What are the benefits of diagnosing dementia early? A mixed methods study

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Abstract

Background and Aims: The prevalence of dementia is rising globally, however, it is estimated that only 60% of people living with dementia in the UK have a formal diagnosis. Over the last decade many countries have taken proactive policy approaches to manage the care and treatment of dementia. They have placed particular emphasis on the "timely" or "early" diagnosis of dementia to enable people with dementia to live well for longer. However, without a reliable diagnostic test for dementia and very few effective treatments, it is unclear what benefits an early diagnosis can be expected to produce.

Therefore, the overall aim of this thesis is to explore the potential benefits of diagnosing dementia early. It is difficult to distinguish an "early" diagnosis from a late diagnosis. Therefore, this thesis aimed to explore whether a diagnosis of Mild Cognitive Impairment (MCI) before dementia could be used as a proxy for early diagnosis, and if an early diagnosis was associated with a reduced risk of mortality, hospitalisation, or emergency department attendance. Furthermore, as previous research has not examined the benefits of an early diagnosis from the perspective of people living with dementia, this thesis aimed to address this gap in the literature. Additionally, non-pharmacological treatments are an important tool in the clinical management of dementia, however, it is not clear how they might benefit people in the early stages of dementia. Therefore, this thesis aimed to explore which outcomes are used in randomised controlled trials testing novel non-pharmacological treatments for mild dementia and mild cognitive impairment.

Methods: This thesis used a convergent parallel mixed methods design, consisting of three phases of investigation.

The first phase was a quantitative study, analysing data extracted from the medical records of 18,555 patients diagnosed with dementia by South London and Maudsley NHS Trust. This phase examined the relationship between an early diagnosis of dementia and hospitalisation, emergency department attendance, and mortality.

The second phase consisted of a qualitative study using semi-structured interviews and thematic analysis, exploring 2 people living with dementia and 12 caregiver's perceptions of the benefits of diagnosing dementia early.

The final phase was a scoping review of outcome measures used by 92 trials testing non-pharmacological treatments for mild dementia and MCI.

The findings from the three phases of investigation were integrated using the triangulation protocol to create cross-cutting meta-themes.

Findings: A diagnosis of MCI before dementia was deemed to be a useful proxy for an early diagnosis. A small proportion (5.6%) of participants in the quantitative phase received an early diagnosis. Those with an early diagnosis had a reduced risk of mortality (HR = 0.86, CI = 0.77–0.97), however, there was no difference in the risk of hospitalisation (HR= 0.99, CI= 0.91 – 1.08), and they were at increased risk of attending the emergency department (HR= 1.09, CI= 1.00 – 1.18).

The results from the qualitative study showed that an early diagnosis enabled people living with dementia and their caregivers to "identify and respond to the evolving needs of the person living with dementia". More specifically, the benefits of an early diagnosis included: understanding early symptoms and/or behaviours to prevent crisis, timely decision making which involves or respects the needs of the person living with dementia, and access to services and treatments to manage decline. However, caregivers felt certain enablers needed to be in place for these benefits to be felt. These included: adequate prognostic information and disease-modifying treatments, the presence of a caregiver, and a willingness to accept the diagnosis or post-diagnostic support.

The scoping review charted 358 outcome measures used in RCTs for new non-pharmacological treatments. Only 78 (22%) of these measures were used more than once. Researchers have prioritised cognitive outcomes over measuring quality of life, making it

difficult to assess whether early treatments can keep people with dementia living well for longer.

The integration of results, using the triangulation protocol, produced four meta-themes capturing the potential benefits of an early diagnosis. These meta-themes vary in the degree to which they are supported by evidence from this thesis.

1) An early diagnosis could initiate early treatment; however, there are gaps in our understanding of the benefits. I found that people with an early diagnosis were more likely to be prescribed anti-dementia drugs, which was welcomed by participants in the qualitative study. However, more research is needed to determine the benefits of initiating early treatment.
2) An early diagnosis can enable people to live for longer. I found people with an early diagnosis had an increased survival, however living for longer may not be perceived as a benefit by those living with dementia and their caregivers.
3) An early diagnosis can reduce the risk of hospitalisation or emergency department attendance. I found participants in the qualitative study felt that an early diagnosis could lead to more responsive treatments from health services. However, the quantitative study found that people with an early diagnosis were at increased risk of attending the emergency department.
4) The benefits of an early diagnosis are dependent on individual and sociological factors. I found that the benefits of an early diagnosis were dependent on individual factors such as the willingness to accept the diagnosis of dementia and the presence of a caregiver; and sociological factors including ethnicity and socio-economic status.

Conclusion: The findings of this thesis indicate that the benefits of an early diagnosis are not as straight forward as previously thought. There is the potential for an early diagnosis to improve outcomes for people living with dementia, however, this is highly dependent on contextual factors and the provision of post-diagnostic support. Future research is needed to

understand how dementia policy, services, and treatments can be improved to maximise their impact on people living with dementia.

Dedication

In loving memory of Barbara Elise Couch

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Chapter 1: Introduction

This thesis aims to investigate the benefits of diagnosing dementia early. In this chapter, I consider the key concepts related to the early diagnosis of dementia. Then, I present the UK dementia policy, which has the early diagnosis of dementia as a key objective. Next, I discuss challenges in the early detection and clinical diagnosis of dementia. Then, I discuss weaknesses in the scientific evidence on the benefits of an early diagnosis, before outlining the rationale and aims of this thesis.

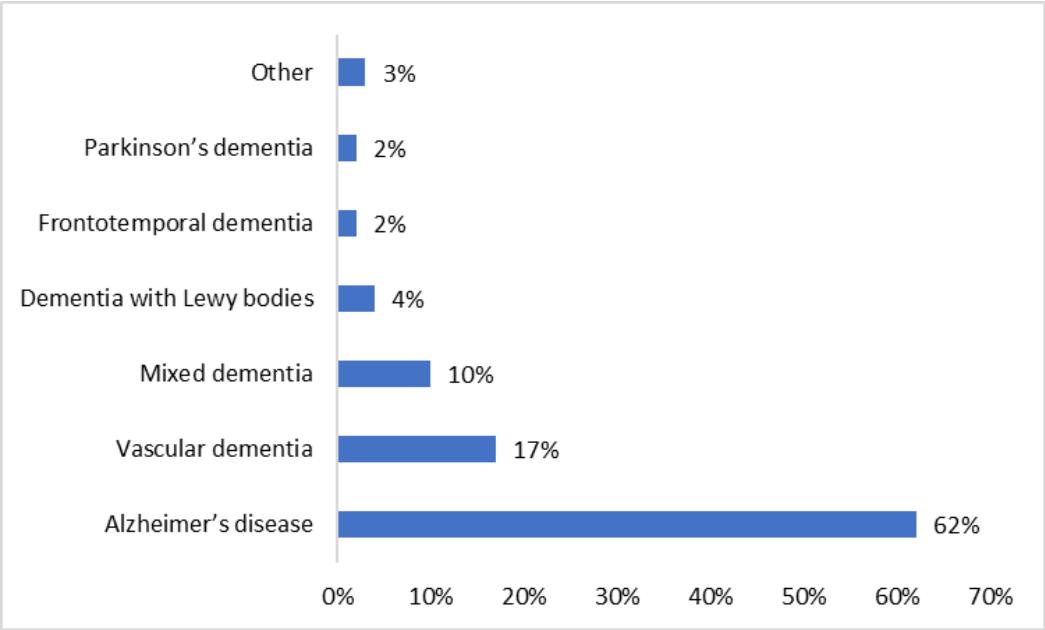
1.1 Introduction

The world's population is ageing. The proportion of older adults aged 65+ is growing and the UN estimates that by 2050 16% of the global population will be over the age of 65 (DESA, 2019). In the UK, not only are the number of older adults increasing but they are also living for longer. In 1951, 4% of older adults were aged 85+ whereas in 2012 this proportion had increased to 14% (Rutherford and Socio, 2012). Older age is associated with an increased risk of developing dementia, with less than 5% of dementia cases occurring before the age of 65 (Livingston et al., 2017). It is estimated that the prevalence of dementia in the UK amongst people aged 65-69 is 1.3%, compared to 32% amongst people aged 95+ (Prince et al., 2014). As the prevalence rises the economic impact of dementia also increases. The global cost of dementia is estimated to be $818 billion (US Dollars); 42.3% of this total is due to formal care, 41.7% is due to informal care, and 16% is due to medical costs (Wimo et al., 2017).

Dementia comes from the Latin words "dems" and "mens", meaning out of one's mind. It is a syndrome that affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement (World Health Organization, 2017), and refers to a number of diseases. Alzheimer's disease is the most common type of dementia followed by vascular dementia, mixed dementia (Alzheimer's disease and vascular dementia), dementia with Lewy bodies, frontotemporal dementia, and dementia with Parkinson's disease. Figure 1.1 presents

the proportion of dementia subtypes in the UK. Each subtype of dementia differs in its clinical presentation and progression.

Figure 1.1 Proportion of Dementia Subtypes in the UK (From Prince et al., 2014)



Dementia progresses from a mild disease, where a person may experience forgetfulness which does not greatly interfere with their everyday living, to moderate and severe dementia, where the level of cognitive impairment becomes more limiting (Wilkosz et al., 2010). There is evidence the neuropathology associated with dementia develops many years before symptoms become apparent (Prince et al., 2011). As the disease progresses, the person living with dementia will experience increased cognitive and physical impairment until they find it difficult to care for themselves and require full-time care (Brodaty et al., 2014). In addition to cognitive and functional impairment, people living with dementia may also experience behavioural and psychological symptoms of dementia, such as agitation and hallucinations (Finkel, 2001). Furthermore, people with dementia may also be living with co-morbid conditions, affecting both the symptoms of their dementia and what care is most appropriate for them to receive (Mondor et al., 2017).

Dementia has a profound effect on those living with the disease. People who are diagnosed with dementia are more likely to report a lower quality of life (Banerjee et al., 2006), have higher levels of depression (Richard et al., 2013) and die sooner than older adults of the same age without dementia (Dewey and Saz, 2001). In addition to every person diagnosed with dementia, there are formal and informal carer givers providing support. Caregivers of people with dementia are more vulnerable to social isolation, depression, feelings of burden, financial hardships and are sometimes described as invisible secondary patients (Brodaty and Donkin, 2009).

1.1.1 Diagnosis rates in the UK

Dementia is an underdiagnosed condition. In 2015, it was estimated that 850,000 people were living with dementia in the UK (Prince et al., 2014) yet only 60% of all people living with dementia were thought to have a formal diagnosis. Since then, there has been a small improvement in the dementia diagnosis rate, reaching 66% in 2017/8 (National Audit Office, 2007). While this improvement is promising, these statistics should be interpreted with caution. It is difficult to assess diagnostic rates, as this requires correctly estimating both the prevalence of dementia within the UK as well as the number of people who have received a formal diagnosis. The prevalence of dementia in the UK has been estimated by a Delphi consensus based on large surveys of the UK population (Knapp et al., 2014). The number of people with a formal diagnosis of dementia has been estimated by looking at the number of people with a diagnosis of dementia recorded in GP registers. GP registers may be lacking in accuracy, which can lead to an underestimation of the true number of people living with dementia.

Additionally, researchers have pointed out that people living with dementia and their family members are not always aware of a dementia diagnosis that is recorded in their patient notes (Amjad et al., 2018). In 2007, it was reported that 60% of mental health teams did not inform the person living with dementia of their diagnosis (National Audit Office, 2007). In these cases,

people living with dementia do not experience any of the outcomes, negative or positive, associated with receiving a diagnosis. However, this is changing and now approximately 80% of people diagnosed with dementia are informed of their diagnosis (Hodge and Hailey, 2013).

It is important to understand why a large proportion of people living with dementia do not have a formal diagnosis. First, we must understand the characteristics of those who do not receive a formal diagnosis. Those living with undiagnosed dementia, both in the UK and globally, tend to be older, unmarried, have less severe dementia, have fewer years of education, and are more likely to live in the community compared to those who have a formal diagnosis (Savva and Arthur, 2015; Lang et al., 2017). It is not clear why these groups are at particular risk of undiagnosed dementia. One theory for the low diagnosis rates amongst men is that men are less likely to seek a diagnosis due to less active help-seeking behaviours, and fear of being stigmatised with dementia (Lang et al., 2017). Previous research has highlighted that the presence of a caregiver increases the likelihood of seeking help for suspected dementia, as they are likely to notice the symptoms and initiate contact with health services (Lagaay et al., 1992). Systematic reviews have suggested that the factors related to missed or delayed diagnoses are complex and can exist at the service, clinician, patient and caregiver level (Bradford et al., 2009). People living with dementia are likely to face multiple barriers; therefore, multifaceted interventions are required to improve diagnosis rates (Parker et al., 2020).

1.1.2 Early diagnosis and dementia policy in the UK

Dementia can have a profound effect on multiple aspects of a person's health and wellbeing. In the absence of a cure, dementia policy in the UK is focused on providing treatment and support which enables people with dementia to live well for longer. Policy initiatives in the UK have not only aimed to increase the number of people diagnosed with dementia, they have also aimed to diagnose it in the earlier stages.

In 2009, the UK government introduced the National Dementia Strategy. The national dementia strategy outlined 17 public health objectives under three broad themes: improving professional knowledge and understanding of dementia, early diagnosis and intervention, and good quality care at all stages of the disease (Department of Health, 2009). To facilitate the implementation of the National Dementia Strategy, they also introduced the Quality Outcomes for People Living with Dementia which highlighted four areas of implementation that would have the greatest impact on people with dementia and their carers: good quality early diagnosis and intervention, improved quality of care in general hospitals, quality care for those living in care homes, and reduction in the use of antipsychotic medication (Department of Health, 2010). In 2015, The Prime Minister's Challenge on Dementia built on the national dementia strategy including objectives outside of health and social care. The key objectives fell under three core areas: improving the health and care of people living with dementia, creating dementia-friendly communities, and improving research programmes for dementia (Department of Health, 2012). This action was renewed by The Prime Minister's Challenge on Dementia 2020, which aimed to make England the best place in the world for dementia care and dementia research. This initiative introduced NHS health checks for adults over the age of 40 to detect the earlier onset of dementia, personalised care plans, and published Care Quality Commission standards for dementia care were also introduced (Department of Health, 2015).

Underpinning the objectives in each of these policies is the early detection and diagnosis of dementia and the provision of high-quality post-diagnostic support. This thesis examines the assumptions and evidence underlying these policy objectives, with a particular focus on the benefits of diagnosing dementia early. These policy objectives promote the narrative that increasing the public awareness of dementia increases the number of people seeking a diagnosis in the early stages of the disease, which in turn leads to the provision of early treatment, which prevents or delays the need for hospital or care home admissions. Table 1.1 presents the outcomes attributed to the early diagnosis in the National Dementia Strategy and

both iterations of the Prime Minister's Challenge on Dementia. However, there are several problems in this narrative, specifically: the challenges in detecting dementia early, weaknesses in the provision of post-diagnostic support, and a lack of evidence on the benefits of an early diagnosis. These problems are interconnected and in the following sections I will examine each one in depth, then summarise how they affect our understanding of the benefits of an early diagnosis of dementia.

Table 1.1 UK dementia policy statements regarding the benefits of early diagnosis

Dementia Policy	**Proposed benefits of early diagnosis**
The National Dementia Strategy (2009)	"The evidence available also points strongly to the value of early diagnosis and intervention to improve quality of life and to delay and prevent unnecessary admission into care homes"
The Prime Minister's Challenge on Dementia (2012)	"Surveys show us that people with dementia would like early diagnosis. And we know that with early intervention, and access to the right services and support, people with dementia can continue to live well for many years."
The Prime Minster's Challenge on Dementia 2020 (2015)	"There is greater awareness now about the importance of support after diagnosis, often termed 'post-diagnosis support', both for improving the individual's quality of life and for the potential to reduce more costly crisis care, for example by avoiding emergency admissions to hospitals and support in care homes"

1.1.3 Early diagnosis or timely diagnosis?

Over the last few years, there has been a shift from advocating an "early diagnosis" to a "timely diagnosis." The terms "early" and "timely" diagnosis have been used somewhat

interchangeably in the scientific literature. There is some overlap between an early diagnosis and a timely diagnosis, for example a timely diagnosis of dementia can be an early diagnosis. However, they have different definitions (see Table 1.2). An early diagnosis may refer to a diagnosis made during the prodromal or pre-symptomatic stage. An early diagnosis can also be in response to the earliest onset of symptoms, where a diagnosis of dementia cannot be confirmed and a diagnosis of Mild Cognitive Impairment (MCI), Subjective Cognitive Impairment (SCI) or Cognitive Impairment No Dementia may be given (Prince et al., 2011) MCI is discussed in more detail in section 1.2.2. There is a greater variation in the definitions of a timely diagnosis. However, each definition of a timely diagnosis highlights the importance of responding to the needs of the person living with dementia. A timely diagnosis, can be in response to the onset of symptoms, but it can also be at a time that best suits the person living with dementia (Brooker et al., 2014, Lepeleire et al., 2008). It is important to note, with regards to a timely diagnosis, that there are people who do not want to be informed of a dementia diagnosis (Boustani et al., 2006). In this case, no diagnosis could also be considered a timely diagnosis.

Table 1.2 Definitions of an early diagnosis and timely diagnosis of dementia

	Early diagnosis	**Timely diagnosis**
Definition(s)	• In response to developing neuropathology, before symptoms become apparent (Prince et al., 2011) • Mild Cognitive Impairment (Albert et al., 2011) • Subjective memory impairment (Prince et al., 2011) • Cognitive impairment no dementia (Hsiung et al., 2006)	• When symptoms are recognised by the person living with dementia and the diagnosing clinician (Lepeleire et al., 2008) • In response to the onset of symptoms (Prince et al., 2011) • At a time when the person living with dementia can most benefit from the diagnosis (Brooker et al., 2014)

While the discourse surrounding the early diagnosis has evolved to become discussions surrounding the timely diagnosis of dementia, it is still important to understand the potential benefits or harms of an early diagnosis. This information can help people living with dementia, their caregivers, health service providers and policymakers make an informed decision about when is the best time for them to seek a timely diagnosis.

1.2 Challenges in the early detection of dementia

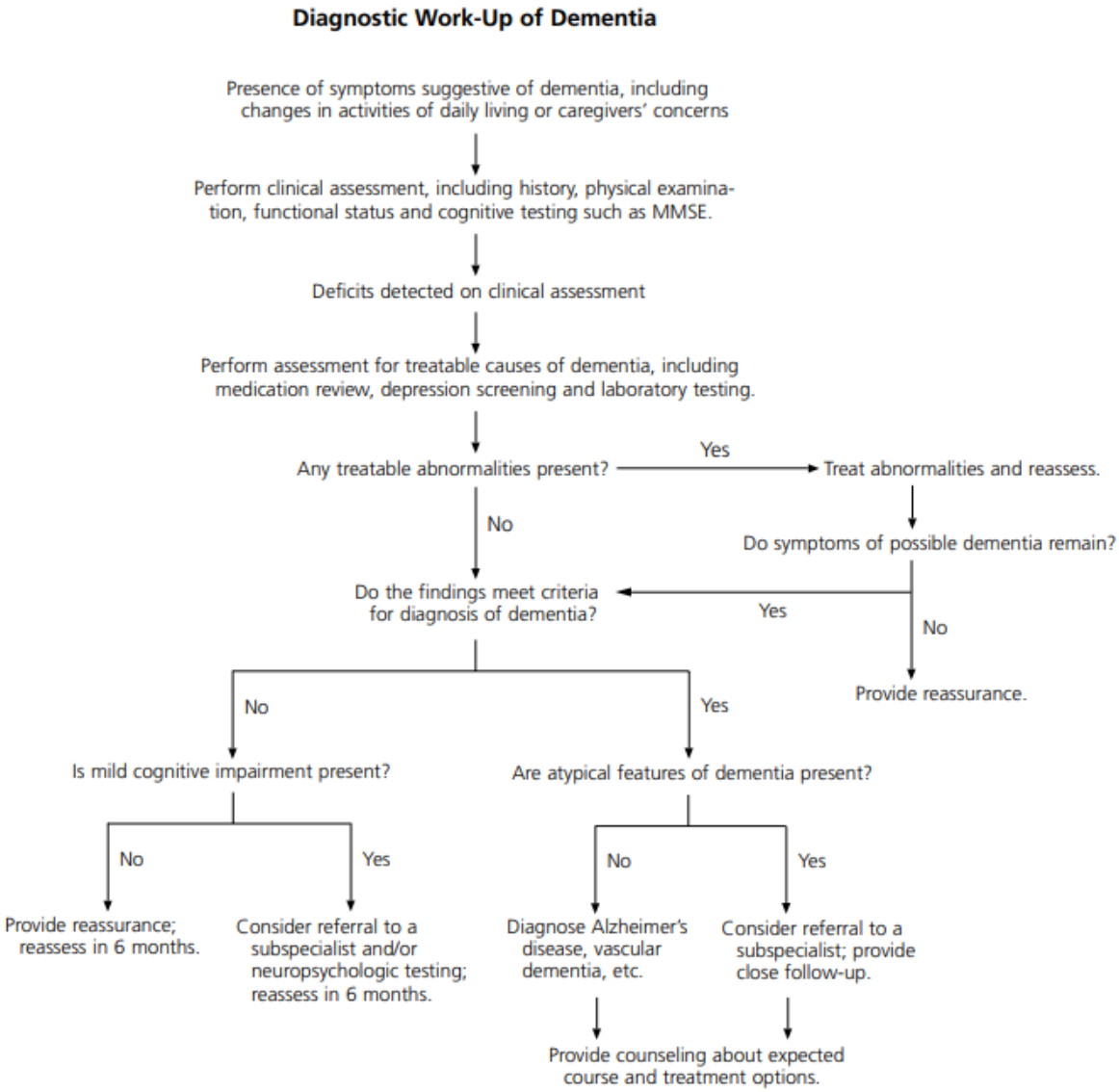
The early diagnosis of dementia is a key objective across the three main dementia policies in the UK. However, dementia is a complex condition to diagnose and clinicians must determine whether the cognitive decline experienced by the patient is greater than would be expected at that age. A definitive diagnosis of dementia cannot be confirmed until post-mortem

examination (Joachim et al., 1988) and is typically given after other causes of cognitive impairment have been excluded. The challenges to making a definitive diagnosis of dementia, especially in the early stages of the disease, can harm efforts to increase the number of people receiving an early diagnosis of dementia.

1.2.1 Making a clinical diagnosis of dementia

In the UK, a diagnosis is made based on DSM-V, NINCDS-ADRDA criteria or ICD-10 criteria (McKhann et al., 2011, Naik and Nygaard, 2008). People with concerns about their memory are referred to specialist memory clinics for a diagnostic assessment. Diagnostic guidelines recommend a systematic assessment of the patient's history, medication, cognitive tests, blood tests, and brain imaging. Figure 1.2 presents how a diagnosis of dementia is determined by clinicians.

Figure 1.2 Process for diagnosing dementia (from SantaCruz and Swagerty Jr, 2001)



1.2.1.1 Patient history

A dementia diagnosis should start with a detailed and structured assessment of the patient's medical history (Livingston et al., 2017). It is recommended that history is taken from both the person with suspected dementia and a close relative or friend (Lam et al., 2019). Interviewing close family members or friends can be helpful because family members may have developed coping strategies which mask their loved one's cognitive impairment (SantaCruz and

Swagerty Jr, 2001) making it difficult to detect cognitive or functional impairment in the early stages of the disease.

1.2.1.2 Cognitive assessments

Cognitive tests can be used to determine the extent of cognitive impairment experienced by the person with suspected dementia. In the UK, primary care clinicians will use a validated cognitive assessment such as the GPCOG or the MMSE (Kukull et al., 1994). The GPCOG can be completed in 6 minutes and is a cost-effective measure for detecting dementia (Tong et al., 2017). It has good sensitivity (0.85) and specificity (0.86) for detecting dementia in the general population (Brodaty et al., 2002). However, this still means 15% of people assessed with the GPGOG may receive a false positive and 14% may receive a false negative.

The MMSE is a popular measure of cognitive impairment in clinical and research settings. Compared to the GPCOG, it is a slightly longer assessment, taking approximately 10 minutes. A Cochrane review of the accuracy of the MMSE for detecting dementia in primary and community setting found good levels of sensitivity (0.85) and specificity (0.90). Like the GPCOG, there is a small risk of false positive and false negatives.

However, sensitivity and specificity can vary greatly depending on what cut-off is used to distinguish between normal and pathological decline, increasing their unreliability in detecting the early stages of dementia. For example, the sensitivity and specificity of the MMSE drop to 0.87 and 0.82 respectively when a score of 25 is used as a cut-off, as compared to a score of 24 (Creavin et al., 2016). While these tests provide a clinically useful assessment of the level of cognitive deterioration experienced by people living with dementia, they are not conclusive. Furthermore, the MMSE is socially (Bertolucci et al., 1994) and culturally biased (Albert et al., 2011, Prince et al., 2003). Of the MMSE, a Cochrane review of diagnostic accuracy, concludes that the MMSE should not be used in isolation to confirm or exclude a diagnosis and scores should be interpreted in the context of the patient's individual circumstances.

1.2.1.3 Cerebral spinal fluid and blood biomarkers

A biomarker is a physical change in the constitution of a host that can be measured and indicates the presence of a disease (Feldman et al., 2008). Currently, there are no reliable blood-based biomarkers, therefore blood tests are used to screen for and exclude reversible causes of cognitive impairment (Livingston et al., 2017). The most advanced biomarkers for dementia are levels of β-amyloid, total tau, and phospho-tau in the cerebral spinal fluid (CSF). These biomarkers are routinely used in research to detect the development of pathologies associated with early-stage dementia up to 15 years before the onset of symptoms (Bateman et al., 2012). However, previous research has highlighted a discrepancy between biomarker pathology and symptomology (Kumar et al., 2020). There are cases in which people will have either β-amyloid plaques or tau-tangles and no symptoms of dementia (Schneider et al., 2009). Similarly, one study found 25% of people with a diagnosis of Alzheimer's disease did not have the associated neuropathology at autopsy. In clinical practice, a lumbar puncture is required to test for these biomarkers and patients can experience negative outcomes from this procedure, including anxiety, pain, and lumbar puncture headaches (Menéndez-González, 2014). Testing CSF has been deemed to be a cost-effective method for detecting early dementia, however, the time taken to conduct an additional lumbar puncture test may cause a further delay to diagnosis (Valcárcel-Nazco et al., 2014). Furthermore, researchers have questioned the utility of the increased diagnostic accuracy from these tests if they do not lead to more tailored and better treatments for dementia (Livingston et al., 2017).

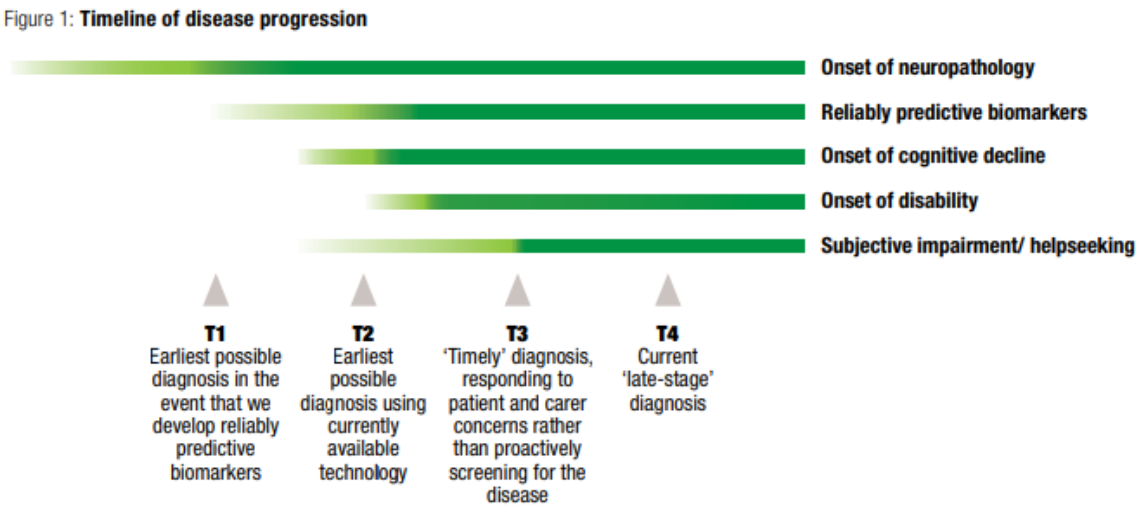
1.2.1.4 Neuroimaging

Structural brain scans, such as CT or MRI, are recommended for confirming a diagnosis and distinguishing between dementia subtypes (Livingston et al., 2017). PET scans can be used to assess levels of β-amyloid and confirm confidence in the accuracy of the diagnosis, however, they are not used in general practice as there is little evidence as to the value they add to the clinical management of dementia (Weston et al., 2016). The following section discusses the value of PET scans for patients diagnosed with MCI.

1.2.2 Mild Cognitive Impairment

The pathological changes in the brain which contribute to the presentation of dementia are thought to start years before the onset of symptoms (T1 and T1 in Figure 1.3). This prodromal stage of dementia is called mild cognitive impairment (MCI), where a person can experience cognitive decline which is greater than expected for their age and level of education but does not interfere with their activities of everyday living (Gauthier et al., 2006). MCI is estimated to be more prevalent than dementia, affecting between 2 and 12% of the population (Sachdev et al., 2015), however, these studies tend to be cross-sectional and do not account for changes over time (van der Flier and Scheltens, 2005). This is important as MCI is not a stable condition, people with MCI may convert to dementia, their cognition may stay the same or they may revert to normal levels of cognitive function (Sachdev et al., 2015).

Figure 1.3 Timeline of disease progression (from Prince et al., 2011)



There are two subtypes of MCI, amnesic and non-amnesic (Petersen et al., 2001). It is estimated that 10.2% of people with MCI convert to dementia per year (Bruscoli and Lovestone, 2004), making it a helpful diagnosis for identifying people who are most at risk of developing dementia. Episodic memory is particularly affected in amnesic MCI, and those with this type of MCI are at greater risk of converting to dementia than those with non-

amnesic MCI (Jahn, 2013). People with non-amnesic dementia and positive β-amyloid PET scan are considered to have “prodromal dementia” (Dubois et al., 2014). It is not clear why some people with MCI develop dementia, whereas others revert to normal cognition. However, age, education, race, co-morbid cardiovascular conductions, diabetes, diet and APOE e4 status have all been found to be associated with an increased risk of converting from MCI to dementia (Welstead et al., 2021).

As MCI is potentially treatable, a diagnosis of MCI presents clinicians with the opportunity to provide treatment, or for the person diagnosed with MCI to make lifestyle changes that may prevent them from converting to dementia. For example, following a Mediterranean diet is associated with a lower risk of converting from MCI to dementia, a diagnosis of MCI presents the patient with the opportunity to make changes to their diet which may, in turn, decrease their risk of dementia (Cooper et al., 2015). However, other than making changes to improve the general health of the person diagnosed with MCI, there are currently no effective pharmacological or non-pharmacological treatments available, limiting the clinical usefulness of this diagnosis.

Additionally, patients may find a diagnosis of MCI confusing. In the USA, the CARE-IDEAS study surveyed 1,845 dyads (caregivers and people living with dementia) who had received a b-amyloid PET scan as part of the clinical investigation for MCI or Dementia (James et al., 2020, Belanger et al., 2019). They found that participants with a diagnosis MCI and a positive β-amyloid scan were less likely to accurately report the results of their test than β-amyloid positive patients with dementia (James et al., 2020). Further qualitative analysis of the sample, found that those who misunderstood their diagnosis had higher levels of cognitive impairment, reported confusion with the terminology to describe their diagnosis and a lack of clarity in the diagnosis and prognosis from the clinician. This is supported by Visser et al (2020) who found that approximately half of clinicians (54%) making a diagnosis of MCI used the name of the condition when explaining the diagnosis to the patient. Furthermore, they found few clinicians gave personalised information regarding the patient's risk of

converting to dementia, and while they did offer advice on the short-term next steps in treatment, they did not offer advice on making plans for the long-term care or treatment of MCI (Visser et al., 2020). Additionally, caregivers were not always present during the diagnostic process or delivery, which could affect their understanding of their loved one's diagnosis.

1.2.3 Misdiagnosis

Due to the imprecision of diagnostic tests for dementia and MCI, there is a risk of misdiagnosis. Individuals who undergo a clinical assessment for dementia can receive a false positive (diagnosed with dementia when they do not have the condition) or false negative (do not receive a diagnosis when they do have dementia). Those who receive a false negative diagnosis are likely to experience a progression of symptoms which are then correctly diagnosed in the later stages of dementia. Much of our understanding of false negative diagnoses can come from research on delayed dementia diagnoses (Bradford et al., 2011, Parker et al., 2020). However, false positive diagnoses present a greater clinical challenge. Those with a false positive diagnosis will not experience the rate of decline, typically associated with dementia. Sometimes this apparent stabilisation of symptoms is attributed to the effects of anti-dementia medications or non-pharmacological treatments (Howard and Schott, 2021). A false positive diagnosis of dementia can come with consequences including unnecessary psychological damage, withdrawing from working and other social activities and exposure to inappropriate treatment with anti-dementia drugs (Howard and Schott, 2021, Philips et al., 2016). As a misdiagnosis is more likely in the earlier stages of dementia, it is important to balance the benefits of an early diagnosis against the risks of a misdiagnosis.

1.3 Outcomes associated with the early diagnosis of dementia

Narratives that support the benefits of an early diagnosis typically follow the same pattern: an early diagnosis allows people living with dementia to access specialist services which

provide post-diagnostic support. They will then be offered drug and non-drug treatments, which can improve the quality of life of people living with dementia and reduce the risk of potential crisis care. The following sections examine the scientific evidence of the benefits of an early diagnosis, and what benefits people living with dementia might expect to gain from receiving treatments and post-diagnostic support.

1.3.1 Scientific evidence of the benefits of an early diagnosis

In the 2011, the authors of the World Alzheimer's Report conducted a systematic review examining the effect of an early diagnosis on five outcomes: memory clinics, disease stage, institutionalisation, disease progression and mortality. This review was limited to epidemiological studies. They identified 8,041 articles, however, only three of these studies examined the timing of the diagnosis in relation to outcomes (Prince et al., 2011). Moreover, these studies demonstrated small effect sizes and were at risk of bias. The authors concluded that an early diagnosis is still likely to be beneficial to people living with dementia and the results of this review were "clearly a case of 'absence of evidence' rather than 'evidence of absence'" (p. 29).

In 2016, another review examined the outcomes associated with a timely diagnosis of dementia. The authors identified nine-studies which examined the consequences of diagnosing dementia early, including qualitative and quantitative studies. However, none of the included studies were "specifically focused on diagnosing AD at the prodromal stage" (p.620) The authors of this review were slightly more circumspect regarding their findings, but they still concluded that an early diagnosis may still be of benefit "Timely diagnosis at the prodromal stage of the disease could offer many potential benefits to patients and caregivers, especially the opportunity to obtain treatment to control symptoms, avoid medications that may worsen symptoms, and, possibly in the future, access to interventions that slow or lessen the disease process." (p. 628)

The conclusions drawn from these two reviews raise an important question: why, in the face of a scarcity of evidence, do the authors still conclude an early diagnosis is beneficial? The presumption of the benefits of an early diagnosis of dementia is pervasive throughout the scientific literature. If we are to create treatments and services that truly meet the needs of people living with dementia, we must critically assess this assumption.

One of the reasons for the paucity of research examining the benefits of an early diagnosis is that is not an easy topic to investigate. Therefore, research assessing the benefits of an early diagnosis does so indirectly. The following section explores how, in the absence of clear evidence, the provision of post diagnostic support, pharmacological and non-pharmacological treatments earlier in the disease may be beneficial to people with early stage dementia.

1.3.2 Provision of post-diagnostic support

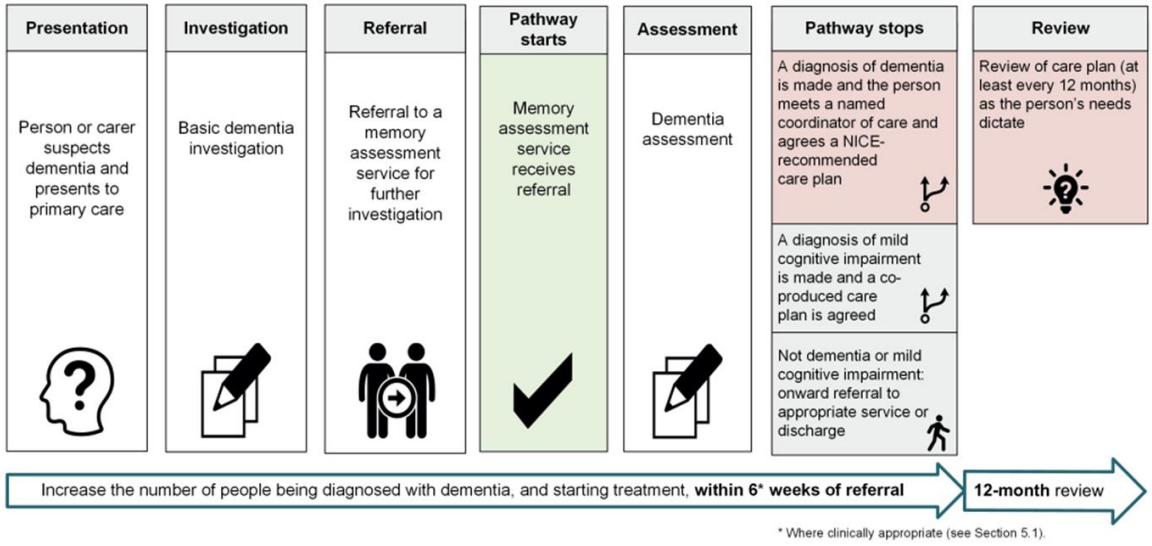
The value of a diagnosis of dementia is contingent on not only how it is delivered, but also on what care and support follows it. It has been argued that an early diagnosis can lead to access to post-diagnostic services which can enable people to live well with dementia. In the UK, guidelines for the diagnosis and treatment of dementia has been outlined by the National Institute for Health and Care Excellence (NICE) as the Dementia Care Pathway (NICE, 2018).

People living with dementia also have access to third sector services following their diagnosis. This includes, but is not limited to, dementia advisors, support groups, memory cafes and alternative sources of advice outside of the health care system. Many of these services do not require a formal diagnosis for access, however people living with dementia and their caregivers are unlikely to learn about these services unless they do receive a formal diagnosis. Furthermore, the effectiveness of support provided outside health and social care settings is less well understood. For example, evidence on the benefits for memory cafes are limited to qualitative studies of caregiver's experiences – although caregivers find memory cafes to be a positive source of information and peer support (Greenwood et al., 2017, Mather, 2006). Another challenge in the provision of post-diagnostic support outside of health services is the

lack of consistency. These services vary greatly depending on where the person living with dementia lives and can change greatly over time. Future research is needed to understand the current provision of post-diagnostic support outside of health services.

1.3.2.1 The Dementia Care Pathway

Figure 1.4 The Dementia Care Pathway (from National Collaborating Centre for Mental Health, 2018)



The Dementia Care Pathway in the UK has two objectives: to improve access to a timely diagnosis and increase the provision of evidence-based post-diagnostic support (National Collaborating Centre for Mental Health, 2018). Figure 1.4 outlines the dementia care pathway. First, the person with suspected dementia presents to their primary care physician with their concerns, the physician assesses their symptoms, and where they feel further investigation is warranted they refer the patient to a specialist memory service. Memory services are designed to be a one-stop shop for people living with dementia, connecting health service, social care and voluntary sector support (Banerjee et al., 2007). When attending the memory service, the patient is assessed with more in-depth cognitive assessments, blood tests and brain scans, where appropriate. After a diagnosis of dementia is confirmed, a care plan which is based on

NICE recommendations is established. The patient is then invited back on an annual basis to review their care plan.

There are many places in which a person may experience roadblocks in the dementia care pathway. For example, a person with suspected memory problems may be reluctant to go to the GP to have their memory problems assessed. Once they have attended the GP, the GP may choose not to refer the patient on for further assessments due to nihilistic beliefs of the value of diagnosis and available treatments (Dhedhi et al., 2014). Failures to identify those with probable dementia in primary care can result in the diagnosis being delayed by 2-3 years (Boise et al., 1999). Once referred to a specialist, there is still a risk of receiving a false positive or false negative diagnosis, due to weaknesses in the available instruments to accurately diagnose dementia. However, this risk is reduced by using a combination of evidence-based investigations depending on the individual circumstances of the patient.

There is no evidence that an earlier access to dementia services can improve health service outcomes for people living with dementia. A survey of GPs in the UK found that participants rated a timely diagnosis as beneficial to people living with dementia, however they also reported a dissatisfaction with the available post-diagnostic services (Fox et al., 2014). Section 1.3.3.3 further discusses weaknesses in the provision of post-diagnostic support in the UK.

1.3.3 The provision of treatments

Two pharmacological and one non-pharmacological treatments are recommended by NICE for the treatment of dementia. The following sections examine how these treatments work, our current understanding of their effectiveness and whether delivering these treatments in the earlier stages of the disease can increase their effectiveness.

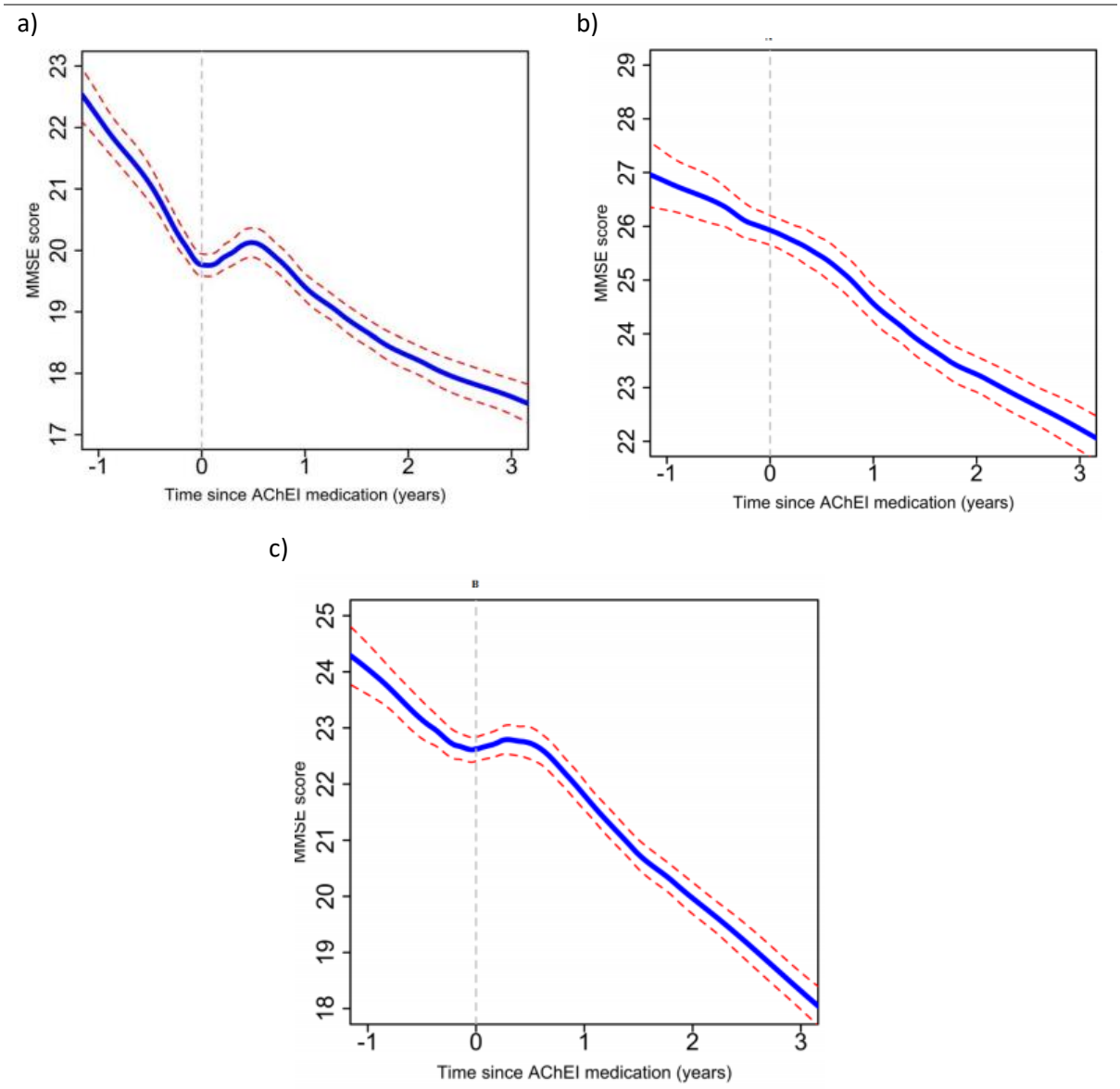
1.3.3.1 Pharmacological treatments

Cholinesterase inhibitors

Three type of acetylcholinesterase inhibitors (AChEIs) – donepezil, galantamine, and rivastigmine – are recommended by NICE for the treatment of mild to moderate Alzheimer's Disease (NICE, 2018). AChEIs do not treat the underlying pathology that causes dementia, they inhibit the enzyme acetylcholinesterase to prevent the breakdown of acetylcholine, a neurotransmitter associated with memory. AChEIs are not recommended for the treatment of MCI, vascular, or frontotemporal dementia.

A Cochrane review of 13 double-blind and placebo-controlled RCTs (of 7,298 participants) testing the effectiveness of AChEIs found that they were associated with increased cognitive performance on the MMSE (mean difference = 1.37, 95% CI = 1.13 – 1.61). A more recent systematic review of 80 RCTs reported more modest benefits to MMSE scores at 3, 6, and 12 months (MD = 1.08, 1.00, and 1.10 respectively) (Birks, 2006). Birks (2006) also reported small improvements in the PLwD's activities of daily living, and neuropsychiatric symptoms, indicating that AChEIs may have benefits to outcomes other than cognition. However, significantly more participants in the treatment groups were lost to follow-up, increasing the risk of bias. This could be partly explained by adverse side effects from the medication, significantly more participants in the treatment group reported adverse events such as nausea, vomiting, and diarrhoea. Another limitation to our understanding of the benefits of AChEIs is the follow-up times used by the included trials, which were limited to 6 months or one year. This is problematic as the median survival time for people living with dementia is 5.7 years following their diagnosis (Waring et al., 2005). However, a large retrospective cohort study of electronic health records found that patients prescribed AChEIs had a significant improvement in cognition in the 6 months following the initiation of treatment, unfortunately, after 6 months their cognition returned to pre-treatment levels of impairment (Perera et al., 2014), see Graph A in Figure 1.5.

Figure 1.5 Trajectory of decline as rated by the MMSE before and after initiation of AChEIs (From Perera et al. 2014)



Note: AChEI initiation date defined as 0

Clinical trials have demonstrated that AChEIs are effective for people living with mild to moderate dementia, with less certain evidence for the later stages of the disease (Livingston et al., 2017). This may indicate that AChEIs are more effective when delivered as early as possible, however, it is not as simple as that. Perera and colleagues (2014) found that people

with less cognitive impairment, as rated by the MMSE, at the time of initiation of AChEI treatment experienced a smaller improvement in cognition, compared to those with a greater degree of cognitive impairment. Graph B in Figure 1.5 shows the trajectory of decline following the initiation of AChEIs for patients with MMSE scores between 25 and 30, whereas Graph C shows the trajectory of decline for patients with MMSE scores between 21 and 24.

Memantine

Memantine is another anti-dementia medication recommended for treating people with more severe Alzheimer's disease, or for those who are intolerant or have a contraindication to ACHEIs (NICE, 2018).

Memantine is effective in treating some of the symptoms of dementia, however, it is slightly less effective than AChEIs. Despite its lower levels of efficacy, it is acceptable to a wider proportion of people living with dementia. A Cochrane review of 44 RCTs of 9,811 patients found memantine was associated with a better cognitive performance in patients with mild to moderate dementia as rated by the ADAS-Cog compared with a placebo (SMD = -0.32, 95% CIs = -0.48 - -0.15) (McShane et al., 2019). Similarly, memantine was associated with increased performance of the clinical global functioning (SMD = -0.20, 95% CIs = -0.28 – -0.13), cognitive functioning (SMD = -0.27, 95% CIs -0.34 -0.21), activities of daily living (SMD = -0.16, 95% CIs -0.24 -0.09) and neuropsychiatric symptoms (SMD = -0.14, 95% CIs -0.21 -0.08) (McShane et al., 2019). Furthermore, there is some initial evidence, albeit low-quality evidence, that memantine may have some benefits to people diagnosed with Parkinson's disease dementia, dementia with Lewy bodies or frontotemporal dementia (Knight et al., 2018). Similar, to studies of AChEIs, participants in the intervention group were more likely to be lost to follow-up, experience adverse effects, and the duration of follow-up in the included trials was limited to 6 months.

1.3.3.2 Non-pharmacological treatments

Non-pharmacological treatments provide an alternative to drug treatments. There is some evidence that non-pharmacological treatments can improve cognition, quality of life and reduce BPSD for people living with dementia (Olazarán et al., 2010) (Livingston et al., 2014) (Olley and Morales, 2018). Non-pharmacological interventions are heterogeneous with varying impact on outcomes. A previous systematic review found that non-pharmacological interventions were more effective: when delivered over a longer period (at a higher dose), when the person with dementia was involved, and when the intervention consisted of multiple components (Pinquart and Sorensen, 2006). Pinquart et al (2006) acknowledged that needs change during the progression of dementia, therefore some treatments may be more effective than others at different stages of the disease. The only non-pharmacological treatment recommended by NICE is cognitive stimulation therapy (CST) (Health and Excellence, 2018). Therefore, the following section will focus on examining the strengths and weaknesses of CST in greater depth.

Cognitive stimulation therapy (CST) is a manualised treatment for people with mild to moderate dementia based on the principles of cognitive stimulation (Spector et al., 2001, Spector et al., 2003). CST is generally delivered to groups of between 8 and 10 people diagnosed with dementia and run for 14 sessions. After an initial programme of CST has finished, there is the option of continuing the treatment by providing maintenance CST (MCST) (Orrell et al., 2005). MSCT follows the same format as CST and runs for 24 sessions. There is also the option for individual CST (iCST) for people who do not want to, or are unable to take part in groups (Yates et al., 2015).

A Cochrane review of RCTs testing CST found it can improve cognition and quality of life for people with dementia (Woods et al., 2012). Participants who had 12 sessions of CST experienced a 1.74 improvement in cognition, as rated by the MMSE, this is comparable to the improvement in cognition elicited by AChEIs. Furthermore, these improvements were considered cost-effective (Woods et al., 2012). Similarly, MCST improves quality of life for

people living with dementia, however, it was not found to have any benefit for cognition. It is not clear whether CST or MCST can reduce feelings of depression or anxiety in people living with dementia. And, so far, research has not found any benefits to caregivers from CST or MCST. While these findings are promising, the studies included in this review had short follow-up times, making it difficult to establish the long-term effectiveness of CST.

NICE guidelines recommend that people living with dementia are offered one course of CST after their diagnosis (NICE, 2018). In addition to the evidence from RCTs, qualitative studies show that people with dementia find taking part in CST groups to be a positive experience. They appreciate having the chance to talk to others and be listened to in a supportive environment (Murray et al., 2016, Spector et al., 2011). They value meeting people who are experiencing similar challenges in their local area. After taking part in the groups, they find it easier to talk to people outside of the group and expand their social circles (Murray et al., 2016). Caregivers may experience similar benefits, however, as CST is not dyadic (offered to both the person living with dementia and caregiver) they can feel excluded from the sessions (Spector et al., 2011). They may not understand what happens during the sessions, and the person they are caring for may not be able to tell them.

While CST is a cost-effective intervention, service providers report that running CST groups requires a lot of time and resources. There is also a worry that people living with dementia have a very positive experience of CST and are then left with no support following the end of the group (NSFT, 2019).

Other non-pharmacological treatments have yet to demonstrate the levels of efficacy and cost-effectiveness to be recommended by NICE, limiting the options available to people living with dementia. An additional barrier to the understanding of which interventions work best in the early stage of the disease is the lack of consistency across studies in which outcome measures are used or considered important. In the scientific literature, there is a wide range of interventions that have been tested for the early stages of dementia. However, the variety

of outcome measures used in these trials makes it difficult to make meaningful comparisons between them (Moniz-Cook et al., 2008).

1.3.3.3 Adherence to the Dementia Care Pathway and NICE Guidelines

To better understand the value of post-diagnostic support, we must first understand weaknesses or gaps in its provision. The Royal College of Psychiatrists has published standards for the post diagnostic support delivered by memory services. This is done through the Memory Services National Accreditation Programme (MSNAP) which regularly audits member services against the published standards. In 2015, there were 222 memory services in England (Hodge and Hailey, 2013). Enrolment in MSNAP is not mandatory and in 2019 91 English memory services were enrolled in the scheme, approximating 41% of all services. MSNAP regularly reviews whether member services are meeting the published standards. In their 2019 review of memory services they found:

- 70% of patients were prescribed medication (available medications were not appropriate for 5% of participants surveyed). Just under half (40%) were not given written information about available medications, and 8% reported that staff did not explain how to take the medication, what it would do, or possible side effects.
- 75% of patients received written information about available psychosocial interventions
- 96% of patients were offered group CST, however, only 51% were offered MCST

This demonstrates that the majority of patients are offered drug or non-drug treatments. However, patients are not provided written information to facilitate decision making. While these statistics show some strengths and weaknesses in the treatment delivered by memory services, they are only limited to services enrolled in the programme and therefore at risk of bias. Furthermore, it is not possible to assess the memory clinic's delivery of all parts of the care pathway. For example, it is not possible to assess the proportion of people diagnosed with dementia who receive an annual follow-up as this is not included in MSNAP standards, despite being a key part of the dementia care pathway. This survey does not compare

outcomes between those who were diagnosed in the early stages of the disease and those who were diagnosed in the later stages of the disease. Future research is needed to understand how the provision of post-diagnostic support affects the outcomes associated with an early diagnosis.

1.4 Rationale and research questions for this thesis

In summary, policy efforts to improve the number of people with a formal diagnosis of dementia during the early stages of the disease have focused on improving public awareness of dementia to increase the number of people seeking a diagnosis for suspected memory problems. Once they have received a diagnosis, people living with dementia will have access to early treatments which will keep them living well for longer. However, initiatives to raise awareness of dementia has only led to a small increase in the proportion of people living with dementia with a formal diagnosis (Mukadam et al., 2015).

Dementia is a challenging condition to diagnose, requiring multiple and lengthy investigations, with a risk of misdiagnosis. Receiving a diagnosis of dementia can be a difficult experience for people living with dementia and their caregivers. A systematic review of 52 qualitative studies exploring experiences of giving or receiving a dementia diagnosis found that the diagnostic process was generally perceived negatively (Yates et al., 2021). Participants with dementia and their caregivers reported a significant emotional impact of the diagnosis including depression, shock, sadness, and grief. However, receiving a diagnosis earlier in the progression of the disease would allow people living with dementia the opportunity to remember their diagnosis and engage with making decisions about treatment and future care (Bradford et al., 2011). It is important to balance these emotional responses to a diagnosis, dementia should ideally be diagnosed early enough that the person living with dementia can participate in decision making, but should also only be given when they are prepared to manage the emotional impact.

UK dementia policies have proposed that an early diagnosis of dementia can lead to improved quality of life, a reduction in crisis care, and delaying admission into care homes. However, there is little empirical evidence to support these claims. There are only two literature reviews which have attempted to summarise the evidence supporting the proposed benefits of an early diagnosis. Alzheimer's Disease International (ADI) published a report assessing the strength of the evidence that early diagnosis and early intervention can lead to the previously mentioned outcomes. They found only three population-based studies which examined the relationship between an early diagnosis and mortality, or cognitive decline, and these studies reported small effects (Prince et al., 2011). Furthermore, when the researchers reviewed statements in published papers summarising the benefits of early diagnosis, they found them largely to be unreferenced and not evidence based. This is supported by a later review of the literature discussing the benefits of diagnosing dementia early, which concluded that there is a paucity of research focused on benefits to people living with dementia or caregivers, and many of the proposed benefits are based on modelling studies rather than patient data (Dubois et al., 2016). Similarly, there are no qualitative studies exploring people living with dementia and their caregiver's perspectives on the value of an early diagnosis.

One of the key challenges in investigating the benefits of an early diagnosis is correctly identifying those who have received an early diagnosis. As cognitive outcomes have lower sensitivity and specificity where patients with dementia are less cognitively impaired, these measures cannot be reliably used to detect those with an early diagnosis. However, as MCI is considered to be prodromal to dementia (Dubois et al., 2014), a diagnosis of MCI recorded before a diagnosis of dementia could be a potentially helpful proxy for investigating the benefits of an early diagnosis.

Not only are there no studies that demonstrate that an early diagnosis can have an impact on any of the outcomes listed above (quality of life, reduction in hospital crisis care, and delaying admission into care homes) (Prince et al., 2011), but we must also question whether these outcomes are, in fact, negative. Admission into care homes has been historically seen as a

negative outcome, however, for many moving to a care home can be a positive choice (Booth, 1989). A study of people with dementia's preferred place of death found that approximately half of people living with dementia (49.8%) wished to be in a care home when they died (Wiggins et al., 2019). This could indicate a shift in attitudes towards care homes.

Furthermore, it is not clear if there is an alignment between the outcomes discussed in dementia policy and the outcomes and measures used in dementia research. Randomised controlled trials play an important role in building our understanding of how an early diagnosis and subsequent early treatment can be beneficial to people living with dementia. However, the value of such trials is dependent on the meaningful selection of outcomes and outcome measures. Interest in developing nonpharmacological treatments for early dementia is growing in the research community, however, meta-analyses weighing the effectiveness of one treatment against another have been limited by the inconsistent use of outcome measures (McDermott et al., 2019). There have been attempts to create consensus guidelines on which outcomes and measures should be used over others, however, it is not clear whether this has translated into practice (Harding et al., 2020). This is a key weakness in both dementia research, policy and practice as RCTs are considered the gold standard of evidence for informing policy and practice (Joffres et al., 2006).

Knowledge of the benefits of an early diagnosis can be generated from data using multiple sources. It can be generated from primary and secondary qualitative and quantitative data. It can also be generated by mapping the existing literature on a topic. A scoping review of outcomes and outcome measures used by non-pharmacological treatments can generate useful information related to the benefits of diagnosing dementia early. This is useful for mapping the current evidence on a topic and identifying its strengths and limitations. While this does not provide an immediate understanding of which treatments are effective, it does highlight areas for further development which can strengthen our understanding of the benefits of an early diagnosis. This is vital for developing robust, evidence-based research, policy and practice guidelines in the future.

A nihilistic attitude to treatments or belief that little can be done for dementia is often cited as a reason for a delayed or missed diagnosis of dementia in primary care (Bradford et al., 2009, Dhedhi et al., 2014). There are pharmacological treatments available for dementia, which are likely to be more effective during the early stages of the disease (Birks, 2006, McShane et al., 2019). However, these medications come with a risk of unpleasant side effects (Birks, 2006, Le Couteur et al., 2013, McShane et al., 2019) and not all patients are given written information regarding available drug treatments (Hodge and Hailey, 2013). Furthermore, AChEIs and memantine are generally limited to those diagnosed with Alzheimer's disease, which represents approximately 62% of people living with dementia in the UK (Prince et al., 2014). While these treatments have been found to have a beneficial effect on cognition, this effect is modest (Perera et al., 2014). Similarly, in terms of non-drug treatments, CST has been found to improve cognition and quality of life for people living with dementia. Most people diagnosed with dementia in England are offered one course of CST (Hodge and Hailey, 2013), however, once they have finished this programme there is often no follow-up available. Furthermore, studies testing non-pharmacological treatments tend to be limited to a select few outcome measures (Moniz-Cook et al., 2008). Making it difficult to make conclusions on their wider utility. So, while it is not correct to argue that nothing can be done for people living with dementia – there are things that can be done – we must also be clear on the limitations of available treatment, and the weaknesses in the evidence on its effectiveness to help patients to weigh up the potential harms and benefits when seeking a diagnosis.

1.4.1 Research questions

Over the last decade, many countries have taken proactive policy approaches to manage the care and treatment of dementia. They have placed particular emphasis on the "timely" or "early" diagnosis of dementia. However, without a reliable diagnostic test for dementia, and with very few effective treatments, it is unclear what benefits an early diagnosis can be expected to produce. Therefore, this thesis aims to answer the question: what benefits are associated with an early diagnosis of dementia? By understanding if an early diagnosis of

dementia is beneficial, and how people with dementia and their caregiver may benefit, we can create policies and services that are more responsive to the needs of those affected by dementia. I will address the overall research question, by exploring the following sub-questions:

1. Can a diagnosis of mild cognitive impairment before dementia be used as an indicator for an early diagnosis?
2. Are people with an early diagnosis, as defined by a diagnosis of MCI before dementia, at less risk of mortality, visiting A&E, or being hospitalised?
3. What potential outcomes of early diagnosis do people with dementia and their carer givers perceive to be the most beneficial or important?
4. What particular circumstances are necessary for people living with dementia and their carers to experience the benefits of an early diagnosis?
5. Which outcomes are measured in randomised controlled trials for non-pharmacological interventions in early dementia and mild cognitive impairment (MCI)? And do they reflect our current understanding of the benefits of early intervention?

1.4.2 Structure of the thesis

To address the research questions, this thesis used a convergent parallel mixed methods design, consisting of three phases of investigation:

1) The secondary data analysis of electronic health care records held by South London and Maudsley NHS Foundation Trust, using linkages to HES and ONS (aims one and two). The results of this phase of investigation are presented across two chapters.

2) A qualitative interview study of people living with dementia or MCI, and their caregivers (aims three and four)

3) A scoping review of outcome measures used to evaluate non-pharmacological interventions in mild cognitive impairment and mild dementia (aim five)

1.4.3 Hypotheses for quantitative phase of investigation

The quantitative phase of investigation aims to investigate whether a diagnosis of MCI can be used as a proxy for an early diagnosis, and if an early diagnosis is associated with a reduced risk of mortality, health service use, or emergency department attendance.

I hypothesise that a diagnosis of MCI before dementia can be used as a proxy for an early diagnosis. However, I hypothesise that an early diagnosis is not associated with a reduced risk of mortality. Nor will participants with an early diagnosis have a reduced risk of hospitalisation or emergency department attendance, compared to those without an early diagnosis.

1.4.4 Chapter summaries

Chapter two outlines the methods used in this thesis. In this chapter I describe the epistemology underpinning this thesis and the selection of a mixed methods design. I then present the included samples, methods of data collection and analysis for each of the individual phases of analysis.

Chapter three presents the results of the first half of the quantitative phase of analysis. In this chapter I examine whether a previously recorded diagnosis of MCI, before dementia, can be used as an indicator for an early diagnosis. I then present whether an early diagnosis is associated with a reduced risk of mortality. This chapter is provided a as the following peer-reviewed publication:

Couch, E., Mueller, C., Perera, G., Lawrence, V. and Prina, M., 2021. The Association Between a Previous Diagnosis of Mild Cognitive Impairment as a Proxy for an Early Diagnosis of Dementia and Mortality: A Study of Secondary Care Electronic Health Records. Journal of Alzheimer's Disease, (Preprint), pp.1-8.

In chapter four, I present the second half of the results from the quantitative phase of analysis. In this chapter, I examine whether an early diagnosis is associated with a reduced risk of hospitalisation or emergency department attendance. This chapter is provided a as the following peer-reviewed publication:

Couch, E., Mueller, C., Perera, G., Lawrence, V. and Prina, M., (In Press) The association between an early diagnosis of dementia and secondary health service use. Age and Ageing.

Chapter five presents the results of the qualitative phase of investigation. In this chapter I explore what people living with dementia and their caregivers perceive the benefits of an early diagnosis to be.

Chapter six presents the results of the scoping review examining which outcome measures have been used by RCTs testing non-pharmacological treatments. This chapter is provided as the following peer-reviewed publication:

Couch, E., Lawrence, V. and Prina, M., 2020. Outcomes tested in non-pharmacological interventions in mild cognitive impairment and mild dementia: A scoping review. BMJ open, 10(4), p.e035980.

Chapter seven summarises the results from each individual phase of analysis. This is followed by a discussion of how the results from each phase of the thesis were integrated to produce cross-cutting meta-themes. Finally, I discuss the implications of the findings of this thesis for policy, future research, and clinical practice.

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Chapter 2: Methods

This chapter outlines the aims of the thesis, associated methods, and study samples. In this chapter, I will present the justification for the mixed methods design of this thesis. I will then present the different methodologies used in this thesis: the quantitative analysis of data from electronic health care records, the thematic analysis of qualitative interviews, and a scoping review of outcome measures used by published studies.

2.1 Mixed Methods

Mixed methods research is broadly defined as research that collects, analyses, and mixes both quantitative and qualitative data and approaches in either a single study or series of studies (Cresswell, 2014). Qualitative and quantitative approaches can be combined at any stage of the research process to be considered mixed methods. However, mixed methods should not just collect and analyse both type of data separately, they should be fully integrated so that the use of qualitative and quantitative methods together is stronger than if they were conducted separately (Johnson et al., 2007). Qualitative and quantitative methods can be viewed as being based on opposing epistemological philosophies, although there are exceptions to this. Balancing these opposing philosophical perspectives to research is one of the key challenges to producing good quality and meaningful mixed methods research (Cresswell, 2014).

2.1.1 Quantitative methods

Quantitative methods are based in positivism, which asserts there is one true reality which can be observed and quantified. Under this paradigm, knowledge is created through deductive reasoning by generating and testing hypothesises (Ryan, 2018). The researcher is separate from participants and maintains objectivity (Phillips et al., 2000, McEvoy and Richards, 2006). In health care research, positivist approaches aim to establish facts about the disease and the body, and its effect in a population. This is rooted in a bio-medical approach as it assumes

that the physiological or biological basis of the disease can be measured, controlled and manipulated (Cresswell, 2014). While positivist approaches can generate much-needed information on how disease affects a population, these approaches have been criticised for giving insufficient attention to the lived experience of disease, and ignoring the social context in which disease occurs and is treated (Corry et al., 2019).

2.1.2 Qualitative methods

Qualitative research is based on multiple epistemological paradigms. Examples of these include constructivism, where there is no objective external reality, instead it is constructed in the mind of the individual (Hansen, 2004); and interpretivism, which posits that there are multiple realities which can be shaped by personal viewpoints, context and meaning (Hesse-Biber, 2010). While there are differences between qualitative paradigms, they are largely based on the assumption that reality cannot be quantified. Qualitative methods allow for the understanding of phenomena from within their context (Blaikie and Priest, 2019). Unlike quantitative research, qualitative methods are not hypothesis-driven but inductive; they are iterative and can be adapted to follow the concerns of the participant (Bryman, 1992). Additionally, in qualitative methods the researcher is a key instrument in the research process, they are central in the collection, analysis and interpretation of the data (Cresswell, 2014). While qualitative methods can allow researchers to explore areas which are not suited to quantitative research, they have been criticised for being highly subjective, without fixed methodologies and therefore at risk of bias (Pope et al., 2000).

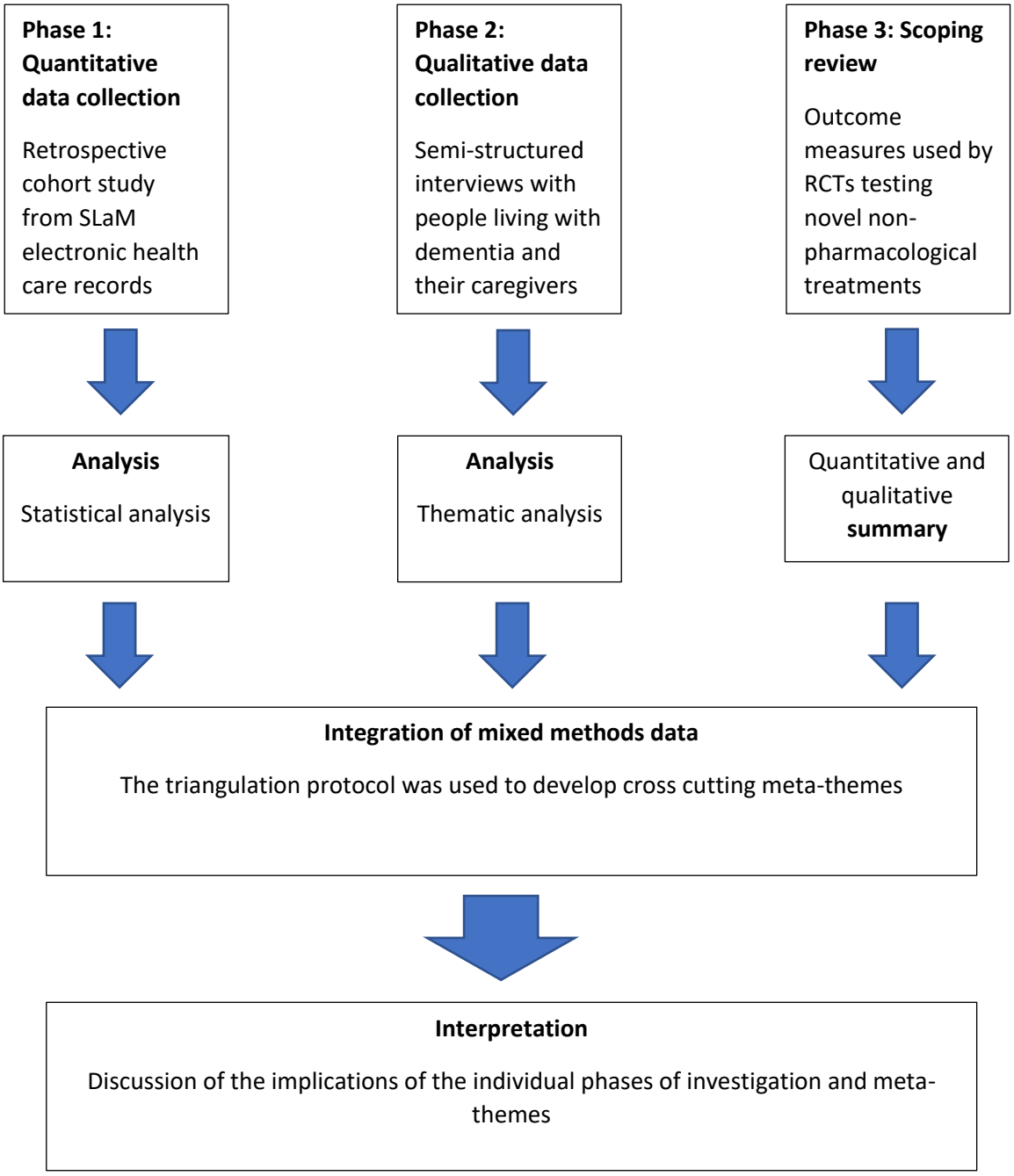
2.2 Choice of Mixed methods for this thesis

This mixed methods thesis will investigate the potential benefits of diagnosing dementia early using a convergent parallel study design. Mixed methods are appropriate for broad and multifaceted research questions, where quantitative or qualitative data alone would not be sufficient to answer the research question (Johnson et al., 2007, Doyle et al., 2009). Mixed

methods research aims to generate insights which are greater than the sum of the individual qualitative and quantitative components (Fetters and Freshwater, 2015).

Under this design, qualitative and quantitative data are collected in parallel, analysed separately and integrated at the interpretation stage. As is often the case in convergent parallel study designs, qualitative and quantitative methods in this design were assigned equal priority (Clark and Creswell, 2008). In this thesis, quantitative methods were used to explore the association between an early diagnosis of dementia and subsequent health service use and risk of mortality in people diagnosed with dementia by South London and Maudsley NHS Trust. Semi-structured interviews and thematic analysis were used to explore people living with dementia's perceptions of the benefits of diagnosing dementia early. A scoping review was used to explore which measures are used to capture the potential benefits of non-pharmacological treatments for early dementia and MCI. Figure 2.1 presents a diagram of the phases of analysis in this thesis.

Figure 2.1 Convergent parallel study design of this thesis



Collecting and analysing mixed methods data allowed me to explore the benefits of an early diagnosis from multiple perspectives. The complexity of dementia requires both quantitative and qualitative knowledge to be generated to create a comprehensive understanding of the disease (Robinson et al., 2011), making mixed-methods research a vital tool for increasing our understanding of how to better care for people living with dementia. The quantitative phase of analysis in this thesis was a retrospective cohort study. While it is not possible to determine causality using this method, it is useful for exploring what factors are related to an early diagnosis of dementia; and whether an early diagnosis is associated with better outcomes. This approach allows researchers to explore trends in how dementia affects the wider population. However, researchers have argued that objective measures (quantitative measures) of the care provided to people living with dementia and their caregivers are at their most meaningful when considered in the qualitative context of the lived experience (Robinson et al., 2011). Additionally, there is a risk that using only quantitative methods in dementia research risk emphasising the biological disease over the personal psychological aspects (Kitwood, 1997). By using qualitative and quantitative methods, I was also able to contextualise the results from one phase of investigation, using the results from another phase of investigation and vice versa.

2.2.1 Pragmatism

One of the key issues in mixed methods research is balancing opposing epistemological philosophies about how reality is constructed and measured (Johnson et al., 2007). Pragmatism is a popular research paradigm in mixed methods as it is not committed to any one system of philosophy and eliminates the need to balance opposing epistemologies (Biesta, 2010). Instead, pragmatism emphasises the aims of the research and advocates for the use of any methods available to address the aims (Yvonne Feilzer, 2010). The partnership between mixed methods research and pragmatism creates a practical and outcome orientated approach to research, which is beneficial for understanding a complex condition like dementia (Robinson et al., 2011).

Furthermore, a pragmatic approach to mixed methods is appropriate to address the aims of this thesis. By allowing for a plurality of methods, pragmatism allowed me to select the best methodology for each component of this study. The benefits of early diagnosis can be at a societal or individual level; there can be benefits in terms of the biological treatment of the disease and there can be benefits in terms of the lived experience. Quantitative methods can be used to quantify the effects of early diagnosis on biological outcomes, such as mortality, and health care outcomes such as hospitalisation. Qualitative methods allow for the exploration of individual experiences and perspectives of early diagnosis and post-diagnostic support, and scoping reviews can be used to summarise the body of evidence on a topic. By combining these methods, I was able to address the aim of this thesis more comprehensively than if I used either of these methods alone. Table 2.1 presents the research questions under investigation in this thesis, the associated design, methods of analysis, and outcomes.

Table 2.1 Research questions and associated design, method of analysis, and outcomes for this thesis

Research questions	Study Design	Method of analysis	Outcome
• Can a diagnosis of mild cognitive impairment before dementia be used as an indicator for an early diagnosis? • Are people with an early diagnosis, as defined by a diagnosis of MCI before dementia, at less risk of mortality, visiting ED or being hospitalised?	Phase 1: The secondary data analysis of electronic health care records held by South London and Maudsley NHS Foundation Trust	Cox regression and negative binomial regression models	Quantitative: hazard ratios for mortality and negative binomial regression for ED and hospitalisations
• What potential outcomes of early diagnosis do people with dementia and their care givers perceive to be the most beneficial or important? • What particular circumstances are necessary for people living with dementia	Phase 2: A qualitative interview study of people living with dementia or MCI, and their carers	Thematic analysis	Qualitative: Themes relating to the research question

and their carers to experience the benefits of an early diagnosis?			
• Which outcomes are measured in randomised controlled trials for non-pharmacological interventions in early dementia and mild cognitive impairment (MCI)? And do they reflect our current understanding of the benefits of early intervention?	Phase 3: A scoping review of outcome measures used to evaluate non-pharmacological interventions in mild cognitive impairment and mild dementia.	Narrative and tabular summary	Quantitative: number of studies using each outcome measure, by type of participant, intervention, and year the study was published Qualitative: Narrative summary of included studies

2.2.2 Rigour in mixed methods research

While there are many benefits to using mixed methods in dementia research, there are also challenges. Pragmatism allows the researcher to use multiple methods to address the research question, however, care should still be taken to integrate findings meaningfully (O'cathain et al., 2008, Johnstone, 2004). Firstly, Robinson et al. (2011) emphasised the importance of developing protocols for collecting and analysing data in advance of commencing the research. I developed protocols for collecting and analysing data for each phase of this thesis in advance. This was usually done as part of the process for applying for approval to conduct each phase of this thesis. Additionally, it is important to consider in advance how the findings from each phase will be integrated. Section 2.4 of this chapter presents how the findings of the different components of this thesis will be integrated using the triangulation protocol. This was established while applying for funding, before starting work on this thesis.

Robinson and colleagues (2011) also argue there are specific considerations for using mixed methods in dementia research. Firstly, the research team undertaking the work should have sufficient training and experience in the methods used in the project. Secondly, protocols for conducting the work should consider the complexity and time requirements for conducting high quality mixed methods research. Finally, mixed methods research in dementia should be patient-centred, and consider the needs of people living with dementia and their caregivers. I have addressed each of these considerations in the design and implementation of each component of this thesis. The supervisory team for this thesis has expertise in each of the methods used. Secondly, when designing the studies in this thesis, I balanced the study design against what is feasible to do during the time I had to complete the thesis. Finally, I used public and patient involvement to ground the aims, design and materials used in this thesis in the needs of people living with dementia. The following section outlines this process in further detail.

2.3 Public and Patient Involvement

Public and patient involvement (PPI) is when people living with the condition of interest works in partnership with research to plan, design, implement, manage, evaluate and/or disseminate research. PPI can be used at any stage of the research process (see Figure 2.2). This process can ensure that research is grounded in the needs of people living with dementia (Bethell et al., 2018), a key consideration in conducting pragmatic mixed methods research (Robinson et al., 2011).

Figure 2.2 PPI and the Research Cycle

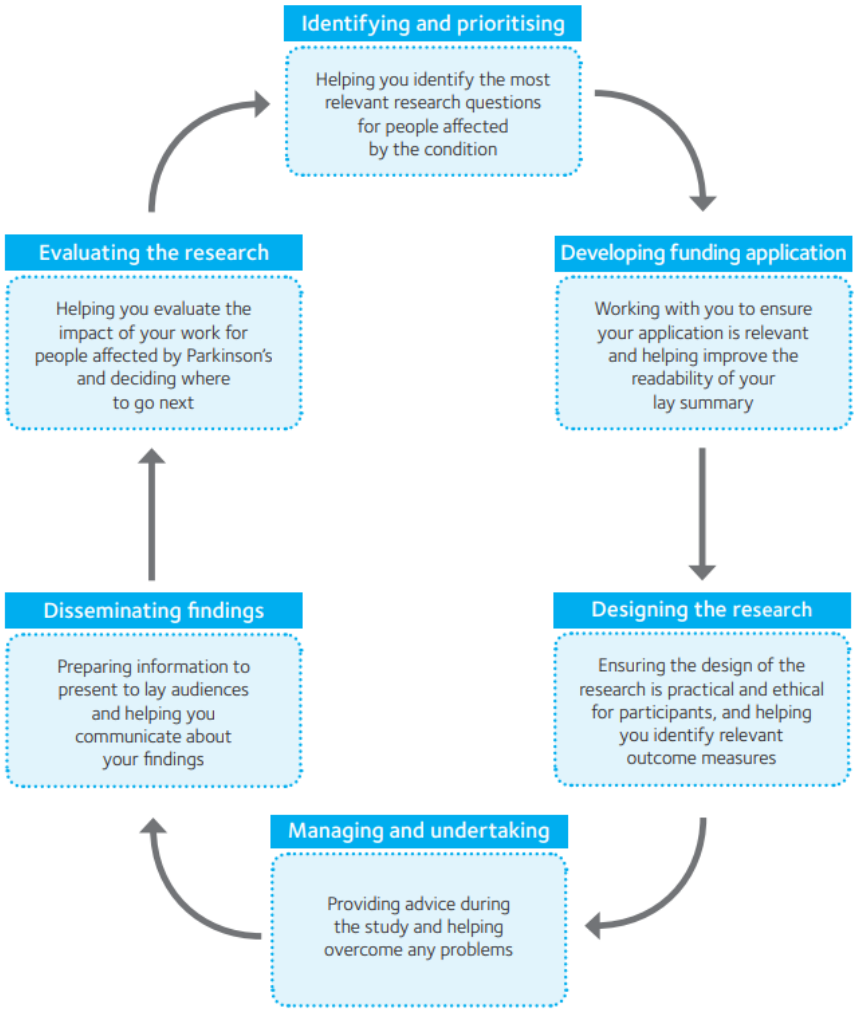


Image from: https://www.parkinsons.org.uk/sites/default/files/2018-/PPI%20Guidance%20for%20Researchers.pdf

PPI can be done in consultation or collaboration with people living with dementia. There are pros and cons to each approach (NIHR, 2018). The collaborative approach sees researchers including at least 2 people with lived experience of dementia in a steering group. This enables volunteers to take an active role, during and potentially after the study. Having members with lived experience in a steering group allows the researcher to continually review their approach and to seek clarification. However, this approach requires careful planning and can be costly. Alternatively, consultation is typically a survey or focus groups with people with lived experience of dementia. This is usually a one-off process, which can be anonymous. This approach to PPI is quick and easy and can deliver a wide range of opinions and perspectives. However, researchers may elicit conflicting perspectives which may not be representative and have little opportunity to clarify or ask follow-up questions. I took a consulting approach to PPI, using an existing PPI group.

South London and Maudsley NHS Foundation Trust (SLaM), the setting for this thesis, has an existing PPI group for people living with dementia. The group is called the SLaM MALADY group and consists of approximately 8 current and past caregivers of people living with dementia. In the early stages of this thesis, I presented my research plans to the group for feedback on the overall research questions. I also consulted them on my dissemination plans for once the work was finished. Finally, I sent my qualitative study materials (topic guide, participant information sheet, and consent form) for the groups written feedback. The PPI group were satisfied with the aims of this thesis. They suggested additions to the topic guides for the qualitative study. Initially, the topic guides were more focused on asking questions about the perceived utility of secondary health services, however the SLaM Malady group encouraged me to include questions on other types of support that is not offered by health services, such as social care. The group reviewed the participant information sheets and consent forms but did not feel any changes were needed.

2.4 Integration of mixed methods findings

A defining feature of mixed methods research is the meaningful integration of quantitative and qualitative findings (Cresswell, 2014). Once the analysis of each component of the thesis was completed, I integrated the findings across the three parts using the triangulation protocol. The triangulation protocol was originally developed for combining multiple qualitative studies but is commonly used for combing mixed methods research (Farmer et al., 2006). The triangulation protocol is used at the interpretation stage of research. This technique involves drawing out the findings from each component of the study and assessing where studies agree, disagree, or where there is silence (O'Cathain et al., 2010). This can be used to identify meta-themes which cut across the whole project (Farmer et al., 2006). The findings of the triangulation protocol are summarised in chapter 7, in a convergence coding matrix which presents the findings of each component of the study and meta-themes on one page.

2.5 Quantitative Methods

2.5.1 Aims

Chapters 3 and 4 assessed the benefits of diagnosing dementia early through the analysis of patient data. One of the key challenges of investigating the benefits of diagnosing dementia early is identifying those who have received an early diagnosis. Therefore, these chapters addressed the following research questions:

1) Can a diagnosis of mild cognitive impairment before dementia be used as an indicator for an early diagnosis in hospital databases?
2) Are people with an early diagnosis, as defined by a diagnosis of MCI before dementia, at less risk of mortality, visiting A&E or being hospitalised?

2.5.2 Setting and Data sources

To address these questions, I conducted an epidemiological study using secondary data extracted from South London and Maudsley's NHS Foundation Trust's (SLaM) Clinical Records Interactive Search (CRIS). SLaM provides secondary care to 1.3 million people in the London boroughs of Lambeth, Lewisham, Southwark, and Croydon, making it the largest mental health care provider in Europe. Compared to the average population in England, a greater proportion of SLaM service users are young adults, have higher levels of education and are from black and minority ethnic backgrounds (Stewart et al., 2009). Among other services, SLaM provides assessment and treatment for people living with dementia, including diagnostic memory services and specialist inpatient services.

Between 2005 and 2006, the health care records held by SLaM were digitised on to the Electronic Patient Journey System (ePJS). ePJS is a single, integrated clinical record which is used across all SLaM services allowing easier recording and sharing of data. The record allows clinicians to record information in structured fields, such as dates, integers, drop-down lists, or in free text fields. It also includes standardised assessments such as the mini-mental state exam (MMSE) for cognition or the Health of the Nation Outcome Scales (HoNOS) as a measure of physical and mental health (Stewart et al., 2009).

In 2008, the SLaM Biomedical Research Centre (SLaM BRC) Case Register was established, which sourced anonymised data from ePJS for analysis in research. The Clinical Records Interactive Search (CRIS) application was developed to facilitate the anonymised extraction of data from ePJS. In addition to containing historical longitudinal data (dating back to 2007), CRIS source files update every 24 hours making new clinical data available for analysis (Perera et al., 2016). CRIS maintains patient confidentially, by using an algorithm to anonymise patient records. The algorithm deidentifies data in structured fields, for example by truncating date of birth to month and year, and by masking patient and carer identifiers in free text fields. The algorithm used for deidentification is successful in masking 98.8% of personally

identifiable data in structured fields and 97.6% of identifiable data in free text fields (Fernandes et al., 2013). The extraction of structured data is relatively simple and is managed by the CRIS algorithm. However, Natural language processing (NLP) hosted through a General Architecture for Text Engineering (GATE) application was used to extract data stored in free text fields (Perera et al., 2016). I used GATE applications to extract data which had previously been tested for accuracy and validity (Perera et al., 2016).

The Mental Health of Older Adults and Dementia (MHOA) clinical speciality has 4,217 active cases (where patients are currently receiving treatment) and 24,842 inactive cases (patients who received treatment from SLaM, but were subsequently discharged) on the SLAM BRC Case Register (Perera et al., 2016). While not all the 29,059 patients who have been or are being treated by the MHOA speciality will have a diagnosis of dementia, there was a large number of participants to sample from.

2.5.3 Ethics

CRIS has received ethical approval from the Oxfordshire Research Ethics Committee C to be used as a data resource for secondary data analysis (reference 18/SC/0372), therefore NHS ethical approval was not needed for this study. However, permission to use CRIS was sought and granted from the CRIS oversight committee before beginning this project.

2.5.4 Measures

2.5.4.1 Diagnostic measures

All participants in this study had received a diagnosis of dementia according to ICD-10 codes F00, F01, F02, and F03 (WHO, 1993). The first date of dementia diagnosis recorded in CRIS was used as the index date.

I used a previously recorded diagnosis of MCI before dementia as a proxy for an early diagnosis. We extracted whether any diagnosis of MCI, as defined by an ICD-10 code of F06.7

was recorded before the index date. This was created as a binary variable (the previous diagnosis of MCI recorded vs no previous diagnosis of MCI recorded).

2.5.4.2 Demographic information

Demographic information at the time of dementia diagnosis were extracted from CRIS. This included gender, age, ethnicity, marital status, and socioeconomic status at the time of dementia diagnosis. Ethnicity is categorised in SLaM records according to standard census codes. For the purposes of the analyses presented in this thesis, we recoded ethnicity as European, Black, Asian, and Other. The martial status of the participant at the time of dementia diagnosis was extracted from structured fields consisting of 8 categories: cohabitating, married, in a civil partnership, single, divorced, widowed, and unknown. These categories were dichotomised to current partner vs not current partner (at time of dementia diagnosis). The socio-economic status of participants was estimated using a neighbourhood index of deprivation from the English Indices of Multiple Deprivation (Smith et al., 2015) and the participant's most recent address. This is presented as a raw score, where a higher score represents higher levels of social deprivation and lower socio-economic status.

2.5.4.3 Symptoms

The mini-mental state exam is used by SLaM clinicians to access patient's cognition. MMSE scores were extracted within 6 months either side of dementia diagnosis, using a GATE hosted NLP application. This application has been found to extract MMSE scores with 97% specificity and 98% sensitivity (Perera et al., 2016). Where multiple MMSE scores were recorded, I used the one closest to the date of dementia diagnosis.

The Health of the Nation Outcome Scales (HoNOS) are collected as part of the minimum dataset (mandatory). The HoNOS is a 12-item instrument covering symptoms of clinical and social wellbeing. The items in the HoNOS include aggression, self-harm, substance use, cognition, physical health, hallucinations, depression, other psychological symptoms, social relationships, general functioning, housing, and activities of daily living. Each item is clinician-

rated on a five-point Likert scale ranging from 0, representing no problems, to 4, representing severe or very severe problems (Wing et al., 1998). Scores from each item can either be summed for an overall score of wellbeing or summarised by subscales with good reliability and validity (Pirkis et al., 2005). In this thesis, I used the HoNOS cognitive, activities of daily living, and physical health subscales, and grouped psychiatric symptoms into the number of symptoms experienced by the participant.

2.5.5 Data linkages for mortality and health service use outcomes

In addition to the data stored in the electronic health care records, CRIS has existing data linkages with the Office of National Statistics (ONS) and the Health Episode Statistics (HES) though NHS Digital (Perera et al., 2016).

ONS mortality data is gathered through the Primary Care Mortality database, which records the data and cause of all deaths in England and Wales (Jewell et al., 2020). This data is collected by the ONS, but access to the data is also managed by NHS digital. Mortality data were collected from the ONS through SLaM's Clinical Data Linkage Service (CDLS) in a three-step process. First, the CDLS sends the request for data along with identifiers (CRIS ID, first name, last name, date of birth, gender, postcode and NHS number) to NHS digital. NHS digital then requests the mortality data from the ONS, who send the data to the CDLS using a secure file transfer service. Mortality data are updated using this process on a daily basis.

The linkage with ONS allows researchers to extract and information from death certificates, including date, place, and cause of death. This linkage was used to extract outcome data for examining the association between early diagnosis and mortality. All causes of mortality were included in this study.

HES data are held and managed by NHS digital. It is a national dataset which contains data on all hospital admissions, outpatient appointments, and emergency department attendances in England (Jewell et al., 2020). The linkage between CRIS and HES follows a similar process as the one described above. CRIS sends identifiers to NHS digital using the CDLS, these data

are then returned using a secure file transfer service. HES data are updated at the end of each financial year, limiting the availability of data for analysis.

HES stores data on all hospital admissions, emergency department attendances, and outpatients visits across England. The linkage between CRIS and HES allowed me to explore the impact of early diagnosis on subsequent health service use.

2.5.5.1 Hospitalisation

Using the HES linkage, I extracted the admission and discharge date for all hospitalisations recorded after the index date, I also extracted data on hospital admissions in the year before their dementia diagnosis. From this data, I created variables for whether the participant was hospitalised after their dementia diagnosis (yes vs. no), whether they were hospitalised in the year before their dementia diagnosis, time to the first hospitalisation, and the cumulative number of days the participant spent in hospital.

2.5.5.2 ED attendance

Also using the HES linkage, I extracted the dates of all ED attendances in the year before dementia diagnosis, and all ED attendances after diagnosis. From this, I created variables for whether the participant attended ED in the year before their diagnosis (yes vs. no), whether they had attended ED at all post-diagnosis (yes vs. no), time to first ED attendance, and the total number of ED attendances after diagnosis.

2.5.6 Description of Cohort

Data were extracted from Patients on the SLaM BRC Case Register, who were over the age of 50 and were diagnosed with any form of dementia between 2nd January 2008 and 4th November 2018. While CRIS data is available from 2006, participants were only included in this study if they had received their first recorded diagnosis of dementia after 2008. This is because we were interested in following patients with a new diagnosis of dementia. Many patients within CRIS, who had a first diagnosis of dementia in 2006 or 2007 were likely to have been diagnosed long before this date and before the CRIS database was created. These

participants are likely to be in the CRIS database, because they were still being actively treated or followed-up by SLaM services (Sommerlad et al., 2018).

Data were extracted from a total of 18,555 SLaM patients. Mortality data were available up until 14th November 2018, however, HES data were only available until 31st March 2017. To maximise the available data for each outcome, I created two cohorts for the analysis of each outcome, with the HES cohort nested in the mortality cohort.

Table 2.2 presents the characteristics of both cohorts.

Table 2.2 Characteristics of Mortality and Health Services Use Cohorts

Demographic Information at Dementia Diagnosis	**Mortality Cohort (n = 18,555)**	**Health Service Use Cohort (N = 15,836)**
Gender (%)		
Male	39.38	39.18
Female	60.62	60.82
Ethnicity (%)		
European (British, Irish, etc)	74.40	74.67
Black (Caribbean, African, other)	16.82	16.49
Asian (Indian Bangladesh, other Asian)	4.65	4.51
Other	4.13	4.33
MCI diagnosed before dementia (%)	5.55	5.10
Mean Age (SD)	80.79 (8.74)	80.84 (8.64)
Mean MMSE Score (SD)	18.55 (6.32)	18.52 (6.30)
Prescribed AChEIs 6 months ± dementia diagnosis (%)	31.85	32.49
Mean Index of deprivation (SD) †	27.34 (11.06)	27.30 (11. 06)
Marital Status (%)		
Current partner	33.36	33.68
No current partner	66.64	66.32
HoNOS Psychiatric symptoms (%)		
No symptoms	35.86	35.06
1 symptom	29.70	29.94
2 symptoms	18.23	18.46
3+ symptoms	16.21	16.54
HoNOS Activities of daily living (%)	61.14	62.13
HoNOS Physical Illness and disability (%)	56.03	56.17

Note: HoNOS= Health of the Nations Outcome Scales

† Higher score indicates more socially deprived

The results from the analysis of mortality data from cohort 1 are presented in chapter 3, and the results from the analysis of health service use data from cohort 2 are presented in chapter 4. The following section presents the method of analysis for each of these chapters.

2.5.7 Statistical analysis

All data were analysed using Stata 15 (StataCorp, 2017).

2.5.7.1 Cox Regression models

Cox regression models were used in chapters 3 and 4. In chapter 3, cox regression models were used to compare the hazard of mortality following a diagnosis of dementia between the early diagnosis and no early diagnosis groups. In chapter 4, cox regression models were used to compare the hazard of first hospitalisation or ED attendance between the early diagnosis and non-early diagnosis group.

Cox regression models, or cox proportional hazards regressions, estimate the time to the outcome of interest between two or more groups while adjusting for a range of confounders. The outcome of cox regression models is presented as hazard ratios (Cox, 1972). Cox regression models are semi-parametric, where the baseline hazard does not need to be defined (Cox, 1972). Furthermore, this analysis is based on the proportional hazards assumption which assumes that the ratio for the hazards between the same group remains constant over time. This assumption can be tested by visually assessing Kaplan-Meier curves representing the differences in survival function between the two groups (Cox, 1972). I also used a Schoenfeld test of residuals to test the proportional hazards assumption. Where variables were found to violate this assumption, they were added to the model as time-varying covariates (Zhang et al., 2018) using the TVC() function on Stata.

2.5.7.2 Negative Binomial Regressions

Negative binomial regressions were used in chapter 4 to compare the number of cumulative days spent in hospital, and the number of ED attendances between the early diagnosis and no early diagnosis groups. Negative binomial regression models are a generalisation of

Poisson Regression models and can be used to compare counts over time (Lawless, 1987). Poisson Regressions can be used to compare rates between two exposure groups while adjusting for confounding factors. Most Poisson regression models are parametric and the mean is equal to the variance. This is not appropriate for data which is overdispersed, containing a lot of ones and zeros (Greene, 1994). The health service use data for this study were overdispersed, therefore Poisson regression was not appropriate for analysing this data. Negative binomial regression does not assume the mean is equal to zero, making it more appropriate for analysing counts where the variance is different to the mean. Negative binomial regressions are performed on a logarithmic scale, therefore, coefficients were exponentiated to Incidence Rate Ratios (IRR).

2.5.7.3 Missing data

The data used in this study were extracted from electronic health care records, meaning data were missing for some participants. MMSE was the most common data item to be missing, 30% of participants did not have an MMSE score within 6 months of their dementia diagnosis. Thirteen per cent of participants were missing one or more items on the HoNOS. All other variables had 1% or less missing data.

To maximise the statistical power of available data for the analysis, missing data were imputed using multiple imputation by chained equations (MICE) (Van Buuren and Oudshoorn, 1999) assuming missing at random. Multiple imputation uses the distribution of the complete data to estimate a set of plausible values for the missing data (White et al., 2011). MICE is used to impute data in datasets with multiple variables which are missing values (Van Buuren and Oudshoorn, 1999). It generates imputations based on a set of imputations models, one for each variable with missing data. As each variable is imputed using its own imputation model, MICE can manage different types of variables at once (e.g. continuous, binary, categorical variables, etc.) (White et al., 2011). Multiple imputation has three basic phases: the imputation phase where missing values are estimated and a complete data set is created; in the analysis phase the imputed dataset is analysed using the chosen method of analysis (e.g. cox

regression); finally at the pooling phase, parameter estimates are obtained for each imputed and analysed dataset and combined for inference (Stata, 2009). In this study, this cycle of imputation was repeated ten times. Ten datasets, including all covariates and outcomes, were imputed using the mi package in Stata before using cox regression models and negative binomial regressions on the imputed datasets.

2.5.8 Strengths, limitations, and alternatives

There are several positives to analysing data held in electronic health records. Firstly, it allows researchers to access a large amount of real-world data with very little expense, and in a short time (Lowrance, 2003). Furthermore, it is possible to extract long term follow-up data (Hopf et al., 2014). This is especially beneficial to this thesis, as there was a finite amount of time available for conducting this work. For pragmatic mixed methods studies to be of high-quality, each component must be feasible to complete in the time available (Robinson et al., 2011). Secondary analysis of data from electronic health care records is useful where it is not possible to conduct a randomised controlled trial. It is not feasible to conduct a randomised controlled trial to address the aims of this study as it would not be ethical to assign participants to an early diagnosis or no early diagnosis group.

However, there are some limitations to analysing data from electronic health care records. The analysis is restricted to what is available in the database (Lowrance, 2003), limiting the research questions the data could be used to answer. Furthermore, there are ethical concerns about using patient data without the explicit consent of the participant (Hopf et al., 2014), however, CRIS has been awarded ethical approval for secondary data analysis and extracted data are anonymised during the extraction process.

2.6 Qualitative methods

2.6.1 Aims

Dementia is a complex condition to diagnose and treat. There has been much debate over when dementia should be diagnosed and what benefits we should expect following an early diagnosis; however, this question has not been explored from the perspective of those living with the disease (either through themselves being diagnosed or friend/family member). Chapter 5 undertook a thematic analysis of semi-structured interviews to investigate the participant's experience of a diagnosis of dementia or mild cognitive impairment and the post-diagnostic care and support they received. This chapter aimed to explore the perceived value and timeliness of post-diagnostic treatment and care from the perspective of those affected by the disease.

The specific objectives were:

1. Explore the perceived long-term and short-term benefits of a dementia diagnosis
2. Explore how the diagnosis of dementia is given and received
3. Understand access to interventions and support following a diagnosis of dementia, and perceived advantages and disadvantages
4. To understand in which circumstances an early diagnosis is perceived to be beneficial

2.6.2 Study Design

2.6.2.1 Setting

This was a single-site study co-sponsored by South London and Maudsley NHS Trust (SLaM) and King's College London. SLaM provides specialist diagnostic and follow-up support, including memory clinics, for people living with dementia in the London Boroughs of Croydon, Lambeth, Lewisham, and Southwark, making it an appropriate setting for addressing the research question.

2.6.2.2 Ethical approval

Ethical approval was granted by the NHS Health Research Authority (HRA) and Health and Care Research Wales Research Ethics Committee (REC) (REC Reference number: 19/WA/0210). See Appendix B for the HRA approval letter.

2.6.3 Recruitment

2.6.3.1 Sample identification

Participants were eligible to participate in this study if they had a diagnosis of dementia or MCI, or if they were a current or former carer for a person living with dementia or MCI. It is important to include people living with dementia as participants in this study, as the Dementia Statements posit people with dementia "have the right to know about and decide if [they] want to be involved in research that looks at cause, cure and care for dementia and be supported to take part." (Dementia Action Alliance, 2017)

A carer was defined as someone providing informal care to the person living with dementia, this can be a family member, friend, or neighbour. Paid carers were not included in this study.

Table 2.3 presents the inclusion and exclusion criteria for this study.

Table 2.3 Inclusion and exclusion criteria for qualitative participants

	Inclusion Criteria	**Exclusion Criteria**
People living with dementia	• Had been diagnosed with dementia or MCI either recorded in their SLaM care notes or confirmed by their GP • Were able to speak English • Lived within the greater London area	• Did not have a diagnosis of dementia or MCI • Had MCI or dementia, but were unable to consent to take part themselves and no consultee was available • Under 18 years old • Lived outside the greater London area
Caregivers	• A current or former carer for someone living with dementia or MCI • Over 18 years old • Able to speak English • Lived within the greater London area	• Not a current or former carer for someone with dementia or mild cognitive impairment • A paid carer • Under 18 years old • Lived outside the Greater London area

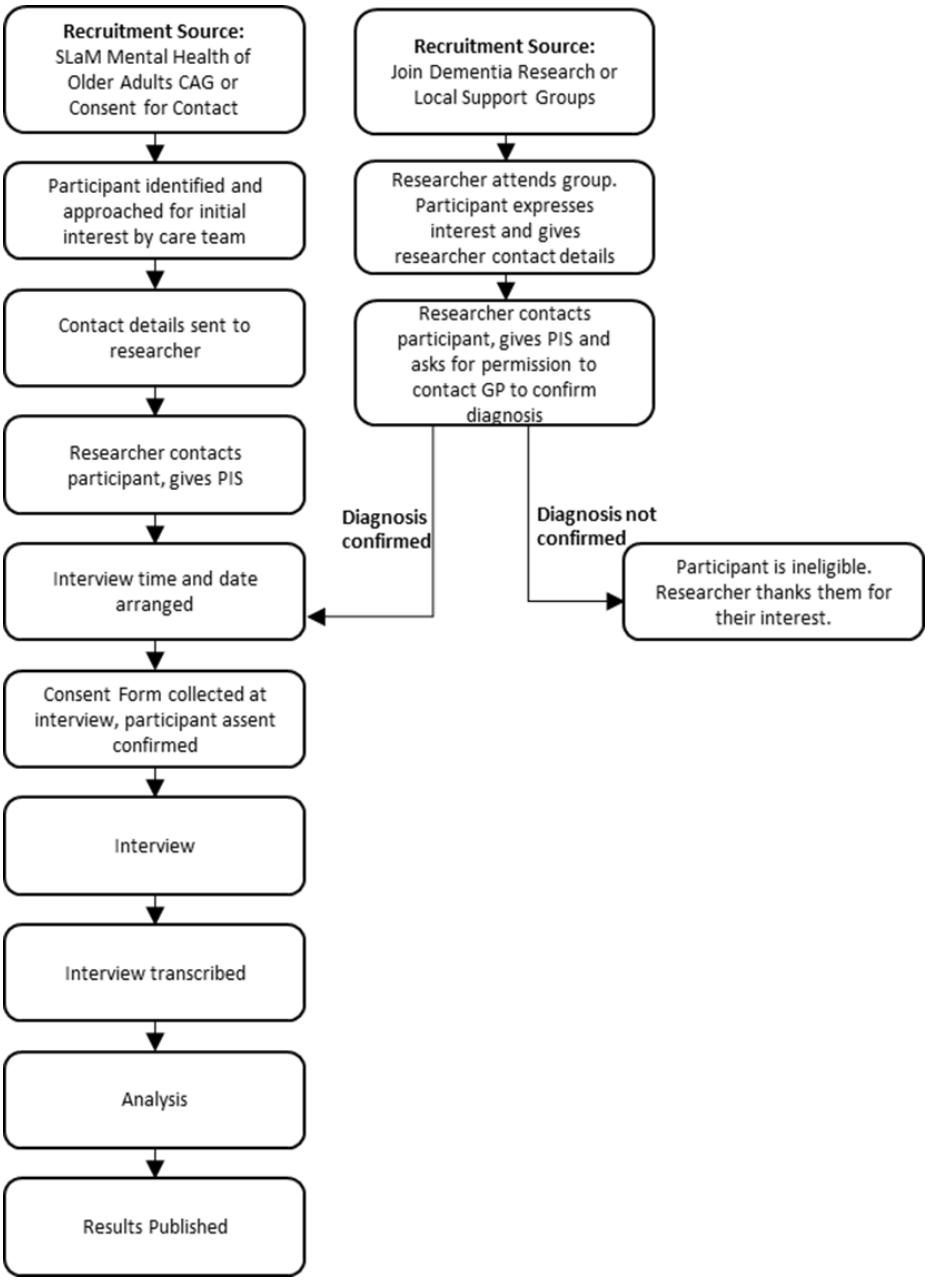
2.6.3.2 Sampling technique and anticipated sample size

I used purposive sampling based on time since diagnosis/disease stage, gender, and amount of social support to explore a diversity of perspectives. Originally, I aimed to recruit between 12 and 20 people living with dementia and 12 and 20 caregivers. However, due to the outbreak of the COVID-19 pandemic during the early stages of conducting this study, I was unable to meet this original target. A total of 2 people living with dementia and 12 caregivers were recruited and interviewed for this study, the characteristics of the included participants are presented in 2.6.4.

2.6.3.3 Recruitment Sources

Figure 2.3 presents the recruitment and data collection procedures for this study.

Figure 2.3 Study Recruitment and Data Collection Procedures



Join Dementia Research

I used the web platform Join Dementia Research (JDR) as my main recruitment tool. This is an online self-registration service which enables volunteers with memory problems or dementia, carers of those with memory problems or dementia, and healthy volunteers, to register their interest in taking part in research.

JDR is funded by the Department of Health, working in partnership with the charities Alzheimer Scotland, Alzheimer's Research UK and Alzheimer's Society and is Health Research Authority (HRA) endorsed. The online service and all associated documentation, methods of contacting volunteers and handling of data, were reviewed by a specially convened HRA committee which included experts in research ethics, data protection, and information governance. A formal endorsement was issued by the HRA in a letter dated 20 May 2014.

The purpose of JDR is to allow such volunteers to be identified by researchers as potentially eligible for their studies. Researchers can then contact volunteers, in line with the volunteers' preferred method of contact, to further discuss potential inclusion.

SLaM Consent for Contact

We aimed to use the SLaM Consent for Contact initiative to recruit patients from the SLaM BRC case register. The C4C programme has been ethically approved by the National Information Board for Health and Social Care, ref ECC 2-08/2010. C4C allows researchers to search the SLaM BRC case register for participants who meet their inclusion criteria and have already given consent to be contacted about taking part in research.

SLaM Mental Health of Older Adults Clinical Academic Group

I also aimed to recruit participants through SLaM's Mental Health of Older Adults Clinical Academic Group (MHOA CAG) database of research volunteers. Participants were first identified by a member of the MHOA CAG team. A member of the participant's clinical care team then approached them for initial interest. If the participant was interested in taking part,

their information was forwarded to the researcher who contacted the participant to provide further information on the study and the PIS.

Local Dementia Support Groups

I contacted local groups which support people with dementia and their carers. In the first instance, I contacted the leader of the group and arranged to present at one of the group meetings. At these meetings, interested participants were given an information sheet and I took their contact details. The following support groups were approached: The Lambeth Healthy Living Club @ Stockwell, Lewisham MindCare Dementia Support, and the Southwark Pensioners Centre.

Where I was more familiar with the organisation leading the support group, for example with the Southwark Pensioners Centre, whom I already had a working relationship with before starting recruitment on this study, centre staff made the initial contact with the participant. After the participant expressed their interest, the centre staff were then able to send me their contact details.

2.6.3.4 Confirmation of dementia or MCI diagnosis

As this study is interested in the participant's experience of post-diagnostic support it was necessary to confirm whether the participants have received a medical diagnosis of MCI or dementia. No additional steps were needed to confirm the diagnosis of participants recruited through SLaM's MHOA CAG, or C4C as these participants were identified by the diagnosis recorded in their care notes.

However, for participants recruited through JDR and local support groups, it was necessary to confirm they have received a formal diagnosis of dementia or MCI. Therefore, when I contacted interested participants to explain the purpose of the study, I also asked the participant for their permission to contact their GP to confirm their diagnosis. After the GP had confirmed their diagnosis of dementia or MCI I arranged an appointment to conduct the interview. See Appendix F for a copy of the letter sent to GPs.

2.6.3.5 Collecting informed consent

The process for collecting informed consent was as follows. When approaching potential participants for recruitment, I sent them a brief email outlining the aims of the study and what their participation would involve. After the participant had replied to say they would be interested in taking part I emailed them a copy of the information sheet and consent form for them to read, along with suggestions for arranging the interview. I made it clear that at this stage, they did not have to complete the consent form, it was for their information. At each stage of this process, I highlighted that participation was optional.

When calling the participant to start the interview, I briefly reminded them of the aims of the study and asked if they had any questions about taking part. I reminded them that the data would be anonymised and that the things they shared during the interview would remain confidential unless I felt they, or someone they knew, was at risk of serious and immediate harm. Where the participant decided to take part, they completed a consent form which was signed by both the participant and me. See Appendix C for the participant information sheet and Appendices D and E for copies of the verbal and written consent forms.

2.6.3.6 Assessing the capacity to give informed consent

When recruiting participants with dementia or mild cognitive impairment, it was necessary to assess their capacity to consent. Capacity was assessed following the guidelines set out by the 2005 Mental Capacity Act. I assessed whether the participant was able to:

- Understand the purpose and nature of the research
- Understand what the research involves, its benefits (or lack of benefits), risks and burdens
- Understand the alternatives to taking part
- Retain the information long enough to make an effective decision
- Make a free choice

Where I did not feel the participant had capacity to decide whether to take part or not, I sought a consultee for advice. The consultee was someone who knows the person living with dementia and who could give an opinion as to whether the person with dementia would want to take part or not. If they felt the person living with dementia would like to take part, they signed the consultee declaration form. If I was unsure whether the participant had capacity, I sought advice from a consultee.

In addition to the consultee declaration form, the person living with dementia also needed to give their verbal or nonverbal assent to taking part. If the participant had made any advanced decisions about taking part in research, these would take precedence.

I recruited two participants with a diagnosis of dementia. Both participants had mild symptoms of dementia and I deemed both to have capacity to give informed consent. However, giving informed consent is a dynamic process (Gupta, 2013), during the interviews I frequently checked that participants were happy to continue with participating in the interview.

2.6.3.7 Adjustments to recruitment due to COVID-19

Collecting consent virtually

Where participants were recruited remotely, consent was collected verbally. This was done over the phone or online, using Microsoft Teams. A verbal consent form was used, where the researcher collecting consent signs on behalf of the participant and a witness verifies consent by signing the consent form.

With the participant's permission, the process of collecting consent was audio recorded. The participant was asked to confirm their name and the date that they are consenting to take part in the study. I signed the consent on behalf of the participant. A witness (VL) listened to the recording and verified consent by signing the consent form. Recordings of the consent taking process were kept for audit purposes and stored separately from the recordings of the interviews.

2.6.3.8 Challenges with recruitment

I started recruitment for this study at the start of January 2019. At the end of January, I paused my PhD to complete a 3-month internship with Age UK ending April 2019. Before starting the internship, I had recruited and interviewed 1 participant from JDR, and I had met with staff at SLaM to plan how I was going to use C4C when I returned to my PhD work. During the time away from my PhD, the COVID-19 outbreak was declared a pandemic and all NHS research, including this study, was suspended. In July, I amended the recruitment and data collection procedures and was able to continue this study virtually.

While I was able to continue with recruitment from July 2019, most of my recruitment channels had closed down. To recruit from SLaM sources, such as C4C or the MHOA CAG, SLaM would have to conduct a risk assessment. However, SLaM was prioritising clinical research, which was either related to COVID-19 or the development of a vaccine, therefore I was not able to get my study risk assessed on time. As a result of this, the only recruitment channels I was left with were JDR and local support groups. JDR was my most successful recruitment channel. I recruited 9 caregivers and 2 participants with dementia. Table 2.4 presents the number of participants approached and enrolled by recruitment source.

Table 2.4 Number of participants by recruitment source

Recruitment Source	**People living with dementia**		**Caregivers**	
	Approached	Enrolled	Approached	Enrolled
Join Dementia Research	18	2	39	9
Local Support Groups	0	0	5	5

It was especially difficult to recruit participants who were living with dementia. There were two reasons for this. Firstly, there were fewer people living with dementia to sample from in my recruitment sources and secondly, my recruitment sources had less reliable data on the

person living with dementia's diagnosis. To illustrate the first point, there were 216 caregivers on JDR compared with 97 people living with dementia. There were varying degrees of engagement with JDR, but the vast majority of people registered on JDR had signed up several years ago and had never engaged with any research studies.

Databases managed by SLaM would have had complete and reliable data on the diagnosis of the person living with dementia and a large number of potential participants to sample from. Whereas, my other recruitment sources had less reliable diagnostic data, and fewer participants to sample from. For example, people who sign up to Join Dementia Research self-identify as having dementia. This means that many of the participants on the Join Dementia Register do not have a formal diagnosis of dementia, rather they have self-diagnosed their memory problems. For example, participant told me they did not have a formal diagnosis after I made an initial contact with them. There were no cases where I wrote to the GP and they did not confirm the dementia diagnosis. Furthermore, the Southwark Pensioners Centre does not keep records of which of their service users have a formal diagnosis of dementia, therefore I was not able to recruit people living with dementia from this recruitment source.

Despite these challenges, I recruited 14 participants in total (2 with dementia and 12 caregivers). With most people working from home and more used to the new remote methods of communication, I found that participants were able to find time to complete the interviews during working hours. Additionally, not having to arrange travel for either myself or the participant meant that I was able to arrange the interview more quickly after the participant expressed an interest in taking part.

2.6.4 Participants

Most participants in this study were female, 75% of caregivers and all participants with dementia were women. The mean time since diagnosis was approximately 4 years for each group. The average age for caregivers at the time of the interview was 61. Participants living

with dementia were slightly older, with a mean age of 79. One of the participants living with dementia was supported by a spouse, whereas the other participant living with dementia was widowed. Most caregivers (75%) were in a current relationship. The majority of caregivers were caring for their parent(s) living with dementia. All participants living with dementia had been diagnosed with dementia, whereas 17% of caregivers were supporting someone who had been diagnosed with mild cognitive impairment. Table 2.5 summarises the characteristics of the included participants.

Table 2.5 Characteristics of participants

Characteristic	**Caregivers (N = 12)**	**People living with dementia (N = 2)**
Gender (%)		
Female	9 (75)	2 (100)
Male	3 (25)	0 (0)
Mean Age (SD)	61 (12.5)	79 (1.4)
Mean time since diagnosis (SD)	4.2 (2.6)	4 (1.4)
Marital Status (%)		
Married or Co-habitating	9 (75)	1 (50)
Divorced, Widowed or Currently Single	3 (25)	1 (50)
Relationship to person living with dementia (%)		N/A
Spouse	4 (33)	
Child of one parent with dementia	4 (33)	
Child of both parents with dementia	3 (25)	
Caregiver to multiple people with dementia	1 (8)	
Type of diagnosis		
Mild cognitive impairment	2 (17)	0 (0)
Dementia	10 (83)	2 (100)

2.6.5 Data collection

2.6.5.1 Semi-Structured interviews

Interviews were semi-structured and based on a topic guide. I chose to use semi-structured interviews as they are more flexible than structured interviews, allowing me to ask clarifying questions, to alter the order in which I asked questions and to explore topics that arose during the interview (Doody and Noonan, 2013). One of the advantages of semi-structured interviews, as compared to structured interviews, is that the researcher can speak to the participant in a more conversational, and less formal style, which can be beneficial for participants living with dementia (Manthorpe and Samsi, 2020). I found that this was particularly helpful for making participants who were nervous about taking part in research feel more comfortable.

2.6.5.2 Topic guide

Interviews were based on topic guides, one guide for interviews with caregivers and one guide for interviews with participants living with dementia (See Appendix A). The topic guide was initially developed in consultation with the SLaM MALADY PPI group. During this consultation, I presented the aims of my research and we discussed what topics might arise during the interview. This helped identify what was important for people with lived experience of dementia. After the consultation, I wrote up the topic guide and sent it to members of the PPI group for written feedback. Further detail on the topics discussed during the interviews will be presented in 2.6.6.

2.6.6 Conducting the interviews

2.6.6.1 Interview setting

Interviews were conducted face to face, over the phone, or online using Teams. Before the pandemic, where interviews were offered face to face, I offered the participants the option to do the interviews in their own home or at my University office. I only conducted one face to face interview and that was done in the participant's home. Conducting the interviews virtually

allowed me to step into the homes of my participants. I felt that this was helpful for making the participant feel more relaxed when speaking to me, and it also gave me valuable contextual information. For example, one interview on Teams was interrupted by the person living with dementia. By seeing the participant interact with the person living with dementia, I noticed there was possibly a strained relationship between the two of them. This opened up a new line of questioning that I would not have considered. Similarly, I was doing the interviews from my home. So, while I was transported to my participants homes, they were also transported into mine. I felt that this was helpful for breaking down the power imbalance between myself, as the researcher, and the participants.

2.6.6.2 Caregivers

For participants recruited through JDR, I generally arranged the interviews over email. This meant that for some of these participants I had very limited knowledge about their situation before calling them to do the interview. For some caregivers, I did not know who they were caring for. Therefore, I used the first part of the call to talk to them more generally, asking them how they were doing before discussing how their participation in the study would work. Then I went through the process of collecting informed consent, before starting the interview. I gave participants the opportunity to ask questions about the study before starting the interview.

After collecting consent, I verbally sign-posted to the participant that we were going to move on to the interview and asked for their verbal assent to continue. I also told them that I was turning on the audio recorder. I started with a general question, either clarifying who they were providing care to or asking when they started to notice the person living with dementia's memory problems. From this point, caregivers usually answered the question and then continued to give further information on related topics. When asking follow-up questions, I waited until a natural break in the participant's speech, where they had finished talking, and asked a question that followed on from the topic that they introduced. I found as the interviews progressed, participants became more confident talking about their experiences and started to talk at greater length moving from one topic to another. I felt it was important to let

participants speak freely and interject as little as possible. This allowed me to formulate follow-up questions which were rooted in the participant's experiences, and not in my assumptions or biases. I kept an eye on the topic guide during the interview and made a note of where these topics arose naturally during the interview. Towards the end of the interview, I would ask questions about the topics which were not covered. Some participants were more comfortable taking the lead in directing the conversation, however, others preferred to give shorter answers to more specific questions. I adapted my interview style to what best suited the participant.

This study aimed to understand the benefits of diagnosing dementia early from the perspective of those living with the disease and their caregivers, however, it was important for me to be aware that the participants may not believe there are any benefits. Therefore, I ensured that I did not use leading questions of language during the interview. Questions aimed to be open-ended and neutral.

During the interviews, I planned to ask questions about finances and end of life care, which some participants might find upsetting or personal. Therefore, when developing the topic guide, I considered how and in what order I was going to ask the questions and how I would phrase difficult questions. After each interview, I reflected on the interview; both considering what the participants said and how I asked the questions. Where I found better ways of managing difficult topics, I amended the topic guide. Additionally, where participants discussed relevant topics which were not previously on the topic guide, I included these in the guide for subsequent interviews. I started with more general questions about when they started to notice memory issues, moving onto their experience of getting a dementia diagnosis and finished with questions about their experience of care and post-diagnostic support. This allowed me to build rapport with the participant and disperse questions on sensitive topics throughout the interview. Another approach I took to building rapport was to reflect what the participant had just said back to them. This is a common technique used by CBT therapists (Westbrook et al., 2011) and I found it useful for clarifying meaning, ensuring the participant

felt heard and for giving me time as the researcher to decide whether I wanted to ask a follow-up question.

When I asked more sensitive questions, I gave the participant advanced warning that I was about to ask a difficult question and told them that they could choose to not answer it. I also had planned a less emotional topic to discuss immediately afterwards. Some questions brought-up strong emotional responses for the participants. Where this happened, I empathised with their response, acknowledging that it is a difficult topic to discuss. I then offered them the chance to take a break or to not answer the question. During these questions, I gave them time to fully express their responses before gently moving the conversation to less emotional topics.

When I had covered all the topics I wished to discuss, I told the participants that I had reached the end of my questions and asked if there was anything they would like to talk about which I had not asked about or if they had any final thoughts or reflections that they wanted to share. Quite often, the participant would summarise their take-home message for me to consider or ask what my plans were for this study. To end the interview, I told the participant I was turning off the recorder, thanked them for their participation and told them they could contact me if they wanted to add to or clarify something they said during the interview. A day or two after the interview, I sent the participant an email thanking them again for taking part in the study.

2.6.6.3 People living with dementia

I followed the same procedures for interviewing people living with dementia, with two adjustments. Firstly, I found it was less helpful for me to ask more factual based questions, for example: “who did you speak to when you first noticed problems with your memory?” because the participant may not remember the answer to this question. Therefore, I rephrased questions about these topics to be more focused on experiences or feelings related to the topic. Secondly, the questions I asked and the answers I received were shorter and more succinct. This helped me to sustain focus during the interview.

I interviewed one participant living with dementia with their caregiver, as the participant was not comfortable using the phone alone. This was an interesting experience, as it allowed me to explore their different perspectives simultaneously, and the caregiver was able to prompt the person living with dementia on some things that they had forgotten. However, I was careful to balance the discussion between the two of them, so that one wasn’t answering for the other.

2.6.7 Analysis

2.6.7.1 Transcription

The interviews were transcribed verbatim for analysis. Verbatim transcription aims to transcribe the recordings exactly how they are heard, including all utterances, sounds and noises a person makes during the interview. Capturing the context of the interviews and non-verbal utterances can increase the reliability and trustworthiness of the transcripts (Stuckey, 2014). Transcription is a time-consuming process, therefore I transcribed 5 of the interviews and had the other 9 transcribed by a professional service. I listened to the recordings while reading the transcripts to immerse myself in the context of the data, to check their accuracy, and fix any mistakes.

2.6.7.2 Thematic analysis

Data were analysed thematically, following the steps outlined by Braun and Clarke (2006). There are 6 steps to thematic analysis: familiarising yourself with the data, generating initial

codes, searching for themes, reviewing themes, naming and defining themes, and producing the report (Braun and Clarke, 2006). The qualitative software NVivo 2020 (QSR, 2020) was used to facilitate thematic analysis.

I first familiarised myself with the data by transcribing some of the interviews, listening back to the interview recordings, reading and re-reading the transcripts. Next, I generated initial inductive and deductive codes. Deductive codes were generated using the topic guide and research questions, this ensured that the analysis remained focused on the aim of the study. Inductive codes were used to ensure the analysis remained grounded in the interview data.

A process of iterative categorisation was used to move from codes to themes (Neale, 2016). In the first step of iterative categorisation, the researcher systematically describes the data contained in each code. In the second stage of iterative categorisation, the researcher reviews the detailed description of the coded data and identifies themes. The themes were then checked against the raw coded data to ensure validity. Themes were then named and given a description. The results of this analysis are presented in chapter 5.

2.6.8 Rigour in qualitative methods

Methods for ensuring rigour are essential for producing high-quality qualitative research. There are multiple approaches to defining rigour. However, the most influential criteria used to determine rigour, or trustworthiness, in qualitative methods comes from Lincoln and Guba. They are credibility, dependability, confirmability, transferability, and authenticity (Lincoln and Guba, 1985). Ensuring rigour is an active process, to be done while conducting the study (Morse, 2015). Table 2.6 presents the definition of each criteria of rigour, alongside the strategies used in this thesis.

Table 2.6 Strategies to ensure rigour

Criterion	Definition	Strategies used in this thesis	Description
Credibility	The truthfulness of the data, or the degree to which participants can recognise themselves in the findings	Triangulation (Denzin, 1978)	In this thesis I used methodological triangulation to confirm credibility. I triangulated the findings of this phase of analysis against the findings of the other phases of analysis
		Peer debriefing (Lincoln and Guba, 1985);	Discussions with my supervisors allowed me to test the fit of emerging themes with the data. It also allowed me to explore my biases and assumptions in relation to the data and analysis
		Negative case analysis (Patton, 1999)	I looked for examples within the data that appeared to contradict the themes. This was important for ensuring the findings best represented the experiences of the participants. I included examples of negative cases in the presentation of the results.
		Member checking (Angen, 2000).	Member checking refers to the presentation of the emerging results to the participants. This was an informal process and

			helped me to check if I was correctly interpreting the data. This is discussed further in section 2.6.8.1.
Dependability	The extent to which the findings are replicable	Inquiry audit (Lincoln and Guba, 1985).	Dependability can be established with another research agrees with the decisions made by the researcher at each stage of the process (Cope, 2014). I used regular supervisions to discuss analytical decisions I made at each stage of the analysis. I presented specific examples of how I moved from codes to categories, and from categories to themes.
Transferability	Applicability of the findings in other contexts	Thick description (Lincoln and Guba, 1985);	Thick description describes presenting a detailed account of the data, paying special attention to the context of the data. By describing the data in sufficient detail it is possible to draw conclusions on the transferability of the findings to other contexts. The results of this study are presented with long and short direct quotes from the participant to ensure a thick description. I have also been careful to contextualise the data I present.

Confirmability	The extent to which the findings are shaped by the participants, rather than the researcher	Reflexivity (Koch and Harrington, 1998);	By keeping a reflexive journal, I was able to explore my own biases and assumptions in relation to the aims of this thesis. The following section (1.6.8.1) discusses reflexivity in greater detail.

2.6.8.1 Reflexivity

Thematic analysis is a subjective and reflexive process of analysis, whereby themes are created by a researcher interpreting patterns of meaning in the data (Braun and Clarke, 2006). Thematic analysis, and qualitative research in general, has been criticised for its subjectivity (Pope et al., 2000), however, Braun and Clarke argue that this is instead a strength of thematic analysis, and qualitative methods in general (Braun and Clarke, 2019). Themes do not passively "emerge" from the data, a researcher is needed to create them. However, it is important for the researcher to be aware of their assumptions or biases, and how they affect the creation of themes.

Reflexivity can be defined as the continual process of reflection by the researcher on their experiences, preconceptions, beliefs, and relationship to the participants (Parahoo, 2006). All of which can affect the researcher's approach to data collection and interpretation (Jootun et al., 2009). In the following paragraphs, I reflect on my position in this research and discuss strategies I used to mitigate this.

Disclosing the personal characteristics of the researcher, including their occupation, knowledge, and professional experience, is an important part of reflexivity in presenting qualitative research. My interest in dementia started while I was working as a care support worker and completing my BSc in Psychology from the University of Kent. Working as a care support worker allowed me to step into the lives of people living with dementia, and to share their joy as well as their struggles. At the same time, during my studies, I was learning how research could be used to develop new interventions and capture their impact. These parallel experiences inspired me to move into health care research, with a specific focus on older adults and dementia. Furthermore, my care working experience instilled in me a desire to promote the voices of people living with dementia.

When I developed the funding application and research proposal for this PhD, I had initially planned to investigate the different pathways through care for people living with dementia.

This original plan was built on the explicit assumption that an early diagnosis could lead to better care for people living with dementia. This was something that I truly believed when I started my PhD. During the first few months of my studies, I was reviewing the literature, while working to refine my research questions, and decided to look for the primary sources which presented evidence on the benefits of an early diagnosis. But I struggled to find any. After reading the 2011's World Alzheimer's Report, which argued that the presumed benefits of an early diagnosis are not evidence based and can be, at best, considered expert opinion, I decided to change the focus of my thesis to address this gap in the literature.

While I had previously believed an early diagnosis to be a good thing, throughout this PhD I grew increasingly sceptical. I found balancing this scepticism difficult when analysing the data from this study. Many of the participants described difficult experiences following the diagnosis of dementia, however they remained positive about diagnosing dementia early. I kept an analytical diary throughout the data collection and analytical phase of this study. Keeping an analytical diary, or memoing, is an important part of the research process. It can help the researcher make the conceptual jump from the raw data to themes (Birks et al., 2008). My analytical diary helped me to balance my ideas of the value of an early diagnosis, against what the participants were telling me. This helped me to stay focused on the aims of the research and follow the experiences of the participants.

All participants in this study were aware that I was a PhD student. Most participants asked about my PhD more generally. I would summarise my findings from the thesis on a whole as well the interviews I had done so far. This elicited interesting insights from the participants, which would open new lines of questioning or helped me to understand if I had been correctly interpreting my data. I also felt this was important for demonstrating the value I felt the interviewee had contributed to this study and the thesis.

2.7 Strengths, limitations, and alternatives

In-depth semi-structured interviews are useful for capturing people's real-life experiences of living with dementia (Manthorpe and Samsi, 2020). They emphasise the social and political context of living with the disease (Doody and Noonan, 2013). Interpretative Phenomenological Analysis (IPA) is an alternative method for addressing the aims of this study. IPA is based on the epistemological assumption that there is no one reality instead, reality is a collection of experiences (Larkin and Thompson, 2012). IPA is a more in-depth method of qualitative data analysis, the researcher goes beyond identifying patterns of meaning as in thematic analysis and looks to understand how participants understand and explain their experiences. While IPA is a good method for understanding personal experiences and psychosocial processes (Larkin and Thompson, 2012), It favours homogenous samples. As I wanted to explore a range of experiences and responses following a diagnosis of dementia, thematic analysis was a more appropriate method. Furthermore, IPA is a time-consuming process making it an unfeasible method of analysis to use during the time available to complete this thesis.

Thematic analysis is a good method of analysis for addressing the aims of the research as it is flexible and allows for the social and psychological interpretation of data. Furthermore, compared with other methods it is quick and relatively easy for novice researchers (Braun and Clarke, 2006). Thematic analysis is a widely used method of qualitative data analysis, with varying levels of quality. During this work, I followed Braun and Clarke's (2006) 15 criteria for conducting high-quality thematic analysis (See Table 2.7).

Table 2.7 Criteria for high quality thematic analysis (From Braun and Clarke, 2006)

Stage of thematic analysis	**Criterion**	**Description**
Transcription	1	The data have been transcribed to an appropriate level of detail, and the transcripts have been checked against the tapes for 'accuracy'.
Coding	2	Each data item has been given equal attention in the coding process.
	3	Themes have not been generated from a few vivid examples (an anecdotal approach), but instead the coding process has been thorough, inclusive, and comprehensive.
	4	All relevant extracts for all each theme have been collated.
	5	Themes have been checked against each other and back to the original data set.
	6	Themes are internally coherent, consistent, and distinctive.
Analysis	7	Data have been analysed - interpreted, made sense of - rather than just paraphrased or described.
	8	Analysis and data match each other / the extracts illustrate the analytic claims.
	9	Analysis tells a convincing and well-organized story about the data and topic.
	10	A good balance between analytic narrative and illustrative extracts is provided.
Overall	11	Enough time has been allocated to complete all phases of the analysis adequately, without rushing a phase or giving it a once-over-lightly.
	12	The assumptions about, and specific approach to, thematic analysis are clearly explicated.
Written report	13	There is a good fit between what you claim you do, and what you show you have done - ie, described method and reported analysis are consistent.
	14	The language and concepts used in the report are consistent with the epistemological position of the analysis.

	15	The researcher is positioned as active in the research process; themes do not just 'emerge'.

2.8 Scoping review

2.8.1 Aims

One of the potential benefits of early diagnosis is access to earlier treatments. It is proposed that treatments at the earlier stages of the disease can enable people with dementia to live well for longer. However, it is not clear what outcome measures are being used to test the effectiveness of non-pharmacological treatments for dementia. The selection of outcome measures is integral to understanding the benefits of early intervention. Therefore, chapter 6 used a scoping review to chart which outcomes are measured in randomised controlled trials for non-pharmacological interventions in early dementia and mild cognitive impairment.

The specific aims of this chapter were to:

1. Chart which outcomes are measured in randomised controlled trials for non-pharmacological interventions in early dementia and mild cognitive impairment (MCI)
2. Explore trends in the use of outcome measures by country, type of intervention and over time

2.8.2 Design

This study was a scoping review of randomised controlled trials of non-drug treatments for mild dementia and mild cognitive impairment. I followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009) and the PRISMA guidelines for Scoping Reviews (PRISMA-ScR) (Page and Moher, 2017) when designing this review. The protocol for this review was registered in advance on PROSPERO (ID: CRD42018102649).

2.8.2.1 Eligibility Criteria

The inclusion and exclusion criteria were based on PICOS (Population, Intervention, Outcomes, and Setting/Study design). The population of interest for this review were those diagnosed with mild dementia or mild cognitive impairment. I was interested in capturing the outcomes used by a broad range of non-pharmacological interventions, therefore any non-pharmacological intervention for mild dementia or MCI was eligible for this review. However, interventions which were not delivered to the person living with dementia was not deemed eligible for inclusion in this review. As the aim of this review was to chart which outcomes are used in studies testing non-pharmacological interventions for mild dementia and MCI, I did not set inclusion or exclusion criteria based on outcomes except for studies only assessing economic outcomes, such as cost-effectiveness. In terms of setting, I only excluded interventions which were conducted in psychiatric inpatient settings or acute hospital settings. These studies were generally staff training interventions rather than interventions delivered directly to the person living with dementia. I also limited this review to only include full RCTs, observational, feasibility, or pilot studies were not included in this review.

2.8.2.2 Search Strategy

EMBASE, Psych Info, Medline and the Cochrane Register of Controlled Trials were searched to identify relevant papers. Two searches were run, the first in February 2018 and a second top-up search was conducted in April 2019. Search terms were based on the Population, Intervention and Study Design of this study's PICOS. Keywords were searched and combined using the "And" and "OR" Boolean operators. The search terms used for identifying non-pharmacological interventions were taken from Olzaran and Colleagues systematic review of the effectiveness of non-pharmacological treatments for dementia (Olazarán et al., 2010), I then added search terms for new non-pharmacological treatments for mild dementia and MCI that I was aware of. I identified additional studies which were relevant to this review by searching the abstracts of the included papers and other systematic reviews on related topics.

2.8.2.3 Selection of sources of evidence

I used EndNote and Rayyan to manage studies identified during the search. Rayyan is an online application for systematic reviews, which allows researchers to create their own labelling system for decision making (Ouzzani et al., 2016). First, the title and abstract of all studies were reviewed in EndNote. Studies which were flagged for full-text review were then uploaded onto Rayyan where the full text was screened against the inclusion and exclusion criteria. A second reviewer screened 10% of all articles at each stage of the review. Reasons for excluding studies were recorded on Rayyan.

2.8.2.4 Data Extraction and Synthesis

I extracted which outcome measures were used by the included studies with references, the description of the intervention, number of comparison groups, the year the study was published, country the research was conducted in, description of the participants, and the author information.

I used the coding feature in NVivo to extract the outcome measures used by the included studies. Each code was labelled as the name of the outcome measure and the reference. I then checked the references for each of the outcome measures and where studies were using the same outcome measures or outcome measures were the same but given different names, I collapsed these codes. I repeated this process until I had a list of the outcome measures used, with references, and the studies which used the measure. A large proportion of the outcome measures used by the included studies were only used once. Where studies were used more than once, I grouped these by domain. For example, measures such as the MMSE, CDR and ADAS-Cog were grouped under the Cognition/Memory Domain. Similarly, I extracted the interventions used by the included studies and grouped these thematically.

I then tabulated the domain of outcome measures used, against the type of intervention, country, and year of publication to explore trends in the use of outcome measures. The results of this summary are presented in chapter 6.

2.8.3 Methodological limitations and alternatives

This review aims to chart which outcome measures are used by non-pharmacological interventions in mild dementia and MCI. I have kept the search strategy and inclusion and exclusion criteria as broad as possible, however, it was necessary to put limits on the types of studies included in this review to make it more feasible. This means studies testing non-pharmacological treatments in rarer types of dementia and studies in hospital settings were not included. Furthermore, only studies which were published in English were included in this review. Due to the language skills of the research team and a limited budget, it was not possible to include papers published in other languages. Therefore, while we have attempted to systematically map which outcome measures have been used in non-pharmacological trials, it is possible that not all studies on this topic are represented in this review.

This study captured and synthesised a broad range of information on this topic, therefore it was necessary to group interventions into broad themes. Therefore, some nuance in the use of outcome measures may have been lost in the categorisation of the outcome measures and interventions.

The findings of this study cannot tell us what the benefits of early diagnosis are in terms of early intervention. However, they do give us an idea of how the benefits of interventions in the early stages of the disease have been conceptualised in previous research. For example, we cannot know if providing non-pharmacological interventions during the early stages of dementia can delay admission into care homes, if no studies are using this as an outcome.

An alternative approach for answering this research question could be to conduct a quantitative study similar to those presented in section 2.5, where I would explore if an early diagnosis increased the likelihood of receiving a non-pharmacological treatment and whether this reduced the risk or mortality, hospitalisation, or ED attendance. However, this was not feasible as there are very few non-pharmacological interventions offered by the NHS and this

data is not easily extractable from CRIS. Therefore, a scoping review of existing research was deemed a more appropriate study design.

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Chapter 3: Quantitative phase (part 1)

This chapter presents the results from the first part of the quantitative phase of analysis. This chapter examines whether a diagnosis of MCI can be used as a proxy for an early diagnosis. Secondly, this chapter investigates the association between an early diagnosis and the subsequent risk of mortality.

This work has been published by the Journal of Alzheimer's Disease therefore, this chapter is presented as the accepted manuscript.

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Title: The association between a previous diagnosis of MCI as a proxy for an early diagnosis of dementia and mortality: A study of secondary care electronic health records

Running title: The early diagnosis of dementia and mortality

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Abstract

Background

Dementia policy states that the early diagnosis of dementia can keep people living well for longer, however, there is little robust evidence to support this. Mild Cognitive Impairment (MCI) is considered a prodrome to dementia and can aid with the earlier diagnosis of dementia.

Objective

The objective of this study was to use a previous diagnosis of MCI, before dementia, as a proxy for early diagnosis to investigate the relationship between an early diagnosis and mortality.

Methods

A retrospective cohort study of electronic health care records from South London and Maudsley NHS. Patients aged 50+, diagnosed with dementia between January 2008 and November 2018 were divided into two groups: those with a previous diagnosis of MCI (early diagnosis) and those without. Cox regression models used to compare the risk of mortality between groups.

Results

Of 18,557 participants, 5.6% (n= 1,030) had an early diagnosis; they had fewer cognitive, psychiatric and functional problems at dementia diagnosis. The early diagnosis group had a reduced hazard of mortality (HR= 0.86, CI= 0.77 – 0.97). However, the magnitude of this effect depended on the scale used to adjust for cognitive difficulties.

Conclusion

A previous diagnosis of MCI is a helpful proxy for early diagnosis. There is some evidence that an early diagnosis is associated with a reduced risk of mortality, however, it is not clear

how MMSE scores affect this relationship. While these findings are promising, we cannot be conclusive on the relationship between an early diagnosis and mortality.

Key Words: dementia, early diagnosis, mild cognitive impairment, MCI, mortality

INTRODUCTION

There is no cure for dementia, therefore current policy and guidelines for the treatment of dementia focus on delaying progression, improving quality of life and increasing survival for people living with dementia [1]. The number of people living and dying with dementia is increasing, it is now the leading cause of death in the UK [2]. The median survival time for people living with dementia is 10.5 years from the onset of symptoms and 5.7 years from the time of diagnosis [3]. However, survival estimates can vary greatly depending on the severity of the disease at the time of diagnosis with those diagnosed with mild dementia experiencing longer survival times and fewer life years lost than those diagnosed with moderate or severe dementia [4].

The early diagnosis of dementia is the cornerstone of the dementia policy in the UK, asserting that an early diagnosis can keep people living well for longer [5-7]. A diagnosis of Mild Cognitive Impairment (MCI) presents the opportunity to identify dementia in the earlier stages of the disease. Current evidence suggests that dementia starts up to 10 years before the onset of symptoms, this asymptomatic phase is followed by an early symptomatic phase, during which people experience mild problems with their memory – and may be diagnosed with MCI– which then progresses to the full disease [8, 9]. Due to the complexity of diagnosing dementia, there is an increased risk of misdiagnosis in the early stages of the disease [10]. Furthermore, the diagnosis of MCI is a grey area, it is not clear how MCI progresses into dementia as not everyone with MCI will go on to develop dementia [11-13]. However, a diagnosis of MCI is considered to be a useful clinical tool for identifying people at risk of developing dementia and could help with the early diagnosis of dementia [8].

While dementia policy in the UK has suggested that diagnosing dementia early can keep people living longer [5-7], there is very little robust evidence to support this. In 2011, Alzheimer's Disease International assessed the strength of the evidence for the proposed benefits of diagnosing dementia early. They found only three population-based studies which

examined the relationship between early diagnosis and mortality, or cognitive decline and these studies reported small effects [14]. Furthermore, when the researchers reviewed statements summarising the benefits of early diagnosis, they found them largely to be unreferenced and not evidenced-based. Furthermore, much of the research into the benefits of diagnosing dementia early is based on modelling and not patient data [15]. More research using real-world data is needed to understand how an early diagnosis can keep people with dementia living well for longer.

One of the challenges of investigating the effects of early diagnosis is how to identify people living with dementia who have received an early diagnosis. While not all people who are diagnosed with MCI will go on to develop dementia, a diagnosis of MCI before dementia could be a helpful proxy for early help-seeking and early diagnosis. Using a previous diagnosis of MCI presents the opportunity to explore the effects of early diagnosis on long-term outcomes, such as mortality, in existing cohort studies and populations ascertained from routinely collected data. Therefore, the aim of this study was to investigate the association between a previous diagnosis of MCI and mortality.

Objectives

To address the overall aim of this study, we used a retrospective cohort design to compare participants who had been diagnosed with MCI before dementia and those who had never received a diagnosis of MCI.

The specific objectives of this study were to:

1) Explore whether a previous diagnosis of MCI – before dementia – can be used as an indicator for early diagnosis or early help-seeking
2) Investigate differences between participants with a previous diagnosis of MCI and those without
3) To investigate the association between a previous diagnosis of MCI and mortality, while taking differences between groups into account.

MATERIALS AND METHODS

Data sources

The data used in this study were extracted from electronic health care records from the South London and Maudsley NHS Trust (SLaM) Biomedical Research Centre Clinical Record Interactive Search (CRIS). SLaM provides specialist dementia care to people living in the catchment areas of Lambeth, Lewisham, Southwark and Croydon. Data are stored both in structured fields and in free text, the extraction of which has been described previously [16, 17]. The CRIS database has full approval for secondary analysis (Oxford Research Ethics Committee C, reference: 08/H0606/ 71+5). This study utilised an existing linkage between CRIS and the Office for National Statistics (ONS) for mortality data.

Sample identification

Data from all SLaM patients who were diagnosed with dementia according to International Classification of Disease (ICD-10) diagnostic criteria [18] between 2nd January 2008 and 4th November 2018 and were over the age of 50 at the time of diagnosis were extracted using CRIS. Date of first dementia diagnosis served as the index date. Dementia diagnosis was determined using structured ICD-10 codes in structured fields in the clinical record, supplemented by a bespoke natural language processing (NLP) algorithm using General Architecture for Text Engineering (GATE) software [19, 20].

Measures

Mild Cognitive Impairment

A diagnosis of MCI according to ICD-10 code F06.7 before the index date was ascertained from structured fields supplemented by free-text using GATE-derived software. This was included as a dichotomous variable (yes/no).

Mortality

Mortality data, including date and cause of death, up until the 14th November 2018 were collected from the data linkage with the ONS. All causes of death were included in this study. Participants were followed-up from the date of diagnosis until death or the census date.

Covariates

Demographic data were extracted from routinely completed fields including age at the time of dementia diagnosis, gender, marital status and ethnicity. Marital status was coded as current partner or no current partner. Ethnicity was coded as European, Black, Asian or Other. Mini-mental state exam (MMSE) scores were extracted from CRIS using NLP. Where patients had multiple MMSE scores, we used the score closest to the date of dementia diagnosis. Data were extracted from the Health of the Nation Outcome Scales (HoNOS), a routine measure of wellbeing in UK mental health and dementia services [21]. The HoNOS subscales are rated on a five-item ordinal scale (from 0 for no problem to 4 for severe or very severe problems), whereby we dichotomized following the clinicians' approach of first considering whether there is a problem requiring intervention (score 2-4) or not (score 0-1). Dichotomized variables based on HoNOS scores have been shown to have predictive validity for mortality in cohorts of patients with dementia assembled from this cohort [22, 23]. We examined HoNOS subscales for clinician-rated cognitive problems, physical illness and disability, activities of daily living and used the remainder to adjust for the presence of psychiatric symptoms experienced by participants and grouped those by number of symptoms (no symptoms, one symptom, two symptoms and three or more symptoms). Two measures of cognitive problems (MMSE and HoNOS) were included in this study as we anticipated multicollinearity between MMSE scores and a previous diagnosis of MCI. Index of Multiple Deprivation was derived from the patient's address at the time of diagnosis [24]. The prescription of acetylcholinesterase inhibitors (AChEIs) up to six months after diagnosis were extracted using GATE hosted applications and were dichotomised (yes/no).

Statistical analysis

Data were analysed using Stata 15 [25]. This was an exploratory study, the exposure under investigation in this study was the prior diagnosis of MCI, referred to as an early diagnosis, and the outcome was all-cause mortality. We used chi-squared tests and t-tests to examine the differences between the two groups, in categorical or dichotomous variables and continuous variable respectively. The significance threshold was set at 0.05 for all analyses.

Kaplan-Meier curves with log-rank tests were used to compare survival between the two groups. Cox regression models were used to investigate the association between early diagnosis and all-cause mortality, age at diagnosis, gender, ethnicity, levels of physical illness, clinician-rated cognitive impairment, prescription of AChEIs and MMSE scores at diagnosis were included in the models to control for confounding. A sensitivity analysis was conducted to compare the dichotomized and ordinal versions of the HoNOS measure of cognition. We checked the proportional hazards assumption was met by using a test of Schoenfeld residuals. Where this assumption was not met, a time interaction for the problematic variables was included in the model.

Missing data

MMSE scores were missing for 30% of participants and 13% of participants were missing one or more items on the HoNOS. All other variables had 1% or less missing data. Missing data were imputed using multiple imputation by chained equations [26], assuming missing at random, to maximise statistical power. Ten datasets, including all covariates and outcomes, were imputed using the mi package in STATA before using cox regression models on the imputed datasets.

RESULTS

Participants

We identified 18,555 patients diagnosed with dementia. The characteristics of the sample are presented in **Table 1**. The mean age of participants was 80.8 (SD = 8.7) years, and the

majority of patients (60.6%) were female, without a current partner (66.6%) and had high levels of physical illness and disability (56%). The majority of participants (35.9%) had no psychiatric symptoms. The average MMSE score was 18.6 (SD = 6.3) and AChEIs were prescribed to one third (31.9%) of participants in this study.

Factors associated with an early diagnosis

Of the 18,555 patients included in this study, 1,030 (5.6%) had a previous diagnosis of MCI recorded. The mean time between the diagnosis of MCI and dementia was 1.2 years (SD = 1.5). In **Table 1** the differences between patients who received an early diagnosis of MCI and those who did not are also presented. T-tests showed that participants with an early diagnosis had better cognition, rated by the MMSE, and higher levels of social deprivation. Chi-squared tests showed participants with an early diagnosis differed in terms of ethnicity, with a greater proportion of white participants receiving an early diagnosis compared to other ethnic groups. Participants with an early diagnosis reported fewer problems with cognition, had fewer psychiatric symptoms and less impaired activities of daily living as rated by the HoNOS. Additionally, a greater proportion of participants with an early diagnosis were prescribed AChEIs following diagnosis.

Early diagnosis and mortality

Between baseline diagnosis of dementia and the census date, there were 10,344 deaths (55.7%) with a median survival time of 4.02 years (IQR = 1.8 – 7.2). Kaplan-Meier curves show increased survival in people with an early diagnosis of MCI (**Figure 1.**) (log-rank test**:** $p<0.01$).

We used cox regression models to further assess the relationship between an early diagnosis and mortality, we added variables which were found to violate the proportional hazards assumption as time-varying covariates (**Table 2**). We ran 11 cox regression models of increasing complexity, adjusting for a range of confounding factors, which showed the hazard of mortality was significantly lower in the early diagnosis groups in all but one of the

models. The hazard ratios ranged between 0.77 and 0.92. A previous diagnosis of MCI remained a significant predictor of a lower mortality risk in models adjusting for demographics and physical illness, psychiatric symptoms, ADL problems, and prescription of AChEIs both individually and simultaneously (Model 9 HR = 0.86, CI = 0.77 – 0.97). Associations remained significant when using HoNOS ratings to adjust for cognitive impairment (Model 10 HR = 0.87, CI= 0.78 – 0.97). Supplementary Table 1 presents models using the full ordinal measure of HoNOS cognition. The hazard ratio for the fully adjusted model shows the same direction of effect as those presented in Table 2 (HR= 0.90, CI= 0.80- 1.01, p=0.07) however, it does not reach the threshold for significance where p=0.05. When using the MMSE to account for cognition in a similar model, associations between a previous MCI diagnosis and mortality were attenuated and no longer significant (Model 11 HR = 0.92, CI = 0.83 – 1.04).

DISCUSSION

In this study of electronic health records from 18,555 participants in routine secondary care, we have found that a previous diagnosis of mild cognitive impairment can be used as an indicator to measure the effects of an early diagnosis or early help-seeking. We found 5.6% of all participants with dementia had previously received a diagnosis of MCI. People with a previous diagnosis of MCI had lower MMSE scores and fewer severe psychiatric symptoms at the time of dementia diagnosis, indicating that they were diagnosed in the earlier stages of the disease. We have found evidence to suggest there is an association between an early diagnosis of MCI and a lower risk of mortality, however, it is not clear how MMSE scores at diagnosis affect this relationship.

While only 5.6% of participants in our sample had a previous diagnosis of MCI, we have demonstrated that a diagnosis of MCI before dementia is a useful tool for measuring early diagnosis/ early help-seeking for memory loss. Participants with a previous diagnosis of MCI had fewer psychiatric symptoms, less impaired cognition (both clinician and MMSE rated) and less impaired activities of daily living at dementia diagnosis. Higher levels of cognitive

decline and behavioural and psychological symptoms of dementia are associated with the later stages of the disease [27, 28]. In our sample, participants who received an early diagnosis were more likely to come from European backgrounds, compared with other ethnic groups. Surprisingly, people with an early diagnosis had higher levels of social deprivation. However, while statistically significant, a difference of 1 point between the groups may not be a clinically significant difference. Our findings indicate there may be systemic differences between those who received a diagnosis of MCI and therefore an earlier diagnosis of dementia. This is consistent with reports that people with MCI are largely a self-selecting group, most receive a diagnosis after requesting a memory assessment [29].

Participants in the sample had a median survival time of 4.0 years, this is slightly less than other studies assessing mortality in dementia which reported average survival times of 5.7 years after diagnosis [3, 30, 31]. Over half of the participants (55.74%) died during the study period. The risk of mortality was between 9-23% lower in participants with a previous diagnosis of MCI compared to those without when adjusting for a range of covariates. There was no statistically significant difference between groups when MMSE scores at dementia diagnoses were included in the cox regression models (Model 11 HR = 0.92; CI = 0.83 – 1.04). However, models controlling for HoNOS rated cognitive impairment showed an early diagnosis was associated with a lower risk of mortality (Model 10 HR = 0.87, CI = 0.78 – 0.97). It is possible that the introduction of MMSE scores nullified the effects due to collinearity between MMSE scores and MCI diagnosis as, typically, a diagnosis of MCI in clinical practice is highly dependent on MMSE scores [32]. However, Models containing the HoNOS measure of cognitive impairment may be lacking statistical power as this is a dichotomous variable, increasing the risk of a false-positive finding [33]. A sensitivity analysis found that models using the full HoNOS measure of cognition were attenuated but did not reach statistical significance. It would be interesting to investigate how cognitive impairment as rated by other measures affected the relationship between an early diagnosis and

mortality. It was not possible to include other measures of cognition in this study, as the variables available for analysis were limited to what is routinely collected.

A greater proportion of people with a previous diagnosis of MCI were prescribed AChEIs within 6 months of their diagnosis of dementia (38.54%, compared with 31.45%). One of the proposed benefits of early diagnosis is access to earlier treatment [5-7, 14]. The findings of this study indicate that people with a previous diagnosis of MCI are more likely to be diagnosed with dementia in the earlier stages of the disease and are more likely to receive treatment with AChEIs at diagnosis. Although antidementia medications have been linked with a reduced risk for mortality and severe cardiovascular events in several observational studies [23, 34, 35], it remains unclear whether this reflects a bias by indication or a direct effect of these medications. As antidementia medications are not appropriate for all people diagnosed with dementia [36], more research is needed to investigate the relationship between an early diagnosis of dementia and mortality related to pharmacological and non-pharmacological treatments.

Despite national initiatives to increase the diagnosis rate of dementia in the UK, only 60% of those with dementia have received a formal diagnosis [29]. The decision to seek help for suspected memory loss is complex. A lack of understanding of the causes and symptoms of dementia, the perception that nothing can be done to treat dementia and fear of stigmatisation can deter people from seeking a diagnosis [37]. There is some evidence that expectations of support following a diagnosis differ between those seeking an early diagnosis for emerging memory problems and those seeking a diagnosis for the later stages of cognitive decline. Those seeking help for early-stage memory loss were more likely to proactively ask about treatment- most commonly medications [8, 38]. Therefore, any benefits of an early diagnosis may be due to proactive help-seeking behaviours rather than post-diagnostic support.

Additionally, people from black and minority backgrounds are less likely to seek timely help for memory problems. This is supported by our finding that white participants were more likely to have an early diagnosis. While we have found some evidence of the potential benefits of an early diagnosis, this remains limited to specific groups of people. Going forwards, it is imperative more research is conducted to understand the real-life benefits of an early diagnosis. This information could help people make a more informed choice about when to seek a diagnosis and the possible consequences. However, it is equally important to address systemic differences in diagnosis rates between different social and ethnic groups.

Strengths and limitations

In this study, we have developed a method to identify people with dementia that have early help-seeking behaviours. This method is easily replicable and can be applied to other hospital databases. The linkage of electronic health care records to a national mortality database allowed us to follow participants from diagnosis to death and excludes the risk of bias from inaccurate mortality records. Generally, studies which explore the progression of dementia or MCI have limited follow-up periods [14]. This study had a large sample size of 18,555 people living with dementia, drawn from a diverse population of patients in routine clinical care, increasing the generalisability of these findings.

There are limitations to this study, which should be considered. While we have shown that a previous diagnosis of MCI can be a helpful proxy for measuring early diagnosis and early help-seeking, it is not a perfect indicator. How the diagnosis of MCI is used differs between clinicians [39], participants may have had a memory assessment before their diagnosis of dementia but were not diagnosed with MCI. Additionally, this study has used a large sample size, however, only a small group of participants had a previous diagnosis of MCI which affects the statistical power of our analysis. We have limited the effect of this by imputing missing data, to maximise the power of the data that was available to us. Additionally, this

study used a cohort design, therefore there may be residual confounding which has not been controlled for.

Conclusions and future directions

In this study, we successfully used the prior diagnosis of MCI in people living with dementia as a proxy for early diagnosis/early help-seeking. Previously, there had been no studies which examined the reported benefits of early diagnosis or early help-seeking for people living with dementia, their caregivers or society, and many of the previously presumed benefits were dependent on the availability of disease-modifying treatments [15]. While we found that only a small percentage of participants received an early diagnosis, they presented a symptom profile associated with the earlier stages of dementia at diagnosis, were more likely to be prescribed ACHEIs and had a lower risk of mortality when adjusting for a dichotomized measure of clinician-rated cognitive impairment. However, this effect was attenuated but no longer significant when using a more sensitive measure of cognition. These findings are promising, however, they are not conclusive on the benefits of an early diagnosis, more research is needed to better understand the association between an early diagnosis and mortality and other long term outcomes.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to report.

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Table 1 Characteristics of participants and factors associated with the early diagnosis of mild cognitive impairment

Demographic Information at Dementia Diagnosis	Total (n=18,555)	Early diagnosis (n=1,030)	No early diagnosis (n = 17,527)	*P*-value
Gender (%)				0.712
Male	39.38	38.83	39.41	
Female	60.62	61.17	60.59	
Ethnicity (%)				0.001*
European (British, Irish, etc)	74.40	79.20	74.11	
Black (Caribbean, African, other)	16.82	14.92	16.93	
Asian (Indian Bangladesh, other Asian)	4.65	3.14	4.74	
Other	4.13	2.75	4.21	
MCI diagnosed before dementia (%)	5.55			
Mean Age (SD)	80.79 (8.74)	80.82 (8.18)	80.79 (8.77)	0.9178
Mean MMSE Score (SD)	18.55 (6.32)	21.59 (5.69)	18.38 (6.31)	<0.001*
Prescribed AChEIs 6 months ± dementia diagnosis (%)	31.85	38.54	31.45	<0.001*
Mean Index of deprivation (SD) †	27.34 (11.06)	28.43 (10.10)	27.27 (11.11)	0.001*
Marital Status (%)				
Current partner	66.64	32.96	33.38	0.784
No current partner	33.36	67.04	66.62	
HoNOS Cognitive impairment	85.12	77.88	85.50	<0.001*
HoNOS Psychiatric symptoms (%)				
No symptoms	35.86	40.58	35.58	0.006**
1 symptom	29.70	29.13	29.74	
2 symptoms	18.23	15.73	18.38	
3+ symptoms	16.21	14.56	16.31	
HoNOS Activities of daily living (%)	61.14	56.52	61.51	<0.001*
HoNOS Physical Illness and disability (%)	56.03	54.87	56.10	0.481

Note: HoNOS= Health of the Nations Outcome Scales

† Higher score indicates more socially deprived
*Significant $p \leq 0.001$
**Significant $p < 0.05$

Table 2 Hazard ratios for the association between a previous diagnosis of mild cognitive impairment and mortality

Early diagnosis		Adjusted HR†	95% CI	p
Model 1	Adjusted for age, gender	0.78	0.70 - 0.86	<0.001 *
Model 2	Adjusted for age, gender, ethnicity, marital status, socioeconomic status	0.77	0.70 - 0.86	<0.001 *
Model 3	Model 2 + physical illness	0.79	0.71 - 0.88	<0.001 *
Model 4	Model 2 + psychiatric symptoms	0.80	0.72 - 0.88	<0.001 *
Model 5	Model 2 + problems with ADLs	0.83	0.74 - 0.93	0.001*
Model 6	Model 2 + prescription of AChEIs	0.81	0.73 - 0.90	<0.001 *
Model 7	Model 2 + cognition (HoNOS)	0.79	0.71 - 0.88	<0.001 *
Model 8	Model 2 + cognition (MMSE)	0.91	0.71 - 1.00	0.046*
Model 9	Model 2 + physical illness, psychiatric symptoms, AChEIs and problems with ADLs	0.86	0.77-0.97	0.01*
Model 10	Model 9 + cognition (HoNOS)	0.87	0.78 - 0.97	0.02*
Model 11	Model 9 + cognition (MMSE)	0.92	0.83 - 1.04	0.177

Note: ADL= Activities of Daily Living; AChEIs= Acetylcholinesterase Inhibitors; HoNOS= Health of the Nation Outcome Scales; MMSE= Mini-Mental State Exam

† Variables found to violate the proportional hazards assumption were added as time-dependent covariates

*p≤0.05

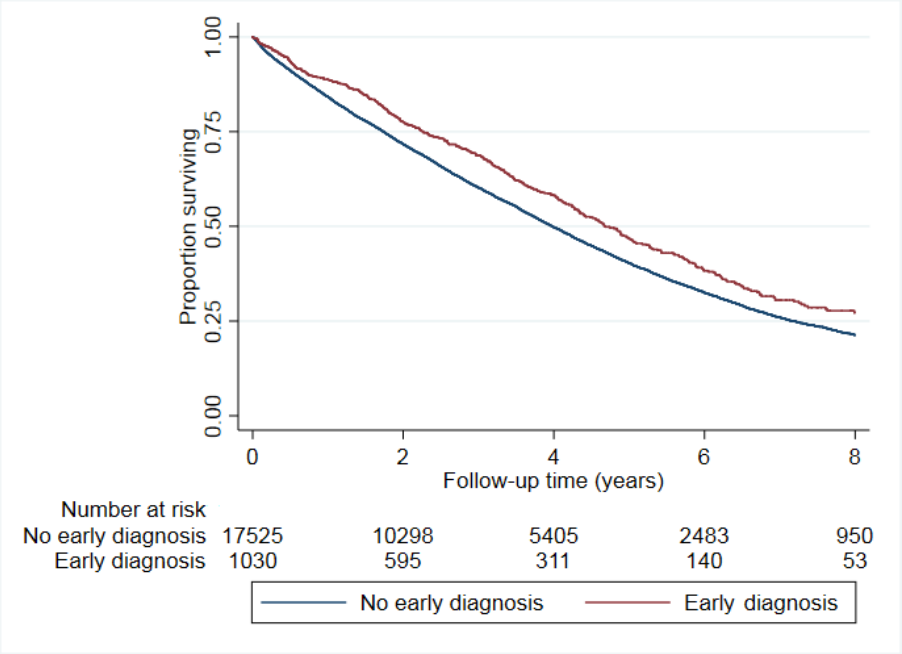

Figure 1 Kaplan-Meier curves comparing survival between a previous of mild cognitive impairment (Early diagnosis) and no previous diagnosis of mild cognitive impairment.

Log-rank test**:** $X^2 = 17.2$, $p<0.01$

3.2 Supplementary materials

Supplementary Table 1 Comparing Hazard Ratios for the association between a previous diagnosis of mild cognitive impairment and mortality using different versions of the HoNOS to adjust for cognitive impairment

Variable used to adjust for cognitive impairment	**Model 1**		**Model 2**	
	HR (95% CI)	p	HR (95% CI)	P
Dichotomised HoNOS	0.79 (0.71 - 0.88)	<0.01*	0.87 (0.78 - 0.97)	0.02*
Ordinal HoNOS	0.83 (0.75- 0.92)	<0.01*	0.90 (0.80 – 1.01)	0.07

*p<0.05

Model 1 adjusted for Adjusted for age, gender, ethnicity, marital status, socioeconomic status and cognitive impairment

Model 2 adjusted for age, gender, ethnicity, marital status, socioeconomic status, physical illness, psychiatric symptoms, AChEIs, problems with ADLs and cognitive impairment

Chapter 4: Quantitative phase (part 2)

This chapter presents the results from the second part of the quantitative phase of analysis. This chapter investigates whether an early diagnosis of dementia is associated with a reduced risk of hospitalisation or emergency department attendance.

This work has been accepted for publication by the Age and Ageing therefore, this chapter is presented as the accepted manuscript.

Couch, E., Mueller, C., Perera, G., Lawrence, V. and Prina, M., (In Press) The association between an early diagnosis of dementia and secondary health service use. Age and Ageing.

Title: The Association between an early diagnosis of dementia and secondary health service use

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The association between an early diagnosis of dementia and secondary health service use

Abstract

Background: Dementia policy suggests diagnosing dementia early can reduce the risk of potentially harmful hospital admissions or emergency department (ED) attendances, however, there is little evidence to support this. A diagnosis of Mild Cognitive Impairment (MCI) before dementia is a helpful proxy to explore early diagnosis. This study investigated the association between an early diagnosis of dementia and subsequent hospitalisations and ED attendances.

Method: A retrospective cohort study of electronic health care records from 15,836 patients from a large secondary care database in South London, UK. Participants were divided into two groups: those with a diagnosis of MCI before dementia, an early diagnosis, and those without. Cox regression models were used to compare the risk of hospitalisation and ED attendance after dementia diagnosis and negative binomial regression models were used to compare the average length of stay and average number of ED attendances.

Results: Participants with an early diagnosis were more likely to attend ED after their diagnosis of dementia (HR= 1.09, CI= 1.00 – 1.18), however there was no difference in the number of ED attendances (IRR= 1.04, CI= 0.95 – 1.13). There was no difference in the risk of hospitalisation (HR= 0.99, CI= 0.91 – 1.08) or length of stay between the groups (IRR= 0.97, CI= 0.85 – 1.12).

Conclusion: The findings of this study do not support the assumption that an early diagnosis reduces the risk of hospitalisation or ED attendance. The patterns of health service use in this paper could reflect help-seeking behaviour before diagnosis or levels of co-morbidity.

Word Count: 2,408

Introduction

The frequent use of emergency services and unplanned hospitalisations is reflective of fractured dementia care [1, 2]. It is not clear what steps need to be taken to reduce people living with dementia's risk of hospitalisation or emergency department (ED) attendance. However, the early diagnosis of dementia has frequently been cited as a way of reducing the need for emergency care or hospitalisation [3]. All European countries with a national dementia strategy highlight the importance of receiving an early or "timely diagnosis" of dementia, to enable people living with dementia to receive treatment and make advance care plans as early as possible to reduce the risk of unnecessary hospitalisations or ED attendances [4]. It is assumed that an early diagnosis of dementia can lead to a reduced risk of hospitalisation or use of emergency services, however, there is little empirical evidence to support this relationship [3, 5, 6].

There is no fixed definition for early diagnosis in dementia. Early diagnosis could be from the onset of neuropathology, many years before the symptoms become apparent, from the use of reliable predictive biomarkers, or the onset of cognitive symptoms [5]. With the current state of evidence, it is possible to diagnose the pathologies that cause dementia early using predictive biomarkers, however, dementia is typically diagnosed in response to the onset of symptoms [5]. Mild cognitive impairment (MCI) is a diagnostic label commonly assigned to the early symptomatic stages of dementia where a full diagnosis cannot be confirmed [7]. Our previous research found people with a diagnosis of MCI before dementia have less severe cognitive, psychiatric and functional symptoms at dementia diagnosis. This profile of symptoms is consistent with the early stages of dementia therefore, a previous diagnosis of MCI is a useful proxy for the early diagnosis of dementia [8].

Aims

In theory, people with an early diagnosis should receive early treatment, have more contact with primary health services ahead of time and be supported to make advanced plans, which reduce the risk of hospitalisation or ED attendance [6]. However, it is unclear whether this happens. Therefore, the primary aim of this study was to examine whether there is any difference in the risk of hospitalisation or ED attendance between participants with an early diagnosis, as defined by a previous diagnosis of MCI, and those without. Secondly, we examined whether the length of stay and number of ED attendances differed between the two groups.

Methods

To address the aims of this study, we conducted a retrospective cohort study using electronic health records from South London and Maudsley NHS Foundation Trust (SLaM). SLaM provides specialist dementia care to people living with dementia in the London boroughs of Lambeth, Lewisham, Southwark and Croydon.

Data sources and linkages

Data from SLaM's electronic medical health care records were extracted through SLaM's Biomedical Research Centre Clinical Record Interactive Search (CRIS). Data is stored in both free text and structured fields, the extraction of which has been previously described [9, 10]. Additionally, we used an existing linkage between CRIS and NHS Digital Health Episode Statistics (HES) to extract data on hospitalisations and visits to ED. HES data were available until 31/03/2017.

Participants

Participants were included in the cohort if they received a diagnosis of dementia according to ICD 10 classifications [11], between 2nd January 2008 and 30th March 2016, and were over the age of 50. The first diagnosis of dementia served as the index date and all participants had at least one year of HES follow-up data available.

Measures

Participants with a diagnosis of MCI, as recorded by an ICD-10 code of F06.7, before the index date were classified as having received an 'early diagnosis'. This was included as a dichotomous variable.

Our primary outcomes of interest were time to first hospitalisation and time to first ED attendance. Our secondary outcomes of interest were the cumulative number of hospital days and number of ED attendances.

As covariates we extracted whether participants were hospitalised or attended ED in the year before Dementia diagnosis, as these are known predictors of ED attendance/hospital admission after diagnosis [12]. Demographic information from the time of dementia diagnosis were extracted including age, gender, ethnicity (coded as European, Black, Asian or Other), marital status and levels of social deprivation. A raw score for neighbourhood index of social deprivation was estimated using the participant's most recent address [13]. Participant's Mini-Mental State Exam (MMSE) scores , which rates the severity of cognitive impairment on a scale of 1-30 (where a higher score indicates less cognitive impairment) [14], at the time of dementia diagnosis were extracted. Participant's scores on the HoNOS 65+, which rates functional and other psychiatric symptoms, were extracted at the time of diagnosis. The number of psychiatric symptoms experienced by participants was grouped by number of symptoms: no symptoms, 1 symptom, 2 symptoms and 3 or more symptoms. We also extracted whether participants were prescribed AChIEs within 6 months of diagnosis, this was dichotomised.

Statistical analysis

All analyses were conducted using Stata 15 [15]. T-tests and Chi-squared test were used to compare baseline differences between the early diagnosis and no early diagnosis groups.

We assessed the risk of hospitalisation and ED attendance after dementia diagnosis using cox regression models. Negative binomial regression models were used to compare the length of stay (number of days) and the number of ED attendances by each group. We used negative binomial regression, rather than Poisson Regression, as data were over dispersed. We present an unadjusted model and a multivariable model adjusted for age, gender, ethnicity, physical illness, marital status, prescription of ACHEIs, number of psychiatric symptoms, MMSE scores, and previous hospitalisation/ED attendance. Follow-up time was included in both models as an exposure variable.

Missing data

Thirty percent of participants were missing MMSE scores and 13% of participants were missing one or more scores on the HoNOS 65+. Missing data were imputed in STATA using multiple imputation by chained equations [16]. All outcomes and covariates were included in the imputation.

Results

Demographics

We identified 15,836 people with dementia, 5.1% of participants (n= 807) were diagnosed with MCI before they were diagnosed with dementia. Table 1 presents the characteristics of included participants. Participants with an early diagnosis were more likely to be white, to be prescribed ACHEIS, have higher levels of social deprivation, less impaired cognition and activities of daily living. A greater proportion of participants with an early diagnosis attended ED before their diagnosis of dementia than those without.

Risk of hospitalisation or ED attendance

Most participants had a hospitalisation (74%) recorded after they were diagnosed with dementia (Table 2). The median time to first hospitalisation after dementia diagnosis was

11.5 months. Adjusted and unadjusted cox regression models showed there was no significant difference in the risk of hospitalisation between the groups.

Over two thirds of participants attended ED after their dementia diagnosis (75.7%). The median time to first ED attendance in the early diagnosis group was 8.9 months, compared with 10.6 months. Adjusted cox regression models showed participants with an early diagnosis were at increased risk of attending ED (HR = 1.09, CI = 1.00 – 1.18, p =0.4).

Length of stay & number of ED attendances

Table 3 presents the mean number of hospital days and ED attendances per 100 person years. Participants with an early diagnosis had a significantly shorter length of stay at 10.8 hospital days compared with 10.27 hospital days (p= 0.01). There was no significant difference in number of ED attendances between the groups.

Negative binomial regressions, adjusted for a range of confounders, showed there was no difference in the count of hospital days between the groups (IRR= 0.97, CI = 0.85 – 1.12). Similarly, there was no difference in the count of ED attendances (IRR= 1.04, CI= 0.95 – 1.13).

Discussion

In this study, we investigated whether an early diagnosis was associated with a decreased risk of hospitalisation or ED attendance after a diagnosis of dementia. We found that participants with an early diagnosis were at greater risk of attending ED than participants without an early diagnosis, however, there was no difference in the number of ED attendances between the groups. There was no difference in the risk of hospitalisation or length of stay between participants with an early diagnosis and those without.

We found a high level of secondary health service use in people with dementia, 74% of participants were hospitalised and 75% attended ED after their diagnosis. The average time

to the first hospitalisation and first ED visit was 11.5 and 10.4 months respectively. This is consistent with previous research which showed that people living with dementia have high rates of admission to hospital within the first year of diagnosis [1]. These are important findings, as the early or timely diagnosis of dementia is a cornerstone of dementia policy in the UK and Europe [4]. Our findings suggest that an early diagnosis, or early help-seeking, alone is not sufficient to reduce the need for potentially harmful hospitalisations and ED attendances. This indicates that we need to think beyond diagnosing dementia early. We do not currently understand how to reduce hospitalisation and ED attendance in people living with dementia. Future research should investigate how post-diagnostic support from health and community services can reduce the risk of using secondary healthcare services.

We found, contrary to popular belief, that the risk of hospitalisation and length of stay did not differ between people with an early diagnosis of dementia compared to those without. Additionally, people with an early diagnosis had a higher risk of attending ED, although there was no difference in the number of times each group attended ED. This group may have had increased contact with health services before their diagnosis of dementia, which increased the likelihood of receiving the early diagnosis of dementia, and this pattern of health service use continued after diagnosis.

Many hospital admissions for people living with dementia are necessary and appropriate. However, people living with dementia are at greater risk of negative outcomes arising from hospitalisation than older adults of the same age without dementia. They may be hospitalised for longer [17, 18], may be less likely to be given appropriate treatment or pain relief [18-20], can experience significant cognitive decline during their admissions, [21] and are at greater risk of developing delirium [18, 22]. Similarly, people living with dementia use ED more than older adults of the same age [23]. ED visits can be difficult for people living with dementia and their carers; they require additional care for their illness and extra support to cope with the unfamiliar environment in ED. ED visits for people living with

dementia are also likely to increase in the last few months of life and are more likely to be emergency referrals, by ambulance or out of hours, indicating visits are made at a time of crisis [2]. It is important that people living with dementia are able to access the health services they need at the time they need it, however more research is needed to understand how to reduce the risk of unnecessary hospitalisation and ED use by people living with dementia.

There is a risk that focusing on diagnosing dementia early and investing in treatments for the early stages of the disease diverts resources from meeting other needs in the later stages, including the treatment of co-morbidities [6]. Previous research has found that people living with dementia tend to access services for their comorbid conditions, rather than for their dementia [1] , and an increased number of co-morbid conditions is associated with increased primary and secondary health service use [24]. Over half of the participants included in this study had high levels of co-morbid physical illness or disability. It is possible that there is no difference in risk of hospitalisations between the two groups because they have similar levels of comorbid conditions and are therefore are accessing services in a similar way. It is not clear how a diagnosis of dementia affects the treatment of comorbid conditions, however, there is evidence that services should take a more holistic approach to treating dementia and comorbid conditions in the hope of reducing hospital admissions and ED visits [24, 25].

Limitations

The cohort from this study came from a secondary care database, which reflects the high levels of service use. Further research is needed to understand the impact of an early diagnosis or early help-seeking on the use of other types of health services, such as primary care. While we have highlighted the possible role of comorbidities in driving high levels of health service use, our data are restricted to HoNOS rated levels of comorbidities without information on individual conditions. This is an interesting avenue for future research. This is

a cohort study, therefore variables used in this study were limited to what is routinely collected, there may be some residual confounding which has not been controlled for. While we have previously found a previous diagnosis of MCI to be a useful proxy for early diagnosis [8], we cannot be conclusive that participants in the early diagnosis group were diagnosed earlier in the disease. Furthermore, in this study, we were not able to differentiate between necessary and avoidable hospitalisations or ED attendances. Finally, the negative findings make it difficult to draw conclusions for clinical practice, however they do have implications for policies which promote the benefits of diagnosing dementia early.

Implications and directions for future research

We have found that early diagnosis alone is not a preventative step for reducing hospitalisations or ED attendances and people with an early diagnosis had an increased risk of attending ED. However, an equal or higher use of health services between people with an early diagnosis and those without is not necessarily a bad thing. People living with dementia should be able to access appropriate health services whenever they are needed. However, people with dementia are at greater risk of negative outcomes following a hospitalisation or ED attendances [18, 23] and should probably be avoided in lieu of other types of support. Previous research in the United States has shown that people living with dementia tend to use medical services, rather than other community care services [26]. Future research is needed to understand the differences in health service and community social care use between people who are diagnosed with dementia, taking comorbid health conditions, the availability of post-diagnostic services and previous patterns of health service use into consideration. It is important to understand where services are being under or over utilised – and why – to make them more responsive to the needs of people living with dementia.

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Table 1 Characteristics of Included Participants

Demographic Information at Dementia Diagnosis	All participants (N = 15,836)	Early diagnosis (N = 807)	No early diagnosis N= (15,029)	P
Gender (%)				0.99
Male	39.18	39.16	39.18	
Female	60.82	60.82	60.82	
Ethnicity (%)				>0.01*
European (British, Irish, etc)	74.67	79.45	74.41	
Black (Caribbean, African, other)	16.49	14.82	16.58	
Asian (Indian Bangladesh, other Asian)	4.51	2.99	4.59	
Other	4.33	2.74	4.42	
MCI diagnosed before dementia (%)	5.10			
Mean Age (SD)	80.84 (8.64)	80.64 (8.19)	80.85 (8.67)	0.49
Mean MMSE Score (SD)	18.52 (6.30)	21.51 (5.74)	18.36 (6.29)	>0.01*
Mean Index of deprivation (SD)	27.30 (11. 06)	28.60 (10.20)	27.24 (11.11)	>0.01*
Prescribed AChEIs 6 months ± dementia diagnosis (%)	32.49	39.78	32.10	>0.01*
Marital Status (%)				0.66
Current partner	33.68	32.95	33.72	
No current partner	66.32	67.05	66.28	
HoNOS65+ Psychiatric symptoms (%)				0.13
No symptoms	35.06	38.79	34.86	
1 symptom	29.94	29.24	29.98	
2 symptoms	18.46	16.85	18.54	
3+ symptoms	16.54	15.12	16.62	
HONOS65+ Activities of daily living (%)	62.13	55.67	62.47	>0.01*
HoNOS65+ Physical Illness and disability (%)	56.17	55.07	56.23	0.55
Health service use in year before dementia diagnosis				
Attended ED (%)	70.34	73.94	70.15	0.03*
Was hospitalised (%)	54.79	54.40	54.81	0.82

*p<0.05

Table 2. Cox regression models comparing time to first hospitalisation and ED attendance after dementia diagnosis between early diagnosis and no early diagnosis group

Outcome	%	Median time to outcome (year)	Risk of outcome			
			Unadjusted HR (95% CI)	P	Adjusted HR‡ (95% CI)	P
Hospitalisation						
All participants	73.96	0.91 (0.27-2.47)				
Early diagnosis	71.50	0.87 (0.28-2.63)	0.96 (0.88-1.04)	0.35	0.99 (0.91-1.08)	0.76
No early diagnosis	74.09	0.91 (0.27-2.46)	**Ref**		**Ref**	
ED Attendance						
All participants	75.73	0.85 (0.26-2.28)				
Early diagnosis	75.22	0.73 (0.23-2.29)	1.03 (0.95-1.11)	0.53	1.09 (1.00-1.18)	0.04 *
No early diagnosis	75.75	0.85 (0.26-2.28)	**Ref**		**Ref**	

‡ Models Adjusted for: age, gender, ethnicity, marital status, MMSE scores at dementia diagnosis, comorbid physical conditions, prescription of ACHEIs, activities of daily living, psychiatric symptoms and hospitalisation /ED attendance before dementia diagnosis
*p< 0.05

Table 3. Mean number of ED attendances and hospital days per 100 person years and Negative binomial regressions comparing length of stay and number of ED attendances between early diagnosis and no early diagnosis group

Outcome	Mean number per 100 person years (95% CIs)	IRR (95% CI)			
		Unadjusted	P	Adjusted‡	P
Hospital days					
All participants	10.26 (10.24 – 10.29)				
Early diagnosis	10.08 (9.95 – 10.21)*	0.89 (0.76-1.01)	0.08	0.97 (0.85-1.12)	0.70
No early diagnosis	10.27 (10.24 – 10.31)	**Ref**		**Ref**	
ED Attendances					
All participants	1.22 (1.21-1.23)				
Early diagnosis	1.26 (1.20 – 1.31)	1.02 (0.93-1.11)	0.68	1.04 (0.95-1.13)	0.38
No early diagnosis	1.22 (1.21 – 1.23)	**Ref**		**Ref**	

*p<0.05

‡Models Adjusted for: age, gender, ethnicity, marital status, MMSE scores at dementia diagnosis, comorbid physical conditions, prescription of ACHEIs, activities of daily living and psychiatric symptoms and follow-up time

Chapter 5: Exploring the perceived benefits of early diagnosis and early intervention in dementia: a qualitative study

This chapter presents the findings of the qualitative phase of analysis which aimed to understand the benefits of an early diagnosis from the perspective of people living with dementia and their caregivers. Semi-structured interviews were conducted with 12 caregivers and two people living with dementia and analysed using thematic analysis. This chapter introduces the aims of this study, followed by a summary of the methods. Finally, this chapter presents the results of the analysis, and discusses the implications of the findings.

5.1 Introduction

The early, or timely, diagnosis of dementia is a key feature of dementia specific policies both in the UK and globally (Brooker, Fontaine, Evans, Bray, & Saad, 2014; Europe, 2012; Prince, Bryce, & Ferri, 2011). A diagnosis is typically given in response to symptoms (Livingston et al., 2017). However, it is possible to diagnose dementia earlier. This can be done using biomarkers to detect the onset of the underlying neuropathology, which is typically asymptomatic (Prince et al., 2011). It is also possible to detect those who are at greater risk of developing dementia. Mild Cognitive Impairment (MCI) is a condition associated with mild levels of cognitive decline and is often considered prodromal to dementia (Mariani, Monastero, & Mecocci, 2007). A diagnosis of MCI presents an additional opportunity for diagnosing dementia early. On the other hand, a timely diagnosis can be described as a diagnosis that is given “at the right time for the individual with consideration of their preferences and unique circumstances” (Watson, Bryant, Sanson-Fisher, Mansfield, & Evans, 2018). This means that a timely diagnosis can be an early or late diagnosis, depending on the preference of the individual. It is important to better understand the benefits of an early diagnosis to help people living with dementia decide when is the best time to seek a diagnosis.

Dementia specific policy in the UK is calling for diagnosing dementia early, stating early diagnosis can lead to living well with dementia for longer and preventing admission into care homes or hospital (Health, 2009). However, there is very little empirical evidence supporting these proposed benefits of an early diagnosis (Prince et al., 2011). While an early diagnosis can facilitate access to early treatment and decision making which might keep people with dementia living well for longer, there are some potential harms. For example, available treatments for dementia are limited in their effectiveness and come with a risk of side effects. Moreover, the focus on early support risks diverting resources from the later stages of the disease (Le Couteur, Doust, Creasey, & Brayne, 2013).

Qualitative research presents the opportunity to understand the perspectives and experiences of people living with dementia at the different stages of the disease (Aminzadeh, Byszewski, Molnar, & Eisner, 2007). Previous qualitative research has reported a wide variety of responses to receiving a diagnosis of dementia some people report negative reactions including fear, anger, anxiety, depression and a threat to personhood (Aminzadeh et al., 2007; Mitchell, McCollum, & Monaghan, 2013). However, a diagnosis of dementia can also confirm suspicions held before the diagnosis, provide a sense of relief and give people living with dementia and their families time to plan for the future and develop positive coping strategies (Cahill, Gibb, Bruce, Headon, & Drury, 2008). A survey of people diagnosed with early dementia or mild cognitive impairment found participants did not experience psychological distress following their diagnosis, in fact they reported less anxiety (Carpenter et al., 2008). However, it is not clear whether these experiences differ depending on the stage of the disease the diagnosis was made.

Previous research has explored the potential benefits of an early or timely diagnosis from the perspective of health care professionals (Dhedhi, Swinglehurst, & Russell, 2014; Iliffe, Manthorpe, & Eden, 2003), caregivers (Boise, Morgan, Kaye, & Camicioli, 1999; de Vugt & Verhey, 2013), general members of the public (Watson et al., 2018) and using economic models (Barnett, Lewis, Blackwell, & Taylor, 2014; Budd, Burns, Guo, L'Italien, & Lapuerta,

2011; Getsios, Blume, Ishak, Maclaine, & Hernández, 2012). However, the perceived benefits of an early diagnosis have not been explored from the perspective of people living with dementia. People living with dementia have advocated for the right to an early diagnosis. In 2019, the Dementia Action Alliance revised the Dementia Statements, which are developed by people living with dementia to reflect their rights on: independence, community/isolation, carers, care and research. These rights are enshrined in the Equality Act, Mental Capacity legislation, Health and care legislation and International Human Rights law. They assert “We have the right to an early and accurate diagnosis, and to receive evidence based, appropriate, compassionate and properly funded care and treatment, from trained people who understand us and how dementia affects us.” (Dementia Action Alliance, 2019)

This study aimed to provide much needed insight on the perceived value of an early diagnosis from the perspective of caregivers and people living with dementia. The objectives of this study were to:

5. Explore the perceived long-term and short-term benefits of a dementia diagnosis
6. Explore how the diagnosis of dementia is given and received
7. Understand access to interventions and support following a diagnosis of dementia, and their perceived advantages and disadvantages
8. Understand in which circumstances an early diagnosis is perceived to be beneficial

This evidence can be used to help develop more responsive and supportive post-diagnostic services, and to help people living with dementia decide when might be the best time to seek a potential diagnosis.

5.2 Methods

This section provides an overview of the methods used in this study. The methods are presented in full in chapter 2.

5.2.1 Design

This study used semi-structured interviews to investigate the participants' experience of a diagnosis of dementia or mild cognitive impairment and what benefits they perceive to be associated with an early diagnosis. Ethical approval was granted by the Wales Research Ethics Committee 5 (Ref: 19/WA/0210).

5.2.2 Sample and recruitment

5.2.2.1 Eligibility Criteria

Participants were included if they have a diagnosis of dementia or MCI, or if they were a current or former carer for a person living with dementia or MCI. A carer was defined as someone providing informal care to the person living with dementia, this could be a family member, friend or neighbour. Paid carers were not included in this study.

It was important to include people living with dementia as participants in this study, as the Dementia Statements posits people with dementia "have the right to know about and decide if [they] want to be involved in research that looks at cause, cure and care for dementia and be supported to take part." (Dementia Action Alliance, 2019). I wrote to the GPs of participants living with dementia, to confirm their diagnosis.

5.2.2.2 Sampling technique and sample size

I used purposive sampling on the basis of time since diagnosis/disease stage, gender and amount of social support to explore a diversity of perspectives. I aimed to recruit between 12-20 participants with dementia and MCI and 12-20 of their carers. I continued recruitment until thematic saturation was reached, where no new information emerged from the data and new data were easily accommodated in the existing framework (Braun & Clarke, 2021; Saunders et al., 2018).

5.2.2.3 Sample identification

Participants were identified through two recruitment channels, Join Dementia Research and local support groups. JDR is an online self-registration service that enables volunteers with

memory problems or dementia, carers of those with memory problems or dementia, and healthy volunteers, to register their interest in taking part in research. The purpose of JDR is to allow such volunteers to be identified by researchers as potentially eligible for their studies. Researchers can then contact volunteers, in line with the volunteers' preferred method of contact, to further discuss potential inclusion.

I also contacted the following local support groups for older adults: The Lambeth Healthy Living Club @ Stockwell, Lewisham MindCare Dementia Support, and the Southwark Pensioners Centre. Staff at these groups made the initial contact with the participant, to determine if they were interested in taking part in this study. When the participant expressed an interest, their contact details were passed on to me.

5.2.3 Procedures

All participants gave their informed consent before participating in the interviews. The COVID-19 pandemic affected the data collection procedures for this study. Before the pandemic, participants had the option of a face to face interview either in their own home or at King's College London. During the pandemic, all interviews were conducted virtually using Microsoft Teams or the phone, depending on the preference of the participant. The interviews were recorded using a password protected and encrypted smart phone.

The interviews were conducted following a topic guide, with one guide for caregivers and another for participants living with dementia. The length of the interviews ranged between 25 minutes and an hour and a half, with an average length of 45 minutes. The interviews followed a topic guide (see appendix A) and started with questions about how and when they started to notice the memory problems. I then moved on to asking questions about their experiences of receiving post-diagnostic support, drug and non-drug treatments, interacting with secondary care services, and their plans for their future. I also included more direct questions about the value of an early diagnosis. The topic guide was initially developed in consultation with the SLaM MALADY PPI group, and was revised iteratively to follow to concerns of the participants. The interviews were conducted between 10th January and 10th December 2020.

5.3 Analysis

The audio recordings of the interviews were transcribed verbatim and uploaded to NVivo 2020 for analysis. I transcribed 5 interviews and 9 interviews were transcribed by a professional service. The interviews were analysed following Braun and Clarke's six steps for thematic analysis: familiarisation with the data, generating initial codes, searching for themes, reviewing themes, naming and defining themes and producing the report. (Braun & Clarke, 2006). Data collection and analysis were done in parallel, this allowed me to familiarise myself with the interviews that I did not transcribe. I listened to the audio-recordings of the interviews while reading the transcripts. I then read the transcripts again and made notes on my initial impression of the interviews. Next, I coded the interviews line-by-line (Gibbs, 2007). This helped me to ensure that all parts of the data were given equal consideration. Some of the codes were deductive, based on the topic guide and aims of the research, whereas other codes were inductive and drawn from the data. This helped me keep the analysis focused on the aims of the study, whilst also capturing the experiences and voices of the participants.

I also used a process of iterative categorisation to move from codes to themes. First, I systematically described the data contained in the codes. Next, I grouped the descriptions into detailed categories, which could incorporate a number of codes, before grouping them again into broader, more abstract themes. Finally, I checked the themes against the raw data to ensure validity, before naming them and giving them a description (Neale, 2016).

5.4 Rigour

I used multiple strategies to minimise the influence of my personal beliefs on my analysis and interpretation of the data. I had regular supervision with my supervisors, where I presented the frameworks I had developed during each phase of the analysis (coding, categorisation, and thematic frameworks). This had two purposes, it allowed my supervisor to audit the analytic decisions I had made, increasing the dependability of my findings (Lincoln & Guba, 1985). It also gave me space to discuss ideas I had during my analysis, to test whether these ideas were well supported by the interview data and explore my position within the analysis

(Lincoln & Guba, 1985). I also used a form of member checking (Angen, 2000), where at the end of the interviews I summarised my findings so far, to test the degree to which my participants recognised themselves in my findings and thus increase the credibility of the analysis. When producing themes, contradictory data is equally important as confirmatory data (Patton, 1999). During the analysis, I was careful to look for examples that did not agree with my themes and explore why this might be the case. Contradictory examples are presented in the findings section. Finally, to aid reflexivity, and ensure the findings of this analysis were shaped by the participants rather than myself, I kept an analytical diary (M. Birks, Chapman, & Francis, 2008; Koch & Harrington, 1998).

5.5 Results

5.5.1 Participants

Interviews were conducted with 12 caregivers and 2 people living with dementia. Table 5.1 presents the characteristics of the included participants. Most caregivers (83%) in this study were still actively caring for the person living with dementia or mild cognitive impairment, two of the participants were former caregivers. All participants living with dementia and all but three caregivers were women. The mean age of participants living with dementia was 79 (SD = 1.4). Caregivers were younger with an average age of 61 (SD = 12.5). The average time since dementia diagnosis was roughly the same for both groups (4.2 years for caregivers and 4 years for people living with dementia).

Table 5.1 Characteristics of included participants

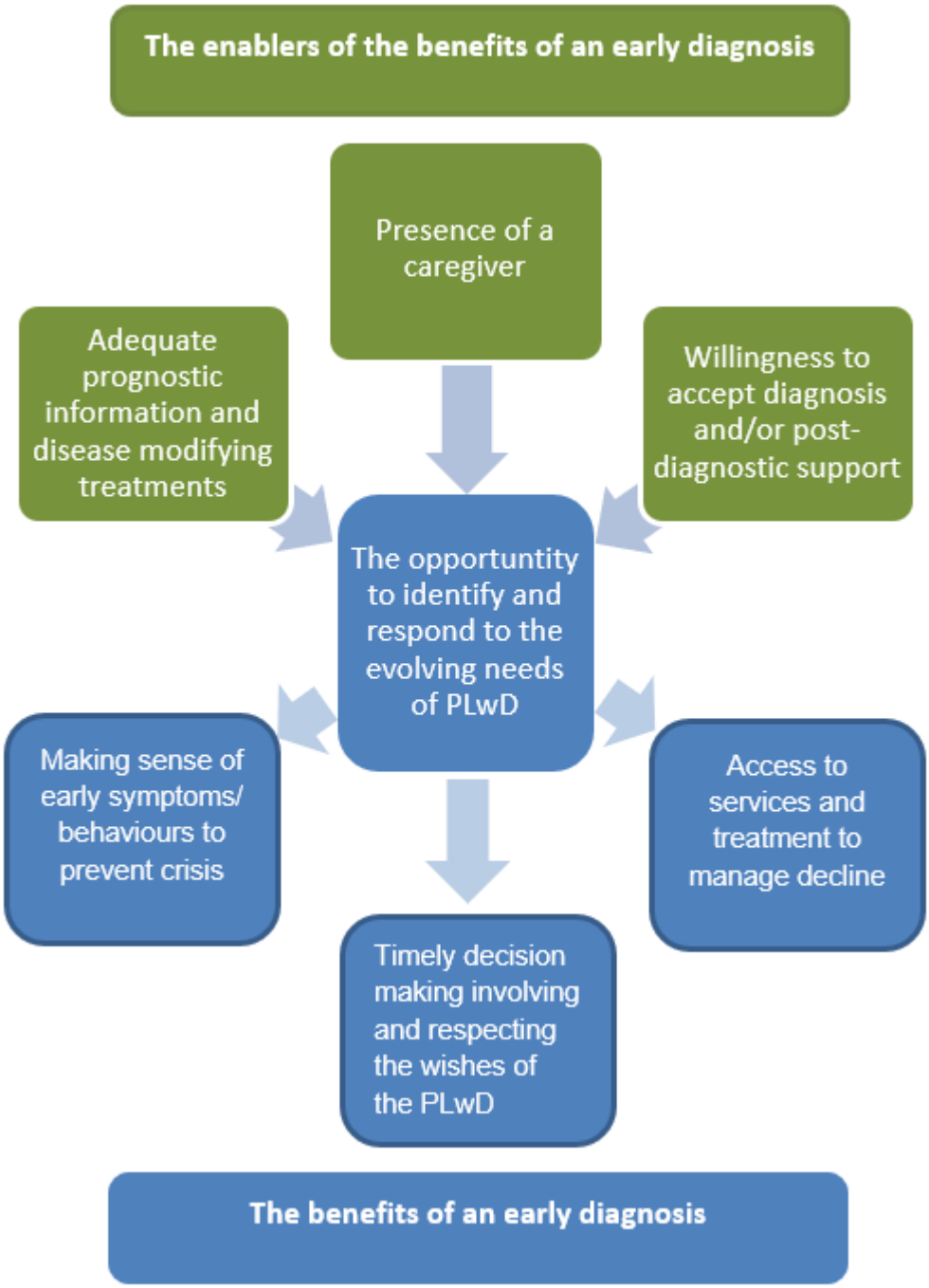
Characteristic	**Caregivers (N = 12)**	**People living with dementia (N = 2)**
Gender (%)		
Female	9 (75)	2 (100)
Male	3 (25)	0 (0)
Mean Age (SD)	61 (12.5)	79 (1.4)
Mean time since diagnosis (SD)	4.2 (2.6)	4 (1.4)
Marital Status (%)		
Married or Co-habitating	9 (75)	1 (50)
Divorced, Widowed or Currently Single	3 (25)	1 (50)
Current caregiver (%)		N/A
Yes	10 (83)	
No	2 (17)	
Relationship to person living with dementia (%)		N/A
Spouse	4 (33)	
Child of one parent with dementia	4 (33)	
Child of both parents with dementia	3 (25)	
Caregiver to multiple people with dementia	1 (8)	
Type of diagnosis		
Mild cognitive impairment	2 (17)	0 (0)
Dementia	10 (83)	2 (100)

5.5.2 An early diagnosis provides the opportunity to identify and respond to the evolving needs of people living with dementia

The key, overarching benefits of an early diagnosis identified in the data were the opportunity to identify and respond to the evolving needs of the person living with dementia. More specifically, an early diagnosis allows people living with dementia and their families the opportunity to make sense of early symptoms or behaviours to prevent crisis, to engage in timely decision making involving the person living with dementia and to access services or treatments to manage the rate or impact of decline.

However, the data indicated that these benefits are only possible under certain circumstances, referred to as enablers of the benefits. Enablers of the benefits of early diagnosis were found to include adequate prognostic information; adequate disease modifying treatments; support from caregiver; and a willingness to accept the diagnosis of dementia and post-diagnostic support. Figure 1 presents a diagram of the themes discussed in this chapter and how they relate to each other. The following sections describe each of these themes and sub-themes in greater detail.

Figure 5.1 The benefits of an early diagnosis and its enablers



Participants described how the needs of the person living with dementia changed over the course of the disease. At first the symptoms associated with dementia were very mild and it was sometimes difficult for participants to detect a change.

However, as time went on, the person living with dementia's symptoms progressed. Participants characterised the decline experienced by the person living with dementia in different ways. For some, the decline was slow and gradual:

"And so, she, so she started losing physical ability gradually. And also gradually her speech got worse." (Carol, caregiver to both parents with dementia)

Whereas for others, the decline was far more accelerated or erratic:

"And it has been a rollercoaster. You know. It's got bad. Then it seems to plateau. Then it's got bad again. And you never know when the next dip is going to happen." (Joanne, caregiver to father with dementia)

Participants struggled with not knowing what was going to happen next. A common misconception amongst participants was that the person living with dementia would not live long after the diagnosis. They found that they were having to manage the emotional and practical pressures of living with dementia for longer than expected.

"But just the, the, I guess, the sort of anguish of the long goodbye. I think maybe an earlier diagnosis would certainly help you prepare, prepare more, I think. Although it doesn't take the pain away from the, the length of time. You know. That is something you just have to... You have to bear with.." (Rebecca, caregiver to mother with dementia)

Participants felt that the value of an early diagnosis lay in access to prognostic information alongside practical advice that would better prepare them to meet the needs of the person living with dementia during all stages of the disease. Participants expressed the view that in the early stages, an early diagnosis can help people living with dementia and their caregivers to better understand the symptoms of dementia and take proactive steps to prevent a crisis.

An earlier diagnosis can facilitate timely, and person-centred decision making. And finally, an early diagnosis can act as a gateway to services and treatment to help manage the symptoms and impact of dementia at all stages of the disease. Table 5.2 presents the themes and sub-themes that are discussed in the following sections.

Table 5.2 The benefits of an early diagnosis

The benefits of an early diagnosis		
Theme	**Sub-themes**	**Examples**
Identifying and responding to the evolving needs of people living with dementia	Making sense of early symptoms/behaviours to prevent crisis	Protecting relationships between family members
		Financial protections for PLwD and other family members
		Personal safety of PLwD
	Timely decision making which involves or respects the wishes of PLwD	Personal Care
		End of life decisions
		Power of attorney
		Priorities for co-morbid physical healthcare
	Access to services or treatment to manage the rate or impact of decline	NHS Treatments
		Preserving identity
		Finding what works at the right time

5.5.3 Making sense of early symptoms/behaviours to prevent crisis

Participant's felt that the value of an early diagnosis lay in helping them to understand the symptoms and behaviours associated with dementia to prevent a crisis. During the early

stages of dementia, participants reported noticing unusual behaviour / changes in the person living with dementia that suggested something was wrong, but were not attributed to possible dementia:

“Um, my mum was getting very aware of the fact that he, um, didn't seem to be able to put identity to names. So, she would mention family members and say, you know, it's [name of relative’s] birthday, or so and so is getting married. And he would just look at her blankly. I put it down to the fact that we have many relatives, and that my mum is very family-orientated, and my dad is less interested in things like birthday cards. So, I put it down to that.” (Joanne, Caregiver)

Similarly, participants living with dementia were less able to remember the specific symptoms that concerned them and prompted them to seek a diagnosis, but still recalled the vague sense that something wasn’t quite right.

Well, it’s simply that I had to think twice. I’d thought I had remembered something, I’d done, and, in fact, I hadn't. I’d, sort of, half done it or, um... I just, kind of, sort of, completed whatever it was I meant to do. Half the time, I used to think it was because one of the dogs had done something or somebody telephoned. But in retrospect, I’d rather... In fact, I probably forgot. (Ann, person living with dementia)

The initial problems associated with memory loss started small and grew larger as time went on. By the time the person living with dementia received a diagnosis, participants had experienced several crises, including a breakdown of relationships between family members and incidents putting the person living with dementia at personal and financial risk. However, one participant acknowledged that it took a crisis for the person she cared for to receive a diagnosis. The impact of the person living with dementia’s willingness to accept a diagnosis on the benefits of an early diagnosis are discussed further in Section 5.5.8.

“So it was really…we could have done with more support earlier, but given his personality I can't honestly see there's a lot else could have been done really until the crisis occurred.” (Catherine, caregiver to multiple people with dementia)

The following sections provide more detail on how an early diagnosis of dementia can protect relationships between family members, the financial interests and personal safety of people living with dementia.

5.5.3.1 Protecting relationships between family members

Participants reported that positive relationships between family members, not just the person living with dementia and their caregiver, were essential for managing the care of the person living with dementia. Caregivers relied on other family members for emotional and practical support.

“I guess we support each other, me and my siblings, we all… but if you were just one person and you were just a single child that wasn’t married and you were dealing with this for one or two parents it would be quite tough. I don’t know who you turn to.” (Fiona, Caregiver to mother with dementia)

Where relationships had been fractured between family members, caregivers felt this had an impact on the care their loved one’s received. One caregiver reflected that if she had been aware that dementia was the cause of her mother’s unusual behaviour, she and her siblings could have worked together to prevent a crisis.

“We weren’t a team. And I think that has had an impact. I think if we’d worked as a team... It’s really embarrassing, but if we’d worked as a team, things might have been different.” (Rebecca, Caregiver)

Two caregivers had a difficult relationship with the person they were caring for. In both cases, the breakdown in these relationships started long before the person living with dementia received a diagnosis. On reflection, one caregiver felt that knowing her husband’s difficult

behaviour was due to dementia, rather than him being “awkward” would have been helpful. By the time her husband’s dementia was diagnosed their relationship had become difficult, leaving her feeling trapped in her new role as a caregiver as her husband’s diagnosis made it clear to her that a divorce was no longer possible. She described how knowing this sooner might have made a difference to their relationship:

“Interviewer: What I'm hearing is it doesn't make much difference whether you're diagnosed early or late. There's… not much for you.

Participant: I think that's, I would say that's correct, yes, but it might make a difference to how you get on with the person, actually…It is an important consideration, because very often it's going to be the partner or the whoever, or a close family member who's going to be the prime carer. Since there is so little support. So, if they know sooner rather than later that this is a disease and not their loved one being a bugger. Then it’s going to be a bit helpful… won't necessarily be easier…” (Sarah, Caregiver to spouse with dementia)

5.5.3.2 Installing financial protections for the person living with dementia and other family members

Making financial plans was a priority after the diagnosis of dementia. Caregivers are not able to intervene in the person living with dementia’s financial affairs without power of attorney, however power of attorney can only be used after a diagnosis of dementia has been given, (the assignment of power of attorney is further discussed in section 5.5.4.1). People who had been living with undiagnosed dementia for a long time were vulnerable to scams and financial abuse. One caregiver discovered after her mother’s diagnosis that she had been a victim of numerous scams:

“When I first started investigating properly her bank account, looking at it, which is, I think, when I retired, she was spending £2000 a year on various home insurances, nuisance call stopping services. It was just... It was heart breaking when I realised.” (Elizabeth, caregiver to mother with MCI)

Similarly, another caregiver described how her mother's undiagnosed dementia put her at risk of financial exploitation: *"Mum literally transferred hundreds of thousands over to [them]." (Rebecca, caregiver).*

One of the potential benefits of an early diagnosis is that it allows people living with dementia and their caregivers to initiate plans and legal processes to protect them from scams and financial exploitation.

Participants reported a need to protect any assets belonging to the person living with dementia, the most important being housing. In general, participants wanted to stay in their homes for as long as possible, however participants were worried that they would need to sell the person living with dementia's home to pay for their care. This was especially a concern where the person living with dementia was living in the same house as their spouse/ caregiver, or where other family members had a financial interest in the house. For example, one participant reported her Dad's diagnosis of dementia prompted her to *"look at what point your home gets taken away from you if you go into care" (Joanne, caregiver)*. Similarly, another participant highlighted the importance of making early financial plans to protect the interests of other family members:

"Because my son helped us to buy this house, he gave a third of the deposit down, he did pay the deposit. So, I wanted to make sure that he wasn't going to lose out of the money that he's put down on the house." (Sheila, caregiver to spouse with dementia)

5.5.3.3 Protecting the personal safety of the personal living with dementia

One of the key ways in which an early diagnosis was considered to protect the personal safety of people living with dementia is in regards to driving. Upon diagnosis, participants with dementia who were still driving were told to inform the DVLA of their diagnosis and have a test to confirm their ability to drive. For both caregivers and people living with dementia, making the decision to stop driving was a significant event. Where the person living with dementia had

to give up driving immediately on diagnosis, participants reported sympathy for this loss of independence but felt concerns around safety were more important:

“And one of the first things he had to do was to give up his car. He wasn’t very happy about that, but that was for safety reasons. We did actually get a test done properly, and his reaction was too slow, so it was just as well.” (Sheila, caregiver)

“I've been there watched an elderly person have a diagnosis test and the person be told ‘well I'm sorry but you really can't have your driving license renewed,’ and behind them there’s been the family going ‘yes!’ Because finally they've got the driving license off Dad [Laughs] rather before he kills someone.” (Catherine, caregiver)

There were two examples where the person living with dementia was still driving. One older person described how her diagnosis made her more aware of her need to be cautious on the road: *“I mean, obviously, now one is more careful, but, I mean, I do drive up to London.” (Ann, person living with dementia).* However, she also reported that health services were able to assess her ability to drive but didn’t want to sign the paperwork needed to allow her to keep her license. She found this lack of support from memory services upsetting.

“Yes, I was very upset about that because I’d done all my... And everybody said that was fine. But when they asked us, you know, sign on the dotted line, and say yes they knew that I came and that I could do all these things, they said oh, well, no, we don’t... We can't do something like that for you. Um, and that's a very pertinent point, you know.” (Ann, person living with dementia)

Participants also reported incidents where the person living with dementia went missing before they were diagnosed with dementia. This could lead to serious consequences for the person living with dementia, as described by one participant:

"Once mum broke out. So, she must have been in a panic. Broke out and went missing in [name of city] for seven hours and..Then badly injured herself on her foot. Someone found her very confused and bleeding, um, because she'd fallen." (Rebecca, caregiver)

By understanding the symptoms and associated risks of dementia earlier in the disease, people living with dementia and their caregivers felt structures could be put in place to ensure the personal safety of the person living with dementia. However, in order for these particular benefits to be felt, people living with dementia need the opportunity to engage in timely decision making.

5.5.4 Timely decision making which involves and respects the wishes of people living with dementia

Participants highlighted several ways in which an early diagnosis of dementia would have allowed them to make practical decisions in a timely manner. During the earlier stages of the disease people living with dementia have a greater ability to be involved in making these decisions, however where this is no longer possible, caregivers tried to respect the wishes of the person living with dementia. Caregivers did sometimes report a conflict between making decisions that respected the person living with dementia's wishes and what is practical. The following section outlines the benefits of timely decision making regarding assigning power of attorney, personal care, end of life decisions and living arrangements.

5.5.4.1 Power of attorney

Most participants went through the legal process of assigning power of attorney as soon as dementia was diagnosed.

"No, we never did. But as soon as we found out he'd got dementia, we started thinking in terms of, um, solicitors. We've done a power of attorney. We've done the will." (Sheila, caregiver)

"Um, and, um, I mean, we did call relatively early on, um, to get some advice. And one of the things we've done is to have Powers of Attorney set up. So, again, that, um, that should mean

that whatever happens, there is somebody responsible who can take any action that's necessary." (Mark, caregiver to spouse living with dementia)

Caregivers also reported health and social care services refused to cooperate with them without power of attorney. One participant described how the person living with dementia's GP would not communicate with her, without proof of power of attorney:

"but he just kept saying I can't talk to you about that and it wasn't till we, we had to send him the power of attorney and persuade him to start talking to us" (Catherine, caregiver)

As discussed in the previous section, power of attorney was essential for enabling caregivers to keep the people living with dementia protected from financial abuse. An early diagnosis can give the person living with dementia the opportunity to assign power of attorney to someone who will make decisions with their best interest at heart. This is important as once power of attorney has been assigned, it cannot be changed. One participant described how easy it might be for someone with power of attorney to take advantage of the person living with dementia.

"I could easily persuade my Aunt in Hackney to do this, but I feel I did take some advice from from the organization you register power of attorney with and they said no way, no, you can't do that." (Catherine, caregiver)

While an early diagnosis does give people living with dementia the opportunity to assign power of attorney to someone who they feel will represent their best interest, things can still go wrong. One participant described how his parents had made plans for assigning power of attorney long before they were diagnosed. Each of his parents had assigned power of attorney to the other, but both developed and were diagnosed with dementia around the same time. This made it incredibly difficult for the participant to intervene and make decisions on his parents' behalf.

"My parents got power of attorney… but gave it to each other. And they both simultaneously lost capacity. And that was that, uh, so we were left without anything, which is why I'm a deputy now. Which is why of course I would say to anybody to avoid ever getting into this situation because we have to go to the court of protection and it's a nightmare. It's extremely slow, it's extremely expensive and troublesome." (James, caregiver to both parents living with dementia)

Despite limitations in the legal processes, caregivers found assigning power of attorney to be so important, that many of them had arranged for their own power of attorney.

"it was about that time that we thought we should take out with my brother as well, um, the possibility of power of attorney for each other. So, we got that started, that process, so that we each 'cause 'cause I said to them and my brother will or any of us could just be in a car crash or something. So isn't it a good idea to get the paperwork in place. I know the system has changed a bit since then, but anyway we did get that set up." (Carol, caregiver)

5.5.4.2 Personal Care

When making decisions about the future care of the person living with dementia, participants wanted to manage the transition into care, whether it be receiving care at home or moving to a residential care home, in a way that would not have a negative impact on the person living with dementia. For all participants, the decision to transition into full time care was an extremely emotional and delicate one, and they worried about getting it right.

"It's just a question of how we transition, at what time. And, and, and getting it right, that I don't make any mistakes which endanger her. That's… Really my worry." (Mark, caregiver)

Similarly, moving home care could provide caregivers with a peace of mind that their loved one was being looked after and kept safe.

"If she lived on her own I would be totally worried about her all the time, not only that she'd fall, but would she leave the gas on, you know, would she leave the doors open or anything…

but since she's in a care home, she's looked after, she's feed so me an my siblings are much, much happier." (Fiona, caregiver)

An early diagnosis gives people the opportunity to be involved in decisions about future care. Participants found it helpful to know the person living with dementia's preference for future care, but highlighted how the rapidly changing social care sector made it difficult to make concrete plans, such as which specific care home the person living with dementia would like to move to. This is summarised by a participant living with dementia:

"I've got, so I've got a list of care homes I know, and I know it's in London, and some that are good. But it's gonna depend so much on whoever's in charge of that care home at that particular point in time, I think." (Helen, person living with dementia)

However, Helen (who is not supported by a caregiver) also discussed the difficulty of making decisions about future care. She felt that this was something health services could support people living with dementia with.

"But I don't know whether I want to be in a care home, or that I want to be in my own home with a carer. And I, I, you know, I think at some point, that would be a useful thing for a psychologist to discuss with people." (Helen, person living with dementia)

When making decisions about care, participants had to balance the preferences of the person living with dementia against their financial resources. Participants who were self-funding had a greater control over deciding what care to introduce and when, whereas participants who were not able to fund their own care were frustrated by a lack of flexibility and reliability from government funded services.

"I thought… I'm lucky, but that's what everybody should be getting. They should be getting that level of support. 'cause everybody else is kind of struggling because they can't afford to pay for all this stuff or not pay so early on." (Sarah, caregiver)

5.5.4.3 End of Life Decisions

Receiving a diagnosis of dementia prompted participants to think about and prepare for death. An early diagnosis can give people the time to decide on their wishes for end of life, caregivers reported making funeral arrangements, palliative care arrangements and discussing do not resuscitate orders (DNRs) with the person they care for:

"we did have a bit of a DNR discussion so that was useful anyway. We've got that." (Sarah, caregiver)

However, confronting their own death can be an incredibly distressing time for participants. One participant who was diagnosed 5 years ago, expected that she would not live for long following her diagnosis, described her "catastrophic" response:

"And I responded with a panic reaction, really. I got rid of all my books and prepared for death, really. I'm not… I mean, not… I wasn't suicidal, but I, you know, I cleared out… My, my house was full of art books and books, and I cleared them all and took them all to the library, so that my stepdaughter, who was my… Um, wouldn't have to deal with them.

And, um, nobody gave me any real support about that or about, you know… I was really left in, in, in limbo. And I think I had a, you know, I had a really catastrophic response, because I was just dismantling the books in my house." (Helen, person living with dementia)

She attributed this response to how the diagnosis was delivered:

"[The Doctor] sort of gave me a whole pile of books, which, really, was totally inappropriate. And that was, I was left with that, and, and, and the confirmation of the diagnosis. But I wasn't given any support about how to deal with it." (Helen, person living with dementia)

Many participants felt that dementia was not worth living with. This was particularly true for female participants who were unmarried and/or did not have children. They described there being a point at which they would not want to live with dementia and would like an option for

euthanasia to be open to them. For the participant above, it would be being unable to recognise loved ones or becoming bed ridden.

"Participant: But I'm, you know, I'm not… I mean, I haven't had any catastrophes at all, but I think, um, I still feel that if I wasn't, if I couldn't recognise people, I certainly don't think I'd want to live. And I don't think if I was bedridden, I'd want to live either. But I suspect that will change as I get nearer to it, frankly.

Interviewer: Yeah. So, not being able to recognise the people that you love, really is something that you couldn't live with.

Participant: Well, I just think it's a waste of time, isn't it?" (Helen, person living with dementia)

This participant felt the later stages of dementia are not worth living with but expressed doubt that she would make the steps to arrange euthanasia. This sentiment was similarly expressed by a caregiver reflecting on what she would do if she suspected she had dementia.

"I do have thoughts. Like I don't think I would do a Still Alice type thing. I would... That I would go off. That I would go off to Switzerland, and you know, and want to... I, I, I don't think I'd want to go through that. But, I don't think... I honestly don't know whether I could do that. But I do not want to have this alone. This long lingering decline." (Rebecca, caregiver)

However, having this as a potential future option brought some feelings of control and relief.

"Participant: Hmm. I think you probably could live with it longer than... You know. If, if you had that option to be... To have your life ended, once you get to a certain stage, then you would... It would be worth living to that stage…

Interviewer: Having that option set up. It sounds like it... What you're describing is a sort of freedom, I guess, or relief.

Participant: Yes. Yes it is. Yes. Yes, it would be very much that… It would be a terrific relief to have that there as an option in the future." (Elizabeth, caregiver)

5.5.5 Access to Services and Treatment to Manage the rate or impact of decline

5.5.5.1 Pharmacological and non-pharmacological treatments for dementia

An early diagnosis provides people living with dementia access to specialist treatment and support. Most participants reported that they or the person they were caring for were offered pharmacological or non-pharmacological treatment from NHS services.

"[she] made the best of all the help on offer um including medication" (Catherine, caregiver)

Participants were prescribed medication: AChEIs and memantine. They were aware that receiving mediation during the early stages of the disease may confer greater benefits, as highlighted by one carer:

"Yeah, I think from my standpoint, um, obviously, as I understand it, the earlier that one is diagnosed, the better chance that some of the drugs will have some effect. But, again, as I understand it, there is nothing, really, at the moment, that makes a big difference. Something like Donepezil can simply slow things down, but, um, but that's about it." (Mark, cargiver)

Many participants also attended memory groups run by NHS memory clinics. One participant living with dementia, found these groups reassuring and had "been to as many as there were." She valued the peer support she received from attending the memory group but highlighted some gender differences in the behaviour of group members. This is discussed future in 5.5.6.2.

"Participant: Yes, I think we've, on the whole, also, we were able to chat amongst ourselves. The men were more withdrawn unless they were... Had completely gone into dementia. And we, I wouldn't say, relaxed, but we were more interested in finding out how others are managed.

Interviewer: That's really interesting. Did you... Did you learn anything from going to these groups?

Participant: Well, I suppose, in a way, a sort of reassurance, I've always thought, well, I must be completely stupid." (Ann, person living with dementia)

Similarly, the other participant with dementia described a positive experience of having supportive psychotherapy following her diagnosis:

"I felt he knew me well, and had sort of allowed me to be the person I was, if you see what I mean." (Helen, person living with dementia)

5.5.5.2 Priorities for co-morbid health care

Participants expressed that people living with dementia had specific needs and priorities when using health services. Being aware of the diagnosis enabled caregivers and health care professionals to make adjustments to better support the person living with dementia. For example, one caregiver whose mother with dementia needed some teeth removed under general anaesthetic in the hospital, explained how understanding her mother's diagnosis enabled her to get more supportive care from hospital services. After explaining her mother's diagnosis, hospital staff allowed her to sit with her mother in the recovery room after the surgery.

"And, the doctor was a bit prickly at first, but... I can't remember exactly what she said. But I just remember thinking, oh gosh, that's not very understanding. But then she came back a few minutes later and said you can actually come right in and hold your mum's hand until she's under the anaesthetic, which I thought was lovely. So that's what I did. And then they allowed me into the recovery room, which again they don't normally do. But they allowed me to just sit quietly while she came around." (Rebecca, caregiver)

Despite the potential to make adjustments for dementia, not all participants' interactions with health services were positive. One caregiver, of both parents living with dementia, felt that each time her parents were discharged from hospital they *"got much, much worse as a result of being in hospital." (Carol, caregiver)*. She felt that if adjustments couldn't be made for her parents living with dementia, then it was better to arrange other types of care rather than

seeking life extending treatments from the hospital. When her mother was diagnosed with a chest infection, she arranged for palliative care, rather than taking her to hospital (It is important to note, her mother had stated her preferences for end of life care following the diagnosis of dementia). She summarised the differences in people with dementia's health care needs following a diagnosis by saying:

"People with dementia should not be kept in hospital. And that, you know, they shouldn't have to fight to come out." (Carol, caregiver)

5.5.5.3 Finding what works at the right time

Participants described many changes in the person living with dementia as the disease progressed including changes in personality and temperament, losing the ability to communicate, perform activities of daily living and the loss of functional abilities.

When faced with new challenges participants were willing to try any new solution that would help the person living with dementia.

"Well, anything that I… If I can, you know, make life easy for him, I do. I'm always prepared to try something else." (Sheila, caregiver)

Caregivers would have to try many products before they found one that worked. Sometimes they would not find a solution to their problem.

"Because otherwise, you know, I've got an iPhone, and an iPhone could be a tremendous… Asset. There's everything in there, you know? But she couldn't use it. She really couldn't use it. I've… So I've got her a very… The most sort of basic, old-fashioned type snap-open phone. And she will occasionally use it. I, I, I… But I bet we've had it about 15 months now and I suspect she's made a dozen phone calls. I don't know." (Mark, caregiver)

One participant, who went through a continual process of "trial and error" to find equipment and products that helped her dad living with dementia to eat, felt that the value of an early diagnosis lay in having information on what symptoms were likely in the future stages of the

disease and time to experiment to find what worked.

"Um, so yeah, so lots of the physical things, we could have done with a lot more guidance about, and advice on equipment earlier on, rather than having to, having to see my dad just starve, because he couldn't eat anything, um, until we worked out the best way of preparing his food." (Joanne, caregiver)

She highlighted that this was a cyclical, ongoing process as *"what worked two years ago doesn't work now."* She also acknowledged that a solution for one person living with dementia, would not work for them all, increasing the difficulty of finding solutions that worked for her Dad.

5.5.5.4 Preserving the identity of the person living with dementia

An early diagnosis enables people living with dementia support so that they can continue their hobbies, preserving their sense of identity. Participants felt it was important for people living with dementia to continue to participate in their hobbies following a diagnosis. One caregiver described how his wife enjoyed being an active member of her church community, and would be upset if she were excluded because of her diagnosis:

"But [she's] very keen to be involved and gets upset if she's not" (Mark, caregiver)

Hobbies that participants wanted to sustain following a diagnosis included watching TV, reading, gardening, music, making pottery and going to church. However, this can become increasingly difficult as their symptoms progress. For example, participants who used to enjoy watching TV or reading books became unable to follow plots

"I'm not getting pleasure from reading books anymore, because I'm finding it difficult to follow plots." (Helen, caregiver)

Another caregiver was advised by the memory service to find activities for her mother to participate in. She was careful to select activities that aligned with her mother's interests:

"Someone from the memory service came round and said. Um, well, what you need to do is make sure you have structure in your day. So I said, Well, you know, she's, she's going to U3A, doing tap dancing and she was in the choir and she likes singing. I looked for other singing classes." (Carol, caregiver)

5.5.6 Enablers of the benefits of an early diagnosis

Participants felt an early diagnosis was valuable, however there were conditions that needed to be met for these benefits to be felt. These enablers of the benefits of an early diagnosis are described in the following sections and include adequate prognostic information with disease modifying treatments, the presence of a caregiver and willingness to accept the diagnosis and/or post diagnostic support. Table 5.3 presents the enablers of the benefits of an early diagnosis.

Table 5.3 The enablers of the benefits of an early diagnosis

Enablers of the benefits of an early diagnosis	
Themes	**Sub-themes**
Adequate prognostic information and disease modifying treatments	Finding individualised information at the right time
	The provision effective and acceptable treatments
Benefits dependent on the presence of a caregiver	Someone to "fight" for support from health services
Willingness to accept diagnosis and/or post-diagnostic support	Active help-seeking behaviours
	Previous family members with dementia

5.5.7 Adequate prognostic information and disease modifying treatments

5.5.7.1 Finding individualised information at the right time

To be able to gain the benefits from making sense of early behaviours, engaging in timely decision making and accessing post diagnostic, participants highlighted the need for finding individualised prognostic information at the right time. Participants were most interested in knowing what symptoms or decline was likely to happen next and practical information on how to treat and manage symptoms. Participants were aware that every person living with dementia and caregiver has a unique experience, and what works for one person does not work for others. This was summed up by a caregiver who looked after both her parents with dementia:

"And, um, I, someone recommended a book to me called Contented Dementia and that I've forgotten who it's by, but that that was very helpful for me in in dealing with my father because he would go into another world and kind of talk rubbish. And I learned just to go with the flow and say Oh yeah, that's right or whatever and just keep everything calm and in fact quite often I was the only person who could get him to take his medications and things like that. So that was very helpful for that. But I never found anything that was helpful for my mother's condition." (Carol, caregiver)

Access to information regarding the person living with dementia's prognosis, good or bad, was deemed to be invaluable.

"if we could have some kind of community-based assessment, somebody with expertise... Who could you know be spend some time [with us] in order to be able to say, Oh yes, I can see what's going on here. I can see how this is going to go. This is what we can do about it. Or there is nothing we can do about it, and I'm afraid inevitably, this is what's going to happen very soon. Or something like that. You know, that's what I wanted." (James, caregiver)

Where participants were not able to access information and support that was relevant to their situation, they could feel isolated.

“I learned a bit from that, but again, I guess every situation is different and I, I haven’t sort of found anybody who I can say, well, that’s just like me and my situation.” (Mark, caregiver)

Participants highlighted the importance of a single source of information for finding individualised advice. Many participants were navigating multiple sources of information, with little success. They reported going to books, support groups, dementia or ageing charities, health and social services, friends and family, newspapers, online videos and doing independent research on google. When describing the ideal dementia service, people often described a one-stop shop which offered advice for both the person living with dementia and their caregiver.

“For the GP to have some sort of specialist or someone who will just, um, help with the support. I think that if there was just one place that you could go to, and that should be based in the GP.” (Elizabeth, caregiver)

“it's at the heart of that thing about, you know social care and physical care and mental care. They shouldn't be separated. It should be, you know, I think it should be one agency doing all of it.” (Carol, caregiver)

Participants wanted regular follow-ups, as this would enable access to individualised information at the right time. They felt that this was important for managing the emotional and practical impacts of a diagnosis. One participant living with dementia felt that she needed support immediately after the diagnosis, which was not offered to her.

“Well, I, I’d like this being fed back to people, about the fact that the diagnosis is catastrophic, and that people should be seen within two weeks of the diagnosis, I think.” (Helen, person living with dementia)

But in general, participants wanted an annual follow-up appointment.

Uh, I would've thought there ought to be somewhere that would give you an annual… You know, an MOT…There ought to be that sort of thing, I would've thought, once a year for the benefit of the carer as well as the benefit of the person. (Mark, caregiver)

"No, I think this thing about the, the, what I had said about, it would be good to have had a point of contact, but it also would have been also would have been good if, you know, the patient could be tested again, maybe after a year and another year. And, and, get feedback on what is happening 'cause I. I'm sure everyone's slightly different. And that would be nice" (Carol, caregiver)

5.5.7.2 Provision of effective and acceptable treatments

Treatments which are both effective and acceptable to people living with dementia are essential for eliciting the benefits of access to treatment following the early diagnosis of dementia. Most participants were offered dementia specific medications; however, they expressed their disappointment when they felt that the medication didn't have the expected effect.

"Because there just may, um, be some help from taking it. In fact there wasn't. We didn't get that on prescription because it is expensive, you know…But it didn't help in anyway." (Jean, caregiver to spouse with MCI)

"Interviewer: Did you notice any difference when she started taking it?

Participant: No.

Interviewer: No?

Participant: Honestly.

Interviewer: Was that disappointing?

Participant: Well, yes, obviously." (Mark, caregiver)

Furthermore, some participants believed that taking anti-dementia medications made the person living with dementia's symptoms worse. One participant living with dementia had

nightmares as a side effect of one type of medication, however on taking a different anti-dementia medication the nightmares went away.

"Uh, yes, no, no nightmares or anything. The others, I used to wake up in sweat and fear. I have no idea what they were." (Ann, caregiver)

Participants described a lengthy process for finding the appropriate combination of medications. One participant said, "it took a while, along the way to get the medication for that right." *(Elizabeth, caregiver)*. An early diagnosis may give people living with dementia more time to find the right medications for their personal needs. However, for some participants, the harms of anti-dementia medication outweighed their potential benefits. One participant realised that the anti-dementia drug (memantine) her Father was prescribed had a contraindication with a medication he was taking for a co-morbid condition, leading to unpleasant side effects. The family decided to take him off memantine.

"And in the end, we looked at the side effects of Memantine, and we looked at the side effects of the, the other bipolar drug, which he had been having. And it very clearly stated not to take the two together. And my dad had every single side effect on the list apart from sudden death, and we were absolutely furious. And we took him off it and he had about 72 hours when he went into a fever. At the time, we thought we had flu, but looking back it was probably withdrawal. We took him off both tablets. And after that weekend of basically sweating out, he drastically improved for about four months." (Joanne, caregiver)

Both participants living with dementia were referred to NHS memory support groups, either Cognitive Stimulation Therapy (CST) or a coping with memory loss group. One participant found that being part of a memory loss group was a helpful, reassuring experience. However, the other participant did not feel taking part in CST met her needs at that stage of her dementia. She attended two CST groups, one predominantly attended by women and one predominantly attended by men. She highlighted how the needs of group members appeared to differ

according to gender. For example, members of the women's group attempted to reshape the focus of the programme to be on the emotional needs of the members.

"the all-women's group moved it from being cognitive stimulation therapy, to being some form of discussion of how, how we felt about it. It was some sort of an, an opportunity to talk about our emotions. But the cognitive stimulation therapy struck me as absolutely futile. And especially in the men's group, where they were all, they were all having to prove to each other that they were, you know, they were still good." (Helen, person living with dementia)

She found the manualised nature of CST did not meet her needs and felt more could have been done to explain what CST was and to give her a choice over her treatment.

"Um, well, I would have liked… I would liked them to ask us if we wanted cognitive, explained cognitive stimulation therapy. Not shove us in it, regardless of where we were." (Helen, person living with dementia)

Similarly, there were gender barriers to accessing caregiver support. One male caregiver did not find going to support groups helpful, as he was unable to find people in a similar situation to himself.

"Uh, and I have been going to lots of groups whenever it's possible. Um, and, uh, I'm just trying to think there... I think there were probably a dozen, uh, uh, Alzheimer's sufferers. Uh, and probably only three... No, probably less than that, actually. Not really... There were probably only two of us who were male carers if you like." (Mark, person living with dementia)

He reflected on how his upbringing and background may have influenced his attitude to help-seeking, and looked to rationalise his need for support.

Yeah, I suppose so, because, uh, you know, I've been somewhat, uh, dismissive, I suppose, of people sitting on their psychiatrist's couch or whatever. I suppose, I was brought up in a fairly, uh, sort of Baptist, um, puritanical sort of background, and you got on and did things, you know? And… This was, a, a, a weakness, if you like. But I think it's, it's possible that, uh,

I can get some help in terms of just… It's trying to assess what I can do better and what is simply an inevitable reaction, I think.

5.5.8 Presence of a caregiver

Many of the perceived benefits of an early diagnosis were contingent on there being a caregiver. The following section discusses how vital caregivers are for advocating for people living with dementia as well as providing everyday support.

5.5.8.1 Caregivers to advocate for the needs of the person living with dementia

For many participants the presence of a caregiver to advocate for the person living with dementia was vital for ensuring a good quality of life. Caregivers reported being aware that the person only got the amount of care they did because they "fought" for it from services.

"I felt that things could be a lot better, and certainly you didn't have someone who's there all the time fighting for the person. I could just imagine there must be hundreds of thousands of people. Not being treated very well." (Carol, caregiver)

"Anyway, so but at the moment, he's getting quite a lot of care. And I really, er, have advocated for him strongly with the social workers to get more help in the house. Um, I'm aware of the fact we're getting a lot more than many people get." (Joanne, caregiver)

When discussing how they arranged support from health services, caregivers described this experience using words of war such as "battle" or "fight". One participant living with dementia used similar words to describe how a person living with dementia may not choose to engage in battle with health services:

"Well, I... When... I, I think so because, um, I think so many people don't have somebody like [Name of Caregiver] behind them, and so they and retreat, rather..." (Ann, person living with dementia)

Another participant living with dementia, who did not have a caregiver, discussed how challenging this lack of support was. She described having "to work hard to be on top of everything now" and worried about her future, where the disease is in the later stages:

"I do feel worried about, about that. And I can't see, to be honest, I mean, the way when people talk about, they can't go out of bed, and they, you know, they find it difficult even to get things to drink. Um, I don't know who… There's certainly nobody here who'd look after me. I'd have to… I don't know what I'd have to do if that happened." (Helen, person living with dementia)

Additionally, without a caregiver she was unable to participate in trials testing new interventions for dementia.

"Oh, and I would quite like also, the other problem was I would have liked to have been on a trial…But because I didn't, haven't got anybody living with me, I couldn't get on a trial." (Helen, person living with dementia.

On reflecting on what they would do if they had dementia, many caregivers said they would want an option for euthanasia (as discussed in section 5.5.4.3). These participants tended to be women who were unmarried and/or did not have children. They felt that not having a caregiver to advocate for their needs could leave them vulnerable to receiving poor care.

"I would probably go to the doctor and then I'd look for a pill… because I don't have any children and I'm single. Uh, so I've just got one brother, I just think. You know they won't have anyone who will… be my advocate like I was with my parents. You know I did all their finances and everything. I just I think it would be a nightmare. Beachy Head or something. I don't know if I can't find a pill." (Carol, caregiver)

"I think that as someone who's chosen to never have children and doesn't want to get married, I, you know, you become… I don't think, I don't think children or marriage are an insurance policy anyway. But you become very aware of the fact that if you start to have Alzheimer's, it's going to be really, really difficult and that you will need to put things in place before you've

completely lost the ability to communicate or fight for your rights or feed yourself, all those sorts of things." (Joanne, caregiver)

5.5.9 Willingness to accept diagnosis and/or post-diagnostic support

An unwillingness to accept a diagnosis of dementia or post-diagnostics support, presented a barrier to many of the benefits of an early diagnosis. People's willingness to accept a diagnosis was influenced by their earlier help-seeking behaviours as well as previous family experiences of dementia.

5.5.9.1 Active help seeking behaviours

Multiple caregivers reported that the person they cared for did not accept their diagnosis of dementia. They generally attributed this acceptance to how the person living with dementia engaged with post-diagnostic support and services:

Yeah, so Pa would go [to the GP] about anything else. He just never admitted about the dementia. (Sarah, caregiver)

Yeah. No, that has been good, I think partly 'cause you know, I'm quite good at understanding the system and I can sure other people would struggle who weren't au fait with all that. But as I say, the biggest obstacle we've had was with my ex-husband in spending four years not acknowledging the situation he was in. That was the most stressful time, and it wasn't because he didn't get the support it was because he wouldn't accept that support. (Catherine, caregiver)

One caregiver described how difficult was balancing the needs of the person living with dementia and their willingness to accept their diagnosis. She felt an early diagnosis gave more time for the person living with dementia to come to terms with the diagnosis and get post-diagnostic support in place.

"And if the person, if the key person with the [early dementia] won't accept that, then I can see it's always going to be a balance, isn't it? Between their freedom and autonomy and the care

system. And I can't really see a way out of that, apart from what I'm doing is trying to get it in place before it happens." (Catherine, caregiver)

Participants worried that if the person living with dementia was not willing to get a diagnosis, or accept their diagnosis, that this could eventually lead to a crisis.

"I said to mum, there's something wrong. I know you don't want to hear it, but there's something wrong. And, I'm worried that it's going to get worse, and you need to be here in, in... You need the support. You need to be here where you can be supported." (Rebecca, caregiver)

Similarly, active help-seeking behaviours are important for enabling caregivers to access support as and when they need it. One of the challenges for caregivers accessing support was their acceptance of their caregiving role. Many caregivers did not perceive themselves to be caregivers. One participant felt that because she didn't provide personal care, that she was not really her mother's caregiver, and therefore did not feel a caregiver support group was applicable to her.

"I think... You know. I mentioned it. It's certainly on a, on a... Because I don't class myself as a carer for mum, because the home do that." (Rebecca, caregiver)

These views were particularly prevalent amongst the male caregivers in this study and may affect their willingness to seek support as discussed in section 5.5.7.2.

"Um, I suppose it depends on, on how you view what does, in inverted commas, carer mean? Um, and, and my immediate reaction, which was what I was alluding to the other day, was that because they weren't, they weren't living with me, I wasn't living with them, I um, perhaps didn't and don't view myself as, as having been their carer." (David, caregiver to both parents with dementia)

"They live in a residential care home. And I am a deputy appointed by the Court of Protection to manage property and financial affairs for them. However, I am effectively the only relative...

And so other than obviously providing the day-to-day care that they receive in the residential care home, I'm the carer in other respects, if that makes sense." (James, caregiver)

5.5.9.2 Previous family members with dementia

People's experience of watching family members live through the disease had a significant impact on how they would act if they suspected they had dementia. Although there is no genetic basis for dementia, many caregivers felt that previous family members having dementia made it almost certain that they themselves would get dementia. How their loved ones coped with being diagnosed with dementia, and how alike they perceived themselves to be, and their previous help-seeking behaviour informed how they would approach a potential diagnosis. However, this did not reduce the fear of getting dementia.

"I mean, this is where I'm different to mum. I know I'd feel a lot of fear, because I'm very like mum in the sense of... I couldn't bear to lose control of the person I am. You know. I'm very dynamic. Um. I have a brain that I use and I I do take pride in my appearance… Despite the fear, I'm adamant that I would face things." (Rebecca, caregiver)

"Um, I would make sure that I got checked. I would make sure that I learned something new because I know that learning something new is, er, very good, like for instance a language, is very good for your memory. I would probably start to put in place some things. So, I'd start to tell a few people, because I'm most like my dad. So, if it's going to happen to anyone, it's probably going to be me. So, I would start to tell people, right, I'm concerned about this thing." (Joanne, caregiver)

5.5.10 Impact of COVID-19

The COVID-19 pandemic started during data collection for this study. Participants described several ways in which the pandemic affected the benefits of an early diagnosis. Firstly, the introduction of lockdown has increased the speed at which people living with dementia's symptoms decline. People living with dementia were classed by the UK government as an at-

risk group, and therefore advised to ‘shield’ at home. This period of isolation had a significant impact on people living with dementia:

“But he really has deteriorated with lockdown physically and mobility wise, because he isn't getting exercises. And he hasn't been seeing a lot of people because he hasn't… So, he hasn’t had to speak because we cater for all of his speech because we know what he needs.” (Joanne, caregiver)

One participant, living with dementia, had not noticed a decline in her symptoms until the pandemic

“I mean at the, at the beginning [after diagnosis], you know, I realised that nothing had changed, really. I was, I was doing like very much as before. I didn’t, I hadn’t really noticed much at all. It’s only in the last year, I’d say, that I’ve noticed. And I think much more with the COVID situation, where I’m isolated.” (Helen, caregiver)

The increase speed of decline associated with the lockdown can make it difficult to respond to early symptoms and get an early diagnosis in the first place. Furthermore, dementia services have been closed or moved online, making it difficult for people living with dementia to access appropriate support when they need it.

“I mean now when I think [name of person living with dementia] actually would benefit from going along to a day centre or something…. I mean there are, there is one day Centre for Lewisham, I think, and then I'm sure that was booked up to the eyeballs, but anyway, it's stopped with COVID of course.” (Sarah, caregiver)

This was a particular shame for participants who had found a service that worked for them and were no longer able to access it.

“I also found another thing, which was a memory afternoon, which was really brilliant. Um, and they're doing it online now, but my dad doesn't really engage with online screens very much.” (Joanne, caregiver)

COVID-19 has had a significant impact on timely decision making for people living with dementia, particularly for arranging care. Where participants had previously made plans for the person living with dementia to move into a care home, they no longer felt comfortable with this decision due to the isolation of care home residents and the increased risk of infection.

They [the participants' children] now agree that really [Name of person living with dementia] should go to a care home when we can't stand it any longer basically. But now with visiting so restricted for care homes, it would be like sending him to prison. I couldn't do it, I couldn't. (Sarah, caregiver)

"Um, I was reluctant, um, but he did go into a nursing home for, um, two weeks. And, within that time he went in, I only saw him once. Er, he had, they… Somebody contracted COVID-19, so I couldn't go and see him." (Sheila, caregiver)

Participants who had arranged for home care also found themselves lacking support due to the pandemic and the lack of personal protective equipment for social care staff.

"Um, so at the beginning for a while, we didn't have any carers, because, because they didn't come in with any PPE." (Joanne, caregiver)

One participant living with dementia found weighing up the risks between home care and a care home during the pandemic incredibly challenging:

And I've also, I mean, I did think I wanted to be at home, um, with, with a carer. But I'm, I'm not sure now with the COVID experience what I want, to be honest. (Helen, person living with dementia)

5.6 Discussion

This study found that the benefits of diagnosing dementia early fell under the overall theme of identifying and responding to the evolving needs of people living with dementia. A better understanding of the symptoms associated with the early stages of the disease enabled people living with dementia and their caregivers to install protections to prevent a crisis.

Furthermore, the confirmation of the diagnosis prompted participants to make plans for the future. When this is done in the early stages of the disease, people living with dementia were better able to engage with this process and communicate their preferences. An early diagnosis allows people living with dementia time to access services and treatment and to "find what works" for their unique situations. However, participants felt that in order to experience the benefits of an early diagnosis, certain enablers needed to be in place. Firstly, they needed access to adequate prognostic information and disease modifying treatments. Secondly, the person living with dementia needed to be willing to accept the diagnosis and post-diagnostic support. And finally, participants felt that these benefits were only possible where there was a caregiver to advocate for the needs of the person living with dementia. These findings are important, as they are the first to examine the value of an early diagnosis from the perspective of those living with the disease. This was the first study to explore the potential benefits of an early diagnosis, from the perspective of those most affected by the disease. Previous research examined the benefits of an early diagnosis from the perspectives of caregivers (Boise et al., 1999; de Vugt & Verhey, 2013) and people living with dementia (Dubois, Padovani, Scheltens, Rossi, & Dell'Agnello, 2016; Le Couteur et al., 2013; Prince et al., 2011). However, by not capturing the experiences of caregivers themselves, these proposed benefits remain theoretical. The findings of this study confirm some of the previously proposed benefits of an early diagnosis from other perspectives. For example, Prince et al (2011) reviewed grey literature on the benefits of diagnosis and found nine rationales supporting an early diagnosis: optimising current medical management; relief gained from better understanding of symptoms; maximising decision-making autonomy; access to services; risk reduction; planning for the future; improving clinical outcomes; avoiding or reducing future costs and diagnosis as a human right. Many of these benefits are reflected in the ones discussed in this study.

5.6.1 Long term vs. short term benefits of an early diagnosis

Participants did not describe a feeling of relief following their diagnosis. This is in contrast with other research, which has suggested a sense of relief is a common and positive response

following a diagnosis of dementia (Cahill et al., 2008). However, participants did suggest that by understanding what was likely to happen next, they were able to make timely plans and access treatment. This would enable them to manage the emotional impact of the disease and develop strategies to cope with the symptoms of dementia. At the time of diagnosis, participants were not aware how long they, or the person they were caring for might live with dementia. The average time since diagnosis in this sample was approximately four years. This is broadly in line with other estimations of survival times following a diagnosis of dementia, where people can live for 10.5 years from the onset of symptoms and 5.7 years after diagnosis (Waring, Doody, Pavlik, Massman, & Chan, 2005). This presented a challenge in identifying and responding to the needs of people living with dementia. Participants found themselves struggling to manage an unanticipated and long decline. This was compounded by a constant cycle of new symptoms developing followed by a period of searching strategies for coping with these new symptoms.

Dubois et al (2016) highlighted a risk of suicide among people living with dementia as a challenge to diagnosing dementia early. This does not consider the complexity of emotional responses to a diagnosis and attitudes towards end of life decisions. Participants in this study were open about their desire for euthanasia should they get dementia and/or their condition deteriorated beyond a certain point. Although it is important to note that these views mostly belonged to caregivers. A previous study of attitudes towards euthanasia found that those who wanted an option to end their life were anticipating an unwanted future, lacking dignity (Lemos Dekker, 2020). This reflects the beliefs of many of the participants in this study, who felt having the option of euthanasia would bring them a sense of relief. However, the participants who wanted euthanasia were primarily single and/or childless women, indicating these beliefs might be linked to social and familial structures. Euthanasia is not legal in the UK, where this study was conducted however, these findings highlight the importance of an early diagnosis in making end of life decisions. People living with dementia should have choice of over their end of life preferences, however it should not feel like their only choice.

The subtheme “making sense of early behaviours to prevent crisis” is similar to “risk reduction” in Prince et al’s (2011) nine rationales for an early diagnosis. The participants in this study discussed the value of an early diagnosis in terms of protecting relationships as well as the person living with dementia from personal or financial harm. Some caregivers in this study reported a deterioration in their relationship between the person they were caring before they were diagnosed with dementia. It is possible that this breakdown in relationships was due to personality changes or the symptoms related to dementia. An early diagnosis would help caregivers to make sense of these early changes in the person living with dementia, and possibly prevent the breakdown of their relationship. This is important as low levels of caregiver burden are predicted by high levels of relationship satisfaction before dementia (Lea Steadman, Tremont, & Duncan Davis, 2007). Similarly, high levels of caregiver burden can lead to a lower quality of life for the person living with dementia (Woods et al., 2014). This indicates that caregiver and person living with dementia outcomes are reciprocally linked, improving one should improve the other.

5.6.2 Access to services and treatments

All participants received some form of treatment following their diagnosis, confirming the benefits of an early diagnosis in terms of access to treatments. Participants were aware that pharmacological treatments that are delivered earlier in the disease are likely to be more effective. However, none of the participants described any benefits of medication to the person living with dementia, and many reported unpleasant side effects. Unfortunately, previous studies have shown that dementia specific medications do come with a risk of side effects (J. S. Birks, 2006; McShane et al., 2019). This can have an impact of the perceived value of treatment in the early diagnosis of the disease. For example, LeCouteur et al (2013) has argued that the side effects and costs of current medications for dementia outweigh the benefits. Furthermore, previous research qualitative research with GPs found participants deemed treatments to be so ineffective that there was no point in giving someone a diagnosis so that they can access them (Dhedhi et al., 2014). While participants were disappointed when

treatment did not work as well as they expected, they were still hopeful that they might find treatments that work for them. This indicates that the participants in this study, may not feel the negatives of early treatments may outweigh its potential benefits.

Participants also reported accessing non-pharmacological treatments. Receiving non-pharmacological interventions can allow the person living with dementia to make best use of their cognitive abilities and develop coping strategies for living with dementia (Kasl-Godley & Gatz, 2000). One participant living with dementia found taking part in a memory support group to be a valuable experience. She found it reassuring to meet other people who were going through similar experiences. However, the other participant living with dementia did not have as positive experience of CST. Previous research has shown that CST can have a beneficial effect on people living with dementia's confidence with speaking in groups, sharing their experiences and cognition (Spector, Gardner, & Orrell, 2011). However, this participant felt the manualised nature of CST, which focuses on reminiscence and orientation, did not give the group the space to discuss their emotional needs following a diagnosis. She highlighted that responses to CST differed depending on the gender of the group members, suggesting that people's needs following a diagnosis of dementia may differ by gender. The data on gendered responses to CST are limited to one person living with dementia. However, this is an interesting area for future research.

Similarly, gender differences in attitudes towards the caregiver role and help seeking in caregivers may be a barrier to the benefits of an early diagnosis. Three male caregivers participated in this study; however, they generally did not perceive themselves to be caregivers as they were not providing personal care. Furthermore, they were more reluctant to seek help following their loved one's diagnosis. A review of the literature of men's experiences of caregiving found that male caregivers wanted to engage with different services to female caregiver, they were less interested in support groups and more interesting in learning specific skills (Mc Donnell & Ryan, 2013). For men and women to equally benefit from an early diagnosis, they need access to services that better reflect their needs.

5.6.3 Implications and future directions

5.6.3.1 Circumstances necessary for the benefits of an early diagnosis

These findings demonstrate that while an early diagnosis can be beneficial, these benefits are dependent on context. People living with dementia and their caregivers can only make sense of early symptoms where prognostic information that is relevant to their situation is easily accessible. Similarly, people living with dementia were able to participate in timely decision making, but only when they were willing to accept their diagnosis. And people living with dementia were able to access treatments, however these would only perceive to be valuable where the treatments were effective and met their individual needs.

It is concerning that participants felt the benefits of an early diagnosis were contingent on the presence of a caregiver. Participants felt that caregivers were essential for advocating for the needs of the person living with dementia. Not all people living with dementia have a caregiver. This sample mainly consists of caregivers, and only one person living with dementia was not supported by a caregiver, therefore participants may have had a heightened awareness of the role of the caregiver in arranging post-diagnostic support. Nonetheless, it is essential that these people living with dementia can experience the same benefits as those who are supported by a caregiver. Future research should examine whether outcomes differ between people with dementia who have a caregiver and those who do not.

These findings demonstrate that an early diagnosis alone does not lead to better outcomes for people living with dementia. Therefore, policy makers should ensure that in addition to creating initiatives to increase the diagnosis rate, they should aim to make services more comprehensive and responsive to the needs of people living with dementia and their caregivers. Participants felt that creating one source of support with annual follow-ups would help improve the quality of care for people living with dementia. It is concerning that participants in this study did not feel they had access to either of these things, as memory clinics in the UK are supposed to serve as a single source of support with annual follow-ups.

5.6.3.2 Covid-19

The COVID-19 pandemic started during the early stages of this study and had a profound effect on the enablers of an early diagnosis. Participants reported that the symptoms associated with dementia have accelerated greatly since the UK introduced a lockdown in March 2020. This is supported by evidence that the isolation with lockdown increased the number of behavioural and psychological symptoms experienced by people living with dementia (Simonetti et al., 2020). With health services closing all but essential services, participants were no longer able to access in person services that they found useful, further affecting the rate of decline. Additionally, care homes have been disproportionally affected by COVID-19 infections and mortality (Mok et al., 2020), making it difficult for people living with dementia to make timely decisions about their future care. Further research is needed to explore the impact of COVID-19 on the benefits of an early diagnosis.

5.6.4 Strengths and limitations

This study provides valuable information on the benefits of an early diagnosis. The perspectives of both caregivers and people living with dementia are represented in the findings of this study. Additionally, this study included the perspectives of male caregivers who are sometimes less represented in dementia research (Mc Donnell & Ryan, 2013). However, the sample consists of far more caregivers than people living with dementia. It was more difficult to recruit people living with dementia than caregivers for this study. Join Dementia Research was the main source of recruitment for this study and there were two barriers to recruiting people from JDR. Firstly, there were fewer people living with dementia to sample from compared to caregivers. Secondly, people on JDR self-identify as having dementia when they register, meaning they may not have a formal diagnosis and were therefore not eligible to participate.

However, the participants in this study are largely white and middle class, affecting the generalisability of these findings. Future research should examine the benefits of an early diagnosis from the perspective of other social and ethnic groups in the UK. This is especially

important as this study found the benefits of an early diagnosis were highly dependent on the participants personal and social circumstances. Similarly, because of the strong relationship between the benefits of an early diagnosis and the structure of local and national services, these findings cannot be generalised outside of the UK. It would be interesting to examine whether people living with dementia in other countries share similar perspectives on the value of an early diagnosis.

5.7 Conclusion

There has been much debate in the literature, as to whether an early diagnosis can be beneficial for people living with dementia. This study demonstrates there are benefits associated with an early diagnosis, but only in conjunction with certain enablers. An early diagnosis gives people living with dementia and their caregiver an opportunity to identify and respond to their evolving needs. Participants highlighted the importance of an early diagnosis to prevent crisis, to engage in timely decision making and facilitate access to treatment and support. However, these benefits were dependant on there being adequate prognostic information, a willingness to accept the diagnosis and a caregiver to advocate on behalf of the person living with dementia. These findings demonstrate weaknesses in the current provision of post-diagnostic support, which enable the benefits of an early diagnosis to be felt.

5.8 References

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Chapter 6: Scoping review

This chapter presents the results from the third phase of analysis. This chapter charts which outcome measures have been used in randomised controlled trials testing novel non-pharmacological treatments for mild cognitive impairment and mild dementia.

This work has been published by the BMJ Open therefore, this chapter is presented as an exact copy of the journal article.

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Outcomes tested in non-pharmacological interventions in mild cognitive impairment and mild dementia: a scoping review

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ABSTRACT

Objectives Non-pharmacological treatments are an important aspect of dementia care. A wide range of interventions have been trialled for mild dementia and mild cognitive impairment (MCI). However, the variety of outcome measures used in these trials makes it difficult to make meaningful comparisons. The objective of this study is to map trends in which outcome measures are used in trials of non-pharmacological treatments in MCI and mild dementia.

Design Scoping review.

Data sources EMBASE, PsychINFO, Medline and the Cochrane Register of Controlled Trials were searched from inception until February 2018. An additional search was conducted in April 2019

Eligibility We included randomised controlled trials (RCTs) testing non-pharmacological interventions for people diagnosed with MCI or mild dementia. Studies were restricted to full RCTs; observational, feasibility and pilot studies were not included.

Charting methods All outcome measures used by included studies were extracted and grouped thematically. Trends in the types of outcome measures used were explored by type of intervention, country and year of publication.

Results 91 studies were included in this review. We extracted 358 individual outcome measures, of which 78 (22%) were used more than once. Cognitive measures were the most frequently used, with the Mini-Mental State Examination being the most popular.

Conclusions Our findings highlight an inconsistency in the use of outcome measures. Cognition has been prioritised over other domains, despite previous research highlighting the importance of quality of life and caregiver measures. To ensure a robust evidence base, more research is needed to highlight which outcome measures should be used over others.

PROSPERO registration number CRD42018102649.

Strengths and limitations of this study

- ► This scoping review has systematically mapped which outcome measures have been used by randomised controlled trials testing non-pharmacological treatments in mild dementia and mild cognitive impairment.
- ► This review has explored how the use of outcome measures varies by diagnosis, type of intervention, country and year of publication.
- ► The papers included in this review were limited to full randomised controlled trials, other study designs may be using different types of outcome measures.
- ► Further research is needed to establish which measures should be used over others.

INTRODUCTION

Delivery of both pharmacological and non-pharmacological treatment in the early stages of dementia has been identified as a global priority.[1 2] Current pharmacological treatments for the cognitive symptoms of dementia have been found to have a greater effect when delivered as early as possible.[3] However, the benefits of delivering non-pharmacological treatments early are less well understood. Non-pharmacological treatments are an important clinical tool for managing dementia as they are more acceptable to some and less prone to side effects, making them a safe alternative to drug treatments.[4] Those diagnosed earlier in the disease have more cognitive abilities available to engage with non-pharmacological treatments and bolster their own methods for coping with the disease.[5] Previous systematic reviews have found non-pharmacological treatments can improve outcomes; however, these reviews were restricted to a small number of outcome measures.[6 7]

Mild cognitive impairment (MCI) has been identified as a potential prodrome for dementia, with approximately 10% of people with MCI converting to a diagnosis of dementia per annum.[8] There is an interest in MCI, as a diagnosis of MCI can facilitate an early diagnosis of dementia and therefore earlier access to dementia services and treatment.[9] MCI is a potentially reversible condition, with many people with MCI

reverting back to normal levels of cognition.[9] Therefore, it is important treatments are available. However, it is not clear which treatments can reverse MCI or prevent conversion to dementia.[3] No drug treatments for MCI have been found to be effective[10 11] and acetylcholinesterase inhibitors are not recommended, however, there is some limited evidence that non-pharmacological interventions may be beneficial.[3 12]

Randomised controlled trials (RCTs) testing non-pharmacological treatments in dementia and MCI are becoming more common. However, they are highly heterogeneous in terms of participants recruited, quality of the study and the types of interventions they are testing, making it difficult to establish the effectiveness of one treatment over another.[6 12 13] Compounding these issues is the inconsistent use of outcome measures in this area of work.[9 14]

Systematic reviews have identified possible benefits of non-pharmacological treatment, yet meta-analyses are difficult to conduct due to the variation in outcome measures used by studies and typically yield small-to-moderate effect sizes.[6 7] It is possible that these small effect sizes are due to the selection of outcome measures which either lack sensitivity or the change following the intervention not being in the area covered by the outcome measure. It is important researchers are clear on which domains their interventions are targeting, and which measures are best able to capture this change.[15] Pharmacological treatments target specific biological pathways underlying the disease; therefore, outcome measures have been chosen to reflect this and typically focus on cognitive and functional decline.[16] Non-pharmacological treatments generally do not target the underlying biological pathway of the disease therefore, outcome measures should theoretically differ between pharmacological and non-pharmacological treatments.[17] However, a review on non-pharmacological approaches to treating found that studies tended to pay little attention to the mechanisms of change underlying the intervention.[4] The expected mechanisms of change should affect which outcomes are used in non-pharmacological treatments for mild dementia and MCI.

In addition to being clear on how change arises in non-pharmacological treatments, there needs to be a more coherent use of outcomes and the measures used to capture these between studies to ensure a broad and robust evidence base.[15] In 2008, the INTERDEM group, a consortium of dementia researchers across Europe, did work to draw a consensus on which outcome measures should be used when evaluating non-pharmacological treatments. They recommended 22 measures across 9 domains including quality of life, mood, global functioning, behaviour, daily living skills, caregiver mood, caregiver burden and staff morale.[15] This guidance does not explore outcomes by the stage of the disease. The outcome measures were selected based on their applicability to European research. The utility of outcome measures may vary by culture,[16] previous reviews exploring the use of outcome measures in dementia research have not investigated how this differs by country.[17]

It is not understood which outcome measures are currently being used in non-pharmacological treatments for early dementia and MCI. Scoping reviews present the opportunity to map the evidence on a topic,[18] unlike a systematic review scoping reviews can be used to summarise the evidence in a heterogeneous body of literature. Therefore, the aim of this scoping review is to map trends in which outcome measures are being used in RCTs for non-pharmacological treatments in MCI and mild dementia.

Objectives

The specific objectives of this scoping review are to:

1. Chart which outcomes measures have been used to assess the effectiveness of non-pharmacological treatments in mild dementia and MCI.
2. Highlight which types of measures have been used most frequently.
3. Explore whether the outcome measures used differ depending on the type of intervention, study population and country the research was conducted in.

METHODS

Protocol registration

The protocol for this review was developed following the guidelines set out by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension (PRISMA) statement[19] and the PRISMA guidelines for Scoping Reviews.[18]

Eligibility criteria

We included RCTs testing non-pharmacological interventions for people diagnosed with MCI or mild dementia. Studies were restricted to full RCTs; observational, feasibility and pilot studies were not included.

Studies were included if they met the following criteria:

- Testing non-pharmacological interventions. Studies were not excluded if participants were also treated with acetylcholinesterase inhibitors.
- Participants had a diagnosis of MCI or mild dementia, which was either diagnosed in clinical practice, or met standardised diagnostic criteria, such as the International Statistical Classification of Diseases or The Diagnostic Statistical Manual of Mental Disorders, The National Institute of Communicative disorders and Stroke and the Alzheimer's Disease and Related Disorders, the International working group on MCI criteria, The Consortium to Establish a Registry for Alzheimer's Disease, The National Institute on Aging-Alzheimer's Associating Diagnostic Guidelines for Alzheimer's Disease, the Petersen Criteria; or was defined by a standardised clinical measure, such as scores between 24 and 18 on the Mini-Mental State Examination (MMSE); scores ≤26 on the Montreal Cognitive Assessment, scores between 15 and 27 on the St Louis University Mental Status, a Clinical

Dementia Rating score of 1 (for dementia) or 0.5 (for MCI); or a 4 (for dementia) or 3 (for MCI) on the Global Deterioration Scale. Studies which include a mix of participants with early dementia and MCI were included, however, studies which included healthy participants and participants with dementia at the later stages of the disease were excluded.

- The intervention was targeted for the person living with dementia or MCI. Dyadic interventions, interventions delivered to both the person living with dementia and their caregivers, were included. Interventions delivered solely to caregivers or healthcare professionals were excluded.
- Participants were living in long-term care facilities or the community.
- Written in English.

Studies were excluded if:

- Only pharmacological interventions were tested.
- The participants were diagnosed with vascular cognitive impairment, young-onset dementia, Parkinson's disease dementia or MCI with Parkinson's disease.
- Participants were living in a psychiatric inpatient or acute hospital setting.
- The intervention had the primary aim of treating major depressive disorder.
- The study tested palliative care interventions or advanced care planning.
- The only outcome measures used were economic outcomes, such as cost-effectiveness, etc.

Information sources and search strategy

To identify potentially relevant studies, we searched EMBASE, PsychINFO, Medline and the Cochrane Register of Controlled Trials from inception until 22 February 2018. An additional search was conducted on 2 April 2019. See online supplementary table 1 for the final search strategy for MEDLINE, which was adapted for the other databases. The final search results were exported into EndNote where duplicates were removed.

Additional papers were identified by searching the references of included papers and other systematic reviews. Conference abstracts and publications were not included.

Selection of sources of evidence

Study selection was managed in Rayyan, where citations were screened against the inclusion and exclusion criteria. Rayyan is an online app for systematic reviews which allows researchers to create their own coding system for decision making.[20] References were first screened by title and abstract, followed by a full-text screening. A second reviewer (MC) screened 10% of the articles at each stage of the review. Disagreements were resolved by discussions with a third reviewer (AMP).

A critical appraisal or assessment of the risk of bias is not necessary for a scoping review.[18] This scoping review is not aiming to critically appraise the cumulative literature of outcome measures for non-pharmacological treatment in MCI and mild dementia, therefore we did not conduct a critical appraisal or risk of bias assessment for this review.

Data charting process and data items

Data from eligible studies were charted using a standardised extraction tool designed for this study. Items deemed most relevant to the review objectives were the diagnosis of the study participants, description of interventions being tested, the number of intervention groups and outcome measures used with references.

Synthesis of results

The charted data were mapped to reflect the objectives of this review. Following data charting, outcome measures which were used more than once across the included studies were grouped by domain. We grouped the interventions thematically by the type of intervention being tested.

We explored which types of outcome measures were used by intervention type, by tabulating the type of intervention against the domain of the outcome measure. We excluded interventions which were only used once from this summary. Results were presented in tables and summarised narratively.

Patient and participant involvement

The South London and Maudsley MALADY group, of current and former carers of people living with dementia, were consulted in the planning of this study.

RESULTS

Included studies

After duplicates were removed, a total of 7056 citations were screened for inclusion, 653 were screened at full text and 74 papers were initially identified. A top-up search in April 2019 identified 119 new citations, 17 were included making the total number of included studies 91 (figure 1).

The studies included in this review are described in table 1, including diagnosis of included participants, number of intervention groups, details on the interventions and comparisons tested and the number of outcomes measures used. The included studies were published between 2002 and 2019.

The majority of studies included in this review were conducted in the USA (n=10), Hong Kong (n=10) and Italy (n=11), followed by mainland China (n=7), Japan (n=8), South Korea (n=8) and Canada (n=6). Studies were also conducted in: Argentina, Australia, Brazil, Czech Republic, Denmark, France, Finland, Germany, Greece, Hungary, Iran, Norway, Pakistan, Singapore, Spain, Taiwan, The Netherlands, Turkey and the UK; these countries had fewer than five included studies each.

Most studies only recruited participants with MCI (n=71), followed by mild dementia only (n=14), and six

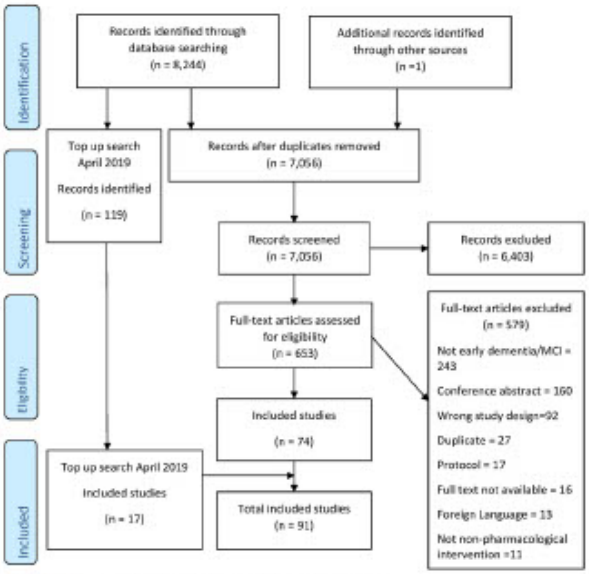

Figure 1 Flow chart of included studies.

studies recruited both participants with MCI and mild dementia.

Results of individual sources of evidence

We extracted 358 individual outcome measures from the included studies, of these 78 (22%) were used more than once. Out of the 78 measures used more than once, 70 (88%) were measures of participants living with dementia (PLWD), 6 measures were used in both the PLWD and their caregiver, 2 measures were only of the caregiver. The number of outcome measures used by each study ranged between 1 and 21 with an average of 6.85.

Types of non-pharmacological interventions

We grouped the interventions thematically by type. The most frequently tested type of intervention was cognitive training (n=37) followed by physical activity (n=25), combined physical activity and cognitive training (n=4), multicomponent psychosocial interventions (n=4) and support groups (n=3). Animal-assisted therapies, art-based therapies, case management, Chinese calligraphy, music-based interventions and reminiscence therapy were each tested in two studies.

A group weight loss programme, mindfulness, social activities, transcranial direct current stimulation, transcutaneous electrical nerve stimulation and Transcranial magnetic stimulation were each trialled once. These interventions were not included in the analysis of trends in outcome measures.

PLWD outcome measures

Table 2 presents the PLWD-specific outcome measures grouped by domain. The most frequently measured domain in PLWD was cognition/memory, which was measured 219 times across the 93 included studies. The most frequent measure of cognition was the MMSE, which was measured 37 times. In addition to measures of memory performance, knowledge of memory strategies was measured 3 times in PLWD.

The next most frequently measured domain in PLWD was behavioural and psychological symptoms of dementia (BPSD), within this depression was the most commonly measured BPSD. The Geriatric Depression Scale was the most used measure in this domain, followed by the Neuropsychiatric Inventory which examines a greater number of symptoms. Other BSPDs measured were apathy and agitation resulting from memory problems.

Quality of life and well-being were measured 15 times across the included studies. Quality of life was measured 15 times using four different instruments, the most popular of which was Logsdon's Quality of Life in Alzheimer's disease scale which was used 7 times.

Measures of everyday living, physical ability, biological outcomes and adherence to the intervention delivered in the study were measured <20 times across the included studies.

Caregiver measures

Eight interventions in this study were dyadic,[21–28] all included outcome measures specific to the caregiver in addition to the PLWD. One study of an intervention solely delivered to the PLWD also included a caregiver-specific measure.[29]

Table 2 also presents the outcome measures administered to caregivers grouped by domain. The Center for Epidemiological Studies Depression Scale and the Zarit Caregiver Burden interview were the only measures which were administered solely to caregivers. The other caregiver measures were also administered to PLWD. The most frequently measured domain in caregivers was depression, followed by caregiver burden. General well-being, knowledge of memory strategies, quality of life and stress were each measured once.

Use of outcome measures over time

RCTs of non-pharmacological treatments in mild dementia and MCI have become more frequent over recent years. Almost half (48%) of studies included in this review were published between 2016 and 2018.

Figure 2 charts trends in outcome measure domains over time. As the number of studies in this area has increased over time, so too has the use of outcome measures in all domains. Cognition/memory has consistently been measured over other domains from the beginning of this sample. The only noticeable trend change is in measures of BPSD, which was generally in line with other domains until around 2012, when it overtakes other domains.

Nearly all studies in 2014 included a measure of everyday living; however, since then, the number of studies including these measures has declined. Where measures of everyday living are being used less, measures of BPSD are being used more.

Similarly, caregiver measures were consistently used until 2011, when in 2010 and 2011 all studies included

Table 1 Included studies

Study	Country	Diagnosis	Number of groups	Group 1	Group 2	Group 3	Group 4	Group 5	Number of measures
Amjad *et al*[37]	Pakistan	MCI	2	Aerobic exercise	Non-aerobic exercise	–	–	–	4
Bae *et al*[38]	Japan	MCI	2	Multi-intervention programme	Active control	–	–	–	10
Baker *et al*[39]	USA	MCI	2	Aerobic exercise	Stretching	–	–	–	11
Belleville *et al*[40]	Canada	MCI	3	Cognitive training	Psychosocial intervention	Control	–	–	7
Biasutti and Mangiacotti[41]	Italy	MCI	2	Cognitive training	Gym activities	–	–	–	4
Bono *et al*[42]	Italy	MCI	2	Animal assisted therapy	Control	–	–	–	4
Burgio *et al*[43]	Italy	MCI	2	Numerical training	Executive training	–	–	–	13
Buschert *et al*[44]	Germany	MCI	2	Cognitive training	Active control	–	–	–	5
Carretti *et al*[45]	Italy	MCI	2	Cognitive training	Active control	–	–	–	16
Cavallo *et al*[46]	Italy	Dementia	2	Cognitive training	Active control	–	–	–	3
Chan *et al*[47]	Hong Kong	MCI	2	Chinese calligraphy	Computer activities	–	–	–	13
Chan *et al*[48]	Hong Kong	MCI	2	Chinese calligraphy	Computer activities	–	–	–	8
Choi and Lee[49]	South Korea	MCI	2	Ground kayaking	Home exercise education	–	–	–	7
Combourieu Donnezan *et al*[50]	France	MCI	4	Physical training	Cognitive training	Simultaneous cognitive and physical training	Control	–	4
DiNapoli *et al*[51]	USA	MCI	2	Individualised social activities	Control	–	–	–	4
Doi *et al*[52]	Japan	MCI	2	Exercise	Active control	–	–	–	4
Doi *et al*[53]	Japan	MCI	3	Dance	Playing musical instruments	Health education group	–	–	4
Drumond Marra *et al*[54]	Brazil	MCI	2	TMS	Sham TMS	–	–	–	6
Emsaki *et al*[55]	Iran	MCI	2	Cognitive training	Active control	–	–	–	9
Eyre *et al*[56]	USA	MCI	2	Yoga	Cognitive training	–	–	–	10
Feng *et al*[57]	China	MCI	2	Single component cognitive training	Multiple component cognitive training	–	–	–	3
Fernández-Calvo *et al*[58]	Spain	Dementia	2	Multi-intervention programme	Control	–	–	–	21
Fiatarone Singh *et al*[59]	Australia	MCI	4	Progressive resistance training and sham cognitive training	Progressive resistance training and cognitive training	Cognitive training	Control	–	12
Finn and McDonald[60]	Australia	MCI	2	Repetition-lag training	Control	–	–	–	6
Fogarty *et al*[61]	Canada	MCI	2	Memory intervention programme and tai chi	Memory intervention programme	–	–	–	5
Förster *et al*[62]	Germany	Both	2	Cognitive training	Control	–	–	–	10
Galante *et al*[63]	Italy	Dementia	2	Cognitive training	Active control	–	–	–	12

Continued

Table 1 Continued

Study	Country	Diagnosis	Number of groups	Group 1	Group 2	Group 3	Group 4	Group 5	Number of measures
Greenaway *et al*[61]	USA	MCI	2	Memory support system (memory rehabilitation) with training	Memory support system without training	–	–	–	15
Hagovská *et al*[64]	Czech Republic	MCI	2	Cognitive training (computer based)	Cognitive training	–	–	–	0
Hagovská *et al*[65]	Czech Republic	MCI	2	Cognitive training and dynamic balance training	Balance training	–	–	–	4
Han *et al*[66]	South Korea	MCI	2	Ubiquitous spaced retrieval-based memory advancement and rehabilitation training	Control	–	–	–	4
Han *et al*[67]	South Korea	Both	2	Multimodal cognitive enhancement therapy	Active control	–	–	–	7
Hattori *et al*[29]	Japan	Dementia	2	Art therapy	Active control	–	–	–	4
Ho *et al*[68]	Hong Kong	Both	3	Dance movement therapy	Physical exercise	Control	–	–	7
Horie *et al*[69]	Brazil	MCI	2	Group weight loss programme	Control	–	–	–	10
Hyer *et al*[70]	USA	MCI	2	Cognitive training (computer based)	Active control	–	–	–	3
Jansen *et al*[22]	The Netherlands	Dementia	2	Case management	Control	–	–	–	5
Jean *et al*[71]	Canada	MCI	2	Cognitive training	Active control	–	–	–	10
Jelcic *et al*[72]	Italy	Dementia	2	Lexical-semantic treatment	Cognitive stimulation	–	–	–	11
Jeong *et al*[73]	South Korea	MCI	2	Cognitive intervention (group based)	Cognitive intervention (home based)	–	–	–	8
Kinsella *et al*[23]	Australia	MCI	2	Cognitive intervention	Control	–	–	–	4
Kohanpour *et al*[74]	Iran	MCI	4	Aerobic exercise	Lavender extract	Aerobic exercise and lavender extract	Control	–	14
Koivisto *et al*[24]	Finland	Dementia	2	Psychosocial intervention	Control	–	–	–	7
Kovács *et al*[75]	Hungary	MCI	2	Multimodal exercise	Control	–	–	–	1
Küster *et al*[76]	Germany	MCI	3	Cognitive training	Physical training	Control	–	–	7
Kwok *et al*[77]	Hong Kong	MCI	2	Cognitive training	Active control	–	–	–	5
Lam *et al*[78]	Hong Kong	MCI	2	Tai Chi	Stretching	–	–	–	4
Lam *et al*[79]	Hong Kong	MCI	4	Cognitive training	Cognitive and physical training	Physical training	Social groups	–	2
Lam *et al*[25]	Hong Kong	Dementia	2	Case management	Control	–	–	–	2
Langoni *et al*[80]	Brazil	MCI	2	Group exercise	Control	–	–	–	14
Law *et al*[81]	Hong Kong	MCI	2	Functional tasks exercise programme	Cognitive training	–	–	–	7
Lazarou *et al*[82]	Greece	MCI	2	Ballroom dancing	Control	–	–	–	5
Li *et al*[83]	China	MCI	2	Computerised cognitive training	Control	–	–	–	4

Continued

Table 1 Continued

Study	Country	Diagnosis	Number of groups	Group 1	Group 2	Group 3	Group 4	Group 5	Number of measures
Lim *et al*[84]	Singapore	MCI	2	Mindfulness	Health education	–	–	–	5
Logsdon *et al*[26]	USA	Dementia	2	Early stage memory loss support group	Control	–	–	–	10
Luijpen *et al*[85]	The Netherlands	MCI	2	TENS	Sham TENS	–	–	–	6
Maffei *et al*[86]	Italy	MCI	2	Multidomain training	Control	–	–	–	10
İnel Manav and Simsek[87]	Turkey	Dementia	2	Reminiscence therapy	Social interview	–	–	–	6
Melendez *et al*[88]	Spain	Both	2	Reminiscence therapy	Control	–	–	–	6
Nagamatsu *et al*[89]	Canada	MCI	2	Aerobic exercise	Resistance training	–	–	–	13
Olsen *et al*[90]	Norway	Both	2	Animal-assisted therapy	Control	–	–	–	9
Pantoni *et al*[91]	Italy	MCI	2	Attention process training	Control	–	–	–	4
Park and Park[92]	South Korea	MCI	2	Cognition-specific computer training	Non-specific computer training	–	–	–	5
Poinsatte *et al*[93]	USA	MCI	2	Aerobic exercise	Stretching	–	–	–	3
Pongan *et al*[94]	France	Dementia	2	Choral singing	Painting	–	–	–	14
Poptsi *et al*[95]	Greece	MCI	5	Paper language tasks	Computer language tasks	Oral language tasks	Active control	Control	4
Qi *et al*[96]	China	MCI	2	Aerobic exercise	Control	–	–	–	3
Rapp *et al*[97]	USA	MCI	2	Memory enhancement training (multicomponent)	Control	–	–	–	9
Rojas *et al*[98]	Argentina	MCI	2	Cognitive intervention	Control	–	–	–	8
Rozzini *et al*[99]	Italy	MCI	2	Cognitive training and AChEIs	AChEIs	–	–	–	7
Savulich *et al*[100]	UK	MCI	2	Cognitive training	Control	–	–	–	9
Scherder *et al*[101]	The Netherlands	MCI	3	Walking	Hand and face exercises	Control	–	–	11
Shimada *et al*[102]	Japan	MCI	2	Physical and cognitive training	Health education group	–	–	–	7
Shimizu *et al*[103]	Japan	MCI	2	Movement music therapy	Single training task	–	–	–	4
Simon *et al*[104]	Brazil	MCI	2	Memory training	Active control	–	–	–	8
Song *et al*[105]	China	MCI	2	Aerobic exercise	Active control	–	–	–	4
Suzuki *et al*[106]	Japan	MCI	2	Multicomponent exercise group	Active control	–	–	–	6
Tappen and Hain[27]	USA	Both	2	Cognitive training (home based)	Life story interview	–	–	–	11
Troyer *et al*[107]	Canada	MCI	2	Multicomponent intervention	Control	–	–	–	6
Tsai *et al*[108]	Taiwan	MCI	3	Aerobic exercise	Resistance training	Control	–	–	7
Tsantali *et al*[109]	Greece	Dementia	3	Cognitive training	Cognitive stimulation	Control	–	–	5
van Uffelen *et al*[110]	The Netherlands	MCI	4	Walking	Placebo activity	Folic acid/ Vitamin b supplements	Placebo pills	–	3

Continued

Table 1 Continued

Study	Country	Diagnosis	Number of groups	Group 1	Group 2	Group 3	Group 4	Group 5	Number of measures
Waldorff *et al*[98]	Denmark	Dementia	2	Multifaceted counselling, education and support	Control	–	–	–	2
Wei *et al*[111]	China	MCI	2	Handball training	Control	–	–	–	8
Yang *et al*[112]	USA	MCI	2	Memory enhancement training	Yoga	–	–	–	3
Yoon *et al*[113]	South Korea	MCI	2	High-speed power strength training	Low-speed strength training	–	–	–	5
Young *et al*[114]	Hong Kong	Dementia	2	Support groups	Control	–	–	–	4
Young *et al*[115]	Hong Kong	MCI	2	Holistic health group	Control	–	–	–	4
Yun *et al*[116]	South Korea	MCI	2	TDS	Sham TDS	–	–	–	1
Zhao *et al*[117]	China	MCI	2	Creative expression therapy	Cognitive training	–	–	–	7
Zhu *et al*[118]	China	MCI	2	Dance	Control	–	–	–	7

MCI, mild cognitive impairment; TDS, transcranial direct current stimulation; TENS, transcutaneous electrical nerve stimulation; TMS, transcranial magnetic stimulation.

a caregiver measure, however since then the use of such measures has declined.

Use of outcome measures by intervention

Table 3 presents diagnosis and type of intervention by the domains measured. Cognition/memory was the most measured domain across all diagnostic groups, followed by BPSD. The third most common domain for MCI studies was physical performance, whereas caregiver measures were the third most common type of measures used in studies of early dementia.

Cognition/memory was measured in all types of intervention. Measures of BPSD were most common in cognitive training interventions and physical activity interventions, however, they were not used by combined cognitive and physical training interventions. Quality of life was measured by studies of case management, cognitive training, psychosocial interventions, physical activity and support groups.

Caregiver measures were used in five types of interventions: case management, cognitive training and psychosocial interventions; followed by arts-based therapy and support groups.

Use of outcome measures by country

Table 4 presents the country the research was conducted in by outcome measure domain. Generally, there was not much variability in the domain of outcome measures used by country. Cognition/memory was the domain most frequently measured by all countries, followed by BPSD. The majority of studies were conducted in China (including Hong Kong and Taiwan), these studies focused on cognition/memory, BPSD and biological outcome measures. Other than China, only three other countries included biological measures (Iran, Pakistan and the USA). The USA had the second largest number of studies included in this review, these studies favoured cognition/memory, BPSD, caregiver measures and quality of life. Out of the 24 countries with studies included in this review, less than half (n=9) included measures of quality of life.

DISCUSSION

In this study, we used a scoping review to map which outcome measures had been used in trials for non-pharmacological treatments of mild dementia and MCI. We extracted 358 individual outcome measures used in 91 trials, only 22% of which were used more than once. We grouped the outcome measures which had been used more than once and examined differences in their use over time, by diagnostic group, country the research was set in and by the type of intervention they were being used to evaluate. Measures of cognition and BPSDs were the most frequently used across all studies and types of intervention.

Perhaps unsurprisingly, measures of cognition or memory are the most prevalent across all countries, diagnostic groups and types of intervention with the MMSE being the most frequently used outcome measure, despite the ADAS-cog having been validated as the gold-standard measure of cognition.[15 30 31] Measuring cognition is central to measuring the progression of dementia and is a clinically and empirically useful outcome to measure in dementia research.[31] However, in this review, we charted 40 different measures of cognition. This indicates that while cognition has been prioritised as an outcome in studies of non-pharmacological interventions, there is no consensus between researchers on which specific

Table 2 Outcome measures by domain and subdomains

Person living with dementia measures Domain and subdomain	Outcome measure	N
Cognition/Memory		**219**
Cognition	MMSE	37
	Trail Making Test	27
	Digit Span Test	12
	ADAS-Cog	10
	Rey Auditory Test	9
	Rivermead Behavioural Memory Test	9
	Stroop Test	7
	MMQ	7
	Novelli Lexical Test	7
	MoCA	6
	CDR	6
	Verbal Fluency	6
	CERAD-NB	5
	Addenbrooke's Cognitive Examination	4
	Boston Naming Test	4
	Rey Osterrieth Complex Figure Task	4
	Montreal Cognitive Test	3
	Attentional Matrices Test	3
	California Verbal Learning Test	3
	Digit Symbol Coding Test	3
	Hopkins Verbal Learning Test	3
	The Wechsler Memory Scale	3
	CAMcog	2
	Cognitive Failures Test	2
	Colour Trails Test	2
	Dementia Rating Scale-2	2
	DSM IV Test	2
	Auditory Verbal Learning Test	2
	Corsi's Block Tapping Test	2
	Frontal Assessment Test	2
	Fuld Object Memory Evaluation	2
	Logical Memory (Subtest of Wechsler Memory Scale)	2
	Prospective and Retrospective Memory Questionnaire	2
	Pyramids & Palm Trees	2
	Questionnaire d'Auto Evaluation de la Memoire	2
	Raven's Coloured Matrices	2
	Repeatable Battery Test	2
	The verbal learning and memory test	2
	Visual Memory Span	2
	Wechsler Adult Intelligence Scale	2
Knowledge of memory strategies	Memory Strategy Toolbox	2
	Strategy Knowledge Repertoire	1
Attention	Test of Everyday Attention	2
Behavioural and psychological symptoms of dementia		**51**
Anxiety/Depression	Geriatric Depression Scale*	21
	Cornell Scale for Depression in Dementia*	7
	Hospital Anxiety and Depression Scale	4
	Beck Depression Inventory	1
Other	Neuropsychiatric Inventory*	12
	Apathy Evaluation Scale	3
	Revised memory and behaviour problem checklist*	
Everyday living		**20**
Activities of daily living	Instrumental Activities of Daily Living*	8
	Bayer Activities of Daily Living Scale	3
	Alzheimer's Disease Cooperative Study Activities of Daily Living Scale	2
	Barthel Index	2
Functional ability	Functional Activities Questionnaire	3
	Functional and Cognitive Assessment Test and Functional Rating Scale for Dementia	2
Physical outcomes		**19**
Physical performance	Timed Up and Go Test	7
	Gait	3
	Handgrip strength	3
	Stride	2
	Walking Speed	2
Physical measures	Weight	2
Quality of life/Well-being		**15**
Quality of life	QoL in Alzheimer's disease*	7
	Dementia Quality of Life Instrument*	3
	EuroQoL EQ 5D*	2
	EQ-VAS	1
Stress	Perceived Stress Scale	1
General Well-being	SF-36	1
Biological outcome		**9**
Brain activity	EEG	4
	MRI	2
Biomarker	BDNF	3

Table 2 Continued

Person living with dementia measures Domain and subdomain	Outcome measure	N
Adherence to intervention		**2**
Adherence to intervention	Adherence	2
Caregiver measures domain	**Outcome measure**	**N**
Depression		**5**
	The Center for Epidemiological Studies Depression Scale*	3
	Geriatric Depression Scale	1
	Beck Depression Inventory	1
Caregiver burden		**2**
	Zarit caregiver burden interview*	2
General well-being		**1**
	SF-36*	1
Knowledge of memory strategies		**1**
	Strategy Knowledge Repertoire	1
Quality of life		**1**
	EQ-VAS	1
Stress		**1**
	Perceived Stress Scale	1

*Measure recommended by INTERDEM Consensus.[14]
CDR, Clinical Dementia Rating; CERAD-NB, Consortium to Establish a Registry for Alzheimer's Disease- Neuropsychological Battery; DSM, Diagnostic Statistical Manual of Mental Disorders; EEG, electroencephalogram; EQ-VAS, EuroQoL Visual Analogue Scales; EuroQoL EQ 5D, EuroQoL 5-dimension; MMQ, Multifactorial Memory Questionnaire; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; SF-36, 36-Item Short Form Survey.

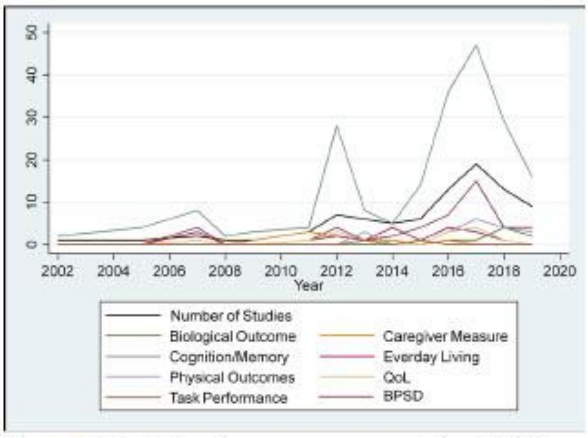

Figure 2 Trends in outcome measures over time. BPSD, behavioural and psychological symptoms of dementia; QoL, quality of life.

measures should be used. In addition to measures of cognitive performance, three studies have also measured participant's knowledge or retention of memory strategies, indicating an interest in long-term coping strategies for memory loss.

Measures of the BPSD have become more common over time, becoming in 2017 the most measured outcome after cognition. There is not much variety in the BPSDs which have been measured. Generally, depression was measured over other BPSDs. Other BPSDs such as agitation were measured less, perhaps because they are more associated with the later stages of the disease and depression is associated with the earlier stages.[32]

Quality of life and well-being were not among the most measured domains. Four measures of quality of life were used 15 times across the included studies and all but one of these measures were dementia-specific measures. It is surprising quality of life has not been measured more, as previous research has stated that in the absence of a cure, healthcare providers have a greater ability to improve quality of life than alter the progression of the disease.[33] Furthermore, both people with MCI and caregivers rated quality of life of the patient as the most important outcome to measure, followed by caregiver quality of life/burden.[34] Indicating while quality of life has been identified as a priority by PLWD, people diagnosed with MCI and their caregivers in previous research, the findings of this study shows this is not being translated into trials of non-pharmacological treatments for early dementia and MCI.

Likewise, caregiver measures had consistent low use across the studies included in this review. We charted eight caregiver measures which were used 11 times across the included studies. Caregiver measures were more commonly used in studies of PLWD, rather than MCI. Previous research has highlighted the profound effect of dementia on their caregivers, with around half of caregivers experiencing high levels of burden.[35] However, a third of caregivers of people with MCI also report extreme levels of burden,[36] yet the findings of this study show this is less investigated.

There was great variability in the types of outcomes being used to evaluate the different types of intervention. All studies measured cognition and all but one measured BPSD. A lack of clarity in how change occurs as a result of non-pharmacological treatments is a fundamental weakness in this area of work.[4] It is unlikely that all interventions being tested in this review could hope to improve cognition, however this is the most prevalent domain of outcome measures. There are a number of practical reasons as to why certain outcomes, and therefore outcome measures are used over others, In the past, pharmacological treatments have been required to include some measure of cognition, functional or global assessment,[17] it is possible that this approach has influenced the choice in outcomes used in non-pharmacological studies. Furthermore, some measures may be used over others for more practical reasons. For example, measures

Table 3 Outcome measure domain by diagnosis and intervention

	Number of studies	BPSD	Biological outcome	Caregiver measure	Cognition/Memory	Everyday living	Physical measures	Physical performance	Quality of life/ Well-being	Task performance
Diagnosis										
Both	6	5	–	1	12	1	–	–	–	–
Dementia	14	16	–	7	42	6	–	–	6	–
MCI	71	30	9	3	163	12	2	17	9	2
Type of intervention										
Animal-assisted therapy	2	2	–	–	2	1	–	–	–	–
Art-based therapy	2	1	–	1	6	1	–	–	–	–
Case management	2	2	–	3	1	–	–	–	1	–
Chinese calligraphy	2	1	1	–	4	–	–	–	–	–
Cognitive training	37	23	2	3	103	11	–	1	6	2
Cognitive training and physical activity	4	–	–	–	14	2	–	2	–	–
Multicomponent psychosocial intervention	4	6	–	3	10	2	–	2	3	–
Music-based intervention	2	1	–	–	7	–	1	2	1	–
Physical activity	25	11	6	–	53	3	1	10	2	–
Reminiscence therapy	2	1	–	–	2	–	–	–	–	–
Support group	3	3	–	1	1	–	–	–	1	–

BPSD, behavioural and psychological symptoms of dementia; MCI, mild cognitive impairment.

which are short to administer and free to use may be priorities over others.[31] Several interventions in this review comprise more than one component, for example, physical activity and cognitive training. In these cases, it may take multiple measures over many domains to accurately capture change. It is vital that outcome measures are selected depending on the domains the intervention is seeking to address.[31]

In 2008, the INTERDEM group recommended 22 outcome measures for use across 9 domains.[15] We found 11 of these 22 measures (50%) were used by the studies included in this review, one of the recommended domains (staff carer morale) was not applicable to the studies included in this review. All measures recommended for measuring patient mood, and patient quality of life were charted in this review. Only one of the recommended measures for the activities of daily living, caregiver mood, caregiver burden and caregiver quality of life domains were charted and no measures under the global measures domain were charted in this review. This indicates that there is some consistency between which measures are recommended and which measures are used, this is largely for patient measures and there is less consistency for caregiver measures.

In this study, we found that the use of outcome measures did not vary much by the country the study was conducted in. In each country, cognition/memory was the most commonly tested domain, followed by BPSD. The importance of outcomes may vary between cultures; therefore, it is important that the outcomes and measures used reflect this.[16] However, due to the limitations of the methodology used we cannot comment on the cultural relevance of the outcome measures charted in this review. Furthermore, articles were only included if they were published in English. It is possible that more culturally appropriate outcomes were used in articles published in the same language as the population under investigation. This is an important area for future research.

Limitations

The findings of this review must be interpreted in the context of the study. To make this review feasible we only included full RCTs, other outcome measures may have been used in different types of studies. Due to time constraints, some subtypes of dementia and cognitive impairment (young-onset, Parkinson's disease dementia and vascular cognitive impairment) were excluded from this review, which limits the applicability of these findings. Further research is needed to explore whether the pattern in the use of outcomes and outcome measures is similar in these groups, compared with the ones included in this review. Furthermore, only outcome measures which were

Table 4 Outcome measure domain by country

Country	Number of studies	BPSD	Biological outcome	Caregiver measure	Cognition/Memory	Functional ability	Physical measures	Physical performance	Quality of life/Well-being	Task performance
Argentina	1	1	0	0	6	1	0	0	0	0
Australia	4	0	0	1	5	1	0	0	0	0
Brazil	5	1	1	0	14	0	0	1	0	0
Canada	6	2	0	0	16	0	0	2	0	0
Mainland China, Hong Kong and Taiwan	20	10	5	1	35	2	0	0	0	1
Czech Republic	3	0	0	0	3	2	0	1	0	0
Denmark	1	2	0	2	1	1	0	0	2	0
Finland	1	1	0	1	3	1	0	0	1	0
France	3	1	0	0	6	0	0	2	1	0
Germany	4	1	0	0	10	0	0	0	1	0
Greece	4	3	0	0	18	2	0	0	1	0
Hungary	1	0	0	0	0	0	0	1	0	0
Iran	3	1	1	0	3	0	1	0	0	0
Italy	11	8	0	0	32	6	0	0	1	0
Japan	8	2	0	1	16	1	1	6	0	0
Norway	1	1	0	0	1	0	0	0	0	0
Pakistan	1	0	1	0	3	0	0	0	0	0
Singapore	1	0	0	0	0	0	0	0	0	0
South Korea	8	5	0	0	14	1	0	4	3	0
Spain	3	2	0	0	2	0	0	0	0	0
The Netherlands	5	0	0	2	10	0	0	0	2	0
Turkey	1	1	0	0	1	0	0	0	0	0
UK	1	3	0	0	1	0	0	0	0	0
USA	10	6	1	3	19	2	0	0	3	1

BPSD, behavioural and psychological symptoms of dementia.

published could be included in this review. The studies included in this study were heterogeneous in terms of participants recruited, interventions tested and outcome measures used, making it difficult to group them thematically. It is possible some nuance is lost in the exploration of broader themes. As with the nature of scoping reviews, we are only able to present which outcome measures have been used in previous research, we are unable to draw conclusions as to which outcome measures should be used over others. Future research should explore which population measures have been validated for and what constitutes a clinically useful change.

Implications and recommendations for future research

The findings of this review indicate there is very little consistency in outcome measures used in RCTs for non-pharmacological interventions in MCI and mild dementia, however we are not able to conclude which measures should be used over others. To create a strong evidence base for non-pharmacological treatments more research, with the involvement of PLWD and their carers, is needed to determine which measures are preferable over a greater number of domains. Additionally, the prevalence of cognitive measures found in this study suggests that researchers are including such measures because there is an expectation to do so. Researchers should be clear on the theory behind how their intervention creates change and use the appropriate outcome measures.

CONCLUSIONS

In summary, this study has found RCTs for non-pharmacological treatments in mild dementia and MCI use a broad range of outcome measures, with a small proportion being used more than once. Excepting measures of cognition, there is very little commonality between studies. Where previous research has set priorities on outcomes preferred by PLWD, people with MCI and caregivers, quality of life, for example, this has not yet

translated into studies measuring new treatments. Further research is needed to understand which outcomes should be prioritised and how they should be measured.

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6.2 Supplementary materials

Supplementary table 1. Search Strategy for OVID

	Search term		Search term continued
1	Early dementia	**39**	self help group
2	Mild dementia	**40**	psychotherapy
3	mild alzheimer*	**41**	CBT
4	early alzheimer*	**42**	Cognitive behavio?ral therap*
5	cognitive impairment	**43**	Cognitive behavioural therap*
6	age related cognitive impairment	**44**	Talking therap*
7	Mild cognitive impairment	**45**	Individual therap*
8	MCI	**46**	Peer support
9	mild neurocognitive disorder	**47**	Counselling
10	**1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9**	**48**	Communication
11	cognitive training	**49**	acupuncture therap*
12	brain training	**50**	acupuncture
13	memory training	**51**	acupuncture points
14	Behavio?r therap*	**52**	Transcranial Magnetic Stimulation
15	Behavio?r modification	**53**	TMS
16	pleasant activit*	**54**	Relaxation therap*
17	Cognitive stimulation therapy	**55**	Therap* relaxation
18	CST	**56**	Relaxation techniques
19	Transcutaneous Electrical Nerve Stimulation	**57**	Early intervention
20	TENS	**58**	Alternative therap*
21	Exercise	**59**	**11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59**
22	exercise therap*	**60**	randomized controlled trial
23	Walking	**61**	randomised controlled trial
24	music therap*	**62**	RCT
15	reminiscence therap*	**63**	Clinical Trial
26	massage therap*	**64**	intervention
27	therap* touch	**65**	**60 OR 61 OR 62 OR 63 OR 64 OR 65**
28	recreation therap*	**66**	early dementia
29	light therap*	**67**	mild dementia
30	therap* light	**68**	mild alzheimer*
31	sensory stimulation	**69**	early alzheimer*
32	multisensory stimulation	**70**	cognitive impairment
33	complementary therap*	**71**	age related cognitive impairment
34	aromatherapy	**72**	Mild cognitive impairment
35	support group	**73**	MCI
36	therap* group	**74**	mild neurocognitive disorder
37	memory group	**75**	**66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75**
38	self help	**76**	**10 AND 59 AND 75**

Supplementary table 2. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	5-6
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5-6
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	6-7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	7
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Table 1
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	9 and Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	9 and Table 2
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Not feasible

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	10-12
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	12
Limitations	20	Discuss the limitations of the scoping review process.	14
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	15
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	15

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.
* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. ;169:467–473. doi: 10.7326/M18-0850

Chapter 7: Discussion

In this chapter, I present an overview of the methods used in this study and their key findings. Next, I discuss how I used the triangulation protocol to integrate the findings from this thesis. The results from the triangulation protocol are presented as meta-themes, followed by a discussion of the strengths and limitations of the findings of this thesis. Finally, I discuss the implications of the findings from the individual phases of analysis and integrated results for policy, future research, and clinical practice.

7.1 Overview of methods and results

This thesis used a mixed-methods design to explore the benefits of an early diagnosis. To address the overall aim of the thesis I conducted three phases of investigation. The first phase of investigation was a retrospective cohort study, using electronic health records from patients who had been diagnosed with dementia by SLaM. During this phase, I investigated whether a previously recorded diagnosis of MCI could be used as a proxy for early diagnosis in quantitative studies. Next, I explored whether an early diagnosis, as defined by a previous diagnosis of MCI, was associated with a reduced risk of mortality, hospitalisation, or health service use. The second phase of investigation was a qualitative study, using semi-structured interviews to explore what benefits people living with dementia and their caregivers perceive to be associated with an early diagnosis of dementia. In the final phase of investigation, I used a scoping review design to chart which measures were used in RCTs testing the effectiveness of non-pharmacological treatments for mild dementia and MCI. I explored whether the use of outcome measures varied by the type of participants or interventions tested and the year of publication. I aimed to explore where the use of outcome measures reflects our understanding of the benefits of an early diagnosis.

7.1.1 Key findings from the individual phases of investigation

Table 7.1 presents the research questions investigated during this thesis, the associated study designs and key findings.

Table 7.1 The phases of investigation, study designs and key findings from this thesis

Research questions	Study Design	Results
Can a diagnosis of mild cognitive impairment before dementia be used as an indicator for an early diagnosis? Are people with an early diagnosis, as defined by a diagnosis of MCI before dementia, at less risk of mortality, visiting ED or being hospitalised?	Phase 1: The secondary data analysis of electronic health care records health by South London and Maudsley NHS Foundation Trust	• A diagnosis of MCI before dementia is a useful proxy for an early diagnosis • Participants with an early diagnosis had fewer symptoms at the time of diagnosis • An early diagnosis was associated with a reduced risk of mortality, but an increased risk of attending ED • There was no difference in the risk of hospitalisation between those with an early diagnosis and those without
What potential outcomes of early diagnosis do people with dementia and their carer givers perceive to be the most beneficial or important?	Phase 2: A qualitative interview study of people living with dementia or MCI, and their carers	• An early diagnosis enables PLwD and caregivers to identify and respond to the evolving needs of people living with dementia. Including: preventing a crisis,

In which particular circumstances is an early diagnosis considered beneficial by people with dementia and their carer givers?		timely decision making and access to services and treatment • There were enablers to the benefits of an early diagnosis including: Adequate prognostic information and treatment, the presence of a caregiver and a willingness to accept the diagnosis
Which outcomes are measured in randomised controlled trials for non-pharmacological interventions in early dementia and mild cognitive impairment (MCI)? And do they reflect our current understanding of the benefits of early intervention?	Phase 3: A scoping review of outcome measures used to evaluate non-pharmacological interventions in mild cognitive impairment and mild dementia.	• There were 91 RCTs testing non-pharmacological interventions in MCI and mild dementia • 358 outcome measures were charted, 78 of which were used more than once • Cognitive measures were the most frequently used followed by BPSD • Caregiver measures and measures of quality of life were less frequently used • The use of outcome measures did not differ by participants, intervention, country or year of publication

During the first phase of investigation, I hypothesised that a diagnosis of MCI could be used as a proxy for an early diagnosis. A small proportion of participants in this study received an early diagnosis (5.6%). These participants had less impaired cognition, activities of daily living and fewer psychiatric symptoms at the time of dementia diagnosis. This profile of symptoms is associated with the earlier stages of the disease, lending confidence to the use of a previously recorded diagnosis of MCI as a proxy for an early diagnosis and confirming my hypothesis. I found that people with an early diagnosis were more likely to be prescribed AChEIs following their diagnosis of dementia. I also hypothesised that an early diagnosis would not be associated with a reduced risk of mortality, hospitalisation or emergency department attendance. Contrary to my hypothesis, participants with an early diagnosis had a reduced risk of mortality compared to those without an early diagnosis (HR = 0.86, CI = 0.77–0.97). However, the benefits of an early diagnosis in terms of health service use were less certain. There was no difference in the risk of hospitalisation between the groups (HR= 0.99, CI= 0.91 – 1.08), however, there was an increased risk of ED attendance for those with an early diagnosis (HR= 1.09, CI= 1.00 – 1.18). There was no difference in the number of days spent in hospital or number of ED attendances between the groups.

The results from the second phase of analysis found that the benefits of an early diagnosis fell under the overall theme of identifying and responding to the evolving needs of dementia. Participants described how a person living with dementia's needs shift as the disease progresses. By diagnosing dementia early, people living with dementia are able to make sense of the symptoms and behaviours associated with the early symptomatic stages of dementia to prevent a crisis. Furthermore, people with an early diagnosis are better able to engage in timely decision making and make plans for the later stages of the disease. Finally, an early diagnosis unlocks access to services and treatments which allow people living with dementia the opportunity to manage and reduce the rate of decline associated with dementia. However, the findings of this study indicated that certain enablers needed to be present to experience the benefits of an early diagnosis. Firstly, participants highlighted the importance of being able

to access prognostic information and effective treatments which addressed their needs at the appropriate time. Secondly, participants felt that the benefits of an early diagnosis were dependent on having a caregiver to advocate on behalf of the person living with dementia. Finally, the benefits of an early diagnosis were dependant on the person with dementia accepting their diagnosis of dementia and the associated post-diagnostic support.

In the final phase of investigation, I extracted the outcome measures used by 91 RCTs testing non-pharmacological interventions. The majority of studies included in this review were testing interventions for participants diagnosed with MCI (N = 72) with fewer studies testing interventions for people living with mild dementia (N = 15) or both participants with MCI and mild dementia (N = 6). The most frequently tested types of interventions were cognitive training (N = 36), physical activity (N = 25), combined cognitive training and physical activity (N = 4), multicomponent psychosocial interventions (N = 4) and support groups (N = 3). I extracted 358 outcome measures used by the included studies. Less than a quarter of these outcome measures were used more than once (22%). Measures of cognition were the most frequently used measures across all studies (N = 219), this did not differ by year or country of publication, type of intervention, or type of participant being tested. The second most measured domain charted was BPSD (N = 51), with depression being the most frequently measured symptom (N = 33). Quality of life was measured 15 times and caregiver measures were used 11 times by the included studies.

7.2 Triangulation of results: The benefits of an early diagnosis

A key feature of mixed methods research is the meaningful integration of qualitative and quantitative data. Therefore, I used the triangulation protocol to identify where the findings over the three phases of investigation overlapped or diverged from each other. This allowed me to draw out meta-themes from the findings of this thesis. Meta-themes were drawn where the findings from two or more phases of investigation overlapped.

Table 7.2 presents a convergence coding matrix, which displays the meta-themes identified, and whether the three phases of investigation agree, partially agree, are in silence or dissonance with the meta-themes.

Table 7.2 Convergence coding matrix displaying meta-themes

Meta-Theme	**Phase 1: Quantitative**	**Phase 2: Qualitative**	**Phase 3: Systematic Review**
An early diagnosis could initiate early treatment; however, there are gaps in our understanding of how these treatments can benefit people with an early diagnosis	A	A	A
An early diagnosis can enable people to live for longer	A	PA	S
An early diagnosis can reduce the risk of hospitalisation or emergency department attendance	D	PA	S
The benefits of an early diagnosis are dependent on individual and sociological factors	PA	A	S

Key: A = agreement; PA = partial agreement; S = Silence; D = Dissonance

7.2.1 Meta-theme 1: An early diagnosis could initiate early treatment; however, there are gaps in our understanding of how these treatments can benefit people with an early diagnosis

This meta-theme suggests that one of the benefits of an early diagnosis is the opportunity to initiate early treatments, however, this thesis also found there are gaps in our understanding of how these early treatments can benefit people with an early diagnosis. Table 7.3 presents the findings from the individual phases of investigation that are relevant to this theme.

Table 7.3 Relevant findings from the individual phases of analysis regarding meta-theme 1: An early diagnosis could initiate early treatment; however, there are gaps in our understanding of how these treatments can benefit people with an early diagnosis

Phase	**Relevant findings**
1: Quantitative	• 38.6% of participants with early diagnosis prescribed AChEIs, compared to 31.5% of participants without an early diagnosis • Data on pharmacological treatments not available • Unclear whether the prescription of AChEIs associated with better outcomes
2: Qualitative	• Access to services and treatments was perceived to be a benefit of an early diagnosis. Participants were aware treatments may be more effective when delivered early in the disease. • participants did not notice any difference in symptoms after taking anti-dementia medications
3: Scoping review	• The investigation of new early treatments for dementia indicates an optimism of the value of early diagnosis in terms of initiating early treatment

- People with an early diagnosis can participate in trials to test new treatments
- This benefit predominantly exists within scientific discourses, wider benefits can only be felt once treatments are found to be effective and become widely available

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Participants in the qualitative phase of this thesis highlighted initiating early treatment as one of the potential benefits of an early diagnosis. Participants in this study received pharmacological treatments (AChEIs and Memantine) and non-pharmacological treatments (support groups and CST) after receiving a diagnosis of dementia. This is supported by findings from the quantitative phase of investigation which found that a greater proportion of participants with an early diagnosis were prescribed AChEI's following a diagnosis of dementia. However, due to how data is stored in the SLaM medical records, it was not possible to analyse whether an early diagnosis of dementia was associated with the prescription of non-pharmacological treatments.

The benefits of an early diagnosis in initiating treatment is supported by the findings of the scoping review. During this phase of investigation, I identified 91 studies testing new non-pharmacological interventions for MCI and mild dementia, 17 of which (18.7%) were published in 2019. This indicates a growing interest in early treatments for dementia within the scientific community. This aligns with the wider discourse in the scientific literature which suggests that an early diagnosis can lead to the provision of early treatments. Furthermore, an early diagnosis allows people living with dementia and their caregivers the opportunity to take part in clinical trials which can aid the effort to find more effective treatments for dementia.

The findings of this thesis are cautiously optimistic regarding the benefits of early treatment in dementia. However, the findings of all three phases of investigation demonstrate there are gaps in the evidence of the benefits of treatments in the early stages of dementia. Firstly, the

studies included in the scoping review used such a wide range of outcome measures that it is difficult to draw conclusions on how they might help people living with dementia and their caregivers. Furthermore, the benefits of early treatments remain theoretical until there is consistency in the use of outcome measures, their effectiveness has been demonstrated, and they become widely available to people living with dementia.

Finally, while it is positive that participants with an early diagnosis in the quantitative study were prescribed AChEIs, it was not clear how taking these medications benefitted participants. This is supported by findings from the qualitative study which found that participants were offered treatment following their diagnosis, however, they did not feel it made any difference to the person living with dementia's symptoms. And in a few cases, participants felt that the medications the person living with dementia were prescribed made things worse. Therefore, this benefit of an early diagnosis was deemed to be dependent on the availability of effective, disease-modifying treatments.

7.2.2 Meta-theme 2: An early diagnosis can enable people to live for longer

The findings of this thesis suggest an early diagnosis of dementia is associated with increased survival following a diagnosis of dementia. However, living for longer with dementia may not be perceived as a benefit by those living with the disease. See Table 7.4.

Table 7.4 Relevant findings from the individual phases of analysis regarding meta-theme 2: An early diagnosis can enable people to live for longer

Phase	Relevant findings
1: Quantitative	• Participants with an early diagnosis had a reduced risk of mortality
2: Qualitative	• Living longer with dementia may not be a benefit for those who are struggling to cope with the disease.

	• Participants discussed the importance of making end of life decisions following an early diagnosis. For some participants, this included making plans for or considering euthanasia.
3: Scoping review	• No measures of mortality were extracted in this review

This meta-theme is supported by findings from the quantitative phase of investigation. People who were diagnosed early were found to have a reduced risk of mortality compared to those without an early diagnosis. However, the strength of the association between an early diagnosis and mortality depended on which measure was used to control for the degree of cognitive impairment at the time of dementia diagnosis. Therefore, these findings should be interpreted cautiously.

The findings of the qualitative study do not provide evidence that an early diagnosis can enable people to live longer with dementia, as the methods used are not appropriate for investigating this outcome. However, they do provide some context as to whether people living with dementia and their caregivers would perceive living longer with dementia to be a good thing. Firstly, participants reported being surprised that the person living with dementia had not deteriorated as quickly as they expected following their diagnosis. This had a negative impact on caregivers' ability to manage the physical and emotional burdens of caregiving. Furthermore, when reflecting on the value of timely decisions following an early diagnosis making some participants (three caregivers and one person living with dementia) discussed considering their options for euthanasia. This indicates that an extended life with dementia may not be considered beneficial for those living with the disease. However, this finding is limited by the small number of people living with dementia in this sample. Further research is needed to explore people with dementia's perspectives of the value of an early diagnosis in terms of extending life.

The findings of the scoping review cannot contribute evidence to this meta-theme as none of the included studies used a measure of mortality. This suggests that this outcome has been assigned less importance than others within the scientific literature.

7.2.3 Meta-theme 3: An early diagnosis can reduce the risk of hospitalisation or emergency department attendance

This theme suggests than an early diagnosis has the potential to reduce the risk of hospitalisation or attending ED. However, the findings of this thesis do not provide strong evidence for this benefit, and the findings of the quantitative study are in dissonance with this theme. See Table 7.5.

Table 7.5 Relevant findings from the individual phases of analysis regarding meta-theme 3: An early diagnosis can reduce the risk of hospitalisation or emergency department attendance

Phase	Relevant findings
1: Quantitative	• Participants with an early diagnosis had an increased risk of ED attendance • There was no difference in the risk of hospitalisation attendance • There was no difference in the length of stay or number of visits to ED between the groups
2: Qualitative	• An early diagnosis of dementia could enable people to receive care that better meets their needs in hospital • Participants acknowledged that interactions with secondary health services were not always positive
3: Scoping review	• No measures of hospitalisation or ED attendance were extracted in this review • This study did not include interventions conducted in inpatient settings

The only findings from this thesis to partially support this theme come from the qualitative phase of investigation. Participants reported being aware that people living with dementia had different needs and priorities from health services following their diagnosis of dementia. Some participants felt that a hospitalisation could have a negative impact on the person living with dementia. The belief that going to the hospital could potentially be harmful to the person living with dementia affected how caregivers made plans for their future care. When her mother developed a chest infection, one caregiver chose to arrange for palliative care to be delivered at home, rather than going to the hospital for treatments. On the other hand, there were cases where knowing a person was living with dementia could lead to better care from hospital

services. An example of this was when one participant's mother with dementia needed a procedure to be done under anaesthetic. The participant was able to tell the clinicians that her mother had dementia and would be distressed when she woke up after the procedure, the clinicians then allowed the caregiver to sit in the recovery room with her mother, which is not usually allowed.

The findings from the quantitative phase of this thesis are in dissonance with this theme. There were high levels of secondary health service use amongst participants in this study. Most participants had a hospitalisation (74%) and/or ED attendance (76%) after their diagnosis of dementia. Furthermore, participants with an early diagnosis were at greater risk of attending ED than participants without an early diagnosis. There was no difference in the risk of hospitalisation between the groups.

None of the outcomes charted during the scoping review measured hospitalisation or ED attendance, therefore it is not possible to conclude how non-pharmacological interventions may affect health service use.

7.2.4 Meta-theme 4: The benefits of an early diagnosis are dependent on individual and sociological factors

This thesis found that the benefits of an early diagnosis are dependent on individual factors and sociological factors. Individual factors are differences between people which lie at the person level, this can include differences in personal characteristics, attitudes, and experiences. The individual factors affecting the benefits of an early diagnosis identified by this thesis are a willingness to seek or accept the diagnosis, active help-seeking behaviours or support from a caregiver. A sociological factor can be described as "the social conditions that affect human behaviour" p.1003 (VandenBos, 2007). The sociological factors found to affect the benefits of an early diagnosis are ethnicity and socio-economic status. Table 7.6 presents the evidence from this thesis that is relevant to this meta-theme.

Table 7.6 Relevant findings from the individual phases of analysis regarding meta-theme 4: The benefits of an early diagnosis are dependent on individual and sociological factors

Phase	Relevant findings
1: Quantitative	• Patterns of health service use following a diagnosis may be influenced by patterns of health service use before diagnosis • Participants with an early diagnosis were more likely to be white • Participants with an early diagnosis had a lower socioeconomic status than participants without an early diagnosis • Participants with a current partner were not more likely to have an early diagnosis
2: Qualitative	• The benefits of an early diagnosis were dependent on the presence of a caregiver to advocate on behalf of the person living with dementia • The benefits of an early diagnosis were contingent on the person living with dementia being willing to accept their diagnosis and post-diagnostic support. Active help-seeking behaviours influenced the acceptance of the diagnosis. • All participants were white and of similar socioeconomic background
3: Scoping review	• Information on participant demographics were not extracted during this review

Firstly, the results of the qualitative phase of investigation found that a key enabler of the benefits of an early diagnosis is the person living with dementia's willingness to accept their diagnosis and following post-diagnostic support. Within this, a person's previous patterns of help-seeking behaviour influenced whether they were likely to accept their diagnosis, with more active help-seeking behaviours reflecting an increased willingness to accept the

diagnosis. This is partially supported by the findings of the quantitative phase of investigation. Participants with an early diagnosis were more likely to attend ED before and after their diagnosis of dementia. This indicates that patterns of help-seeking before a diagnosis of dementia can endure afterwards. However, it was not possible to extract data on the person living with dementia's willingness to accept their diagnosis, therefore this data can only lend limited support to this finding.

The qualitative study also found the presence of a caregiver was a key enabler of the benefits of an early diagnosis. A caregiver was perceived to be essential for advocating on behalf of the person living with dementia and for getting the necessary care from health and social care services. When reflecting on what they might do if they were to develop dementia, caregivers who did not have their own identified caregiver were more worried about their future. This is somewhat in dissonance with the findings of the quantitative study, which found that an equal proportion of participants with and without an early diagnosis were supported by a caregiver, as defined by the presence of a current partner. However, caregivers are not always family members or a current partner. Most of the caregivers who participated in the qualitative studies were children of the person living with dementia. An additional limitation to this meta-theme is that participants in the qualitative phase of analysis were primarily caregivers therefore, they may have placed greater emphasis on the role of the caregiver than people living with dementia. Therefore, these findings should be interpreted with caution.

The quantitative study found sociological differences between the participants with an early diagnosis and those without. A greater proportion of participants with an early diagnosis were white, compared with any other ethnic group. Furthermore, participants with an early diagnosis had a lower socio-economic status (SES) compared to those without an early diagnosis. While it might have been hypothesised that participants with an early diagnosis would be of higher socioeconomic status, there was only a difference of one point between the group which may not equate to a clinically significant difference. Additionally, the London boroughs served by SLaM have become gentrified in recent years, with estates for low income families being

redeveloped into housing for wealthier homeowners (Davidson and Lees, 2005, Lees and Hubbard, 2020). As SES was estimated using the participants postcode, the SES scores presented in this study may not represent the current demographics of these areas.

The findings of the scoping review are not able to lend support or dissonance with this theme, as I did not extract data on the characteristics of participants in the included studies.

7.3 Strengths and limitations

This thesis used a convergent parallel design, where the results from the individual strands of investigation were integrated at the interpretation phase using the triangulation protocol. Integration in mixed methods research aims to produce an outcome that is greater than the sum of its individual qualitative and quantitative components (Fetters and Freshwater, 2015). Meaning, researchers aim to offer insights from mixed methods data that might not be found by looking at qualitative and quantitative data separately (Bryman, 2007). However, there are strengths and limitations of both the individual phases of analysis and of the integration of mixed methods results which must be considered when drawing conclusions in this thesis.

7.3.1 Individual results

One of the proposed strengths of mixed methods research is that the weaknesses of one methodology can be offset by the strengths of another. The following paragraphs present the strengths and weaknesses of the three phases of investigation in this thesis and considers the extent to which they complement each other (see Table 7.7).

Table 7.7 Strengths and weaknesses of the individual phases of analysis

Phase	Strengths	Limitations
1: Quantitative	• Real world data • Data-linkages which reduce risk of bias • Large and diverse dataset	• Variables limited to what is routinely collected • Missing data • MCI before dementia is only a proxy for early diagnosis • Small proportion of participants with an early diagnosis
2: Qualitative	• Grounded in needs and priorities of people living with dementia • Rich description of the lived experience in relation to an early diagnosis • Exploring outcomes outside of the health service management of dementia	• Most participants were caregivers, there were only two participants with dementia • Sample was lacking in diversity
3: Scoping review	• Provided a summary on a broad topic • Exposed weaknesses in the literature	• Did not synthesise evidence on the benefits of non-pharmacological treatments • Some rarer type of dementia were excluded • Few of the included studies were from the UK

Using mixed methods increased the outcomes I was able to explore in relation to the research question. The use of electronic health records as a source of data in the quantitative phase has two advantages, first it allowed me to study the potential benefits of an early diagnosis using real-world data from people living with dementia. This has been cited as a weakness in research on the benefits of an early diagnosis (Dubois et al., 2016). Secondly, I was able to use existing data linkages between SLaM and the ONS and HES, which provided me with more complete data for the outcomes I analysed, increasing the reliability of my findings. However, the variables available for analysis were limited to what is routinely collected. For example, it was not possible to extract data on the provision on non-pharmacological treatments. Therefore, it was only possible to investigate the benefits of an early diagnosis in relation to health service outcomes. Whereas, qualitative methods allow for the deeper exploration of the lived experience of dementia. In this phase of analysis, I was not limited to asking questions about the value of an early diagnosis in relation to health service outcomes. Therefore, I was able to explore how an early diagnosis of dementia might be beneficial in other areas of everyday life. On the other hand, scoping reviews are useful for drawing together all the literature on a given topic. This provided me with the opportunity to explore the how the benefits of an early diagnosis of dementia are conceptualised in the scientific literature. The use of these methods allowed me to explore the potential benefits of an early diagnosis more comprehensively then if I were to use one of these methods alone.

Furthermore, using mixed methods can increase the credibility of the results from the individual phases of analysis. The quantitative phase of analysis was useful for exploring trends within a population but was less able to explain why these trends were observed. In the qualitative study, I was able to contextualise and explore reasons why these trends were observed. Furthermore, the use of PPI for developing the research questions and topic guides allowed me to ground the aims of this study in the needs and priorities of people living with dementia. Similarly, similarities between the qualitative and quantitative phases of investigation lent the qualitative findings more credibility and vice-versa.

However, all phases of investigation are limited by issues of generalisability. Qualitative research does not aim to produce generalisable findings, however, the participants, in this phase of investigation were lacking in diversity. Participants were largely white, middle class, caregivers meaning their experiences may not be representative applicable of all those included in the quantitative phase of investigation. Furthermore, the sample under investigation consisted of 12 caregivers, but only two people living with dementia. The views of people living with dementia may differ from those of caregivers, therefore we cannot conclude that the findings of this phase of investigation are representative of people living with dementia. Similarly, while the quantitative phase included a large and diverse sample of 18,555 participants, these findings cannot be generalised outside of South London. Likewise, the scoping review excluded studies with participants with rarer forms of dementia and few of the included studies were conducted in the UK, limiting the degree to which it can be triangulated against the other components of the thesis.

7.3.2 Integrated results

The potential benefits of an early diagnosis can be explored from multiple perspectives. This thesis aimed aims to explore the benefits of an early diagnosis through the perceptions of people living with dementia and their caregivers, at a population level and through previously published literature on the topic.

One of the challenges of integrating mixed methods research is the degree to which findings from disparate study designs can or should be integrated. This thesis was conducted under the epistemological perspective of pragmatism, which is not committed to any one system of philosophy. On a practical level, it was challenging to compare the results of such different strands of investigation. Furthermore, on an epistemological level, there is disagreement over the degree to which you can integrate mixed-methods details. By using a pragmatic approach to address the aims of the thesis, I did not need to balance the opposing epistemologies (Biesta, 2010). Pragmatism acknowledges that both qualitative and quantitative methods are

valuable for furthering our understanding of complex social issues (Yvonne Feilzer, 2010). Therefore, I was able to select the most appropriate research design for each phase of investigation. While this approach was beneficial, it does limit the conclusions I could draw from this thesis.

It can be difficult to assess how well qualitative and quantitative data have been integrated. Bryman (2007) argues that in a high-quality integration the findings of one component of a mixed-methods design are substantially enhanced by the findings of the other components. In this thesis, the findings of the qualitative study provide a rich description of the trends presented in the quantitative chapters. Similarly, the findings of the quantitative phase of investigation lend validation to the findings of the qualitative phase of the investigation and vice versa. The scoping review aims to address a gap that could not be addressed in the quantitative phase of investigation. By triangulating these findings, I was able to draw cross-cutting meta-themes, which allowed me to make interpretations that take all chapters of this thesis into account.

One of the challenges when integrating mixed methods data is the degree to which the findings of one phase of investigation takes priority over the findings of the other phases (Bryman, 2007). This may be for example, where the findings of one phase are deemed by the researcher to be more interesting and therefore assigned a higher priority during integration (Bryman, 2007). The qualitative chapter was the last empirical chapter I completed, when integrating the data across this thesis I considered cross-checking the findings of the other phases of investigation against the thematic framework I developed in the qualitative chapter. I was concerned that by doing this, I would be giving greater priority to the findings of the qualitative phase over the other two phases of investigation. Although, the findings of the qualitative study provide a compelling and inductive investigation of the benefits of an early diagnosis, this was not compatible with the convergent parallel design of this thesis. Therefore, I coded my findings and grouped these into meta-themes instead.

Assessing where studies agree, partially agree, are in silence or dissonance allowed me to explore the implications of my findings at a broader level. However, there was not much agreement between the phases of investigation in this thesis. All components of this thesis presented evidence supporting meta-theme one (an early diagnosis can initiate early treatment; however, these have limited effectiveness), lending this theme greater credibility. Whereas, there wasn't a total agreement for any other of the meta-themes drawn from this thesis. This is likely to be due to the complexity of the phenomena this thesis is seeking to explore.

The scoping review is in silence with most of the meta-themes for this thesis. Silence is expected when integrating mixed methods studies (O'Cathain et al., 2010), however, it is important to explore why this silence has occurred. There are two reasons why the findings of the scoping review are in silence with most meta-themes. Firstly, the findings of the scoping review may be in silence with the meta-theme because that particular outcome was not extracted as part of the results. An example of this is in meta-theme two (An early diagnosis can enable people to live for longer) were the findings of the scoping review were not able to agree or disagree with this meta-theme because none of the included studies used mortality as an outcome measure. The second reason why there may be silence between the findings of the scoping review and the meta-theme is that some data were not extracted as part of the scoping review procedures. For example, in meta-theme 4 (The benefits of an early diagnosis are dependent on individual and sociological factors) I did not extract data on participant characteristics when conducting the scoping review as this was outside of the aims and scope of the review, therefore I was not able to assess whether there were any differences in the types of participants studied by RCTs of non-pharmacological treatments. This is supported by Farmer and colleagues who suggest that silence may occur due to differences in the contents of the datasets or inherent differences in the methods used (Farmer et al., 2006).

7.4 Discussion

The following section discusses the implications of the findings from this thesis with regards to policy, future research, and clinical practice

7.4.1 Implications for policy

7.4.1.1 The benefits of an early diagnosis as proposed by UK policy

UK dementia policy suggests an early diagnosis and access to earlier treatment can confer several benefits to people living with dementia (Health, 2009). However, the evidence from this thesis does not support these proposed benefits. Table 7.8 presents the benefits of an early diagnosis proposed by UK policy, alongside evidence from this thesis that lends support or disagrees with the proposed benefit.

Table 7.8 The proposed benefits of an early diagnosis and evidence from this thesis

Proposed benefit	**Evidence from this thesis**
Improve quality of life	Few studies in the scoping review included a measure of quality of life Participants in the qualitative study felt an early diagnosis had the potential to improve quality of life, but certain enablers needed to be in place for this to happen
Delay and prevent unnecessary admission into care homes	No studies in the scoping review included a measure for care home admission Findings from the qualitative study show participants perceived an early diagnosis to be beneficial in making timely decisions about future care.
People with dementia can live well for longer	Meta-theme two shows that people with an early diagnosis may live for longer, but this may not be considered a benefit

Reducing costly crisis care	Meta-theme three shows an early diagnosis could theoretically prevent the need for crisis care, however, this is not currently happening in practice.

This thesis did not produce much evidence that an early diagnosis can improve the quality of life for people living with dementia. The results of the scoping review found that only a small proportion of RCTs testing novel non-pharmacological treatments for early dementia included a measure of quality of life. Furthermore, the use of quality of life as an outcome measure has declined over time. Indicating that quality of life has been assigned lower priority in the scientific literature than other outcomes, such as cognition. While it is not possible to draw inferences on the potential of non-pharmacological treatments to improve quality of life for people living with dementia, the absence of these measures highlights a key weakness in the scientific evidence supporting this proposed benefit of an early diagnosis. This is concerning as people living with dementia and their caregivers have rated quality of life as the most important outcome. Participants in the qualitative study did not explicitly discuss quality of life. However, participants felt by being able to identify and respond to the evolving needs of the person living with dementia, they would be able to live better. This indicates that from the perspective of caregivers and people living with dementia, an early diagnosis could have a beneficial impact on quality of life. Although, they also described how this benefit could only be felt if people living with dementia have access to timely prognostic information and disease modifying treatments, were willing to accept their diagnosis and were supported by a caregiver.

The findings of this thesis cannot contribute much evidence to whether an early diagnosis is associated with a reduced risk of care home admission, however, it does contribute to the debate on whether admission to a care home is perceived as a negative outcome. Similar to measures of quality of life, the scoping review did not chart any measures of care home admission. Indicating that this outcome has been assigned lower priority in the scientific

literature. UK policy presents admission into a care home as a negative outcome, however, there is some evidence that attitudes are changing. A care home is the second most preferred place of death (at home was the most preferred) for people living with dementia (Wiggins et al., 2019). This emphasises the importance of allowing people with dementia to make decisions regarding their future care.

The findings of the qualitative study found that one of the perceived benefits of an early diagnosis is the opportunity to make timely decisions about care. However, participants felt it was difficult to be sure when is the right time for the person living with dementia to transition to the next stage of care and worried about the potential negative consequences. This is supported by a qualitative study exploring social care professional's views on the optimal time to transition care, which found participants felt it was important that people living with dementia should stay at home for as long as possible, so long as they are safe (Cole et al., 2021). However, the findings of the qualitative chapter also showed that making timely decisions about care was limited by the perceived volatility of the care sector and the amount of private funding available to the participant. Participants from the qualitative study, worried that if they picked a care home too far ahead of time, the manager of the home would change before they moved in. Furthermore, those who had no access to private funds, were frustrated with the lack of choice over care. However, if people living with dementia who are funding their care privately move to a care home too early, there is a risk they will run out of private funds (Cole et al., 2021). Therefore, an early diagnosis may be beneficial in terms of making timely decisions about care, however, this is dependent on how care is funded and made available to people living with dementia.

Another of the proposed benefits of an early diagnosis from UK policy is that it can enable people with dementia to live well for longer. It's not clear what is exactly is meant by "living well for longer", but research on chronic disability has defined living well as 'the best achievable state of health that encompasses all dimensions of physical, mental and social well-being' (Wallace et al., 2012). Meta-theme two, an early diagnosis can enable people to

live for longer, demonstrated that an early diagnosis was associated with increased survival, however, I did not investigate whether an early diagnosis of dementia was associated with a reduced trajectory of physical or cognitive decline. Meaning that participants were living longer, but it was unclear if they were staying well for longer. This is an important area for further research.

Furthermore, the emphasis on living well with dementia has been criticised as it can deny suffering. As suffering to some degree is an inescapable reality of living with a terminal illness, it is important that clinicians, researchers and policymakers recognise this and investigate ways to alleviate this (Bartlett et al., 2017). Some participants, both living with dementia and their caregivers, in the qualitative phase feared a long life with dementia and discussed the value of an early diagnosis in weighing up options for euthanasia. This indicates that not all people diagnosed with dementia want to live well, some do not want to live with dementia at all (Wilkinson, 2015). Therefore, not only is there little evidence that an early diagnosis can keep people with dementia living well for longer; as a policy objective, it may not reflect the needs or reality of living with dementia.

It has been proposed that an early diagnosis of dementia can reduce the risk of costly, and potentially harmful crisis care. The findings of meta-theme three demonstrate a divergence in the evidence on this potential benefit of an early diagnosis. The findings of the quantitative study did not support the hypothesis that an early diagnosis can lead to fewer hospital admissions or visits to the ED. On the contrary, participants with an early diagnosis had an increased risk of attending ED. However, a greater proportion of participants with an early diagnosis had also attended the ED before their diagnosis, indicating that patterns of health service use may continue after diagnosis. This is concerning as ED attendances can be reflective of fractured care for people living with dementia (Sleeman et al., 2018). On the other hand, the findings of the qualitative study presented mixed evidence for the potential for an early diagnosis to lead to more responsive health care from secondary care services. By receiving a formal diagnosis, there was the opportunity for people living with dementia to

receive care and support that was appropriate to their condition. A review of nursing practices for supporting people living with dementia in hospital found that getting to know the person and building a relationship, involvement of families, flexible and creative care approaches, use of comfort and communication were essential for delivering quality person-centred care (Baillie et al., 2012). However, where the person was not receiving person-centred care in hospital settings, participants in the qualitative study felt that going to the hospital did more harm than good. The findings of this thesis do not support the policy statement that an early diagnosis reduces the risk of hospitalisation. Future research should investigate the role of post-diagnostic support and social care provision in reducing hospitalisations and ED attendances.

7.4.2 Implications for Research

The findings of this thesis do not support the discourses used in scientific papers to justify the benefits of an early diagnosis. In 2011, the authors of the World Alzheimer's report reviewed statements in peer-review journals supporting the benefits of an early diagnosis. They found the assertions to be lacking in empirical support, stating "Many were unreferenced, and where references were provided these were generally to other papers making similar, non-evidence-based assertions. These statements should therefore be considered, at best, to represent expert opinion" p.27 (Prince et al., 2011). The findings of the thesis indicate the benefits of an early diagnosis are nuanced and highly dependent on contextual factors. By not critically assessing the beliefs held by the scientific community, there is a risk of missing important areas of investigation which can improve the lives and care of people living with dementia. The following paragraphs consider the implications of the findings of the thesis for future research.

7.4.2.1 Detecting dementia early

There is considerable effort being made in research that can identify dementia earlier in the disease. One of the most promising developments in this area is the potential for a blood test to detect dementia while pre-symptomatic (Janelidze et al., 2020). While these are exciting

scientific developments, they must also go hand in hand with developments in the clinical and social management of dementia. An unintended consequence of the drive to find a cure for dementia is that there has been less investment in other areas of dementia research (Pickett et al., 2018). Previous research testing novel biomarkers for the early stages of the disease have questioned the clinical utility of such efforts without corresponding treatments (Livingston et al., 2017). This is supported by the findings of this thesis, which demonstrates that an early diagnosis alone, is not sufficient to improve outcomes for people living with dementia. As we come closer to more reliable predictive tests for dementia, research is needed to understand the advantages and disadvantages of an early diagnosis, and how to improve the clinical management of the early stages of dementia.

More critical research is needed to assess the potential benefits of an early diagnosis, using all types of study designs. The findings of the quantitative phase of investigation presented a method for identifying those with an early diagnosis in epidemiological datasets. This can be used to explore the potential benefits (as well as harms) with other outcomes. However, it is also important that people living with dementia and their caregivers are also represented in research on the benefits of an early diagnosis. The absence of the voices of people living with dementia has been noted in multiple areas of study. While this thesis has aimed to explore the benefits of an early diagnosis from the perspective of those affected by the disease, only two people living with dementia were interviewed. Therefore, the findings of this thesis may be more reflective of the views of caregivers than people living with dementia. Further qualitative research with a larger sample of people living with dementia is needed to understand what they perceive to be the benefits of an early diagnosis. As qualitative methods provide important insights into the lived experience of dementia, they should not be neglected in favour of other methods of investigation. Systematic reviews are considered to be the gold standard of evidence on a topic, however, the paucity of research on the benefits of an early diagnosis makes it difficult to draw together research on this area.

7.4.2.2 Research to find new disease-modifying treatments

There is also a need for a greater number of effective treatments for the early stages of dementia. If we are to follow the principles of person-centred care in the post-diagnostic support for people living with dementia, then we should be offering a range of treatments where the person living with dementia can pick the one that best suits their needs. However, the options for dementia-specific treatments within the UK's National Health Service are limited to two types of drug treatments (AChEIs and memantine) and two types of non-pharmacological treatments (support groups and CST) (Department of Health, 2007). For more treatments to become widely available, more research is needed in this area. The scoping review indicated that many treatments are being trialled in early dementia and MCI, however the variety of outcome measures used in research in this area limit the degree to which studies can be compared to each other. This issue is not unique to non-pharmacological treatments, pharmacological treatments tend to use cognitive outcomes over other outcomes. Although this is to be expected to some extent, as pharmacological treatments aim to address the underlying pathology that causes dementia and its symptoms. However, people living with dementia, MCI and their caregivers have rated quality of life as the most important outcome. Cognitive outcomes have previously been used as a proxy measure of quality of life in pharmacological trials, however, research has shown that cognition is not correlated with quality of life (Banerjee et al., 2006). For new treatments that make a difference to the lives of people with dementia and their caregiver, researchers must be more consistent in their use of outcome measures and include the domains which are the most important to the people impacted by dementia.

Future research on the benefits of early treatments in dementia should also consider the role of caregivers. Caregivers are often necessary for the person living with dementia to take part in clinical trials, however, they are often not included in the intervention and caregiver measures are not captured. A participant living with dementia in the qualitative phase of analysis voiced her frustration at not being able to take part in clinical trials for novel dementia

treatments because she was not supported by a caregiver. The presence of a caregiver to act as a proxy is common in many clinical trials. This presents a barrier for some people who receive an early diagnosis to take part in research to find a cure, which is a commonly cited benefit of an early diagnosis (Dubois et al., 2016). Another interesting area for future research is the value of dyadic treatments for the person living with dementia and their caregivers. Of the 91 included studies in the scoping review, only 8 were dyadic. Another weakness in our understanding of the benefits of early interventions for caregivers is the lack of caregiver measures used, out of the 78 measures we charted which were used more than once only 11 were caregiver measures. The caregiver's and the person living with dementia's outcomes are reciprocally linked (Lea Steadman et al., 2007, Woods et al., 2014). We should ensure that both groups should equally benefit from taking part in research seeking to find new treatments for dementia.

7.4.2.3 Inequalities in the benefits of an early diagnosis

Meta-theme 4 of this thesis showed that the benefits of an early diagnosis were contingent on individual and sociological differences. Future research must investigate the causes and ways of eliminating inequality in the benefits of an early diagnosis. The quantitative phase of investigation found that a greater proportion of people with an early diagnosis were white compared with those from other ethnic groups. However, participants without an early diagnosis had a higher SES. It is possible that people with an early diagnosis were more likely to be white and of lower SES due to shifting demographics in South London. Despite having a greater risk of dementia (Adelman et al., 2009, APPGo, 2013), there is evidence that people from minority ethnic groups are likely to present to services later than white people with dementia (Mukadam et al., 2011). To increase equity in the benefits of an early diagnosis, we must first understand why minority ethnic groups do not receive an early diagnosis. A qualitative study of reasons for a delayed diagnosis found that participants from minority ethnic groups reported not seeking a diagnosis until caring for the person living with dementia at home was unmanageable (Mukadam et al., 2011). This is supported by findings that people

from minority ethnic groups were more likely to seek a diagnosis in response to a crisis (Hinton et al., 2004). Next, we must understand the perceived harms and benefits of an early diagnosis from the perspective of those who belong to minority groups. It is a limitation of the qualitative phase of investigation that all the participants were white, therefore the conclusions from this study cannot be applied to minority groups. This is an important area for future research.

The qualitative phase of investigation found that the presence of a caregiver was perceived to be an enabler of the benefits of an early diagnosis. Participants felt that people who did not have the support of a caregiver were at risk of receiving poorer care. Approximately 75% of people living with dementia in the USA are supported by a family or friend acting as an informal caregiver (Schulz and Martire, 2004). The effects of caregiving on caregivers is well documented. They are at greater risk of caregiver burden depression, anxiety, and a financial burden (Brodaty and Donkin, 2009). However, there are no studies on the impact of not having an informal caregiver on people living with dementia. Future research is needed to understand whether people living with dementia who are not supported by a caregiver have different outcomes compared to those supported by a caregiver.

7.4.3 Implications for practice

7.4.3.1 The timely diagnosis of dementia

In recent years, the discourse surrounding the diagnosis of dementia has shifted from advocating for an “early diagnosis” to advocating for a “timely diagnosis”. This largely due to an increased awareness of the need for person-centred approaches to giving a diagnosis of dementia (Watson et al., 2018). An early diagnosis is given as soon as possible, however, a timely diagnosis, which respects the preferences of the patient, may be given at the onset of symptoms or not at all (Dhedhi et al., 2014). Several large surveys have found that almost all people (between 92-96%) would want to be told of their diagnosis if they had dementia (Dautzenberg et al., 2003, Turnbull et al., 2003, Watson et al., 2018). Furthermore, one survey of health care users over the age of 18 in Australia found that 88% of respondents would like

to receive their diagnosis as early as possible (Watson et al., 2018). While these findings indicate that for most people a timely diagnosis is an early diagnosis, the participants of this study were making a hypothetical judgement. These methods cannot capture the nuanced experience of the onset of dementia, where it is difficult to distinguish the symptoms from normal ageing. The findings of the qualitative chapter of this thesis indicate that a willingness to accept the diagnosis is key to unlocking the benefits of an early diagnosis.

This supports the idea that a timely diagnosis may be beneficial to people living with dementia. However, perceptions of a timely diagnosis may differ between the person living with dementia and their caregiver. A systematic review of preferences in the disclosure of the diagnosis found that most caregivers wanted to be informed of the diagnosis (Werner et al., 2013). This may be linked to the caregiver's desire to make practical plans to support the person living with dementia. Indeed, research has shown that within three months of the diagnosis, caregivers have started to access and organise practical support for themselves and the person living with dementia (Vernooij-Dassen et al., 2006). This is also reflected in the findings of the qualitative study, where most of the participants were caregivers. Timely decision making and access to services and treatments were perceived to be benefits of an early diagnosis. Therefore, a timely diagnosis should also aim to balance the needs and values of both the person living with dementia and the caregiver.

One previously identified barrier to a timely diagnosis is the attitudes and beliefs of the clinicians making the diagnosis. Research has found that GPs can be reluctant to make a diagnosis due to the perception that nothing can be done (Dhedhi et al., 2014). The findings of this thesis, particularly meta-themes one (early diagnosis and mortality) and meta-themes two (early diagnosis and health service use), do not provide evidence against these nihilistic attitudes. However, they also do not present evidence that there is no value to an early diagnosis. Meta-theme one highlighted that across the phases of analysis, access to earlier treatment was a reoccurring benefit. However, it also highlighted that it was not clear how well these treatments worked, or the differences they made to people living with dementia.

However, participants in the qualitative study were hopeful they would find services, treatments or coping strategies that worked for them. As a diagnosis of dementia unlocks access to post-diagnostic support, we must do more to reduce this barrier to a timely diagnosis.

7.4.3.2 Post diagnostic support

It is essential that people living with dementia not only have access to a high quality and timely diagnosis, they must also be able to receive high-quality and timely post-diagnostic support. The findings of this thesis highlight several weaknesses in the provision of post-diagnostic support in the UK. Firstly, there is a gap between UK dementia policy and practice. The dementia care pathway recommends that people living with dementia should receive an annual follow-up from the memory clinic. Participants in the qualitative phase felt that having a regular follow-up appointment would enable them to receive timely prognostic information and advice which would help them better cope with the symptoms of dementia. However, this was generally not happening in practice. Secondly, evidence from the quantitative phase of investigation suggested that the provision of post-diagnostic support in the UK was not sufficient to keep people living with dementia from being hospitalised or attending the ED. Two-thirds of all participants in the quantitative phase of investigation had a hospitalisation and/or ED attendance, reflecting a high use of secondary health care. However, as we were not able to distinguish between essential and emergency hospitalisations in this study, I am limited on the conclusions I can draw on this point. The study of whether an early diagnosis leads to an increase or decrease in emergency hospitalisations is an important area for further research.

Participants in the qualitative phase also reported a desire for a single source of information, where people living with dementia and their caregivers would be able to receive advice for both managing dementia and co-morbid diseases. Memory clinics were initially developed to be a single point of contact for managing the care of people living with dementia. The Croydon Memory Service Model was developed to be responsive to the needs of people living with

dementia (Banerjee et al., 2007). Within this model of service delivery, a diagnosis of dementia would be made by those with specialist training, then a management plan would be drawn up for the person living with dementia in consultation with multi-disciplinary teams and patients have access to specialist dementia advisors (Willis et al., 2010). However, in the development of the Croydon Memory Service Model, there were no explicitly stated goals for including or evaluating the management of co-morbid conditions). People living with dementia are more likely to have multi-morbidity (as defined by two or more long term diseases (Salive, 2013)) than cognitively healthy older adults of the same age. This was reflected in the findings of the quantitative phase where 56% of the sample had a high level of co-morbid illness and/or disability. Clinical guidelines have been criticised for their focus on singular disorders, which do not take multiple conditions into account (Guthrie et al., 2012). There is evidence that treatments that focus on singular disorders do not work as well for individuals with multiple conditions (Banerjee, 2015) and people living with dementia and co-morbid conditions have poorer outcomes. For example, people living with dementia are less likely to be diagnosed with treatable diseases (Larson et al., 1984). As memory clinics were initially designed to manage the care for people living with dementia, further research is needed to explore how these services can better support people with dementia and multi-morbidity.

7.5 Conclusions

The findings of this thesis show that the benefits of an early diagnosis are not as straight forward as previously thought. Policy objectives supporting the drive to diagnose more people earlier in the disease are lacking in empirical support and may not reflect the needs of people living with dementia. Where disease modifying treatments are not available, people living with dementia and their caregivers value services and support which can improve quality of life. Policy should therefore focus on initiatives to improve post-diagnostic support for all people living with dementia. The thesis has highlighted inequalities both in who receives an early diagnosis and how they benefit from it. Accessing treatments and support is a key benefit of an early diagnosis. However, more research is needed to make a greater number of

pharmacological and non-pharmacological treatments available for the early stages of dementia. It is also important that we review how services deliver care for people living with dementia. Previous dementia policy has created memory services to be a one stop shop for people living with dementia. This initiative is welcomed by people living with dementia and their caregivers; however, it is not clear that these services are operating in the way they were intended to. Creating more responsive services which enable the benefits of an early diagnosis does not necessarily mean we should look to develop new models of care; it can mean creating standards, initiatives, and indicators that these standards are being met in practice.

7.6 References

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Appendix A: Topic guides

Identifying the benefits of early diagnosis in dementia

Topic guide for carers

Experiences of the person living with dementia receiving the diagnosis

Tell me about when you first started to notice problems with [name of PLwD]'s memory?

What did you initially attribute [PLwD]'s to? What did you think was causing their memory problems?

Did you speak to anyone about [PLwD's] memory problems?

When did you decide to seek help for [name of PLwD's] memory problems?

Would you usually go to the doctors?

Can you tell me about the experience of getting the diagnosis of dementia? Prompt on:

- Expectations of diagnosis (e.g. what did you expect to happen? Were those expectations met? Hopes? Worries?)
- What was the process of getting a diagnosis? E.g. memory tests
- What was the impact of the diagnosis on you (e.g. emotional, practical etc.)
- What was impact on [PLwD]? (e.g. emotional, practical, etc.)
- What was helpful/unhelpful in this experience?

Reflecting on your experience of diagnosis, are there any ways in which you think finding out about [PLwD]'s diagnosis sooner would have helped, or do you feel you found out at the right time? Why?

What did the diagnosis mean for [PLwD]?

Experiences of post-diagnostic support

When you went for the diagnosis, did you expect [PLwD] to receive any treatment (e.g. drug treatment, cognitive therapies, group support)?

Did you or [PLwD] receive any treatment or support?

Prompt on:

- Common dementia drug treatments
- Cognitive stimulation therapy
- Occupational therapy

- Support groups
- Invitations to take part in research
- Carer's assessment
- Carer's support group
- Local authority services

If yes, can you tell me a little bit more. What was your experience of receiving this treatment/support? What was helpful or unhelpful.

Did you stop using this treatment/support? If yes, why?

Did you access any other forms of support? (e.g. church) Why? Can you describe what type of support you received and how this was helpful or unhelpful?

What support do you think is needed for PLwD or cargivers, especially in the early stages of dementia?

Is there any support that you didn't have but wish you did? If yes, what was it and how would this have helped?

Did the diagnosis change how you think or feel about memory problems?

Experiences of Health Services

Have you used any health services including:

- GP
- A&E
- hospital stays
- care homes

If yes, tell me about that experience? Why did you use this service? What was helpful or unhelpful?

Planning for the future

- Have you or [PLwD] made any plans for their future?
- If yes, can you tell me about them?
- How has [PLwD]'s diagnosis affected these plans? Did your plans change as they disease has been progressing?

Concluding questions

Thank you for answering my questions, is there anything else you would like to tell me about your experiences which I haven't asked about?

Identifying the benefits of early diagnosis in dementia

Topic guide for PLwD

Experiences of the person living with dementia receiving the diagnosis

Tell me about when you first started to notice problems with your memory?

What did you think was causing your memory problems? Did you think it was a problem?

How did you decide to seek help for your memory problems?

Can you tell me about the experience of getting the diagnosis of dementia? Prompt on:

- Expectations of diagnosis (e.g. what did you expect to happen? Were those expectations met?)
- What was the impact of the diagnosis on you (e.g. emotional, practical etc.)
- What was helpful/unhelpful in this experience?

Reflecting on your experience of diagnosis, are there any ways in which you think finding out about [PLwD]'s diagnosis sooner would have helped, or do you feel you found out at the right time? Why?

Experiences of post-diagnostic support

When you went for the diagnosis, did you expect to receive any treatment or support?

Did you receive this treatment or support?

What treatment/support did you receive?

Prompt on:

- Common dementia drug treatments
- Cognitive stimulation therapy
- Occupational therapy
- Support groups
- Invitations to take part in research

If yes, can you tell me a little bit more. What was your experience of receiving this treatment/support? What was helpful or unhelpful.

Did you stop using this treatment/support? If yes, why?

Did you access any other forms of support? (e.g. church) Why? Can you describe what type of support you received and how this was helpful or unhelpful?

Was there any support which you did receive, which you wish you had received earlier?

Is there any support that you didn't have but wish you did? If yes, what was it and how would this have helped?

Experiences of Health Services

Have you used any health services including:

- GP
- A&E
- hospital stays
- care homes

If yes, tell me about that experience? Why did you use this service? What was helpful or unhelpful?

Planning for the future

- Have you made any plans for their future?
- If yes, can you tell me about them?
- How has you diagnosis affected these plans? Did your plans change as the disease has been progressing?

Concluding questions

Thank you for answering my questions, is there anything else you would like to tell me about your experiences which I haven't asked about?

Appendix B: HRA Approval Letter for Qualitative Study

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Matthew Prina
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24 September 2019

Dear Dr Prina

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Exploring the perceived benefits of early diagnosis and early intervention in dementia: a qualitative study**
IRAS project ID:	**241432**
REC reference:	**19/WA/0210**
Sponsor	**King's College London**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **241432**. Please quote this on all correspondence.

Yours sincerely,
Anne Gell

Email: HCRW.approvals@wales.nhs.uk

Copy to: *Dr Carol Cooley*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [King's College London Insurance]		09 July 2018
GP/consultant information sheets or letters [Letter to GP]	1	01 August 2019
Interview schedules or topic guides for participants [Carers]	1	01 August 2019
Interview schedules or topic guides for participants [Provisional Topic Guide]	1	28 May 2019
IRAS Application Form [IRAS_Form_27062019]		27 June 2019
Letter from funder		12 April 2017
Letter from sponsor [Letter from Sponsor]		26 June 2019
Other [Consultee Consent Form]	2	27 March 2019
Other [Consultee Information Sheet]	4	31 July 2019
Participant consent form [Participant Consent Form]	5	31 July 2019
Participant information sheet (PIS) [Participant Information Sheet]	4	31 July 2019
Research protocol or project proposal [Exploring the benefits of early diagnosis and early intervention protocol]	3	20 June 2019
Response to Request for Further Information		03 August 2019
Summary CV for Chief Investigator (CI) [Dr Matthew Prina CV]		
Summary CV for student [Elyse Couch CV]		
Summary CV for supervisor (student research) [Dr Vanessa Lawrence CV]		

IRAS project ID	241432

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
Single site, same sponsor.	This is a single site study sponsored by the participating NHS organisation. You should work with your sponsor R&D office to make arrangements to set up the study. The sponsor R&D office will confirm to you when the study can start following issue of HRA and HCRW Approval	Single site, same sponsor.	No funding available to sites.	Local Collaborator required at site.	Use of identifiable patient records held by an NHS organisation to identify potential participants without their prior consent should be undertaken by a member of the direct care team for the patient, so it would not normally be acceptable for this to be done by staff not employed by that organisation. The activities at the participating NHS organisation will be undertaken by local staff therefore it is expected that adequate contractual relationship with the host organisation are already in place. Where contractual arrangements are not already in place, network/external staff (or similar) undertaking research activities would be expected to obtain Honorary Research Contracts on the basis of a Research Passport (if university employed) or a Letter of Access on the basis of an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). Enhanced DBS checks (incl. appropriate barred list checks) and occupational health clearance would be appropriate.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.

Appendix C: Participant information sheet

NHS South London and Maudsley NHS Foundation Trust

KING'S College LONDON

Exploring the benefits of early diagnosis and intervention in dementia

Information sheet for participants (V5 22/06/2020)

IRAS ID: 241432

Invitation to take part in a research study

We would like to invite you to take part in a research study. Before deciding whether you would like to take part, it is important for you to understand what it will involve. Please take time to read the following information carefully. Please feel free to ask us if there is anything that is not clear, or if you would like more information. It is important you understand that you do not have to take part and that if you do agree to participate you are free to withdraw at any time without having to give a reason.

What is the study about?

The number of people living with dementia in the UK is growing. Dementia is a difficult condition to treat and manage. It is thought that early diagnosis can lead to better outcomes for people with dementia including living well for longer however, the scientific evidence to support these statements is weak.

Policy in the UK has highlighted the importance of early diagnosis in the management of dementia. Early diagnosis means diagnosing dementia as soon as the symptoms become apparent, but this can be a challenge. Mild cognitive impairment is a condition where a person experiences cognitive impairment that is greater than expected for their age but does not meet the criteria for dementia. A significant proportion, but not all, of people who have mild cognitive impairment go on to develop dementia; this means that a diagnosis of mild cognitive impairment presents the opportunity to diagnose dementia early.

Although the scientific evidence of the benefits of early diagnosis is not clear, many people living with dementia believe an early diagnosis is important. Therefore, the aim of this study is to understand what people who have been diagnosed with dementia or mild cognitive impairment and their carers think are the benefits of diagnosing dementia early.

This study forms part of a PhD project investigating the benefits of diagnosing dementia early.

Why have I been invited to take part?

We are inviting you to participate because you have received a diagnosis of dementia, or mild cognitive impairment, or you are caring for someone with a diagnosis of dementia or mild cognitive impairment.

We would like to interview you to understand your experiences of diagnosis and any treatment or support you received after the diagnosis.

Do I have to take part?

We would like to invite you to take part in the study, but whether or not you do so is entirely up to you. If you decide not to take part, you do not have to give a reason, and this will not affect you or your care in any way.

How long do I have to decide?

There are no time limits on making this decision. You may take your time to decide whether you want to take part.

What will happen in the study?

In the study, we will interview between 12 and 20 people with a diagnosis of dementia or mild cognitive impairment and between 12 and 20 of their carers. Interviews will be one on one between the participant and the researcher. Interviews can be held face to face, over the phone or online on Microsoft Teams. Where is it

not safe to meet in person due to COVID-19, all interviews will be done over the phone or online. The interview will be audio recorded. We will ask participants questions about their diagnosis and what treatments and support they have had since their diagnosis.

Once the interview has been completed, the audio recording will be transcribed into a word document. We will analyse all the interviews together to identify common themes.

Why are you asking for the details of my GP?

If you have not been referred to the study by South London and Maudsley NHS Foundation Trust, we need to contact your GP prior to your taking part to confirm you have received a medical diagnosis of dementia or mild cognitive impairment.

Once you are enrolled in the study, the researcher would only contact your GP if they feel there is a significant risk to yourself or others.

What will happen if I take part?

Before agreeing to take part, a researcher will explain the study to you and provide this information sheet. You will have the opportunity to ask the researcher any questions you have about taking part. If you do want to take part the researcher will ask you to sign a consent form. If you are taking part by phone or online the researcher will ask for verbal consent.

Once you have given your consent to take part in the study researcher will contact you to arrange a time and place to do the interview. The interview can be done at a time and place of your choosing. You will be reimbursed for any travel costs. However, where it is not safe to meet face to face, due to COVID-19, interviews will only take place over the phone or on Microsoft Teams.

On the day of the interview the researcher will ask you questions from a pre-prepared list, this will take approximately 45 minutes. With your permission we would like to audio-record the interview.

What are the possible benefits of taking part?

While there are no direct benefits to you for taking part, the information that you provide will be valuable in helping us understand how health services can better support people who are diagnosed with dementia.

What are the potential disadvantages and risks of taking part?

There are limited disadvantages to taking part and no risks. Potential disadvantages include the time commitment required to participate in the study and you may find talking about your experiences distressing. The researcher will try to minimize this by offering you a break, to skip the question, or to end the interview. All information will be kept strictly confidential and will only be accessed by members of the research team.

How will my information be kept confidential?

All information you give will be kept anonymous. You will be assigned a participant ID number when you enroll in the study and the audio recording of your interview will be saved using your participant ID and not your name.

The answers you give during the interview will remain confidential unless the researcher feels there is a significant risk to yourself or others. The researcher will tell you if they need to break confidentiality.

The audio recording of your interview may be transcribed by the transcription service Way with Words. This service is NHS approved and will keep the recordings confidential. See here for more information on their privacy policy:
https://waywithwords.net/privacy-policy/

How will my data be used in compliance with General Data Protection Regulation?

King's College London (KCL) is the lead sponsor for this study based in the United Kingdom. We will be using information from you [and your medical records] in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. KCL will keep identifiable information about you for 1 year after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

For more information about Microsoft Teams privacy policy, please follow this link: https://docs.microsoft.com/en-us/microsoftteams/security-compliance-overview.

You can find out more about how we use your information by contacting the Chief Investigator Dr Matthew Prina, Matthew.Prina@kcl.ac.uk, or visiting the KCL website: https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research.aspx.

South London and Maudsley NHS Foundation Trust will collect information from you and/or your medical records for this research study in accordance with our instructions.

South London and Maudsley NHS Foundation Trust will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is

recorded for your care, and to oversee the quality of the study. Individuals from King's College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. South London and Maudsley NHS Foundation Trust will pass these details to King's College London along with the information collected from you and/or your medical records. The only people in King's College London who will have access to information that identifies you will be people who need to contact you to invite you to take part in the study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

All the data you provide will be stored in accordance with General Data Protection Regulation. Paper copies of consent forms will be stored in locked filing cabinets and electronic copies will be saved on an encrypted, password protected computer which is only accessible to members of the research team. The paper and electronic copies of the data you provide will be kept for 7 years after the end of the study.

Why do you want to keep my contact details for two years?

We would like to keep your contact details for up to two years after the study to let you know about other opportunities for future involvement in this study. This is optional, if you say no this will not affect your participation and your contact details will be kept for one year in accordance with General Data Protection Regulation.

What will happen if I don't want to carry on with the study?

You are free to change your mind at any time, without any consequences. Please contact the researcher and let them know that you would like to withdraw.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researcher who will do their best to answer your questions. You can also contact the chief investigator Dr Mathew Prina (matthew.prina@kcl.ac.uk). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. The address for the Patient Advice and Liaison Service (PALS) where you can complain is provided on page 8 of this document.

Who is organizing and funding the research?

This research is funded by a PhD studentship from the Economic Social Research Council's London Interdisciplinary Social Science Doctoral Training Partnership. It is being led by King's College London and is sponsored by South London and Maudsley NHS Foundation Trust.

How have patients and the public been involved in this study?

Public and patient involvement in this study has been provided by the MALADY Dementia Service User and Carer advisory group at The National Institute for Health Research Biomedical Research Centre. The group has provided feedback on the study design, topics to be discussed in the interviews, recruitment methods, and dissemination plans. They have also provided feedback on the participant information sheets and consent forms.

Who has reviewed and approved this study?

This study has been reviewed and approved by Health and Care Research Wales (REC ID: 19/WA/0210).

What will happen to the results of this study?

When the study has been completed the results will be presented in a final study report, at national and international meetings and published in scientific and academic journals. No individual will be

identified in any publication or meeting. Copies of the published results will be available on request.

What do I do now?

Thank you for taking the time to consider the study and for reading this information. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

PALs

PALS, The Maudsley Hospital, Denmark Hill, London SE5 8AZ

Freephone: 0800 731 2864

Email: pals@slam.nhs.uk

Who do I contact for information?

If you would like more information about this research project, please contact:

Elyse Couch
PhD Student
Health Service and Population Research Department
Institute of Psychiatry, Psychology and Neuroscience, King's College London
David Goldberg Centre
De Crespigny Park, Denmark Hill
London SE5 8AF

Email: elyse.couch@kcl.ac.uk
Telephone: 07403169417

Thank you for considering taking part in this research study

Appendix D: Consent form (before COVID-19)

NHS South London and Maudsley NHS Foundation Trust

KING'S College LONDON

Exploring the benefits of early diagnosis and intervention in dementia

Consent form for participants (V5 31/07/19)

To be completed by researcher:	IRAS ID: 241432
Participant ID: _ _ _	Participant DOB _ _ / _ _ / _ _ _ _

Please initial by each statement to show you have read it and agree	**Initials**
I have read and understood the information sheet dated 31/07/19 (version 4) and have had the chance to ask questions	
I understand that my participation in the research interview is voluntary and that I can change my mind at any time	
I understand that participation in this research involves being audio-recorded. I give permission for the interview to be audio-recorded, on the understanding that the interview will be transcribed, and direct quotations may be reproduced in reports and publications, but all identifying information will be removed.	
I give permission for the research team to contact my GP about my participation in this study. I am aware that my GP may be notified if there are concerns about my health or safety during my participation in this study.	
I give permission for the research team to contact my GP to confirm my diagnosis or dementia or mild cognitive impairment (this does not apply to participants who are carers)	
I understand that relevant sections of my medical notes (excluding carers) and/or data collected during the study, may be looked at by individuals from King's College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records/data	
I agree to take part in the above study	

OPTIONAL

I agree for my contact details to be kept for 2 years after the end of the study to let me know about opportunities for future involvement with this research team	

Name of Participant	Participant's signature and date
Name of Researcher	Researcher's signature and date

(Original to be retained and filed, 1 copy for the participant, 1 copy for Sponsor if required.)

Appendix E: Verbal consent form

NHS South London and Maudsley NHS Foundation Trust

KING'S College LONDON

Exploring the benefits of early diagnosis and intervention in dementia

Consent form for participants (verbal consent) (V1 22/06/2020)

To be completed by researcher:	IRAS ID: 241432
Participant ID: _ _ _	Participant DOB _ _/ _ _/_ _ _ _

The researcher taking consent should read aloud each statement to the participant and then initial each box if the participant confirms that they understand and are in agreement.	**Initials**
I have read and understood the information sheet dated 22/06/2020 (version 5) and have had the chance to ask questions	
I understand that my participation in the research interview is voluntary and that I can change my mind at any time	
I understand that participation in this research involves being audio-recorded. I give permission for the interview to be audio-recorded, on the understanding that the interview will be transcribed, and direct quotations may be reproduced in reports and publications, but all identifying information will be removed.	
I give permission for the research team to contact my GP about my participation in this study. I am aware that my GP may be notified if there are concerns about my health or safety during my participation in this study.	
I give permission for the research team to contact my GP to confirm my diagnosis or dementia or mild cognitive impairment (this does not apply to participants who are carers)	N/A
I understand that relevant sections of my medical notes (excluding carers) and/or data collected during the study, may be looked at by individuals from King's College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records/data	N/A
I agree to take part in the above study	

OPTIONAL

I agree for my contact details to be kept for 2 years after the end of the study to let me know about opportunities for future involvement with this research team	

Complete the Boxes below

Name of person taking consent:	Date:	Signature:
Name of witness:	Date:	Signature:

(Original to be retained and filed, 1 copy for the participant, 1 copy for Sponsor if required.)

Appendix F: Letter to GP

Dr Matthew Prina

Health Services and Population Research Department
King's College London
PO33 David Goldberg Centre
De Crespigny Park, Denmark Hill
London SE5 8AF

[GP Name]

[GP ADDRESS]

Dear Dr [GP Name]

Re: [Participant name], [Participant date of birth]

Your patient has expressed an interest in taking part in a study exploring the benefits of early diagnosis and early intervention in dementia. This is a qualitative study, where we are interviewing approximately 16 people diagnosed with dementia or mild cognitive impairment and approximately 16 of their carers to understand their experiences of diagnosis and the support they received afterwards.

Before your patient can take part this this study, we must confirm they have received a medical diagnosis of dementia or mild cognitive impairment. Please can you confirm your patient has been diagnosed with dementia or mild cognitive impairment by sending a letter to the above address.

I have enclosed a copy of the patients consent form, and a copy of the participant information sheet for your information.

If you have any questions, please do not hesitate to contact me on [researcher phone number].

Yours Sincerely,

Dr Matthew Prina

Encs: Participant Consent Form
Patient Information Sheet, version XX dated XX