrictive.

Arrangements for appointing consultees

The REC considered the arrangements set out in the application for appointing consultees under Section 32 of the Mental Capacity Act to advise on whether participants lacking capacity should take part and on what their wishes and feelings would be likely to be if they had capacity.

After discussion the REC agreed that reasonable arrangements were in place for identifying personal consultees, and for appointing nominated consultees independent of the project where no person can be identified to act as a personal consultee.

Information for consultees

The REC reviewed the information to be provided to consultees about the proposed research and their role and responsibilities as a consultee.

The REC was satisfied that the information was adequate to enable consultees to give informed advice about the participation of persons lacking capacity.

Additional safeguards

The REC was satisfied that reasonable arrangements would be in place to comply with the additional safeguards set out in Section 33 of the Mental Capacity Act.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS Sites - Site Specific Assessment (SSA)

The REC decided that the research did not require Site-Specific Assessment at non-NHS sites as it involves no clinical interventions and the REC was satisfied that the risk to participants is likely to be negligible, and the study procedures will not significantly interfere with participants' freedom of action or privacy or be unduly invasive or restrictive.

The Committee agrees that all non-NHS sites in this study should be exempt from site-specific assessment (SSA). There is no need to submit the Site-Specific Information Form to any Research Ethics Committee.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study:

- There is a rogue reference to a 'consent form' rather than a declaration form at the bottom of the consultee's declaration form – please correct this.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Evidence of insurance or indemnity		25 July 2013
Investigator CV	Dr Cooper	
Letter of invitation to participant	Letter to Family Carers, v1	28 January 2014
Letter of invitation to participant	Letter to Family Carers v2	20 February 2014
Participant Consent Form: Family Carer	2	28 January 2014
Participant Consent Form: Resident	2	28 January 2014
Participant Consent Form: Staff	3	20 February 2014
Participant Consent Form: Consultee Declaration Form	3	20 February 2014
Participant Information Sheet: Consultee for mid study loss of capacity	1	28 January 2014
Participant Information Sheet: Consultee	3	20 February 2014
Participant Information Sheet: Family Carer	3	20 February 2014
Participant Information Sheet: Resident	3	20 February 2014
Participant Information Sheet: Resident Short Version	3	20 February 2014
Participant Information Sheet: Staff	3	20 February 2014
Protocol	1	24 October 2013
Questionnaire: CSRI		
Questionnaire: DEMQOL - Carer		
Questionnaire: Neuropsychiatric Interview		
Questionnaire: DEMQOL		
Questionnaire: TESS - NH/RC		
Questionnaire: Staff Measures		
Questionnaire: Home Ratings		
Questionnaire: Carer Interview		
Questionnaire: Staff Proxy Measures		
Questionnaire: CDR - UK/English		
REC application	143438	02 December 2013
Response to Request for Further Information		28 January 2014
Response to Request for Further Information		20 February 2014

NHS
Health Research Authority

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

14/LO/0034	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Jan Downer
Chair

Email: nrescommittee.london-harrow@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Mr Dave Wilson, University College London*

A Research Ethics Committee established by the Health Research Authority

Appendix 8 – Noticeable Problems Checklist (NPC)

Care home number: ⌊ ⌋⌊ ⌋⌊ ⌋

Resident number: ⌊ ⌋⌊ ⌋⌊ ⌋

Date: ⌊ ⌋⌊ ⌋⌊ ⌋⌊2⌋⌊0⌋⌊ ⌋⌊ ⌋

Resident Eligibility Form

1. Does this resident have a diagnosis of dementia? **YES/NO**

*If **YES**, you do not need to fill in the Noticeable problems checklist, skip to **q2.***

Noticeable Problems Checklist

Does [name of person]...have noticeable problems in		Yes	No
NPC1	Remembering recent events?	☐	☐
NPC2	Working out how to do some basic every day tasks such as dressing, making tea, going to the toilet?	☐	☐
NPC3	Knowing the time?	☐	☐
NPC4	Knowing where he/she is?	☐	☐
NPC5	Correctly naming persons seen regularly?	☐	☐
NPC6	Keeping in touch with a conversation?	☐	☐

NPC TOTAL _____

*A score of **2-5** indicates possible dementia, a score of **5+** indicates probable dementia.*

2. Is the resident eligible for this study? **YES/NO**

*Does the resident have a **diagnosis of dementia** OR a **NPC score of 2 or above?***

Capacity:

1. Does this resident have capacity to agree to the study? **YES/NO**

Appendix 9 - MARQUE WS2 information sheet for residents

VERSION 5 28/5/14 resident

University College London
6th Floor Maple House
149 Tottenham Court Road
London, W1T 7NF
Tel: 0207 679 9367

Participant Information Sheet
Quality of life in care homes study

We are asking whether you would like to take part in a research project. We want to find out about the quality of life of people with memory problems who live in care homes, and what makes their quality of life better or worse. We plan to use this information to develop a new training programme for care home staff to improve resident's quality of life. Before you decide whether to take part it is important that you understand why the research is being done and what this study will involve. Please take time to read the following information carefully and discuss it with relatives and friends if you wish. Ask us if there is anything that is not clear or if you would like more information.

- Part 1 tells you why the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of this study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?
We want to find out about the quality of life people with memory problems who live in care homes experience, and what makes it better or worse. We plan to use this information to develop a new training programme for care home staff to improve resident's quality of life.

Why have I been invited?
Because you are a resident in a care home that is taking part in the study. Fifty care homes across England are taking part in all.

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do you will be given the information sheet to keep. You are free at any point to withdraw without giving a reason.

Division of Psychiatry
6th Floor Maple House, 149 Tottenham Court Road, University College London, London, W1T 7NF
Tel: +44 (0)20 7679 9367
a.kadri@ucl.ac.uk
http://www.ucl.ac.uk/psychiatry/marque

What will happen to me if I take part?
A researcher will visit you at your care home and ask you some questions about your quality of life. The researcher will then visit you 4 more times over then next year and half to ask you these questions again to see how your experiences might have changed. We will ask for your NHS number and date of birth and use this to collect long term data from the Office of National Statistics about your future health.

What do I have to do?
We estimate it will take around 15 minutes for you to complete the questions about your quality of life on each of the five occasions. We would like to ask a family member or friend some questions about how they see your quality of life, and care home staff questions about your background, health and social care and wellbeing. You may decide that you do not want or feel able to answer questions yourself but you are happy for us to approach these people about you.

What are the possible disadvantages and risks of taking part?

We don't expect the survey to be upsetting, but if taking part brings up issues for you that you would like to talk about you can ask speak to one of our team. You may also find it helpful to ring the Alzheimer's Society National Dementia Helpline on 0300 222 1122. The Helpline is usually open from 9am to 5pm Monday to Friday and Saturday and Sunday 10am - 4pm.

What are the possible benefits of taking part?
We cannot promise the study will help you but the information we get might help us develop ways to improve the quality of life of people with memory problems living in care homes.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?
All interviews are confidential and you will not be identified in any publications. If any person in the study tells us that they or someone else is being harmed we will ask their permission to disclose the information to the care home manager or other appropriate responsible person. We respect confidentiality but cannot keep it a secret if anyone is being harmed.
Contact
Please contact Hannah Savage, Administrative Assistant on 020 7679 9367 or at h.savage@ucl.ac.uk for further information.

This completes Part 1 of the Information Sheet. If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with Dr Claudia Cooper (principal investigator for the study) (0207 679 9250) who will do her best to answer your questions. If you remain unhappy and wish to complain formally about any aspect of the way you have been approached or treated during the course of this study, you

may contact the Research Governance Sponsor of this study, University College London. Please write to Joint Research Office, 149 Tottenham Court Road, London, W1T 7DN quoting study 08/0043 quoting study 08/0043.

In the unlikely event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against UCL but you may have to pay your legal costs.

What will happen to the results of the research study?
We intend to publish results in relevant conference proceedings and publications. Please tell the researchers if you would like a copy of any publications and we would be happy to send them to you when they are published. You will not be identified in any report/publication.

Who is organising and funding the research?
The research is organised by University College London and funded by the ESRC & the NIHR.

Who has reviewed the study?
All proposals for research using human subjects are reviewed by an Ethics Committee before they can proceed. This proposal was reviewed by Harrow Research Ethics Committee.

You will be given a copy of the information sheet and a signed consent form to keep. Thank you for considering taking part or taking time to read this sheet.

Appendix 10 - MARQUE WS2 resident consent form

Version 4 28/05/14

UCL

Care home Number: ⌊ ⌋ ⌊ ⌋ ⌊ ⌋

Resident Number: ⌊ ⌋ ⌊ ⌋ ⌊ ⌋

Date: ⌊ ⌋ ⌊ ⌋ ⌊ ⌋ ⌊2⌋⌊0⌋ ⌊ ⌋ ⌊ ⌋

RESIDENT CONSENT FORM

Quality of life in care homes study

Principal investigator: Dr Claudia Cooper

Please **initial** box

1. I confirm that I have read and understand the information sheet dated 28/5/14 (version 5) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without my medical care or legal rights being affected, and my request will be respected. ☐
3. I understand that relevant sections of data collected during the study, may be looked at by responsible individuals from University College London, the NHS Trust, or regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I agree to researchers interviewing care home staff and [family carer name]_____about me. ☐
5. I agree to researchers obtaining data about my future health from National Records. ☐
6. I agree to take part in the study. ☐

Name of person giving consent	Date	Signature

Researcher	Date	Signature

1

Appendix 11 – MARQUE WS2 consultee information sheet

VERSION 6 28/5/14 consultees

University College London
6th Floor Maple House
149 Tottenham Court Road
London, W1T 7NF
Tel: 0207 679 9367

Consultee Information Sheet
Quality of life in care homes study

You are being invited to act as a 'consultee' for _____ because s/he is unable to make a decision for him/herself. You are being asked to advise the researcher about this person's wishes and feelings and whether they would have wished to join this research. Before you decide, it is important you understand what being a consultee means, why the research is being done and what it will involve. Please take time to read this information carefully and talk to others about the study if you wish. Ask us if anything is not clear or if you would like more information. Take time to decide whether you wish to be a consultee.

What does it mean to be a consultee?

A consultee is someone who knows a person who doesn't have capacity well and is willing and able to offer an opinion on what that person's wishes would have been if they were still able to decide themselves whether to take part. You do not have to act as a consultee if you do not want to. If you decide to act as consultee, you will be asked to sign a Consultee Form. If you think that this person would not have wanted to take part, then the researchers will respect this. Please remember that you are not being asked for your personal views on the research but only what the person's wishes would have been were they being asked to take part in this research. Think about the broad aims of the research, the risks and benefits and what taking part will mean for this person. At any stage, you can advise the researcher that in your opinion the person would no longer wish to remain in the study.

Why have I been asked to be a consultee?

You may have been asked because you know the patient personally, as a friend, partner, or relative, and they would trust you to help with this decision. Or, you may be a member of the care home staff, and you have the patient's best interests in mind.

About the study

We want to find out about the quality of life people with memory problems who live in care homes experience, and what makes their quality of life better or worse. We plan to use this information to develop a new training programme for care home staff to improve resident's quality of life. Before you decide whether to take part it is

important that you understand why the research is being done and what this study will involve. Please take time to read the following information carefully and discuss it with relatives, friends, and colleagues if you wish. Ask us if there is anything that is not clear or if you would like more information.

- Part 1 tells you why the purpose of this study and what will happen to the resident you are advising us about if they take part.
- Part 2 gives you more detailed information about the conduct of this study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?
We want to find out about the quality of life people with memory problems who live in care homes experience, and what makes it better or worse. We plan to use this information to develop a new training programme for care home staff to improve resident's quality of life.

Why have I been asked?
Because the resident you are being asked to act as consultee for lives in a care home that is taking part in the study. Fifty care homes across England are taking part in all.

Do they have to take part?
No. It is up to you to advise on whether or not the resident would have wanted to take part. If they do you will be given the information sheet to keep. You are free at any point to request the person you are consultee for is withdrawn from the study without giving a reason.

What will happen to them if they take part?
A researcher will visit the resident at their care home and ask them some questions about their quality of life. The researcher will then visit them 4 more times over then next year and half to ask them these questions again to see how their experiences might have changed. We will ask for their NHS number and date of birth and use this to collect long term data from the Office of National Statistics about their future health.

What do they have to do?
We estimate it will take around 15 minutes for them to complete the questions about their quality of life on each of the five occasions. Not all participants will be able to answer these questions, and we will ask your advice about this. For all residents taking part, including those who cannot answer questions themselves, we would like to ask a family member or friend some questions about how they see their quality of life (this may be you if you are their carer), and care home staff questions about their background, health and social care and wellbeing.

What are the possible disadvantages and risks of taking part?

We don't expect the survey to be upsetting, but if taking part brings up issues for you or the resident that you or they would like to talk about you can ask speak to one of our team. You may also find it helpful to ring the Alzheimer's Society National Dementia Helpline on 0300 222 1122. The Helpline is usually open from 9am to 5pm Monday to Friday and Saturday and Sunday 10am - 4pm.

What are the possible benefits of taking part?

We cannot promise the study will help the resident you are advising us about but the information we get might help us develop ways to improve the quality of life of people with memory problems living in care homes.

What if there is a problem?

Any complaint about the way the resident you are advising us about has been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

All interviews are confidential and the resident you are advising us about will not be identified in any report/publication. If any person in the study tells us that they or someone else is being harmed we will ask their permission to disclose the information to the care home manager or other appropriate responsible person. We respect confidentiality but cannot keep it a secret if anyone is being harmed.

Contact

Please contact Hannah Savage, Administrative Assistant on 020 7679 9367 or h.savage@ucl.ac.uk for further information.

This completes Part 1 of the Information Sheet. If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with Dr Claudia Cooper (principal investigator for the study) (0207 679 9250) who will do her best to answer your questions. If you remain unhappy and wish to complain formally about any aspect of the way you or the resident you are advising us about have been approached or treated during the course of this study, you may contact the Research Governance Sponsor of this study, University College London. Please write to Joint Research Office, 149 Tottenham Court Road, London, W1T 7DN quoting study 08/0043 quoting study 08/0043.

In the unlikely event that something does go wrong and the resident you are advising us about is harmed and this is due to someone's negligence then they may have

grounds for a legal action for compensation against University College London but you may have to pay your legal costs.

What will happen to the results of the research study?
We intend to publish results in relevant conference proceedings and publications. Please tell the researchers if you would like a copy of any publications and we would be happy to send them to you when they are published. The resident you are advising us about will not be identified in any report/publication.

Appendix 12 – MARQUE WS2 consultee declaration form

version 5 28/5/14

Care home Number: [ ][ ][ ]
Resident Number: [ ][ ][ ]
Carer Number: [ ][ ] OR Staff Number [5][ ][ ][ ]
Date: [ ][ ][ ][ ][2][0][ ][ ]

CONSULTEE DECLARATION FORM
Quality of life in care homes study
Principal investigator: Dr Claudia Cooper

Please initial box

1. I confirm that I have read and understand the information sheet dated 28/5/14 (version 6) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that participation of the person about whom I am giving advice is voluntary and that I am free to advise they should be withdrawn at any time, without giving any reason, without their medical care or legal rights being affected, and my request will be respected. ☐
3. I understand that relevant sections of data collected during the study, may be looked at by responsible individuals from University College London, the NHS Trust, or regulatory authorities, where it is relevant to their taking part in this research. ☐
4. I agree to researchers interviewing care home staff and [family carer name]_____ about of the person about whom I am giving advice. ☐
5. I agree to researchers obtaining data about the future health of the person for whom I am giving advice from National Records. ☐
6. I advise that _____ would in my view want to take part in the above study if they could decide. ☐

Name of consultee:	Date	Signature
Name of researcher	Date	Signature

5

Appendix 13 – Home census

Care home Number:

Date:

Home Census

Home details

What mental health trust does the care home belong to?

1. Type of accommodation			
Privately managed		Council managed	
Housing association managed		Charity managed	
		Other *Please complete **q1a***	
		1a.Specify other *Only complete is 'Other' is selected.*	

2. Type of care home			
Nursing		Personal care	
Nursing and Personal care			

3. Is the home dementia registered?	YES/NO
4. Is the home dementia specialist? *(i.e. all residents should have dementia)*	YES/NO
5. Total number of resident places in home	

Care Quality Commission rating
This can be found at: www.cqc.org.uk

✓ **'All standards met' – 1**

✗ **'Not all standards met' – 2**

⊗ **'Enforcement action' – 3**

6. Standards of treating people with respect and involving them in their care	
7. Standards of providing care, treating and support that meets people's needs	
8. Standards of caring for people safely and protecting them from harm	
9. Standards of staffing	
10. Standards of quality and suitability of management	

11. Date of last CQC inspection: __/__/____
Please date this from the last follow up, rather than the last full inspection.

Dementia Policy

12. Is the policy that all newly admitted residents with dementia are cared for in a specialist area, separate to other residents, where their physical needs do not preclude this?	YES/NO
13. Is there a special unit for residents with behavioural disturbances relating to dementia, aside from the area above?	YES/NO
14. Does the home have specific team for dementia care?	YES/NO
15. Is it typical that, as residents needs change over time, they are moved to different locations within the home (e.g to a nursing area, closer to staff offices, to a specialist team)?	YES/NO

Home Organisation

16. Is the care home divided into units? *If NO, please skip to Q19.*		YES/NO
17. If YES, please allocate each unit an ID number	**Name**	**ID Number**
18. Does each unit have a specific staff team?		YES/NO

Care home Number: [ ][ ][ ]

Date: [ ][ ][ ][ ][2][0][ ][ ]

Home statistics measured for the last 24 hours

The census period is 24 hours BEFORE the day of the interview, ending at completion of previous night shift

19. How many qualified nursing staff were rostered on during the day	0-60
20. How many care staff, other than above, were rostered on during the day	0-60
21. How many qualified nursing staff were rostered on during the night	0-60
22. How many care staff, other than above, were rostered on during the night	0-60
23. Number of staff in 24 hours period who were agency/bank	0-20
24. Number of residents present in home (ie, if in hospital, or away, do not count)	0-200
25. Number of residents with dementia present in home (ie if in hospital, or away, do not count) *Amount AFTER noticeable problems checklist* Complete this after the interview is complete	0-200
26. Number of residents currently in hospital	0-80

Home statistics measured for the last 7 days

27. Number of permanent registered nursing staff (including those on sick/carer/compassionate leave)	0-200
28. Number of permanent other care staff (including those on sick/carer/compassionate leave)	1-500
29. Number of registered nursing staff from those above on sick/carer/ compassionate leave in the last week	0-20
30. Number of other care staff from those above on sick/carer/ compassionate leave in the last week	0-50

Activity sessions taking place in the last 7 days

Before entering activities into the database please refer to the 'activities reference list'

Activity *If any activity has occurred on more than one occasion, please put the average number of residents attending/ average duration of activity.* *Only include activities organised by the care home.*	**a. Individual or Group**	**b. Duration** (in hours)	**c. No. of occasions**	**d. No. residents attending**
e.g. Sensory activity	*Individual*	*3 hours*	*4*	*13*

Care home Number: [ ][ ][ ]

Date: [ ][ ][ ][ ][2][0][ ][ ]

Home statistics measured for the last 6 months

32. Has the care home provided dementia specific training in the last 6 months *If **NO**, skip to question 36*			YES/NO
33. Who was the training for?			
Nurses		Care staff	
Nurses & Care staff		All staff	
34. How many sessions of dementia specific care training were provided			
35. On average, how long were the sessions?			

36. Number of registered nurses who have joined as permanent staff in last 6 months.	0-50
37. Number of other care staff who have joined as permanent staff in last 6 months.	0-100

Appendix 14 – Medication CRF

Care home Number: ⌊ ⌋ ⌋ ⌋
Resident Number: ⌊ ⌋ ⌋ ⌋
Staff number: ⌊5⌋ ⌋ ⌋ ⌋
Date: ⌊ ⌋ ⌋⌊ ⌋ ⌋⌊2⌋0⌋ ⌋ ⌋

MEDICATION

4 WEEKS				Date range (2 weeks, same as CMAI): _ _/_ _/ _ _ - _ _/_ _/ _ _ Number of days resident not in home during above 2 weeks (if applicable): _ _					
Drug name	Prescribed dosage	Prescribed frequency	Duration of prescription	PRN? *If yes please complete boxes to the right*	Route of administration/ format	Total number of doses offered	Total number of doses refused	No. of days medication given	Indication (if given) *reason for taking*
				Please give maximum dosage for PRN prescription. If compound, please give strength of each component.					

Appendix 15 – Relevant drugs

Simple, non-opioid	**NSAID oral**
Paracetamol	Ibuprofen
Nefopam	Aspirin
	Naproxen
Weak opioid	Meloxicam
Codeine	Diclofenac
Dihydrocodeine	
Meptazinol	**Anxiolytics and hypnotics**
	Lorazepam
Strong opioids	Diazepam
Buprenorphine	Midazolam
Fentanyl	Oxazepam
Morphine	Clonazepam
Diamorphine	Buspirone
Oxycodone	Zopiclone
Methadone	Nitrazepam
Tramadol	Temazepam
	Zolpidem
Compound analgesics	Clobazam
Co-codamol	Lormetazepam
Co-dydramol	Medazepam
Co-codaprin	
	Antidepressants
Antipsychotics	Amitriptyline
Levomepromazine	Mirtazapine
Amisulpride	Venlafaxine
Quetiapine	Sertraline
Flupentixol	Paroxetine
Sulpiride	Citalopram
Promazine	Fluoxetine
Aripiprazole	Duloxetine
Trifluoperazine	Lofepramine
Clozapine	Phenelzine
Olanzapine	Trazodone
Risperidone	
Haloperidol	
Chlorpromazine	

Appendix 16 – Cohen-Mansfield Agitation Inventory (CMAI)

Care home Number:
Resident Number:
Staff number: 5
Date: 2 0

Cohen-Mansfield Agitation Inventory:

How often have each of the behaviours below happened over the last 2 weeks?

	Never	Less than once a week	1-2 times a week	Several times a week	1-2 times a day	Several times a day	Several times an hour
1. Pacing and aimless wandering							
2. Inappropriate dressing or disrobing							
3. Spitting (including while feeding) *(Do not include spitting into tissue, toilet or onto ground outside)*							
4. Cursing or verbal aggression							
5. Constant unwarranted request for attention or help.							
6. Repetitive sentences or questions *(Do not include complaining)*							
7. Hitting (including self) *(Including hitting furniture)*							
8. Kicking							
9. Grabbing onto people or things inappropriately							
10. Pushing							
11. Throwing things							
12. Making strange noises							
13. Screaming							
14. Biting							
15. Scratching							
16. Trying to get to a different place							

	Never	Less than once a week	1-2 times a week	Several times a week	1-2 times a day	Several times a day	Several times an hour
17. Intentional falling							
18. Complaining							
19. Negativism *(Bad attitude, doesn't like anything, nothing is right.)*							
20. Eating or drinking inappropriate substances							
21. Hurting self or others							
22. Handling things inappropriately *(Picking up things that don't belong to them, playing with food, rummaging through drawers)*							
23. Hiding things							
24. Hoarding things							
25. Tearing things or destroying property							
26. Performing repetitive mannerisms							
27. Making verbal sexual advances							
28. Making physical sexual advances or exposing genitals							
29. General restlessness							

Appendix 17 – Clinical Dementia Rating (CDR)

Care home Number: ⌊ ⊥ ⊥ ⊥ ⌋
Resident Number: ⌊ ⊥ ⊥ ⊥ ⌋
Staff number: ⌊5⊥ ⊥ ⊥ ⊥ ⌋
Date: ⌊ ⊥ ⊥⌊ ⊥ ⊥⌊2⊥0⊥ ⊥

Clinical Dementia Rating Worksheet

This is a semi-structured interview. Please ask all of the following questions. Ask any additional questions necessary to determine the subject's CDR. Please record information from the additional questions.

MEMORY QUESTIONS

1. Does the resident have a problem with his/her memory or thinking?	YES/NO
1a. If yes, is this a consistent problem (as opposed to inconsistent)?	YES/NO
2. Can the resident recall recent events?	Always/Usually/Sometimes/never With / without prompting
3. Has there been some decline in memory whilst the resident has been with you?	YES/NO
4. Does the resident completely forget an event you would have considered significant or meaningful to them? (e.g. the celebration of a wedding anniversary or family birthday party).	Always/Usually/Sometimes/never With / without prompting
5. Does the resident forget pertinent details of the major event?	Always/Usually/Sometimes/never With / without prompting
6. Does the resident completely forget important information from the distant past (e.g., birthdate, wedding date, place of employment)?	Always/Usually/Sometimes/never With / without prompting

	None 0	**Questionable** 0.5	**Mild** 1	**Moderate** 2	**Severe** 3
Memory	No memory loss or slight inconstant forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain

ORIENTATION QUESTIONS

How often does the resident know of the exact.....

1. Date of the month?	Always/Usually/Sometimes/ /never With / Without Prompting
2. Month?	Always/Usually/Sometimes//never With / Without Prompting
3. Year?	Always/Usually/Sometimes/never With / Without Prompting
4. Day of the week?	Always/Usually/Sometimes/never With / Without Prompting
5. Does the resident have difficulty with time relationships (e.g. whether it is before or after lunch)?	Always/Usually/Sometimes/ /never With / Without Prompting
6. How often can the resident find her way around indoors?	Always/Usually/Sometimes/never With / Without Prompting

	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographical disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only

Care home Number: ⌊ ⌋ ⌋ ⌋
Resident Number: ⌊ ⌋ ⌋ ⌋
Staff number: ⌊5⌋ ⌋ ⌋ ⌋
Date: ⌊ ⌋ ⌋⌊ ⌋ ⌋⌊2⌋0⌋ ⌋

JUDGEMENT AND PROBLEM SOLVING QUESTIONS

1.Thinking about his/her ability to handle a small personal budget	Is able to manage a small personal budget. Has a personal budget but needs assistance keeping track of it. Not applicable
2. Is the resident capable of interacting in a socially appropriate way with other residents? *e.g. choosing who to sit next to at meal times, responding appropriately to another distressed resident.*	Always/Usually/Sometimes/never
3. Is the resident capable of interacting in a socially appropriate way with staff? *e.g. appropriate topics of conversation, appropriately asking for assistance.*	Always/Usually/Sometimes/never
4. Does the resident have the ability to request when they need personal appointments? *e.g. to see the chiropodist, have a haircut, see a dentist.*	Always/Usually/Sometimes/never
5. Can the resident understand situations or explanations? *e.g. why dinner is late, the fire alarm being tested.*	Always/Usually/Sometimes/never
6. Does the resident behave appropriately in social situations and interactions with other people?	Always/Usually/Sometimes/never

	None 0	**Questionable** 0.5	**Mild** 1	**Moderate** 2	**Severe** 3
Judgement and Problem Solving	Solves everyday problems and handles business and financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences, social judgment usually maintained	Severely impaired in handling problems similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems

COMMUNITY AFFAIRS QUESTIONS

1. Is the resident an active member of the home community?	Yes/No *Prompt for further explanation*
2. Is the resident able to join in activities organised in the home?	Yes/No Usually/Sometimes/Rarely/Don't know
3. Does the resident interact well with other residents at social functions/activities?	Usually/Sometimes/Rarely/Don't know
4. Does the resident interact well with staff in social at social functions/activities?	Usually/Sometimes/Rarely/Don't know
5. Is the resident able to engage in family visits both: **- within the home** **- outside of the home**	Yes/No/Not applicable
6. Does the resident use the outside areas of the home through choice? *e.g. the garden area*	Yes/No/Not applicable

	None 0	**Questionable** 0.5	**Mild** 1	**Moderate** 2	**Severe** 3
Community Affairs	Independent function at usual level in job, shopping, and volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection	No pretence of independent function outside home; Appears well enough to be taken to functions outside a family home	No pretence of independent function outside home; Appears too ill to be taken to functions outside a family home

Care home Number: ⌊ ⌋ ⌋ ⌋
Resident Number: ⌊ ⌋ ⌋ ⌋
Staff number: ⌊5⌋ ⌋ ⌋ ⌋
Date: ⌊ ⌋ ⌋⌊ ⌋ ⌋⌊2⌋0⌋ ⌋

HOME AND HOBBIES FOR INFORMANT

1. What hobbies can the resident still do well?
Hobbies they used to enjoy e.g. knitting, following sports, reading the daily paper, skittles.

Prompt for frequency

2. How engaged is the resident in the home environment?
e.g. does the resident take an interest in watering plants, making their own bed, helping to set or clean the table, gardening?

Prompt for frequency

	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Home and Hobbies	Life at home, hobbies and intellectual interests well maintained	Life at home, hobbies and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult chores abandoned more complicated hobbies and interests abandoned	Only simple chores preserved; very restricted interests, poorly maintained	No significant function in home

PERSONAL CARE QUESTIONS

What is your estimate of his/her mental ability in the following areas?

1. Dressing *(The Dementia Scale of Blessed)*	Unaided	Occasionally misplaced buttons etc.	Wrong sequence, commonly forgotten items.	Unable to dress.
2. Washing, grooming.	Unaided	Needs prompting	Sometimes needs help	Always or nearly always needs help
3. Eating habits	Cleanly; proper utensils	Messily; spoon	Simple solids	Always or nearly always needs help
4. Sphincter control *(The Dementia Scale of Blessed)*	Normally complete control	Occasionally wets the bed	Frequently wets the bed	Doubly incontinent

	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Personal Care	Fully capable self-care	Fully capable self-care	Needs prompting	Requires assistance in dressing, hygiene, keeping of personal effects	Requires much help with personal care; frequent incontinence

Care home Number: ⌊ ⌋ ⌋ ⌋
Resident Number: ⌊ ⌋ ⌋ ⌋
Staff number: ⌊5⌋ ⌋ ⌋ ⌋
Date: ⌊ ⌋ ⌋⌊ ⌋ ⌋⌊2⌋0⌋ ⌋

To be completed in Research office

	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory					
Orientation					
Judgment and Problem solving					
Community affairs					
Home and Hobbies					
Personal care					

Rating ☐

Check this box If you want to confirm your rating with another researcher ☐

Check this box if the rating has been confirmed by another researcher ☐

Appendix 18 - Table describing prescribing prevalence of psychotropic classes and drugs at each study visit, and mean daily dose

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
Psychotropics	Baseline	822 (57.7%) [55.1-60.2]	655 (46.0%) [43.4-48.6]	64 (4.5%) [3.5-5.7]	102 (7.2%) [5.9-8.6]	na
	4-month	690 (56.8%) [54.0-59.6]	540 (44.4%) [41.7-47.3]	47 (3.9%) [2.9-5.1]	103 (8.5%) [7.0-10.2]	na
	12-month	491 (57.4%) [54.0-60.6]	371 (43.3%) [40.0-46.7]	46 (5.4%) [4.0-7.1]	74 (8.6%) [6.9-10.7]	na
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Anxiolytics and hypnotics	Baseline	310 (21.8%) [19.7-24.0]	160 (11.2%) [9.7-13.0]	118 (8.3%) [7.0-9.8]	31 (2.2%) [5.9-8.6]	na
	4-month	276 (22.7%) [20.4-25.2]	139 (11.4%) [9.8-13.4]	109 (9.0%) [7.5-10.7]	28 (2.3%) [1.6-3.3]	na
	12-month	195 (22.8%) [20.1-25.7]	87 (10.2%) [8.3-12.4]	87 (10.2%) [8.3-12.4]	21 (2.5%) [1.6-3.7]	na
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
Buspirone	Baseline	3 (0.2%) [0.1-0.7]	2 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.5]	0 (0%)	11.7 (5.8) 5-15
	4-month	2 (0.2%) [0.0-0.6]	2 (0.2%) [0.0-0.6]	0 (0%)	0 (0%)	10.0 (7.1) 5-15
	12-month	1 (0.1%) [0.0-0.8]	1 (0.1%) [0.0-0.8]	0 (0%)	0 (0%)	5.0 (0.0)
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (3, 3) (exc. withdrawn residents)					
Clobazam	Baseline	1 (0.1%) [0.0-0.5]	0 (0%)	1 (0.1%) [0.0-0.5]	0 (0%)	10 (0)
	4-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 1 (N/A) (inc. withdrawn residents), 1 (N/A) (exc. withdrawn residents)					
Clonazepam	Baseline	21 (1.5%) [1.0-2.3]	17 (1.2%) [0.7-1.9]	4 (0.3%) [0.1-0.8]	0 (0%)	0.7 (0.4) 0.25-1.5
	4-month	15 (1.2%) [0.7-2.0]	14 (1.2%) [0.7-1.9]	1 (0.1%) [0.0-0.6]	0 (0%)	0.8 (0.5) 0.25-2

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	14 (1.6%) [1.0-2.7]	12 (1.4%) [0.8-2.5]	2 (0.2%) [0.1-0.9]	0 (0%)	1.0 (0.7) 0.25-2.7
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Diazepam	Baseline	46 (3.2%) [2.4-4.3]	17 (1.2%) [0.7-1.9]	27 (1.9%) [1.3-2.8]	2 (0.1%) [0.0-0.6]	5.2 (3.9) 0.5-20
	4-month	43 (3.5%) [2.6-4.7]	13 (1.1%) [0.6-1.8]	28 (2.3%) [1.6-3.3]	2 (0.2%) [0.0-0.7]	4.6 (2.7) 2-12
	12-month	26 (3.0%) [2.1-4.4]	8 (0.9%) [0.5-1.9]	18 (2.1%) [1.3-3.3]	0 (0%)	6.2 (5.3) 1-20
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Lorazepam	Baseline	120 (8.4%) [7.1-10.0]	38 (2.7%) [1.9-3.6]	80 (5.6%) [4.5-6.9]	2 (0.1%) [0.0-0.6]	1.5 (0.9) 0.5-4
	4-month	112 (9.2%) [7.7-11.0]	39 (3.2%) [2.4-4.4]	69 (5.7%) [4.5-7.1]	4 (0.3%) [0.1-0.9]	1.5 (1.2) 0.5-9
	12-month	80 (9.3%) [7.6-11.5]	22 (2.6%) [1.7-3.9]	56 (6.5%) [5.1-8.4]	2 (0.2%) [0.1-0.9]	1.5 (0.8) 0.5-4

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2.5, 3) (exc. withdrawn residents)					
Lormetazepam	Baseline	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	0 (0%)	1.0 (0)
	4-month	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	1.0 (0)
	12-month	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	1.0 (0)
	Median (IQR) study visits that drug is prescribed: 3 (N/A) (inc. withdrawn residents), 3 (N/A) (exc. withdrawn residents)					
Midazolam	Baseline	23 (1.6%) [1.1-2.4]	0 (0%)	22 (1.5%) [1.0-2.3]	0 (0%)	34.5 (22.2) 2.5-60
	4-month	25 (2.1%) [1.4-3.0]	1 (0.1%) [0.0-0.5]	24 (1.7%) [1.1-2.5]	0 (0%)	78.8 (63.5) 20-240
	12-month	23 (2.7%) [1.8-4.0]	4 (0.5%) [0.1-1.2]	19 (2.2%) [1.3-3.4]	0 (0%)	43.0 (26.3) 20-120
	Median (IQR) study visits that drug is prescribed: 3 (3, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Nitrazepam	Baseline	4 (0.3%)	4 (0.3%)	0 (0%)	0 (0%)	5.9 (1.2)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[0.1-0.7]	[0.1-0.7]			5-7.5
	4-month	5 (0.4%) [0.2-1.0]	5 (0.4%) [0.2-1.0]	0 (0%)	0 (0%)	5.0 (1.8) 2.5-7.5
	12-month	4 (0.4%) [0.1-1.2]	4 (0.4%) [0.1-1.2]	0 (0%)	0 (0%)	5.6 (1.3) 5-7.5
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2.5 (1.5, 3) (exc. withdrawn residents)					
Oxazepam	Baseline	5 (0.4%) [0.1-0.8]	1 (0.1%) [0.0-0.5]	3 (0.2%) [0.1-0.7]	1 (0.1%) [0.0-0.5]	17.5 (9.6) 10-30
	4-month	4 (0.3%) [0.1-0.9]	1 (0.1%) [0.0-0.6]	3 (0.2%) [0.1-0.8]	0 (0%)	20 (0.0)
	12-month	3 (0.4%) [0.1-1.1]	1 (0.1%) [0.0-0.8]	2 (0.2%) [0.1-0.9]	0 (0%)	15.0 (7.1) 10-20
	Median (IQR) study visits that drug is prescribed: 3 (3, 3) (inc. withdrawn residents), 3 (2.5, 3) (exc. withdrawn residents)					
Temazepam	Baseline	14 (1.0%) [0.6-1.7]	13 (0.9%) [0.5-1.6]	1 (0.1%) [0.0-0.5]	0 (0%)	12.1 (6.4) 5-20

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	4-month	11 (0.9%) [0.5-1.6]	11 (0.9%) [0.5-1.6]	0 (0%)	0 (0%)	12.3 (6.5) 5-20
	12-month	6 (0.7%) [0.3-1.6]	6 (0.7%) [0.3-1.6]	0 (0%)	0 (0%)	10.8 (4.9) 5-20
	Median (IQR) study visits that drug is prescribed: 2.5 (2, 3) (inc. withdrawn residents), 3 (3, 3) (exc. withdrawn residents)					
Zolpidem	Baseline	5 (0.4%) [0.1-0.8]	5 (0.4%) [0.1-0.8]	0 (0%)	0 (0%)	5 (0)
	4-month	5 (0.4%) [0.2-1.0]	5 (0.4%) [0.2-1.0]	0 (0%)	0 (0%)	5 (0)
	12-month	4 (0.5%) [0.1-1.2]	3 (0.4%) [0.1-1.0]	1 (0.1%) [0.0-0.6]	0 (0%)	5.0 (0.0)
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 2 (2, 3) (exc. withdrawn residents)					
Zopiclone	Baseline	119 (8.4%) [7.0-9.9]	100 (7.0%) [5.8-8.5]	18 (1.3%) [0.8-2.0]	1 (0.1%) [0.0-0.5]	5.2 (2.0) 3.5-15
	4-month	98 (8.1%) [6.7-9.7]	82 (6.7%) [5.5-8.3]	15 (1.2%) [0.7-2.0]	1 (0.1%) [0.0-0.5]	4.9 (1.7) 3.75-7.5

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	12-month	68 (7.9%) [6.3-10.0]	50 (5.8%) [4.5-7.6]	18 (2.1%) [1.3-3.3]	0 (0%)	5.0 (1.8) 3.75-7.5
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2.5 (2, 3) (exc. withdrawn residents)					
Antidepressants	Baseline	578 (40.6%) [38.0-43.1]	573 (40.2%) [37.7-42.8]	3 (0.2%) [0.1-0.6]	1 (0.1%) [0.0-0.4]	na
	4-month	485 (40.0%) [37.2-42.7]	482 (39.7) [37.0-42.5]	2 (0.2%) [0.0-0.7]	1 (0.1%) [0.0-0.6]	na
	12-month	337 (39.4%) [36.1-42.7]	335 (39.1%) [35.9-42.5]	2 (0.2%) [0.1-0.9]	0 (0%)	na
	Median (IQR) study visits that drug is prescribed: 2 (1.5, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Amitriptyline	Baseline	33 (2.3%) [0.7-2.3]	31 (2.2%) [1.5-3.1]	2 (0.1%) [0.0-0.5]	0 (0%)	18.0 (18.3) 5-100
	4-month	30 (2.5%) [1.7-3.5]	30 (2.5%) [1.7-3.5]	0 (0%)	0 (0%)	19.0 (20.0) 5-100
	12-month	17 (2.0%) [1.2-3.2]	17 (2.0%) [1.2-3.2]	0 (0%)	0 (0%)	25.0 (25.7) 5-100

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Citalopram	Baseline	217 (15.2%) 13.5-17.2]	217 (15.2%) 13.5-17.2]	0 (0%)	0 (0%)	17.3 (9.1) 5-100
	4-month	172 (14.2%) [12.2-16.2]	172 (14.2%) [12.2-16.2]	0 (0%)	0 (0%)	17.6 (13.1) 5-160
	12-month	117 (13.7%) [11.4-16.2]	117 (13.7%) [11.4-16.2]	0 (0%)	0 (0%)	17.8 (9.6) 10-80
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Duloxetine	Baseline	9 (0.6%) [0.3-1.2]	9 (0.6%) [0.3-1.2]	0 (0%)	0 (0%)	45.0 (16.0) 30-60
	4-month	8 (0.7%) [0.3-1.3]	8 (0.7%) [0.3-1.3]	0 (0%)	0 (0%)	43.1 (18.7) 15-60
	12-month	6 (0.7%) [0.3-1.5]	6 (0.7%) [0.3-1.5]	0 (0%)	0 (0%)	48.3 (13.3) 30-60
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2.5 (1, 3) (exc. withdrawn residents)					
Fluoxetine	Baseline	31 (2.2%)	31 (2.2%)	0 (0%)	0 (0%)	23.0 (7.9)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[1.5-3.1]	[1.5-3.1]			10-40
	4-month	26 (2.1%) [1.4-3.1]	26 (2.1%) [1.4-3.1]	0 (0%)	0 (0%)	25.8 (13.9) 10-80
	12-month	13 (1.5%) [0.8-2.6]	13 (1.5%) [0.8-2.6]	0 (0%)	0 (0%)	21.5 (5.5) 20-40
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Lofepramine	Baseline	6 (0.7%) [0.3-1.5]	6 (0.7%) [0.3-1.5]	0 (0%)	0 (0%)	122.5 (75.9) 35-210
	4-month	5 (0.4%) [0.1-1.0]	5 (0.4%) [0.1-1.0]	0 (0%)	0 (0%)	70.0 (0.0)
	12-month	2 (0.2%) [0.0-0.8]	2 (0.2%) [0.0-0.8]	0 (0%)	0 (0%)	140.0 (99.0) 70-210
	Median (IQR) study visits that drug is prescribed: 1 (1, 1) (inc. withdrawn residents), 1 (1, 1) (exc. withdrawn residents)					
Mirtazapine	Baseline	159 (11.2%) [9.6-12.9]	159 (11.2%) [9.6-12.9]	0 (0%)	0 (0%)	28.0 (11.3) 7.5-45
	4-month	136 (11.2%)	136 (11.2%)	0 (0%)	0 (0%)	27.5 (12.1)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[8.5-13.1]	[8.5-13.1]			5-75
	12-month	94 (11.0%) [8.9-13.3]	94 (11.0%) [8.9-13.3]	0 (0%)	0 (0%)	28.9 (11.1) 7.5-45
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Paroxetine	Baseline	12 (0.8%) [0.5-1.5]	12 (0.8%) [0.5-1.5]	0 (0%)	0 (0%)	22.5 (6.2) 10-30
	4-month	10 (0.8%) [0.4-1.5]	10 (0.8%) [0.4-1.5]	0 (0%)	0 (0%)	23.3 (5.0) 20-30
	12-month	9 (1.1%) [0.5-2.0]	9 (1.1%) [0.5-2.0]	0 (0%)	0 (0%)	22.2 (6.7) 10-30
	Median (IQR) study visits that drug is prescribed: 3 (2.5, 3) (inc. withdrawn residents), 3 (3, 3) (exc. withdrawn residents)					
Phenelzine	Baseline	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	0 (0%)	30.0 (0.0)
	4-month	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	0 (0%)	30.0 (0.0)
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	Median (IQR) study visits that drug is prescribed: 2 (2, 2) (inc. withdrawn residents), 2 (2, 2) (exc. withdrawn residents)					
Sertraline	Baseline	81 (5.7%) [4.6-7.0]	80 (5.6) [4.5-6.9]	0 (0%)	0 (0%)	85.6 (67.8) 25-500
	4-month	75 (6.2%) [4.9-7.7]	75 (6.2%) [4.9-7.7]	0 (0%)	0 (0%)	77.8 (42.6) [25-200]
	12-month	64 (7.5%) [5.8-9.4]	64 (7.5%) [5.8-9.4]	0 (0%)	0 (0%)	75.0 (42.0) 25-200
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Trazodone	Baseline	62 (4.4%) [3.4-5.5]	60 (4.2%) [3.3-5.4]	2 (0.1%) [0.0-0.6]	0 (0%)	92.8 (53.6) 25-250
	4-month	47 (3.9%) [2.9-5.1]	44 3.6%) [2.7-4.8]	2 (0.2%) [0.0-0.7]	1 (0.1%) [0.0-0.5]	92.1 (45.8) 10-200
	12-month	30 (3.5%) P2.5-5.0]	28 (3.3%) [2.3-4.7]	2 (0.2%) [0.1-0.9]	0 (0%)	91.7 (47.9) 25-200
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (1, 3) (exc. withdrawn residents)					
Venlafaxine	Baseline	17 (1.2%)	17 (1.2%)	0 (0%)	0 (0%)	113.8 (53.7)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[0.7-1.9]	[0.7-1.9]			22-225
	4-month	16 (1.3%) [0.8-2.1]	16 (1.3%) [0.8-2.1]	0 (0%)	0 (0%)	124.2 (56.0) 37.5-225
	12-month	14 (1.6%) [0.9-2.7]	14 (1.6%) [0.9-2.7]	0 (0%)	0 (0%)	133.9 (52.4) 75-225
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Antipsychotics	Baseline	246 (17.3%) [15.4-19.3]	219 (15.4%) [13.6-17.3]	19 (1.3%) [0.9-2.1]	8 (0.6%) [0.3-1.1]	na
	4-month	209 (17.2%) [15.2-19.4]	189 (15.6%) 13.6-17.7]	14 (1.2%) [0.6-1.9]	6 (0.5%) [0.2-1.1]	na
	12-month	158 (18.5%) [16.0-21.2]	136 (15.9%) [13.6-18.5]	14 (1.6%) [1.0 -2.7]	8 (0.9) [0.5-1.9]	na
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Amisulpride	Baseline	16 (1.1%) [0.7-1.8]	16 (1.1%) [0.7-1.8]	0 (0%)	0 (0%)	98.4 (97.7) 25-400
	4-month	11 (0.9%)	10 (0.8%)	0 (0%)	1 (0.1%)	87.5 (66.9)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[0.5-1.6]	[0.4-1.5]		[0.0-0.5]	25-200
	12-month	9 (1.1%) [0.5-2.0]	9 (1.1%) [0.5-2.0]	0 (0%)	0 (0%)	133.3 (136.4) 25-400
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Aripiprazole	Baseline	6 (0.4%) [0.2-0.9]	6 (0.4%) [0.2-0.9]	0 (0%)	0 (0%)	12.1 (7.5) 2.5-20
	4-month	5 (0.4%) [0.1-1.0]	5 (0.4%) [0.1-1.0]	0 (0%)	0 (0%)	14 (6.5) 5-20
	12-month	5 (0.6%) [0.2-1.4]	5 (0.6%) [0.2-1.4]	0 (0%)	0 (0%)	9.0 (4.2) 5-15
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 2.5 (1, 3) (exc. withdrawn residents)					
Chlorpromazine	Baseline	1 (0.1) [0.0-0.5]	1 (0.1) [0.0-0.5]	0 (0%)	0 (0%)	179.0 (0.0)
	4-month	1 (0.1%) [0.0-0.5]	1 (0.1%) [0.0-0.5]	0 (0%)	0 (0%)	175.0 (0.0)
	12-month	0 (0%)	0 (0%)	0 (0%)	0 (0%)	na

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
	Median (IQR) study visits that drug is prescribed: 2 (2, 2) (inc. withdrawn residents), 2 (2, 2) (exc. withdrawn residents)					
Clozapine	Baseline	2.0 (0.1%) [0.0-0.6]	2.0 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	275.0 (35.4) 250-300
	4-month	2 (0.2%) [0.0-0.6]	2 (0.2%) [0.0-0.6]	0 (0%)	0 (0%)	275.0 (35.4) 250-300
	12-month	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	250.0 (0.0)
	Median (IQR) study visits that drug is prescribed: 2.5 (2, 3) (inc. withdrawn residents), 3 (3, 3) (exc. withdrawn residents)					
Flupentixol	Baseline	4 (0.3%) [0.1-0.7]	4 (0.3%) [0.1-0.7]	0 (0%)	0 (0%)	2.0 (1.4) 1-3.6
	4-month	4 (0.3%) [0.1-0.8]	4 (0.3%) [0.1-0.8]	0 (0%)	0 (0%)	1.0 (0.3) 0.7-1.3
	12-month	3 (0.4%) [0.1-1.0]	3 (0.4%) [0.1-1.0]	0 (0%)	0 (0%)	1.1 (0.6) 0.7-1.5
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 2.5 (1.5, 3) (exc. withdrawn residents)					
Haloperidol	Baseline	16 (1.1%)	7 (0.5%)	9 (0.6%)	0 (0%)	4.3 (4.2)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[0.7-1.8]	[0.2-1.0]	[0.3-1.2]		1-15
	4-month	16 (1.3%) [0.8-2.1]	9 (0.7%) [0.4-1.4]	7 (0.6%) [0.3-1.2]	0 (0%)	6.0 (8.9) 1-30
	12-month	13 (1.5%) [0.8-2.6]	6 (0.7%) [0.3-1.6]	7 (0.8%) [0.4-1.7]	0 (0%)	2.9 (3.3) [1-11.5]
	Median (IQR) study visits that drug is prescribed: 3 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Levomepromazine	Baseline	4 (0.3%) [0.1-0.7]	0 (0%)	4 (0.3%) [0.1-0.7]	0 (0%)	137.5 (147.4) 12.5-300
	4-month	2 (0.2%) [0.0-0.6]	0 (0%)	2 (0.2%) [0.0-0.6]	0 (0%)	81.3 (97.2) 12.5-150
	12-month	3 (0.4%) [0.1-1.0]	1 (0.1%) [0.0-0.6]	2 (0.2%) [0.0-0.8]	0 (0%)	25.0 (0.0)
	Median (IQR) study visits that drug is prescribed: 3 (3, 3) (inc. withdrawn residents), 1 (1, 1) (exc. withdrawn residents)					
Olanzapine	Baseline	23 (1.6%) [1.1-2.4]	23 (1.6%) [1.1-2.4]	0 (0%)	0 (0%)	6.7 (5.9) 2.5-20
	4-month	19 (1.6%)	19 (1.6%)	0 (0%)	0 (0%)	6.7 (6.3)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[0.9-2.4]	[0.9-2.4]			2.5-20
	12-month	17 (2.0%) [1.2-3.2]	17 (2.0%) [1.2-3.2]	0 (0%)	0 (0%)	6.9 (6.0) 2.5-20
	Median (IQR) study visits that drug is prescribed: 3 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Promazine	Baseline	14 (1.0%) [0.6-1.7]	6 (0.4%) [0.2-0.9]	7 (0.5%) [0.2-1.0]	1 (0.1%) [0.0-0.5]	63.2 (47.9) 10-200
	4-month	9 (0.7%) [0.4-1.4]	5 (0.4%) [0.2-1.0]	2 (0.2%) [0.0-0.7]	2 (0.2%) [0.0-0.7]	53.9 (58.2) 10-200
	12-month	5 (0.6%) [0.2-1.4]	3 (0.4%) [0.1-1.1]	2 (0.2%) [0.1-0.9]	0 (0%)	85.0 (69.8) 25-200
	Median (IQR) study visits that drug is prescribed: 2.5 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Quetiapine	Baseline	58 (4.1%) [3.2-5.2]	55 (3.9%) [3.0-5.0]	1 (0.1%) [0.0-0.5]	2 (0.1%) [0.0-0.6]	69.6 (61.3) 10-300
	4-month	54 (4.4%) [3.4-5.8]	52 (4.3%) [3.3-5.6]	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	75.2 (76.2) 12.5-400
	12-month	39 (4.6%)	38 (4.4%)	0 (0%)	1 (0.1%)	68.9 (81.5)

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
		[3.3-6.2]	[3.2-6.0]		[0.0-0.6]	12.5-400
	Median (IQR) study visits that drug is prescribed: 2 (2, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Risperidone	Baseline	106 (7.4%) [6.2-8.9]	103 (7.2%) [6.0-8.7]	3 (0.2%) [0.1-0.7]	0 (0%)	0.9 (0.8) 0.25-6
	4-month	86 (7.1%) [5.8-8.7]	81 (6.7%) [5.4-8.2]	3 (0.2%) [0.1-0.8]	2 (0.2%) [0.0-0.7]	1.0 (0.9) 0.25-6
	12-month	65 (7.6%) [6.0-9.6]	57 (6.7%) [5.2-8.5]	4 (0.5%) [0.2-1.2]	4 (0.5%) [0.2-1.2]	1.2 (1.1) 0.25-6.25
	Median (IQR) study visits that drug is prescribed: 2 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					
Sulpiride	Baseline	5 (0.4%) [0.1-0.8]	5 (0.4%) [0.1-0.8]	0 (0%)	0 (0%)	140 (54.8) 100-200
	4-month	5 (0.4%) [0.2-1.0]	5 (0.4%) [0.2-1.0]	0 (0%)	0 (0%)	108.0 (57.6) 40-200
	12-month	3 (0.4%) [0.1-1.1]	3 (0.4%) [0.1-1.1]	0 (0%)	0 (0%)	180.0 (192.9) 40-400
	Median (IQR) study visits that drug is prescribed: 2.5 (1, 3) (inc. withdrawn residents), 3 (2, 3) (exc. withdrawn residents)					

	Study visit	Total N (%) [95% CI]	Regular only N (%) [95% CI]	PRN only N (%) [95% CI]	Both regular + PRN N (%) [95% CI]	Daily dose (mg) Mean (SD) range
Trifluoperazine	Baseline	2 (0.1%) [0.0-0.6]	2 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	6.5 (4.9) 3-10
	4-month	2 (0.2%) [0.0-0.7]	2 (0.2%) [0.0-0.7]	0 (0%)	0 (0%)	6.5 (4.9) 3-10
	12-month	1 (0.1%) [0.0-0.6]	1 (0.1%) [0.0-0.6]	0 (0%)	0 (0%)	5.0 (0.0)
	Median (IQR) study visits that drug is prescribed: 2.5 (2, 3) (inc. withdrawn residents), 3 (3, 3) (exc. withdrawn residents)					

Appendix 20 – Published *British Journal of Psychiatry Open* paper

Prevalence of and associations with agitation in residents with dementia living in care homes: MARQUE cross-sectional study

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Background
Agitation is reportedly the most common neuropsychiatric symptom in care home residents with dementia.

Aims
To report, in a large care home survey, prevalence and determinants of agitation in residents with dementia.

Method
We interviewed staff from 86 care homes between 13 January 2014 and 12 November 2015 about residents with dementia with respect to agitation (Cohen-Mansfield Agitation Inventory (CMAI)), quality of life (DEMQOL-proxy) and dementia severity (Clinical Dementia Rating). We also interviewed residents and their relatives. We used random effects models adjusted for resident age, gender, dementia severity and care home type with CMAI as a continuous score.

Results
Out of 3053 (86.2%) residents who had dementia, 1489 (52.7%) eligible residents participated. Fifteen per cent of residents with very mild dementia had clinically significant agitation compared with 33% with mild (odds ratios (ORs)=4.49 95% confidence interval (CI)=2.30) and 45% with moderate or severe dementia (OR=6.95 95% CI=3.63, 13.31 and OR=6.23 95% CI=3.25, 11.94, respectively). More agitation was associated with lower quality of life (regression coefficient (rc)=−0.53; 95% CI=−0.61, −0.46) but not with staffing or resident ratio (rc=0.03; 95% CI=−0.04, 0.11), level of residents' engagement in home activities (rc=3.21; 95% CI=−0.82, 7.21) or family visit numbers (rc=−0.03; 95% CI=−0.15, 0.08). It was correlated with antipsychotic use (rc=6.45; 95% CI=3.98, 8.91).

Conclusions
Care home residents with dementia and agitation have lower quality of life. More staffing time and activities as currently provided are not associated with lower agitation levels. New approaches to develop staff skills in understanding and responding to the underlying reasons for individual resident's agitation require development and testing.

Declaration of interest
None.

Agitation is often considered a symptom of distress in people with dementia,[1,2] leading to family distress and burden.[3,4] It accounts for about 12% of health and social care costs for people with dementia.[2,3,5] Agitation refers to a range of behaviours including restlessness, pacing, repetitive vocalisations and verbally or physically aggressive behaviour[1,6] It is the most common neuropsychiatric symptom,[7–9] and it is more persistent when more severe.[10] In community settings, its prevalence increases with dementia severity. Prevalence is around 10% in people with mild cognitive impairment,[11] 15% in people with dementia presenting to memory clinics[12] and 30% in those living in the community.[13,14]

Many people with dementia and agitation are admitted to care homes, with the relationship between agitation and admission mediated by carer distress.[4,15] Although we may, therefore, expect many residents of care homes to be agitated, there have been no large, representative studies to determine whether this is the case, or how agitation levels relate to dementia severity in care homes. In a UK survey of 233 care home residents, agitation was the most common clinically significant neuropsychiatric symptom, with 40% of participants experiencing some symptoms.[16] In the largest care homes study of agitation to date, among 1322 people with dementia in 59 units in the Netherlands, 85% showed at least one symptom of agitation, most frequently general restlessness.[16,17] Physical aggression was more common in people with very severe dementia, and disinhibition, irritability and verbally agitated behaviours were more common in moderate dementia.[18] Agitation has been associated with lower quality of life in small care home studies.[19–21]

Symptoms of agitation are often conceptualised as arising from unmet need[22] in a person unable to identify, communicate and respond to their own needs, who also has brain pathology predisposing to disinhibition and repetitive behaviour. This model is supported by findings from small randomised controlled trials that activities, sensory interventions, structured music therapy and interventions to improve staff communication, prevent or reduce agitation.[23] Nonetheless, there is no good evidence that care home residents with dementia are less agitated or have a higher quality of life, when they have access to more activity or social interaction (from family visits or a higher number of staff). This is particularly important given the need to provide ways to manage agitation alternative to antipsychotic prescribing,[24,25] levels of which may now be steady, despite initiatives to reduce their use.[26,27]

This is the largest study of residents with dementia in care homes to date. Our primary aim is to discover how common clinically significant agitation is and test our hypothesis that in residents with dementia, higher levels of agitation are associated with lower quality of life. Our secondary hypotheses from the literature above suggesting that agitation is caused by dementia and unfulfilled needs in terms of less social interaction, stimulation and activity are that agitation is associated with: (1) more severe dementia, (2) fewer staff numbers per resident, (3) fewer family visits and (4) lower care home activity levels. We will also explore the relationship of agitation to psychotropic medication prescription and care home environment.

Method

This study reports the Managing Agitation and Raising QUality of lifE in dementia (MARQUE) longitudinal care home study baseline findings. It received ethical approval from the London (Harrow) NRES Committee (14/LO/0034).

Setting and sampling

We recruited care homes across England. Our sampling frame comprised each provider type (voluntary, state and private), care provision (nursing, residential) and reflected English care home provision where people with dementia resided to ensure external validity and generalisability. We defined care home clusters as units within care homes in which staff and managers worked separately. If staff in units cross-covered each other we defined this as one cluster.

Procedures

We recruited through third sector partners, NHS trusts and clinicians, a Department of Health newsletter and the NIHR Clinical Research Network. We sought care home managers' agreement for each home's inclusion. Each manager provided a staff list and identified residents with a known clinical dementia diagnosis. Care home staff completed the Noticeable Problems Checklist (NPC)[28] for all residents without a known diagnosis of dementia, to identify those with probable undiagnosed dementia. The NPC is a six-item questionnaire covering memory, basic self-care, orientation, naming familiar people and ability to follow conversations, which has been used by non-clinicians and which has been validated against clinical diagnosis.[28,29] Eligible participants were all residents with an existing dementia diagnosis or those who screened positive for dementia, and their family and care home staff.

Staff asked residents, whom they judged as having decisional competence for consent, if researchers could approach them. Residents who had decisional competence for consent were asked for written informed consent to the study. Consultees were asked to make this decision for those lacking capacity in line with the Mental Capacity Act (2005). For all other residents, the staff tried to contact the next-of-kin (to participate in family carer interviews) and asked if the researchers could contact them. Participating staff and relatives gave written informed consent. We asked a staff member working closely with each resident with dementia to rate proxy measures for the resident and then asked the relative to do the same. In addition, all consenting staff providing hands-on care completed questionnaires about themselves as did consenting relatives. All participants were recruited between 13 January 2014 and 12 November 2015.

Measures

Trained research assistants interviewed staff and residents in a private room at the care home. We interviewed family carers in their preferred location: in the care home, their own home or the researcher's office.

Care home measures

We recorded information about the care home, including whether it was a residential or nursing home, number of residents (in total and with dementia), staff numbers, and programmed activities with number of attendees.

We used the Therapeutic Environment Screening Survey for Nursing Homes and Residential Care (TESS-NH/RC), which has satisfactory psychometric properties, to rate the care home's physical environment.[30] The TESS sums 15 environmental items, each scoring from 0 to 2 (facility maintenance, cleanliness, handrails, call buttons, light intensity, light glare, light evenness, hallway length (shorter is better), homelikeness, room autonomy, the presence of telephones, tactile stimulation, visual stimulation, privacy and outdoor areas) into the Environmental Quality Score (EQS). Higher scores indicate better environmental quality.[31]

Residents measures

We recorded demographic information and completed the following measures:

1. Agitation: our primary outcome was the Cohen-Mansfield Agitation Inventory (CMAI), a 29-item questionnaire with construct validity and reliability to measure agitation in people with dementia in care homes.[32,33] The CMAI is an informant questionnaire and each item scores from 1 to 7, with 1 meaning 'never' and 7 'several times per hour'. The score sums individual items and ranges from 29 to 203. A score of >45 is usually regarded as clinically significant agitation.[34]
2. Quality of life: The DEMQOL and DEMQOL proxy are responsive, valid and reliable measures of quality of life in people with dementia.[35,36] The DEMQOL-Proxy is a 31-item interviewer-administered questionnaire answered by a professional or family carer. The people with dementia who were able to were asked to complete the DEMQOL, a 28-item interviewer-administered questionnaire.[36] As the DEMQOL has fewer questions than the DEMQOL proxy, the totals are not directly comparable.
3. Dementia severity: Staff gave information so the researcher could rate the severity of dementia by the Clinical Dementia Rating (CDR).[37] This is a reliable and valid instrument for rating severity of dementia.[38] It is used to rate performance in memory, orientation, judgment and problem-solving, community affairs, home and hobbies, and personal care, and this information was used to classify dementia severity of included residents into very mild, mild, moderate or severe.
4. Neuropsychiatric symptoms: the Neuropsychiatric Inventory (NPI)[39] is a validated instrument with 12 domains of neuropsychiatric symptoms, including agitation. Each domain scores between 0 and 12 with higher scores meaning increasing severity. A score of ≥4 on any domain is usually considered clinically significant severity.[14] A summed scored can be calculated for total neuropsychiatric symptoms.

Staff self-rated measures

Staff working in the care home provided their demographic details and working patterns.

Family carer measures

We asked relatives visiting residents at least monthly to complete the DEMQOL-proxy[36] and tell us how often they visited. We recorded their gender and relationship to the person with dementia.

Analysis

We used Stata version 14 for all analyses.[40] Characteristics of care homes and people with dementia, including CMAI scores and presence of significant agitation, are summarised by frequency (%) mean (standard deviation (s.d.)) or median (interquartile range (IQR)) as appropriate. To obtain values more relevant to the types of care home in England, we weighted estimates, using population

information about the distribution of care home types (nursing or residential and private sector or voluntary, local authority (LA) and National Health Service (NHS)). Probability weights were based on available figures in England from the Care Quality Commission (CQC) from 31 December 2012. At this time, 73% of the total 17 592 care homes were residential homes. The remaining 27% were either nursing homes or both nursing and residential. Seventy five per cent of care homes in England were private whereas 25% were 'voluntary' (non-profit sector), LA or NHS. In calculating the weights, we assumed that the percentage of residential and nursing homes was the same within the private sector and voluntary, LA and NHS.

To investigate our primary and secondary hypotheses, we used random effects models to account for care home or unit clustering and adjusted for residents' age, gender, CDR dementia severity and care home type (residential or nursing or both, dementia specialist, dementia registered). For the primary hypothesis, we also fitted a three-level model accounting for clustering by staff member, as some provided information about multiple residents in the home. We carried out analyses with CMAI as a continuous score. As we found some skewness in model residuals for this outcome, we checked results in sensitivity analyses based on generalised linear models with a gamma distribution. In further sensitivity analyses, we fitted models with CMAI as two groups defined by presence of clinically significant agitation (CMAI>45). Again we controlled for residents' age, gender, dementia severity, care home type (residential, nursing or both, dementia specialist, dementia registered). We also carried out an additional sensitivity analysis with significant agitation defined by the NPI agitation domain score (significant agitation is a score ≥4) in place of CMAI.

Results

Study participation

Out of the 114 care homes we contacted, 86 (75.4%) participated. Of the 28 who did not participate, 21 were nursing or mixed nursing and residential and 7 were residential only. Among the 28 care homes, 22 did not wish to participate, 5 were too busy or had a new manager and 1 was excluded as in another research project. We therefore recruited 86 care homes: 7 homes were divided into >1 cluster, totalling 18 clusters. The sample, therefore, was 97 clusters.

Our flow diagram (Fig. 1) shows residents' recruitment to the study. After considering pre-existing clinical dementia diagnosis and those who screened positive on the NPC, 3053 (86.2%) residents within the care homes had probable dementia and thus were eligible. Out of the 2825 residents who were approached, 1489 (52.7%) participated. The common reasons for non-participation were refusal (27.3%) and staff being unable to contact the family consultee (17.6%). Of the participating residents, 300 (20.1%) had capacity to consent to the study and we used a consultee for the remainder. We have no data for six residents for whom we had consent, as five died and one moved before data were collected, so our analyses are based on 1483 people. Out of 1483, 1281 (86.4%) had a pre-existing clinical diagnosis of dementia and the remainder scored positive on the NPC. The number of recruited residents per cluster ranged from 2 to 55 (median 14).

In total, 1281 (86.4%) of consenting residents had an identified family member who agreed to participate. A total of 1701 care home staff consented. Numbers of staff per cluster ranged from 3 to 54 (median 15). Care home and staff characteristics are summarised in Table 1.

Sample characteristics

Table 2 shows recruited residents' and relatives' demographic characteristics. Approximately equal proportions of residents were classified as having severe, moderate, or mild or very mild dementia. Around two-thirds of identified family members were women and a similar proportion were sons or daughters. The median number of visits residents received from their main family carer was six each month.

Table 3 summarises agitation, quality of life scores and psychotropic medication. Staff and family members' total quality of life proxy ratings were similar, however, the correlations between family- and staff-rated DEMQOL was low at 0.35. More than half the residents were prescribed psychotropic medication, most commonly antidepressants (40%).

Agitation levels and correlates

A total of 209 (14.7%) residents did not have symptoms of agitation, whereas 569 (40%) had clinically significant agitation according to CMAI and 465 (32%) on the NPI (Table 3). Fifteen (13%) of those with very mild dementia had clinically significant levels of agitation (CMAI cases). In comparison, the prevalence was higher in other CDR categories (mild dementia 102 (33%), moderate dementia 212 (45%), severe dementia 239 (45%)). A random effects logistic regression model adjusted for resident's age, gender, care home type (residential, nursing or both, dementia specialist, dementia registered) showed significantly greater odds of CMAI caseness in participants with mild, moderate and severe compared with very mild dementia. (odds ratios (ORs): mild dementia 4.49, 95% confidence interval (CI)=2.30 to 8.74; moderate dementia 6.95, 95% CI=3.63 to 13.31; and severe dementia 6.23, 95% CI=3.25 to 11.94).

Average CMAI score in those with very mild dementia was 37.0, s.d.=10.4, which was lower than other CDR categories (mild 43.5, s.d.=15.6; moderate 48.7, s.d.=19.0; severe 48.3, s.d.=19.7). A random effects model adjusted for resident's age, gender, care home type (residential, nursing or both, dementia specialist, dementia registered) indicated significant CMAI differences between very mild and other CDR categories (mild dementia coefficient 7.35, 95% CI=3.55 to 11.44; moderate dementia 11.04, 95% CI=7.34 to 14.71; severe dementia 9.70, 95% CI=6.01 to 13.39).

Higher agitation levels were significantly associated with lower staff and family ratings of the resident's quality of life, and with prescription of antipsychotics and hypnotics but not analgesics or antidepressants (Table 4). Agitation levels were not associated with frequency of family visits, time spent in activities per resident, staff ratios, number of residents or quality of the environment.

Sensitivity analyses

Sensitivity analyses based on agitation caseness showed exactly the same pattern (Table 5) as did analyses with models based on a gamma distribution. Analyses with caseness based on NPI agitation scores also showed similar associations except increased staff numbers and staff:resident ratios were associated with increased resident agitation (adjusted analysis for higher staff numbers to NPI agitation caseness, OR=1.010 (95% CI 1.003, 1.017)) (Table 6). The significant relationship with staff-rated quality of life was also maintained in a three-level model incorporating clustering by staff member (adjusted regression coefficient −0.53, (95% CI: −0.61 to −0.46)). Information about the number of family visits each month was missing for 15% of people. A sensitivity analysis assuming this equated to no visits did not change the results.

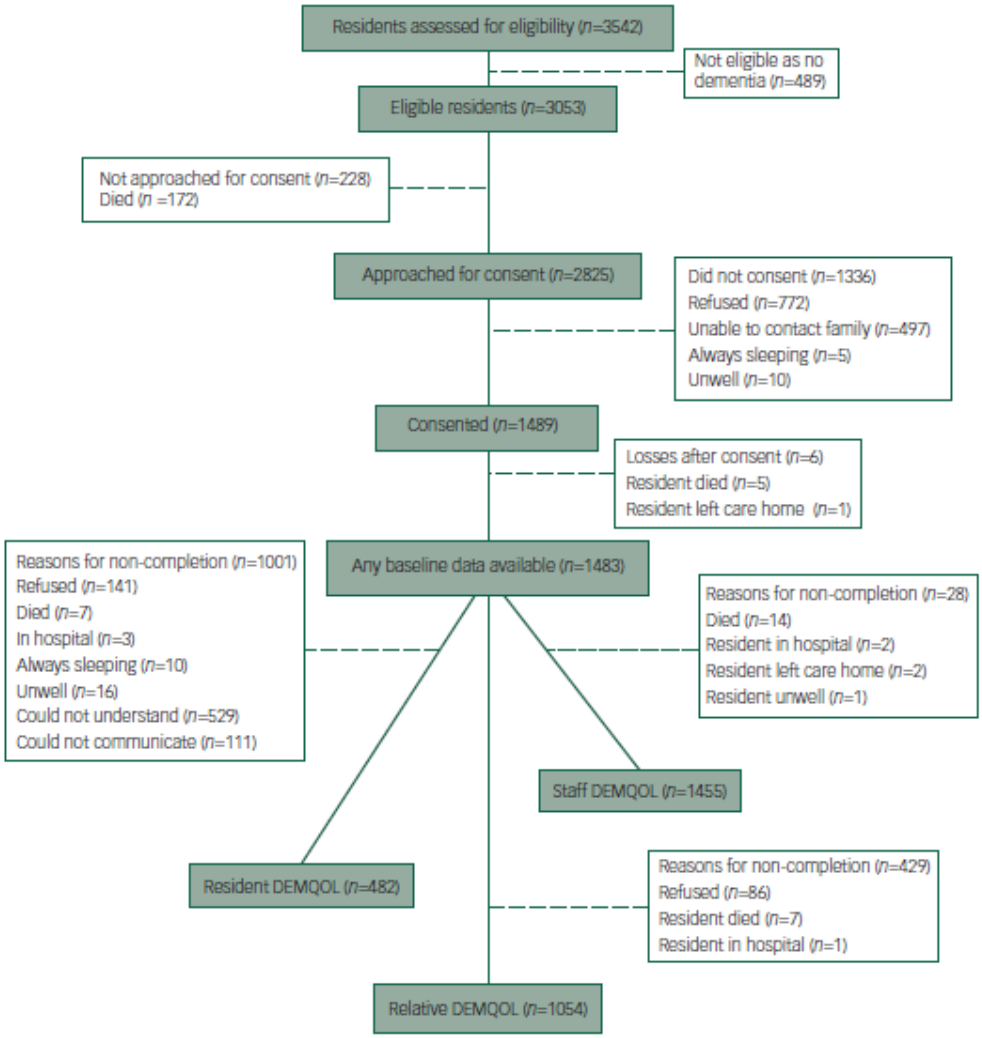

Fig 1 MARQUE baseline flow diagram of recruited residents.

Discussion

We found that 86% of care home residents had dementia. Of those, 40% had clinically significant agitation symptoms and 86% had some symptoms. Those who were agitated had a lower quality of life as rated by staff and family carers, confirming our hypothesis that agitation in care home residents with dementia is associated with lower quality of life. Earlier studies had suggested that there may be relationship but a recent systematic review found there was insufficient available evidence to draw conclusions.[20,21,41]

Agitation in care home residents is, as in the community, associated with more severe (as opposed to very mild) dementia. This relationship is not linear, with 45% of those with both moderate and severe dementia having clinically significant agitation. This indicates that agitation is not wholly a symptom of worsening brain pathology or it would parallel cognition in its severity. The high prevalence of agitation in care homes probably relates to the greater likelihood of people with agitation moving to a care home and the high prevalence of moderate and more severe dementia within care homes, as well as a lack of effective strategies to manage it.

Improving the overall environment, good staffing levels and overall time spent in activities is desirable. Although these factors differed among the homes in the study, they were not associated with levels of agitation. Our analysis did not find that lower staff numbers in care homes were related to agitation. There was a non-significant trend towards higher staff/resident ratios and more agitation (Table 4). This might be because additional staff members were booked to manage the most agitated residents, and because the quality rather than quantity of interaction is important. The number of staff present does not capture what they do and the degree to which individual residents' needs are met. In addition, there are laws about statutory minimum levels of staffing, so while there is some variation in staffing levels between homes, it is not huge. A recent intervention study of a variety of strategies taught to staff including social interaction and exercise found that none of the strategies reduced agitation.[42] It may be that staff also require the skills to communicate with residents who have

Table 1 Care home or unit and staff characteristics (numbers are frequency (%) unless stated otherwise)

Care homes or units characteristic *n*=97	Unweighted	Weighted for England[a]
Home or unit type		
Nursing	13 (13%)	5%
Personal care (residential)	39 (40%)	73%
Nursing and personal care	45 (46%)	22%
Dementia registered home	86 (89%)	88%
Dementia specialist home	42 (43%)	45%
Environmental quality score (TESS) mean (s.d.) *n*=86	16 (3)	16 (2)
Care home activity participation (hours per person per week) median (IQR) *n*=89 (range: 0.30–18.87 hours)	2.07 (1.43, 3.08)	2.15 (1.40, 3.70)
Total number of resident places in the home median (IQR)	38 (27, 54)	36 (26, 51)
Total permanent nursing and care staff in previous week median (IQR) *n*=96	32 (20, 50)	27 (16, 42)
Staff/resident ratio mean (s.d.) *n*=96	1:1 (1:2.22)	1:1.08 (1:2)
Staff		
Staff works days only *n*=1693	1150 (68%)	68%
Staff works any other shift pattern	543 (32%)	32%

IQR, interquartile range.
a. For the MARQUE cohort, 28 care homes were private residential, 50 private nursing or nursing and residential, 11 non-private residential and 8 non-private nursing or nursing and residential. Probability weights were calculated as number of care homes in the given category in England or number of care homes in the same category in MARQUE.

Table 2 Sociodemographic characteristics of baseline MARQUE cohort (Numbers are frequency (%) unless otherwise stated)

Resident characteristic	Unweighted	Weighted for England[a]
Male *n*=1483	457 (31%)	28%
Age, years: mean (s.d.) *n*=1437	85 (9)	86 (8)
Ethnicity *n*=1452		
White British	1281 (88%)	91%
White Irish	43 (3%)	2%
White other	50 (3%)	3%
Black British, Caribbean, African	33 (2%)	2%
Asian or Asian British, Indian Pakistani, Bangladeshi	13 (1%)	0.5%
Mixed: White and Black Caribbean	1 (0.1%)	0.03%
Chinese	2 (0.1%)	0.1%
Other	29 (2%)	2%
Dementia severity (CDR) *n*=1458		
Very mild	114 (8%)	10%
Mild	313 (21%)	23%
Moderate	482 (33%)	33%
Severe	549 (38%)	34%
Family member characteristic		
Male *n*=1102	341 (31%)	32%
Age, years: mean (s.d.) *n*=1048	63 (11)	63 (11)
Relationship *n*=1101		
Spouse	209 (19%)	15%
Son or daughter	674 (61%)	65%
Son or daughter-in-law	28 (3%)	2%
Grandchild	15 (1%)	2%
Friend	38 (3%)	3%
Other	137 (12%)	13%
Number of family visits per month: median (IQR) *n*=1243	6 (3, 13)	4 (2, 13)

CDR, Clinical Dementia Rating; IQR, interquartile range.
a. For the MARQUE cohort, 28 care homes were private residential, 50 private nursing or nursing and residential, 11 non-private residential and 8 non-private nursing or nursing and residential. Probability weights were calculated as number of care homes in the given category in England or number of care homes in the same category in MARQUE.

difficulty knowing or conveying what they need, and to identify the needs of individual agitated residents.

In a cross-sectional study, the number of family visits a month may reflect a resident's needs, with relatives visiting more when a resident is more unwell and, conversely, with relatives visiting those who are most impaired less frequently with few perceived opportunities for communication.[43] Individuals whose relatives have been unable to manage are more likely to be admitted to care homes and their family members are often themselves distressed. Seeing family can trigger feelings of loss, particularly when they leave. Therefore some family carers may avoid visiting. We measured how often the main family carer visited and did not account for other visitors. Thus it may be too simplistic to expect that agitation may be related to this measure.

Perhaps more extensive participation in activities was not associated with reduced agitation because only less agitated residents are approached to take part, as they are more likely to agree to join in an activity, to remain there and be less disruptive. A recent ethnographic study found that residents with the highest levels of needs were not included in activities.[44]

Previous estimates of the proportion of residents in care homes with dementia are similar to ours but they vary depending on the type of care home, with lower proportions of people with dementia in residential than nursing homes and the highest proportion in designated homes for elderly residents with mental illness.[16,45] Unsurprisingly, residents with agitation are more likely to be taking antipsychotics and sedatives as medication is a frequently used management strategy for these behaviours. In contrast, residents with agitation are no more likely to be prescribed analgesics or antidepressants. This suggests that staff do not consider that agitation may be a manifestation of pain, despite some trial evidence that it can be.[26,46] Encouragingly, we reported lower antipsychotic use that appears to have been halved (to 15%) because an influential 2010 report recommended that they are used less.[47] However, we report higher rates of antidepressants prescriptions compared with the 2010 report. Both these trends are consistent with international studies.[48–50]

We did not find a link between the quality of the environment (measured by the TESS in our study) and quality of life. Surprisingly, the one other study to investigate this found that quality of life was negatively associated with a good environment.[51] Thus a good environment may not be enough to improve quality of life. An improved environment may be of little benefit to some individuals, especially if they remain in one room of the care home and do not routinely access the better space, the outdoors and natural light.

The staff and family mean total proxy ratings of quality of life on the whole group of residents were similar and this is in line with a systematic review and meta-analysis of previous reported studies using other quality of life measures for people with dementia;[52] the correlation between the ratings regarding individuals was not high. This also showed that staff and families have previously taken into consideration different factors when considering quality of life and we will explore this further in this study to help us understand the role of different proxy raters.

Table 3 Resident agitation, quality of life and medication (numbers are frequency (%) or median (IQR))

Resident characteristic	Unweighted	Weighted for England
Agitation		
CMAI		
Agitation case (CMAI) *n*=1424	569 (40%)	41%
CMAI total *n*=1424	41 (33, 55)	41 (32, 56)
NPI		
Positive NPI agitation (stem question) *n*=1450	833 (57%)	57%
NPI agitation (frequency*severity 4+) *n*=1449	465 (32%)	31%
Quality of life (DEMQOL)		
Resident completed *n*=482	92 (80, 101)	94 (83, 102)
Staff proxy *n*=1455	104 (95, 110)	104 (95, 111)
Family proxy *n*=1054	101 (90, 109)	102 (90, 109)
Medication prescribed *n*=1483		
Any psychotropic medication[a]	825 (56%)	54%
Antipsychotics	248 (17%)	15%
Antidepressants	587 (40%)	39%
Anxiolytics or hypnotics[b]	285 (19%)	18%
Analgesia	961 (65%)	64%

CMAI, Cohen-Mansfield Agitation Inventory; IQR, interquartile range.
a. Any of antidepressants, antipsychotics, hypnotics or anxiolytics.
b. Not including melatonin as not classed as a psychotropic drug (16 residents were prescribed melatonin).

Table 4 Regression analysis of relationship of quality of life and other factors to agitation score (CMAI)

	Adjusted regression coefficient	95% confidence interval
Quality of life (DEMQOL)		
Staff proxy *n*=1391	−0.53	(−0.61, −0.46)
Family proxy *n*=1004	−0.26	(−0.33, −0.18)
Resident completed *n*=447	−0.06	(−0.14, 0.03)
Number of family visits per month *n*=1182	−0.03	(−0.15, 0.08)
Number of resident places in cluster *n*=1396	−0.02	(−0.10, 0.05)
Care home activity participation (hours per person per week) *n*=1263	0.46	(−0.15, 1.07)
Total number of permanent nursing and care staff in the previous 7 days *n*=1344	0.03	(−0.04, 0.11)
Environmental quality score on the TESS *n*=1263	−0.07	(−0.72, 0.57)
Staff/resident ratio *n*=1344	3.21	(−0.82, 7.24)
Medication prescribed (yes or no) *n*=1483		
Any psychotropic=1483	2.82	(0.94, 4.70)
Antipsychotic=587	6.45	(3.98, 8.91)
Antidepressants=587	−0.21	(−2.07, 1.65)
Hypnotics and anxiolytics[a]=285	7.59	(5.20, 9.98)
Analgesia=961	−0.80	(−2.79, 1.18)

CMAI, Cohen-Mansfield Agitation Inventory; TESS, Therapeutic Environment Screening Survey.
a. Not including melatonin as not classed as a psychotropic drug (16 residents were prescribed melatonin).

Table 5 Relationship of quality of life and other factors to CMAI caseness

	Adjusted odds ratio	95% confidence interval
Quality of life (DEMQOL)		
Staff proxy *n*=1391	0.936	(0.925, 0.947)
Family proxy *n*=1004	0.972	(0.962, 0.982)
Resident completed *n*=447	0.987	(0.972, 1.003)
Number of family visits per month *n*=1182	0.984	(0.914, 1.059)
Staff/resident ratio *n*=1344	1.589	(0.995, 2.538)
Number of beds in cluster *n*=1396	0.996	(0.987, 1.005)
Care home activity participation (hours per person per week) *n*=1263	0.984	(0.914, 1.059)
Staff numbers *n*=1344	1.003	(0.995, 1.012)
Environmental quality score on the TESS *n*=1263	0.969	(0.900, 1.043)
Medication prescribed (yes or no)		
Any psychotropic *n*=1483	1.445	(1.127, 1.853)
Antipsychotic *n*=248	1.881	(1.362, 2.598)
Antidepressants *n*=587	0.962	(0.753, 1.229)
Hypnotics and anxiolytics[a] *n*=285	2.250	(1.645, 3.079)
Analgesia *n*=961	0.987	(0.760, 1.283)

CMAI, Cohen-Mansfield agitation inventory; TESS, Therapeutic Environment Screening Survey.
a. Not including melatonin as not classed as a psychotropic drug (16 residents were prescribed melatonin).

Table 6 Relationship between quality of life and other factors with NPI agitation caseness

	Adjusted odds ratio	95% confidence interval
Quality of life (DEMQOL)		
Staff proxy DEMQOL *n*=1415	0.957	(0.947, 0.968)
Family proxy DEMQOL *n*=1018	0.981	(0.972, 0.991)
Resident DEMQOL *n*=456	0.996	(0.980, 1.012)
Number of family visits per month *n*=1199	0.990	(0.976, 1.005)
Staff/resident ratio *N*=1368	1.582	(1.031, 2.426)
Number of beds in cluster *n*=1421	1.003	(0.995, 1.011)
Care home activity participation (hours per person per week) *n*=1285	1.050	(0.985, 1.119)
Staff numbers *n*=1368	1.010	(1.003, 1.017)
Environmental quality score on the TESS *n*=1281	1.011	(0.946, 1.080)
Medication prescribed (yes or no)		
Any psychotropic *n*=1421	1.538	(1.189, 1.989)
Antipsychotic *n*=1421	1.425	(1.034, 1.962)
Antidepressants *n*=1421	1.264	(0.985, 1.621)
Hypnotics and anxiolytics[a] *n*=1421	1.776	(1.303, 2.420)
Analgesia *n*=1421	1.012	(0.777, 1.318)

CMAI, Cohen-Mansfield agitation inventory; TESS, Therapeutic Environment Screening Survey.
a. Not including melatonin as not classed as a psychotropic drug (16 residents were prescribed melatonin).

This study is large and weighted for representativeness; it covered varied homes throughout England and was planned to ensure external generalisability. Sensitivity analyses found the same results. Most homes approached agreed to participate. It may, however, be that homes which feel more confident about being scrutinised are more likely to agree to research and those residents or their families who refused participation or who could not be contacted were more agitated or had more severe dementia. A slightly higher proportion of nursing homes refused to participate. We may, therefore, have underestimated the prevalence of agitation, although our figures are similar to those in previous studies.[8,17]

We conclude that most residents in care homes have dementia and many are agitated with low quality of life. This indicates that new interventions are needed to reduce agitation. For those persons with dementia, agitation and a lowered quality of life, our findings from this survey suggest that investing in more of the current systems of care (increasing staff to resident ratios and activities within the care home and improving the environment) are unlikely to be sufficient to reduce agitation. We suggest that future research should focus on applying personalised approaches to managing agitation in residents with dementia, while also determining which specific individualised activities would be of greatest benefit. Tools should be provided for staff to understand, communicate with and engage individual residents to enable them to analyse the underlying reasons for agitation, which may include pain, discomfort, loneliness and boredom. This would enable care homes to deliver personalised interventions to reduce agitation and increase quality of life of their residents.

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Appendix 21 – Published *International Journal of Geriatric Psychiatry* paper

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RESEARCH ARTICLE

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Carer coping and resident agitation as predictors of quality of life in care home residents living with dementia: Managing Agitation and Raising Quality of Life (MARQUE) English national care home prospective cohort study

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Objectives: The objectives of the study are (1) to test our primary hypothesis that carers using more dysfunctional coping strategies predict lower quality of life in care home residents living with dementia, and this is moderated by levels of resident agitation, and (2) to explore relationships between carer dysfunctional coping strategy use, agitation, quality of life, and resident survival.

Methods: In the largest prospective cohort to date, we interviewed carers from 97 care home units (baseline, 4, 8, 12, 16 months) about quality of life (DEMQOL-Proxy) and agitation (Cohen-Mansfield Agitation Inventory) of 1483 residents living with dementia. At baseline, we interviewed 1566 carers about coping strategies (Brief COPE), averaging scores across care home units.

Results: Carer dysfunctional coping strategies did not predict resident quality of life over 16 months (0.03, 95% CI −0.40 to 0.46). Lower resident quality of life was longitudinally associated with worse Cohen-Mansfield Agitation Inventory score (−0.25, 95% CI −0.26 to −0.23). Survival was not associated with carer dysfunctional coping, resident quality of life, or agitation scores.

Conclusions: Carer dysfunctional coping did not predict resident quality of life. Levels of resident agitation were consistently high and related to lower quality of life, over 16 months. Lack of association between carer dysfunctional coping and resident quality of life may reflect the influence of the care home or an insensitivity of aggregated coping strategy scores. The lack of relationship with survival indicates that agitation is not explained mainly by illness. Scalable interventions to reduce agitation in care home residents living with dementia are urgently needed.

KEYWORDS
agitation, care homes, dementia, quality of life

1 | INTRODUCTION

A third of people living with dementia experience symptoms of agitation, such as restlessness, pacing, shouting, and verbal or physical aggression[1] These are more common in people living with moderate and severe compared to mild dementia.[2] People living with dementia who are agitated are more likely to move to a care home, and family carer burnout can mediate this relationship.[3] Fewer than half of nursing home residents report good quality of life,[4] but there is a dearth of robust research about what enables or interferes with living well with dementia, or cost-effective ways to maintain and improve quality of life in this setting.[5,6] Reflecting the difficulties experienced by family carers precipitating care home admission, within the care home, carers also report difficulties caring for people with agitation.[3] In this article, "carer" means an employed member of a care home team.

Agitation may be 1 determinant of poorer quality of life for people living with dementia in care homes,[2] because symptoms can make delivering care very challenging.[3] This association is likely to be driven by impairments in the abilities of care home residents with dementia to communicate and the needs that they have which are unmet, as well as dementia-related neurodegenerative changes.[7] The Needs-Driven, Dementia-Compromised Behaviour theory posits that in dementia, problem behaviours arise from unmet needs or goals, including emotional (communication, comfort, physical contact), recreational (stimulation, including touch, music; enjoyable activities), or physical needs (eg, pain relief, thirst, hunger).[8] People living with dementia may not know or be able to communicate their wishes. When carers are unavailable, unaware, or inadequately skilled in communicating, a lack of understanding or attendance to these individual needs may increase agitation.

Carers are likely to cope with the stress of caring for people living with dementia in different ways, with differing impacts on residents. In family carers of people living with dementia at home, dysfunctional coping such as avoidance, behavioural disengagement, or venting[9] was found to mediate the relationship between their reported burden and use of potentially abusive behaviours.[10] We therefore hypothesised that carers' dysfunctional coping strategies may similarly impact upon quality of life of residents. We expected a stronger relationship among residents who experienced more symptoms of agitation as they would require carers to use more coping strategies and thus be more vulnerable to dysfunctional strategies.

We previously reported cross-sectional, baseline data from the Managing Agitation and Raising Quality of Life (MARQUE) research programme's naturalistic cohort study where agitation was associated with poorer quality of life in care home residents living with dementia in England.[2] Currently, we report the longitudinal findings from this 16-month cohort study. Our primary hypothesis was that carers using more dysfunctional coping strategies predicted lower resident quality of life, moderated by levels of resident agitation. To consider an alternative model that agitation is mainly or wholly explained by greater physical and cognitive illness severity, we tested our hypothesis that higher levels of agitation predicts decreased survival.

Key points

- A third of people living with dementia experience symptoms of agitation, such as restlessness, pacing, shouting, and verbal or physical aggression, which is associated with poorer quality of life in care home residents living with dementia in England.
- Carer dysfunctional coping strategies may negatively impact upon quality of life of residents, perhaps most prominently among residents experiencing more symptoms of agitation as they would require carers to use more coping strategies and thus be more vulnerable to dysfunctional strategies.
- Based on study results, lower resident quality of life was longitudinally associated with greater agitation and carers' dysfunctional coping strategies did not predict quality of life over 16 months.
- Scalable interventions to reduce agitation in care home residents living with dementia are urgently needed.

2 | METHODS

Ethical approval was received from the National Research Ethics Committee London-Harrow 14/LO/0034 (06/03/14).

2.1 | Setting and sampling

Care homes across England were recruited through third sector partners, NHS trusts and clinicians, Care England, the NIHR Clinical Research Network, and the Enabling Research in Care Homes network. To ensure external validity and generalisability, our sampling frame comprised each provider type (voluntary, state, and private) and care provision (nursing, residential). We defined care home clusters as units within care homes with distinct care teams, managers, and activity schedules. If carers in units cross-covered each other, we defined this as 1 cluster. The use of the term "cluster" in this study denotes a care home unit and is the unit of analysis.

2.2 | Procedure

Care home managers agreed to the unit or home taking part in the study. Managers identified residents with a known clinical diagnosis of dementia using care home records. For all residents without a known dementia diagnosis, the Noticeable Problems Checklist (NPC)[11] was completed by a member of the care team. This is a 6-item validated questionnaire covering memory, basic self-care, orientation, naming familiar people, and ability to follow conversations. Eligible participants were all residents with an existing dementia diagnosis or NPC score >2.

Carers asked eligible residents judged to have capacity to consent to the study if researchers could approach them. Willing residents were approached by research assistants who assessed their decisional capacity and, if appropriate, followed informed consent procedures to

invite residents to consent into the study. With all other residents, the care home contacted the next of kin, asking if researchers could contact them. As per the Mental Capacity Act (2005), the next of kin was invited to act as a personal consultee to make a decision about research participation on behalf of the resident. If there was no appropriate personal consultee, a professional consultee was sought.

Individuals named as next of kin agreeable to research contact were asked to consent to providing personal demographic information and information about how frequently they visit the resident. They were invited to complete a proxy measure of resident quality of life.

Care home managers also provided a staff list, and permanent carers providing hands-on care were invited to complete measures about coping, burnout, and care practices. Bank carers were eligible to participate if they exclusively worked in that care home or cluster. All carers gave written informed consent.

Care home managers identified appropriate members of the care team to complete proxy measures about consented residents' dementia severity, agitation, and quality of life.

All participants were recruited between 13 January 2014 and 12 November 2015.

2.3 | Measures

Trained research assistants interviewed carers and residents at the care home. At baseline, researchers met with relatives at their preferred venue, usually the care home, their own home, or the research office. Interviews were carried out at baseline, 4, 8, 12, and 16 months, except for carer self-report measures and care home-level measures, which were captured at baseline only. Relatives completed follow-up measures with a research assistant via telephone or face to face.

2.3.1 | Care home-level measures

We recorded information about whether the care home provided personal care, nursing care, or both, and whether it was dementia-registered or a dementia specialist home.

2.3.2 | Resident measures

We recorded demographic details and information about the use of prescribed medications over the previous 28 days. The following measures were administered:

1. Quality of life: The DEMQOL and DEMQOL-Proxy are responsive, valid, and reliable measures of quality of life in people living with dementia. The DEMQOL-Proxy is a 31-item interviewer-administered questionnaire answered by a professional or family carer. The score range is 31 to 124. The people with dementia who were able to were asked to complete the DEMQOL, a 28-item interviewer-administered questionnaire. Scoring range for this instrument is 28 to 121. As the DEMQOL has fewer questions than the DEMQOL-Proxy, the totals are not directly comparable.[12,13] Higher scores indicate better quality of life.
2. Agitation: Agitation was measured using the Cohen-Mansfield Agitation Inventory (CMAI), a 29-item questionnaire with construct validity and interrater and test-retest reliability to measure agitation in people with dementia in care homes.[14,15] The CMAI is an informant questionnaire, and each item scores from 1 to 7, with 1 meaning "never" and 7 "several times per hour." The score sums individual items and ranges from 29 to 203. A score of >45 is usually regarded as clinically significant agitation.[16]
3. Dementia severity: Staff gave information so the researcher could rate the severity of dementia using the Clinical Dementia Rating. This is a reliable and valid instrument for rating severity of dementia.[17] It is used to rate performance in memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care, and this information was used to classify dementia severity into very mild, mild, moderate, or severe. An adaptation of the Clinical Dementia Rating was used; research assistants did not undergo the Washington University online training. However, they followed the structured grid during the interview.

2.3.3 | Staff self-reported measures

Staff measures were at baseline only. All consenting carers completed the Brief Coping Orientations to Problems Experienced (Brief COPE) measure. This is a multidimensional coping inventory widely used to assess the different ways in which people manage in response to stress.[18] Coping styles appear to be fairly constant over time.[19] It is a self-report questionnaire,[9] and participants score each strategy from 1 (not doing it at all) to 4 (doing it a lot). These have been grouped into 3 larger subscales that show adequate psychometric properties in dementia family carers[19]: problem-focussed (active coping, instrumental support and planning), emotion-focussed (acceptance, emotional support, humour, positive reframing, and religion), and dysfunctional coping (behavioural disengagement, denial, self-distraction, self-blame, substance use, and venting). Mean values per care home cluster were calculated.

2.3.4 | Family carer measures

We recorded family carers' demographics and asked them to complete a proxy measure of quality of life (DEMQOL-Proxy[13]) and tell us how often they visited the person with dementia.

3 | ANALYSIS

Data were analysed using Stata version 14. Mixed effects linear regression models were used to examine the relationship between quality of life scores over 16 months and baseline dysfunctional coping level within the care home cluster. Three level models were used to allow for the repeated measurements over time and clustering by care home cluster. Interaction terms were included in the models to consider differential effects by CMAI agitation score. Models were initially unadjusted. Fully adjusted models included time, sex, age, dementia severity, marital status, and visits by the main family carer. Assumptions of fitted models were investigated. Because of the severely skewed distribution of CMAI scores, all models were refitted using a dichotomous measurement representing CMAI caseness (CMAI case defined using cutoff score >45). Models were also refitted using the family carer proxy-rated DEMQOL score in place of carer proxy-rated score.

Associations between time to death and coping, agitation, and quality of life were analysed using Cox proportional hazards models

with shared frailties to account for clustering by care home cluster. Unadjusted and adjusted models were fitted. Adjustments were made for resident age, sex, dementia severity, antipsychotic use, marital status, number of times a month the family carer visited the resident, and the number of British National Formulary subchapters the residents' prescribed medication encompassed (representing a measure of resident's physical comorbidity (19)).

3.1 | Sample size justification

In a previous trial, the correlation between dysfunctional coping in family carers and the quality of life of the person with dementia was −0.31.[20] To detect this magnitude of correlation with 90% power and 5% significance requires 105 people living with dementia.[21] Adjusting for clustering by care team (estimated average team size: 40 people living with dementia, intracluster correlation (0.075),[22] impact of confounding (variance inflation factor = 2),[23] and an expected average 2.5 repeated measurements/person (based on 30% dropout/year) and correlation between repeated quality of life measurements of 0.75 (from START trial data (20)) required a total sample size of 700. This number was inflated to 2800 to allow investigation of the interaction between coping strategy and high and low agitation groups.

During the study, it became apparent that the average cluster size would be less than 40. With a smaller cluster size and more clusters, fewer people living with dementia are required to maintain power at 90%. Recalculations indicate that with 15 per cluster, the overall

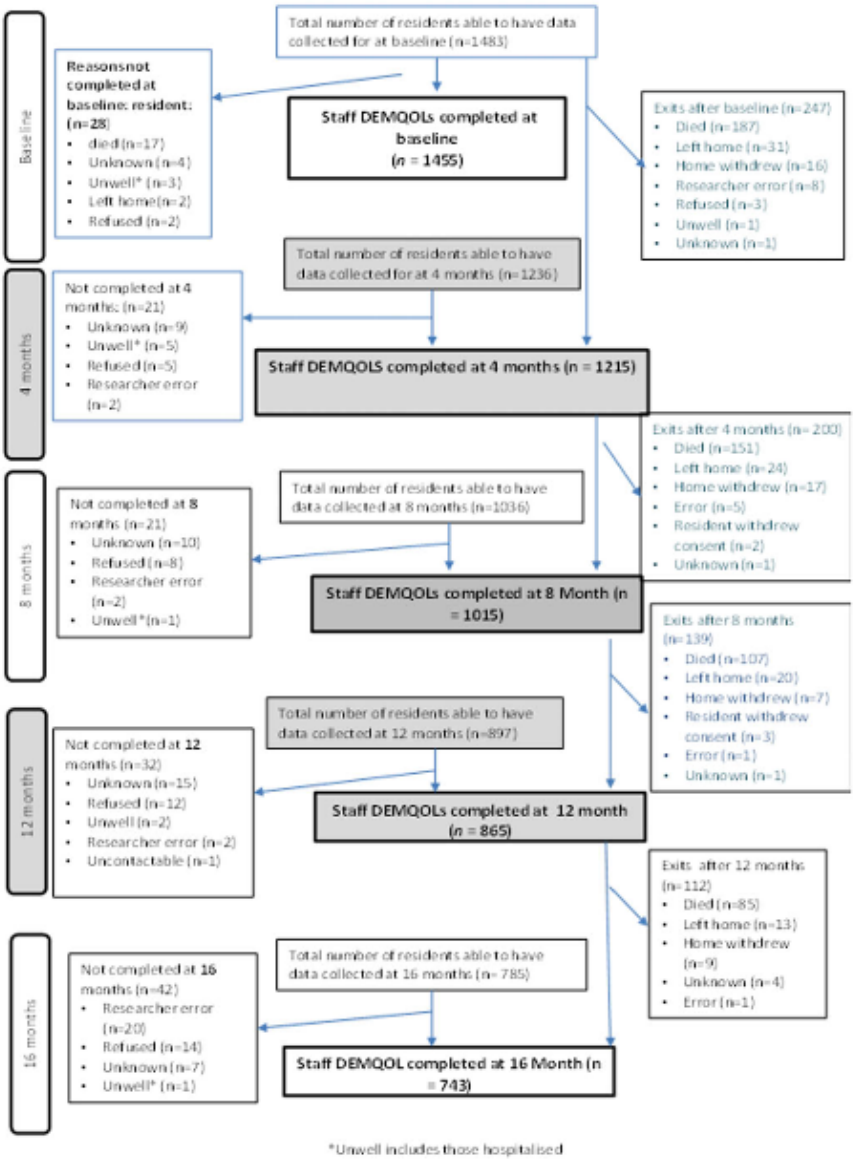

FIGURE 1 Flow diagram for completion of primary outcomes (carer-rated DEMQOL) [Colour figure can be viewed at wileyonlinelibrary.com]

target would be 1466 people living with dementia (requiring 97 clusters). This was achieved in the study, and extra power gained by an increase in the number of repeated measures per resident (3.6 rather than 2.5 originally anticipated).

4 | RESULTS

4.1 | Recruitment and retention

We contacted 114 care homes, and 75% (n = 86) agreed to participate. Seven homes were subdivided into >1 cluster, totalling 18 clusters. The sample at baseline, therefore, was 97 clusters. Of these, 39 provided personal care, 13 nursing care, and 45 nursing and personal care. There were 86 care home units registered as providing dementia care, and 42 as providing dementia-specialist care.

The total number of eligible care home residents was 3035 (86.2%); of these, 2825 (93.1%) were approached by researchers (directly or through a proxy); 1489 (52.7%) consented to participation. The common reasons for nonparticipation were refusal (27.3%) and the care team being unable to contact the family consultee to ask permission for researchers to contact them (17.6%). Three hundred (20.1%) had capacity to consent to the study at baseline, and we used consultees for the remainder; 1281 (86.0%) had a pre-existing clinical diagnosis of dementia, and the remainder scored >2 on the NPC. There were 6 consented residents who died before data were collected, so analyses at baseline are based on 1483. The number of recruited residents per cluster ranged from 2 to 55 (median 14). One thousand eighty-one (86.0%) of consenting residents had an identified family member who agreed to participate. One thousand five hundred sixty-six carers completed the measure of coping. Numbers of carers per cluster ranged from 3 to 54 (median 15).

Our flow diagram (Figure 1) shows resident recruitment to and retention in the study. Median follow-up time was 1.34 years (interquartile range (IQR): 0.68 to 1.44). Four care homes withdrew from the study after baseline; in 2 cases, this was because the home closed; 1 unit withdrew because the study was perceived as too time consuming and 1 unit did not give a reason.

4.2 | Sample description

The majority of participants were female, widowed, and 71% were living with moderate to severe dementia (Table 1). They took a median of 7 medications, and had a mean age of 85 years. They received a median of 6 visits a month from the family carer who completed their DEMQOL-Proxy. At baseline, the median (IQR) for paid carer dysfunctional coping scores was 16 (13 to 20; N = 1566). Aggregated at care home level, the median score was 17 (IQR 16 to 18; N = 97). Agitation and quality of life scores remained fairly stable and changed little over time (Table 2).

4.3 | Relationship of dysfunctional coping and CMAI scores to quality of life

Contrary to our hypothesis, there was no evidence of an association between resident quality of life over 16 months and carer baseline dysfunctional coping scores (0.06, 95% CI −0.39 to 0.52; N = 1457) or even after adjusting for sex, age, dementia severity, marital status, and visits by the main family carer (0.03, 95% CI −0.40 to 0.46; N = 1174). Carer proxy-rated DEMQOL scores over 16 months were associated with CMAI scores over 16 months, indicating lower quality of life scores for those with worse agitation. This association was evident in unadjusted analyses (coefficient −0.25, 95% confidence interval (CI) −0.27 to −0.23; N = 1450) and in the fully adjusted model that included

TABLE 1 Characteristics, dementia severity, agitation scores, quality of life, medication, and antipsychotic use of participating residents at baseline

Variable	N	Frequency (%) Unless Stated Otherwise
Female	1483	1026 (69%)
Age	1437	Mean (SD): 85 (9)
Family visits from main carer per month	1243	Median (IQR): 6 (3, 13)
Marital status	1424	
Married/common law		345 (24%)
Single, separated, divorced		287 (20%)
Widowed		792 (56%)
Dementia severity	1458	
Mild or very mild		427 (29%)
Moderate		482 (33%)
Severe		549 (38%)
Number of medications taken	1483	Median (IQR): 7 (5, 10)
Antipsychotic use	1483	248 (17%)
CMAI	1424	Median (IQR): 41 (33, 55)
CMAI >45	1424	569 (40%)
DEMQOL staff proxy	1455	Median (IQR): 104 (95, 110)
DEMQOL family carer proxy	1054	Median (IQR): 101 (90, 109)

Abbreviations: SD, standard deviation; IQR, interquartile range.

TABLE 2 CMAI and DEMQOL scores over time

	Median (IQR) Unless Stated Otherwise				
	Baseline	4 months	8 months	12 months	16 months
CMAI	41 (33, 55) N = 1424	39 (32, 54) N = 1201	40 (32, 53) N = 999	39 (32, 55) N = 851	39 (31, 52) N = 737
CMAI >45: frequency (%)	569 (40%) N = 1424	460 (38%) N = 1201	367 (37%) N = 999	320 (38%) N = 851	260 (35%) N = 737
DEMQOL staff proxy	104 (95, 110) N = 1455	105 (94, 111) N = 1215	106 (97, 111) N = 1015	106 (98, 111) N = 865	106 (99, 11) N = 743
DEMQOL family carer proxy	101 (90, 109) N = 1054	103 (92, 109) N = 699	103 (93, 1009) N = 536	102 (94, 109) N = 414	104 (93, 109) N = 318

Abbreviation: IQR, interquartile range.

dysfunctional coping strategy use and the other potential confounders (−0.25, 95% CI −0.26 to −0.23; N = 1174). Dysfunctional coping was not a significant predictor in this model. The model extended to include an agitation (CMAI) by dysfunctional coping interaction term showed no evidence that the relationship between quality of life score over 16 months and coping was changed by level of agitation ($P = 0.147$). Alternative models where CMAI caseness was used in place of CMAI score gave similar conclusions (CMAI case cutoff >45 score). Cohen-Mansfield Agitation Inventory caseness over 16 months was associated with lower quality of life scores over 16 months (adjusted difference in means −6.96, 95% CI −7.70, −6.23; N = 1174), but there was no evidence of an interaction with dysfunctional coping ($P = 0.269$). In models that used family carer proxy-rated DEMQOL score in place of carer proxy-rated score, results were again very similar: CMAI score predicted quality of life over 16 months in a fully adjusted model (−0.06, 95% CI −0.08 to −0.03; N = 994), and dysfunctional coping use score did not (0.35, 95% CI −0.16 to 0.85; N = 994).

4.4 | Predictors of survival

Five hundred eight of 1470 participants died during the study period; median time to death was 7.4 months (interquartile range 4.2 to 11.6). In models adjusted for age, sex, dementia severity, number of medications, and whether taking antipsychotics (N = 1146) including CMAI caseness (score of 46+), neither CMAI caseness hazard ratio (HR 0.80, 95% CI 0.64-1.01), baseline staff proxy DEMQOL score (HR 1.00, 1.00 to 1.01), nor baseline dysfunctional coping score (HR 1.00, 0.94 to 1.08) were significant predictors of survival (Table 3). When we repeated analyses using CMAI score instead of caseness, results were very similar. As expected, those living with mild or moderate dementia, younger residents, and women survived longer. Taking antipsychotic medication or number of medication classes were not significant predictors of survival.

TABLE 3 Fully adjusted (N = 1146) survival models

	Hazard Ratio	95% Confidence Interval
Baseline CMAI 46+	0.800	0.635, 1.007
Baseline staff proxy DEMQOL	0.999	0.990, 1.009
Baseline dysfunctional coping	1.003	0.936, 1.076
Resident age	1.056	1.040, 1.072
Sex		
Male	Ref.	
Female	0.636	0.502, 0.806
Dementia severity		
Mild	0.500	0.377, 0.663
Moderate	0.656	0.516, 0.834
Severe	Ref.	
Number of medications taken	1.009	0.980, 1.039
Antipsychotic use	0.998	0.747, 1.333
Marital status		
Married/common law	Ref.	
Single, separated, divorced	1.262	0.889, 1.791
Widowed	1.014	0.756, 1.361
Family visits from main carer per month	1.011	0.999, 1.023

5 | DISCUSSION

In this well-powered, naturalistic care home study, the largest to date, we did not demonstrate our primary hypothesis that greater use of dysfunctional coping strategies by carers would predict lower resident quality of life or greater levels of agitation. Levels of agitation and quality of life of residents living with dementia, rated by paid carers, remained fairly constant over the 16-month follow-up period. Higher levels of resident agitation predicted lower quality of life. These longitudinal findings build on those reporting this association in cross-sectional data.[2] We hypothesised that higher levels of agitation would predict survival, but this was not supported by these data.

We hypothesised that being cared for by carers who use dysfunctional care strategies would lower resident quality of life, in particular, among residents who had symptoms of agitation when they were first recruited and therefore require more carer coping. Although it seems logical that caring practices will impact on quality of life, we did not demonstrate our hypothesis. Carers cope with caring challenges within a set of multilevel systems that determine how care is delivered and therefore residents experience life. For homes that are part of a bigger chain, there is a wider macro system of the provider organisation; for all homes, there is a meso system of the care home and a microsystem of a shift or team influences. While most care homes intend to deliver person-centred care, in reality, care work is often task-focussed and stressful[24] with a discrepancy between how people would like to care and the reality of what they feel able to achieve.[25] Home policies can limit the individual coping strategies that are permissible within that system. There may be linguistic barriers too.[26]

Availability and accessibility of pleasant, meaningful activities for residents with dementia may be important in preventing agitation, and we did not measure the activities individual residents engaged in. We reported from MARQUE baseline analyses that the overall environment, good staffing levels, and overall time spent in activities

in a particular home were not associated with agitation or quality of life.[2] We did not measure carer burden, and we do not know whether paid carers who reported using dysfunctional coping strategies were talking about this in reaction to the stresses of caring, to organisational issues (such as poor pay or conditions), or to other life stresses.

An alternative explanation for not demonstrating our primary hypothesis is that the coping strategies carers reported in the Brief COPE did not sufficiently capture the interpersonal dynamics between residents and carers when someone became agitated. While the Brief COPE is a valid measure of general coping style, our study design could not capture how a carer's prevailing style of coping was influenced and modified by different caring situations and care recipients. Future research may benefit from integrating more in-depth observational measures that capture this. A further explanation could be that carers may be reluctant to report dysfunctional coping, or may not carry out care in line with their self-perceived care practices in an environment which they do not control. The Brief COPE has been validated and used widely with family carers of people with dementia[19] but less so with paid carers, although it has been used across a range of populations including nurses.[27] It is possible that residents or their families who refused participation or who could not be contacted were more agitated or had more severe dementia. We approached carers while they were at work and providing care, so perhaps those who struggled to cope were more likely to refuse.

In adjusted models, neither agitation nor quality of life predicted survival. This may be because those who are less agitated enter care homes at a later stage of dementia and an older age and thus survived less long. This would also explain our findings that neither antipsychotics nor number of medication classes predicted survival once age, sex, and dementia stage were known. The lack of relationship with survival indicates that agitation is not mainly explained by illness.

The lack of a link between quality of life and agitation and home environment, carer coping, physical illness, or survival may indicate that agitation is complex and an end point with complex aetiologies. The Needs-Based Dementia-Compromised Behaviour model will not be the only story; there is increasing evidence that symptoms such as agitation are caused by structural deficits in neural networks. A recent synthetic review suggests structural and functional deficits in brain regions associated with emotional regulation and salience.[28] Agitation may therefore arise from a reduced capacity to regulate emotional responses and/or attentional resources, and possibly reduced problem-solving ability. It could be that fear or anxiety or misunderstanding others' actions drives agitation, and future work should consider multiple theoretical perspectives.

We provide here the most comprehensive social evidence to date of a longitudinal link between agitation and quality of life for care home residents living with dementia. Residents' significant levels of agitation did not reduce over time. This may be because although they became more familiar with the care home, they also have a more severe level of dementia. It is unsurprising that living with agitation for periods of months and years negatively impacts quality of life. Effective, scalable care home interventions to reduce agitation and promote quality of life are thus needed and important. Within the MARQUE programme, we have developed and are evaluating a care team intervention to reduce agitation and improve quality of life of residents living with dementia.

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CONFLICT OF INTEREST

None declared.

DATA ACCESSIBILITY STATEMENT

Data will be made available on the UCL Research Data Repository (http://www.ucl.ac.uk/isd/services/research-it/research-data/repository).

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