AN ECONOMIC ANALYSIS OF THE QUALITY OF PRIMARY CARE FOR THE MANAGEMENT OF COMORBIDITIES IN PATIENTS LIVING WITH DEMENTIA

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Thesis submitted for the degree of Doctor of Philosophy (PhD)

DECLARATION

I, Thomas James Stephens, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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ABSTRACT

The thesis examines the quality of primary care services across a range of comorbid conditions in patients with dementia. The key aims were to assess whether their dementia diagnoses may hinder access to high quality care compared to patients without a cognitive impairment older adults, the health implications of this, and whether quality could be modified. An economic framework is proposed, suggesting that the quality of care received is a function of the supply and demand for quality. Patients with dementia may have a diminishing demand for quality due to a decreased comprehension of their health status as cognitive function declines. On the supply side, quality care provided by physicians may be a function of the availability of resources and the motivation to provide high quality care, which could be financial or not.

A systematic literature review and meta-analysis was conducted and highlighted that a diagnosis of dementia is associated with not meeting quality indicators for a range of non-dementia conditions. Subsequent analysis on the English Longitudinal Survey of Ageing, including care quality indicators specifically selected for UK older adults, supports these findings in suggesting that quality is unequal between patients with dementia and patients without cognitive impairments. Further analysis showed that meeting some of these indicators was associated with improved survival and could reduce social care use in patients with dementia, implying that care quality should be improved.

In order to assess how care quality and the consequential health outcomes could be improved for patients with dementia, later analyses in this thesis aimed to identify interventions or policies that could improve care quality. Pay-for-performance measures (the Quality and Outcomes Framework) as well as higher levels of cognitive function in patients with dementia appear to be associated with higher quality care. I developed an early model to evaluate the potential cost-effectiveness of introducing a cognition and independence promoting intervention or expanding the QOF to provide additional incentives for patients with dementia. Expanding the QOF does not appear to be cost-effective compared to current practices, though there may be some benefit in promoting cognition and independence in patients with dementia. However, further research on the valuation of health in patients with dementia is required to validate these findings within current willingness-to-pay frameworks for healthcare.

The findings of this thesis show that there are some inequalities in the delivery of high-quality primary care, to the detriment of health of patients with dementia. It is

implicated that there may be economically efficient strategies to improve health outcomes for patients with dementia by promoting independence.

Impact Statement

The Health and Social Care Act states that care providers should "reduce inequalities between patients with respect to their ability to access health services" as well as "reduce inequalities between patients with respect to the outcomes achieved for them by the provision of health services". NICE guidelines advocate that people living with dementia should have "equivalent access to diagnosis, treatment and care services for comorbidities to people who do not have dementia". This thesis demonstrates that patients diagnosed with comorbid dementia are less likely to receive care meeting indicators of care quality in contravention to these recommendations, and that this could be leading to expanded inequalities in health outcomes.

Patients with dementia are significantly less likely to receive certain care processes for diabetes, hypertension, osteoporosis, or smoking cessation, and potentially several other conditions. This research has shown that this could have a detrimental effect on patients' survival as well as increasing demands on social care services. It has also been found in this thesis that it may be possible for care quality in patients with dementia to be increased either through targeted reimbursement schemes or by promoting independence and improving cognitive function through psychosocial interventions. Subject to confirmatory evidence, using these strategies to improve care quality could be an economically efficient use of NHS resources.

The findings presented in this thesis may provide an evidence base for changing clinical practice for patients with dementia. This may involve potentially placing more weight on the future health benefits of managing comorbidities, rather than short-term goals of avoiding discomfort of certain medical treatments for those with deteriorating cognitive function. The results could also support an update to the current schemes used to reimburse general practitioners, such as the Quality and Outcomes Framework in the UK. Targeted reimbursement to GPs could be used to improve the probability that care is delivered to patients with dementia if this could provide clinical benefits to them.

In addition, this thesis contributes a new school of thought to the clinical and economic evaluation of treatments for dementia. Cognitive interventions or disease-modifying therapies may have compound benefits for patients with dementia in improving the quality of care for comorbid conditions as well as improving cognitive function. Therefore, effectiveness and cost-effectiveness evaluations may historically have had too narrower scope.

With regards to dissemination of the research, the systematic review and meta-analysis in Chapter 2 is currently under review in *BMC Geriatrics*. The results of the review demonstrates that patients with dementia are less likely to meet quality indicators. An analysis related to Chapter 4, showing that better primary care quality is associated to improved survival in older adults, was accepted for a podium presentation at the EuHEA Conference in 2020. Further manuscripts related to Chapters 4 and 5 are in development for submission in the first half of 2021.

Presenting selected findings from this thesis at primary or geriatric care conferences could increase the likelihood of changes to clinical policy and practice, which I am considering for 2022. Future dissemination activities, such as engaging with policy makers could increase investment into future research to the benefit of patients with dementia, though these are not currently planned.

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Acronyms & Abbreviations

ACE	Angiotensin-Converting Enzyme
AChEI	Acetylcholinesterase Inhibitor
ACOVE	Assessing Care of Vulnerable Elders
ACS	Acute Coronary Syndrome
AD	Alzheimer's Disease
ADAS-Cog	Alzheimer's Disease Assessment Scale - Cognitive Subscale
ADL	Activities of Daily Living
AHRQ	Agency for Healthcare Research and Quality
AIC	Akaike Information Criterion
ARB	Angiotensin II Receptor Blockers
BIC	Bayesian Information Criterion
BMI	Body Mass Index
BNF	British National Formulary
BP	Blood Pressure
CCB	Calcium Channel Blocker
CDF	Cancer Drugs Fund
CDR	Clinical Dementia Rating
CEAC	Cost-Effectiveness Acceptability Curve
CHD	Coronary Heart Disease
CHF	Swiss Francs
CI	Confidence Interval
CKD	Chronic Kidney Disease
COC	Cost of Capital
COPD	Chronic Obstructive Pulmonary Disease
CrI	Credible Interval
CVD	Cardiovascular Disease
DAG	Directed Acyclic Graph
DALY	Disability-Adjusted Life Year
DEMQOL	Quality of Life Assessment in Dementia
DES	Discrete Event Simulation
DESMOND	Diabetes Education and Self-Management for Ongoing and Newly Diagnosed
df	Degrees of Freedom
DLB	Dementia with Lewy Bodies
DM	Diabetes Mellitus
DSA	Deterministic Sensitivity Analysis
DSU	Decision Support Unit
ELSA	English Longitudinal Study of Ageing
eMIT	Electronic Marketing Information Tool
EQ-5D	EuroQol Five Dimensions
EVPI	Expected Value of Perfect Information
EVPPI	Expected Value of Partial Perfect Information
EVSI	Expected Value of Sampling Information
FTD	Frontotemporal Dementia
FTE	Full Time Equivalent
GMS	General Medical Services
GP	General Practitioner
HDI	Human Development Index

HDL	High-Density Lipoprotein
HF	Heart Failure
HKSJ	Hartung-Knapp-Sidik-Jonkman
HR	Hazard Ratio
HRQoL	Health-Related Quality of Life
HSE	Health Survey for England
HTA	Health Technology Assessment
IADL	Instrumental Activities of Daily Living
ICER	Incremental Cost-Effectiveness Ratio
IFS	Institutionalisation-Free Survival
IQ	Intelligence Quotient
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
IRR	Incidence Rate Ratio
MAKS	Motor Stimulation, Activities of Daily Living, Cognitive Stimulation, and Spiritual Training
MAUI	Multi-Attribute Utility Instruments
MCI	Mild Cognitive Impairment
MEC	Marginal Efficiency of Capital
MI	Myocardial Infarction
MICE	Multiple Imputation by Chained Equations
MMSE	Mini Mental State Evaluation
MOOSE	Meta-analysis Of Observational Studies in Epidemiology
N/A	Not Applicable
NDCI	Non-Dementia Cognitive Impairment
NG	NICE Guideline
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPI	Neuropsychiatric Inventory
NRT	Nicotine Replacement Therapy
OR	Odds Ratio
OS	Overall Survival
P4P	Pay-for-Performance
PCA	Principal Components Analysis
PCT	Primary Care Trust
PRIDE	Promoting Independence in Dementia
PRO	Patient Reported Outcome
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
PYAR	Person Years at Risk
QALY	Quality-Adjusted Life Year
QoC	Quality of Care
QOF	Quality and Outcomes Framework
RCT	Randomised Controlled Trial
ROC	Receiver Operating Characteristic
RR	Relative Risk
SA	Stable Angina
SD	Standard Deviation
SE	Standard Error
SWLS	Satisfaction with Life Scale

TA	Technology Appraisal
TAU	Treatment as Usual
TIA	Transient Ischaemic Attack
TSD	Technical Support Document
TTO	Time Trade-Off
UA	Unstable Angina
UK	United Kingdom
USA	United States of America
VBA	Visual Basic for Applications
VD	Vascular Dementia
WTP	Willingness-to-Pay

CHAPTER 1

INTRODUCTION

1.1. BACKGROUND

There are approximately 7.7 million new cases of dementia globally each year,[1] and it is a leading cause of death in the England and Wales.[2] Dementia currently costs the UK economy £17 billion a year, and this cost will increase to over £50 billion over the next 30 years.[3] People with dementia often face multimorbidity.[4] With a growing impetus towards enabling people with dementia to remain resident in the community for longer before institutionalisation,[5 6] there may be an increased need to provide holistic management and appropriate care for all of their comorbidities, as well as the dementia condition itself, within community care services.

Primary care providers are charged with the demanding job of diagnosing, managing, and supporting those in ill health, as well as promoting population health. Arguably, the principal goal of these services is to increase the length or quality of life for patients in their care. Data collected on these health outcomes can serve two purposes: prospective data (e.g., clinical trial results) can be used to inform decision-making, and retrospective data (e.g., registry analysis) could be a valuable measure of a health system's performance. However, use of measures of health outcomes can distort perspectives on performance. Exogenous factors in the care processes may lead to poorer outcomes, such as age or comorbidities,[7] and so outcomes may not directly reflect weaknesses in the health care system. However, if better care leads to better outcomes despite exogenous factors, evaluating a health system's performance by examining the quality of the processes of care may be more valid.

The Agency for Healthcare Research and Quality (AHRQ) defines quality health care "as doing the right thing for the right patient, at the right time, in the right way to achieve the best possible results".[8] This focus on "doing" and the actions of care is supported in the framework proposed by Avedis Donabedian, which conceptualises three dimensions for the quality of care: the structure and setting of where care is delivered, the processes and medical practices that are followed, and the outcomes and impact on health status.[9] Process evaluation in health care refers to when there is a need for a service, as defined by best practice or evidence-based medicine, and

whether or not this service was delivered. Process indicators are considered to be more sensitive measures of care quality than outcomes measures because poor outcomes do not always occur when there is an error in care.[10]

Assessing quality of care is also pertinent economically. Much of the work of economists in health care is focussed on the cost-effectiveness of interventions, assessing the efficiency of resource use, or cost-containment and the financial management of health care institutions. Care quality can fit into each of these domains from the perspective of a healthcare payer or provider. Audits of quality could be used to optimise efficiency in spending and healthcare practitioner time by using evidence on the effectiveness of interventions and processes to rank actions within a financially constrained health care system. The increased supply of primary care staff has a measurable effect on the quality of care processes.[11] Therefore quality can reflect the use of health care resources, as well as the funding for and availability of these resources. Quality of care could therefore be a significant topic of economic interest.

In addition to the effects of the supply of care on quality, the demand side of the equation may also have an impact. This may have particular implications for patients with dementia. In improving care for patients living with dementia, it may be relevant to explore how cognitive function influences the quality of services being provided. A loss of understanding of their health status in these patients may negatively affect demand for care, while a loss of independence may be instrumental in hindering access to care. Patients with advanced dementia often do not recognise the need for therapeutic interventions, or actively reject treatments.[12] Similarly, physicians may be less inclined to provide treatments for non-cognitive conditions to patients with a poor mental prognosis or unstable condition, given a possible reduction in the marginal benefit of treatment. When treating patients with advanced dementia physicians are advised to weigh up the benefits of treatment against the burden imposed as most medical interventions may cause some discomfort to these patients.[12 13] As the severity of dementia increases, the therapeutic benefit of interventions may be limited due to reduced life expectancy and decreased efficacy.[12] Current guidelines therefore advocate that aggressive treatments should only be provided in the earliest stages of Alzheimer's disease whereas, in the more advanced stages, treatment of comorbidities should be more conservative.[12]

This thesis aims to explore whether there are differences in the quality of health care services provided to patients for non-dementia conditions between patients with cognitive impairments and those without, as well as the factors that may be driving

these differences, and explore strategies for maximising primary care quality in patients living with dementia.

Dementia & Cognitive Impairments

Dementia is characterised by the progressive decline of cognitive and functional abilities, sufficient to interfere with usual functioning.[14] Although memory is the most commonly associated symptom of dementia, other cognitive domains such as orientation, comprehension, and judgement are affected.[15] The main symptoms of different dementias and cognitive impairments are summarised in Table 1.1. Dementia has a gradual onset with decline stretching over 5-8 years on average.[16]

The different types of dementia are characterised by their underlying pathology. The most common form is Alzheimer's disease, accounting for 60-70% of cases,[17] and causes mass neuronal death which reduces brain weight by 30-40%.[18] The second most common form is vascular dementia, which is caused by reduced blood flow and a reduced supply of nutrients and oxygen to the brain.[17] Dementia with Lewy Bodies and dementia in Parkinson's disease are the other most prevalent forms. Other forms of dementia can be caused by a variety of pathologies affecting frontal cortex functions are often referred to as frontotemporal dementia.[19] Prior to the onset of dementia, there can be a prodromal stage where cognitive deficits greater than those witnessed in normal aging appear. This state is referred to as 'mild cognitive impairment' (MCI).[20]

Table 1.1. Clinical symptoms of different cognitive impairments and dementia diagnoses

Symptom	MCI	AD	VD	DLB	FTD	Late Stage
Memory Loss	✓	✓				✓
Mood Changes	✓		✓		✓	✓
ADL Impairments	✓	✓				✓
Difficulties Finding Words		✓			✓	✓
Difficulties Following Conversations	✓				✓	✓
Anxiety		✓				✓
Attention & Reasoning Problems			✓	✓		
Confusion		✓		✓		
Difficulty Concentrating	✓					
Disorientation in Time/Place	✓					
Falls & Fainting				✓		
Incontinence						✓
Lack of Social Awareness					✓	
Movement Problems			✓			
Obsessive Behaviours					✓	
Repetitive Questioning		✓				
Sleep Disturbances				✓		
Visual Hallucinations				✓		

Abbreviations: AD, Alzheimer's disease; ADL, activities of daily living; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; MCI, mild cognitive impairment; VD, vascular dementia. **Source:** NHS Choices[21]

Dementia is predominantly diagnosed in primary care, and typically GPs refer less than one in five patients with dementia to a specialist.[22] The role of the primary care physician in treating and managing patients with dementia is therefore significant. It is estimated that 40% of dementia patients in the UK die in the community,[23 24] and other European evidence suggests over half of people with dementia live at home,[25 26] making the primary care physician a principal point of contact with the health care service for patients with dementia. Caring for people with dementia requires a holistic approach, incorporating the management of cognitive and behavioural symptoms, social and supportive care, as well as considering the needs of the carer.[27] High quality healthcare is important to maintain quality of life and support independence for people with dementia.[28-30]

Healthcare, Social Care, & Quality of Care

Health care is composed of health care systems and actions taken within them designed to improve health or well-being.[31] For patients living with dementia, social care also forms a large part of the care delivered to them.[32] Social care refers to the non-medical services that support individuals who are in social need but the exact definition of social care as an entity is somewhat loose.[32] Government policy in the UK over recent years has promoted social care, and the Care Standards Act 2000 outlined the regulation and inspection of social care services helping to define it as a profession.[32]

The integration of health and social care services for patients with dementia has been taking place in practice for a number of years, reflecting the awareness that people living with dementia have a range of care needs.[32] The integration of health and social care seeks to improve the quality of care patients receive by ensuring services are coordinated around their needs. Maximising the quality of care across services is only successfully achieved when the perspective of the health service user is the organising principle behind service delivery.[33]

A systematic review conducted as part of the National Institute for Health and Care Excellence (NICE) guideline on the care and management of dementia concluded that there were improvements in quality of life and reductions in the rates of entry into long-term care for people living with dementia when patients were offered case management, integrating health and social care, over usual care.[34] Evidence has also suggested that case management models reduce the total costs of care.[35] As the elderly population grows, and with it multimorbidity amongst patients, the need to coordinate care across teams for improvements will become more important,[36] perhaps particularly so for patients living with dementia where the collaboration between

various clinical and social care teams is required. Therefore, an efficacious and high-quality primary care service considering all the comorbidities and care needs of patients with dementia to maximise health outcomes is desirable.

The NHS defines quality care as care that is clinically effective, care that is safe, and care that provides a positive experience for the patient.[37] In defining quality, one clarifies standards that should be upheld which can then be measured and audited to inform improvement strategies. This can drive competition between units in a health care system to be at the forefront of quality and can lead to higher rates of commissioning and reimbursement, as has been implemented by pay-for-performance schemes like the Quality and Outcomes Framework (QOF) in the United Kingdom.

When evaluating health care systems, Donabedian outlined a framework to consider them in terms of structures, processes, and outcomes.[7 9] The approach of disaggregating the system is considered a necessity when examining health care.[31] The outcomes and structures are not specifically components of care, but rather consequence of care and channels through which it is delivered, respectively.

Health care structures are organisational factors that shape the system in which care is provided,[38] such as the human resources, equipment, and buildings. These can be organised in particular ways to develop different health structures, for example having a system to facilitate the booking of appointments and improve access to care. Structural features are necessary to provide care but they do not guarantee it.[31] Evaluating the quality of structures is concerned with aspects of care such as the adequacy of facilities and equipment, the administration and fiscal management of institutions, and the qualifications of staff.[7] The assessment of structure as a measure of quality is based on the notion that given the proper settings and means in which to provide care, good quality care will follow. The principal limitation with this assumption is that the relationship between structure and outcomes is not well established.[7] Nonetheless, structural aspects such as health care supply have been suggested to impact the processes of care,[11] implying that the availability of resources should be considered when evaluating health care units on their adherence to process measures.

Outcomes are the consequences of care and can be defined as both the health outcomes as well as user evaluation or service satisfaction. Both structures and processes can influence the outcomes of care. Outcome measures can be considered indicative of quality, as there is little dispute over whether recovery from illness or increased survival demonstrates the effectiveness of care. However, outcomes may not be the

desired or relevant measure. Outcomes can reflect the power of care and interventions to achieve results in a given circumstance, but not strictly whether the best care or intervention has been given in a specific circumstance. Some outcome measures are not practical for analysis, such as the time between an error in a process of care and the outcome of that error in chronic conditions.[7] Additionally, many factors other than the course of care taken may influence outcomes, such as case mix and comorbidities on mortality outcomes, and these factors must be held constant in order to draw valid conclusions about outcome measures. Therefore, although outcomes may be the ultimate validators for the effectiveness of treatment, it is questionable as to whether they can be used to validate care quality.

The processes of care are the interactions between patients and the health care system and can be defined as the actual delivery and receipt of care, whereby processes can largely be classified into two key grouping: clinical care and interpersonal care.[31] Clinical care refers to the medical processes involved in treating a health problem, whereas interpersonal care includes "the management of the social and psychological interaction between client and practitioner" or the patient-centeredness of care.[38] When evaluating the quality of processes in health care, one is not only interested in the power of medical science and technology, but also whether the correct and good medical science and technology care has been applied.[7] Previous research has demonstrated that process measures are more efficient indicators of quality compared to outcome measures, and require substantially less data collection to determine statistically significant differences in quality.[39] In addition, process measures can be directly attributable to the actions of care providers, rather than be influenced by extraneous variables which may impact upon outcomes.[40] Consequently, process indicators would appear to be the best indicators of care quality, particularly in primary care where the clinical outcomes of treatment are not always immediately obvious.[10]

Quality measures can indicate how up-to-date a physician's knowledge and available resources are in line with the latest health and medical sciences and technologies and how well they are delivered.[7] Campbell and colleagues suggest there are two dimensions to quality: access (i.e., patients getting the care that they need) and effectiveness (i.e., whether the care was received effective in terms of both clinical effect and patient satisfaction).[31] The aim of health care is to maximise the health benefit relative to the need, therefore quality should be assessed based on the needs of the individual.[31]

Evaluating the level of quality between groups is unlikely to provide much insight into why differences in the quality received between groups may exist. Efficacy and safety

considerations, as well as the resources available, may play a role. However, patients themselves could be instrumental in limiting their access to high quality care in failing to identify a pertinent issue, denying themselves access to potential treatments, or by rejecting care offered which they feel does not take into account their personal preferences. Therefore, there are numerous potential barriers to quality care delivery outside of the domain of delivery.

Ferlie & Shortell postulate that strategies for improving quality can be at four levels of the care system: the individual level (e.g., education strategies), the group level (e.g., developing multidisciplinary teams), the organisation level (i.e., organisational learning), and the larger system level (e.g., national guidelines and auditing or accrediting bodies).[36] Strategies focussing on individuals alone are rarely effective unless used in conjunction with other interventions, [41 42] because medicine is generally practiced as part of a team within the health care system.[36] More efficacious mechanisms for improving care quality require the alignment of financing and regulatory policy with the goals of health care providers to deliver better care, with providers promoting coordinated and collaborative care in teams developed based on the needs of the patient and the skills of its members.[36] Different aspects of this ideal scenario could be targeted when considering the feasibility of the scheme and the impact it could have on quality. Schemes which influence both the individual (demand side) and the health care provider (supply side) could be more efficacious.

1.2. Aims

Project Overview

Evaluating the quality of care services received may be of pertinence to the cognitively impaired. Patients living with dementia may have difficulty in accessing high quality health care services, especially in primary care where a greater level of patient decision-making and control is required. However, the association between cognitive impairment and care quality may not be unidirectional or homogenous across all conditions and care domains. Given that these patients may also face the additional burden of ill health, the implicit demand for care rises. By identifying factors influencing access to, and the quality of, care services for patients with diminishing cognitive function, it can support the development of intervention strategies to maximise care quality and improve health outcomes.

The overall aim of this thesis is to utilise health economic and econometric methods to identify and evaluate strategies for improving care quality for patients living with dementia. These should have a meaningful effect on health, determined from the

welfarist perspective of the efficient maximisation of outcomes. Within this, I aimed to explore four separate facets of the relationship between care quality and dementia:

(1) The current extent of the differences in the quality of the processes of care received between those with cognitive impairment or dementia and those without in the management of their comorbidities;
(2) Whether any observed differences in the quality of care received have a meaningful impact on patient health or payer-relevant economic outcomes;
(3) Whether patient or health policy factors are associated with greater care quality where differences currently exist, or are factors which could explain inequalities in care between patient groups, and thus form the basis of an intervention strategy; and,
(4) What would be the clinical and economic implications of introducing potential interventions to improve care quality for patients with dementia and where are the evidence gaps?

The field of health economics is well suited to respond to these questions. Health economics seeks to facilitate decision-making by offering an explicit framework based on the principle of efficiency, by maximising the benefits from available resources whilst recognising concerns on equity.[43] In identifying how a dementia diagnosis may impact care quality and in turn the impact this has on health outcomes of patients and the long-term economic consequences, evidence can be generated to inform decision-making at all levels of the healthcare delivery system, from frontline practitioners to policy makers, incorporating both the costs and benefits of alternative models of care for patients with dementia.

For this thesis, the focus has been on middle-aged and older adults (aged at least 50 years) given the lower prevalence of dementia in younger populations – an estimated 0.3% of dementia cases in the UK are in people under 50.[44] There are therefore greater expected economic and population-level clinical implications for this population.

To provide context to the empirical analyses, I have developed an economic framework which outlines the possible association between cognitive impairment and the quality of care services received using a supply and demand framework, derived from the human capital model for health (the Grossman model).[45] These models are later used to form the basis for assessing the impact of specific personal, social and economic factors on the supply and demand of quality care. To initially illustrate the size of the disparity in quality of care received between patients with cognitive impairments and those without, I have conducted a systematic literature review and

meta-analysis of quality metrics. This association was also assessed using a longitudinal sample of English older adults from the English Longitudinal Study of Ageing (ELSA) to compare how receipt of 39 indicators of care quality differs with a dementia diagnosis or by level of cognitive function.

For process measures of care quality to be valid they must demonstrate that variations in the process lead to differences in relevant outcomes.[10] The NICE guidance on evaluating new guidelines and health technologies recommends that outcomes be measured using quality-adjusted life years (QALYs) where possible.[46] The QALY is a composite of health-related quality of life (HRQoL) and life expectancy, and so takes into account both morbidity and mortality. To assess the impact of differences in the quality of care on outcomes, an analysis was conducted on the association between meeting quality indicators and various metrics of health. This analysis also incorporates an outcome associated with increased independence in patients with dementia, in assessing if high quality care could delay institutionalisation and a move to residential care, or reduce the volume of support provided by social services.

To reduce inequalities in health, a potential strategy is to reduce inequalities in health care quality. I conducted a further analysis to assess whether pay-for-performance measures or providing cognitive interventions could improve care quality for patients with dementia, by increasing supply or demand for quality, respectively. An empirical analysis on the ELSA data was used to assess these associations, leading to the final study in this thesis which aimed to identify if these potential interventions would be economically feasible and justifiable in terms of cost-effectiveness, and what additional evidence would be needed to make robust inferences on the case.

The last chapter concludes the thesis by drawing together the findings from each study conducted and the implications for policy and practice. Furthermore, limitations of the analyses are presented, as well as suggestions for relevant future research.

Research Implications

In showing that dementia and poor cognitive function is associated with a lower quality of care received, it serves to further expand the list of burdens placed upon an individual with dementia, hence emphasising the need for effort to be placed on improving the cognitive outcomes in dementia patients. The recent update to the NICE guidance on the care and management of dementia advocates that people living with dementia should have "equivalent access to diagnosis, treatment and care services for comorbidities *[compared]* to people who do not have dementia".[34] This thesis aims to

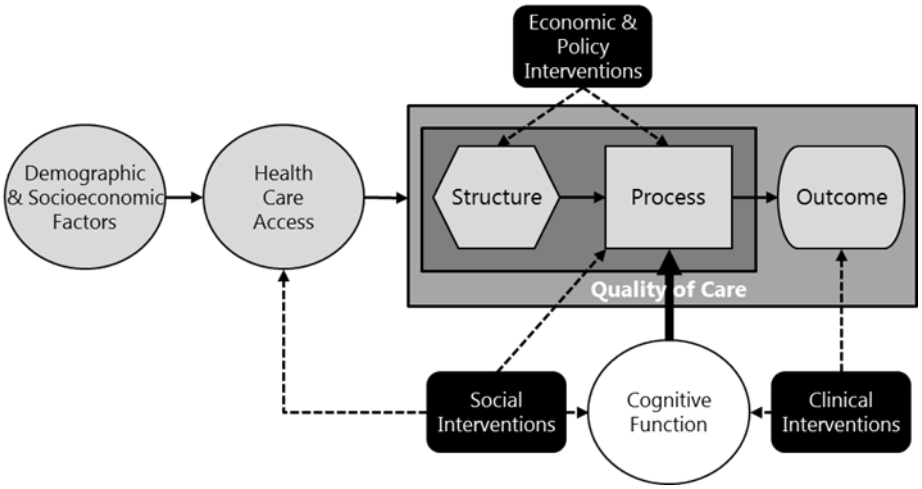

Figure 1.1. The link between structure, process, and outcomes and the implications of interventions on the relationship between cognitive function and quality processes in health care. Adapted and updated from Peabody et al. (2006)[47]

assess whether this is the case in current practice and the implications of deviations from this guideline.

If some of the clinical consequences associated with having dementia could be alleviated with improved cognition and greater independence, this could support access to better formal care and perhaps delay or avoid admittance to care homes or hospitalisation. An association between cognitive impairment and the quality of health care processes provides numerous implications for intervention. These include policy interventions to improve the quality of care through increased supply or treatment guidelines, providing social interventions to improve support for patients with cognitive impairment facilitating access to care and demand for quality, or clinical interventions to reduce the rate of cognitive decline in patients (Figure 1.1). With a demonstrated link between the structure, processes, and outcomes of care, these should all have a measurable benefit on the patient's quality of life.

1.3. Theoretical & Economic Frameworks

Theoretical Perspective

For this thesis I have adopted a perspective on the boundary of welfarism and extra-welfarism. Welfarism refers to an approach whereby one judges the state of society and distributions of goods within it by the welfare of the people concerned. Welfarist economists aim to maximise societal welfare within budget constraints,[48 49] whilst extra-welfarists aim to maximise health effects within a resource-constrained health system.[49-51] Welfarism implies that the distribution of economic goods is evaluated by the effect it has on the welfare of the persons concerned. Within this study, the aim is

to derive an optimal treatment paradigm for patients with dementia that is Pareto efficient and maximises utility within the resource constraints.

However, there are some limitations to the welfarist approach, such as distributional concerns when valuing human life that could favour diseases of the affluent and the most productive over diseases of the poor or sedentary.[48 50 52] Using human capital approaches to monetise health outcomes are likely to discriminate against those with dementia as most will be outside the labour force.[53-56]

The extra-welfarist approach is generally considered to be more straightforward to operationalise in healthcare, where outcomes are measured in health alone rather than aggregate welfare. However, extra-welfarism may neglect some important outcomes in this analysis. Extra-welfarists do not define the output of healthcare in terms of preferences for health in relation to overall welfare, but according to its contribution to health itself. In terms of economic evaluation, the extra-welfarist approach usually takes the form of cost-effectiveness analysis or cost-utility analysis with outcomes measured in health-related terms, such as QALYs.[57] However, the improvement in outcomes due to an intervention is challenging to measure in dementia as quality of life measurements such as the EQ-5D are not sensitive to the severity of dementia,[58] and the QALY from the perspective of the extra-welfarist doesn't include the benefits to the caregiver, and the costs do not incorporate those associated with private care, such as self-paid nursing homes. Therefore, although this approach is widely used in health economics and is easy to implement, it may not always provide useful information to decision makers about how to allocate scarce resources.

Given that one of the aims of welfarism is to determine whether the goal is worth achieving, while extra-welfarism aims to determine the least costly way to achieve a goal,[48 59] within the structure of this thesis, the welfarist approach applies to Chapter 2 through 5 when assessing care differences and the consequences of this, whilst the extra-welfarist approach is adopted in Chapter 6 in appraising the potential cost-effectiveness of improving care quality from the perspective of a healthcare payer.

The Role of Cognitive Impairments in Influencing the Quality of Care

The first aim of this thesis is to assess if patients with dementia are less likely to receive high quality care for their comorbidities, though the rationale for this may not be immediately clear. It is unlikely that a person with dementia presenting themselves to a GP with a health complaint would be denied certain diagnostic procedures or treatment purely on the discrimination and stigmatisation of their condition. Rather, it is hypothesised that any differences in the quality of care can be explained in terms of

the supply and demand for quality. Identifying factors influencing access to, and the quality of, primary care in patients with diminishing cognitive function would support the development of intervention strategies to maximise care quality and improve health outcomes.

The human capital model considers health as a commodity.[45] We can invest in health to improve our "stock" of health by eating well, exercising, or seeing a physician to cure our ailments, or we can divest our stock through behaviours such as smoking. The greater our stock of health is, the more healthy days we have and are able to go about our usual activities.[45] Our demand for health services is related to our desire for health stock.[60] However, in order to demand health services it is assumed that we have knowledge that our health is suboptimal. Jönsson and colleagues demonstrated that self-reported HRQoL in patients with dementia was not sensitive to disease severity or progression, but carer-reported proxy measures were significantly lower and deteriorated further as the disease progressed.[58] Assuming that a decline in cognitive function, such as impaired comprehension or health literacy, is associated with a lower understanding of our health stock and health care needs then demand for health care services is likely to fall. As quality processes in health care reflect the use of a service when it is needed, quality will fall as a consequence.

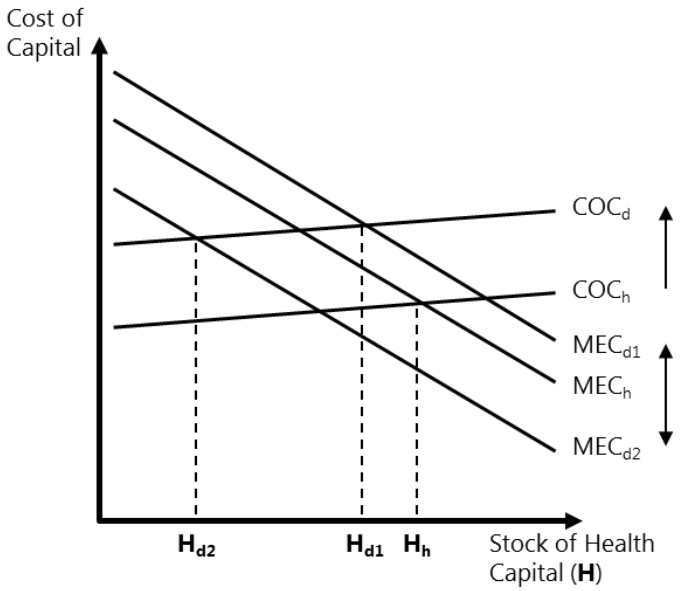

Figure 1.2. The cost of capital (COC) increases with the disease burden associated with dementia (d). The optimal health capital in a healthy population (H_h) given the equilibrium with the marginal efficiency of capital (MEC) can fluctuate with disease and changes in the depreciation rate of health associated disease. Thus, the optimal health stock in early dementia (H_{d1}) and severe dementia (H_{d2}) can differ as a result of the effectiveness of care in different stages of the disease.

The relationship between cognitive function and demand for health services may not be linear. In investment literature, the optimal stock of capital is the amount at which the cost of capital (the "cost" or time invested in obtaining health stock) equals the marginal efficiency of capital (the amount of healthy time you can expect from investing in health). People will not want to invest more in their health than they can expect as a return on investment. The cost of capital curve is presumed to be positively sloped, as it can be assumed that visiting your GP is less of an investment than progressing through secondary care. Conversely, the marginal efficiency of capital curve can be expected to have a negative slope as investors are assumed to rank investments by their expected rate of return. Exogenous changes in the cost of capital and marginal efficiency of capital change the optimal health level. The cost of capital reflects not only the cost of obtaining health care, but also the depreciation of your investments in health requiring further investments to maintain health – visiting the GP once only has a limited treatment benefit. A patient with dementia can expect their health to deteriorate much quicker than a healthy person. As such, the cost of capital increases and shifts the schedule upwards. The marginal efficiency is also subject to change in patients with dementia. In the early stages of the disease, patients may value improvements in health in order to sustain their productive lifespan, but in the latter stages the marginal benefits of care are lower, and patients may actively refuse treatments. This may shift the marginal efficiency of capital curve to the right and left respectively (Figure 1.2).

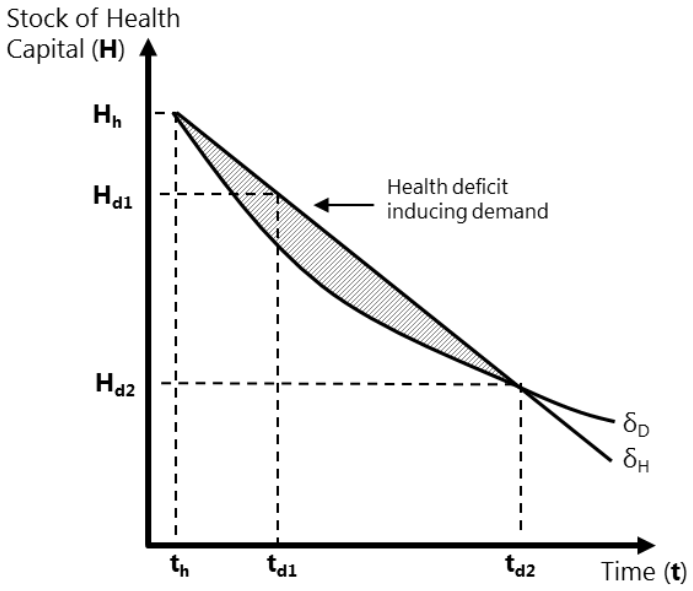

Figure 1.3. An unexpected increase in the depreciation rate (δ) upon diagnosis with dementia (D) can reduce health capital below the optimal stock inducing demand for services.

Consequently, this suggests that the optimal health level for patients with mild dementia is not much lower than the standard population but is significantly lower in the severely impaired. In line with this, research has found that those with mild dementia had a utility score of 0.64, and 0.33 in those with severe dementia,[58] compared with the English population average for that age group of 0.70.[61]

A non-monotonicity of demand may stem from the depreciation in health. As well as impacting the desired level of health stock, depreciation also directly impacts health stock. Upon diagnosis of a chronic condition such as dementia, the depreciation rate in health changes as the decline in health may be more rapid than for those without dementia, thus pushing the health status below the desired level and increasing demand for health care services (Figure 1.3). This helps to explain why the elderly are the most prolific users of health services,[60 62] where additional diagnoses and multimorbidity can increase demand.

Therefore, the relationship between cognitive impairment and demand for care may not be unidirectional, but rather there may be an increased demand for care in the early stages of dementia and decreased demand in the more advanced stages of impairment. Both of these influencing factors on demand could be modulated by external forces. For example, people with dementia with an immediate family caregiver may seek care on their behalf, thus driving demand for health care services up. However, family carers for patients may delay seeking care on their behalf in order to protect the self-image of the patient.[63]

In addition to demand, evaluating factors influencing the supply of quality care is a salient issue. Formal service providers should provide quality, evidence-based care and support for patients with dementia and their families.[64] When services focus effort on adapting services to the needs of dementia patients they can improve quality of life for both the patient and their carers.[65-67]

In addition to the clinical rationale, a considerable proportion of the remuneration to GP practices has depended on meeting quality process indicators since 2004. The QOF is the world's largest health related pay-for-performance scheme,[68] providing an additional 25% of income to practices.[69] Points are accrued for meeting quality indicators across several domains, and since its inception over 50% of points apply to clinical indicators, though now take a much more prominent role.[70 71] Therefore, high quality care based on indicators is paramount for maximum reimbursement.

Within the QOF calculations, it is possible to exclude medical records of individual patients from counting towards reimbursement points, known as "exception

reporting". The clause intends to account for patients who are unable or unwilling to be treated and safeguarding patients against inappropriate treatment by physicians seeking to maximise their income, though it has been considered an opportunity for doctors to game the system.[69] Retrospective analysis has found that this was probably not the case, with only 5.3% of patients being reported as exceptions.[72] However, it was found that physicians were most likely to exclude patients from indicators related to more complex treatments and targets, than from routine checks and simpler procedures.[72] One of the reasons doctors are allowed to exclude patients from indicators is when "the patient has a supervening condition that makes treatment of their condition inappropriate".[73] Although a somewhat pessimistic view of GPs, patients with dementia could be included under this umbrella for exclusion reporting. Assuming that providing high quality care is associated with a greater upfront cost to GPs, either directly in the resources consumed, or indirectly in terms of opportunity costs, profits could be maximised by meeting indicators included in the QOF for patients who are not cases for exception reporting. This could lead to worse quality care for patients with dementia as GPs will attempt to minimise their upfront costs by not treating patients with complex comorbidities, but by excluding them from reporting so their reimbursement remains unaffected.

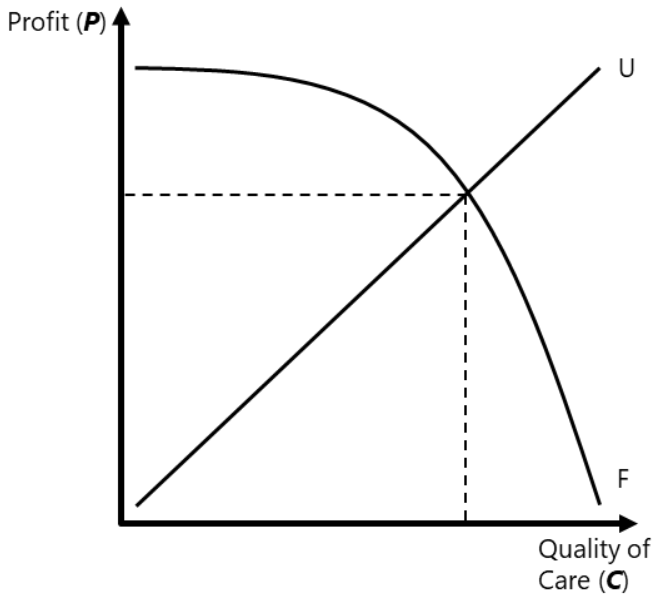

Figure 1.4. The supply of quality care from the physician (C) has a measurable impact on their profits (P), defining the production frontier (F). The physician's utility (U) is a function of both increased profits and the increased other motivations associated with providing better quality care. Physician-level variations on the weights of profit and job satisfaction on utility can vary quality. Patient-level variations in the complexity of condition can shift the production frontier, reducing profits, so a greater weight on job satisfaction or a greater level of reimbursement is required to maintain quality in these patients.

It is an unfair assumption to brand GPs as purely profit maximisers, but they are also unlikely to be purely altruistic with regard to ensuring the best outcomes for their patients. Instead, they may be considered as utility maximisers, much like the patients. Work-related utility for GPs is likely to be the result of a balance between the financial gains of the role and other motivations to provide high quality care (Figure 1.4). These motivations could include the job satisfaction achieved from greater patient satisfaction and the kudos or the pressure of penalisation by professional bodies from failing to adhere to guidelines during audits, amongst others.

An alternative view on the supply of quality could be reflected by the marginal benefit of treatment to patients. For example, general health targets such as managing cholesterol in a patient with diabetes may not be especially pertinent for a patient with severe dementia but reducing the risk of falls through proper assessment may improve their quality of life in the short-term. Therefore, a degree of clinical judgement and adopting a patient-centred approach to match the needs and preferences of this population would be appropriate.

Both supply side and demand side factors are theoretically modifiable in the interactions providing care to patients with dementia. Factors for consideration are interventions to improve cognition, the support networks for patients with dementia, the best practice guidelines for treating these patients and quantification of the benefits of care, as well as the resources and reimbursement available for providing care. This thesis will explore how these factors influence the relationship between a dementia diagnosis and care quality for the management of comorbidities.

CHAPTER 2

CARE QUALITY FOR THE COGNITIVELY IMPAIRED
A SYSTEMATIC REVIEW AND META-ANALYSIS OF DIFFERENCES

2.1. INTRODUCTION

The recent growth in the number of older adults, and with it the increasing prevalence of dementia,[74] has led to an added burden on health care systems in terms of the cost of managing and caring for patients living with dementia.[75] People with dementia often feel happier if they can remain independent and in their own homes as long as possible, and have been demonstrated to have a higher quality of life than those residing in nursing homes.[76] To assist in sustaining community living, it may therefore be desirable to optimise the quality of community care services in treating and managing health complaints in patients living with dementia, as to offset future comorbidity cost burdens as well as potentially limit rates of institutionalisation.

Patients with dementia form a vulnerable group and face the additional burdens associated with ageing such as multimorbidity, frailty, and polypharmacy.[4] Research has shown that the general quality of care for older adults is below optimal,[4] and therefore it is possible that the added challenges of cognitive impairment leave room for improvements in the quality of care for this patient group. In UK primary care, having comorbid dementia has been shown to be a consistently cost-limiting factor in terms of consultations, medication, and investigations for patient's other comorbidities, which could possibly be associated with inadequate care.[77]

Little is known about how dementia or other cognitive impairments may be associated with the quality of healthcare received by patients and delineating the nature of this association may set the framework for developing quality improvement programmes to optimise outcomes for these patients. The aim of this systematic review and meta-analysis was to extend current knowledge on the association between dementia, or non-dementia cognitive impairments, and care quality. Quantitative evidence has been synthesised on the differences in meeting indicators of care quality in non-dementia settings, considering a psychometrically assessed cognitive impairment or clinical dementia diagnosis as the exposure variable. Estimates of the association between measures of impaired cognition and the odds or rates of meeting indicators of quality health care have been produced. Additionally, subgroups analyses were conducted to

explore whether this association is subject to variation in different conditions or disease areas, different countries or treatment settings, by the type of process underlying the indicator, or whether the patient had been diagnosed with dementia versus a non-dementia cognitive impairment.

2.2. Methods

Data Sources & Searches

A systematic review and meta-analysis of observational studies was carried out following the recommendations of the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group.[78] Studies were sought from selected databases via Ovid (MEDLINE, Embase, PsycINFO, and the Cochrane Library), published between 1 January 1990 and 31 May 2018. The cut-off start date was selected based on the assumption that findings from older studies would be less reflective of current practices. Reference lists of included studies were scrutinised for additional relevant publications. For studies to be included in the review abstracts had to be available in English, however there were no language restrictions on articles. I developed the search strategies including the terms 'dementia', 'Alzheimer's disease', and 'cognitive impairment', which were cross-referenced to the terms 'quality of health care', 'quality indicators', and 'process assessment'. The MEDLINE search strategy can be found in Appendix 2.1, and the syntax was adapted for use in the other databases.

Eligibility & Study Selection

Eligibility criteria for studies to be included in the review have been derived using the MOOSE[78] guidelines (Table 2.1). To be included, studies had to be original research meeting the criteria below:

- Observational studies conducted in a developed country of older adult patients (aged ≥ 50 years) with diagnosed dementia or a psychometrically evaluated cognitive impairment (e.g., suspected dementia based on the Mini Mental State Evaluation score) and a comparator population without an assessed cognitive impairment.
- Reported on the relation between cognitive impairment and at least one of the following factors related to the process of care: (1) the proportion or rates of patients meeting a quality indicator defined by guidelines or best practice; (2) the proportion or rates of patients receiving a care process where there is a clinically defined need; (3) metrics of the patient-centeredness of care; or (4) other statistically determined associations between cognition and care quality (e.g., regression coefficients).

Table 2.1. Study selection criteria

	Inclusion Criteria	Exclusion Criteria
Population	▪ Aged ≥ 50 years ▪ Conducted in a developed country (Human Development Index ≥ 0.8)	▪ Younger populations ▪ Conducted in a developing nation, or a nation without adequate/universal health coverage and low HDI
Exposure	▪ Clinically diagnosed or psychometrically evaluated cognitive impairment (i.e., dementia diagnosis or Mini Mental State Evaluation score)	▪ Inadequate assessment of cognitive impairment or where the level of cognitive impairment is not well defined
Control	▪ Non-cognitively impaired patients of comparable demographics and clinical background	▪ Incomparable populations in terms of age, other comorbidities, or treatment setting
Outcomes	The relationship between cognitive impairment and at least one of the following processes of care: ▪ The proportion or rate of patients meeting a quality indicator as defined by treatment guidelines or best practice; ▪ The proportion or rate of patients receiving a specific process where there is a clinically defined need (e.g., prescription of anticoagulants for patients with high-risk atrial fibrillation); or, ▪ Metrics of patient-centeredness (e.g., whether patients' wishes about their care are met)	▪ Studies assessing the quality of care in dementia-related settings whereby having a cognitive impairment would be a direct predictor of the type of care received (i.e., care in memory clinics) ▪ Studies comparing the efficacy of care rather than the receipt of care
Study Design	▪ Observational/epidemiological studies of real-world treatment patterns ▪ Systematic reviews of relevant studies	▪ Randomised trials where a cognitive impairment may have a direct impact on the type or quality of care received ▪ Case studies
Restrictions	▪ Abstract published in English ▪ Published between January 1990 and May 2018	▪ Studies published pre-1990

Systematic reviews of relevant publications were included and used to identify original research that could be included in the analysis. Articles were excluded if they assessed quality of care in dementia-related settings whereby having a cognitive impairment could potentially be a predictor of the type of care received; if studies only evaluated the efficacy of care rather than the receipt of care; if they were randomised interventional studies where the intervention could reasonably be expected to have an impact on the quality or type of care received, or where cognitively impaired patients consistently receive a specific type of care; if they were case studies; or studies conducted in a country without adequate health insurance or coverage. Opinion letters, editorials, and letters were excluded. Case studies or those with an insufficient sample

size to assess differences in the quality of care between the cognitive populations were also excluded.

Identified studies were reviewed in two rounds. The first round consisted of critically screening the title, abstract, and keywords. Concurrently with the first round of screening, a colleague reviewed a subset (10%) of identified studies independently. The robustness of the study selection criteria and agreement was assessed using the Gwet's AC_1 statistic.[79] Disagreements were resolved in discussion. Studies selected for inclusion in the first round had the full text article reviewed in the second round. In this round, studies were scrutinised to ensure a valid and reliable metric of both quality and cognitive impairment was used.

Data Extraction

The following data were extracted from the included articles: study characteristics (country, treatment setting, study design, inclusion criteria, method used to identify cognitive impairment, quality of care metric, and method of analysis), patient characteristics (age, sex), outcomes, and key conclusions. If a regression-adjusted odds ratio for binary indicators of care quality was reported in the study, which accounted for patient-level factors influencing access to or the need for care, this was extracted and favoured over raw results for the base case analysis. A sensitivity analysis was also conducted using the unadjusted results.

Quality Assessment & Publication Bias

Study quality was assessed using the RTI Item Bank[80] to judge methodological quality of included studies. This measure was developed in response to the need for a comprehensive assessment of bias in observational studies, where traditional measures of bias in randomised-controlled trials do not consistently apply. Of the original 16 questions developed for the scale, five were excluded for use in this study due to lack of relevance to the types of study included. The remaining questions assessed bias in recruitment, inclusion criteria, study protocol, measures and scales, follow up, confounding, and the precision of the results. Studies were subsequently classified as "low risk", "possible risk", "probable risk", or "unsure" and categorised across the domains of attrition bias, confounding, detection bias, precision, selection bias, and selective reporting. When assessing whether confounding variables had been accounted for in analyses, included potential confounders were age, sex, non-dementia comorbidities, and those related to health care access or residence status. Other variables associated with dementia, such as activity of daily living impairments, were

not necessary for adjustment, as these are a common characteristic of this population. Publication bias was assessed using funnel plots.

Analytical Approach

To summarise the dichotomous differences in the proportion of quality indicators met between patients with a cognitive impairment and/or dementia and those without from included studies, odds ratios and the corresponding 95% confidence intervals (CI) were calculated. Results of these studies were then synthesised in a meta-analysis, as described below. Where results of included papers could not be included in the meta-analysis, due to outcomes being reported on a continuous scale or in a method inconsistent with those included in the meta-analysis (e.g., insufficient data to estimate appropriate effect sizes and/or standard errors), these were discussed separately.

Heterogeneity was assessed by means of the I^2 statistic, which reflects the amount of heterogeneity between studies beyond sampling variation and is robust to the number of studies and choice of effect measure.[81] The I^2 statistic summarises observed heterogeneity on the percentage scale, with 0% indicating no heterogeneity and 25%, 50%, and 75% considered to be low, medium, and high levels of heterogeneity.[81] If the I^2 statistic indicated considerable heterogeneity, the summary odds ratio was estimated using a random effects model. Although the DerSimonian-Laird method[82] is commonly used, it may lead to statistically significant results even when there is moderate or substantial heterogeneity.[83-88] The Hartung-Knapp-Sidik-Jonkman (HKSJ)[84 85 89] method has been demonstrated to be more robust and perform better than the DerSimonian-Laird method when there is considerable heterogeneity and/or when the number of studies included in the meta-analysis is small.[83-90] Subsequently, confidence intervals of summary odds ratios were adjusted using the HKSJ method. As multiple quality indicators could be obtained from the same study, a meta-analysis via a multilevel model including a random intercept at the study level was also conducted to assess the sensitivity of results. Multilevel models have been recommended when multiple measures of an outcome, in this case metrics of care quality, are included.[91]

To explore heterogeneity between studies, the effect of study specific characteristics on outcome variables was also explored using subgroup analysis for each of the following categorical variables: disease area or condition for which the quality indicator applies to, the country in which the study was conducted, the underlying process or type of quality the indicator assesses (i.e., prescription of medication, receipt of surgery, monitoring and testing procedures, rehabilitative or supportive care, patient-centred care, or the outcomes of care), the setting care was delivered

(community care, inpatient care, or residential care), and the type of cognitive impairment (diagnosed dementia or a psychometrically assessed impairment). To assess whether any of the subgroup definitions themselves were drivers of care quality differences, any subgroup where the difference in care quality between cognitively impaired people or patients with dementia and those with neither cognitive impairment was statistically significant, these covariates were included in a meta-regression to assess the impact on the summary odds ratio. All subgroup analysis and meta-regression models were run using the DerSimonion-Laird weighting with results adjusted using the HKSJ method, and sensitivity assessed using a multilevel model with a random intercept at the study level.

To assess the impact of using adjusted odds ratios from logistic regressions in the meta-analysis, a separate meta-analysis was conducted using only results which were not adjusted for by regression methods to assess the impact on the summary odds ratio. This was compared to a restricted meta-analysis using the adjusted odds ratios, where several studies from the main analysis were excluded as absolute number counts and sample sizes were not reported in these studies.

The *R* software package add-in '`metafor`'[92] was used to conduct the meta-analyses and meta-regressions. Microsoft Excel 2016 (Microsoft, Redmond, WA) was used to produce forest plots to visualise summary odds ratios and their corresponding confidence intervals.

2.3. Results

Study Characteristics

The literature search yielded 5,643 unique records. Of these, 294 full text articles were assessed for eligibility and 37 were included articles in the analysis (Figure 2.1). Agreement between reviewers was high (89.1%) and the Gwet's AC_1 statistic indicated substantial inter-rater reliability (0.86), suggesting that the interpretation of inclusion criteria was consistent across reviewers. The included studies

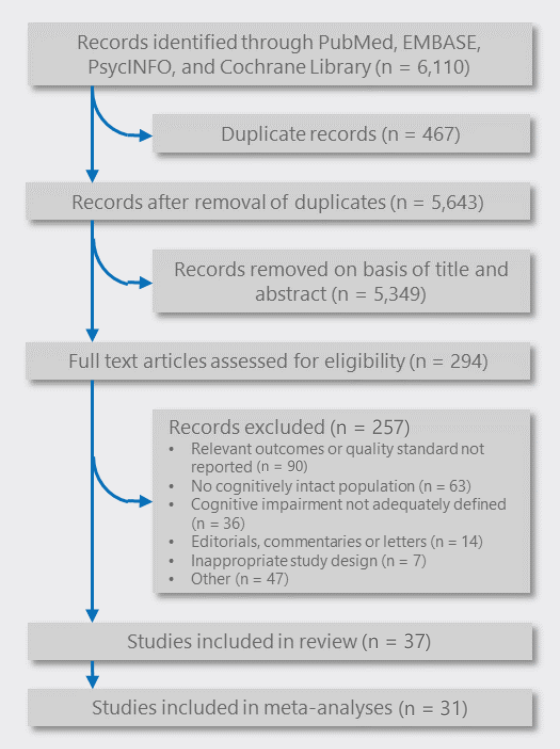

Figure 2.1. Flowchart of study selection. 'Other' includes outcomes or cognitive function reported on non-relevant scale, or care being related to dementia treatment setting, amongst others.

were published between 1999 and 2018 and provided data on 73 different binary quality indicators and 15 other outcomes, covering 21 diseases or conditions in total, and 12 countries (see Appendix 2.2 for details of study characteristics). Sample sizes for indicators ranged from 58 to 491,754 with a weighted average prevalence of any cognitive impairment of 18.6% (interquartile range between individual studies 3.1% to 46.3%). Three studies (eight indicators) did not report sample sizes relating to the study groups and indicators.[93-95] From these studies, and 14 others,[96-109] extracted odds ratios included in the meta-analysis were covariate-adjusted from a logistic regression.

Twenty-three studies used a cross-sectional design, and ten and four studies used a cohort or case-control design, respectively. Twelve studies were conducted in the USA, eight in the UK, four in Canada, three in Germany, two each in France, Italy, and Sweden, and one each for Denmark, Netherlands, Norway, and Taiwan. The majority of studies were conducted in a community care setting (51%), with 30% of studies in an inpatient setting, and five studies reflect care for patients in residential care. Two studies assessed outcomes separately for both those in residing the in community and those in residential care. [110 111]

Details of methodological quality of included studies is provided in Appendix 2.3. Included studies had a low risk of selection and reporting bias or confounding. The risk of detection bias was occasionally unclear due to the measures used to infer quality of care from retrospective database analyses in some studies. For cohort studies, the risk of attrition bias was often high or unclear due to poor reporting on the impact of differential follow-up. The funnel plots suggested limited publication bias but high heterogeneity (Figure 2.2).

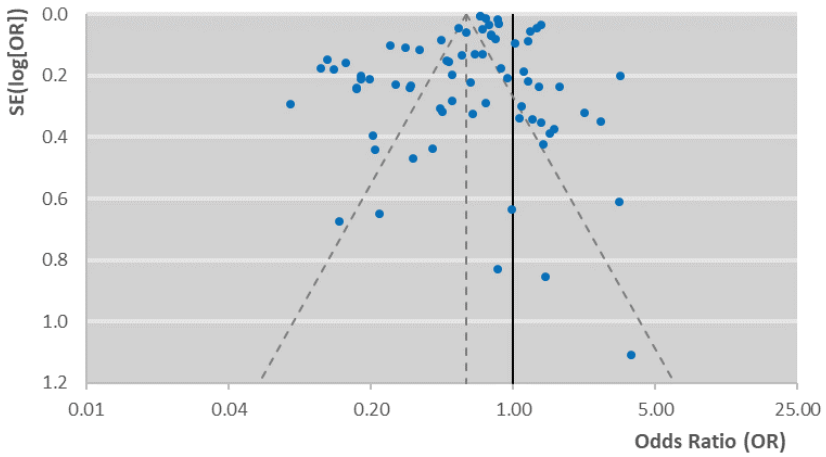

Figure 2.2. Funnel plots of quality of care in cognitively impaired patients for dichotomous quality indicators. The dotted vertical line represents the point estimate from the meta-analysis, and the dotted diagonal lines represent the 95% confidence interval for the given standard error.

Quality of Care

As heterogeneity was high, as indicated by the I^2 statistic, only random effects models are reported. The summary odds ratio of care quality was 0.59 (95% CI 0.48 to 0.71; k = 73 indicators, j = 31 studies) for patients with dementia or a cognitive impairment relative to patients who were not cognitively impaired (Figure 2.3), indicating that fewer patients will meet defined indicators of quality healthcare if they have a cognitive impairment or dementia. The Q statistic indicated a significant dispersion of results across studies (Q = 2062.29, df = 72, $p < 0.001$). Based on the I^2 statistic, 99.8% of the total variance was related to true heterogeneity between records (indicators within studies). To assess the role of clustering within studies, the meta-analysis via multilevel linear model captured some of the between-study variance ($\sigma^2 = 0.38$) and attenuated the summary odds ratio though this remained statistically significant (OR 0.67, 95% CI 0.53 to 0.84).

Sensitivity Analysis

Of the 73 indicators included in the meta-analysis, 24 were regression-adjusted for covariates. However, for nine of these unadjusted results were not available. In order to assess the impact of including unadjusted results in the meta-analysis, first the main analysis was reconducted using adjusted results excluding these studies. This did not noticeably change the effect size in either models using the HKSJ adjustment (OR 0.57, 95% CI 0.46 to 0.70; k = 64; j = 28), or the random intercept at the study level (OR 0.66, 95% CI 0.52 to 0.85). However, including unadjusted results in the analysis further reduced the odds of cognitively impaired patients receiving high quality care in both the HKSJ-adjusted model (OR 0.54, 95% CI 0.43 to 0.67) and the multilevel model (OR 0.60, 95% CI 0.45 to 0.80).

Subgroup Analyses & Effect Modifiers

Several exploratory subgroup analyses were conducted (Table 2.2). Given the high level of heterogeneity across studies indicated by the Q and I^2 statistics, the disease area, country, type of quality indicator, and the treatment setting significantly affected the odds ratios of meeting quality indicators (all analyses, $p < 0.001$). Likewise, the type of cognitive impairment significantly affected the odds ratio, with patients with diagnosed dementia having significantly lower odds of meeting quality indicators than their counterparts without a cognitive impairment, though this association did not hold in patients with a psychometrically assessed cognitive impairment.

Author (Year)	Disease	Indicator	No of Events / Total		Odds Ratio Random (95% CI)	Weight (%)	Odds Ratio Random (95% CI)
			Intact	Impaired			
Banach (2012)	Influenza	Received Vaccination	281 / 352	297 / 337		1.1	1.69 (1.07 to 2.69)†
Béjot (2015)	Stroke	Comprehensive Assessment	275 / 654	49 / 149		1.2	0.62 (0.40 to 0.96)†
Byers (2017)	Mood Disorder	Received Specialist Care	NR / 434	NR / 137		0.8	2.23 (1.19 to 4.18)†
Cancian (2013)	CVD	Received Beta Blockers	771 / 1,606	102 / 229		1.8	0.56 (0.43 to 0.73)
Christensen (2017)	Various	Preventative Home Visits	251 / 2,884	81 / 214		1.3	3.35 (2.26 to 4.96)†
Connolly (2013)	Atrial Fibrillation	Received Anticoagulants	3693 / 4,058	75 / 99		1.1	0.31 (0.19 to 0.50)
Connolly (2013)	CVD	Smoking Cessation Advice	11,247 / 12,225	23 / 48		0.9	0.08 (0.05 to 0.14)
Connolly (2013)	CHD	ACE Inhibitor After MI	1,523 / 1,813	11 / 21		0.5	0.21 (0.09 to 0.50)
Connolly (2013)	CHD	Blood Pressure Recorded	11,978 / 12,338	167 / 195		1.3	0.18 (0.12 to 0.27)
Connolly (2013)	CHD	Cholesterol Recorded	11,339 / 12,338	113 / 195		1.7	0.12 (0.09 to 0.16)
Connolly (2013)	CHD	Received Flu Vaccine	9,890 / 12,338	152 / 195		1.5	0.87 (0.62 to 1.23)
Connolly (2013)	Diabetes	Blood Pressure Recorded	12,445 / 12,832	115 / 136		1.1	0.17 (0.11 to 0.27)
Connolly (2013)	Diabetes	Cholesterol Recorded	12,062 / 12,832	113 / 136		1.1	0.31 (0.20 to 0.49)
Connolly (2013)	Diabetes	Hb1Ac Recorded	12,085 / 12,832	101 / 136		1.3	0.18 (0.12 to 0.26)
Connolly (2013)	Diabetes	Neuropathy Testing	10,523 / 12,832	51 / 136		1.5	0.13 (0.09 to 0.19)
Connolly (2013)	Diabetes	Retinal Screening	10,891 / 12,832	53 / 136		1.5	0.11 (0.08 to 0.16)
Connolly (2013)	Diabetes	Serum Creatinine Test	12,141 / 12,832	112 / 136		1.2	0.27 (0.17 to 0.42)
Connolly (2013)	Hypertension	Blood Pressure Recorded	37,742 / 41,665	324 / 438		2.0	0.30 (0.24 to 0.37)
Connolly (2013)	Stroke	Blood Pressure Recorded	5,084 / 5,308	139 / 170		1.3	0.20 (0.13 to 0.30)
Connolly (2013)	Stroke	Cholesterol Recorded	4,708 / 5,308	92 / 170		1.6	0.15 (0.11 to 0.21)
Connolly (2013)	Stroke	Received Flu Vaccine	3,977 / 5,308	131 / 170		1.4	1.12 (0.78 to 1.62)
Dreischulte (2014)	Atrial Fibrillation	Received Anticoagulants	8,717 / 19,458	144 / 1,007		2.1	0.25 (0.20 to 0.31)†
Fleming (2016)	Colorectal Cancer	Chemotherapy After Metastasis	NR	NR		0.5	0.40 (0.17 to 0.94)†
Fung (2017)	CKD	Received Nephrology Care	14,308 / 36,960	675 / 2,709		2.5	0.71 (0.64 to 0.78)†
Gershon (2014)	COPD	Pulmonary Function Test	171,672 / 467,125	4,764 / 24,629		2.6	0.73 (0.71 to 0.75)†
Giangregorio (2009)	Osteoporosis	Receiving Drug	57 / 125	149 / 395		1.8	0.71 (0.55 to 0.92)†
Grant (2013)	Incontinence	Drug Treatment	4,223 / 23,083	1,309 / 8,987		2.5	0.76 (0.71 to 0.81)
Han (2007)	ACS	Cardiac Catheterisation	126 / 180	9 / 21		0.4	0.32 (0.13 to 0.81)
Hoffmann (2011)	Pain	Pain Medication When Needed	3,301 / 7,385	878 / 1,848		2.4	0.78 (0.69 to 0.89)†
Holt (2012)	Atrial Fibrillation	Received Anticoagulants	17,934 / 33,661	108 / 380		2.0	0.35 (0.28 to 0.44)
Huang (2013)	Smoking	Cessation Prescription	37,714 / 281,749	17 / 684		1.1	0.17 (0.11 to 0.27)†
Kimmick (2014)	Breast Cancer	Guideline Concordance	4,029 / 6,170	94 / 269		0.8	0.45 (0.24 to 0.84)†
Klarin (2003)	CVD	Received Antithrombotics	NR	NR		1.1	1.34 (0.84 to 2.13)†
Klarin (2003)	CVD	Received ACE Inhibitor	NR	NR		0.8	0.44 (0.24 to 0.80)†
Klarin (2003)	CVD	Received Beta Blockers	NR	NR		0.9	0.50 (0.29 to 0.87)†
Klarin (2003)	CVD	Received Calcium Channel	NR	NR		0.9	0.73 (0.41 to 1.29)†
Klarin (2003)	CVD	Received Cardiac Therapy	NR	NR		1.2	1.19 (0.77 to 1.83)†
Klarin (2003)	CVD	Received Diuretics	NR	NR		1.3	0.94 (0.63 to 1.41)†
Lin (2012)	ACS	Drug Treatment	2,889 / 3,670	1,299 / 1,835		2.3	0.78 (0.68 to 0.89)†
Müther (2010)	Diabetes	Prescribed Medication	41 / 69	46 / 69		0.6	1.37 (0.68 to 2.73)
Müther (2010)	Hypertension	Prescribed Medication	163 / 181	154 / 181		0.7	0.63 (0.33 to 1.19)
Müther (2010)	High Cholesterol	Prescribed Medication	30 / 108	32 / 108		0.8	1.09 (0.61 to 1.97)
Nilsson (2011)	Hip Fracture	Receiving Occupational Therapy	132 / 147	34 / 53		0.5	0.20 (0.09 to 0.44)
Nygaard (2005)	Pain	Pain Medication When Needed	7 / 21	8 / 67		0.2	0.22 (0.06 to 0.76)†
Nygaard (2005)	Pain	Pain Medication When Needed	7 / 21	10 / 37		0.2	0.98 (0.28 to 3.40)†
Preuss (2016)	Atrial Fibrillation	Received Oral Anticoagulants	573 / 806	67 / 121		1.3	0.50 (0.34 to 0.74)
Raijmakers (2018)	Palliative Care	Dying in Preferred Place	383 / 536	80 / 166		0.3	3.33 (1.01 to 10.99)†
Raijmakers (2018)	Palliative Care	Dying at Home if Preferred	NR	NR		0.2	0.14 (0.04 to 0.52)†
Saposnik (2011)	Stroke	Admitted to Stroke Unit	5,814 / 8,602	442 / 702		2.2	0.82 (0.69 to 0.96)
Saposnik (2011)	Stroke	Antihypertensive Therapy	6,627 / 8,602	543 / 702		2.2	1.02 (0.85 to 1.22)
Saposnik (2011)	Stroke	Carotid Imaging	6,957 / 8,602	458 / 702		2.2	0.44 (0.38 to 0.52)
Saposnik (2011)	Stroke	Dysphagia Screening	5,827 / 8,602	501 / 702		2.2	1.19 (1.00 to 1.41)
Saposnik (2011)	Stroke	Received Anticoagulants	1,280 / 2,457	69 / 201		1.7	0.48 (0.36 to 0.65)
Saposnik (2011)	Stroke	Received Anticoagulants	7,985 / 8,602	627 / 702		1.9	0.65 (0.50 to 0.83)
Saposnik (2011)	Stroke	Received Anticoagulants	1,264 / 1,715	120 / 211		1.7	0.47 (0.35 to 0.63)
Scowcroft (2013)	Atrial Fibrillation	Received Anticoagulants	35,743 / 75,999	1,376 / 5,382		2.4	0.59 (0.52 to 0.66)†
Shah (2012)	Influenza	Received Vaccination	278,940 / 373,414	3,604 / 5,048		2.5	0.85 (0.79 to 0.90)
Shah (2012)	Influenza	Received Vaccination	4,447 / 5,524	2,984 / 3,582		2.4	1.21 (1.08 to 1.35)
Thorpe (2012)	Diabetes	Cholesterol Recorded	193,074 / 244,088	27,099 / 44,717		2.6	0.69 (0.68 to 0.69)
Thorpe (2012)	Diabetes	Hb1Ac Recorded	197,223 / 244,088	32,778 / 44,717		2.6	0.83 (0.81 to 0.86)
Thorpe (2012)	Diabetes	Retinal Screening	154,508 / 244,088	23,342 / 44,717		2.6	0.69 (0.68 to 0.70)
Vitagliano (2004)	CVD	Received Beta Blockers	22,046 / 43,227	771 / 2,143		2.5	0.54 (0.49 to 0.59)
Wachterman (2016)	Palliative Care	Received Palliative Care Consultation	31,057 / 54,077	2,382 / 3,676		2.5	1.36 (1.27 to 1.46)
Wachterman (2016)	Palliative Care	Palliative Care Rated Excellent	17,872 / 31,761	1,409 / 2,244		2.5	1.31 (1.20 to 1.43)
Zinn (2004)	Stroke	Speech Therapy Evaluation	40 / 98	25 / 54		0.7	1.25 (0.64 to 2.44)
Zinn (2004)	Stroke	Occupational Therapy Evaluation	63 / 98	40 / 54		0.6	1.59 (0.76 to 3.31)
Zinn (2004)	Stroke	Diagnostic CT/MRI Performed	51 / 98	29 / 54		0.7	1.07 (0.55 to 2.08)
Zinn (2004)	Stroke	Communication Evaluation	90 / 95	52 / 54		0.1	1.44 (0.27 to 7.71)
Zinn (2004)	Stroke	Depression Evaluation	42 / 113	17 / 36		0.6	1.51 (0.71 to 3.23)
Zinn (2004)	Stroke	Social Functioning Evaluation	24 / 110	11 / 39		0.5	1.41 (0.61 to 3.23)
Zinn (2004)	Stroke	Cognition Evaluation	81 / 86	62 / 63		0.1	3.83 (0.44 to 33.6)
Zinn (2004)	Stroke	Cognitive Goals Listed	31 / 92	33 / 57		0.7	2.71 (1.37 to 5.34)
Zinn (2004)	Stroke	Physical Goals Listed	113 / 120	27 / 29		0.1	0.84 (0.16 to 4.25)
Total (95% CI)						**100.0**	**0.59 (0.48 to 0.71)**

Test for heterogeneity: $\tau^2 = 0.04$, $\chi^2 = 2140.26$, df = 82, $p < 0.001$, $I^2 = 96.2\%$

Test for overall effect: $t = -6.81$, $p < 0.001$

0.01 0.04 0.20 1.00 5.00 25.00

Favours Intact Favours Impaired

† Adjusted odds ratio

Figure 2.3. Forest plot of the association between a dementia diagnosis or cognitive impairment and binary indicators of care quality

Table 2.2. Subgroup analyses on the association between cognitive impairments and care quality

Subgroup Analysis	Odds Ratio (95% CI)	Test for Residual Heterogeneity				Test for Moderators		
		Q	df	*p*	I^2	df1	df2	*p*
Disease Area		965.2	53	<0.001	99.7%	20	53	<0.001
ACS	0.54 (0.18 to 1.63)							
Atrial Fibrillation	0.38 (0.20 to 0.74)							
CVD	0.60 (0.36 to 1.00)*							
CHD	0.25 (0.12 to 0.55)*							
Diabetes	0.34 (0.21 to 0.54)*							
Hypertension	0.42 (0.14 to 1.22)							
High Cholesterol	1.09 (0.23 to 5.20)							
Stroke	0.74 (0.51 to 1.07)							
Cancer	0.43 (0.14 to 1.34)							
CKD	0.71 (0.17 to 3.01)							
COPD	0.73 (0.17 to 3.09)							
Influenza	1.19 (0.51 to 2.77)							
Osteoporosis	0.71 (0.16 to 3.07)							
Fractures	0.20 (0.04 to 1.05)							
Incontinence	0.76 (0.18 to 3.23)							
Anxiety	2.23 (0.46 to 10.76)							
Pain	0.58 (0.22 to 1.52)							
Smoking	0.17 (0.04 to 0.77)*							
Various	1.57 (0.71 to 3.47)							
Palliative Care	1.34 (0.48 to 3.72)							
Country		1955.2	62	<0.001	99.6%	11	62	<0.001
Canada	0.69 (0.45 to 1.06)							
Denmark	3.35 (0.88 to 12.77)							
France	0.62 (0.16 to 2.40)							
Germany	0.81 (0.44 to 1.49)							
Italy	0.87 (0.23 to 3.22)							
Netherlands	0.74 (0.21 to 2.62)							
Norway	0.45 (0.13 to 1.53)							
Sweden	0.68 (0.40 to 1.14)							
UK	0.29 (0.22 to 0.38)*							
USA	1.01 (0.73 to 1.38)							
Taiwan	0.78 (0.22 to 2.82)							
Indicator Type		1447.3	68	<0.001	99.7%	5	68	<0.001
Patient-Centred	1.49 (0.81 to 2.74)							
Drug Therapy	0.65 (0.50 to 0.83)*							
Rehabilitation	0.82 (0.51 to 1.34)							
Surgery	0.45 (0.10 to 2.08)							
Testing	0.33 (0.24 to 0.46)*							
Main Treatment Setting		1784.0	70	<0.001	99.7%	3	70	<0.001
Community Care	0.47 (0.37 to 0.59)*							
Inpatient Care	0.85 (0.63 to 1.16)							
Residential Care	0.55 (0.20 to 1.51)							
Cognitive Impairment		2039.8	71	<0.001	99.7%	2	71	<0.001
Dementia	0.49 (0.40 to 0.60)*							
Scale Assessed	1.11 (0.75 to 1.65)							

Abbreviations: ACS, acute coronary syndrome; CVD, cardiovascular disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CHD, coronary heart disease

* Quality of care was significantly lower ($p < 0.05$) for patients with diagnosed dementia and/or a psychometrically assessed cognitive assessment.

Table 2.3. Results of cross-category mixed-effects meta-regression model on the impact of cognitive impairment of indicators of care quality

Subgroup Analysis	Odds Ratio (95% CI)	Test for Residual Heterogeneity				Test for Moderators		
		Q	df	*p*	I^2	df1	df2	*p*
Atrial Fibrillation	0.60 (0.31 to 1.17)	1079.5	62	<0.001	99.5%	10	62	<0.001
CVD	0.40 (0.22 to 0.72)*							
CHD	0.67 (0.32 to 1.40)							
Diabetes	0.82 (0.47 to 1.44)							
Smoking	0.31 (0.08 to 1.16)							
UK	0.45 (0.29 to 0.68)*							
Drug Therapy	1.02 (0.66 to 1.58)							
Testing	0.53 (0.31 to 0.89)*							
Community Care	1.44 (0.93 to 2.23)							
Dementia	0.59 (0.38 to 0.91)*							
Constant	1.41 (0.92 to 2.14)							

Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease

* Quality of care was significantly lower ($p < 0.05$) for patients with diagnosed dementia and/or a psychometrically assessed cognitive assessment.

Subgroups where the odds of receiving high quality care were significantly lower for cognitively impaired patients were quality indicators for treating certain vascular diseases (atrial fibrillation, cardiovascular disease, coronary heart disease, or diabetes mellitus) or smoking cessation. Studies conducted in the UK and those in a community care setting also demonstrated significantly lower odds of cognitively impaired patients meeting quality indicators. The group of patients with diagnosed dementia or cognitive impairment also had lower odds of receiving drug treatments or testing or monitoring procedures than patients without cognitive impairments. In the fully adjusted model incorporating the significant predictors from each category, the intercept showed no differences in care quality and identified that the areas where a reduction in care quality is observed is for care for cardiovascular disease, or the need for testing or monitoring procedures (Table 2.3). However key drivers of a reduction in care quality appeared to be having a diagnosis of dementia or in studies conducted in the UK.

The results of the analyses using multilevel models came to comparable conclusions with regards to cardiovascular disease, smoking, testing or monitoring procedures, and dementia diagnoses, but also identified significantly worse quality care for diabetes and fractures. However, the effect for UK based studies was no longer statistically significant in the fully adjusted analysis, but studies conducted in Denmark were found to be significantly positive effect modifier. All results can be found in Appendix 2.4.

Additional Findings

Seven studies contributed findings that could not be included in the meta-analysis. Most of these studies presented findings in line with those of the meta-analysis, suggesting that patients with dementia or cognitive impairments receive worse quality care than patients without any cognitive impairment. However, one study demonstrated that there were no significant differences in adherence to quality indicators between demented and non-demented residents in a single Italian nursing home for diagnostic or treatment-related processes, but there was a strong, albeit non-significant, trend for poorer screening and prevention processes.[112]

Cognitive function was the biggest patient-level predictor of the quality of care provided to impaired older adults in nursing homes in Quebec, Canada, with better quality care being received by those who were less impaired.[113] A diagnosis of dementia was significantly associated with delayed or forgone initiation of anti-osteoporosis treatment following hip fracture in the UK.[114] Rates of prolonged use of indwelling urinary catheters amongst older patients with urinary incontinence were found to be increased in patients with dementia, contrary to treatment guidelines.[115]

A French cohort study also identified that patients with Alzheimer's disease and related syndromes received significantly fewer glycated haemoglobin tests, fewer cholesterol tests, fewer microalbuminuria tests, and fewer eye examinations, and that the differences in the rates of tests between demented and non-demented patients increased over time.[116] They also demonstrated that there were higher rates of hospitalisations due to diabetes-related complications amongst those patients with Alzheimer's disease. This was supported by a US studied showing significantly lower rates of glycated haemoglobin tests, fasting glucose tests, cholesterol tests, serum creatinine tests, and retinal screening in patients with diabetes who were diagnosed with dementia compared to those who were not.[110] However, it was identified that the disparities between those diagnosed with dementia and those not were reduced after admission to a nursing home. Patients with diagnosed dementia and atrial fibrillation who were receiving warfarin had no significant differences in the rates of international normalised ratio (INR) tests during treatment compared with those without dementia.[117]

2.4. Discussion

Principal Findings

This is the first meta-analysis comparing the quality of care between patients based on either cognitive impairment status. This meta-analysis synthesised data on the

association between the presence of dementia or another cognitive impairment in patients and the quality of care received, demonstrating that these are significantly associated with poorer quality care (summary OR 0.59, 95% CI 0.48 to 0.71). In fully adjusted analyses, it was noted that this association was largely driven by a diagnosis of dementia rather than a psychometrically assessed cognitive impairment, and that poor quality care persisted for patients being treated for certain vascular conditions or receiving testing or monitoring procedures. The less pronounced differences in quality between those patients who are cognitively impaired and those who are not in secondary care and residential care in the subgroup analysis could be attributed to patients and their informal carers having a reduced role in driving their demand for care due to increased observation and care management. However, for those individual effect modifiers in subgroup analyses and meta-regressions not showing significant effects these results should be interpreted with caution, given that some modifiers had few studies to determine its influence on results.

The results suggest that the effect is only present in those patients with a diagnosis of dementia rather than those with a non-dementia cognitive impairment. It is plausible that there are additional factors associated with dementia diagnosis beyond solely a cognitive impairment that impacts care, such as the general deterioration in health and functional status limiting access to care or the feasibility of it being provided. However, as the severity of cognitive impairment was not accounted for in the analyses, a diagnosis of dementia in the included studies may be associated with a more severe cognitive impairment which could be associated with worse quality care. Nevertheless, there is a drive to increase the early diagnosis of dementia, and people with more severe impairments are more likely to be in contact with healthcare services.

Further aspects of the study population and design may have affected outcomes, such as not accounting for the impact of multimorbidity on indicator outcomes. Given that dementia and comorbidities can affect the functional status and life expectancy of patients, this may influence treatment decisions with regard to what treatments and processes patients are fit enough to receive or will cause discomfort to these patients.[13] [106] Whilst this may be true in some cases, it is not in others. For example, people with dementia may be unable to follow instructions and therefore providing occupational therapy following hip fracture may be less clinically relevant.[118] However, prescribing anti-osteoporosis drugs to this population may be beneficial given that these patients are more likely to fall and experience further fractures.[103] On a similar note, the trend for higher rates of influenza vaccinations in demented patients may be because people

with dementia are at a greater risk of lower respiratory tract infections and so physicians may provide stronger recommendations for vaccination.[96]

In those with vascular conditions, improved survival rates have been observed in frail elders who are prescribed beta-blockers and present an opportunity to improve care, though it is possible that prolonged survival is not the primary goal of care in certain older and frail patients.[119] Primary care providers feel that patients with dementia are more difficult to manage than those with certain cardiac conditions, and that they feel that they could improve quality of life more for cardiac patients.[120] This may result in under treatment of conditions in some cases.[121] Severe dementia may be a valid reason for not conducting diagnostic or prognostic assessments if the affected patient is unable to follow instructions and complete testing, and desires to limit the number of invasive procedures, however mild dementia is not a valid reason in itself and therefore it is important to ensure preconceived notions are not barriers to such testing.[97 102]

Considering the patient driven demand for care services, the quality observed may also be influenced by having dementia. Patients with advanced dementia often do not recognise the need for therapeutic interventions, or actively reject treatments.[12] A decline in cognitive function may be associated with an impaired understanding of their health status or an inability to properly communicate health complaints and therefore limits the patient's, and health care professional's, recognition of health complaints that need to be treated.[104] In situations where the patient is not monitored and cannot be relied upon to take charge of their own care then the prescription of services may be redundant.[122] However, one included study evaluating the receipt of pain medication found that those with a diagnosis of dementia had lower odds of receiving pain medication when needed, but with those with only suspected dementia did not. This may indicate that the diagnosis of dementia, not simply the presence of a profound cognitive impairment, stigmatises patients and impacts the receipt of care.[123] The association between the quality of care provided for diabetes and cognitive function has been shown to be modulated by the levels of social support the patient received.[124] Therefore, increased social support and integrating the management of care across its delivery may be a driver of improved quality. This might help to explain why the differences in quality between the cognitive groups were less pronounced in secondary care and, to an extent, residential care because patients are less likely to have to be the drivers of their demand for care due to increased observation and care management. It should be noted that this study only highlights the differences in the quality of care observed and cannot differentiate the reasons for poorer quality care.

Strengths & Limitations

This systematic review indicates that having dementia is strongly associated with the quality of care received. The use of meta-analytical techniques aims to produce more robust estimates of associations than individual studies. The use of the Hartung-Knapp-Sidik-Jonkman method produces a more robust estimate of the confidence intervals of the effect size, and by assessing publication bias and the effects of heterogeneity on the estimates using subgroup analyses, meta-regression, and multilevel models, this serves to further increase the validity and reliability of the summary estimates. However, many the analyses were conducted on existing databases and in some cases differences between the cognitive cohorts were determined post hoc in ancillary analyses. Therefore, the data and analyses were always not hypothesis driven and powered for making such inferences.

Overall methodological bias was low, although the statistical methods used to identify exposure effects on observational data are subject to a potential lack of precision and some confounding. When estimating the effects of an intervention on outcomes, the randomised controlled trial provides a strong evidence base for the presence or absence of a differential effect. In estimating the effects of cognitive impairment on quality of care, laboratory settings cannot be used because patients cannot be randomised to having dementia or not and the quality of care can easily be manipulated within the trial. Therefore, observational data is a much more relevant source. However, observational data is subject to confounding by several other variables: patients living with dementia may be burdened with more comorbidities, be older, and subsequently less able to travel, or have an informal caregiver at home. Therefore, the observed differences may not be directly attributable to their impairment. Making statistical adjustments, matching subjects on key variables, and including covariates in the analysis might serve to better represent the treatment effects. The sensitivity analysis shows that including regression-adjusted results on 23 indicators serves to slightly attenuate the summary odds ratio and therefore if all indicators included adjusted results the summary odds ratio may move to a less marked difference in quality between the cognitive groups. However, care quality has been assessed in a number of different ways within this analysis. This presents one potential additional source of bias as this variation can lead to bias in interpreting the impact of dementia or cognitive impairment on quality of care, when quality of care can be defined in so many ways.

The included results of identified papers demonstrated considerable heterogeneity. This is not unexpected due to the differences in population and indicators between

studies. Although the summary effect sizes suggest a significant association with dementia, this could be largely due to the method of data synthesis and the fact that studies with a greater weight showed a stronger association with poorer quality care. Therefore, the robustness of the summary estimates come into question. Due to the range of outcomes and different indicators of quality, the appropriateness of the higher-level analyses may be limited. For example, it is questionable as to whether the rates of influenza vaccination are indicative of the same care quality as glycaemic control in diabetes patients. The summary odds ratios are weighted by the inter- and intra-study variance rather than the clinical relevance. It is therefore advocated that the higher-level analyses and summary effect sizes should be considered indicative of the trends in quality, whereas the lower-order analyses are more accurate representations of quality.

In addition, the search terms used to identify studies focussed on papers relating to the concept of quality of care, rather than a comprehensive search of studies related to a number of a priori determined quality indicators. Therefore, the studies included in this review are unlikely to be exhaustive.

Clinical & Research Implications

The recent NICE guidance on the care and management of dementia advocates that people with dementia should have equal access to care services as those without dementia.[34] It is pertinent to ensure that care for the general health and other medical conditions of patients with cognitive impairments is of a sufficient standard to maintain quality of life.[28-30] These findings do not clarify the nature of the association between cognitive impairments and care quality, specifically whether dementia is a condition that is causatively linked to poorer quality care or whether it is a marker of some other aspect of the patient's condition, such as frailty, or demand and need for quality health care, whose link to quality is confounded by other variables. Subsequent research should aim to assess the reasons for the observed differences in care quality between patients with dementia and people without. Irrespective, the results have practical implications with regard to patient management. When treating patients with advanced dementia, physicians should weigh up the benefits of treatment against the burden imposed,[12] such as stress, as most medical interventions can cause some discomfort to these patients.[13] The impact of forgoing quality care needs to be quantified in order to facilitate decision-making. If sacrificing care in favour of avoiding discomfort leads to early mortality or increased morbidity, then the impact of this on both the patient living with dementia and their caregivers should be assessed.

From an economic standpoint, attempting to increase care quality across the board may not be feasible. Given the burden and strain currently placed on health services, increasing the clinician's time demands per individual patient by increasing the rate of procedures would require a considerable expansion of human and physical resources. A recent publication has suggested that up to an additional 70,000 GPs would need to be hired in order to meet quality indicator targets in primary care in the UK.[11] Therefore, any attempt to improve quality should be outcomes focussed within the capacity framework and involve the prioritisation of procedures based on their expected impact on patient and population health.

Conclusions

As observed from studies in the real-world setting, the likelihood of meeting quality indicators across medical conditions is lower for patients with dementia, though not for those with non-dementia cognitive impairments. The lower rates of high-quality care observed in those with dementia potentially serves to expand the list of burdens placed on these individuals in terms of future health outcomes beyond the impact of dementia itself. With regards to the economic framework presented in Chapter 1, it appears that a dementia diagnosis plays a role in the quality of care in some of the evaluated settings, but that cognitive impairment alone is not a driver of care quality. Therefore, there could be a reduced demand for quality due to other facets of dementia limiting access to care, or a reduced supply of quality as physicians are less willing to provide care as the diagnosis of dementia creates an assumption on the limits of the marginal benefit of care. Further evidence is required to examine the reasons for, and the impact of, these care quality differences, taking into consideration comorbidities and clinical needs.

CHAPTER 3

QUALITY OF CARE PROCESSES IN ENGLISH ADULTS
THE ASSOCIATION WITH IMPAIRED COGNITIVE FUNCTION IN ELSA

3.1. INTRODUCTION

The systematic review and meta-analysis presented in the previous chapter highlighted significant differences in the quality of care received between those with dementia and those without, however several aspects of the relationship remain unappraised and new questions are postulated. Indicators in the previous chapter were often defined by potential clinical need or good practice, but the relationship between cognitive impairment and specific guidelines and care standards for older adults, where factors such as multimorbidity and frailty are likely to have been considered in the development of the indicators may be pertinent to explore.

Given that multimorbidity may influence treatment decisions based on fitness or discomfort,[13 106] and patients with dementia are observed to have a higher number of comorbidities,[125] the differences in care quality observed in the meta-analysis may be attributable to factors correlated with dementia rather than the condition itself. As was observed in the previous chapter, including individual study results that were adjusted for patient-level covariates served to attenuate the summary odds ratio, and so conducting analyses adjusting on relevant variables influencing access to and the supply of care may isolate the exposure effects of cognitive impairment on the quality of care received. Additionally, the relationship between the level of cognitive function and the quality of care received was not assessed. Including measures on the severity of cognitive impairment in the analyses may provide further granularity in explaining the observed differences.

The results of the meta-analysis also showed that the differences in the observed quality of care were greater in UK based studies. This posits questions as to why such differences were observed here but not in other countries and what can be done in terms of financing, organisation, or policy changes within the NHS to reduce the disparity in patient-relevant terms.

The aims of this chapter are twofold: the first is to generate contemporary estimates of the quality of primary care services provided to patients with cognitive impairments and dementia in the UK, and the second is to develop a dataset for further analyses in

this thesis, subject to the findings of this chapter. These analyses include (a) assessing the impact of poor-quality care for patients with dementia or a cognitive impairment and (b) appraising methods for improving quality.

3.2. Methods

Data Sources

The analysis used data from the English Longitudinal Study of Aging (ELSA) – a longitudinal panel study of people aged 50 and over, providing a representative sample of people living in private households in England.[126] The initial sample was drawn from households that participated in the Health Survey for England (HSE) in 1998, 1999, or 2001. Subsequent refresher samples have been drawn from later waves of HSE. Approximately 9,000 to 12,000 respondents are included at each wave, selected to be representative of people aged 50 years and over, living in private households in England.[126] There is a trend for more females to be included (approximately 55%) and nearly half were aged over 65 years at the first interview, however the average age has increased with time.[126-129] Respondents have been interviewed at biennial intervals and includes data collected on the quality of health care received, health status, cognitive function, demographic, and socioeconomic factors. For this analysis, data from waves 2 to 5 (surveyed in 2004 – 2005, 2006 – 2007, 2008 – 2009, and 2010 – 2011, respectively) of ELSA. These waves were selected due to having the most complete data on quality of care, with consistent measures of cognitive function being used.

Dementia & Cognitive Impairment Assessment

Self-reported cases of doctor diagnosed 'Alzheimer's disease' or 'dementia, senility, or other serious memory impairment' were included as two separate responses in ELSA. There was evidence of responses from individual respondents crossing between these two responses between waves. Therefore, responses were synthesised into a single variable of a dementia diagnosis. If respondents were interviewed at more than one wave and at a later wave the diagnosis of dementia was disputed, all cases of previous impairment from the same patient were adjusted accordingly on the assumption of an error in reporting at a previous wave. Given this analysis only includes wave 2 to 5, this assumes that all cases of dementia that are undisputed as of wave 5 are true cases of dementia. Using this method, the reported prevalence of dementia in the ELSA sample was between 0.9% and 1.9% depending on the study wave (between 1.4% and 3.2% in the sample aged over 65 years). Despite most respondents in ELSA being resident in the community, where the prevalence of dementia may be lower than in care homes,[44] there may still be underreporting of

diagnoses or undiagnosed cases given the recorded prevalence of dementia in England is roughly 4.3% in people aged over 65 years, and 0.8% in the general population.[130]

Prior to 2009, it was estimated that around a third of patients living with dementia had received a formal diagnosis, compared with two-thirds in more recent years.[131] This suggests that the prevalence of dementia (both diagnosed and undiagnosed) in the ELSA sample could be around 3% across all waves. To capture these patients, and potentially any unreported prodromal cognitive deficits such as mild cognitive impairment, a proxy variable for capturing cognitive impairment was developed. In addition, this population serves to validate the conclusions of the meta-analysis, where patients with cognitive impairments without a diagnosis of dementia did not have any significant differences in the quality of care received compared to patients without either cognitively impairment.

A battery of cognitive function tests is included in ELSA. Measures of memory (immediate and delayed recall) and executive function (verbal fluency and speed of mental processing) are commonly cited as the preferred measures of cognitive function in ELSA.[132-136] Memory was measured using: (1) immediate recall of a list of 10 words presented aurally, and (2) delayed recall of the same word-list after five minutes during which time they completed other survey questions. Executive function was evaluated using: (1) a semantic verbal fluency task where participants were asked to name as many animals as possible in one minute, and (2) a mental processing task where participants were handed a page of randomly generated letters set out in rows and columns and asked to cross out as many of the target letters ("P" and "W") as possible within one minute which was appraised for (a) how much of the task was done (speed), and (b) how accurate the completed portion of the exercise was (accuracy). Scores on both memory tasks, verbal fluency, and processing speed were normally distributed with no evidence of floor or ceiling effects.

ELSA includes other metrics of cognitive function, such as self-rated memory, orientation in time, and numerical ability, however these tests were chosen not to be used *a priori* due to the presence of ceiling effects or because they capture educational performance rather than cognitive function. The selected variables were also favoured over other methods for assessing cognitive function in ELSA, such as the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), because the IQCODE is a proxy-assessed measure of impairment where the respondent was unable to complete the self-report measures for cognitive or medical reasons. At wave 2 this would have left a viable sample of 72 respondents with at least one metric of care quality, of which only three respondents would be classified as having no cognitive

impairment. This sample would have been significantly underpowered for making inferences between the two populations of interest. Any attempt to expand the sample based on other criteria would not have been valid.

Latent variables for memory and executive function were developed using multilevel confirmatory factor analysis of the included ELSA scales. Multilevel models were favoured to account for the patient-level correlation between waves. The accuracy of mental processing was both bounded (0 to 100%) and positively skewed, as so was arcsine square root transformed for the analysis. Eigenvalues from a principal components analysis (PCA) indicated the presence of a single factor on both memory and executive function domains. Up to 10% of data was missing on the selected cognitive function assessments, and missingness was correlated both with advanced age and a diagnosis of dementia. Data were therefore considered to be missing not at random according to Rubin's definitions,[137] as missing cognitive function data was assumed to be associated with poor cognitive function. As multiple imputation methods are generally not considered appropriate for use in the case of data missing not at random,[138 139] to account for the missing data in the cognitive function scales, the full information maximum likelihood approach was adopted in estimating latent values and factor loadings, integrating both age and dementia diagnoses into the model (see Appendix 3.1). Patient-level scores for both memory and executive function were developed from the factor loadings. To assess the face validity of this cognitive score, known predictors of cognitive function (age, race, and education)[140] and risk factors for dementia (diabetes, hypertension, high cholesterol and BMI)[141] were regressed onto the scores (see Appendix 3.2 for results).

For this study, the diagnostic criteria for MCI proposed by Petersen (2004) have been adopted, which consider a cognitive decline that is not normal for age, reflecting either an amnestic (memory) impairment or non-amnestic (executive function) impairment.[20] However, what is an appropriate cut-off or deviation from the norm to define a cognitive impairment has not been defined. In order to determine the optimal cut-off, a range of threshold below norms standardised by five-year age groups (50-54 year, 55-59 years, … 90+ years) were explored. The cut-offs were aligned with definitions of below average or low scores on the standard IQ test[142] (from the mean score to 3 standard deviations below, see Appendix 3.3) to see which maximised the sensitivity and specificity of identifying diagnosed cognitive impairments (Alzheimer's disease or dementia) using a receiver operating characteristic (ROC) curve. Using this cut-off, a binary indicator of cognitive impairment on each domain was synthesised into a single variable for cognitive impairment. A categorical variable

was then defined including three levels of impairment: no determined cognitive impairment, cognitively impaired without diagnosed dementia (henceforth referred to as non-dementia cognitive impairment [NDCI]), and diagnosed dementia. To assess the impact of the severity of cognitive impairment on quality of care, two variables representing the quintiles of the latent age-standardised memory and executive function scores were also developed.

Quality of Care Indicators

ELSA includes 39 indicators of care quality covering 14 medical conditions (see Appendix 3.4 for details). The conditions covered are cerebrovascular disease (stroke), depression, diabetes mellitus, falls, hearing problems, high cholesterol, hypertension, ischaemic heart disease, osteoarthritis, osteoporosis, pain management, smoking cessation, urinary incontinence, and problems with vision (cataracts).

In the interview, ELSA respondents are asked a plethora of questions pertaining to the quality of processes in healthcare and these questions load onto indicators to determine whether the respondent received evidence-based healthcare standards for conditions they have. The indicators included in ELSA were derived from a list originally developed for RAND's 'Assessing Care of Vulnerable Elders' (ACOVE) project in the USA, and were chosen according to their prevalence, impact, effectiveness of prevention or treatment, importance in older people, feasibility of measurement, and the potential for quality improvement.[40 143] These indicators were rated for validity in England by an expert panel of clinicians.[144] All indicators were intended to assess the quality of the delivery of care to a minimum acceptable standard, rather than the optimal level,[145] and are based on self-report by patients. Each indicator comprises an eligibility statement describing the patient group to which the indicator applies (e.g., "If aged 50 or over and has diabetes"), and a question to ascertain whether or not the quality standard has been met (e.g., "In the past year, has any doctor or nurse examined your bare feet?"). Therefore, all indicators provide a binary answer to whether or not the minimal acceptable standard of care has been met.

All 39 quality indicators were evaluated at wave 2, however at subsequent waves only selected questions were asked. Appendix 3.7 summarises the availability of each quality indicator at each wave. Only ELSA respondents who were eligible for at least one quality indicator at any wave were retained for the analysis.

For this analysis, indicators have been classified in four different ways: overall quality of care, clinical categories (geriatric or general medical condition), disease categories, and process categories. The clinical categories defined indicators by disease and

whether these conditions were more prevalent in geriatric populations (falls, hearing problems, osteoarthritis, osteoporosis, urinary incontinence, vision problems) or general medical care (stroke, depression, diabetes, high cholesterol, hypertension, ischaemic heart disease, pain management, smoking cessation). The rationale for including these groupings is that the supply of care may be modified by the perceived need, where improving outcomes for certain geriatric conditions may be considered more relevant for increasing comfort in patients with dementia, compared to improving the long-term prognosis associated with general medical or cardiovascular conditions. The process categories defined indicators based on the underlying process of care involved, including pharmacotherapy, rehabilitative/supportive care, surgery or surgical referrals, diagnosis, prognosis and monitoring, and patient-centred care. Appendix 3.4 summaries how individual indicators load onto each category.

Covariates

To reduce the impact of selection bias and attempt to elicit the effect size of the association between cognitive impairment and health care quality, the analyses were adjusted for variables thought to influence health care access and those that may independently influence health care quality, as well as potential confounders. However, those traits that are common in patients with dementia (e.g., challenges with activities of daily living) were not included in the analysis in order to derive estimates of the association with the condition of dementia as a whole, rather than specifically a diagnosis of the condition and not the symptoms. Covariates were selected by generating direct acyclic graphs of the available variables using the DAGitty tool [146] to identify the adjustment needed to determine the total effect of dementia or cognitive impairment on care quality.

Certain area-level factors associated with healthcare access and supply were included in the analyses to account for the structural aspects of quality, as defined by the Donabedian framework. The area-level measures included were GP density, and the percentage of indicators met on the organisational domain of the Quality and Outcomes Framework (QOF).

The density of GPs was defined at the number of full-time equivalent (FTE) GPs per 1,000 registered patients in the Primary Care Trusts (PCT) the ELSA respondent was resident in at the time of the interview. PCTs were responsible for commissioning health care services during the data collection period of this analysis. Residence codes by PCT were obtained on special license from the data owners. Data on the number of FTE GPs and registered patients as of 30th September each year between 2004 and 2011 was obtained from NHS Digital.[147] Those figures closest to the month of the

interview were applied in the analysis. Previous research has shown that this measure of primary care supply was a significant predictor of health care quality measures in ELSA.[11]

As mentioned in Chapter 1, the QOF is a pay-for-performance contract for GPs in England. At the time of data collection in the included ELSA waves, indicators were grouped into four key domains: clinical (indicators akin to those captured in ELSA), organisational (e.g., record keeping and practice management), patient experience (whether patient surveys were conducted), and additional services (e.g., screening and health surveillance). The exact list of indicators included within each domain has changed over the years, with the organisational and patient experience domains being removed from the QOF since 2012 when virtually all practices scored 100%.[148] NHS Digital has published statistics at the PCT level regarding the proportion of indicators met on each of these domains for the year running from April to March from 2004/05 onwards.[149] As the metrics on the clinical domain reflect process indicators and are aligned with those in ELSA, only results from the QOF reflecting health care supply and structural factors were considered of relevance. Whilst no longer included in the QOF, the score on the organisational domain reflects supply relevant factors such as the data quality (completeness and timeliness) of patient records, the ease in contacting the practice and booking appointments, how up to date practice staff's training and skills are, and its coordination with social care services, and was therefore included in the analyses.

From 2006 onwards there were 152 PCTs in England, though prior to this there were 303. As residence codes were only permitted for 93 districts based on the 152 PCT structure by the data guardians (collapsing major city boroughs into a single district, e.g., London), I developed a mapping tool comparing which practices were in which PCT before and after the change from 303 to 152 PCTs. If boundaries between PCTs were changed, resulting in a fraction of the practices from one of the 303 PCTs not becoming part of one of the 152 PCTs, the mapping algorithm assumed that all practices in the old PCT followed the majority into the new PCT. This resulted in 33 practices (0.4%) being allocated to the wrong 152 structure PCT. To collapse the data on the 152 PCTs into the 93 districts provided, results from each PCT were weighted based on the number of respondents from each of the PCTs, kindly provided by the data guardians.

Patient-level variables were included in the models after assessing those requiring adjustment. Quintiles of total net wealth was included to capture socioeconomic differences in the burden of disease and access to healthcare, and marital status or

cohabitation as a proxy for informal care availability. Given that previous research has demonstrated gender differences in perceptions and acceptance of care,[150] sex was included as a covariate. Although age is strongly correlated with dementia and may therefore be considered to be captured within the exposure variable, as the measure of cognitive impairment used was based on an age-standardised variable the inclusion of five-year age band was used to capture other age-related effects, such as frailty and comorbidities. Further measures of comorbidity burden, as patient-level markers of overall healthcare resource need, were defined as categories of the number of diagnosed chronic (e.g., respiratory, musculoskeletal, psychological diagnoses) and cardiovascular (e.g., ischaemic heart disease, hypertension, diabetes) conditions. Alzheimer's disease or other dementias were excluded from comorbidity counts given these were captured elsewhere. Educational attainment was not included as a covariate. Although this commonly adjusted for and can be a proxy variable for health literacy and socioeconomic status, higher level qualifications are associated with a reduced risk of dementia.[151]

Missing Data

On the dataset derived for the analyses, the data on model predictors was largely complete except for net (non-pension) wealth, where 2.3% of observations were missing. However, 4.5% of quality indicators were missing responses, ranging from between 0.0% and 11.2% depending on the indicator. The appraisal of missingness for indicators was based on the assumption that data were complete for the denominators (i.e., the clinical need for a process assessed by the quality indicator) on the grounds that there were very few missing results on diagnoses reported by patients and there is a lack of clinical and methodological justification for generating assumptions on missing medical diagnoses. Although missingness was low overall, for several quality indicators this was correlated with having dementia or a cognitive impairment. Other correlates of missingness were older age, comorbidities, and challenges in performing activities of daily living. As some reasons for missingness can be accounted for in the model, using Rubin's definitions the data were assumed to be missing at random within these groups.[137] Imputation of missing data on the outcome variable when only covariates from the substantive model are included in the imputation model is often considered inappropriate as it purportedly does not yield an increase in information.[152] However, there is a growing impetus to impute outcome variables,[152] and previous research has shown that including incomplete dependent variables in the imputation model can improve imputations of the independent variables.[153] As quality of care is also to be used as a predictor in future analyses and data is available on variables not

involved in the current substantive model (further details below and in Chapter 4), it was deemed appropriate to impute outcome data on quality of care. The amount of missing data on quality indicators by cognitive group in reported in Appendix 3.5.

Multiple imputation is a statistical method which produces a number of imputed datasets of plausible values for missing data by using the available data to model the likely distribution of missing data.[154-156] The method is not designed to estimate exactly the missing values, but to correctly reflect the uncertainty around the missing data to improve estimation of parameters of analysis (i.e., regression coefficients). Analyses are conducted separately on each imputed dataset and then combined using Rubin's rules.[157] Specification of the imputation model was multilevel to account for both respondent-level factors in health care access and quality, and situational factors between waves for individual respondents. Variables included in the model were the cognitive variable, quality indicators, and the covariates above. In addition, whether the respondent was dead or resident in a nursing home or hospital by the next wave of ELSA, self-rated health, and metrics of quality of life and subjective wellbeing were also included so a single imputation model could be used for all planned analyses. Further details on these variables can be found in Chapter 4. Multiple imputation by chained equations (MICE) was used with regression models for each outcome, using linear regressions or bounded linear regressions for continuous variables (age, wealth, number of comorbidities, GP density, proportion of QOF points obtained on the organisational domain, and quality of life measures), logistic regressions for binary variables (cognitive impairment, quality indicators, sex, marital status, institutionalisation, and mortality), and ordinal logistic regressions for ordinal variables (socioeconomic classification, self-rated health, and frequency of help with ADLs). As the volume of missing data was low overall but associated with the primary exposure (diagnosed dementia), it was determined that a moderate number of imputations were required and so 50 datasets were imputed. For sensitivity, analyses were repeated only using complete cases and results are reported in Appendix 3.8.

Econometric Approach

A hierarchical regression model was used to account for indicators being clustered within study waves and individual respondents. Participants in ELSA only respond to the indicators they are eligible for, meaning that they are unlikely to respond to all 39 indicators, but may respond to more than one. Multilevel models can account for the random-effects in quality at the indicator and respondent-level for unmeasured covariates and variance in quality between indicators. The model used was:

$$C_{ijk} = \alpha + \beta f_{jk} + \delta Z_{jk} + \mu_i + \mu_k + \varepsilon_{ijk},$$

where C is the care quality associated with indicator i at wave j for individual k, β is the coefficient of interest of the association with a dementia diagnosis or NDCI f, δ is a vector of covariates Z, μ_i and μ_k are the indicator and respondent-level random-effect error components, and ε represents the error term. As all of the quality of care indicators C are binary values (met/unmet), logistic regression models were used.

Models analysing the impact of dementia and cognitive impairment on quality of care on subgroups of indicators will be run using the same model but limiting the observations according to the indicator groupings discussed in Appendix 3.4. As mentioned above, the models were run clustering quality indicators at five levels: overall quality of care, whether for geriatric or general medical conditions, treatments for specific diseases, categorisation by the type of process involved, and at the individual indicator level. Univariate models, excluding the covariates δZ, were also analysed for overall quality of care and by geriatric or general medical conditions. The analyses by severity of cognitive impairment were also only conducted on these three outcome groups.

For the pooled analyses, statistical significance was determined at the 5% level. For the analyses at the individual indicator level, given the potentially small number of respondents with diagnosed dementia eligible for the indicator the statistical power to detect differences at the 5% would be substantially reduced. Therefore, for these analyses, statistical significance was set at the 10% level to reduce the probability of a type II error and false interpretation of an outcome that may be clinically meaningful and could be assessed with further research.

3.3. Results

The latent cognitive function scores and the cognitive impairment index developed were all significantly associated with known predictors of dementia (see Appendix 3.2), as expected, providing some face validity to the estimates. The result of the ROC curve analysis indicated that a cut-off of 1.33 standard deviations below the mean maximised the sensitivity and specificity in identifying patients with dementia (see Appendix 3.3). Assuming that deviations from the mean have a similar clinical interpretation across metrics of cognition, this is aligned with a cut-off of 80 on the IQ test which is the marker of a borderline intellectual deficit.[142]

Table 3.1 summaries the characteristics of the overall evaluated population. Details of the population at each wave can be found in Appendix 3.6. The proportion of the

sample with diagnosed dementia between waves 2 and 5 were 0.9%, 1.7%, 1.6%, and 1.8%, respectively. The estimated prevalence of a NDCI declined from 13.9% at wave 2 to 9.8% at wave 5. Of the 126 patients who did not have diagnosed dementia upon first entry into the study but later reported a diagnosis, 51.6% of these were identified to have a NDCI at a previous wave. The mean age of the sample ranged from 65 to 67 years, approximately 55% were females, the majority were married or cohabiting, and nearly three-quarters had at least one diagnosed condition besides dementia. Patients with a dementia diagnosis were older and had more comorbidities. Both respondents with a NDCI or dementia were more likely to be male, be living alone or unmarried, and were less wealthy than respondents without a cognitive impairment.

Table 3.1. Characteristics of the sample

	No Impairment	Cognitive Impairment	Diagnosed Dementia	*p*-value
Observations	20,014	2,601	348	
Respondents	9,536	1,980	227	
Age, Mean (SD)	67.8 (9.8)	67.0 (9.5)	76.8 (9.9)	< 0.001
Age Groups				< 0.001
▪ 50 - 54	1,517 (7.6%)	240 (9.2%)	5 (1.4%)	
▪ 55 - 59	3,320 (16.6%)	460 (17.7%)	22 (6.3%)	
▪ 60 - 64	3,525 (17.6%)	461 (17.7%)	28 (8.0%)	
▪ 65 - 69	3,166 (15.8%)	420 (16.1%)	27 (7.8%)	
▪ 70 - 74	3,134 (15.7%)	427 (16.4%)	42 (12.1%)	
▪ 75 - 79	2,486 (12.4%)	327 (12.6%)	56 (16.1%)	
▪ 80 - 84	1,724 (8.6%)	174 (6.7%)	73 (21.0%)	
▪ 85 – 89	929 (4.6%)	77 (3.0%)	79 (22.7%)	
▪ ≥ 90	213 (1.1%)	15 (0.6%)	16 (4.6%)	
Female	11,395 (56.9%)	1,307 (50.2%)	172 (49.4%)	< 0.001
Married and/or Cohabiting	13,609 (68.0%)	1,573 (60.5%)	210 (60.3%)	< 0.001
Diagnosed Chronic Conditions				< 0.001
▪ None	7,588 (37.9%)	980 (37.7%)	99 (28.4%)	
▪ 1	8,058 (40.3%)	962 (37.0%)	132 (37.9%)	
▪ 2 or 3	4,149 (20.7%)	607 (23.3%)	104 (29.9%)	
▪ 4 or more	219 (1.1%)	52 (2.0%)	13 (3.7%)	
Diagnosed Cardiovascular Conditions				< 0.001
▪ None	4,629 (23.1%)	596 (22.9%)	48 (13.8%)	
▪ 1	7,524 (37.6%)	932 (35.8%)	111 (31.9%)	
▪ 2 or 3	7,094 (35.4%)	929 (35.7%)	147 (42.2%)	
▪ 4 or more	767 (3.8%)	144 (5.5%)	42 (12.1%)	
Net Non-Pension Wealth, Mean (SD)	£ 287,019 (480,147)	£ 163,969 (228,644)	£ 185,397 (214,446)	< 0.001
Eligible Quality Indicators, Mean (SD)	2.60 (2.15)	3.03 (2.56)	2.78 (2.34)	< 0.001
GPs per 1,000 Patients, Mean (SD)	0.57 (0.06)	0.56 (0.06)	0.57 (0.06)	< 0.001
QOF Organisational Domain, Mean (SD)	94.1% (0.04)	93.1% (0.05)	94.7% (0.04)	< 0.001

Notes: Values are *n* (%) unless otherwise stated. *p*-values for differences between cognitive groups were calculated using ANOVA or χ^2 tests as appropriate.

Quality of Care

Summary statistics for all the quality of care indicators are given by disease/condition, process type, and combined for general medical conditions, geriatrics conditions, and overall in Table 3.2. Statistics for each individual indicator are given in Appendix 3.7. On average, the number of quality indicators each respondent was eligible for at each wave was 2.7, 1.3, 1.6, and 1.7. The probability that quality of care standards were met across all 39 indicators combined at wave 2 was 64.8% in the observed dataset. At subsequent waves, with varying numbers of indicators included, the proportion of quality indicators met was 61.2%, 63.0%, and 68.7% for waves 3 to 5, respectively. The proportion of individual indictors met across all waves ranged from 18% to 100%.

Overall Associations with Dementia & Cognitive Impairment

The results combining all available quality of care indicators across all includes waves of ELSA are reported in Table 3.3, along with the results by clinical category (general medication or geriatric condition). The main finding is that a diagnosis of dementia is correlated with lower odds of meeting quality indicators than for patients without a cognitive impairment, particularly for the treatment of general medical conditions, and slightly less so for the treatment of geriatric conditions and only statistically significant

Table 3.2. Summary of outcomes on quality indicator groups

Indicator Group	Proportion Met	Standard Deviation	ELSA Wave(s)	Observations	Number of Indicators
Overall	64.7%	0.478	2 – 5	58,199	39
General Medical	75.0%	0.433	2 – 5	39,571	23
Geriatric	42.8%	0.495	2 – 5	18,628	16
Cerebrovascular Disease	40.7%	0.492	2 – 5	437	1
Depression	65.7%	0.475	2 & 4	1,348	3
Diabetes	69.0%	0.463	2 – 5	14,278	7
Falls	42.1%	0.494	2 & 4	615	2
Hearing Problems	79.1%	0.407	2	1,733	2
Hyperlipidaemia	63.7%	0.481	2	3,393	2
Hypertension	82.3%	0.382	2 – 5	15,069	3
Ischaemic Heart Disease	92.7%	0.260	2 & 5	1,775	5
Osteoarthritis	33.8%	0.473	2 – 5	12,662	5
Osteoporosis	67.6%	0.468	2 & 5	1,072	2
Pain	78.1%	0.414	2 & 4	631	1
Smoking	78.1%	0.413	2 & 5	2,640	1
Urinary Incontinence	51.1%	0.500	2	1,318	4
Vision Problems	53.6%	0.499	2 & 5	1,228	1
Pharmacotherapy	79.9%	0.401	2 – 5	21,268	12
Rehabilitative/Supportive Care	66.6%	0.472	2 – 5	5,091	4
Surgery	48.4%	0.500	2 – 5	1,976	2
Diagnosis	56.2%	0.496	2 & 4	3,464	7
Prognosis & Monitoring	83.0%	0.376	2 – 5	8,226	5
Patient-Centred Care	45.5%	0.498	2 – 5	20,909	9

Notes: Number of indicators reported is the maximum number included at wave 2

Table 3.3. Logistic regression models for the probability of meeting quality of care indicators – overall and by clinical categories

	All Indicators		General Medical		Geriatric	
	OR	95% CI	OR	95% CI	OR	95% CI
Observations (Respondents)	60,522 (10,418)		41,619 (8,845)		18,903 (5,586)	
Univariate Analyses						
Cognitive Impairment						
▪ No Impairment	*Ref*		*Ref*		*Ref*	
▪ Non-Dementia Impairment	1.14**	1.02 to 1.28	0.93	0.83 to 1.05	1.34***	1.11 to 1.61
▪ Diagnosed Dementia	0.43***	0.31 to 0.59	0.38***	0.27 to 0.53	0.61*	0.36 to 1.03
Multivariate Analyses						
Cognitive Impairment						
▪ No Impairment	*Ref*		*Ref*		*Ref*	
▪ Non-Dementia Impairment	1.14**	1.02 to 1.27	1.02	0.90 to 1.15	1.23**	1.03 to 1.48
▪ Diagnosed Dementia	0.36***	0.26 to 0.49	0.28***	0.19 to 0.39	0.59**	0.36 to 0.98
Age (years)						
▪ 50 – 54	*Ref*		*Ref*		*Ref*	
▪ 55 – 59	1.15*	0.98 to 1.35	1.28***	1.07 to 1.53	0.92	0.69 to 1.22
▪ 60 – 64	1.11	0.94 to 1.31	1.30***	1.08 to 1.58	0.96	0.72 to 1.29
▪ 65 – 69	1.16*	0.98 to 1.38	1.51***	1.24 to 1.84	1.06	0.79 to 1.42
▪ 70 – 74	1.18*	1.00 to 1.40	1.58***	1.30 to 1.93	1.19	0.89 to 1.60
▪ 75 – 79	1.20**	1.00 to 1.43	1.50***	1.22 to 1.85	1.39**	1.02 to 1.88
▪ 80 – 84	1.09	0.90 to 1.32	1.30**	1.03 to 1.63	1.55***	1.13 to 2.13
▪ 85 – 89	1.13	0.90 to 1.42	1.25	0.94 to 1.67	1.73***	1.21 to 2.46
▪ ≥ 90	0.63**	0.42 to 0.94	0.57**	0.33 to 0.97	1.09	0.64 to 1.85
Female	0.79***	0.72 to 0.87	0.90*	0.81 to 1.01	1.07	0.93 to 1.24
Married and/or Cohabiting	1.11**	1.01 to 1.23	1.21***	1.07 to 1.36	1.14*	0.98 to 1.33
Chronic Comorbidity Index						
▪ None	*Ref*		*Ref*		*Ref*	
▪ 1	0.60***	0.54 to 0.65	1.22***	1.10 to 1.35	0.44***	0.36 to 0.53
▪ 2 or 3	0.49***	0.44 to 0.55	1.15**	1.01 to 1.32	0.47***	0.38 to 0.57
▪ 4 or more	0.38***	0.28 to 0.51	0.97	0.65 to 1.45	0.47***	0.31 to 0.71
Cardiovascular Comorbidities						
▪ None	*Ref*		*Ref*		*Ref*	
▪ 1	1.77***	1.58 to 1.98	1.06	0.89 to 1.25	0.96	0.83 to 1.10
▪ 2 or 3	2.86***	2.56 to 3.21	1.41***	1.19 to 1.67	1.06	0.91 to 1.23
▪ 4 or more	3.38***	2.84 to 4.03	1.55***	1.24 to 1.95	1.02	0.75 to 1.38
Net Non-Pension Wealth						
▪ 1st Quintile (Least Wealthy)	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	0.90*	0.79 to 1.01	0.94	0.82 to 1.09	0.94	0.78 to 1.12
▪ 3rd Quintile	0.98	0.87 to 1.11	1.05	0.91 to 1.22	0.99	0.82 to 1.20
▪ 4th Quintile	0.91	0.80 to 1.04	1.02	0.87 to 1.19	0.96	0.78 to 1.18
▪ 5th Quintile (Wealthiest)	0.84**	0.73 to 0.97	1.01	0.85 to 1.20	0.88	0.71 to 1.10
GPs per 1,000 Patients	1.66	0.76 to 3.64	1.46	0.56 to 3.81	2.57	0.80 to 8.22
QOF Organisation Domain (%)	1.04***	1.03 to 1.05	1.10***	1.09 to 1.11	0.93***	0.91 to 0.94

Abbreviations: CI, confidence interval; OR, odds ratio

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

in the multivariate analysis. However, patients with a NDCI had significantly higher odds of meeting care quality indicators for geriatric conditions than patients with no impairment, driving a trend for higher quality. Trends were consistent between the univariate and multivariate analyses, however covariate adjustment served to attenuate the differences for patients with NDCI but exacerbate them for those with dementia.

With consideration to the covariates, advancing age showed a trend for increased odds of receiving care that meets the minimum acceptable standards, and that overall females are significantly less likely than males to receive care meeting the quality indicators. The presence of a partner was associated with better quality care. The impact of comorbidities was mixed, with a higher comorbidity burden of chronic conditions reducing the odds of meeting indicators for geriatric conditions and overall, which showing increases in the odds of meeting indicators for general medical conditions. Cardiovascular comorbidity burden was demonstrated to increase the odds of meeting quality indicators for general medical conditions and this was carried over to the analysis of all indicators.

Supply of primary care, as measured by GP density, was positively correlated with quality of care though not statistically significant. The organisational domain of the QOF was observed to have a positive effect on the quality of care for general medical conditions, but a detrimental effect on the quality of care for geriatric conditions.

Associations by Disease Area or Process Type

The results for each of the disease domains is presented in Table 3.4, and for each of the process types in Table 3.5. All analyses used the multilevel modelling approach with indicators clustered with individual respondents except for the analysis on vision problems (cataracts) given that data was only collected on a single indicator and respondents were only asked once (despite being collected in two waves), therefore a standard logistic regression model was used. All the models control for the same covariates as before (not reported).

A statistically significant negative effect of a dementia diagnosis on quality of care was observed at the 5% level in indicators for treating diabetes, hypertension, and osteoporosis, when compared to patients without an impairment. In addition, patients with dementia were significantly less likely to receive drug treatment for conditions, undergo prognostic tests or ongoing monitoring of conditions, or receive a patient-centred approach to their care. However, a strong, though not statistically significant, trend for better quality care for the treatment of falls was observed in this patient group. In the sample, no patients with a dementia diagnosis were eligible for quality indicators associated with the treatment of pain. Patients with a NDCI were significantly more likely to meet quality indicators for vision problems and hypertension, though demonstrated a trend for worse quality care for the treatment of ischaemic heart disease and stroke. There was also a trend for these patients to receive more drug treatment for their conditions than patients without cognitive impairments.

Table 3.4. Results for the probability of meeting quality of care indicators by disease area or risk factor

Disease Area	Observations	Non-Dementia CI		Diagnosed Dementia	
	(Respondents)	OR	95% CI	OR	95% CI
Cerebrovascular Disease	437 (253)	0.58	0.26 to 1.28	0.68	0.13 to 3.48
Depression	1,348 (695)	0.94	0.56 to 1.59	1.23	0.33 to 4.60
Diabetes	14,727 (1,538)	0.93	0.77 to 1.11	0.29***	0.17 to 0.48
Falls	615 (293)	1.61	0.84 to 3.06	2.90	0.66 to 12.78
Hearing Problems	1,733 (1,047)	1.16	0.81 to 1.65	1.11	0.40 to 3.12
Hyperlipidaemia	3,393 (1,708)	0.94	0.75 to 1.18	0.54	0.21 to 1.37
Hypertension	16,591 (6,056)	1.28**	1.01 to 1.63	0.14***	0.08 to 0.28
Ischaemic Heart Disease	890 (636)	0.63*	0.37 to 1.08	0.84	0.20 to 3.54
Osteoarthritis	12,830 (3,962)	1.04	0.84 to 1.29	0.57*	0.30 to 1.09
Osteoporosis	1,107 (847)	0.97	0.51 to 1.87	0.10**	0.02 to 0.60
Pain	626 (615)	1.21	0.69 to 2.10	*No Observations*	
Smoking	2,699 (2,097)	0.95	0.66 to 1.36	0.32*	0.09 to 1.16
Urinary Incontinence	1,332 (333)	1.19	0.85 to 1.66	0.94	0.42 to 2.12
Vision Problems	1,286 (1,286)	1.48**	1.04 to 2.10	0.75	0.37 to 1.53

Table 3.5. Results for the probability of meeting quality of care indicators by healthcare process type

Indicator Process Type	Observations	Non-Dementia CI		Diagnosed Dementia	
	(Respondents)	OR	95% CI	OR	95% CI
Pharmacotherapy	20,305 (8,152)	1.14*	0.99 - 1.31	0.32***	0.22 - 0.45
Rehabilitative/ Supportive Care	5,090 (3,620)	1.24	0.92 - 1.66	0.85	0.32 - 2.30
Surgical Referrals	1,974 (1,594)	1.51	0.72 - 3.16	0.51	0.08 - 3.34
Diagnosis & Testing	3,414 (2,095)	1.06	0.83 - 1.36	0.68	0.36 - 1.30
Prognosis & Monitoring	7,980 (1,678)	1.01	0.81 - 1.27	0.32***	0.17 - 0.60
Patient-Centred Care	20,858 (6,320)	0.90	0.76 - 1.06	0.49***	0.29 - 0.83

Abbreviations: CI, confidence interval; OR, odds ratio

Notes: All odds ratios and confidence intervals given are with reference to population without a cognitive impairment or dementia (OR = 1). * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Associations by Individual Quality Indicators

The estimates of the impact of the dementia and NDCI, adjusted for the covariates, on each of the indicators of quality of care separately are presented in Table 3.6. Results are only reported for 36 indicators as for the remaining three there was either no variation in outcome (patients receiving antiplatelets for coronary heart disease) or insufficient variation in outcome to fit the models (patients on warfarin receiving frequent INR tests, and treatment for women diagnosed with osteoporosis). For four indicators, there were insufficient observations to estimate an odds ratio for respondents with diagnosed dementia. A statistically significant effect ($p < 0.1$) of dementia diagnosis was observed on seven of the indicators. All but one of these (falls assessment) showed a negative association between dementia diagnosis and quality of care. A statistically significant effect of a NDCI was also observed on seven indicators.

Table 3.6. Logistic regression models for the probability of meeting quality of care indicators by indicator

Quality Indicator	Observations (Respondents)	Non-Dementia CI		Diagnosed Dementia	
		OR	95% CI	OR	95% CI
Stroke Antihypertensives	437 (253)	0.58	0.26 to 1.28	0.68	0.13 to 3.48
Depression Suicide	751 (681)	1.12	0.59 to 2.13	0.85	0.17 to 4.27
Depression Treatment	559 (517)	0.75	0.40 to 1.39	1.32	0.16 to 11.21
Depression Review	34 (34)	0.14	0.00 to 5.25	*Insufficient Observations*	
Diabetes HbA1c	3,076 (1,415)	1.02	0.74 to 1.41	1.19	0.42 to 3.36
Diabetes Proteinuria	1,261 (808)	0.62**	0.40 to 0.97	0.54	0.13 to 2.17
Diabetes Cholesterol	235 (235)	0.77	0.25 to 2.42	*Insufficient Observations*	
Diabetes ACE Inhibitor	1,972 (1,217)	0.88	0.61 to 1.27	0.94	0.39 to 2.26
Diabetes Foot Check	3,445 (1,538)	1.11	0.77 to 1.59	0.15***	0.06 to 0.37
Diabetes Training	2,367 (1,289)	0.54**	0.34 to 0.88	0.30*	0.07 to 1.22
Diabetes Knowledge	2,367 (1,289)	0.83	0.55 to 1.24	0.13***	0.04 to 0.37
Falls History	304 (291)	1.08	0.55 to 2.09	1.03	0.24 to 4.48
Falls Assessment	308 (293)	2.22**	1.13 to 4.37	6.50**	1.17 to 35.97
Hearing Evaluation	1,047 (1,047)	0.97	0.63 to 1.48	0.60	0.19 to 1.87
Hearing Rehabilitation	677 (677)	1.74	0.89 to 3.42	*Insufficient Observations*	
Cholesterol Explanation	1,705 (1,705)	0.90	0.64 to 1.27	0.83	0.20 to 3.35
Cholesterol Preferences	1,688 (1,688)	0.97	0.72 to 1.31	0.31	0.06 to 1.47
Hypertension Treatment	13,267 (6,056)	1.54***	1.18 to 2.01	0.09***	0.05 to 0.16
Blood Pressure Explanation	1,662 (1,662)	0.71**	0.52 to 0.97	2.76	0.44 to 17.21
Blood Pressure Choice	1,662 (1,662)	0.81	0.60 to 1.10	1.84	0.57 to 5.95
IHD Cholesterol	269 (269)	0.39**	0.16 to 0.95	0.52	0.04 to 7.37
IHD Smoking	251 (207)	0.88	0.25 to 3.07	0.99	0.05 to 19.39
MI Beta Blockers	197 (197)	0.95	0.35 to 2.58	0.99	0.04 to 25.33
Osteoarthritis Exercise	1,446 (1,116)	0.81	0.48 to 1.36	1.69	0.30 to 9.56
Osteoarthritis Education	7,271 (3,879)	1.08	0.82 to 1.41	0.86	0.43 to 1.71
Osteoarthritis Paracetamol	1,616 (1,599)	1.28	0.91 to 1.79	0.95	0.15 to 6.09
Osteoarthritis Referral	688 (542)	0.85	0.42 to 1.71	2.10	0.19 to 22.62
OA Treatment Purpose	1,803 (1,466)	0.93	0.58 to 1.49	0.73	0.14 to 3.83
Osteoporosis Supplements	920 (847)	0.99	0.51 to 1.92	0.11**	0.02 to 0.70
Pain Treatment	626 (615)	1.21	0.69 to 2.10	*No Observations*	
Smoking Cessation	2,699 (2,097)	0.95	0.66 to 1.36	0.32*	0.09 to 1.16
Incontinence History	333 (333)	1.69	0.79 to 3.61	3.36	0.67 to 16.93
Incontinence Examination	333 (333)	1.02	0.54 to 1.92	0.39	0.07 to 2.15
Incontinence Treatment	333 (333)	1.56	0.81 to 3.03	2.69	0.47 to 15.45
Urinalysis	333 (333)	0.82	0.40 to 1.67	0.29	0.06 to 1.40
Cataracts Surgery	1,286 (1,286)	1.48**	1.04 to 2.10	0.75	0.37 to 1.53

Notes: All odds ratios and confidence intervals given are with reference to the population without a cognitive impairment or dementia (OR = 1). * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

For all of these except those related to hypertension and cataracts, the direction of effect was the same as for a dementia diagnosis. Patients with a NDCI were more likely than non-impaired patients to receive treatment for hypertension, but less likely to have a patient-centred approach to their treatment. As mentioned above, patients with a NDCI were significantly more likely to meet quality indicators for vision problems. The indicators with a significant relationship, whether positive or negative, with either a dementia diagnosis or a NDCI were:

- Have you had a urine test for protein in the last 12 months? (Diabetes Proteinuria)
- In the past year, has any doctor or nurse examined your bare feet? (Diabetes Foot Check)
- Have you ever participated in a course or class about diabetes, or received special training on how you can live with your diabetes from day to day? (Diabetes Training)
- How much do you think you known about managing your diabetes? (Diabetes Knowledge)
- Did a doctor or nurse or physiotherapist test your balance or strength or watch how you walk to understand why you fell; or did a doctor or nurse or physiotherapist recommend any additional tests, such as heart tests or brain scans to understand why you fell? (Falls Assessment)
- Did a doctor or nurse ever suggest you take any medication to lower your blood pressure? (Hypertension Treatment)
- Has a doctor or nurse explained high blood pressure in a way you could understand at any time since you were first told you had high blood pressure? (Blood Pressure Explanation)
- Has any doctor talked to you about how to lower your cholesterol? This would include changing your diet, losing weight, getting more exercise, or taking medication. (IHD Cholesterol)
- Has any doctor or nurse recommended taking calcium pills or Vitamin D? (Osteoporosis Supplements)
- Has a doctor or nurse ever advised you to stop smoking; or has any doctor or nurse ever told you about any nicotine products, such as nicotine patches, chewing gum, lozenges, or other similar products at all to help you give up smoking? (Smoking Cessation)
- Did any doctor or optician recommend that you have your cataracts removed? (Cataracts Surgery)

Associations by Severity of Cognitive Impairment

Given that cognitive impairment was determined by a composite of both memory and executive function, severity of cognitive impairment was estimated based on quintiles of age-standardised scores on each of these domains. Models were run including both domains together, and then independently, both overall and by clinical category, including the same covariates as before, and results are presented in Table 3.7.

The results show that on overall quality of care (all indicators combined) there is little effect of the severity of cognitive impairment, though patients in the third quintile

Table 3.7. Logistic regression models for the probability of meeting quality of care indicators – (A) by level of memory and executive function, (B) by memory alone, and (C) by executive function alone

	All Indicators		General Medical		Geriatric	
	OR	95% CI	OR	95% CI	OR	95% CI
Observations (Respondents)	60,522 (10,418)		41,619 (8,845)		18,903 (5,586)	
A						
Memory						
▪ 1st Quintile	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	1.02	0.94 - 1.10	1.03	0.93 - 1.14	1.01	0.86 - 1.17
▪ 3rd Quintile	0.95	0.87 - 1.05	0.90*	0.79 - 1.02	1.03	0.86 - 1.24
▪ 4th Quintile	1.08	0.97 - 1.20	1.08	0.94 - 1.24	1.11	0.91 - 1.37
▪ 5th Quintile	1.11*	0.98 - 1.26	1.03	0.87 - 1.21	1.28**	1.01 - 1.63
Executive Function						
▪ 1st Quintile	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	0.96	0.88 - 1.04	1.04	0.94 - 1.15	0.88*	0.75 - 1.02
▪ 3rd Quintile	0.89**	0.81 - 0.98	0.96	0.85 - 1.09	0.81**	0.67 - 0.98
▪ 4th Quintile	0.98	0.87 - 1.09	1.18**	1.02 - 1.36	0.78**	0.63 - 0.96
▪ 5th Quintile	0.90	0.79 - 1.03	1.23**	1.03 - 1.46	0.68***	0.53 - 0.87
B						
Memory						
▪ 1st Quintile	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	0.98	0.92 - 1.04	1.04	0.96 - 1.13	0.91*	0.81 - 1.02
▪ 3rd Quintile	0.89***	0.84 - 0.95	0.92**	0.84 - 1.00	0.87**	0.77 - 0.98
▪ 4th Quintile	1.03	0.96 - 1.10	1.19***	1.09 - 1.29	0.89*	0.78 - 1.00
▪ 5th Quintile	1.03	0.96 - 1.11	1.22***	1.11 - 1.34	0.94	0.83 - 1.06
C						
Executive Function						
▪ 1st Quintile	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	0.96	0.90 - 1.02	1.03	0.95 - 1.12	0.89**	0.79 - 1.00
▪ 3rd Quintile	0.89***	0.84 - 0.95	0.93*	0.86 - 1.01	0.85**	0.76 - 0.96
▪ 4th Quintile	1.03	0.96 - 1.10	1.20***	1.10 - 1.31	0.87**	0.77 - 0.99
▪ 5th Quintile	0.99	0.92 - 1.06	1.26***	1.15 - 1.39	0.84***	0.74 - 0.96

Notes: The first quintiles refer to respondents with age-standardised scores on each domain that were the lowest (worst cognitive function), with each subsequent quintile representing improved cognitive function. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

(average cognitive function) have lower odds of meeting quality indicators. For general medical indicators, there is a positive association between level of executive function and quality of care. There is also a positive trend between memory and quality of care, though this is only significant when not adjusting for executive function. There was a significant negative association between executive function and quality of care for geriatric conditions. When adjusting for executive function, there was a non-significant trend for patients with better memory to receive better quality care. However, when assessed independently, it was observed that patients who performed better on memory measures received significantly worse quality care.

3.4. Discussion

Principal Findings

The first aim of this chapter was to derive a dataset for on which further analyses could be conducted regarding the impact of, and solutions to, poor quality care for patients with cognitive impairment or dementia. The use of ELSA has provided a comprehensive dataset of quality of care indicators relevant to older patients in which to inform the role care quality plays in this relationship. The metric of cognitive impairment developed for those without a diagnosis of dementia carries some validity, given its association with prevalent dementia, future incidences of dementia, and known predictors of cognitive function and risk factors for dementia. The sample size for respondents diagnosed with dementia, however, is rather small meaning further analyses on this subgroup of patients may not be powered for making inferences.

The other aim of this chapter was to quantify the association between a diagnosis of dementia, or an undiagnosed or unreported cognitive impairment, and the quality of primary care services provided to patients in the UK. The results of this analysis are comparable to those from the meta-analysis in the previous chapter, in that patients with a dementia diagnosis were observed to less frequently receive minimum acceptable standards of care than patients without a cognitive impairment. Patients with low executive function or poor memory, but without a dementia diagnosis, had comparable or marginally improved levels of care quality compared to those without cognitive impairments, depending on the type of condition treatment was for. Care quality for geriatric conditions was also negatively correlated with severity of the impairment.

Taking a more granular view, patients with dementia were significantly less likely to meet indicators for diabetes, hypertension, or osteoporosis, though significantly more patients with dementia had comprehensive assessment for why they had a fall. For respondents with a NDCI, few significant effects were observed at the disease level, suggesting they potentially receive worse quality care than patients without a cognitive impairment for ischaemic heart disease, but are significantly more likely to be referred to have surgery to remove cataracts or have high quality care for hypertension. These findings are somewhat inconsistent with the higher-level findings for overall quality of care or geriatric quality of care, suggesting that the small effect sizes require larger sample sizes to achieve statistical significance.

For the analyses at the indicator level, results can be challenging to interpret for the group of patients with diagnosed dementia given the small sample sizes. Despite using

a significance level of 10% in an attempt to reclaim some statistical power, the number of patients with dementia for the 32 indicators analyses were conducted on ranged from two to 129 (median 11.5, see Appendix 3.5). Therefore, inferences on the differences between cognitive groups for indicators with limited respondents with dementia may not be especially valid or reliable.

The results of the complete cases analysis demonstrate the impact of missing data on the results (see Appendix 3.8). For respondents with a NDCI, the point estimate for geriatric quality of care has changed very little, supported by the very low levels of missing data on quality of care outcomes. Whereas for general medical care 4.6% of observations had missing data, and the inference differs between the analyses, from showing a negative association to no association. For respondents with diagnosed dementia the inferences have changed significantly when accounting for the missing data. The complete cases analyses showed no significant differences in quality care for patients with dementia. Assuming the correct specification of the imputation model, the impact of missing data in this subgroup was substantial, which is not unexpected given that 26% of indicator results were deemed to be missing. Based on the hypothesis noted above that patients with missing data on the cognitive domain are those with the worst cognitive function, and this translates to missing data on other domains, then it stands to reason that patients with dementia in more severe forms are the least likely to meet the quality indicators, in line with the results for the imputed analyses. Estimates of the effect of other correlates of missingness of the quality of care data (age and comorbidities) on the outcome did not change between the complete cases and imputed analyses.

As to why patients with a NDCI had limited differences in care quality compared with patients without a cognitive impairment, or even improvements in quality, whilst care quality for patients with diagnosed dementia was lower, I have identified two possible reasons. The first relates to weaknesses in the cognitive impairment measure, and the second pertains to whether there are additional factors associated with a diagnosis of dementia beyond cognitive impairment that impacts the quality of care, such as the general deterioration in health and functional status limiting access to care or the feasibility of it being provided. As such, a metric for undiagnosed dementia should perhaps incorporate impairments in activities of daily living, and emotional or behavioural symptoms, differentiating it from some of the diagnostic criteria for MCI. The defined NDCI metric was age-standardised and therefore naïve to other age-related factors that may have a compound effect or interaction with other covariates to influence care quality.

With regards to covariates and further predictors of care quality, the results show that the comorbidity burden has a substantial impact on the quality of care received. Having multiple diagnosed chronic conditions was associated with worse quality care for geriatric conditions. This may be because these chronic conditions are associated with older populations (e.g., Parkinson's disease, osteoarthritis, osteoporosis) and therefore is reflective of higher care demands for geriatric conditions and so upon presenting to a GP, the limited time and resources available mean that certain conditions or factors need to be deprioritised. However, for cardiovascular conditions, a greater comorbidity burden was associated with better quality care on the general medical domain. Many of the general medical indicators included are for cardiovascular and related conditions. Given the comorbid nature of conditions and risk factors such as diabetes, hypertension, ischaemic heart disease, treatments for one are often for the primary or secondary prevention of another.[71] Therefore a greater comorbidity burden to reflect a greater need. In addition, it has been postulated that the main benefits of the clinical indicators in the QOF are for patients aged 40 to 74 years with cardiovascular disease,[158] and therefore there may be greater incentive for GPs to treat this patient group, increasing quality against the included metrics.

Covariate adjustment also had a small influence on the association between a dementia diagnosis and care quality. Conversely to what was identified in the meta-analysis in the previous chapter, covariate adjustment exacerbated the differences between patients with dementia and the patients without a cognitive impairment. However, adjusted did slightly attenuate the differences for patients with a non-dementia cognitive impairment, in line with the meta-analysis.

Strengths & Limitations

A strength of this analysis lies with the quality of the data, where a number of evidence-based indicators of care quality have been derived for inclusion. However, sample sizes for certain indicators were small in some patient groups leading to a lack of statistical power to detect differences, despite the imputation of missing data. The multilevel approach taken in the regression analyses allowed for the exploitation of multiple responses from individual respondents in order to take a wider perspective on the impact of cognitive function on care quality. Although other data sources evaluating quality are available, such as the QOF, these do not always account for necessary patient-level characteristics required in this analysis. However, leveraging data from the QOF and on GP density at the PCT level to some extent captures practice-level characteristics and the structural aspects of quality, such as resources, funding, and the framework for providing high quality clinical care to patients.

However, this analysis is not without its limitations. With the exception of cognitive function testing, all variables were based on self-reported outcomes – including those in patients with cognitive impairments or dementia, though a family member or caregiver may have been present during the interview. Although previous research has demonstrated a strong correlation between self-reported processes using quality indicators and processes recorded in medical records,[145 159] one study reported that indicators relating to communication and non-prescription treatments had significantly higher pass rates on the self-reported indicators.[159] This means that patients may remember care which was not documented in the records, or may report receiving care which they did not receive.[11] The inverse may be true for patients with a serious memory impairment, where certain indicators require respondents to comment on whether some process of care was conducted over the past 12 months.

The quality indicators included in this study also only pertain to a certain number of conditions and processes, whereby a patient has received a diagnosis for this condition. It is therefore not possible to make inferences that apply to the entire domain of care where other relevant health conditions have been excluded. As treatment for a condition and the quality indicator is dependent on a diagnosis of disease, the differential effects of cognitive impairment on diagnosis have not been accounted for – if patients with dementia or cognitive impairment are less likely to receive a diagnosis for certain conditions, perhaps for similar reasons that lead to worse quality care, then the quality of care for undiagnosed conditions goes unreported.

The use of observational data to determine the effect of an exposure on an outcome is subject to several limitations surrounding selection bias, and is why the randomised controlled trial, or a synthesis of these, remains the preferred method for estimating effects of exposures or interventions for evidence-based medicine. However, as patients cannot be randomised to have a diagnosis of dementia, and the outcome of care quality is determined by the parties involved as a potential consequence of the exposure, rather than directly by the exposure variable itself, a randomised controlled trial would not be possible. Alternative analytic approaches, such as a nested case-control study which is generally ranked higher on the hierarchy of evidence than cross-sectional studies,[160 161] could have been used. However, these methods were deemed to be more challenging to apply relative to the benefits gained from their use given the obstacles associated with matching and choosing matching variables when using a proxy for dementia diagnoses, as well as the small sample sizes in the diagnosed dementia group for which a regression analysis can be better powered.[162] The use of directed acyclic graphs to determine relevant patient-level variables for inclusion in

the analysis, alongside the structural aspects of care captured at the PCT level, suggests that the estimates derived in this study should reflect treatment decisions for patients based on their cognitive status as opposed to other confounding variables.

Given the inconsistency in results between the complete cases analysis and models with imputed data, one must consider the benefits of imputation. When data are missing at random, use of methods such as multiple imputation may lead to unbiased results.[138] Previous work has suggested that complete case analysis may be used if the proportion of missing data is low, approximately 5% as a rule of thumb, and if missingness due to exposure is implausible.[163 164] Although the proportion of missing data was low overall, this was strongly correlated with having a diagnosis of dementia and therefore is assumed to have introduced bias into the analysis. Imputing data for these patients was therefore considered to be the preferred strategy.

However, it is worth highlighting that two separate models for missing data were used: one to impute missing data on quality of care and other covariates, and other to estimate cognitive function scores. Whilst this violates conventional practice it was deemed acceptable here given the differing mechanisms of missingness and analytical methods required, and it was assumed that the determination of cognitive impairment in the population would be independent of the quality of care received. Regardless, the inferences for the group of patients with diagnosed dementia are unlikely to change as the quality of care for those with a NDCI and for those with no assessed impairment was largely comparable, and so minor variations in which patients are defined as cognitively impaired is assumed to have little effect on the odds ratios for patients with dementia.

Clinical & Research Implications

Over these past two chapters, a meta-analysis and now an analysis on a large observational dataset have suggested that there are significant differences between patients with diagnosed dementia and those without any assessed cognitive impairment with regards to meeting indicators of health care quality in the UK. The meta-analysis presented in the last chapter failed to determine whether dementia is a condition that is causatively linked to poorer quality care. Whilst this study does not provide concrete evidence for this, the use of directed acyclic graphs and appropriately adjusted regression analyses introduces a quasi-experimental method for assessing the effect of an exposure on an outcome. Therefore, the results could reflect the treatment decisions for patients based on a diagnosis of dementia. This suggests that there is a clinical decision, either determined by the treating physician, the patient, their caregiver, or all of these parties, to not provide processes associated with high quality

healthcare in older adults. The clinical implications of this are uncertain, given that the physicians are presumably balancing delivery of care that is considered to be within the best interest of patients, with the time and resources to deliver care. The research implication, from the perspective of a health economist, is to develop evidence to inform decision making as to whether this is (a) best for the patients and society in terms of preferences and health outcomes, and (b) an efficient use of healthcare resources.

Conclusions

The results of this study provide further evidence from a real-world setting that patients with diagnosed dementia have a lower probability of meeting indicators for a minimum acceptable standard of care across several diseases and domains. Whilst there are some associations observed between patients with low cognitive function but without a diagnosis of dementia, which were not observed in the previous chapter, these are often positively associated, particularly for care in geriatric domains which were not well captured in the systematic review. Although the analysis is subject to some limitations in deriving reliable inferences, it provides a short list of areas in which care quality substantially differs for patients with dementia, namely in the treatment and monitoring of diabetes, hypertension, and osteoporosis. The patient impact of this, as well as the role that general practitioners may have to play in improving care quality on these domains needs to be determined. The findings of this study are particularly pertinent as the role of primary care services is changing within NHS England, with more services being transferred from hospitals to community care[165] and therefore GPs may be left with less time per patient to meet quality guidelines. If this is the case, then even greater detriments and differences in quality may be observed.

CHAPTER 4

CAN QUALITY CARE IMPROVE HEALTH OUTCOMES?
AN ASSESSMENT OF THE ASSOCIATION IN PATIENTS WITH DEMENTIA

4.1. INTRODUCTION

The findings of the previous two chapters have highlighted that patients living with dementia are less likely to meet indicators for acceptable standards of care for the treatment of their comorbid conditions. Whilst an inequality in care quality has been observed, in some situations inequalities in care could be justified with regards to treatment need or the inappropriateness of certain care processes. To establish whether this inequality is an inequity, in that the difference in care quality is unjust, is dependent on what would constitute an unfair distribution of health outcomes.

A number of the included quality indicators in the English Longitudinal Study of Ageing (ELSA) used in the previous chapter were derived for the assessment of care quality in older adults, based on those from the 'Assessing Care of Vulnerable Elders' (ACOVE) project.[40 143] The intention of these indicators is to assess quality in areas that represent priorities for treatment in older adults to improve health outcomes and reduce health inequalities. However, there is a discussion about the applicability of the goals of care for the general older adult population compared with those with dementia and poor prognoses. For these patients the goals of care may be more comfort-orientated based on what is considered a relevant outcome for these patients, particularly for those in the end-stages of the disease.[166-168] Therefore, the differences in care quality observed in the previous analyses should have a measurable impact on health outcomes or quality of life for patients with dementia in order to be considered an area for improvement. If care quality is associated with better outcomes, then it could be determined that the differences in care quality represent an unjust health inequity.

For process measures of care quality to be valid they must demonstrate that variations in the process lead to differences in relevant outcomes.[10] If these processes are not important predictors of outcome, then redirecting resources to improve the quality would increase the costs of care without producing measurable benefits in health outcomes.[10] Using metrics of care outcomes are not especially valuable measures of the quality of care (see Chapter 1), but these are important measures of the benefit

patients receive. By establishing a link between care quality and care outcomes it further emphasises the need to improve care quality. If a health care consumer or payer considers good quality care to be desirable as it has a measurable impact on health or quality of life, then demand for care is likely to increase with the quality of care.

The aims of this chapter are to assess the implications of meeting quality indicators versus failure to meet these indicators for patients with dementia in terms of health outcomes, general wellbeing, and wider care resource use. The primary outcomes of interest in this analysis were survival and health-related quality of life. Other outcomes of interest were self-rated health, subjective wellbeing, and other domains of quality of life in older adults, as well as social care resource use for assistance with activities of daily living (ADL), and time to institutionalisation.

4.2. Methods

Data Source & Population

The analysis uses a dataset derived from waves 2 to 5 of the English Longitudinal Study of Aging (ELSA). As noted in the last chapter, dementia diagnoses, cognitive function, quality of care, and a range of covariates were available in the dataset. In addition, further data during follow-up such as current health status and survival were available, described in detail below. Later follow-up data from waves 6, 7, and 8 of ELSA were also reviewed to identify time-dependent outcomes such as death or subsequent institutionalisation for those respondents who were included at later waves. Waves 6 to 8 of ELSA were surveyed in 2012/13, 2014/15, and 2016/17, respectively. The analyses in this chapter focus on the outcomes of different levels of care quality for patients with dementia. Therefore, those patients identified in ELSA with a reported diagnosis of dementia (see §3.2) form the population for the analysis given the statistically significant observed differences in the quality of care in this group reported in the previous chapter. The analysis uses a mixed cross-sectional and longitudinal design, stratifying patients by the care quality received over time.

Quality of Care

The quality of care indicators forming the base of this analysis are the same as used in Chapter 3. In brief, there were up to 39 care quality indicators included in ELSA which were derived from those defined during the 'Assessing Care of Vulnerable Elders' (ACOVE) project,[40 143] and selected from this list given their relevance to UK older adults.[144]

In the previous chapter, quality of care was assessed on a range of indicators, with each respondent eligible for up to 91 indicators depending on the wave of ELSA and

their diagnosed conditions (see Table 3.2 for groupings). Outcomes on each indicator could differ within each respondent, reflecting whether care standards had been met for that specific indicator in the time preceding the current interview for that respondent. As individual respondents at specific time points could meet some indicators but not others, multilevel models were used in the previous chapter to account for clustering at the respondent on the combined effect sizes. Conversely, each of the outcome variables in this analysis has only one unique observation per wave (e.g., current health-related quality of life, or death by the next wave of data collection). There has been research into methods on statistical techniques for the analyses of repeated outcome measures, but much less emphasis has been put on repeated independent variables on a single outcome.[169] For simplicity, a single variable of care quality was defined per respondent at each wave as their average care quality across all indicators they were eligible for. The choice to use the average instead of conducting analyses on each individual indicator was based on the grounds that very few observations are available for patients with dementia for some indicators, and therefore reliable analyses could therefore not be conducted.

As very few quality indicators in the previous chapter had perfect scores for patients without a cognitive impairment, along with the associations with other covariates in the analyses, it is assumed that there are other factors beyond cognition or dementia that influence whether a quality indicator is met. Therefore, meeting quality indicators on all domains may not be feasible for all patients. I therefore considered that the new metric of care quality for patients with dementia should only include indicators where a diagnosis of dementia was associated with worse quality care than for patients without a cognitive impairment. The results of this analysis should therefore provide an estimate of the potential health and quality of life gains that could be attained if care quality were equal between those diagnosed with dementia and those without a cognitive impairment.

All quality indicators that were negatively associated with a diagnosis of dementia (i.e., patients with dementia received worse quality care) at the 10% level in the previous chapter were assumed to be significantly associated with a dementia diagnosis and included in the new indicator for care quality. This includes:

- In the past year, has any doctor or nurse examined your bare feet? (Diabetes Foot Check)
- Have you ever participated in a course or class about diabetes, or received special training on how you can live with your diabetes from day to day? (Diabetes Training)

- How much do you think you known about managing your diabetes? (Diabetes Knowledge)
- Did a doctor or nurse ever suggest you take any medication to lower your blood pressure? (Hypertension Treatment)
- Has any doctor or nurse recommended taking calcium pills or Vitamin D? (Osteoporosis Supplements)
- Has a doctor or nurse ever advised you to stop smoking; or has any doctor or nurse ever told you about any nicotine products, such as nicotine patches, chewing gum, lozenges, or other similar products at all to help you give up smoking? (Smoking Cessation)

The care quality metric was defined as the average score across all quality indicators they were eligible for from the list above. Further details on the indicators can be found in Appendices 3.4 and 3.7. The new quality metrics were calculated from indicator responses for all 50 imputed datasets separately and the regression models used allowed for multiple imputed datasets and combined results using Rubin's rules.[157]

Primary Outcomes

The two most important goals of health care are to increase the length of life and improve the quality of life of the treated patients.[170] In order to determine a fair and efficient allocation of health care resources, the gains from a range of healthcare interventions must be comparable so that, for example, investment decisions on a life-prolonging intervention in oncology can be compared to those for an intervention to alleviate symptoms in major depression, in much the same way that a banker may consider financial returns from a range of possible investment schemes. The outcome most commonly used by health technology assessment (HTA) bodies and payers/decision makers in health care, such as NICE in England and Wales, to quantify health benefits of an intervention is the quality-adjusted life year (QALY). Given that some interventions can improve length of life, and others can improve quality of life, the QALY is a metric for rating gains on both of these outcomes on the same scale. Quality of life estimates are based in utility theory and methods for its estimation require weighting so that perfect health has the same value as a year of healthy life, and death is assigned a quality of life value of zero.

Estimating QALYs requires estimates of both survival and quality of life. As an example, consider two treatments (Interventions A and B), where with Intervention A the patient lives for three years in a health state associated with a quality of life of 0.65 (65% of "perfect" health), and then a further two years with a quality of life of 0.55. For a patient receiving Intervention B, they live for around five and a half years with

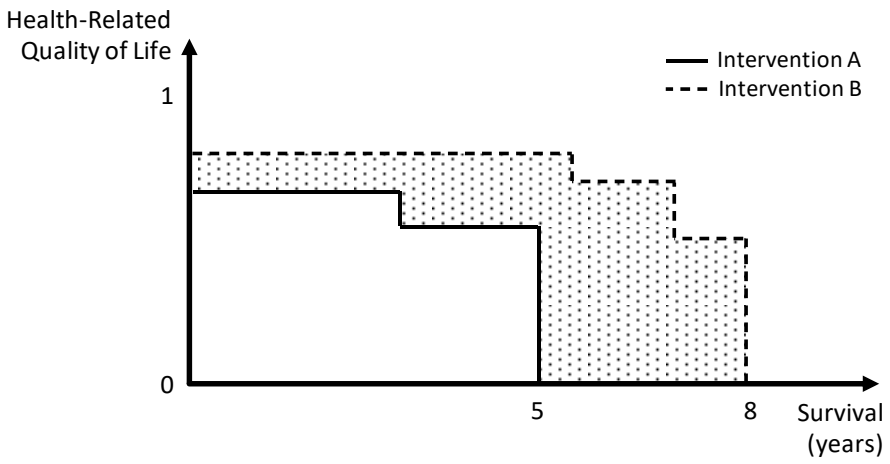

Figure 4.1. Example of the calculation of quality-adjusted life years

a quality of life of 0.8, followed by a gradual decline in health, with a year and a half with a quality of life weight of 0.7, and then a further year at 0.5. The QALYs for each patient can be calculated as follows:

$$QALY_A = (3 \times 0.65) + (2 \times 0.55) = 3.05$$

$$QALY_B = (5.5 \times 0.8) + (1.5 \times 0.7) + (1 \times 0.5) = 5.95$$

The patient receiving Intervention B accumulates more QALYs over the observed period, which can be seen from Figure 4.1 where this patient gains both length of life and quality of life over the patient receiving Intervention A.

Given that the QALY is the preferred metric for decision making in the UK,[171] it was determined that survival and health-related quality of life changes associated with differences in quality of healthcare should be the primary outcomes of the analysis.

Survival was calculated as the time from the date of the interview until the date of death or next interview. End of life and mortality datasets are developed at each wave of ELSA to capture previous respondents who have passed away. All respondents who had a recorded date of death were assumed to have died, and all remaining patients were censored for death at the date of their last known interview (up to wave 8). For confidentiality reasons, date of death in ELSA is only recorded by year and season (December to February; March to May; June to August; September to November) and interview date is only reported by month and year. For censored observations, follow-up time for survival could be calculated to the nearest month. For those respondents who had died, time windows for death were calculated based on the seasonal data reported and adjusted for any implausible outcomes. For example, the respondent cannot have died prior to the last interview participated in, but must have died prior to

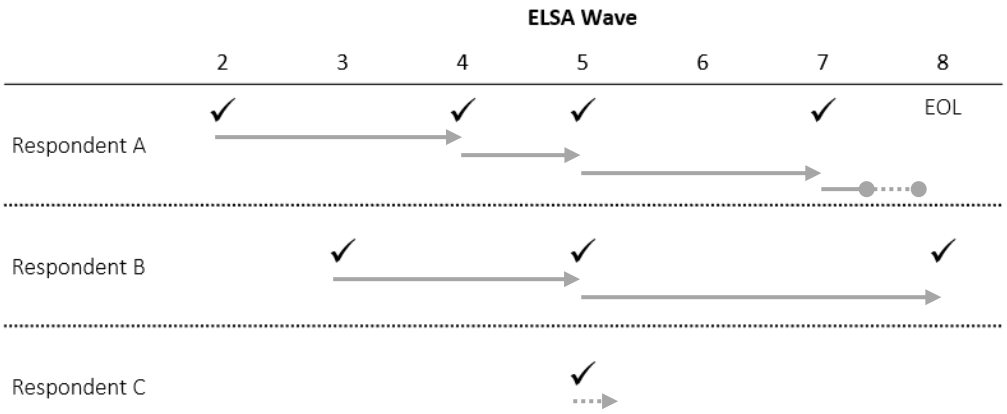

Figure 4.2. Estimation of the survival time windows. Respondent A was interviewed (✓) at wave 2 and again at wave 4 and so is censored for survival based on the quality of care received at wave 2, and again between waves 4 and 5, and waves 5 and 7. An end-of-life interview (EOL) was included at wave 8 and the respondent was known to have died (●) in a three-month period between waves 7 and 8, shown by the dotted line representing the minimum and maximum survival times. Respondent B has no observed death and was therefore assumed to be censored at the date of their last interview at wave 7. Respondent C was only included in one wave of ELSA and was censored for survival, assuming a minimum follow-up of one day.

data collection about their death). Survival time was calculated in months for all respondents at all waves separately. Minimum and maximum survival times were calculated for patients with a recorded death based on the upper and lower limits of the mortality window (see Figure 4.2). Note that respondents who participated in multiple waves and eventually died will be censored for death at all waves except for their last observed wave participated in up to wave 5. This allows for time/wave-dependent predictors of survival with multiple observations per subject using the counting process formulation.[172 173]

To measure health-related quality of life, weights are applied to a normal (healthy) state. The preferred approach by economists is that this is measured by utility (i.e., preference) for one health state over another. Preference measures for estimating quality of life weights include the time trade-off (TTO) exercise or standard gamble. The TTO involves respondents being asked to choose between living in a health state with symptoms or criteria associated with a disease or worse quality of life for a certain amount of time, or a state of perfect health for a shorter period of time, thereby making a choice to trade time for health. The utility is defined as the proportion of time when the two states are considered equally desirable (i.e., 10 years in the health state is equivalent to 8 years in perfect health, deriving a utility of 0.8). The standard gamble involves a similar approach, where respondents are asked to choose between two scenarios: one with a single outcome of remaining in a health state for a given time, and one with two outcomes associated with a probability or risk (e.g., living in full health for *x* years or dying immediately). The exercise is repeated, and the probability

of immediate death is varied, until respondents are indifferent between scenarios. The utility is derived from the probability of death at the point of indifference. For example, if the probability of death is 50% then the value of the "safe" health state is 50% of that of full health and so the utility is 0.5. Both methods are subject to limitations and require respondents to consider somewhat abstract concepts like trading life, and so alternative methods have been derived to make data collection in studies more manageable. Multi-attribute utility instruments (MAUI) often use scales of the severity of commonly cited domains of health-related quality of life, such as pain, fatigue, anxiety, activities of daily living, and others that are not symptoms specific to any one disease or condition. Respondents complete these questionnaires based on their current health state to determine markers of quality of life. Studies can then be designed to collect both utility measures (such as TTO or standard gamble) and data on MAUIs to estimate what utility is associated with which outcomes on the questionnaire to derive utility value sets associated with the MAUI. As neither a direct elicitation of utility nor a MAUI with a utility value set was collected as part of ELSA, an alternative method for valuing health was required.

The EQ-5D is a MAUI consisting of five questions relating to different dimensions of quality of life (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). The NICE reference case states that the EQ-5D is the preferred measure of health-related quality of life in adults, however NICE recognise that this data may not always be available and that mapping methods can be used to derive utilities.[171] The preference for the EQ-5D is based on the fact that it is standardised and has been validated in many patient populations, as well as it has a UK-specific value set for utilities. Mapping methods involve the use of an algorithm to predict utility values using data on other indicators of health or quality of life. To estimate utility values for the ELSA sample, I developed a mapping algorithm from the Health Survey for England (HSE). Five waves of the HSE (years 2003, 2004, 2005, 2006 and 2008) collected EQ-5D data and were synthesised and used to derive the mapping algorithm. Full details on the estimation and validation of the mapping algorithm can be found in Appendix 4.1. In brief, the algorithm captures predictors of general health, including age, sex, socioeconomic factors, self-rated health, functional limitations, depression, and diagnoses, as well as the additional burden of multimorbidity. As part of the estimation process of the algorithm, I conducted several validation exercises and the algorithm was demonstrated to be a reasonable predictor of utilities derived from the three-response-level version of the EQ-5D. Based on the mapping algorithm from the HSE, I estimated utilities for ELSA respondents that would approximately

reflect EQ-5D valuations at each wave. This approach was favoured over the quality of life measure collected in ELSA, the CASP-19, as no utilities value set is available for the CASP-19, and the was specifically designed not to capture health-related quality of life but rather subjective quality of life associated with the higher domains of Maslow's hierarchy of needs in older adults.[174]

Other Outcomes of Interest

Utility is the preferred metric of the value of health by economists, however as mentioned in Chapter 1, measures like the EQ-5D have been demonstrated to not be sensitive to changes in severity or progression in patients with dementia.[58] Psychologists generally equate the value of health with subjective wellbeing[175] and there has been discussion in the economic literature as to whether 'experienced utility' (the hedonic experience of an outcome)[176] may be a more appropriate valuation of health over preference-based utility measures given that the experience of a disease is dynamic and individual to the patient.[177] This may be particularly true for dementia patients, where dementia is a life-limiting condition and therefore the goals may be aligned with other terminal illnesses such as relieving discomfort or distress, rather than increasing the length of life or aiming for curative care.[178 179] Therefore, measures of patient value of their health and their wider quality of life or subjective wellbeing were also considered of relevance for this analysis.

Although captured as part of the measures used to derive utility values, how respondents perceive their health was deemed to be a relevant outcome. Self-rated health has been demonstrated to account for 41% of the variation in health-related quality of life utility weights.[180] Participants in ELSA were asked to report how good their health was in general, and data across waves 2 to 5 were synthesised to provide the responses of very good, good, fair, or poor.

Life satisfaction is believed to be one of the three core constructs on subjective wellbeing, alongside happiness/anxiety and self-worth/achievement.[175] The Satisfaction with Life Scale (SWLS)[181] consists of five items answered over a seven point Likert scale from strongly agree to strongly disagree, with higher scores indicating better life satisfaction. The SWLS has also been demonstrated to be correlated with preference-based measures of utility.[182]

Although the CASP-19 was not considered an appropriate metric of health-related quality of life for this analysis, it has been validated as a metric of other relevant aspects of quality of life in older adults,[183] particularly needs satisfaction with respect to the four main domains: control, autonomy, self-realisation, and pleasure.[174]

Respondents rate 19 items such as 'My health stops me from doing the things I want to do' and 'Shortage of money stops me from doing the things I want to do' with response options of often, sometimes, not often, or never. Total scores can range from 0 to 57, with higher scores equating to better quality of life. The CASP-19 has been demonstrated to be responsive to changes in variables that reflect some aspects of quality of life in a longitudinal analysis on ELSA,[184] including health and socioeconomic indicators.

Further outcomes were included to assess the association between quality indicators of processes in primary care and other care resource use, such as social or residential care. To assess to association with other aspects of care delivery, the number of activities of daily living that respondents received help with from a local authority worker or social services were appraised. At the included waves of ELSA, data were collected on whether respondents received help with up to six instrumental activities of daily living:

- Moving around the house
- Washing and/or dressing
- Preparing a meal or eating
- Shopping and/or doing work around the house
- Using the phone and/or managing money
- Taking medication

Whether patients had difficulty with these six activities were derived from questions on challenges with IADLs, and those respondents facing difficulties were asked if a number of parties assisted them in conducting them, such as a friend, a family member, a social worker, or a nurse. For this analysis it was considered that any publicly funded assistance would be relevant, given the NICE perspective of costing should reflect that of the NHS or Personal Social Services.[171] This included local authority workers, social services arranged care, nursing, or other health or social services. Help from friends, neighbours, family members, and privately funded care were therefore not considered. The total number of activities the respondent has difficult with, and the number of difficulties receiving help with, were summed for each respondent at each wave.

In previous cost-effectiveness analyses in dementia and Alzheimer's disease, time to institutionalisation has been a key driver of cost-effectiveness given the expected major step change in costs compared to patients in the community, as well as being a predictor of quality of life given the associated functional and health limitations that

often warrant institutionalisation.[185] As ELSA was designed to assess ageing in the community, all respondents are resident in the community at the time of recruitment, though can continue to be interviewed at later waves after moving to an institution. For the purposes of this analysis, institutionalisation was defined as residence in a care home (i.e., nursing home, residential care home, or mixed function home) for any respondent who was alive at the wave of interview. As only the year moved to nursing home is reported these patients, a time window for institutionalisation was calculated as per for date of death assuming a 12-month window for the year of institutionalisation, adjusted for implausible dates that fall either before the previous interview or after the current interview. For previous respondents who had passed away between interviews, data from the end-of-life interview was used to infer institutionalisation. Data collected in the end-of-life interview include place of death, time stay in place of death prior to death, other places stayed overnight during the two years before death, and the time spent in these other places. Based on place of death, three rules were introduced to determine if respondents were institutionalised before death:

- If place of death was in a nursing home, residential care home, or mixed function home then the respondent was assumed to be institutionalised
- If place of death was in a hospital or hospice then the deceased person must have stayed there for one month in the last two years before death, or for at least one month combined between hospital and hospice, or stayed in a nursing home, residential care home, or mixed function home for at least one day prior to hospitalisation in order to capture those patients intended to be moved to a care home but illness or accident warranted a move to hospital
- If deceased person died anywhere else, there must be a record of a combined total stay of at least one week in the past two years in a nursing home, residential care home, or mixed function home

To derive the time in each institution, time in any place prior to death is reported in each of the boundaries of one day or more, but less than one week; one week or more but less than one month; one month or more but less than three months; three months or more but less than six months; six months or more but less than a year; and a year or more. Based on this, minimum and maximum times before death the patient was institutionalised were calculated, incorporating all time in care homes of any type, as well as the time spent in the place of death. For example, for a patient who died at home and stayed there for between three and six months in the two years before death but has stayed in a care home for between one and three months, the minimum time

before death they could have been institutionalised was assumed to be four months but could have been up to nine months. These time windows were then combined with the date of death windows to create estimates of the dates of institutionalisation (i.e., the maximum possible time in an institution before the earliest date of death reflects the earliest date of institutionalisation, and the minimum possible time in an institution before the latest date of death reflects the latest date of institutionalisation). For all respondents not considered to have been institutionalised, they were censored for institutionalisation at the dates derived for survival (i.e., date of last interview or date of death). In addition to time to institutionalisation, institutionalisation-free survival was computed as the time between the date of interview and the first of institutionalisation, death, the next interview, or loss to follow-up.

Covariates

To derive the effects of exposure on outcomes in observational studies, reducing the impact of selection bias and adjustment for variables thought to confound care quality and health or economic outcomes is required. The covariates explored for possible inclusion in the analysis were the same as those included in the previous chapter. This included age, sex, whether the respondent was married or cohabiting, quintiles of total net (non-pension) wealth, the comorbidity burden of chronic conditions (e.g., respiratory, musculoskeletal, psychological diagnoses) or cardiovascular conditions (e.g., ischaemic heart disease, hypertension, diabetes). The area level factors derived from Primary Care Trusts (PCT) are the number of full-time equivalent GPs per 1,000 registered patients, and the organisational domain of the Quality and Outcomes Framework, as well as area itself.

In addition to those covariates included in the previous chapter, functional impairments associated with inability to perform activities of daily living or instrumental activities of daily living were considered given the alignment of constructs of one domain of the EQ-5D, and the presumed possible association with demands for additional care warranting earlier institutionalisation. The number of ADL or IADL impairments were derived from a list of questions in ELSA. Problems with ADLs were captured with ten items related to mobility (e.g., walking, climbing stairs, moving around), and the six IADL items mentioned above (e.g., washing, dressing, eating, etc.)

Covariates for inclusion in regression models for each of the outcomes were identified as those highlighted as being required for adjustment to estimate the direct effect of care quality on outcomes generating directed acyclic graphs of the available variables and using the DAGitty tool.[146]

Missing Data

Missing data on self-rated health and total scores on the SWLS were imputed as part of the same imputation model used for quality indicators outlined in the previous chapter, including all observations at all waves. For self-rated health, 2.7% of observations were missing data overall, however this was 35.1% for patients with dementia, and for the SWLS 17.7% and 59.8% of data were missing overall and for patients with dementia, respectively. Given that right censoring was assumed for survival and time to institutionalisation, data were assumed not to be missing and were not imputed. There were no missing values for the mapped EQ-5D values, and after accounting for eligibility (i.e., problems with IADLs) there were no missing data on number of IADLs respondents were receiving help with from local authority workers. As mentioned above, missing data on quality indicators were aggregated for all imputed datasets to derive the new quality of care metrics.

Econometric Approach

Hierarchical regression models were used to account for outcomes being reported at multiple study waves by individual respondents. For outcomes measured at a fixed time point – utilities, self-rated health, SWLS, CASP-19, and the number of IADLs respondents received help with – the multilevel models accounting for a random intercept at the respondent level were specified as:

$$\theta_{jk} = \alpha + \beta C_{jk} + \delta Z_{jk} + \mu_k + \varepsilon_{jk}$$

where θ is the exposure effect for individual k at ELSA wave j, β is the coefficient of interest to be estimated as the impact of a meeting the included care quality indicators C, δ is the vector of the covariates Z specific to the regression model, μ_k is the respondent-specific error component capturing the unobserved heterogeneity at this level, and ε represents the error term. It is assumed that μ_k is independent of the error term and the regressors.

For outcomes measured on a discrete or continuous scale, coefficients were estimated using linear regression models within the multilevel framework. This included the mapped utility values, the SWLS, and the CASP-19. Ordered logit regression models were used for self-rated health.

To estimate the association between care quality and the number of IADLs respondents received assistance with from social services, a negative binomial model was used using the number of IADLs the respondent reported difficulties in performing as the exposure. The negative binomial regression was preferred over a Poisson model given overdispersion of responses, particularly those reporting no help.

This model also included an additional level to account for respondents living with PCTs as funding for social services and the number of social workers employed can differ between local authorities.

Cox models for time to event outcomes (survival, time to institutionalisation, and institutionalisation-free survival) were conducted for both the minimum and maximum times to the event. Although survival analytic methods are available for interval data, methods accounting for the combination of multiple imputed datasets, the counting process for survival outcomes associated for multiple study waves per respondent, and interval data on the date of death were not identified in either the Stata or *R* software packages. For analyses including institutionalisation outcomes, a stratification by PCT was included as there may be area level factors influencing access to residential care.

Table 4.1. Characteristics of the samples

Characteristic	*N* = 263
Included Quality Indicators Met, Mean (SE)	55.5% (0.03)
Included Quality Indicators Eligible, Mean (SD)	1.68 (1.09)
Age, Mean (SD)	76.6 (10.0)
Age Groups	
▪ 50 - 54	4 (1.5%)
▪ 55 - 59	18 (6.8%)
▪ 60 - 64	22 (8.4%)
▪ 65 - 69	22 (8.4%)
▪ 70 - 74	27 (10.3%)
▪ 75 - 79	44 (16.7%)
▪ 80 - 84	58 (22.1%)
▪ 85 - 89	55 (20.9%)
▪ ≥ 90	13 (4.9%)
Female	133 (50.6%)
Married and/or Cohabiting	158 (60.1%)
Chronic Comorbidity Index	
▪ None	73 (27.8%)
▪ 1	103 (39.2%)
▪ 2 or 3	79 (30.0%)
▪ 4 or More	8 (3.0%)
Cardiovascular Comorbidities	
▪ None	14 (5.3%)
▪ 1	73 (27.8%)
▪ 2 or 3	136 (51.7%)
▪ 4 or More	40 (15.2%)
№ Challenges with Mobility, Mean (SD)	5.16 (3.19)
№ Challenges with IADLs, Mean (SD)	3.17 (2.30)
Net Non-Pension Wealth, Mean (SE)	£ 178,545 (21,584)
GPs per 1,000 Patients, Mean (SD)	0.57 (0.06)
QOF Organisational Domain, Mean (SD)	94.9% (0.04)

Notes: Variables with imputed values (proportion of indicators met, net wealth) are derived from regression models of the imputed datasets. Proportion of indicators passed and the number of indicators eligible only reflect those included in each of the quality metrics.

Given the small sample sizes and the challenges associated with assessing the effects of exposures using observational data, a statistical significance level was not formally defined. However, if the 90% confidence interval did not cross 0 for regression coefficients, or 1 for odds ratios, hazard ratios, or incidence rate ratios, these were considered associations of interest. As the analysis was exploratory and no formal definition of statistical significance was included, it was determined that all endpoints could be analysed without the need for gatekeeping to control for type I error. All analyses were conducted using Stata/SE 15.1 (StataCorp, College Station, TX).

4.3. Results

Up to 263 observations were available for respondents in ELSA with a diagnosis of dementia and who were eligible for at least one indicator associated with worse quality care for patients with dementia compared to patients without cognitive impairments. Sample characteristics are presented in Table 4.1. Characteristics are presented without stratification by quality of care, given that there is some variation in allocation between imputed datasets. A summary for the effects of care quality in both samples on all endpoints is presented in Table 4.2. Comprehensive reporting of all models can be found in Appendix 4.2.

Primary Outcomes

The survival estimates are from 176 unique respondents with follow-up ranging between one and 145 months from first interview to death or censoring (median 25 months), during which time there were 68 observed deaths. Figure 4.3 shows the minimum and maximum survival for this group. Median survival time in this group was 78 months (95% CI 48 to not reached) and 71 months (95% CI 53 to not reached) for the minimum and maximum survival times, respectively. The Kaplan-Meier curves

Table 4.2. Summary of associations between quality of care and health outcomes, for each 10% increase in average care quality

Outcome (Metric)	Result	90% CI	*p*-value
Survival, Min (HR)	0.93	0.88 to 0.98	0.017
Survival, Max (HR)	0.92	0.87 to 0.97	0.008
EQ-5D Utilities (β)	0.00	0.00 to 0.01	0.325
Self-Rated Health (OR)	1.04	0.97 to 1.11	0.401
SWLS (β)	0.00	-0.01 to 0.01	0.966
CASP-19 (β)	-0.05	-0.30 to 0.21	0.766
ADLs Helped With (IRR)	0.92	0.88 to 0.97	0.009
Time to Institutionalisation, Min (HR)	0.85	0.68 to 1.07	0.237
Time to Institutionalisation, Max (HR)	0.74	0.49 to 1.11	0.219
Institutionalisation-Free Survival, Min (HR)	0.86	0.75 to 0.99	0.076
Institutionalisation-Free Survival, Max (HR)	0.84	0.66 to 1.08	0.251

Abbreviations: CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio; OR, odds ratio

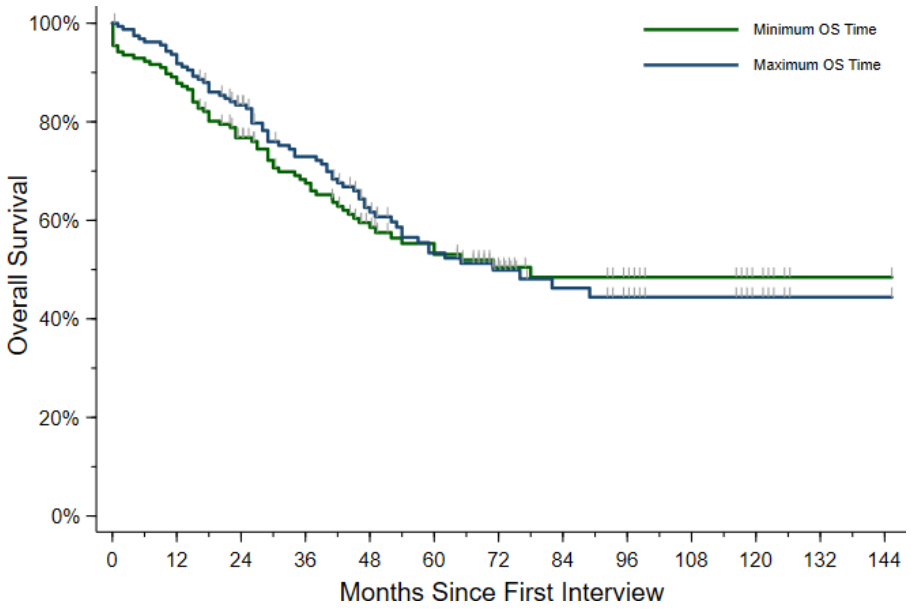

Figure 4.3. Overall survival (minimum and maximum survival times).

are not stratified by care quality given that this was time varying. After adjustment for age, sex, GP density, and the QOF organisational domain, each ten-percent increase in average care quality was associated with a 7% decrease in the hazards of death.

In addition, advanced age was significantly associated with increased hazards of death ($p < 0.001$ in all models), and female sex and higher scores on the organisational domain of the QOF were significantly associated with reduced mortality (see Appendix 4.2). There were no observable trends between health-related quality of life, as measured by the mapped EQ-5D utility values, and the care quality indicators in either group.

Other Outcomes

Having higher care quality averaged across indicators respondents were eligible for was significantly associated with a lower number of IADLs respondents received help with from social services or nurses. The rate of help with IADLs, compared to the number of IADLs the respondent reported difficulty in performing, was over 8% lower for a 10% increase in average care quality in both evaluated patient groups.

Of the 176 subjects followed up for survival in the group including indicators with any association with dementia, 26 were institutionalised at the time of their first included interview and were therefore excluded from the time to institutionalisation analyses. This provided 215 observations from 150 respondents, of which 20 were assessed to later have been institutionalised under the definitions outlined above and thus data were immature with the median not reached (Figure 4.4). Of the same group of

respondents, a further 37 died prior to institutionalisation, giving a total of 57 events for institutionalisation-free survival (Figure 4.5). After adjustment for age, gender, whether married or cohabiting, difficulties in performing IADLs, and comorbidities, as well as stratification by PCT, there was a trend for care quality to be associated with prolonged time to institutionalisation or institutionalisation-free survival, however this only met the predefined criteria for an association of interest ($p < 0.1$) in one of the analyses (minimum estimated institutionalisation-free survival). It is possible that a 10% increase in average care quality can reduce the hazard of institutionalisation or pre-institutionalisation death by around 15%.

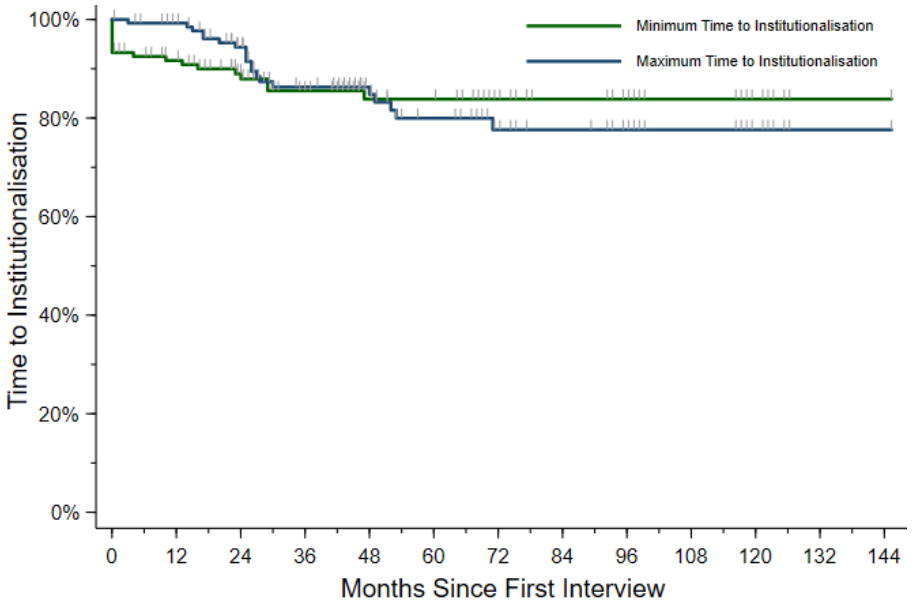

Figure 4.4. Time to institutionalisation (minimum and maximum survival times).

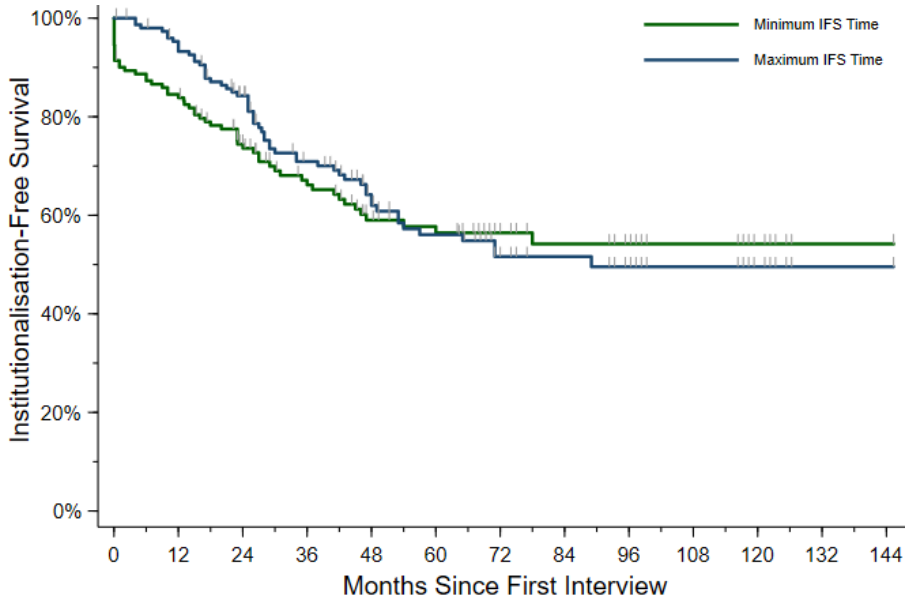

Figure 4.5. Institutionalisation-free survival (minimum and maximum survival times).

There was no observations association between care quality and self-rated health, satisfaction with life, or scores on the CASP-19.

4.4. Discussion

Principal Findings

In the previous chapter it was shown that care quality as measured on six indicators was significantly lower in patients with dementia compared to patients without an assessed cognitive impairment. The analyses in this chapter have shown that higher quality care on these indicators is associated with improved survival, meeting the pre-specified metric for an outcome of interest ($p < 0.1$).

Care quality also appeared to be associated with a reduced number of IADLs respondents were assisted with by social services or nurses. It is possible that care quality is also associated with delaying or avoiding institutionalisation, however a limited number of institutionalisation events means this finding is uncertain and hampers making statistical inferences on this association.

There was little observed association between the quality of primary care services and utilities mapped to the EQ-5D, self-rated health, life satisfaction, or quality of life. The lack of association with outcomes that were not analysed in time-dependent models, such as health-related quality of life, may reflect that most indicators are indicative of care provided over the past 12 months, and therefore differential health benefits may not have had the time to materialise. However, given the limited number of longitudinal observations for patients with dementia, a cross-sectional analysis was required to maximise use of the available data. These patient-reported outcomes have also not been validated in patients with dementia and may not be especially relevant. For example, the DEMQOL, a validated patient-reported outcome measure for use in patients with dementia, focusses questions on the past week with a strong component related to their emotional state over the past week, along with questions related to social relationships, ability to conduct activities of daily living, and some specifically related to memory.[186] Conversely, the Satisfaction with Life Scale and the CASP-19 focus on much broader, and potentially subjective, domains associated with the value of achievements and structure in life, with both long-term retrospective as well as prospective components, whereas the EQ-5D contains a much greater physical health focus.

The conceptual link between some of the included quality indicators and the key outcomes of interest is not explicit and may explain a lack of sensitivity. For example, not all patients with diabetes undergoing an examination of their bare feet to check for

signs of neuropathy, poor circulation, and infection or injury will have had the need to have future health events averted, and not all those initiating supplements for osteoporosis will be at risk of fracture. However, for other indicators this link is more robust, as appropriate diabetes education has been demonstrated to reduce the risk of hospitalisation for diabetic complications, cardiovascular events, and mortality,[187-189] and a meta-analysis has shown that the initiation of hypertension treatment reduces the risk of mortality and cardiovascular events.[190] Whilst not all quality indicators included in the exposure variables are clearly linked to the measured outcomes, the choice to assess the effect on all outcomes using an aggregate measure of care quality allowed for estimations of the overall benefit received by patients by improving care quality where is has been demonstrated to be lacking for patients with dementia. Supplements for osteoporosis may not be so clearly linked to survival as opposed to improving care for hypertension or the management of diabetes, though the risk of post-fracture mortality may be reduced. Regardless, it was deemed relevant to include all metrics of care quality in analyses of associations with all outcomes to assess the impact of the inequalities in health care quality for patients with dementia.

The results suggest that higher care quality is not associated with wider aspects of patient's perception of value, such as life satisfaction, control, autonomy, pleasure, and self-realisation. These findings neglect to directly account for the role of patient satisfaction with care processes and the potential discomfort or distress associated with care for patients with dementia. As current decision making on health care interventions and funding is based on a social welfare function combining health-related quality of life and survival, a value mechanism for these assessments would need to be identified to integrate patient satisfaction into economic evaluations. However, previous research has shown that patient satisfaction with the quality of care was not associated with clinical effectiveness or health-related quality of life,[170] implying that a change to the framework would be required if this were to be included.

Strengths & Limitations

Survival was one of only two outcomes were flagged to be of interest based on the pre-specified criteria. For analyses related to survival, two models were required due to a lack of granularity in the data in order to identify the exact date of death. Therefore, the results of this analysis are subject to some uncertainty as to the exact hazard ratio and its confidence interval. Despite this, the results between the minimum and maximum date of death were comparable both in terms of the point estimates and uncertainty, providing some support to the conclusion that care quality is protective of survival.

None of the quality of life measures, health-related or otherwise, demonstrated an association with care quality on the included indicators. Whilst these scales and metrics have been validated in older adults, there are some questions as to their appropriateness in the evaluated population. For the mapping algorithm for EQ-5D utilities, dementia is not explicitly called out as a covariate due to the lack of recording at the HSE waves used to developed to algorithm. Although correlates of dementia are included in the algorithm, such as functional limitations, depression, and psychiatric diagnoses, I was unable to validate the algorithm in a population with a diagnosis of dementia and therefore its applicability is uncertain. A previous analysis mapping of the same health metrics in different populations based on diagnosed conditions has shown to produce different mapping algorithms between the populations,[191] suggesting that there may be a possibility for inconsistent results if a dementia-specific algorithm was developed. In addition, the algorithm developed for this analysis has only been internally validated on the HSE sample which only included respondents living in the community, and therefore the utility values developed for institutionalised patients may not be valid.

To measure other potentially relevant aspects of quality of life in older adults the SWLS and CASP-19 were used. However, these facets of quality of life may not reflect aspects which are sensitive to change in the treatment of dementia. The current goals of care for dementia focus on relieving discomfort and distress, though life satisfaction does not relate to the outcomes or experience of care but rather general wellbeing, which may well be influenced by care but not explicitly so. Whereas the CASP-19 is designed to measure quality of life in the 'third age', characterised by freedom from work and family constraints, rather than factors in later life associated with functional decline and dependence.[184] Given that all quality of life measures were based on self-report by respondents, there are also additional challenges associated with memory or executive function impairments in the patients which may hinder analyses, though the impact of this cannot be assessed within the current dataset.

The self-reported outcome measures also lack some support in economic theory. As the metrics are not derived from preference measures, the answers respondents give may be open to interpretation. Using scales such as these can encounter numerous biases, where respondents demonstrate aversion to extreme values on a scale, introducing bias on the scaling between "excellent" and "poor" health, particularly in the absence of relevant anchoring points (such as perfect health or death). Such normative measures of outcome make objective inferences regarding the appropriate

allocation of resources to improve care quality and in turn health-related quality of life outcomes challenging to obtain.

Perhaps the most significant limitation of this analysis lies in using observational data to assess the effects of exposures. Whilst using observational data to assess the associations between dementia and care quality is perhaps essential, assessing the effects of an intervention like improving care quality on health outcomes is better assessed using randomised trial evidence to alleviate the effects of selection bias. Whilst the use of directed acyclic graphs or matching can identify confounding variables which may help isolate the effects of exposure, there is a school of thought that failure to account for unmeasured confounders can exacerbate differences in the allocated groups and therefore these methods are not a valid substitute for randomisation.[192] [193] Additionally, the sample sizes included are somewhat smaller than that of trials which would be conventionally used for regulatory approval or reimbursement and so consideration to the statistical power of results should be given. Accordingly, the findings of this study should be considered hypothesis generating, warranting further research and validation prior to informing policy decisions.

Clinical & Research Implications

There is now some evidence that meeting care quality indicators for comorbidities in patients with dementia patients, where care quality is lower than for other patient groups, could have a tangible benefit to patients. Therefore, the key clinical implication is regarding a discussion on the goals of care. The current goals of care in patients with dementia are to avoid discomfort and improve quality of life and independence during the decline in health associated with the condition. Whilst discomfort was not directly assessed here, other aspects of quality of life in older adults was and these were largely unaffected by meeting quality indicators. However, survival was improved and there is a possibility that independence could be increased as a result of care quality, as the number of IADLs assisted with by social care workers could reflect a shift in the provider of care, and there was also a trend for delaying time to institutionalisation suggesting that patients could have the independence to remain in the community for longer.

For these clinical implications to have weight, however, three key research implications have been identified. The main priority is to delineate whether the observed effects are correct, and therefore developing and conducting an appropriate study to assess the effects of care quality (e.g., a randomised trial) would be beneficial. Having the statistical power to assess the benefits on time to institutionalisation would be a consideration, as this is a patient-relevant metric of independence and quality of

life, and a key driver of value in pharmaceutical trials of Alzheimer's disease.[185] In addition, including dementia-relevant outcomes to assess the impact of care quality for their comorbidities on their dementia-related quality of life would be relevant in designing a more holistic and integrated care programme. Research implications that can perhaps begin to be answered within this thesis are two-fold: (1) what is a mechanism, policy, or intervention that could improve care quality for this group of patients, and (2) if a method for improving care quality could be identified, is it a cost-effective use of healthcare resources, where are the uncertainties in its benefits, and what additional research would be needed to plug the data gaps to reduce uncertainty?

Conclusions

Higher quality care appears to reduce the hazards of mortality, is associated with reduced use of other care resources, and can potentially delay institutionalisation in people living with dementia, without hampering health-related or wider quality of life. This therefore may prove to be a cost-effective method of improving outcomes in this population. These inferences need robust randomised evidence in order to ascertain the potential magnitude of the benefits, as well as an evaluation of methods for enabling physicians to meet care quality indicators. Modelling methods can be used to explore the potential cost-effectiveness and the additional benefits of research.

CHAPTER 5

ASSESSING QUALITY-MODULATING MECHANISMS
CORRELATES OF HIGH QUALITY CARE IN PATIENTS WITH DEMENTIA

5.1. INTRODUCTION

In Chapters 2 and 3 it was shown that a diagnosis of dementia can lead to inequalities in health care quality with regards to patients with dementia having a lower probability of meeting quality indicators. Evidence from the previous chapter has demonstrated that this inequality in health care quality may lead to a health inequity in that failure to meet these quality indicators was associated with poorer survival outcomes. Under the Health and Social Care Act 2012, Clinical Commissioning Groups have a duty to "reduce inequalities between patients with respect to their ability to access health services" as well as "reduce inequalities between patients with respect to the outcomes achieved for them by the provision of health services".[194] There is therefore a need to ascertain why there are differences in care quality, or to develop mechanisms for improving care quality for patients with dementia to alleviate differences in primary care quality between those with dementia and those without. Within this chapter, the aim is to evaluate the effects of exposure variables that could potentially form the basis of intervention strategies for patients with dementia. The results could then be used to determine whether these represent options for (a) improving the care quality received for patients with dementia, and (b) reduce the inequality observed in care quality between patients with dementia and the those without.

As outlined in Chapter 1, two main factors modulating the quality of care are proposed: the demand for high quality care and the supply of it. Figure 5.1 shows the potential associations between a subset of possible demand-side and supply-side factors in the relationship with care quality in patients with dementia.

Within the human capital for health model, demand for care lies with the health care consumer (e.g., patients and their families or caregivers), who can either not seek care or elect not to receive it when offered. With regards to clinical quality indicators, this can be a result of a lack of access to care due to mobility issues or the lack of social support to facilitate attending care facilities, or also as a potential consequence of the lack of knowledge or mental capacity to make decisions. When patients or their caregivers elect not to receive care it may be because they believe that they are acting

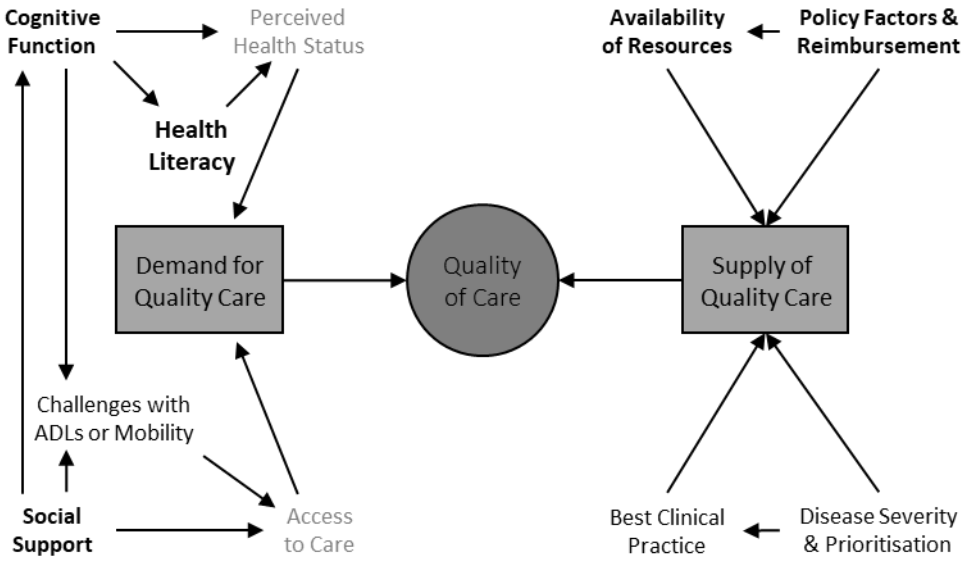

Figure 5.1. The figure represents the core variables that may drive factors of supply or demand for high quality care. Latent or unmeasured variables are written in pale grey text. Potentially modifiable variables are emboldened.

in their best interests, and this modulates their demand for care processes. As outlined in the theoretical framework in Chapter 1, as a patient's cognition declines, they may have a diminished understanding of their health status or reduced ability to obtain health-related knowledge, both of which may restrict decision-making ability. Patients with dementia with reduced mental capacity or those who have their decision-making opportunities limited by their informal caregivers tend not to be involved in the decision-making process related to health care.[195]

Within the diagram above, cognitive function, health literacy, and social support are considered potentially modifiable on the demand side. Health literacy could be considered the product of education in patients capable of receiving it, cognitive function can be modulated by drugs and other interventions, and social support networks can be improved through formal services or by supporting access to social groups. Conversely, challenges with activities of daily living (ADL) or mobility are assumed to be the product of comorbidities or dementia and cognitive decline itself, amongst other exogenous factors, which are not shown in the figure. Given that health literacy in patients with dementia is likely to be contingent on cognitive ability if they receive health education, cognitive function may be a more relevant variable for assessing associations with care quality in this population. As for social support, to understand its relationship with care quality, the role of cognitive function as a mediator on the pathway needs to be understood and therefore cognitive function may reflect a more relevant variable for exploration.

The supply of care is controlled by health care practitioners, institutions, or payers. Deficiencies in quality could be attributed to these actors either electing not to supply care or not having the resources to do so. Referring to the economic framework proposed in Chapter 1, if physicians do not supply care this is unlikely to be an act of malice or solely for the purposes of profit maximisation, but rather based on what is currently determined to be the best course of action due to clinical or policy reasons, or resource availability. In the world of evidence-based medicine, where advice and guidelines are dynamic in response to new clinical and economic evidence, physicians may be acting upon the perceived best course of action at the time, considering resources. For example, the use of paracetamol for controlling osteoarthritis pain was included in the ACOVE-2 indicators and former NICE guidelines, but is now being phased out as a guideline following trial evidence to suggest a lack of efficacy.[196] Therefore, new evidence may alter the supply of care that meets quality indicators. Whilst best clinical practice may change and influence care quality, this is not directly considered to be a potential intervention strategy to improve care quality as best clinical practice defines care quality.

Non-clinical factors influencing the delivery system for improvements in care quality are likely initiated by two main mechanisms: the availability of current resources, or policy factors and reimbursement for care, including incentives to provide care. Previously published work has shown that a greater density of GPs was associated with meeting quality indicators.[11] Therefore the supply of care may influence the quality of care. Whilst increasing healthcare resources is desirable and is likely to provide benefits across multiple domains, the delay in observing these benefits would probably be substantial given the time needed to train additional healthcare practitioners. Additionally, the cost associated with recruiting and retaining the additional staff needed to meet quality indicators in the long-term could be considerable. More rapid, affordable, and simple schemes to improve care quality could focus on leveraging the delivery systems already in place, or strengthen those where training and recruitment is less time- and budget-consuming. Incentives could be explicit in a financial motivation to provide care, or implicit via an increased ability to provide care through better organisation and management or an increase in capacity. Therefore, could policy interventions such as pay-for-performance schemes or reallocating existing resources and functions work to improve care quality?

The world's largest healthcare-related pay-for-performance scheme is the Quality and Outcomes Framework, introduced into the UK National Health Service in the 2004/05 fiscal year.[148] The QOF includes various indicators for specific processes within

clinical care and for improving the operation of general practices, and has reduced variations in quality between practices.[197] However, there has been some evidence to suggest that practices are prioritising care activities included as indicators in the QOF because of their reliance on income at the expense of other aspects of care.[198 199] If some of the indicators or conditions where patients with dementia were lacking care quality are disproportionately associated with a diagnosis of dementia (e.g., common comorbid condition in this patient group), the absence of relevant QOF indicators may explain some of the disparity in care quality. Given that nearly 99% of practices in England participate in the QOF, and derive on average 10% to 15% of practice income from the scheme,[200] it presents a potential mechanism for improving care. Whilst, it has been suggested that pay-for-performance measures may improve care quality overall, they may increase healthcare disparities due to individual patient needs and challenges in care.[201 202] A review of studies evaluating the QOF concluded that the scheme has led to improvements in the quality of chronic disease management but that there are still some disparities in care,[203] though more recent research has shown that financial incentives in the QOF have served to reduce inequalities in the delivery of care.[197] Therefore, a tailored financial incentive framework targeting the inequalities in care processes for patients with dementia could represent a top-down mechanism or a macro-level intervention for improving primary care quality.

The objectives of this chapter were to assess the relationship between cognitive function or the inclusion of clinical indicators in a pay-for-performance scheme on the quality indicators associated with poorer quality care for patients with dementia. In turn it is also of interest to assess if these exposures are associated with reductions in the inequalities in care quality observed compared to patients without dementia. This could then lay the foundations for potential intervention strategies for improving care quality and health outcomes for patients with dementia.

5.2. Methods

Population & Outcomes

The analyses are based on the dataset developed over the previous chapters derived from waves 2 to 5 of the English Longitudinal Study of Aging (ELSA). Only quality indicators where a dementia diagnosis was associated with significantly worse quality care at the 10% level in the analyses in Chapter 3 are included in this chapter, given the demonstrated associated with survival and social care use in Chapter 4. These indicators were:

- In the past year, has any doctor or nurse examined your bare feet? (Diabetes Foot Check)
- Have you ever participated in a course or class about diabetes, or received special training on how you can live with your diabetes from day to day? (Diabetes Training)
- How much do you think you known about managing your diabetes? (Diabetes Knowledge)
- Did a doctor or nurse ever suggest you take any medication to lower your blood pressure? (Hypertension Treatment)
- Has any doctor or nurse recommended taking calcium pills or Vitamin D? (Osteoporosis Supplements)
- Has a doctor or nurse ever advised you to stop smoking; or has any doctor or nurse ever told you about any nicotine products, such as nicotine patches, chewing gum, lozenges, or other similar products at all to help you give up smoking? (Smoking Cessation)

As per the analysis in Chapter 3, all six indicators provide a binary response to whether or not the minimal acceptable standard of care has been met.

Given that some cognitive interventions, both pharmacological and psychosocial, may not be relevant or indicated for certain populations, and that the population assessed may produce an interaction between exposure and outcome, a subgroup of patients was considered for the analyses on cognitive function. Most studies assessing the efficacy of cognitive stimulation measures on cognition have focussed on patients with mild or moderate dementia, excluding those with Mini Mental State Examination (MMSE) scores of less than 10,[204] and there is evidence that the greatest improvements in cognitive function as a result of intervention are obtained in those with less severe disease at baseline.[205] Therefore, for the analysis on assessing the role of cognitive function on care quality, patients with the most severe impairment were excluded in the subgroup analysis (see below).

Cognitive Function

The measure of cognitive function developed in Chapter 3 of this thesis focussed on deriving a metric of relative cognitive function, determined from age-standardised measures in order to develop a proxy metric of mild cognitive impairment or undiagnosed dementia. Studies appraising the benefits of cognitive interventions on cognitive function typically assess outcomes on absolute measures of cognitive function, such as the MMSE or the Alzheimer's disease Assessment Scale-Cognition

(ADAS-Cog). Therefore, a comparable measure was sought for these analyses instead of using the previously developed metric.

The study investigators of ELSA have defined a cognitive function index composed of a memory index and an executive function index, derived from a similar list of variables as used in the previously defined cognitive function metric. This included immediate recall of a list of 10 words, and delayed recall of the same word list after some intermediate tasks, verbal fluency as measured by the number of animals mentioned in one minute, and the speed of mental processing as measured by the position reached in a letter finding task on a grid (see §3.2 for further details). The last two tasks were recoded on a scale of 0 to 9 and 1 to 8 respectively, with higher scores representing more animals named or further position in the letter grid reached. The same letter grid was also used to assess the accuracy of mental processing by counting the number of letters meant to be identified that were missed. Actual numbers missed were recoded on a scale of 1 to 6, with more letters missed equating to a lower recoded score. In addition, two further metrics of cognitive function are included in the index: orientation in time and a prospective memory test. Orientation in time is based on the equivalent question in the MMSE and was assessed by asking respondents to give the current day, month, year, and the day of the week, and is scored from 0 to 4. Prospective memory concerns memory for future actions. Near the beginning of the cognitive assessment respondents are informed that they should write their initials in the top left-hand corner of a page attached to a clipboard when they are later handed the clipboard during the interview. Respondents are awarded a maximum of three points for this task, reflecting that they either performed the tasks correctly without being prompted (3 points), wrote their initials elsewhere on the page or wrote something else (e.g., their name) in the top left-hand corner without being prompted (2 points), did some other action without being prompted (1 point) or did nothing or a prompt was needed to perform the task (0 points).

The final cognitive function index has a maximum attainable score of 50 and minimum score of two, with higher scores on the index reflecting greater cognitive function. The list of tasks included in the ELSA cognitive function index aligns with a majority of those included in the ADAS-Cog, with a comparable scoring system.[206] The memory index and the executive function index defined in ELSA are strongly correlated with the memory (r = 0.94) and executive function (r = 0.81) latent variables defined in Chapter 3. Given the strong correlation with the previously defined variables, multiple imputation using linear regression of these variables along with age and a dementia diagnosis were used to derive cognitive index scores for those with missing data.

To define the subgroup with mild or moderate dementia, a cut-off was needed. The cognitive index in ELSA does not explicitly differentiate between mild, moderate, and severe dementia with the use of predefined cut-offs. The most commonly used stratification of dementia severity uses MMSE scores, with severe dementia defined as a score below 10.[204] However, there is no mapping algorithm available between the MMSE and ELSA index to estimate a cut-off. Instead, the cut-off was approximated by mapping to the prevalence of severe dementia in the UK. This assumes that the scores on the cognitive index in patients with dementia in ELSA are representative of cognitive function in patients with dementia in general, and that those with the lowest scores on the index would be the most severe cases. The estimated prevalence of severe dementia in patients with dementia aged over 60 in the UK is 12%.[44] When matched to the ELSA cognitive index, the lowest 12% of scores equated to those scoring 10 or less. Therefore, a score of 10 or below was assumed to indicate severe dementia. Given the uncertainties associated with this approach, sensitivity analyses were considered for the lowest 5% of scores (less than or equal to 7) and the lowest 20% of scores (less than or equal to 12).

Pay-For-Performance Measures

To assess whether including a clinical indicator in the QOF has a measurable impact on observed quality, those indicators included in the QOF were mapped to those in ELSA (Table 5.1). A binary variable was created to reflect indicators in ELSA where a comparable metric was included as a payment indicator in the QOF. In addition, the number of points attainable for the indicator in the QOF was captured. As indicators with more points provide the potential for greater reimbursement, this metric was assumed to reflect the potential financial gain to GPs for meeting the indicator.

Table 5.1. ELSA quality of care indicators reflected in the QOF and the points available

ELSA Wave	Wave 2	Wave 3		Wave 4		Wave 5	
QOF Year	2004/05	2005/06	2006/07	2007/08	2008/09	2009/10	2010/11
Diabetes Foot Check	DM9/10 (6)	DM9/10 (6)	DM9/10 (6)	DM9/10 (6)	DM9/10 (6)	DM9/10 (6)	DM9/10 (6)
Diabetes Training	N	N	N	N	N	N/A	N/A
Diabetes Knowledge	N	N	N	N	N	N/A	N/A
Hypertension Treatment	BP5 (56)	BP5 (56)	BP5 (57)	BP5 (57)	BP5 (57)	BP5 (57)	BP5 (57)
Osteoporosis Supplements	N	N/A	N/A	N/A	N/A	N	N
Smoking Cessation	Multiple (33)	N/A	N/A	N/A	N/A	SMOKE4 (30)	SMOKE4 (30)

Notes: Comparable QOF indicator was not available (N) or the indicator was not collected in ELSA at that wave (N/A). Numbers in brackets reflect the total points available for the indicator.

No indicators pertaining to providing training on self-management or assessing self-management skills for diabetes were included in the QOF in any of the evaluated years, and neither were indicators related to the treatment or management of osteoporosis.

Smoking cessation advice is reimbursed in the QOF related to the diagnosis of various conditions. In 2004/05, QOF indicators for smoking cessation advice were specific to those with coronary heart disease, stroke or transient ischemic attack, hypertension, diabetes, chronic obstructive pulmonary disease, or asthma. From 2008/09 onwards, schizophrenia, bipolar affective disorder, or any other psychoses were added to this list. Given that most respondents were diagnosed with at least one of these conditions, the indicator was assumed to be comparable to that recorded in ELSA. Two indicators in the QOF refer to an examination of the feet of patients with diabetes for the measurement of foot sensation for signs of neuropathy or peripheral pulses (DM 9: 'The percentage of patients with diabetes with a record of presence or absence of peripheral pulses in the previous 15 months', and DM 10 'The percentage of patients with diabetes with a record of neuropathy testing in the previous 15 months') which were assumed to be comparable to the indicator in ELSA.

Whilst several indicators for the treatment and management of hypertension are included, these mostly refer to targets for managing hypertension (e.g., BP 5: 'The percentage of patients with hypertension in whom the last blood pressure [measured in the previous 9 months] is 150/90 or less'). Although this does not correspond directly to a prescription for blood pressure lowering medication, the rationale given in QOF documentation for the inclusion of this indicator is to assess the response to pharmacological measures for reducing hypertension,[207] and therefore it would implicitly indicate that these patients are receiving medication to lower blood pressure. Therefore, it is assumed that this QOF indicator would stimulate physicians to prescribe blood pressure lowering medications and is aligned with the care quality goals captured in the ELSA indicator.

COVARIATES

Covariates for each analysis were selected based on the minimal sufficient adjustment needed for confounders, based on the list of covariates previously discussed in Chapters 3 and 4. I developed a directed acyclic graph (DAG) considering potential associations identified in previous chapters and conditional independencies were tested using the output from the DAGitty software.[146]

The relationship between cognitive function in patients with dementia and care quality was adjusted for the minimum required confounders identified from the DAG of all

Table 5.2. Proportion of total DALYs lost to each disease area or risk factor included in ELSA as part of total DALYs lost in the UK for each year the QOF indicators were updated

ELSA Disease Area	GBD Category	2004	2006	2008	2009
Diabetes	Diabetes Mellitus	1.96%	1.98%	2.05%	2.09%
Hypertension	High Systolic Blood Pressure	10.38%	9.36%	8.57%	8.17%
Osteoporosis	Low Bone Mineral Density	0.60%	0.62%	0.64%	0.65%
Smoking	Smoking	13.76%	13.10%	12.50%	12.20%

included variables. These were age, sex, chronic comorbidities, whether married or cohabiting, and the number of difficulties with mobility. For the analyses assessing the potential reduction in inequalities in quality, the same covariates were used as presented in the models in Chapter 3, namely demographics (age, sex, and net wealth), clinical factors (chronic and cardiovascular comorbidities), informal caregiving and access to care (whether married and/or cohabiting and number of close relationships), and health care supply (GPs per 1,000 registered patients).

Analyses on pay-for-performance measures were adjusted for GP supply as this was assumed to be correlated with a physician's ability to provide high quality care based on capacity. In addition, burden of disease was also included to capture a physician's clinical motivation to provide care. The burden of disease was measured using the estimated proportion of total disability-adjusted life years (DALYs) attributable to the condition or risk factor in the UK for each year the QOF quality indicators were updated. Values were obtained from the Global Burden of Disease visualisation hub from the Institute of Health Metrics and Evaluation at the University of Washington.[208] Table 5.2 shows the burden of disease estimates included in the analyses. Given that the number of points available for each indicator on the QOF can reflect the clinical pertinence of the indicator as well as the associated level of reimbursement, there may be some collinearity between the DALYs associated with the condition and the points available. Accordingly, a scenario excluding the burden of disease measured by the DALYs was also considered.

Statistical Analyses

To assess the research questions, a two-stage approach was adopted. First the relationship between the exposure (i.e., inclusion in the QOF or higher cognitive function) and quality of care on the key quality indicators was assessed in the subgroup of patients with diagnosed dementia. If this association were statistically significant at the 10% level ($p < 0.1$), the variable reflecting the intervention strategy would be included as a covariate in an analysis assessing the association between a diagnosis of dementia and care quality (akin to that presented in Chapter 3) to see if this alters the previously observed association. In addition, a further model was conducted for each

exposure considering an interaction between a diagnosis of dementia and the additional exposure variable to assess if the effects of the exposure on care quality are different in patients with dementia compared to those without cognitive impairments.

To ascertain if the exposure variable has a meaningful impact on reducing the inequalities in care quality, *post hoc* analyses were conducted to estimate the adjusted probability of meeting the quality indicator in patients with dementia, or the scale of the change in exposure needed, and comparing this to the observed quality care in the population without a cognitive impairment.

Multilevel regression models were used to account for quality of care indicators being clustered within individual respondents and reported at multiple study waves. The multilevel models included random intercepts with indicators clustered within respondents to estimate the effect of exposures on care quality, specified as:

$$C_{ijk} = \alpha + \beta E_{jk} + \delta Z_{jk} + \mu_i + \mu_k + \varepsilon_{ijk},$$

where C is the quality of care associated with indicator i at ELSA wave j for individual k, β is the coefficient of interest to be estimated as the magnitude of the association of the exposure E, δ is a vector of the covariates Z, μ_i and μ_k are the indicator and respondent-specific random-effect error components, and ε represents the error term. Including the random-intercept at the indicator level is considered pertinent as the indicators are fundamentally different despite the fact they are intended to measure the latent concept of care quality. As all the quality of care indicators are binary (met/unmet), logistic regression models were used.

It was determined *a priori* that if both cognitive function and pay-for-performance were significantly associated with care quality improvements in their individual models, then a further regression model considering a combined approach would be evaluated. This would permit assessment of whether there is an interaction between the supply and demand sides of care quality.

The models for assessing the reduction in inequalities of care were comparable to those specified above and in Chapter 3:

$$C_{ijk} = \alpha + \beta f_{jk} + \beta E_{jk} + (\beta f E_{jk}) + \delta Z_{jk} + \mu_i + \mu_k + \varepsilon_{ijk},$$

where the coefficient to be estimated β of a dementia diagnosis f is to assess if the exposure or intervention strategy E confounds the relationship with care quality C. The interaction term fE will also be captured in a second model.

Given that these analyses are being conducted on the subset of quality indicators that were significantly associated with a dementia diagnosis, the model was also run

without the exposure effects to estimate the baseline difference in care quality for this group, which is not reflected by the models presented in Chapter 3. This analysis was also conducted for the subgroups given above. All analyses were conducted using Stata/SE 15.1 (StataCorp, College Station, TX).

5.3. Results

Sample characteristics for the population used to assess the effects of the potential intervention strategies are aligned with those reported in the previous chapter. To assess inequalities in care, the patients without cognitive impairment (as defined in

Table 5.3. Characteristics of the sample

	Diagnosed Dementia	No Impairment
N	263	14,620
Included Quality Indicators Met, Mean (SE)	55.5% (0.03)	76.8% (0.00)
Included Quality Indicators Eligible, Mean (SD)	1.68 (1.09)	1.46 (0.93)
Eligible Indicators Included in QOF, Mean (SD)	85.0% (0.27)	88.4% (0.25)
ELSA Cognitive Index, Mean (SD)	16.5 (6.5)	29.8 (5.8)
Age, Mean (SD)	76.6 (10.0)	67.7 (9.8)
Age Groups		
▪ 50 - 54	4 (1.5%)	1,130 (7.7%)
▪ 55 - 59	18 (6.8%)	2,425 (16.6%)
▪ 60 - 64	22 (8.4%)	2,571 (17.6%)
▪ 65 - 69	22 (8.4%)	2,263 (15.5%)
▪ 70 - 74	27 (10.3%)	2,329 (15.9%)
▪ 75 - 79	44 (16.7%)	1,874 (12.8%)
▪ 80 - 84	58 (22.1%)	1,240 (8.5%)
▪ 85 - 89	55 (20.9%)	662 (4.5%)
▪ ≥ 90	13 (4.9%)	126 (0.9%)
Female	133 (50.6%)	8,045 (55.0%)
Married and/or Cohabiting	158 (60.1%)	9,863 (67.5%)
Number of Close Relationships		
▪ 0 or 1	190 (72.4%)	1,077 (7.4%)
▪ 2 or 3	36 (13.8%)	1,421 (9.7%)
▪ 4 or 5	23 (8.6%)	3,733 (25.5%)
▪ 6 to 9	11 (4.1%)	6,569 (44.9%)
▪ 10 or more	3 (1.1%)	1,819 (12.4%)
Diagnosed Chronic Conditions		
▪ None	73 (27.8%)	6,515 (44.6%)
▪ 1	103 (39.2%)	5,300 (36.3%)
▪ 2 or 3	79 (30.0%)	2,656 (18.2%)
▪ 4 or more	8 (3.0%)	149 (1.0%)
Diagnosed Cardiovascular Conditions		
▪ None	14 (5.3%)	1,431 (9.8%)
▪ 1	73 (27.8%)	5,842 (40.0%)
▪ 2 or 3	136 (51.7%)	6,602 (45.2%)
▪ 4 or more	40 (15.2%)	745 (5.1%)
Net Non-Pension Wealth, Mean (SE)	£ 178,545 (21,584)	£ 271,407 (4,749)
GPs per 1,000 Patients, Mean (SD)	0.57 (0.05)	0.57 (0.06)

Notes: Variables with imputed values (proportion of indicators met, close relationships, net wealth) derived from regression models of the imputed datasets. Proportion of indicators passed and the number of indicators eligible only reflect those included in each of the quality metrics.

Chapter 3) who were eligible for the same quality indicators were utilised. Sample characteristics for both patient groups are presented in Table 5.3. As observed previously, patients with dementia tended to be older, have lower cognitive function, have fewer close relationships, and a greater comorbidity burden, as well as being less wealthy. In this subset of the overall ELSA sample with respondents who were eligible for the included quality indicators, the overall quality of care for patients with dementia was significantly lower than for patients without cognitive impairment (OR 0.25, 95% CI 0.15 to 0.40; see Appendix 5.1 for full results) after adjustment for covariates. Results were comparable in the subgroup with a cognitive index score of greater than 10 (OR 0.22, 95% CI 0.13 to 0.36).

Cognitive Function

In the full population of patients with dementia, there was no observed association between cognitive function and care quality (Table 5.4). However, when assessing associations in the subgroup considered to have mild or moderate dementia, each additional point on the ELSA cognitive index was associated with a 13% increase in the odds of meeting quality indicators. This interaction between effect size and severity was further supported with sensitivity analyses, demonstrating a stronger association when restricted to patients with a cognitive score greater than 12, and a weaker relationship that was not statistically significant when restricted to those with a cognitive score greater than 7.

When including cognitive function as a covariate to assess the impact on inequalities in care, higher cognitive function was associated with higher quality care for all patients, though a dementia diagnoses was still significantly associated with lower quality care (Table 5.5). Further analysis showed a significant interaction between dementia diagnosis and the ELSA cognitive index, implying that cognitive function

Table 5.4. Logistic regression models for the association between cognitive function index scores and the probability meeting quality of care indicators

	Adjusted OR	90% CI
Cognitive Function in All Patients with Dementia		
ELSA Cognitive Index	1.01	0.94 to 1.08
Cognitive Function in Patients with an ELSA Cognitive Index Score > 10		
ELSA Cognitive Index	1.13**	1.02 to 1.25
Cognitive Function in Patients with an ELSA Cognitive Index Score > 7		
ELSA Cognitive Index	1.06	0.98 to 1.14
Cognitive Function in Patients with an ELSA Cognitive Index Score > 12		
ELSA Cognitive Index	1.25**	1.08 to 1.44

Abbreviations: CI, confidence interval; OR, odds ratio
Notes: Odds ratios for covariates not shown. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Table 5.5. Logistic regression models for the association of cognitive function with reducing inequalities in the quality of care received by patients with mild or moderate dementia, and the mean cognitive index score required to have comparable care quality (<10% difference with the non-impaired) and the increase needed based on observed cognitive function (17.7)

	Adjusted OR	Cognitive Score Required (Increase)
Excluding Interaction Term		
Diagnosed Dementia	0.13***	>50 (N/A)
ELSA Cognitive Index	1.03***	
Including Interaction with Dementia Diagnosis		
Diagnosed Dementia	0.01***	24.9 (7.5)
ELSA Cognitive Index	1.03***	
Interaction (Dementia * ELSA Cognitive Index)	1.19***	

Abbreviations: CI, confidence interval; OR, odds ratio

Notes: Odds ratios for covariates not shown. Cognitive score to reach a comparable level of cognitive function to patients without a cognitive impairment not possible without interaction term as score would exceed maximum for scale. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

has a greater impact on care quality in patients with dementia and improvements in cognitive function may help to reduce some of the inequalities in care quality. Post hoc analysis to determine the cognitive score required to increase care quality to within 10% of that of patients without a cognitive impairment was a mean cognitive index in the population of patients with mild or moderate dementia of 24.9 when considering the interaction term, representing a 7.5-point increase on the observed mean score.

Pay-for-Performance

Inclusion of a clinical indicator in the QOF was significantly associated with better quality care as observed in ELSA, increasing the odds of patients with dementia meeting the quality indicator by nearly six-fold (Table 5.6). With adjustment for the proportion of total UK DALYs lost to the disease or risk factor, the number of points (and the level of reimbursement) associated with quality indicators was not significantly associated with care quality. However, when excluding the burden of disease, the number of QOF points was a significant predictor, with more points being associated with better quality care, without altering the relationship between the inclusion of the indicator in the QOF and quality of care.

Table 5.6. Logistic regression models for the association of pay-for-performance measures with the probability of patients with dementia meeting quality of care indicators

	Adjusted OR	90% CI
Including Points Associated with Reimbursement		
Indicator Included in QOF	5.70***	2.09 – 15.52
QOF Points Available	1.02	0.99 – 1.04
Excluding Burden of Disease as Covariate		
Indicator Included in QOF	5.80***	2.14 – 15.71
QOF Points Available	1.03**	1.01 – 1.04

Table 5.7. Logistic regression models for the association of pay-for-performance measures with reducing inequalities in the quality of care received by patients with dementia, and the estimated quality of care for patients with dementia in a pay-for-performance scheme including all quality indicators for dementia patients only and the difference compared to non-cognitively impaired patients

	Adjusted OR	Dementia-Specific P4P Scheme Care Quality (Diff. vs. Non-Impaired)
Excluding Interaction Terms		
Diagnosed Dementia	0.25***	75.2% (-15.5%)
Indicator Included in QOF	8.09***	
QOF Points Available	1.01***	
Including Interaction with Dementia Diagnosis		
Diagnosed Dementia	0.20***	75.6% (-15.0%)
Indicator Included in QOF	8.16***	
QOF Points Available	1.01***	
Interaction (Dementia * Inclusion in QOF)	0.84	
Interaction (Dementia * QOF Points)	1.01	

Abbreviations: CI, confidence interval; OR, odds ratio; P4P, pay-for-performance
Notes: Odds ratios for covariates not shown. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

The effect of including indicators in the QOF appears to benefit both patients with dementia and those without as the inequalities in care were sustained after adjustment for the QOF (Table 5.7). Interaction terms between dementia diagnosis and QOF indicators were also not statistically significant, suggesting a comparable effect on care quality between the patient groups and comparable diagnoses that would be eligible for care. Therefore, in its current format the QOF does not reduce inequalities in care. If all care quality indicators associated with poorer quality care were included in a pay-for-performance scheme for dementia patients only, compared to the current QOF, the difference compared to patients without a cognitive impairment would be reduced to 15.5% from 24.8%, with the estimated overall probability of meeting indicators increased to 75.2% from 65.9%.

Combined Exposures

Given that both cognitive function and pay-for-performance were significantly associated with care quality, a model considering both exposures as factors to improve care quality was assessed in patients with milder dementia. Models were adjusted for all covariates mentioned for both analyses above, namely demographics (age and sex), clinical factors (comorbidities), access to care (whether married or cohabiting, difficulties with mobility, and GP density), and burden of disease (UK DALYs lost to the condition). The analysis shows comparable results to the individual models, with both inclusion in the QOF and cognitive function being significantly associated with higher quality care (Table 5.8).

Table 5.8. Logistic regression models for the association of cognitive function and pay-for-performance measures with the probability of patients with mild or moderate dementia meeting quality of care indicators

	Adjusted OR	90% CI
Indicator Included in QOF	5.32**	1.51 to 18.73
QOF Points Available	1.03	1.00 to 1.06
ELSA Cognitive Index	1.13*	1.02 to 1.26

Table 5.9. Logistic regression models for the association of cognitive function and pay-for-performance with reducing inequalities in the quality of care received by patients with mild or moderate dementia, and the mean cognitive index score required to have comparable care quality (<10% difference with the non-impaired) and the increase needed based on observed cognitive function (17.7)

	Adjusted OR	Cognitive Score Required (Increase)
Diagnosed Dementia	0.01***	
Indicator Included in QOF	9.56***	
QOF Points Available	1.01***	23.5 (6.1)
ELSA Cognitive Index	1.02**	
Interaction (Dementia * ELSA Cognitive Index)	1.18***	

Abbreviations: CI, confidence interval; OR, odds ratio
Notes: Odds ratios for covariates not shown. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

When combined, a diagnosis of dementia was still significantly associated with worse quality care for patients with dementia (Table 5.9), however the increase in cognitive function required to develop comparable levels of care quality to patients without a cognitive impairment is reduced when compared to assessing cognitive function alone (6.1 vs. 7.5 points).

5.4. Discussion

Principal Findings

Both pay-for-performance measures and cognitive function to some extent appear to be associated with improved care quality in patients with dementia, with the latter being limited to patients with mild or moderate dementia, with a greater effect in less severe populations. However, neither of these factors alone fully explained the differences in observed care quality between patients with dementia and those without. Therefore, there must be other aspects of the dementia condition and its treatment which limit the receipt of high-quality care.

Referring to Figure 5.1, it is perhaps that access to care for patients with dementia is limiting demand and best clinical practice limits supply. To reduce inequalities, it may be important to support patients with dementia to access care and to educate physicians and update guidelines to reflect the potential benefits of meeting quality indicators in this patient group. Therefore, schemes which aim to focus on cognitive gains or additional reimbursement should be combined with education, to patients or providers

respectively, on the intentions of the scheme so that relevant parties are aware of the benefits of treatment.

The association of cognitive function with care quality was statistically significant in patients with mild or moderate dementia and so programmes to improve cognitive function targeted to these patients may generate improvements in primary care quality. However, a 7.5-point increase in the ELSA cognitive function score would be required to reduce inequalities to levels of care comparable to those observed in patients without cognitive impairment. To put that in context, based on a meta-analysis of studies on the impact of cognitive stimulation on ADAS-Cog scores, programmes on average reduced ADAS-Cog scores (associated with cognitive improvements) by 0.53.[204] Assuming transferability of these findings to the ELSA cognitive index, rescaling from a 0 to 70 declining scale to a 2 to 50 increasing scale, cognitive stimulation programmes would increase scores by 0.36, increasing the regression-adjusted proportion of indicators met from 50.6% to 52.5%, but still substantially below the 92.3% observed in patients with cognitive impairment.

For patients with milder dementia, lower cognitive function is associated with poorer quality care, but not when considering all severities. This may mean there is a threshold of cognitive function, where decision making or management and demand for care shifts from the patients to caregivers. The results presented here provide some support the economic framework outlined in Chapter 1. As lower cognitive function may limit perceptions and understanding of one's own health status, this may reduce demand for healthcare in line with a diminished demand to improve our health stock due to the dearth of knowledge about the depleted health stocks, in line with Grossman's human capital model.

Inclusion of clinical indicators in the QOF was significantly associated with improvements in care quality for patients with dementia, though had little effect in reducing the differences in care quality compared to those without cognitive impairment. Despite this, a potential strategy for improving care quality and reducing inequalities in care could be considered. The effect of including a quality indicator in the QOF on the improvements in care quality (log odds ratio 2.10) was greater than the detriments to care quality in those with a diagnosis of dementia (log odds ratio -1.37), and therefore it is plausible that a pay-for-performance scheme which is solely targeted to patients with dementia rather than the general population may serve to reduce the inequalities in overall care quality. This is contingent on the assumption that supply of care can influence care quality independent of the demand of care, and that an exogenous shift in the provision of care would increase observed quality

without requiring additional effort from patients. Based on the analyses considering both exposures, this is deemed feasible as effect sizes remained unchanged for pay-for-performance and cognitive function, implying that these have independent, additive effects on care quality, rather than an interaction with one facilitating the other.

However, a dementia-focussed pay-for-performance scheme may pose an ethical issue in providing specific funding for care for patients with dementia whilst neglecting other patient groups, as was faced by the Cancer Drugs Fund (CDF) in the UK.[209-211] There are also questions on the feasibility of such a scheme. It has previously been commented that pay-for-performance schemes will generally not be suitable for improving care in patients with more complex problems,[148] and that a key factor to success in using economic incentives to reduce health inequalities is whether external factors lead to certain patients being more likely to be identified and treated.[212] There is some evidence to suggest that targeting treatment programmes to individuals with high-risks of health complications can widen socioeconomic inequities.[213] Also, where aspects of care quality and the relationship with outcomes are not easily measurable to inform reimbursement, alternative mechanisms for improving care quality are required, such as allowances for the additional time taken to provide high quality care.[148] However, whilst patients with dementia represent a group with complex health needs requiring holistic care, the analyses presented over the previous chapters show that measurable care indicators are associated with better health outcomes in this population, and that pay-for-performance schemes are associated with higher quality care. Engelgau and colleagues commented that for health schemes focussing on disease risk, such as the screening and primary prevention measures in ELSA where patients with dementia were shown to have worse quality care, to reduce inequities these approaches must have greater targets and investments among disadvantaged populations. [212] This would therefore suggest that to reduce inequalities in care quality, targeting investment to patients with dementia may be a viable strategy. By using the existing QOF indicators in conjunction with a dementia comorbidity flag, incentives could boost indicators met in this patient population. For example, the QOF now includes a reimbursement indicator for an annual review of the care plan for patients with dementia,[71] which could be expanded to include additional clinical domains. Therefore, whilst pay-for-performance schemes may not optimise primary care for patients with dementia across the board, it could present an economically efficient method of improving it.

It is of note that the number of points associated with each indicator on the QOF, and so the corresponding level of reimbursement associated with the indicator, was not demonstrated to be statistically significantly associated with improvements in care quality after adjustment for the burden of disease. The points associated with the indicator reflect aspects of disease severity, and therefore there is some collinearity with disease burden regarding the clinical motivation of physicians to provide care. As such, the variance of these predictors in the model containing both QOF points and DALYs lost may have been inflated in the regression, as demonstrated by the sensitivity analysis excluding the associated DALYs with the condition. The analyses allowed for the estimation of the impact of the volume of reimbursement independent of clinical pertinence on care quality. The findings suggest that beyond the burden of disease and the notion of some reimbursement for their actions, the specific volume of reimbursement is not a significant motivator of care quality and therefore primary care physicians may not have profit maximisation as a major consideration in delivering care.

Strengths & Limitations

This analysis has helped to identify some potential intervention strategies for improving care quality in patients with dementia. These can potentially leverage pre-existing frameworks or treatment programmes that have been deemed desirable on other grounds and could be a target for increased investment to improve care quality. The analysis also benefits from looking at a subgroup who are most likely to be able to partake and benefit from one of the potential intervention strategies, defined as patients with a level of cognitive function sufficient to engage in a cognition-boosting programme. However, the downside to consider with cognitive intervention strategies is that these are targeted to patients with mild or moderate dementia and their implementation may fail to provide strategies to improve care quality for those with severe dementia, potentially widening the inequalities in care quality compared to current practices. However, it is estimated that over three-quarters of patients with severe dementia are in residential care and have lower healthcare costs,[44] and therefore their primary care needs may differ.

There are, of course, challenges in making robust inferences on causal effects on observational data, especially when considering aspects with complex feedback loops. For example, cognitive function or greater independence may increase the demand for high quality healthcare, but higher quality care and the associated health gains may increase independence and sustain cognitive function. Therefore, conducting cross-sectional analyses on these outcomes may hinder the validity of these findings to

inform potential intervention strategies. However, given the longitudinal missing data in ELSA, with many patients living with dementia only included at one wave, assessing a sequential nature of cause and effect was deemed not possible.

On a similar note, the analysis also assumes an immediacy of effect. Whereas it is feasible for pay-for-performance metrics to have an instant influence on treatment decisions following their implementation, a full cognitive intervention programme is typically conducted across several weeks,[204 214 215] and further time may elapse before the patient has a health complaint that needs treating. It would therefore be desirable to conduct a cohort study, assessing the relationship between cognition or cognitive decline and health care resource use/quality prior to a cognitive stimulation programme, during the programme, and long-term follow-up to assess if and when changes in care quality are observed.

Clinical & Research Implications

The findings of this analysis could have major policy implications with regards to the care and management for patients with dementia. However, the evidence requirements for policy changes determine the further research implications. Whilst it has been established that there are inequalities in the quality of primary care services for patients with dementia, and that reductions in care quality on the observed domains are associated with potentially undesirable health consequences, whether the identified strategies represent an economically efficient use of health care resources within reasonable budget constraints remains to be seen. In turn, to inform robust conclusions from these analyses high quality clinical data must be generated on the gains in care quality associated with intervention strategies, along with the long-term health gains associated with the improvements in care quality, that would come for a high-quality randomised trial. Given the time and expense associated with generating such evidence, early economic modelling could be used to inform decisions on the feasibility of these strategies being potentially cost-effective interventions and whether or not to fund additional research.

In terms of clinical implications, these will be determined as a result of policy implications. If funding becomes available to reimburse physicians for meeting quality indicators for patients with dementia, or for local dementia services to provide cognitive training and stimulation, then the implication would be for clinicians and commissioners to ensure these services are provided. The QOF is declining in popularity with GPs due to the administrative demands of the scheme and that recent indicators either focus on managerial practices rather than clinical benefits, or that the indicators have a poor evidence base.[216] The Royal College of General Practitioners

have called for it to be replaced by a reimbursement system that encourages a more holistic approach to patient care.[217] This leaves questions about its future and the relevance of results of this analysis. Indeed, NHS England has commented in the past that it was committed to removing the QOF altogether.[218] That said, the scheme remains but there is a preference for the focus of the QOF to shift to improving health in a way that has meaning for individual patients.[219] A recent NHS review of the QOF concluded it would be desirable to take a broader definition of high-quality care and recognise changes in clinical evidence and practice.[220] Therefore, could updating the QOF to provide equality of outcomes for patients, rather than equality of opportunity, reinvigorate the scheme?

The potential value of an association between cognitive function on care quality may be limited. Trial evidence has shown that whilst acetylcholinesterase inhibitors and other Alzheimer's disease drugs are superior to placebo on measures such as the ADAS-Cog or MMSE, cognitive function still deteriorates whilst using these drugs,[185] and similar results are observed for cognitive stimulation measures.[204 214 215] Whilst it was not captured by this analysis as many patients with dementia were only included at one wave, longitudinal studies to assess how limiting the decline in cognitive function over time can improve care quality in the long-term would be of value. Such research may be of particular interest given that improved cognitive function may also have other benefits beyond improving care quality, such as quality of life and wellbeing, and reduction in support needed with ADLs, and thereby increasing the potential value of interventions targeting it.

Conclusions

Based on the analyses conducted, better cognitive function was associated with higher quality care for patients with less severe dementia, potentially supporting the hypothesis that increased cognitive function increases the demand for high quality healthcare. Engaging in cognitive interventions to improve cognitive function may improve access to high quality healthcare that can improve long-term health outcomes, as well as potentially providing additional short-term quality of life and wellbeing gains. For those patients unable to engage in cognitive interventions, perhaps proactive measures to increase demand are required, such as registries monitoring comorbidities and care needs partnered with social support to increase access to care.

Pay-for-performance schemes that aim to motivate health care providers to increase the supply of high-quality care also appear to improve care quality for patients with dementia, however this improvement in care quality is also observed in patients without cognitive impairments and therefore does not reduce inequalities in quality.

A targeted pay-for-performance scheme with a focus on indicators specific to patients with dementia could be used to optimise and target the time spend within existing healthcare interactions to improve both care quality and health outcomes for these patients, whilst reducing inequalities in quality compared to patients without cognitive impairments. Whilst improvements in care quality as a result of these exposures may be feasible, the clinical and cost-effectiveness of additional financial incentives to physicians or widespread cognitive interventions to improve quality and reduce inequalities on top of treatment costs needs to be appraised and validated, as well as the impact of physicians' disinvestment of time in care for other patients.

The findings of this chapter suggest that the supply and demand for quality health care could be modifiable by influencing the actions of the healthcare provider or healthcare consumer. The consumer-driven demand may be increased with greater cognitive function, potentially associated with an increased knowledge of their health status and health literacy, in line with the economic framework presented in Chapter 1. The increase of the supply of quality care could be modulated by an economic or reimbursement mechanism, however financial rewards do not seem to be the sole driver of better-quality care. Therefore, pay-for-performance mechanisms may also be an avenue for knowledge dissemination in terms of the clinical value of care as well as the economic value they provide. Both factors could play some role in the actions of physicians, assuming a framework of utility maximisation based on financial and non-financial incentives as outlined in Figure 1.4.

CHAPTER 6

EARLY ECONOMIC EVALUATION OF STRATEGIES FOR IMPROVING CARE QUALITY FOR DEMENTIA PATIENTS

6.1. BACKGROUND & OBJECTIVES

The costs of dementia with regard to health and social care are substantial, with an estimated at £8.8 billion spent per year on healthcare and publicly funded social care for patients with dementia in the UK, plus a further cost of £17.3 billion for privately funded social care, informal care, and other services.[44] With an increasing prevalence of dementia, optimising the delivery of care and allocation of resources to ensure these funds are spent in the best possible way to maximise health outcomes for patients with dementia and their caregivers is a pertinent issue.

Over the previous chapters it has been shown that patients with dementia are less likely to meet quality indicators for the management of some of their comorbid conditions, and that failure to meet these indicators is associated with poorer survival and greater social care use. However, the analyses have also determined that both patient (cognitive function) and policy (pay-for-performance) factors are associated with meeting these quality indicators. In assessing whether these variables could form the basis of a viable intervention strategy, and if collecting high quality clinical data of the effectiveness of these potential interventions could be worthwhile, economic modelling can be used.

This study aims to make early assessments on the cost-effectiveness of potential care quality improving strategies for patients with dementia to provide a basis for funders to make inferences on the value of conducting additional research as to whether these interventions are efficacious in clinical practice.

Early modelling for cost-effectiveness analysis differs from modelling for submission to health technology assessment (HTA) agencies and payers in its objectives and data sources. When submitting to HTA authorities for reimbursement, the objective of the model is to assess whether a proposed intervention or strategy is an economically efficient use of health care resources within reasonable budget constraints, and should be based on the best available evidence to reduce uncertainty in decision making. Conversely, early modelling is typically based on earlier or naïve data and tends to focus more on whether further action should be taken, such as evidence generation

(e.g., conducting a large, randomised, phase 3 trial for a pharmaceutical) to prepare for reimbursement.[221] Early modelling is increasingly being used during clinical development to inform research design to mitigate potential risks that may be perceived by healthcare payers associated with reimbursement.[222] Provisional estimates of the cost-effectiveness can be used to inform "go, no-go" decisions on investment of research and development resources based on the commercial viability of the product, such as the probability of reimbursement at a given price, or as to whether the economically justifiable price for a given willingness-to-pay (WTP) per QALY would be acceptable to a technology developer given their costs.[221] Whilst early modelling has been most widely used in the pharmaceutical industry, its value spills over into other areas where investment decisions may be required.[223] Given the known limitations with making causal assumptions and deriving efficacy from observational data, early modelling could be used to estimate the potential cost-effectiveness of the derived intervention strategies from the English Longitudinal Study of Ageing (ELSA) data to determine whether further evidence should be collected to confirm the effectiveness and cost-effectiveness.

In the opening chapter to this thesis, a framework was proposed outlining that care quality can either be directly modulated by the economic and policy factors driving the provision of care, or that clinical or social interventions could influence patient-level factors (including cognitive function) to increase the demand for care quality (see Figure 1.1). In the previous chapter it was demonstrated that pay-for-performance in the Quality and Outcomes Framework (QOF) was positively associated with care quality, highlighting that economic interventions could be used to improve care quality. This association was sustained even after adjustment for cognitive function, suggesting that potential intervention strategies may be independent of each other with regards to supply and demand.

Whilst the QOF represents a pre-existing framework for improving care quality, and its association with outcomes has already been assessed in this thesis, how cognitive function could be influenced and modulated was not directly appraised in the previous chapter.

Promoting independence is a commonly cited goal for patients with dementia and involves embracing a patient-centred approach to care that allows the maintenance of autonomy.[224] Promoting independence includes encouraging participation in daily activities, supporting physical activity, and providing opportunities for social engagement.[224 225] A further core component of the promotion of independence is the maintenance of cognitive abilities, which can be sustained or improved through

physical and social activity,[136 226] as well as through cognitive interventions.[204 214 215] The PRIDE (Promoting Independence in Dementia) intervention is a self-management intervention for patients with early dementia. The PRIDE intervention has been developed though epidemiological investigation into the risk and protective factors associated with dementia, and a qualitative exploration on the themes of memory and independence, alongside existing literature.[227]

The PRIDE intervention is currently being evaluated in a feasibility randomised controlled trial (RCT), aiming to assess the feasibility and acceptability of conducting a future large-scale definitive RCT with regards to recruitment, inclusion criteria, sample size, trial and intervention procedures, and the appropriateness of outcome measures.[227] Given that there is no evidence to date on the efficacy of this intervention on improving cognition and its potential indirect effects on care quality, a provisional estimate of the efficacy of the intervention is developed in this model to support the potential value assessments of conducting a definitive RCT.

6.2. Decision Problem

Table 6.1 captures the decision problem and scope of the analysis included in this chapter. The decision problem addresses the long-term effectiveness and cost-effectiveness of expanding the QOF to include indicators specifically in patients with dementia that are not currently included in the QOF, or provide additional reimbursement associated with comorbid dementia for indicators already included in the QOF. The selected indicators include those where care quality is lacking for patients with dementia. Additionally, the long-term effectiveness and cost-effectiveness of introducing a self-management intervention for dementia (the PRIDE intervention) is also addressed in patients with milder dementia.

The expansion of the QOF is assumed to include additional indicators for patients with dementia, focusing on providing reimbursement to GP practices for referring patients with dementia to a self-management intervention for their diabetes and providing dietary supplements to patients with osteoporosis to improve bone density, as well as boosting the reimbursement attainable for providing antihypertensives to patients with dementia and high blood pressure, providing smoking cessation advice and treatment, and conducting annual foot checks for those with comorbid diabetes.

Table 6.1. Scope of the analysis

Population	People living with dementia (aged 50+) in the community with comorbid diabetes, hypertension, or osteoporosis, or who currently smoke	People living with mild or moderate dementia (aged 50+) in the community with comorbid diabetes, hypertension, or osteoporosis, or who currently smoke

Interventions	Expanded QOF scheme for patients with dementia	▪ Expanded QOF scheme for patients with dementia ▪ The PRIDE intervention ▪ Both of the above in combination
Comparators	Treatment as usual	▪ Each of the interventions above ▪ Treatment as usual
Outcomes	▪ Survival ▪ Admissions to hospital or care homes ▪ Health-related quality of life ▪ Avoided ill health and symptom reduction / resolution of comorbid illness ▪ Quality of primary care services ▪ Resource use and costs ▪ Cost-effectiveness	

The PRIDE intervention is based on a manual focussing on social, physical, and cognitive domains, with which patients with mild dementia are guided through three facilitated sessions, tailored to meet the individual's needs. The topics covered in the PRIDE intervention are:

- **Finding a balance**: helping the person to better manage their time and the resources needed to perform activities and balancing with rest and relaxation
- **Social connections**: information on how others can support the person with dementia, and how their support network could be enhanced
- **Keeping going**: finding motivation to do activities and navigating practical considerations in maintaining activities
- **Making decisions**: supporting decision-making with examples and activities
- **Getting your message across**: helping the person with dementia to communicate via activities and case stories
- **Receiving a diagnosis**: managing worries associated with diagnosis and discussing the diagnosis with others
- **Keeping mentally active:** encouraging the patient to maintain cognitive activities through stimulating activities
- **Keeping physically active**: enabling the patient to maintain an active lifestyle
- **Keeping socially active**: helping the patient to maintain their social roles

The first six topics may support gains in care quality with regards to improving discussions with healthcare professionals and informal caregivers or allowing patients to be more engaged in their healthcare decisions.[195] However, given that cognitive function is the main focus of anticipated gains in care quality for this analysis, the cognitive benefits of keeping physically, mentally, and socially active are those captured in this early assessment given it is these factors which have been appraised for their impact on cognitive function in previous research.[136 204 214 215 226]

The choice of the patient groups is informed by the assumption that all patients could be involved in the expansion of the QOF, but that initiating a self-management intervention would require a certain level of baseline cognitive function in order to be able to engage in the intervention. For completeness, the expansion of the QOF programme is also considered in this patient subgroup, as well as both interventions in combination. The analysis aims to assess the impact of these interventions on costs, survival, and health-related quality of life, with consideration to the impact they may have on the quality of primary care services.

The interventions will be compared to treatment as usual, defined as care for patients with dementia and their relevant comorbidities without any additional treatment beyond current practice to improve their cognitive function nor providing wider reimbursement to GPs with regards to quality indicators. Costs of treatment as usual will include those related to the QOF at present and for the management of dementia.

Results will be expressed in line with the NICE reference case in terms of the incremental cost per quality-adjusted life year (QALY), considering costs from the perspective from the National Health Service (NHS) and personal social services (PSS) in England, and benefits from the perspective of the patient.[171] Given that the QOF is currently funded by the NHS, an extension to this would also likely be funded by the NHS. The PRIDE intervention could be funded by the NHS or other public sector body which funds social care programmes (e.g., local government), or be self-funded. As a conservative estimate of the cost-effectiveness from an NHS/PSS perspective, the costs of the intervention are included in this analysis.

6.3. Previous Economic Models

No known previous models have assessed the cost-effectiveness of a pay-for-performance scheme specifically for patients with dementia, nor the cost-effectiveness of the PRIDE intervention. Analyses have been conducted on pay-for-performance schemes in the general population, as well as for other self-management and cognitive interventions in patients with dementia, and these models may provide valuable insight into the model design or inputs.

A targeted literature review to identify previous cost-effectiveness models in patients with dementia, or those looking at cognitive interventions or changes in cognitive function, or for pay-for-performance schemes was conducted in MEDLINE (see Appendix 6.1 for the search strategy). In addition, NICE guidance was screened for those appraisals including economic models assessing the same areas. Only modelling studies were considered, as opposed to cost-effectiveness analyses conducted

alongside trials, given the requirements for extrapolation of outcomes to a lifetime horizon. Models which focussed only on populations of patients with severe dementia or moderate to severe dementia were not considered given that the target population for community-based interventions is likely to be for more mild cases. Models that did not discriminate by level of dementia severity were also included (i.e., included mild to severe patients). Models must have reported results on a cost-per-QALY basis to be included, have been published in English, and have a full-text manuscript available (abstracts were not included).

Ten published models were considered of relevance, though three of these were the same model adapted to different countries. A summary of the main modelling approaches is provided below, with references to which aspects of each model provided input or inspiration to this model detailed throughout this chapter. Most of these models focussed on patients with dementia, with one analysis looking at the cost-effectiveness of pay-for-performance schemes. No modelling studies were identified specifically for self-management interventions to improve cognition.

A NICE technology appraisal (TA217) evaluated the cost-effectiveness of acetylcholinesterase inhibitors (AChEI) and memantine for Alzheimer's disease.[228] Within this appraisal, a systematic review of modelling studies was conducted which included 27 papers, of which three were considered relevant to potentially inform the modelling approach for this analysis. In addition, three de novo cost-effectiveness models were included in the report: one developed by Lundbeck (the manufacturer of memantine), one by Eisai/Pfizer (the manufacturers of donepezil – an AChEI), and one developed by the TA assessment group (PenTAG). The model submitted by Eisai/Pfizer for the economic evaluation of donepezil in mild to moderate Alzheimer's disease and the model developed by the PenTAG were deemed potentially relevant. The Eisai/Pfizer model was a discrete event simulation, where patient's MMSE (Mini Mental State Evaluation) score, NPI (Neuropsychiatric Inventory – measure of behavioural change) score, and the number of difficulties in performing (instrumental) activities of daily living (IADL/ADL) were modelled over time to estimate the time to the next event. The events included stopping treatment, a GP visit, or death, with utilities accumulated between events. Patient utilities are estimated as a function of the MMSE score, NPI, whether they are living in an institution, and if they are living with their caregiver. The model also included caregiver utilities, estimated as a function of the caregiver age and sex, the age of the patient, the patient's MMSE and NPI scores and ADL/IADL impairments, as well as whether or not they were receiving antipsychotic medications. Routine monthly costs of medical care beyond drug

treatment and specific events were also included, including the cost of institutionalisation. This model was also found to be published,[229] as well as adapted to Germany.[230] The model developed by PenTAG was a little more simplistic, using a Markov approach based on health states for patients resident in the community or those institutionalised (i.e., in long-term residential care or hospitalised). The model was based on time-to-institutionalisation data from a UK cohort. Within the pre-institutionalised state there were gradual increases in costs and gradual reductions in HRQoL dependent on the time to institutionalisation.

The three models of relevance identified from the systematic review in TA217 appraised the cost-effectiveness of donepezil in Taiwan,[231] Spain,[232] and Germany.[233] All three studies used a fairly simple, single dimensional approach using a Markov structure, which tracked patients through three or four health states based on disease severity (defined by either MMSE score or the Clinical Dementia Rating [CDR] scale), with death as an absorbing health state. Transitions between states were not time-dependent in any model. Across all models the main treatment effect was to reduce the rate of disease progression. Costs and quality of life estimates were based on simple assumption of annual values capturing the health care resource costs by disease severity, and fixed utilities within health states. The model authors were self-critical with regards to assumptions on the association between disease severity and survival,[233] and that approaches may not capture all patient-relevant factors in Alzheimer's disease.[231 233]

In the development of the NICE guideline on the assessment and management of dementia (NG97), a simple economic model was developed to assess the cost-effectiveness of non-pharmacological interventions influencing cognition. This model used an area-under-the-curve approach to determine how MMSE scores change over time, considering an intervention phase (where cognitive function improves), a follow-up phase (where it is sustained), and a convergence phase (where it deteriorates back to the untreated level). They assumed that non-pharmacological interventions would have no effect on mortality, there would be no additional improvements in cognition after the intervention has ended, and that wider healthcare resource use does not change as a result of the programme (e.g., no beneficial effects on hospital stays or GP appointments).

A further model in dementia patients looked at the cost-effectiveness of earlier diagnoses and initiation of treatment compared to standard practice.[234] The authors developed a simple model extrapolating MMSE scores over 10 years, along with utilities modelled using the same algorithm as in the Eisai/Pfizer model. The costs of

care were assigned based on resource use observed in a French cohort, matched to UK relevant prices. They explored the cost-effectiveness of a hypothetical scenario of introducing symptomatic treatment or a disease-modifying therapy prior to the current time of diagnosis and how this may alter utilities gained, to estimate cost thresholds within UK willingness-to-pay thresholds.

One modelling study was identified which aimed to assess the cost-effectiveness of continuing the QOF compared to stopping it by developing a lifetime simulation model.[158] The authors considered that most benefits of the QOF are targeted at to a cohort of 40-74 year olds with cardiovascular disease or associated risk factors. The core focus of their approach was to assume a mortality reduction with the presence of the QOF, for which the inverse was used to estimate survival in an age- and sex-matched cohort to the UK at present. This was used to determine the incidence of fatal cardiovascular events, and the morbidity and quality of life impact of non-fatal cardiovascular events was indirectly estimated, along with the total costs of the QOF programme, the cost of cardiovascular events, and the cost to the NHS associated with prolonged life. This approach informs that external data can be used to estimate the excess mortality and quality of life loss in the presence of imperfect care quality, and the wider impact of investing in pay-for-performance schemes.

Based on the studies identified, a range of key criteria were considered for integration in the model design:

- **Drivers of disease progression**: Cognitive function is the key factor used to model the trajectory of dementia, with behavioural changes and challenges in performing activities of daily living also used to predict key events in the life course and changes in quality of life. The natural history of dementia was also considered to be unidirectional, in that the disease always progresses but gains in cognition can be achieved in the short-term.
- **Treatment-effect duration**: Gains in cognitive function are likely to be for a limited term only, and therefore modelling how these can improve and deteriorate over time in response to the intervention and disease progression is likely to be required.
- **Mortality**: Dementia was largely considered to be a terminal condition, with death playing a key role in outcomes in the models, with how survival is influenced by treatment being a driver of results.
- **Institutionalisation**: Some models included a move to residential care or long-term hospitalisation as a key event or outcome for measuring quality of

life or treatment effects, but for others it was just a marker of a step-change in costs. Regardless, it appears to be a key factor for consideration.

- **Routine care:** The costs of manging dementia were typically substantial, with routine care exceeding intervention costs. Therefore, capturing how costs of care may increase as a result of prolonged survival may be important in cost-effectiveness assessments.
- **Comorbidities:** A substantial component of the costs and outcomes of pay-for-performance and care quality improvement schemes are not just the costs of the scheme itself, but rather the investments in healthcare in the long-term due to providing better quality care. The health outcomes across the lifetime because of better care are also key to capture.

6.4. Model Structure

The choice of model structure was informed by a number of decisions, within a multidimensional framework. The purpose of the model is to evaluate potential interventions for patients living with dementia, though the interventions are not specifically targeting the treatment of dementia. The model should have to ability to assess the impact of the interventions on the morbidity and mortality associated with the comorbidities for which care quality is aiming to be improved for, whilst also considering the natural history and progression of dementia. The key clinical outcome associated with improvements in care quality was identified to be survival in Chapter 4, along with a possible association with institutionalisation, and therefore time-to-event analysis needed to be incorporated into the structure.

Given the complexity of the patient transitions and events that could occur over the lifetime, individual patient simulation methods (e.g., discrete event simulation; DES) would appear preferable. Indeed, it has been argued that the complexity of the disease and the heterogeneity of disease progression in patients is best reflected using DES approaches,[235 236] and the Assessment Group for the NICE TA217 evaluated the relevance of DES approaches at length.[228] With sufficient data, this approach would also permit inclusion of future events associated with comorbidities, such as cardiovascular events due to the lack of antihypertensive treatment, if risk equations could be developed.

Ultimately the Assessment Group decided to use a state transition (Markov) model due to the challenges in using aggregate trial data of the interventions in a model requiring patient-level data, as the patient-level data not being available to them. I reached a similar conclusion for this model in that whilst patient-level data is available

from ELSA for modelling certain aspects of the patients' prognosis, there is insufficient data on the consequences of changes in health care quality, such as morbidity and health care utilisation associated with the complications of long-term conditions. In addition, some form of cohort-based approach would be required with regards to assessing the impact of the QOF. The scheme reimburses practices based on the proportion of patients on their lists who are eligible for a particular indicator meeting the care practices within that indicator. Therefore, a binary metric of whether a quality indicator has been met on a patient-level is not informative of the level of reimbursement attainable by the practice, but rather assessing the overall quality of care within a cohort of patients representing a single GP practice is required.

Upon settling on a cohort-based approach, several further questions were outlined for determining specific health states and how to capture the relevant costs and effects:

- Which aspects of the progression of dementia or events across the life course of a patient with dementia lead to a step-change in the costs of health or social care or key changes in health-related quality of life, and what role would the prolonging of survival have on lifetime costs?
- Which measures of dementia progression are predictive of health and social care costs or health-related quality of life?
- Which long-term events or complications are associated with the included quality of care indicators from ELSA, and which of these are associated with morbidity or health-related quality of life losses or surplus health and social care utilisation?

Based on the overview of the previously conducted models, three key factors arise as predictors of long-term costs and outcomes in patients with dementia: cognitive function, ability to conduct (instrumental) activities of daily living, and institutionalisation. Consideration was given to how a multidimensional model could account for these factors. Both cognitive function and IADLs would have to be incorporated into the model and sensitive to changes over time and treatment, given the impact of the PRIDE intervention and the possible impact of higher quality care on the number of IADLs assisted with by social workers. In addition, it has been noted in the past that basing a disease progression model in Alzheimer's disease on the decline in cognitive function alone is inadequate given that it is not strongly associated with health-related quality of life or costs.[237] [238] However, developing a model structure which tracks the progression of cognition and functional ability simultaneously would require multiple health states, with each additional health state exponentially increasing the number of transitions and with it, the patient numbers

needed to estimate the transition probabilities. Given the limited data and the provisional nature of the cost-effectiveness assessment a simpler approach was favoured, akin to that used by the Technology Assessment Group in NICE TA217,[228] focussing on time to institutionalisation. In their model they identified institutionalisation as being the key driver of changes in costs. The definition of institutionalisation used in the TA217 model was akin to that applied in Chapter 4 as living in a residential care home, nursing home, mixed function home, or in hospital on a long-term or permanent basis.[228]

As participants in ELSA are required to be resident in the community at their first interview, and so analyses conducted in the previous chapters were largely done so on those resident in the community, the distinction between pre- and post-institutionalisation was deemed relevant for the new model. Especially given that the PRIDE intervention is designed for patients with milder dementia who are more likely to be resident in the community and benefit from the promotion of independence. In addition, the modelled intention of the interventions is to improve primary care quality and patients with dementia who are living in residential care are less prolific users of primary care services than those who are resident in the community.[44]

A three-state structure formed the basis of the model for capturing the progression of disease for patients with dementia. The three states are: pre-institutionalisation, institutionalised, and death. Using the definitions of overall survival and institutionalisation-free survival as applied in Chapter 4, a partitioned-survival model was used, as commonly applied in oncology. These models involve the independent extrapolation of the overall survival curve as well as a second time-to-event outcome composed of an intermediate event that may be prognostic of death, as well as deaths prior to this event. Health state occupancy is then estimated as the disaggregation of the area under or between the sequential extrapolated curves (see Figure 6.1).

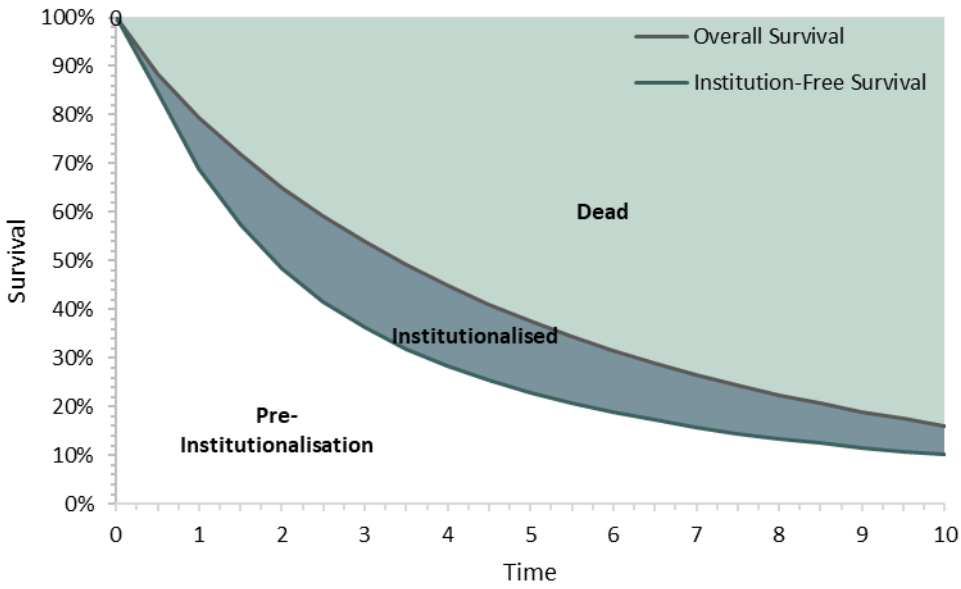

Figure 6.1. Partitioned-survival model structure

Within this model structure, patients are assumed to be resident in the community at baseline and from here can either transition to long-term care or die. Once institutionalised, patients are assumed to only transition to death. As all modelled patients are resident in the community at baseline, and that it is assumed that once an individual becomes institutionalised they do not return to the pre-institutionalised state, a partitioned survival framework can be used in this scenario over a Markov model accounting for specific transitions. This structure also permits for the hazard ratios derived for the impact of care quality on survival to be directly applied in the model to the overall survival curve.

Much like in the model used in NICE TA217, cognition and IADLs are modelled over time independently of health state transitions as secondary dimensions to capture the impact on health-related quality of life and costs. Comorbidity burden, as influenced by changes in the quality of care, are considered as a third dimension. As mortality and dementia-related morbidity are already assumed to be captured by the model, as well as the impact of care quality on mortality, the morbidity and health changes associated with comorbidities are captured in terms of event and disutilities related to the conditions and the care provided (see below) and are therefore not directly linked to model health states but considered as events within health states.

A time horizon of 20 years was selected in the base case to align with the NICE guidelines for health technology assessment recommendation that all important differences costs or outcomes would be reflected.[171] By this time, it was estimated that

less than 10% of the cohort would be alive and that less than 5% would still be resident in the community. Whilst 20 years is not a full lifetime horizon, given the uncertainties in extrapolating survival and that key differences in care quality are expected earlier in the patient lifetime this was deemed an appropriate duration. Scenarios of five and 30 years were also considered. A cycle length of 12 months was applied in the model. Although ELSA data was collected biennially, the derived time window defined for death or institutionalisation for each patient was less than one year (see §4.2). In addition, as QOF payments reflect care quality over the previous year, these costs should be captured within a 12-month cycle. Both costs and health effects were discounted at 3.5% per annum as per NICE reference case, with a discount rate of 1.5% considered separately for costs and outcomes in scenario analyses.[171]

6.5. Clinical Parameters & Variables

Health State Occupancy

As mentioned above, health state occupancy was defined by the extrapolation of overall survival and institutionalisation-free survival using data from the ELSA. A subset of participants from ELSA were included in the model, defined as those living in the community at their first included interview following a diagnosis of dementia and at least one comorbid condition or risk factor making them eligible for the quality indicators associated with poorer quality care for patients with dementia in Chapter 3 (the index date). These factors were physician diagnosed diabetes, hypertension, or osteoporosis, or current cigarette smoking. This created a sample of 147 patients, or 128 patients in the subset with mild or moderate severity dementia at baseline as defined by a score greater than 10 on the cognitive function index from ELSA. Patient characteristics at model baseline are summarised in Table 6.2.

For each respondent in ELSA, time from the index date to the date of death, defined as the time window with the year and season of death or censoring (date of last ELSA interview up to wave 8) was calculated. Further details on the method for calculating the minimum and maximum times to death based on the reported ELSA data are given in Chapter 4 (see §4.2). Of the patients with all dementia severities, 51 had an observed death during follow-up, whereas only 42 respondents with mild or moderate dementia at baseline had died by the end of follow-up. Institutionalisation-free survival was defined as the time from the index date until the first of institutionalisation, death, or censoring. Institutionalisation was calculated as the time window in which the respondent moved to a nursing home, residential care home, or prolonged stay in

Table 6.2. Baseline characteristics of patients used to inform the treatment as usual arm

	All Severities	Mild or Moderate Dementia
N	147	128
Age, Mean (SD)	76.2 (10.1)	75.5 (10.3)
Years Since Dementia Diagnosis, Mean (SD)[†]	4.3 (8.2)	4.7 (8.7)
ELSA Cognitive Function Index, Mean (SD)	16.8 (7.0)	18.1 (6.6)
Female, n (%)	75 (51.0%)	63 (49.2%)
Married and/or Cohabiting, n (%)	89 (60.5%)	78 (60.9%)
White Ethnicity, n (%)[‡]	139 (94.6%)	120 (93.8%)
Challenges with IADLs, n (%)		
▪ None	43 (29.3%)	39 (30.5%)
▪ 1 – 2	22 (15.0%)	20 (15.6%)
▪ 3 – 4	34 (23.1%)	28 (21.9%)
▪ 5 – 6	48 (32.7%)	41 (32.0%)
Diabetes, n (%)	35 (23.8%)	31 (24.2%)
Hypertension, n (%)	123 (83.7%)	108 (84.4%)
Osteoporosis, n (%)	11 (7.5%)	9 (7.0%)
Smoking Status, n (%)		
▪ Non-Smoker	57 (38.8%)	50 (39.1%)
▪ Ex-Smoker	78 (53.1%)	67 (52.3%)
▪ Light Smoker (<10 Cigarettes per Day)	1 (0.7%)	1 (0.8%)
▪ Moderate Smoker (10-19 Cigarettes per Day)	6 (4.1%)	5 (3.9%)
▪ Heavy Smoker (≥20 Cigarettes per Day)	5 (3.4%)	5 (3.9%)
Multiple Comorbidities or Risk Factors, n (%)[‖]	37 (25.2%)	34 (26.6%)
Total Number of ELSA Interviews Included, n (%)		
▪ 1	91 (61.9%)	77 (60.2%)
▪ 2	40 (27.2%)	36 (28.1%)
▪ 3	13 (8.8%)	12 (9.4%)
▪ 4	3 (2.0%)	3 (2.3%)
Median Follow-Up for Survival (95% CI), Months	70 (49 to 75)	70 (65 to 92)

[†]Data only available for 138 respondents with all severities and 122 respondents with mild or moderate dementia. [‡]ELSA data collapses ethnicity into white or non-white to preserve anonymity given low numbers of non-white respondents. [‖]Only considers diabetes, hypertension, osteoporosis, or current smoker.

hospital or a hospice prior to death, using the same method reported in Chapter 4. During follow-up, 58 respondents become institutionalised or died prior to institutionalisation in the group including all severities of dementia, compared to 46 in the mild or moderate dementia subgroup. Given the relative immaturity of the time to event data, the curves for overall survival (OS) and institutionalisation-free survival (IFS) needed to be extrapolated.

Estimates for long-term OS and IFS were derived by fitting parametric survival distributions to the ELSA data in accordance with the guidance from the NICE Decision Support Unit (DSU) Technical Support Document (TSD) 14.[239] This involves a systematic process of deriving the appropriate analysis method, extrapolating curves, and selecting optimal fits for inclusion in the model.

Table 6.3. Goodness of fit statistics for the overall survival curves

Distribution	All Severities		Mild or Moderate Dementia	
	AIC	BIC	AIC	BIC
Weibull	590.5	596.5	488.6	494.3
Loglogistic	590.7	596.7	488.8	494.5
Gompertz	591.2	597.2	490.6	496.3
Generalised Gamma	592.5	601.5	490.6	499.1
Lognormal	596.7	602.7	492.6	498.3
Exponential	598.5	601.5	499.9	502.8

Notes: Distributions are ranked by AIC (equal order for both populations). AIC, Akaike information criterion; BIC, Bayesian information criterion.

Given that the data from ELSA representing treatment as usual are from a single group of patients (i.e., non-comparative), the first stage of the algorithm assessing proportional hazards between exposures was not considered. Only standard parametric hazard functions (exponential, Weibull, Gompertz, lognormal, loglogistic, and generalised gamma) were considered in the extrapolations rather than more complex functional forms (e.g., Royston-Parmar cubic splines or mixture models). These other models were excluded *a priori* as I considered that it would not be plausible to statistically define or observe a group of responders versus non-responders to higher quality care after disaggregating the sample into those receiving high- or low-quality care as this was a time-varying factor. In addition, given the advanced age of included patients, the plateau in survival typically observed with these methods would be unrealistic. Curves were fitted using the *R* package `flexsurv` which uses a maximum likelihood function which can account for the interval-censored time to event data.[240] The distributions used in the base case model were selected based on a visual inspection of the survival curves relative to the Kaplan-Meier curves, goodness-of-fit statistics (the Akaike information criterion [AIC] and the Bayesian information criterion [BIC]), plausibility of the underlying hazard function, and comparison to external data.

The AIC and BIC estimates for the extrapolated curves are presented in Table 6.3 and Table 6.4 for OS and IFS, respectively. As can been seen, there is very little variation in the goodness of fit statistics.

Figure 6.2 shows the comparison of extrapolated overall survival curves, including an adjustment so that the hazard of death any in any given year is greater than that observed in the general population. These were derived from lifetables from England and Wales for the period 2017 to 2019 obtained from the Office for National Statistics assuming a baseline age of 76 as per the included sample.[241] All curves fairly closely follow the Kaplan-Meier for the first four years of the analysis for both the group with

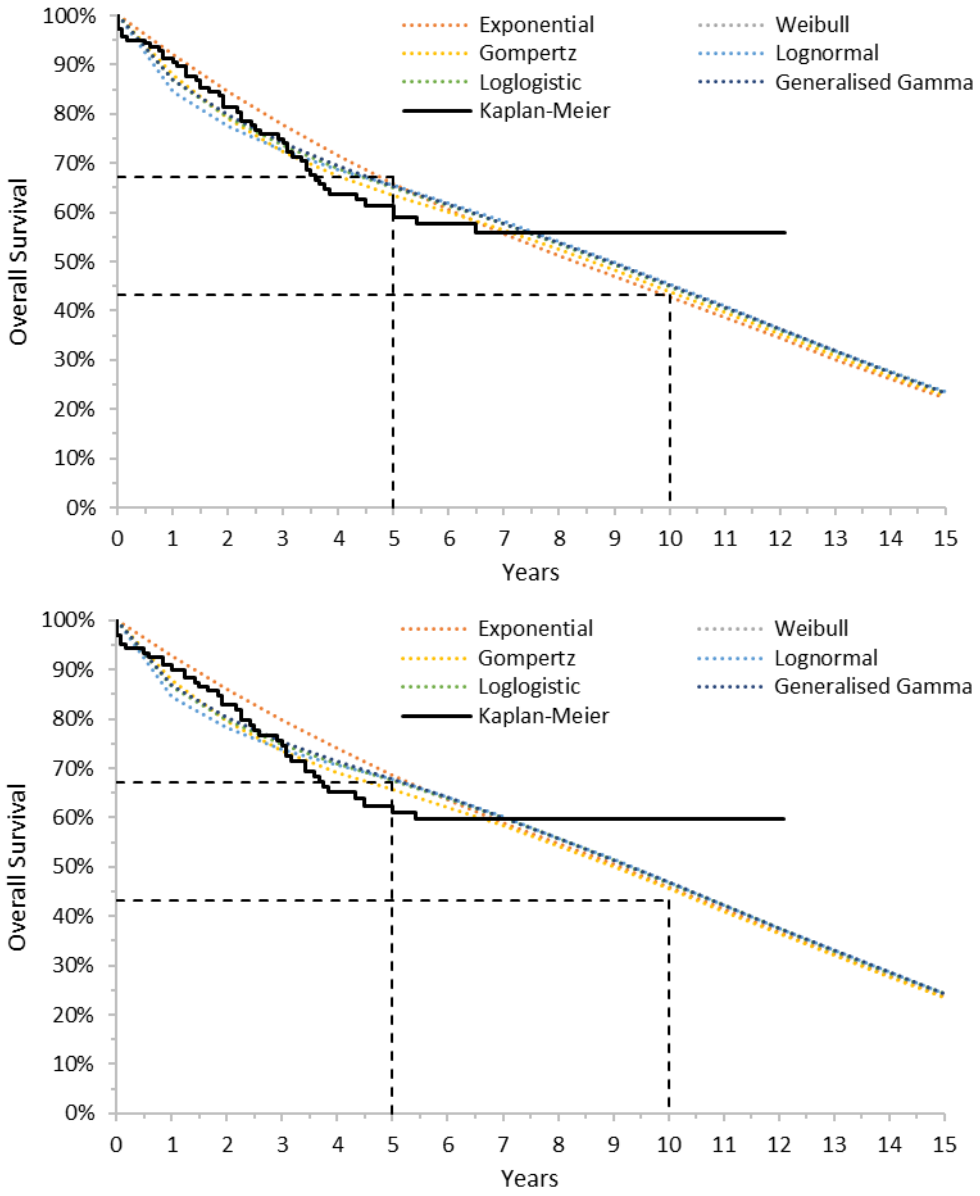

Figure 6.2. Comparison of extrapolated overall survival curves for the population including all dementia severities (top) and mild or moderate dementia (bottom)

all severities of dementia and the mild/moderate group. After this point, despite a brief overestimation of survival, curves in both patient groups dip below the observed plateau. The prolonged survival observed on the Kaplan-Meier is likely to be attributable to high censoring and a limited number of patients in the tail, and therefore it is considered reasonable that survival would be less than this in practice. On visual inspection, the Gompertz and loglogistic distributions provided the best fit to the early period of the Kaplan-Meier curve for both patient groups for OS.

Table 6.4. Goodness of fit statistics for the institutionalisation-free survival curves

Distribution	All Severities		Mild or Moderate Dementia	
	AIC	BIC	AIC	BIC
Weibull	591.1	597.1	474.9	480.6
Generalised Gamma	591.9	600.9	476.2	484.8
Loglogistic	593.4	599.4	476.2	481.9
Lognormal	596.3	602.3	477.8	483.5
Gompertz	629.0	635.0	507.4	513.1
Exponential	651.9	654.9	529.1	532.0

Notes: Distributions are ranked by AIC (equal order for both populations). AIC, Akaike information criterion; BIC, Bayesian information criterion.

For comparison to external estimates, relative survival estimates by age group for patients with dementia compared to the general population were obtained.[242] These were applied to the lifetable survival estimates for England and Wales. Based on this, five-year survival was estimated at 67% and ten-year survival at 43%, which roughly aligns with all extrapolated curves in patients regardless of severity, with the Weibull, lognormal, and loglogistic distributions being the most optimistic in terms of long-term survival. For patients with mild and moderate dementia, all curves are aligned with the external data at five years but overestimated at 10 years. However, improved cognitive function has previously been demonstrated to be associated with longer survival,[228] and therefore in this population survival may be expected to be longer when compared to all severities of dementia.

IFS was also adjusted for all-cause mortality, given that patients who become institutionalised must do so before death, and the deaths of those patients who do not become institutionalised are captured within the curve. The extrapolated curves for IFS for all patients and those with mild or moderate dementia are shown in Figure 6.3. Based on visual inspection, the generalised gamma distribution provided the best fit for both patient groups.

As the ELSA data is obtained from a prevalent cohort, and practices on institutionalisation and the move to long-term care are changing for patients with dementia,[44] [243] there was no known reliable source of external validation for institutionalisation-free survival. However, I deemed this to be of limited consequence given that in the base case no modelled effect of care quality on institutionalisation was included, based on the non-significant results obtained in Chapter 4.

Based on the assessment, the Gompertz distribution was selected for OS in the base case for both patient populations, with the loglogistic distribution being applied in

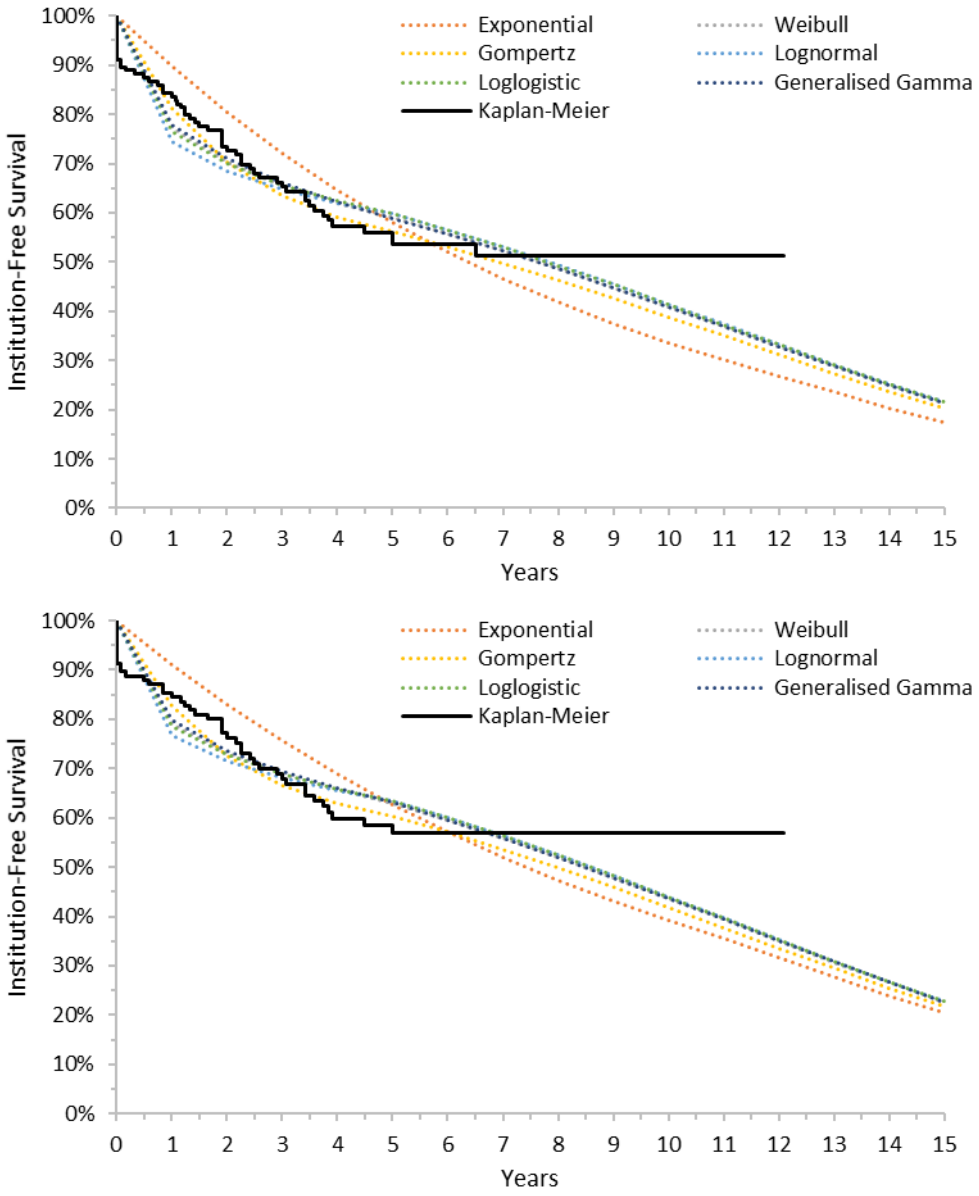

Figure 6.3. Comparison of extrapolated institutionalisation-free survival curves for the population including all dementia severities (top) and mild or moderate dementia (bottom)

scenario analyses. For IFS, the generalised gamma and Weibull distributions were selected for the base case and scenario analysis, respectively, for both patient groups. Given the numerous uncertainties associated with early modelling, and the various assumptions associated with the parameters in the model, it is important to represent the uncertainty in the model as fully as possible. Accordingly, a probabilistic base case was favoured. The Cholesky decomposition was derived from the covariance matrices for the fitted parametric curves for probabilistic sampling of the curve parameters. Figure 6.4 and Figure 6.5 show the mean of the samples of the survival estimates of

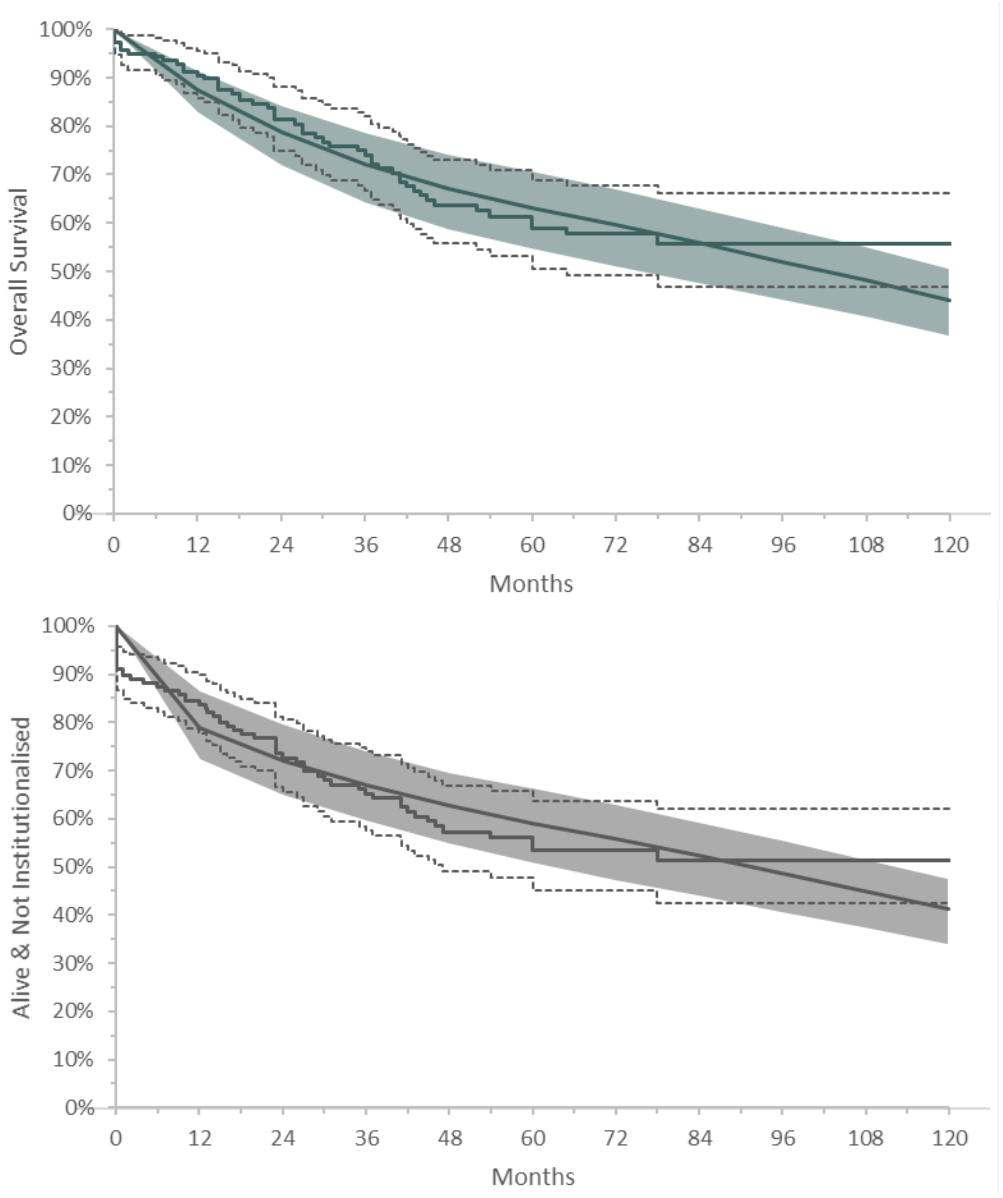

Figure 6.4. Kaplan-Meier curves for overall survival (top) and institutionalisation-free survival (bottom) showing probabilistically sampled mean survival extrapolation and 95% credible intervals for all patients with dementia and at least one comorbid condition or risk factor

the selected base case curves for the first 10 years in the model, as well as the 95% credible intervals of these, compared to the Kaplan-Meier curves from ELSA and their 95% confidence intervals. As can be seen, the sampled estimates provide a reasonable representation of the observed uncertainty in the study data.

Cognitive Function

As improving cognitive function through the promotion of independence is one of the interventions, and cognition is a predictor of costs,[228] modelling cognitive function was required. Dementia is a progressive condition, and it was therefore assumed that cognition would decline with time. A series of time variables were defined *a priori* to

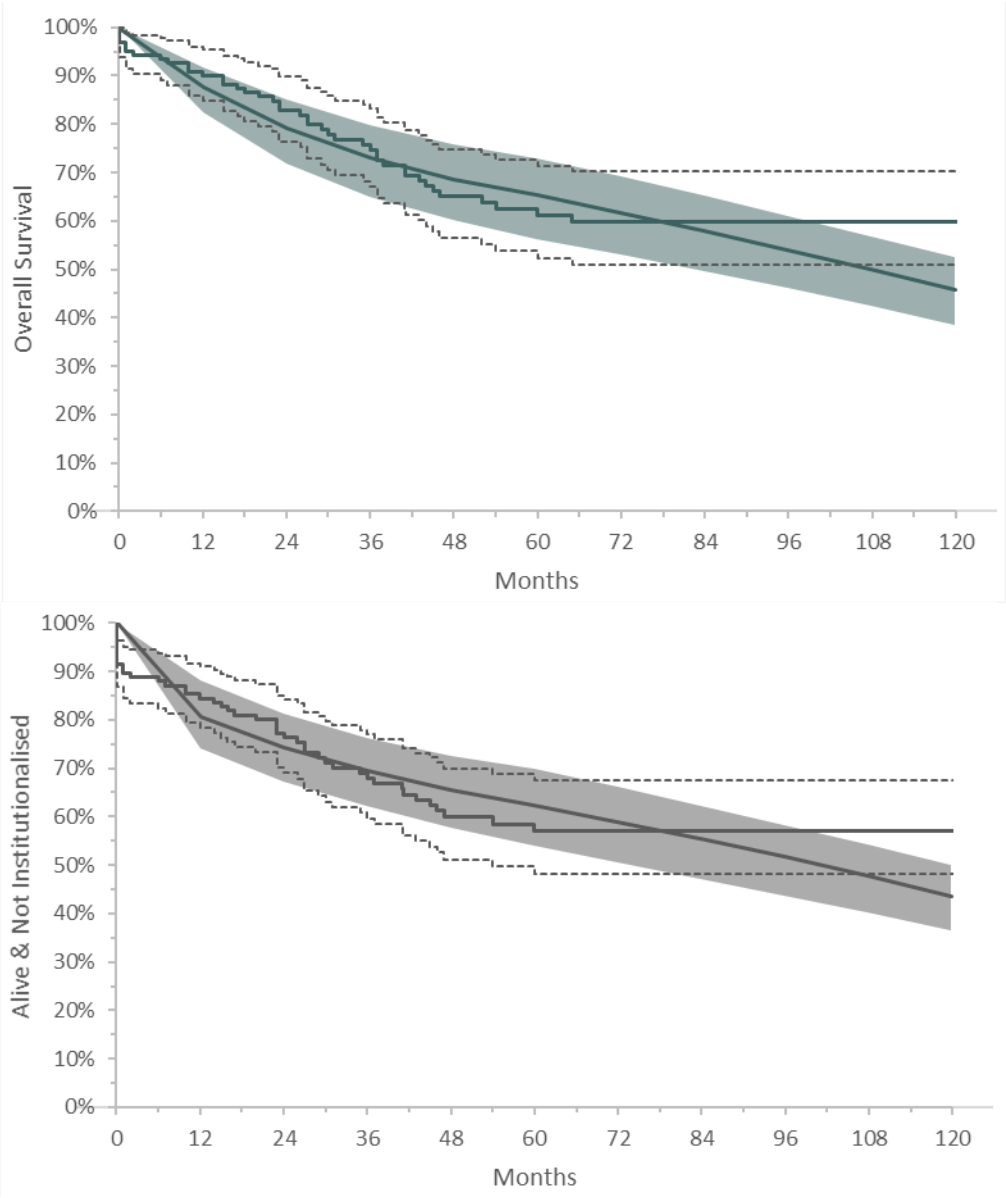

Figure 6.5. Kaplan-Meier curve for overall survival (top) and institutionalisation-free survival (bottom) showing probabilistically sampled mean survival extrapolation and 95% credible intervals for patients with mild or moderate dementia and at least one comorbid condition or risk factor

be tested to ascertain which provided the best fit to the underlying data. Fit was determined in terms of minimising the BIC, as well as statistical significance of the time variables in the analysis model, and face validity of the extrapolated estimates. The BIC was selected over AIC to apply a heavier penalty on additional parameters to avoid overfitting the models. The selected time variables were age (centred at the model baseline age), time elapsed since first interview (both with and without an adjustment for age), as well as time to death. Time to death was considered as an ordinal variable with levels of less than one year, one to two years, two to three years, three to four years, or greater than four years. These categories were selected to align

with model cycles, and because there are a limited number of patients with observed deaths with more than four years of follow-up. In addition, in NICE TA217 the Assessment Group showed that MMSE scores are somewhat stabilised with at least four years of institutionalisation-free survival remaining.[228] For those with an observed death, the time to death was derived from the number of months prior to the midpoint of the date of death interval that the interview was recorded. For those who were censored for death, if the interview date was more than four years prior to the censoring date, the observation was included in the category of greater than four years as patients have been observed to live for at least four more years, otherwise these observations were classified as an "unknown date of death" so that all observations could be included in analysis models permitting comparisons on the BIC.

For those models where the time variable was continuous (age and time since first interview), fractional polynomials were used to assess the association with cognitive function. Fractional polynomials are an extension of conventional polynomial models for determining the functional form of a continuous predictor and offer considerable flexibility in fitting non-linear data.[244] Considering a continuous covariate, *t*, in a linear model the first-order fractional polynomial model is:

$$y = \beta_0 + \beta_1 t^p$$

where the power, *p*, is selected from the set -2, -1, -0.5, 0, 0.5, 1, 2, 3, with $t^0 = \log(t)$. A second-order fractional polynomial, using the same list of powers, is defined as:

$$y = \beta_0 + \beta_1 t^{p_1} + \beta_2 t^{p_2}$$

Table 6.5. Models for the decline in cognitive function over time for patients with all dementia severities

Parameter	β	95% CI	*p*-value	BIC
Age (First-Order Fractional Polynomial; $p = 1$)				
Baseline Cognitive Function	16.82	15.95 to 17.69	< 0.001	1385.25
Years Since Baseline	-0.43	-0.51 to -0.34	< 0.001	
Years Since First Interview (Second-Order Fractional Polynomial; $p_1 = -0.05$, $p_2 = -0.05$)				
Constant	9.12	2.29 to 15.94	0.009	1461.79
Years Since Baseline 1 ($p = -0.05$)	9.55	0.52 to 18.58	0.038	
Years Since Baseline 2 ($p = -0.05$)	1.55	0.08 to 3.02	0.039	
Years Before Death				
Constant	20.05	18.66 to 21.43	< 0.001	1441.02
Time to Death				
▪ More Than 4 Years	*Ref*			
▪ 3 to 4 Years	-4.18	-7.13 to -1.23	0.006	
▪ 2 to 3 Years	-4.39	-7.66 to -1.12	0.009	
▪ 1 to 2 Years	-7.89	-10.81 to -4.97	< 0.001	
▪ Less Than 1 Year	-5.18	-8.05 to -2.31	< 0.001	
▪ Date of Death Unknown	-5.31	-7.27 to -3.35	< 0.001	

Notes: The age variable was centred at the model baseline age to assess decline over time and so is reported as years since baseline. Years since first interview includes an adjustment to add one day (1/365.25) to the time since baseline to permit calculation of the fractional polynomial.

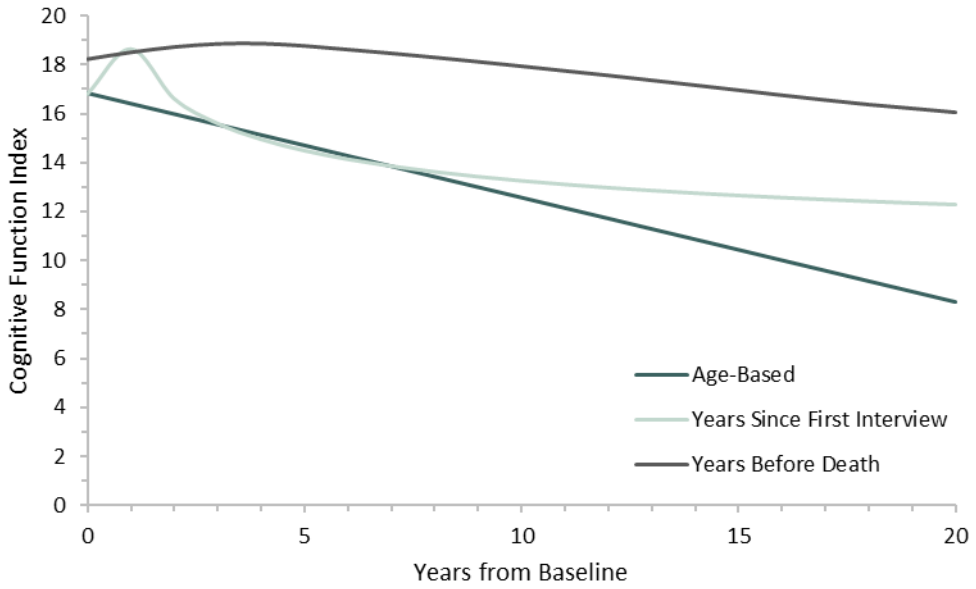

Figure 6.6. Cognitive function scores over time for the group of patients irrespective of dementia severity

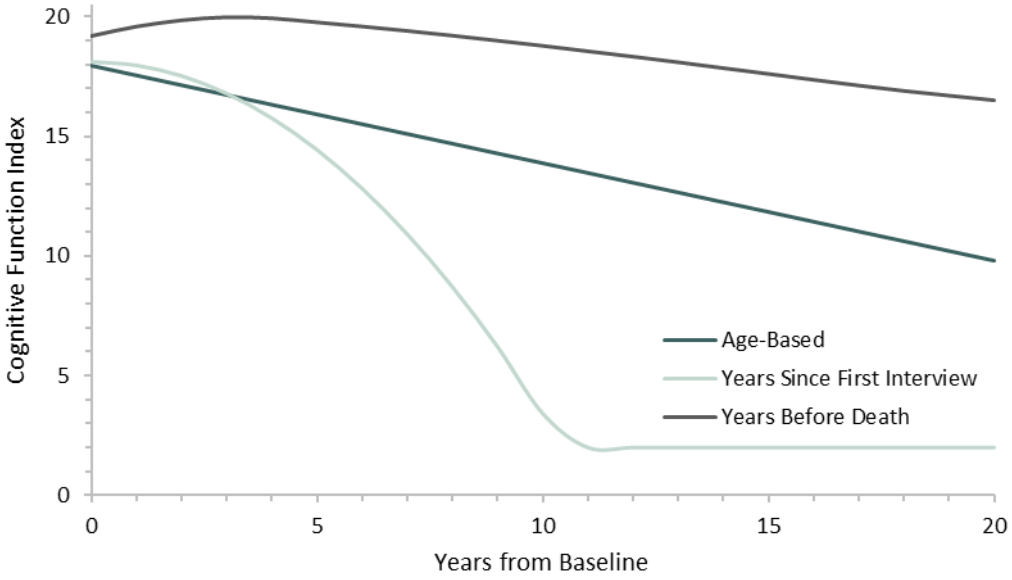

Figure 6.7. Cognitive function scores for the group of patients with mild or moderate dementia

If $p_1 = p_2$ then the model becomes a 'repeated powers' model and the second term is further multiplied by the natural log of t:

$$y = \beta_0 + \beta_1 t^p + \beta_2 t^p \log t$$

For the time to death models, as the time variables was not continuous, a standard linear regression model was used, estimating individual coefficients for each time category. The results for analyses, showing only the best fitting fractional polynomials for age and time since first interview, are shown in Table 6.5 and Figure 6.6 for all severities and Table 6.6 and Figure 6.7 for those with mild or moderate dementia. For

Table 6.6. Models for the decline in cognitive function for patients with mild or moderate dementia

Parameter	β	95% CI	*p*-value	BIC
Age (First-Order Fractional Polynomial; $p = 1$)				
Baseline Cognitive Function	17.97	17.08 to 18.86	< 0.001	1210.38
Years Since Baseline	-0.41	-0.50 to -0.32	< 0.001	
Years Since First Interview (First-Order Fractional Polynomial; $p = 2$)				
Constant	18.11	16.98 to 19.24	< 0.001	1269.88
Years Since Baseline ($p = 2$)	-0.15	-0.23 to -0.06	< 0.001	
Years Before Death				
Constant	21.31	19.95 to 22.67	< 0.001	1251.35
Time to Death				
▪ More Than 4 Years	*Ref*			
▪ 3 to 4 Years	-4.75	-7.77 to -1.73	0.002	
▪ 2 to 3 Years	-5.23	-8.36 to -2.11	0.001	
▪ 1 to 2 Years	-8.73	-11.87 to -5.58	< 0.001	
▪ Less Than 1 Year	-6.86	-9.71 to -4.00	< 0.001	
▪ Date of Death Unknown	-5.34	-7.25 to -3.44	< 0.001	

Notes: The age variable was centred at the model baseline age to assess decline over time and so is reported as years since baseline. Years since first interview includes an adjustment to add one day (1/365.25) to the time since baseline to permit calculation of the fractional polynomial.

the age-based model, the linear prediction (first order fractional polynomial, $p = 1$) was the best fitting model for both patient groups, and for years since first interview a second-order, repeated powers model ($p = -0.5$) was the best fitting for all severities and a first-order squared model ($p = 2$) for mild or moderate dementia.

The models assessing time since first interview provided the worst fit to the data and some potentially spurious results with regards to stabilisation of cognitive function in the long-term for all patients with dementia compared to a significant drop off for mild or moderate dementia (to the scale minimum score of two). Therefore, this predictor was rejected for use in the model. Despite statistically significant time variables, the regression for time to death did not provide the best fit and showed limited decline in function in the model. In addition, the assumption that cognitive function improves in the year before death compared to the previous year is dubious, and the number of missing death dates meant not all patients in the sample are used in estimating relevant coefficients. Accordingly, the age-based model was selected for both patient groups.

Quality of Care Measures

Care quality was considered in the model in terms of the six quality indicators shown to be significantly associated with a diagnosis of dementia in Chapter 3, that were further shown to be associated with improved survival when met in Chapter 4, and that were sensitive to the intervention strategies assessed in Chapter 5, namely:

- In the past year, has any doctor or nurse examined your bare feet? (Diabetes Foot Check)

- Have you ever participated in a course or class about diabetes, or received special training on how you can live with your diabetes from day to day? (Diabetes Training)
- How much do you think you known about managing your diabetes? (Diabetes Knowledge)
- Did a doctor or nurse ever suggest you take any medication to lower your blood pressure? (Hypertension Treatment)
- Has any doctor or nurse recommended taking calcium pills or Vitamin D? (Osteoporosis Supplements)
- Has a doctor or nurse ever advised you to stop smoking; or has any doctor or nurse ever told you about any nicotine products, such as nicotine patches, chewing gum, lozenges, or other similar products at all to help you give up smoking? (Smoking Cessation)

For modelling purposes, the proportion of people eligible for each condition and the observed baseline quality of care was assumed to be independent for each dementia severity group. Although it is not possible to exclude that the small differences reported in Table 6.2 are attributable to random noise, it is feasible that comorbidities may be associated with the course of dementia (e.g., cardiovascular disease as a risk for dementia) and those of lower severities may have a different comorbidity profile. For diabetes, hypertension, and osteoporosis, the proportion of the population eligible for these indicators was assumed to be homogenous over time and equal to those presented in Table 6.2. As smoking cessation advice would only be given to current smokers, it is assumed that discontinuation of smoking due to advice and treatment should be captured as the proportion of smokers should decrease over time. In the cost-effectiveness assessment of the QOF indicator for smoking cessation advice and treatment,[245] the authors considered an annual background quit rate of 2% based on published sources.[246 247] In addition, long-term abstinence rates were estimated for those receiving treatment where this was 3.30% for those receiving nicotine replacement therapy (NRT) and 4.23% for those receiving drug treatment (bupropion or varenicline), assuming that 73.1% of patients would receive NRT. The annual probability of discontinuing smoking was then derived from the proportion meeting the quality of care indicator during that year, assuming that these patients would get the additional benefit of NRT or drug treatment.

To estimate the baseline quality of care for each indicator, percentages were derived from the ELSA data for the included patient populations. For quality indicators associated with processes of care (diabetes foot check, diabetes training, hypertension

treatment, osteoporosis supplements, and smoking cessation), proportions were derived from ELSA using a multilevel regression model with a random intercept at the subject level to account for potential within subject correlation between scores at different waves. Time variables (year of data collection, time from first interview, and age) were explored as covariates in the analyses to assess whether these had any influence on observed quality of care, however there were no statistically significant effects.

As institutionalisation may influence both the supply and demand for primary care services, as patients may have more direct contact with other care workers, this was considered as a covariate for those quality indicators that may be repeated over time. The Diabetes Foot Check indicator in ELSA has an explicit time period attached to it, as does the comparable indicator in the QOF that advocates a foot examination should be conducted each year.[71] Whilst the Smoking Cessation indicator in ELSA does not include a time period, the QOF indicators for providing smoking cessation advice suggest that all smokers should be offered support and treatment to quit every 24 months, and those with selected cardiovascular, peripheral vascular, metabolic, respiratory, or psychotic comorbidities should be offered support and treatment annually.[71] Therefore, these two indicators were assumed to be dynamic with regards to institutionalisation and demand and access to care. For drug treatment for hypertension and osteoporosis, it was assumed that institutionalisation would not be a specific reason for treatment discontinuation as this is not specifically mentioned in the NICE guidance for the management of either condition. Similarly, for those eligible for diabetes training this course of treatment was assumed to only apply to those living in the community, as the prognosis for patients with dementia following institutionalisation is poor,[228] and therefore the benefits of self-management of their condition are likely to be limited. The modelled baseline quality of care for each of these indicators in each patient group are shown in Table 6.7.

For diabetes knowledge, as this is not explicitly an aspect of healthcare, this was deemed to be indirectly influenced by diabetes training. Within ELSA, all patients with dementia who met the training indicator claimed to have the knowledge they need

Table 6.7. Observed quality of care in ELSA for the modelled population

Quality Indicator	All Severities		Mild or Moderate Dementia	
	Community	Institution	Community	Institution
Diabetes Foot Check	71.2%	7.9%	70.4%	9.3%
Diabetes Training	15.8%	N/A	18.2%	N/A
Hypertension Treatment	64.4%	N/A	60.2%	N/A
Osteoporosis Supplements	28.6%	N/A	33.1%	N/A
Smoking Cessation	73.5%	0.0%	72.4%	0.0%

to manage their diabetes, along with a proportion of those who had not received training (27.5% of patients irrespective of severity, and 26.7% of those with mild or moderate dementia). Therefore, in the base case it was assumed that 27.5% or 26.7% of patients eligible for the Diabetes Knowledge indicator would already meet the indicator, plus all those who also met the Diabetes Training indicator (a total of 43.3% of patients with diabetes for treatment as usual).

Diabetes Training is expected to be delivered to a prevalent cohort, and therefore it is assumed that the increase in knowledge as a result of training would be observed in the first model cycle. To account for the benefits of improving care quality, any additional patients who met the Diabetes Training indicator in the other treatment arms would therefore also meet the Diabetes Knowledge indicator. In a scenario analysis it was arbitrarily assumed that only 80% of those additional patients who received training would improve their self-perceived knowledge about managing their diabetes on the assumption that for patients with impaired cognition this training may not be 100% effective. In a similar vein, the assumption that this knowledge would deteriorate over time with the progression of dementia was also assessed. A regression model assessing the association between the cognitive function index from ELSA and

Table 6.8. Predictors of meeting the diabetes knowledge in the first cycle and the decline over time

Parameter		Est.	
Baseline Diabetes Knowledge without Training (All Severities)		27.5%	
Baseline Diabetes Knowledge without Training (Mild/Moderate)		26.7%	
Parameter	**OR**	**95% CI**	***p*-value**
Diagnosed Dementia	0.02	0.00 to 0.43	0.013
Cognitive Function Index	**1.03**	**1.00 to 1.06**	**0.056**
Dementia * Cognitive Function	**1.15**	**0.95 to 1.39**	**0.145**
Age (years)	1.00	0.98 to 1.02	0.682
Female	1.26	0.89 to 1.80	0.192
Diagnosed Chronic Comorbidities			
▪ None	*Ref*		
▪ 1	0.85	0.39 to 1.87	0.688
▪ 2 to 3	1.04	0.49 to 2.20	0.925
▪ 4 or more	0.86	0.37 to 2.02	0.728
Diagnosed Cardiovascular Comorbidities			
▪ None	*Ref*		
▪ 1	0.87	0.62 to 1.22	0.421
▪ 2 to 3	0.57	0.37 to 0.88	0.011
▪ 4 or more	0.86	0.21 to 3.47	0.831
Net Non-Pension Wealth			
▪ 1st Quintile (Least Wealthy)	*Ref*		
▪ 2nd Quintile	1.25	0.81 to 1.92	0.318
▪ 3rd Quintile	2.25	1.38 to 3.67	0.001
▪ 4th Quintile	2.06	1.20 to 3.53	0.009
▪ 5th Quintile (Wealthiest)	1.89	1.04 to 3.44	0.037

Notes: The emboldened lines refer to those applied in the cost-effectiveness model to assess the decline in a patient's self-perceived knowledge about managing their diabetes as a result of the progression of dementia

the Diabetes Knowledge indicator was developed, again using a multilevel model at the patient level. Due to the small number of observations within patients with dementia and comorbid diabetes who were eligible for the knowledge indicator, the regression model was developed in all patients using a covariate for a dementia diagnosis, as well as an interaction term between dementia diagnosis and cognitive function. The model was also adjusted for age, sex, comorbidities, and wealth based on the directed acyclic graph developed for Chapter 3 to assess the impact of dementia and cognitive impairment on quality of care indicators. Cognitive function was found to be a predictor of the Diabetes Knowledge indicator, with higher cognitive function associated with an increased probability of meeting the indicator, and this association was stronger in patients with dementia (see Table 6.8). Although this was not statistically significant at the 5% level, the effect size was considered substantial enough to warrant inclusion.

Efficacy of Interventions

The impact of the different intervention strategies on the quality of care was derived from the results presented in Chapter 5. The odds ratios for the effect of the potential interventions are presented in Table 6.9.

Pay-for-Performance

For pay-for-performance schemes, effect estimates were included for whether or not the indicator was included in the QOF, and the number of points available. The preferred analysis for inclusion in the model included the adjustment for the proportion of total disability-adjusted life years lost in the UK attributable to the condition or risk factor. Although with this adjustment, the number of points available for the QOF indicator was no longer statistically significant, as this factor is a driver of costs with regards to reimbursement for the indicator it was included in the model. Including the

Table 6.9. Efficacy of intervention strategies on care quality

	OR	95% CI
Pay-for-Performance (All Severities)		
Indicator Included in QOF	5.70	1.72 to 18.83
QOF Points Available (per point)	1.02	0.98 to 1.05
Pay-for-Performance (Mild or Moderate Dementia)		
Indicator Included in QOF	4.65	1.32 to 16.38
QOF Points Available (per point)	1.02	0.98 to 1.05
Improved Cognitive Function (Mild or Moderate Dementia)		
ELSA Cognitive Function Index (per point)	1.13	1.00 to 1.28
Combined Scheme (Mild or Moderate Dementia)		
Indicator Included in QOF	5.32	1.19 to 23.84
QOF Points Available (per point)	1.03	0.99 to 1.07
ELSA Cognitive Function Index (per point)	1.13	1.00 to 1.28

gains of additional points associated with hypertension treatment, diabetes foot check, and smoking cessation advice was deemed pertinent as, although these indicators are currently included in the QOF, it is feasible that there is a benefit on clinical practice beyond actual reimbursement level through the implied importance of their inclusion in a dementia-specific pay-for-performance scheme. As the analysis model presented in the previous chapter included all patients irrespective of their dementia severity, the analysis was repeated restricting observations to those considered to have mild or moderate dementia to generate estimates applicable to the second population appraised in the model. The effect of increased cognitive function and a combined scheme of a broader QOF scheme and cognitive stimulation were based on the effect estimates presented in the previous chapter, only for those patients with mild or moderate dementia.

For the application of a broader QOF scheme in the model, the effect of inclusion of the indicator in the QOF and the number of points was applied with regards to the 2019/20 General Medical Services (GMS) contract for England.[71] Although the number of points applicable to individual indicators has changed between the time of data collection for the included ELSA waves, this was considered to not influence efficacy for either treatment as usual or the arms including an expanded QOF. The definition used for the expanded pay-for-performance scheme for patients with dementia considered that all indicators not previously in the QOF would be included for these patients (Osteoporosis Supplements and Diabetes Training, with an indirect effect on Diabetes Knowledge) as well as a "comorbidity bonus" awarded to GP practices for meeting indicators in patients with dementia. This was included by increasing the number of points attainable for each of the indicators associated with care processes, specifically for patients with dementia. In the base case, this was assumed to be three additional points for each indicator as this is the median number of points awarded for indicators in the 2019/20 GMS contract. Scenarios were also considered for other values, ranging from no additional points up to 30.

The points awarded for the "Osteoporosis Supplements" indicator in patients with dementia was assumed to also be three points. This is based on the former indicator in the QOF for those patients with osteoporosis and a prior fragility fracture who should be treated with an appropriate bone-sparing agent, where this was awarded up to three points.[248] For Diabetes Training, up to 11 points were awarded for this indicator. This value was selected based on the current reimbursement awarded to practices for referring patients with diabetes to a structured education programme within nine months of diagnosis.[71] Whilst the QOF currently includes an indicator related to

diabetes training, within its definition it is only applicable to incident cases of diabetes. Given that the model assessing a population with dementia and prevalent diabetes, this indicator was assumed to not be applicable to the population in the base case as for all modelled patients, more than nine months had elapsed since their diabetes diagnosis. However, since this indicator has been included in the QOF since 2011 it is feasible that rates of diabetes training are now higher than observed in the ELSA data. Therefore, a scenario analysis is included accounting for the inclusion of this indicator in the treatment as usual arm as well, thus increasing quality of care for all arms over the observed data from ELSA. In this case, the expansion of pay-for-performance for patients with dementia only includes Osteoporosis Supplements, plus the potential additional benefit of broader reimbursement (more points attainable for patients with dementia) for the other quality indicators.

A further scenario was considered whereby the points for Osteoporosis Supplements and Diabetes Training were more than halved (one and five points, respectively) given that patients with dementia may receive less clinical benefit from the care in the indicators compared to those without dementia given their poorer prognosis.

PRIDE Intervention

The three core factors within the PRIDE intervention that are purported to improve cognitive function are keeping physically active, keeping socially active, and keeping mentally active. To assess the effects of exercise and social integration on cognitive function, further analyses were conducted on the ELSA data set. However, as the receipt or engagement in cognitive interventions was not captured in ELSA, to what extent cognitive function can be improved needed to be derived from external sources.

Given that patients with dementia are burdened with comorbidities and functional decline that may limit their ability to engage in more vigorous forms of exercise, self-reported difficulties with mobility were also considered in determining a physical activity metric. Mobility was measured in ELSA using six ADLs: walking 100 yards; sitting for about two hours; getting up from a chair after sitting for long periods; climbing several flights of stairs without resting; climbing a single flight of stairs without resting; and stooping, kneeling, or crouching. Given the lack of a direct link to physical activity, sitting for two hours was not considered, and similarly climbing several flights of stairs was also excluded as this was considered as a more demanding version of climbing a single flight of stairs. For simplicity, I defined a binary metric for difficulty with mobility based on these. Any respondent reporting difficulties on fewer than two of the remaining domains were considered to not be mobility impaired.

Self-reported physical activity levels were obtained from ELSA. Three ordinal variables are included in ELSA reporting the frequency that the respondent engages in vigorous, moderate, or mild sports or activities. Mild activities include doing laundry and home repairs, moderate activities were those such as cleaning the car or walking at a moderate pace, and vigorous activities include cycling, aerobics, or digging with a spade. Responses are given in the range of "more than once a week", "once a week", "one to three times a month", or "hardly ever or never". To define a possible exposure variable related to an exercise intervention, levels of physical activity and mobility impairment were combined to make a binary variable of whether the respondent engaged in a certain level of physical activity relative to their ability. Previous analysis using ELSA data which assessed the association between physical activity and dementia considered that engaging in any physical activity at least once per week constituted some activity and was associated with a reduced risk of dementia and the level of cognitive decline post-diagnosis.[226] Therefore, it was determined that respondents with mobility impairments would have a physical activity level equivalent to an exercise-related intervention if they engaged in any mild, moderate, or vigorous sports or activities at least one per week. For respondents without a mobility impairment, this was defined as engaging in vigorous sports or activities at least once per week, or moderate sports or activities more than once a week.

To define social engagement and the extent respondents were keeping socially active, a range of concepts were considered. Although many studies of social relationships in later life tend to focus on the volume of contact,[249] both the quantity of social contact (social engagement) and the quality of social interactions (loneliness) have been linked to morbidity, mortality, and cognitive function, and may therefore fit within the analytical frameworks.[136] [250] Previous analyses on the ELSA data set have demonstrated an association between loneliness, the number of close relationships, marital status, and subsequent dementia diagnoses.[251] Whilst social isolation was not significantly associated with an increased hazard of a dementia diagnosis in their analyses, it is not excluded here given the assessment of different concepts in a post-diagnosis population. The association between marital status or cohabitation has already been assessed in this thesis and demonstrated to have a positive association with care quality, potentially attributable to the presence of an informal caregiver. However, given that marriage is not a practical expectation for the outcome of intervention, it is only considered as a covariate for adjustment in analyses. As loneliness is likely to be consequence of social engagement, as well as personal

perception on the quality of these engagements, it was not considered to be directly modifiable by intervention.

Social contact with regards to the number of close relationships or the level of social isolation could be targeted with social interventions. The number of close relationships includes the total count of self-reported number of children, other family members (except partner or children), and friends with whom respondents have a close relationship, grouped into five categories (0 or 1, 2 or 3, 4 or 5, 6 to 9, and 10 or more). Social isolation was defined as the extent of contact the respondent has with their social network or involvement in social clubs and organisations. Respondents reported on how often they had contact with their children, other family members (except partner or children), and friends on a six-point scale, ranging from "three or more times a week" to "less than once a year or never". Contact could be meeting face-to-face, speaking on the telephone, or having written/e-mail contact. For each social group, the respondent was awarded a point if they had contact with that social tie less than once a month. An additional point was given if the respondent did not participate in any social clubs, sports clubs, churches, or residents' groups. Scores ranged from 0 to 4, with higher scores indicating greater social isolation. These variable definitions have been used in previous analyses on ELSA data.[136 250 251]

As social isolation may be a more modifiable concept permitting intervention, in that a more socially active person could have contact with those they have close relationships with more frequently, as well as capturing the benefit of engagement in clubs in societies, this was considered as the exposure. The number of close relationships the respondent has was used as a covariate in the analyses to adjust for the ability to reduce social isolation.

To assess the potential joint effect of physical activity and social isolation on cognitive function, given the combined intervention in the PRIDE programme, a single regression model was run to test the association. The model was adjusted for age, sex, social factors beyond isolation (number of close relationships and whether married or cohabiting), and factors influencing ability to engage in exercise (number of mobility problems and diagnosed chronic comorbidities), including a random-intercept at the respondent-level given that there may be some correlation within respondents between waves. Both factors were significantly associated with cognitive function, with those engaging in exercise programmes having 1.6 more points on the cognitive function index, and each level of decline in social isolation (greater engagement) being associated with a 0.8-point increase in cognitive function (Table 6.10). A sensitivity

Table 6.10. Associations between physical activity, social isolation, and the ELSA cognitive function index in patients with mild or moderate dementia

Exposure Variable	β	95% CI
Engages in Physical Activity	1.58	0.31 to 2.84
Social Isolation (per level)	-0.76	-1.45 to -0.06

analysis was also conducted to assess an interaction between the physical activity metric and level of mobility impairment to assess the strength of the assumptions when combining activity level with level of impairment. A significant interaction was not observed, suggesting no difference in effect on cognitive function for respondents with mobility impairments engaging in mild physical activity or those without mobility impairments engaging in moderate or vigorous activity.

To apply these effect sizes in the economic model, estimates of the improvement in exercise level and reductions in social isolation in response to the PRIDE intervention were required.

A systematic review and meta-analysis of studies on exercise interventions for older adults identified studies reporting adherence and uptake levels.[252] Only one of the included studies in this review included patients with dementia who were resident in the community based on a self-managed exercise programme.[253] During the course of the intervention and follow-up, they reported that on average participants met 75% of their exercise goals. It was therefore assumed that by the end of the facilitated sessions of the PRIDE intervention (two months), 75% of participants would be engaging in physical activity. The standard level of engagement in exercise was estimated from ELSA and modelled to decline with age for those receiving treatment as usual. At baseline, this was 14.4% of respondents, reducing to just 6.5% after 5 years. The same rate of discontinuation associated with age was also applied to the intervention group after the PRIDE intervention ended (after the second month) along with a supplementary discontinuation rate of 12.5% per annum, derived from attrition rates in trials of exercise interventions.[252] Therefore, 18.0% of surviving participants in the PRIDE intervention would still be engaging in some physical activity after 5 years.

It was assumed that social isolation would increase with age as a patient's condition may leave them unable to partake in social clubs or have difficulty communicating with friends. A model was developed on the ELSA data assessing the association between social isolation score and time, showing a mean score of 2.53 (out of four) at baseline up to 2.97 after 10 years. It was assumed that during the intervention (up to 2 months) all respondents would improve by 1-point as the PRIDE intervention may be considered as a sociable activity akin to joining a group or organisation, and therefore

reflects one domain of the social isolation score. Following this time, it was assumed that 85% of participants would continue to have reduced social isolation by 1-point, either through joining a social group or increasing contact with friends or family. The estimate of 85% was derived from the attrition rate in a study of a social support intervention for patients with dementia.[254] This study represented the most appropriate estimate in this patient population from a range of studies included in two systematic reviews of social interventions in older adults.[255] [256] The estimate of reductions in social isolation may potentially be conservative, as it assumes that those sustaining social contact only do so within one domain (i.e., social clubs or increased contact with friends). The effect of increased social engagement was assumed to be sustained until the patient developed severe dementia (modelled ELSA cognitive index score of 10 or less in the base case), at which point this was equal to those who had received treatment as usual.

No known previous studies have used the ELSA cognitive function index to assess the efficacy of cognitive interventions. The most common outcome measures for cognitive function in studies are the MMSE and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog). As the scoring properties of the ADAS-Cog are more aligned with that of the ELSA cognitive function index, in that the MMSE can be positively skewed with regards to normal cognition and/or mild dementia, outcomes measured on the ADAS-Cog were deemed more likely to be transferable.

Huntley and colleagues conducted a systematic review and meta-analysis of various cognitive interventions and concluded that cognitive stimulation represented the most efficacious approach, with a standardised mean difference versus no treatment on the ADAS-Cog of -0.26 (95% CI -0.44 to -0.08).[204] The keeping mentally active component of the PRIDE intervention also draws upon cognitive stimulation therapy research.[257] Group cognitive stimulation is recommended by NICE for patients with dementia as of 2018,[34] though to date the cost-effectiveness analyses considered by NICE has not considered its effect on primary care quality for other conditions.

As noted in the economic model developed as part of NICE NG97, interventions effecting cognition do not have an instant and sustained effect, but rather work in three phases: intervention, follow-up, and convergence.[34] In the intervention phase, treatment is initiated and begins to have an impact on improving cognition until treatment discontinuation or a plateau is reached, at which point the relative treatment effect can be sustained (or marginally decline) for a period. After a time, the relative effect declines to the extent that cognitive function converges with that of those who had not received treatment and the disease continues to follow its natural course.

Accordingly, a single point estimate for a meta-analysis is not especially informative for inclusion in the cost-effectiveness model. Therefore, the studies in the meta-analysis by Huntley *et al* were reanalysed using a meta-regression model including a covariate for the duration of the course of treatment. Analyses were conducted using the *R* package `metafor`, to fit a multilevel meta-regression model with the mean difference in change from baseline score as the outcome, duration of follow-up during treatment as the predictor, and a random-intercept at the study level to account for the repeated measures with studies. Table 6.11 shows the input values extracted from the studies in meta-analysis by Huntley, and Figure 6.8 shows the meta-regression results. As can be seen, time was shown the have a statistically significant association (p = 0.025) with the improvement in the ADAS-Cog scores during a cognitive stimulation training programme when compared to no cognitive intervention. Each additional month of treatment was associated with a decline of -0.42 points on the ADAS-Cog (95% CI -0.78 to -0.05). Whilst most of the included cognitive interventions were not self-managed, a previous meta-analysis has identified that computer-based and self-managed cognitive interventions led to superior results compared to face-to-face and group interventions in cognition,[214] and therefore results from the meta-regression may be conservative when applied to the provisional efficacy of the PRIDE intervention.

Table 6.11. Studies included in the meta-regression of cognitive stimulation on the ADAS-Cog over time

Study	Intervention (N)	Change from Baseline (SD)	Comparator (N)	Change from Baseline (SD)	Follow-Up
Bottino 2005[258]	Cognitive Rehabilitation + AChEI (6)	-2.2 (5.7)	AChEI (7)	0.4 (5.2)	5 months
Chapman 2004[259]	Cognitive Communication + AChEI (23)	4.9 (5.4)	AChEI (26)	5.6 (5.8)	12 months
Coen 2011[260]	Cognitive Stimulation (13)	-0.2 (7.2)	No Intervention (12)	-2.3 (4.1)	7 weeks
Graessel 2011[261]	MAKS Therapy (31)	-0.1 (11.0)	Treatment as Usual (30)	5.2 (12.5)	1 year
Onder 2005[262]	Reality Orientation + AChEI (79)	-0.4 (6.7)	AChEI (77)	2.5 (6.5)	25 weeks
Requena 2006[263]	Cognitive Stimulation + AChEI (20)	-6.4 (7.7) -3.4 (10.7)	AChEI (30)	6.6 (11.6) 8.6 (9.4)	1 year 2 years
	Cognitive Stimulation (18)	-3.9 (15.4) -2.3 (14.6)	No Treatment (18)	9.3 (8.3) 18.7 (9.4)	1 year 2 years
Spector 2003[264]	Reality Orientation (21)	4.3 (9.5)	No Intervention (14)	-1.0 (11.2)	7 weeks
Tarraga 2006[265]	Cognitive Stimulation + AChEI (15)	-2.5 (4.1) -1.1 (4.4)	AChEI (12)	1.1 (3.4) 1.8 (3.4)	12 weeks 24 weeks

Abbreviations: AChEI, acetylcholinesterase inhibitor; MAKS, motor stimulation, activities of daily living, cognitive stimulation, and spiritual training; SD, standard deviation

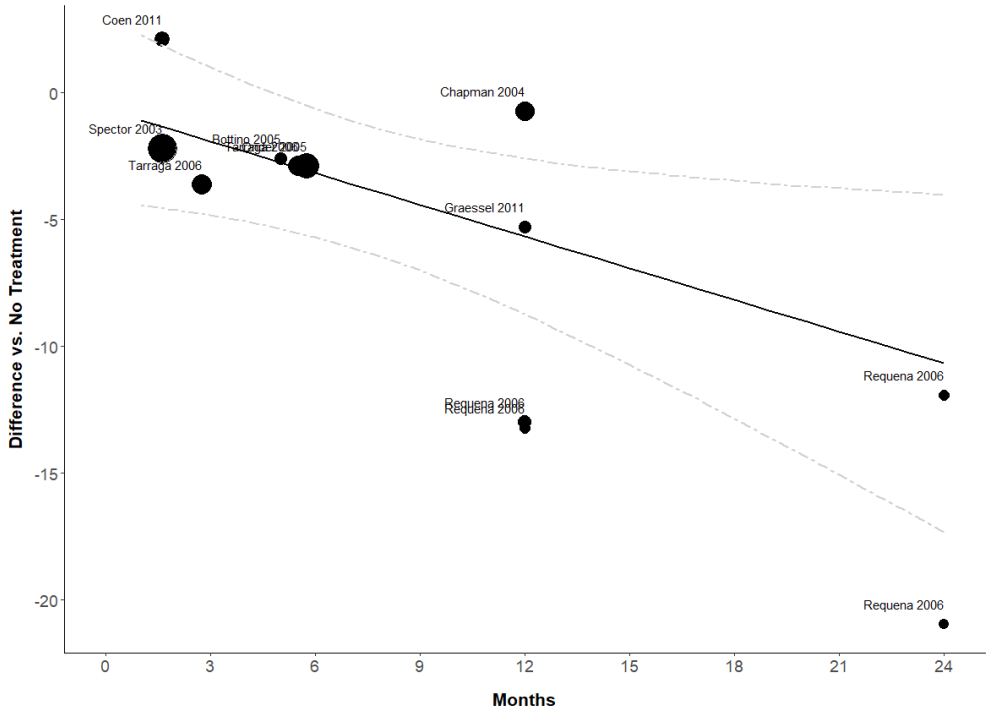

Figure 6.8. Meta-regression analysis of cognitive stimulation training programmes compared to no cognition intervention on the ADAS-Cog, with a statistically significant coefficient for time (p = 0.025)

The effect from the meta-regression was rescaled to fit the ELSA cognitive index. The ADAS-Cog is measured on a scale of 0 to 70, with higher score indicating greater cognitive impairment, whereas the ELSA index in measured from 2 to 50 with lower scores indicating greater impairment. Accordingly, each point decline on the ADAS-Cog was assumed to equate to a 0.69-point increase on the ELSA cognitive index.

For applying this within the model, three additional parameters needed to be considered for the intervention, follow-up, and convergence phases: at what time point patients stop gaining from the intervention (maximum cognitive function), how long this gain is sustained, and how rapid the decline in cognitive function is following the loss of effect. With regards to the time to maximum effect, although the PRIDE intervention programme only lasts two months, this is meant to train participants to self-manage their condition and have the tools to continue gaining independence. As none of the included studies reported continuous changes in cognitive function, an assumption was required as to when peak gains may be achieved with a self-managed cognitive programme. In the base case this was assumed to be six months.

For the follow-up phase and convergence phases, a waning of the treatment effect was applied. In a systematic review of computer-based cognitive interventions, studies

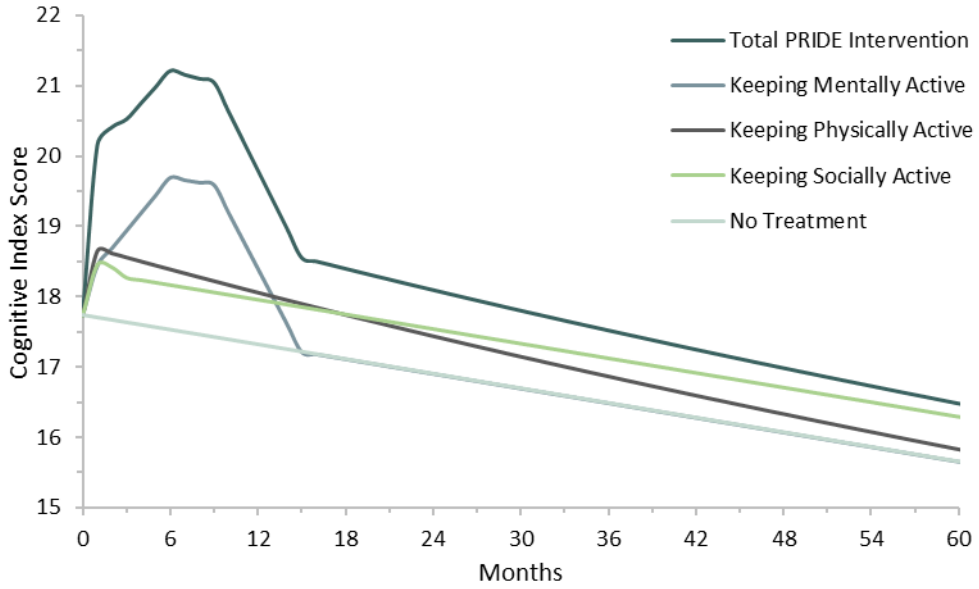

Figure 6.9. Modelled cognitive function scores for the PRIDE intervention and treatment as usual for the base case scenario for patients with mild or moderate dementia

reporting on cognition during follow-up demonstrated that the effects of treatment were maintained for two to three months after the intervention.[214] Accordingly, it was assumed that the treatment effect was sustained for three months (up to month nine in the base case) at which point the convergence phase began. In the economic model for NG97, the convergence phase was assumed to last for six months,[34] and so the same assumption was applied here. Therefore, between months 9 and 15 in the base case, the incremental gain in cognitive function due to cognitive stimulation was assumed to decline linearly from the modelled maximum to no addition gain.

Table 6.12. Parameters defining the benefit from the PRIDE intervention on cognitive function

Parameter	Base Case	Optimistic Scenario	Conservative Scenario
Duration of Cognitive Stimulation Intervention Benefits (Intervention Phase)	6 months	12 months	2 months
Duration of Cognitive Stimulation Effect (Follow-Up Phase)	3 months	3 months	2 months
Duration of Cognitive Stimulation Effect Waning Period (Convergence Phase)	6 months	9 months	1 month
Exercise Uptake	75%	95%	40%
Rate of Exercise Discontinuation	12.5% per year plus age-related discontinuations	Age-related discontinuation only	25% per year plus age-related discontinuations
Participants Increasing Social Engagement	85%	100%	60%
Volume of Social Engagement (Social Isolation Points Reduction)	1	1.5	1
Duration of Increase in Social Engagement	Until cognitive index < 10	Until cognitive index < 7	Until cognitive index < 12

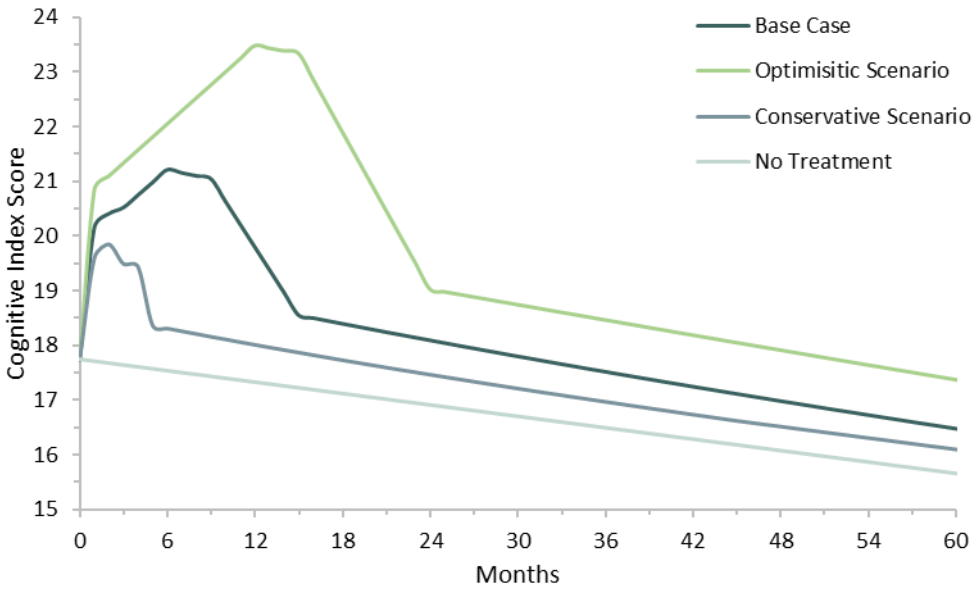

Figure 6.10. Cognitive function scores for the PRIDE intervention in each of the three main scenarios

Figure 6.9 shows the model inputs for the gains in cognitive function attributable to each aspect of the PRIDE intervention. Given the uncertainties associated with these assumptions, optimistic and conservative scenarios were defined alongside the base case. Table 6.12 shows the parameters for the assumptions associated with cognitive function in each scenario, with the modelled effects shown in Figure 6.10.

Impact of Care Quality & Interventions

The impact of care quality on model outcomes was assessed using the parameter estimates derived in Chapter 4. In the base case, improved care quality was assumed to impact overall survival as well as the number of IADLs the patient receives help with whilst resident in the community, in line with the statistically significant effects observed. A scenario analysis was also considered including a benefit of care quality on institutionalisation-free survival. Analysis models from Chapter 4 were repeated for those with mild or moderate dementia to determine effect sizes in this subgroup.

As the time to event analyses were conducted on both the minimum and maximum estimated survival windows (see §4.2), for application in the model these estimates were combined using Rubin's rules. The choice to combine estimates rather than select one model over the other was considered appropriate given the minimal differences in effect sizes between minimum and maximum survival times. Rubin's rules were favour over other methods of synthesising estimates (such as meta-analysis) were preferred as these preserve the variance of the estimates, where in other cases they

Table 6.13. Effect sizes for each 10% increase in average in care quality on time-to-event outcomes and NHS/PSS provided assistance with IADLs

Outcome	All Severities		Mild or Moderate Dementia	
	Est.	95% CI	Est.	95% CI
Overall Survival, HR (Min. OS)	0.93	0.87 to 0.98	0.90	0.84 to 0.97
Overall Survival, HR (Max. OS)	0.92	0.86 to 0.98	0.90	0.84 to 0.97
Overall Survival, HR (Pooled)	0.92	0.86 to 0.98	0.90	0.84 to 0.97
Institutionalisation-Free Survival, HR (Min. IFS)	0.96	0.89 to 1.03	0.93	0.85 to 1.02
Institutionalisation-Free Survival, HR (Max. IFS)	0.86	0.73 to 1.02	0.93	0.85 to 1.02
Institutionalisation-Free Survival, HR (Pooled)	0.84	0.63 to 1.13	0.93	0.85 to 1.02
IADLs Helped with by Social Services, IRR	0.92	0.87 to 0.98	0.90	0.85 to 0.96

Abbreviations: CI, confidence interval; HR, hazard ratio; IADL, instrumental activities of daily living; IFS, institutionalisation-free survival; IRR, incidence rate ratio; OS, overall survival

may be inappropriately reduced on the assumption of data coming from independent samples. Effect sizes in both populations are reported in Table 6.13.

For application in the model, these were assumed to be time-varying parameters based on the weighted average care quality for that treatment in the previous model cycle. The weighted average overall care quality for each arm was derived from the care quality on each indicator along with the proportion of the cohort eligible for each indicator, accounting for those eligible for multiple indicators. As care quality is estimated as a percentage, hazard ratios were adjusted accordingly. For the scenario analyses where the IFS hazard ratio for care quality was included, this was based on the overall average care quality for those patients who were pre-institutionalisation only rather than in the full cohort.

Certain aspects of the PRIDE intervention may have wider benefits on health outcomes, beyond those attained through improving care quality, such as exercise or reducing cognitive decline. Consequently, the association between engaging in physical activity, the level of social isolation, or cognitive function and overall survival, institutionalisation-free survival, the number of difficulties respondents have with IADLs, and the number of IADLs respondents receive help with from social services was assessed. Directed acyclic graphs were used to identify confounders permitting the direct estimation of exercise and social isolation on outcomes (excluding potential indirect effects via improvements in cognitive function) as well as the total effect of cognitive function on outcomes, adjusted for the indirect effect mediated by care quality. OS analyses were adjusted for care quality, age, and comorbidities, as well as cognitive function where appropriate. IFS analyses and the self-reported number of difficulties were adjusted for age, marital status, the number of close relationships, and issues with mobility. The number of IADLs that

respondents received help with from social services or local authority workers was adjusted for care quality, comorbidities, and whether married or cohabiting. As per in Chapter 4, time to event outcomes were conducted using Cox regression models considering time-varying covariates using the counting process, and outcomes related to IADLs were assessed using negative binomial regression models. Analyses were conducted in mild or moderate dementia only given these patients were eligible for the PRIDE intervention.

Table 6.14 presents the results for the statistically significant associations. Cognitive function was observed to have a direct effect on OS and IFS, independent of care quality, and did not confound the observed significant association between care quality and overall survival (adjusted HR [per 10% change in care quality] 0.90, 95% CI 0.84 to 0.97, in the pooled analysis). Given cognitive gains in response to medication are associated with improved survival, this was deemed to feasibly be a causal relationship.[228] Better cognitive function and engaging in physical activity were also associated with a lower number of the number of self-reported difficulties with IADLs. These associations were also considered potentially causative rather than just a correlation associated with the decline of cognitive and functional skills in dementia, as several of the included IADLs would require cognitive skills to successfully perform them (e.g., taking medication, using the telephone, managing money). Lower social isolation was also associated with a lower number of IADLs the respondent received help with from social services, independent of care quality.

Health Impact of Comorbidities

To assess the costs and quality of life impact of improving care quality, I conducted a pragmatic literature search to identify cost-utility models with a UK base case appraising care programmes comparable to those captured in the quality indicators.

Table 6.14. Direct effects of PRIDE intervention on outcomes, not mediated by care quality

Exposure	Outcome	Est.	95% CI	*p*-value
Cognitive Function	Overall Survival, HR (Min. OS)	0.90	0.81 to 0.99	0.009
	Overall Survival, HR (Max. OS)	0.89	0.81 to 0.98	0.010
	Overall Survival, HR (Pooled)	0.89	0.81 to 0.99	0.014
	Institutionalisation-Free Survival, HR (Min. IFS)	0.93	0.86 to 0.99	0.034
	Institutionalisation-Free Survival, HR (Max. IFS)	0.93	0.87 to 1.00	0.047
	Institutionalisation-Free Survival, HR (Pooled)	0.93	0.87 to 1.00	0.021
	Difficulties with IADLs, IRR	0.96	0.94 to 0.99	0.006
Exercise	Difficulties with IADLs, IRR	0.72	0.54 to 0.96	0.026
Social Isolation	IADLs Helped with by Social Services, IRR	1.68	1.25 to 2.27	0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; IADL, instrumental activities of daily living; IFS, institutionalisation-free survival; IRR, incidence rate ratio; OS, overall survival

The considered treatments related to the indicators were:

- Foot examinations and/or orthotic footwear for patients with diabetes
- Self-management interventions or training for patients with diabetes
- Blood pressure lowering medications for patients with hypertension
- Pharmaceutical management or dietary supplements for patients with osteoporosis or deemed at risk of fracture
- Smoking cessation advice, nicotine replacement therapy, or pharmaceutical treatment for current smokers

Targeted search syntax was used in PubMed including "cost-effectiveness", "economic model", and related terms, as well as each of the conditions or risk factors for the included indicators. Results were restricted to the past 15 years from the search date (January 2005 to December 2019). In addition, NICE guidance and technology appraisals were screened for those potentially appraising the cost-effectiveness of treatments relevant to the quality indicators, as well as the NICE database of standards and indicators to determine if a previous assessment on the cost-effectiveness of a similar quality indicator had been conducted.

Cost-effectiveness analyses were ranked based on their relevance with respect to the quality indicator, to older adult patients (no analyses were identified specifically in patients with dementia), the country for the analysis (United Kingdom or England were preferred, otherwise Western Europe), and the comprehensiveness and quality of the analysis. Given the provisional nature of the cost-effectiveness assessment, those models that represented the simplest method for incorporating the costs and impacts of meeting quality indicators were also favoured.

For the impact of improved care quality on indicators related to diabetes and smoking, simple assumptions were applied with regards to quality of life decrements or additional costs based on aggregate results for previously published models. Further details can be found in sections 6.6 and 6.7 below. For long-term complications associated with the treatment of hypertension or osteoporosis, no suitable aggregate data from published models was found. Instead, additional functionality was included in the model to account for future events associated with treatment for these conditions, based on modelling approaches applied previously in NICE appraisals.

Hypertension Treatment

For the treatment of hypertension, this was based on the model developed for NICE guideline 136.[266] The benefit of antihypertensive treatment is that it reduces the risk of having a cardiovascular event.[266] The model is based around the QRISK®2 score –

a cardiovascular disease (CVD) risk score that estimates the risk of a person developing CVD over the next 10 years, developed and validated in UK patients.[267 268] The QRISK score is calculated as a function of demographics, current health status, and selected risk factors with results presented as the cumulative probability of having a transient ischaemic attack (TIA), stroke, unstable angina, stable angina, or myocardial infarction. The QRISK score is recommended by NICE for risk calculation of cardiovascular events.[266]

The QRISK-2 score is derived from a regression equation based on a Cox model including the hazards of demographic and clinical factors applied to baseline hazard. The QRISK2®-2015 equation is publicly available via the open source software script.[269] The equation follows the form:

$$Q = 1 - S_0(t)^{\exp(\alpha)}$$

where $S_0(t)$ is the baseline hazard of a cardiovascular event after 10 years and α is the patient-specific relative hazard of a cardiovascular event as a function of age, sex, ethnicity, smoking status, diagnosed diabetes, chronic kidney disease, atrial fibrillation, or rheumatoid arthritis, as well as a history of cardiovascular disease in a first degree relative or whether the patient is currently on blood pressure treatment. In addition, optional information can be included regarding UK postcode to derive area-level deprivation (Townsend score), total to high-density lipoprotein (HDL) cholesterol ratio, systolic blood pressure, and body mass index (BMI). These variables are mean-centred and therefore missing data is assumed to be equal to the population means in the initial datasets used to derive the QRISK algorithm. Data on the demographics and diagnoses were obtained from the ELSA data for all patients. Cholesterol levels, blood pressure, and height and weight measurements were collected during the nurse visits at every second wave of ELSA (waves two and four in the included dataset), however even within these waves there was a significant proportion of missing data for patients with dementia. Data were included in the calculation of QRISK scores for patients where available and was assumed equal to the mean values for the cholesterol to HDL ratio and BMI where missing. For blood pressure, given that the associated quality indicator applies to people with hypertension, it was assumed that patients with missing data had a systolic blood pressure of 140mmHg for those aged 79 or less and 150mmHg for those aged over 80. These are the cut-offs for reimbursement in the 2019/20 QOF and pass rates on this indicator have been consistently high over time,[71] and therefore this was considered to be a reasonable proxy as the limited data points in ELSA would not allow for reliable imputation. Area-level deprivation as measured by the Townsend score was assumed

to be equal to the national average as the Primary Care Trust codes obtained from the data guardians do not provide sufficient granularity to map to published scores by area. In addition, it is not reported on the incidence of cardiovascular disease in first degree relatives in ELSA and so instead of each patient having a binary variable associated with this predictor, the proportion of patients in the QRISK estimation sample reporting this was applied to each patient (12.6% for females and 9.7% for males).[268]

As QRISK2 scores increase with age, and as the cost-effectiveness model follows a cohort of patients across the lifetime, it is appropriate to model how the QRISK2 score would develop across the model horizon. The relationship between age and risk in the QRISK algorithm is non-linear, and so fractional polynomial models were utilised to model changes over time. Given that observations on the QRISK2 score derived from the ELSA data can come from multiple waves including the same respondents, and therefore covariates beyond age may be homogenous over time, a multilevel model was applied including a random intercept at the respondent level. In addition, as the QRISK2 score is represented as a percentage, a generalised linear model with a binomial likelihood and logit link was used. Age was selected as the time variable for the analyses, rather than time since first interview, to maximise use of the available data given that the majority of respondents were only interviewed at one wave in the included analyses but may have been followed up across multiple waves for survival. The QRISK2 algorithm is specific to each gender, and so I extrapolated the scores independently for males and females and weighted the individual extrapolations in the model. The best fitting models were selected by minimising the deviance (-2*loglikelihood) and the BIC. Analyses were conducted using Stata/SE 15.1 (StataCorp, College Station, TX).

For males, the best fitting model was the first-order fractional polynomial to the power of -0.5, and for females a first-order cubic model (p = 3) was preferred. Figure 6.11 shows the fitted scores compared to the observed scores.

For application in the model, as the QRISK score estimates the 10-year probability of a cardiovascular event, the annual rate of a cardiovascular event was estimated using an exponential distribution:

$$r = \frac{-\ln(1 - p_{10})}{10}$$

where r is the annual rate and p_{10} is the 10-year probability of a cardiovascular event. This was converted to an annual probability of an event using the formula:

$$p_1 = 1 - \exp(-r)$$

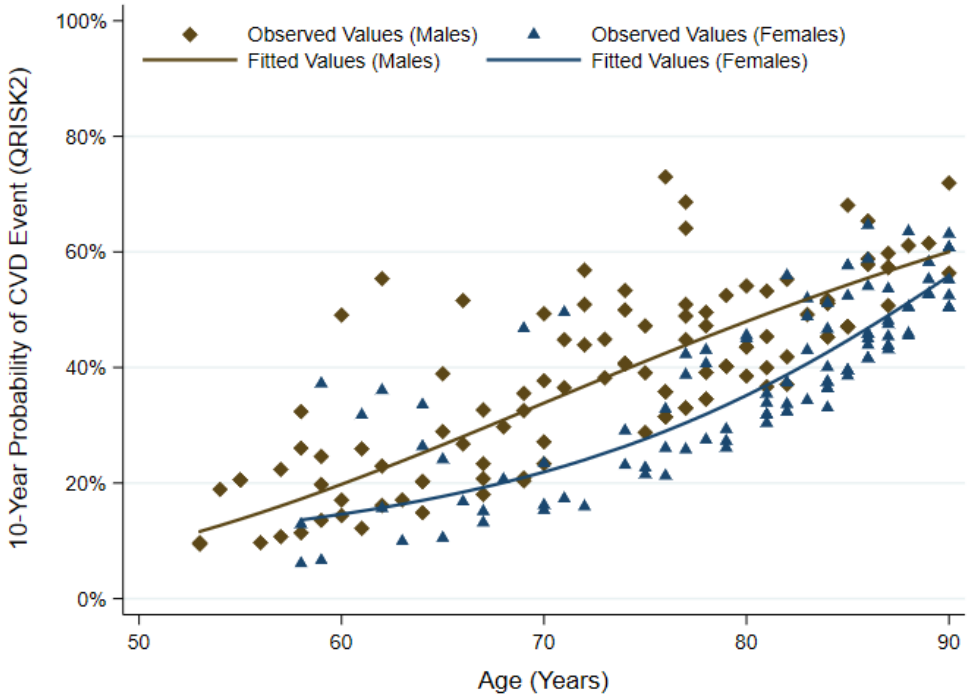

Figure 6.11. Fitted QRISK2®-2015 scores to ELSA patients with hypertension

This aligns with the method applied in NICE NG136 to derive the total annual probability of a cardiovascular event.[266]

As the 10-year probability of a cardiovascular event changes with each year of age, the cumulative probability of a cardiovascular event after 10 years in the model does not align with the predicted values at baseline for 10 years in the future. Based on the ELSA data, the total 10-year probability of a cardiovascular event at baseline is 35.9%, but the modelled cumulative probability of an event (assuming no treatment or death from other causes) after 10 years is 38.5%. This would suggest that the baseline hazard function does not follow an exponential distribution, but in fact a distribution where the baseline hazard decreases with time, but this is compensated for by the increase in the hazard ratio associated with time. Therefore, there are potential limitations in the specification of the model, however given the high mortality rates for patients in this age group with dementia and other comorbidities, and that the deviation is limited in the earlier periods of the model, the impact of this variation on costs and health outcomes is expected to be negligible.

To assess the benefit of antihypertensive treatment, the non-fatal cardiovascular events included in NG136 were incorporated. Only non-fatal events were considered as cardiovascular death was assumed to be captured by the overall survival curve. The included events were stable angina (SA), unstable angina (UA), myocardial infarction

(MI), transient ischaemic attack (TIA), stroke, and heart failure (HF). Note that heart failure is not included as a CVD event in the calculation of the QRISK2 score, however the NICE committee agreed that it was important to include in the analyses as antihypertensive treatment can reduce the risk of heart failure, and so annual probabilities of a cardiovascular event were adjusted accordingly.

To estimate which non-fatal cardiovascular event was experienced, a distribution was applied based on that use in NICE guidance 181 for estimating the distribution of cardiovascular events based on four UK based studies,[270] which was also applied in NG136. Given that death due to cardiovascular disease is also included in the estimation of the QRISK score, this proportion was also extracted in order to accurately ascertain the proportion of non-fatal events. The proportion of patients experiencing heart failure was estimated from a study in lipid modification for the reduction in risk of cardiovascular events,[271] as per the method applied in NG136.

Accordingly, to total proportion of modelled events relative to that in the QRISK score is greater than 100%. Table 6.15 shows the modelled distributions of events relative to the QRISK2 score by age and sex, as the risk of experiencing different cardiovascular events was observed to differ within these groups in the underlying data. These proportions were applied to the annual probability of experiencing a cardiovascular event derived from the QRISK2 score for the subgroup of patients with hypertension and adjusted for mortality in each treatment arm.

For simplicity, only the first cardiovascular event was modelled in this analysis as it was assumed that the impact of including further events would be limited given the relatively low incidence of first events due to the short survival in patients with dementia. The analysts behind the model for NG136 also excluded subsequent

Table 6.15. Relative distributions of cardiovascular events including heart failure

Age	SA	UA	MI	TIA	Stroke	HF	CVD Death	Total CVD Risk Relative to QRISK
Males								
50 to 54	30.7%	10.7%	29.5%	6.0%	12.9%	7.1%	10.1%	107.1%
55 to 64	32.8%	7.1%	17.2%	8.9%	20.6%	12.4%	13.4%	112.4%
65 to 74	21.4%	8.3%	17.3%	10.0%	27.0%	16.0%	16.0%	116.0%
75+	19.1%	8.1%	16.1%	8.0%	34.3%	26.1%	14.3%	126.1%
Females								
50 to 54	32.4%	11.7%	8.0%	16.0%	22.9%	6.3%	9.1%	106.3%
55 to 64	34.6%	7.3%	9.2%	9.5%	28.8%	10.6%	10.6%	110.6%
65 to 74	20.2%	5.2%	12.1%	7.3%	38.2%	18.5%	17.1%	118.5%
75+	14.9%	3.4%	10.2%	9.8%	46.4%	25.2%	15.2%	125.2%

Abbreviations: CVD, cardiovascular disease; HF, heart failure; MI, myocardial infarction; SA, stable angina; TIA, transient ischaemic attack; UA, unstable angina

cardiovascular events on the grounds of limited data of the effect of antihypertensive treatment on subsequent events, as most trials censor patients at their first event.[266] Whilst patients may experience multiple cardiovascular events with inadequately treated hypertension, the estimated benefit and cost-effectiveness of improving rates of antihypertensive treatment are likely to be conservative as a result of the assumption.

To estimate the benefit of treatment with antihypertensives, relative risks (RR) of events were derived from the analyses applied in NICE NG136. Here the analysts leveraged a systematic review and meta-analysis on the benefit of antihypertensives compared to no treatment in patients with hypertension,[190] along with age-adjustments for the relative efficacy based on a further meta-analysis of cohort studies identifying subgroup effects.[272] Treatment effects were considered specific to age, sex, and class of cardiovascular event: coronary heart disease (stable angina, unstable angina, or myocardial infarction), stroke events (TIA, or stroke), or heart failure. Table 6.16 shows the included relative risks for those receiving antihypertensive treatment. For inclusion in the model, weighted relative risks were calculated based on the quality of care indicator for "Hypertension Treatment". Those patients meeting the indicator were assumed to benefit from antihypertensive treatments, considering the equation:

$$RR_i = \exp\left(Q_i \log RR_0\right)$$

where Q is the modelled care quality for the intervention i, which adjusts the relative risk of antihypertensive treatment (RR_0) to be specific to the intervention. As relative risks are ratios and have a lognormal distribution, the influence of covariances on the modelled relative risk was considered on the log scale. Note that this calculation was applied to all interventions, including treatment as usual, as a proportion of patients with dementia in ELSA were receiving antihypertensive treatment and therefore met the indicator.

Table 6.16. Relative risks of cardiovascular events with antihypertensive treatment

Age (years)	50 to 54	55 to 64	65 to 74	75+
CHD Events				
Males	0.84	0.86	0.91	0.90
Females	0.84	0.86	0.90	0.89
Stroke Events				
Males	0.83	0.86	0.93	0.92
Females	0.82	0.86	0.92	0.90
Heart Failure Events				
Males	0.84	0.87	0.94	0.94
Females	0.83	0.87	0.93	0.91

Abbreviations: CHD, coronary heart disease

Osteoporosis Supplements

For modelling the effects of supplements on osteoporosis, a similar approach as to the treatment of hypertension was adopted, inspired by the methods applied in the model developed for NICE TA464 (bisphosphonates for treating osteoporosis).[273] The model in this analysis used a discrete event simulation (DES) which assessed the risk of fracture based on a range of patient-level characteristics. The DES approach was justified on the assumption that age and fracture risk would not be uniform across cohorts and would have a non-linear relationship with cost-effectiveness due to both the varying probability of fracture aligned with the development of risk factors, and the increased risk of death. Given that the cohort of patients with dementia and comorbid osteoporosis in this analysis is likely to be much more homogenous in terms of age and comorbidities, I deemed these factors to be relatively low risk and so a DES was not required.

Despite the differences between core modelling methods, the underlying approach used in TA464 for deriving the risk of a fracture was deemed to be applicable to this model. The main predictors of fracture used in their model were the FRAX® and QFracture® risk factors tools, which are recommended by NICE for estimating the cumulative risk of fracture over a period of time (10 years for FRAX, or one to 10 years for QFracture).[274] Much like the QRISK scores, these risk factor tools consider a range of demographic and clinical variables at the patient level to derive a probability of experiencing a fracture in the future. As the algorithm for the QFracture®-2016 score is publicly available via the open source software,[275] as well as having a functional form permitting the changing risk of fracture over time,[273] this was used to determine the underlying baseline risk of fracture. The QFracture score reports the cumulative probability of experiencing a hip, wrist, vertebral, or proximal humerus (shoulder) fracture over the defined time period, as these are the sites most strongly associated with osteoporosis.[273]

Like the QRISK scores, the QFracture score takes the form $Q = 1 - S_0(t)^{\exp(\alpha)}$, where α is the patient-specific hazard derived from demographics (age, sex, ethnicity, and whether resident in a nursing home), health behaviours and risk factors (smoking status, alcohol consumption, and BMI), current drug treatments (antidepressants, steroids, or oestrogen/hormone replacement therapy), diagnoses, and a family history of osteoporosis or hip fracture. The included diagnoses are history of falls or fractures, dementia, cancer, asthma, diabetes, cardiovascular disease, chronic liver disease, chronic kidney disease, Parkinson's disease, rheumatoid arthritis, malabsorption (Crohn's disease, ulcerative colitis, or coeliac disease), endocrine problems

(thyrotoxicosis, hyperparathyroidism, or Cushing's syndrome), or epilepsy. As several of the factors are dynamic over time with the model (age, institutionalisation, smoking status, fractures, and cardiovascular disease), the average hazard of the cohort was estimated over time within the model rather than extrapolated based on the observed data from ELSA. For simplicity, all other variables were assumed to be homogenous over time. Whilst this is a naïve assumption, as across the time horizon patients may become diagnosed with other conditions or initiate new treatments which would alter the hazard of fracture, this is assumed to be sufficiently captured by probabilistic sampling of covariates. As several of the variables (chronic kidney disease, chronic liver disease, malabsorption, endocrine problems, epilepsy, steroid use, oestrogen, and parental history of osteoporosis) were not collected in ELSA, these were assumed to be equal to the population averages in the dataset used to derive the QFracture score.[276]

In NICE TA464, it was identified that the underlying hazard of fracture in the QFracture score follows a Gompertz distribution over time.[273] Whereas the QFracture score can be calculated over a one year time horizon, the relationship between time to fracture from the Gompertz model is not equal to the increase in hazard due to age in risk factors. For example, the cumulative probability of fracture after ten years at model baseline (4.5%) is not the same as the sum of the individual hazards using one-year intervals calculated over 10 years, updating age each year but keeping all other risk factors equal (3.1%). With the parameters in the model, the QFracture hazard ratio could be recalculated each model cycle with the change in risk factors, however the QFracture reports do not issue guidance for handling time-varying covariates. As there

Table 6.17. Relative distributions of as a proportion of the QFracture score, derived from Kanis 2001[277]

Age	Hip	Vertebral	Proximal Humerus	Wrist
Males				
50 to 54	10.4%	48.5%	16.2%	25.0%
55 to 59	18.4%	32.2%	8.5%	41.0%
60 to 64	23.9%	40.4%	10.7%	25.0%
65 to 69	30.8%	27.2%	10.3%	31.7%
70 to 74	38.4%	38.6%	15.9%	7.0%
75 to 79	49.1%	32.3%	9.4%	9.2%
80 to 84	57.3%	27.9%	7.1%	7.7%
85+	61.7%	22.8%	9.4%	6.1%
Females				
50 to 54	5.5%	21.7%	16.7%	56.2%
55 to 59	10.9%	19.0%	15.3%	54.8%
60 to 64	15.3%	25.8%	10.7%	48.2%
65 to 69	20.7%	23.4%	18.9%	37.0%
70 to 74	28.3%	27.0%	13.4%	31.3%
75 to 79	37.9%	24.9%	14.1%	23.1%
80 to 84	53.3%	18.4%	9.3%	19.1%
85+	55.5%	17.6%	12.0%	14.8%

is no defined approach, to account for this the model in TA464 "resampled" the QFracture score (i.e., reset the baseline hazard function, updated with risk factors at the current time) after five and 10 years in their model.[273] For consistency in assessing the benefit of treatment for osteoporosis, the same assumption has been applied here.

The QFracture score can estimate the total probability of experiencing an osteoporotic fracture of the hip, vertebra, proximal humerus, or wrist, or the single probability of a hip fracture. In line with NICE TA464, the QFracture score for multiple sites was adopted in the model as dietary supplementation was assumed to affect the risk of multiple fracture types by increasing bone density. However, within this, the QFracture score does not provide individual predictions on the risk of each fracture type. In order to estimate which site the incident fracture occurred at, a distribution was applied based on fracture rates from a Swedish epidemiological study reporting outcomes by age and gender,[277] which was also used in TA464. Table 6.17 shows the distributions applied to the risk of fracture derived from the QFracture score. The Assessment Group in TA464 identified that this method potentially underestimates the risk of a hip fracture, an overestimates the risk of other fractures, though considered the overall risk of bias in the analysis to be low.[273] Given that the probability of any fracture is relatively small in this model, considering the limited number of patients with comorbid osteoporosis, the potential bias was assumed to be limited as well.

Although the QFracture score only estimates the probability of fracture of the hip, spine, wrist, or shoulder, other fracture sites (sternum, tibia and fibula, scapula, pelvis

Table 6.18. Multipliers applied to the rate of hip, proximal humerus, and wrist fractures to include fractures at other sites, derived from Kanis 2001[277]

Age	Hip Multiplier	Proximal Humerus Multiplier	Wrist Multiplier
Males			
50 to 54	1.36	1.52	5.36
55 to 59	1.27	1.83	6.89
60 to 64	1.18	1.69	4.48
65 to 69	1.15	1.70	4.57
70 to 74	1.09	1.59	12.67
75 to 79	1.05	1.78	7.03
80 to 84	1.05	2.06	15.34
85+	1.04	1.92	13.06
Females			
50 to 54	1.26	1.88	1.49
55 to 59	1.19	2.08	1.57
60 to 64	1.20	2.26	1.37
65 to 69	1.13	1.75	1.70
70 to 74	1.11	1.93	1.61
75 to 79	1.09	1.90	2.23
80 to 84	1.07	2.33	2.50
85+	1.08	2.14	3.56

femoral shaft, humeral shaft, clavicle, ribs) have been incorporated by increasing the incidence of the four main fractures (see Table 6.18). This was based on the same epidemiological study used to estimate distributions of the initial four sites,[277] generating multipliers for comparable sites following the method applied in NICE TA464.[273] The groupings of fracture types in TA464 were determined in discussion with clinical advisors based on excess mortality risk and costs, and considered to be:

- **Hip:** femoral shaft
- **Proximal humerus:** tibia, fibula, pelvis, and humeral shaft
- **Wrist:** clavicle, scapula, rib, and sternum

To estimate the effects of calcium or vitamin D supplementation on the risk of fracture, as per the quality indicator included in ELSA, estimates of relative efficacy were obtained from the literature. As NICE TA464 evaluated the cost-effectiveness of bisphosphonates, a further study from the pragmatic literature review was utilised. This cost-effectiveness model evaluated the cost-effectiveness of calcium and vitamin D supplementation in elderly patients with osteoporosis from the perspective of the Belgian healthcare payer.[278] Whilst the core modelling approach applied in this analysis differed from that used in TA464, as a Markov model was used instead, Belgian data on the incidence of fractures stratified by age, sex, and site (hip, vertebral, wrist, or other) was used in a similar method to that used in TA464. To estimate the relative effectiveness of supplementation, the authors conducted a literature review and identified several meta-analyses evaluating the effects of vitamin D with calcium on fracture rates in older adults. To align with the inputs to their model, results from the three included meta-analyses of RCTs and have also been applied here. Calcium with vitamin D supplementation was estimated to reduce the risk of hip fracture by 18% (RR 0.82, 95% CI 0.71 to 0.94; number of RCTs (k) = 6; total number of patients (n) = 45,509)[279] and 13% for vertebral fractures (RR 0.87, 95% CI 0.75 to 1.01; n = 45,184).[280] For other sites, this was assumed to be equivalent to efficacy estimates for non-vertebral fractures (excluding hip) where supplementation reduced the risk of fracture by 20% (RR 0.80, 95% CI 0.72 to 0.89; k = 9; n = 33,265).[281]

In line with the assumptions of the Belgian model, patients were assumed to receive supplementation for three years, during which time the relative risks of fracture were applied. Previous models in osteoporosis have also considered an offset time, where the treatment effect is not lost immediately upon discontinuation but rather declines over time.[273 278 282] In both of the models used to inform the current analysis, the offset time was set to be equal to the modelled duration of treatment.[273 278] The same assumption was applied here, and therefore it was assumed that all patients receiving

calcium and vitamin D supplements would have the full effect treatment for three years, and then this would decline linearly over the subsequent three years (i.e., risk of fracture equal to no treatment after six years). As for the relative risks associated with hypertension treatment, weighted relative risks based on the quality of care indicator for "Osteoporosis Supplements" were calculated. Again, the calculation of the weighted relative risk was applied to all treatment strategies, including treatment as usual, as some were receiving supplements in the ELSA population already.

6.6. Measurement & Valuation of Health Effects

Health effects were captured in the model in terms of health state utilities and health decrements attributed to events associated with the care quality indicators. Adverse events of treatment, such as those associated with increased use of antihypertensives or osteoporosis supplements were not included as the estimated impact was deemed to be limited given the marginal change in uptake and relative infrequency of adverse events. A previous cost-effectiveness analysis demonstrated that exclusion of adverse events from a model of hypertension treatment had minimal effect on the incremental QALYs gained.[266]

NICE guidelines advocating the inclusion of caregiver utilities for intervention which may impact social care.[171] Whilst this thesis has demonstrated that care quality can reduce demands on the number of IADLs assisted with, caregiver utilities were excluded. The rationale for this decision stems from the findings in NICE TA217, where very limited data on the utility of carers of people with Alzheimer's disease was identified from the literature, and the one study that was considered relevant suggested that the caregiver's utility remains fairly stable until the patient's progresses to severe dementia when the carer's quality of life starts to improve.[283] The Assessment Group for TA217 considered this to most likely be due to the patient moving to institutionalised care. In their model, caregiver utilities were only applied in the pre-institutionalised state. If the same assumption were to be applied here, given that care quality was not considered to have an impact on time to institutionalisation, there would be minimal further differentiation of intervention strategies by including caregiver utilities. This is potentially a conservative assumption with regards to the PRIDE intervention, where gains in cognitive function are modelled to marginally improve institutionalisation-free survival.

Health State Utilities

In line with the model structure, utilities were sought for the pre- and post-institutionalised health states, with consideration to the most appropriate data source.

As noted in TA217, there are recorded differences between self-reported quality of life ratings in patients with dementia and those valued by caregivers.[58 284-287] It has been purported that some of these differences could be attributed to caregivers reporting on the impact of dementia on their own quality of life.[288 289] However, the Assessment Group concluded differences may be attributable to the patients themselves given that there is no evidence that patients with Alzheimer's disease can reliably and consistently provide self-ratings of utility.[228] They therefore opted to use carer proxy ratings in their model.

This rationale does not necessarily apply to the utilities available from the ELSA data, as the EQ-5D utilities estimated in Chapter 4 have been derived from demographics and comorbidities rather than a rating instrument (see Appendix 4.2 for details on the estimation algorithm). However, two variables with some of the greatest impact on estimated utility were self-rated health and recent feelings of depression, both of which require some understanding of the patients own health status, which may be limited in dementia. Despite this, having access to patient-level data on utility values is valuable as it permits the assessment of associations with other variables in the model. Health state utilities were therefore derived from the estimated EQ-5D values in the base case.

Utilities were estimated using a linear mixed effects model considering a fixed effect for institutionalisation, a fractional polynomial adjustment for age, and respondent as a random-effect. The fractional polynomial adjustment for age was justified by previous analysis that has demonstrated a polynomial decline in utility with age in the UK general population,[290] and it was assumed that utilities may decline more rapidly that this in the sample given the decline dementia may impact health-related quality of life. Previous utility analyses in patients with Alzheimer's disease have shown sharp declines on proxy-rated quality of life associated with decreasing MMSE scores.[58]

Table 6.19. Utility estimation regression model

Parameter	Est.	95% CI	*p*-value
All Severities			
Constant	0.439	0.333 to 0.545	< 0.001
Age (p_1 = 2)	0.078	0.027 to 0.130	0.003
Age (p_2 = 2)	-0.050	-0.085 to -0.015	0.006
Institutionalised	-0.017	-0.112 to 0.078	0.724
Mild or Moderate Dementia			
Constant	0.455	0.347 to 0.564	< 0.001
Age (p_1 = 2)	0.066	0.012 to 0.120	0.017
Age (p_2 = 2)	-0.042	-0.079 to -0.005	0.027
Institutionalised	-0.016	-0.118 to 0.086	0.751

Notes: Age is rescaled to avoid fitting to unobserved data as only patients over 50 years of age were included. Modelled age variable = (age – 50) / 10.

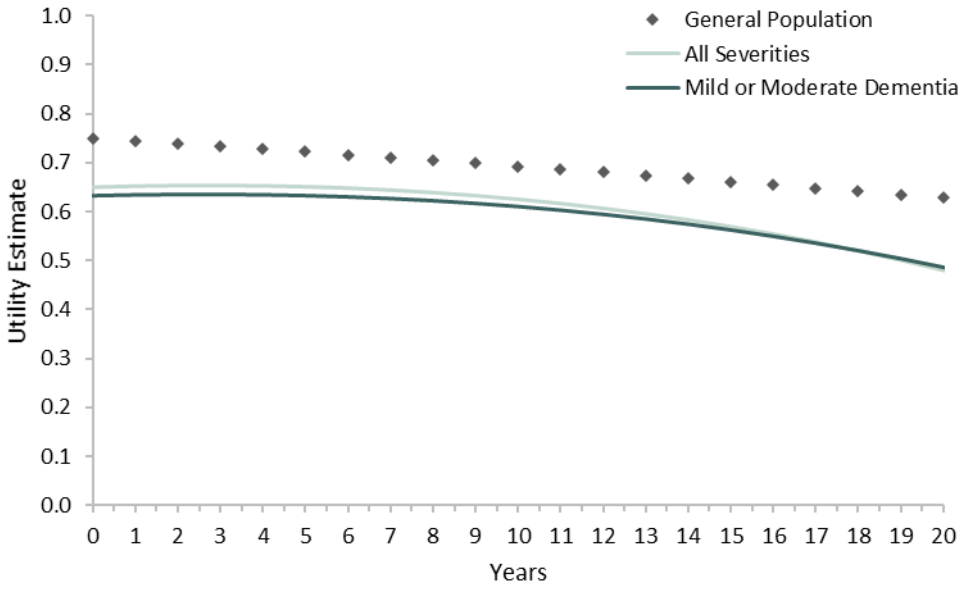

Figure 6.12. Modelled pre-institutionalisation utilities over time compared to those for the age- and sex-matched general population

Table 6.19 shows the regression model results and Figure 6.12 shows the modelled results over time. As can be seen, there is a decline in utility with age, which increases faster in patients with dementia than the general population after around 10 years. Notably, after adjustment for age, there was no significant change in utility associated with institutionalisation. However, there were a limited number of post-institutionalisation interviews conducted (16 in respondents regardless of severity, and 14 in those with mild or moderate dementia at model baseline) and therefore there may be limitations with the estimation of this parameter. In TA217, the Assessment Group assumed that institutionalisation would be associated with the development of severe dementia, which was associated with a substantial decline in proxy rated quality of life. Therefore, in the base case I have opted to take the same value from the literature for the institutionalised health state and use the regression results in a scenario analysis. The selected value comes from a Swedish study of carer-proxy ratings on the EQ-5D stratified by MMSE score, and for those with an MMSE score of less than 10 (severe dementia) the estimate was 0.33.[58] As noted in TA217, severe dementia appears to be a good proxy for institutionalisation as analysis of the patient-level data used in their model showed that the mean time at which participants reached MMSE of less than 10 was around two weeks prior to institutionalisation.

As a sensitivity analysis, proxy-rated utilities were obtained from the literature and applied in the model for both health states. Most quality of life studies identified by the literature review in NICE TA217 reported utilities stratified by disease severity on

Table 6.20. Utility values applied in the model

Scenario	Population	Pre-Institutionalisation		Institutionalised	
		Value	Source	Value	Source
Base Case	All Severities	0.650	ELSA (Data on File)	0.337	Jönsson 2006[58]
	Mild or Moderate	0.631			
Scenario 1	All Severities	0.650	ELSA (Data on File)	0.633	ELSA (Data on File)
	Mild or Moderate	0.631		0.615	
Scenario 2	Both	0.617	Andersen 2004[291]	0.552	Andersen 2004[291]

Notes: Values in the table are reported for the first model cycle, including adjustments for age from the original source where required. All values are age-adjusted over model cycles.

the MMSE or the CDR, neither of which are known to be mappable to measures included in ELSA. However, one identified study reported utilities rated on the EQ-5D by residential status aligned with the health states in the model.[291] Table 6.20 shows the various utilities applied in the model. Where utility values were sourced from the literature, these were age-adjusted using UK norms.[290]

In addition to the basic health state utilities, analyses were conducted to determine whether any other dynamic aspects in the model as a result of the interventions could impact health-related quality of life. In Chapter 4 it was determined that care quality itself was not significantly associated with the estimated EQ-5D values, however there is published evidence to suggest that cognitive function and ability to perform IADLs may impact quality of life in patients with dementia.[58 283-285 287 291] In addition, physical activity may have other health benefits improving quality of life,[292] and reductions in social isolation is plausibly linked to improved mental health.[293] Accordingly, regression models were developed to determine the direct association between these factors and the estimated EQ-5D utilities.

Of the evaluated variables, only the number of self-reported challenges in performing IADLs was significantly associated with utility. After adjustment for age, comorbidities, whether married or cohabiting, and social isolation (minimum sufficient adjustment to elicit direct effects from the DAG), each additional self-reported difficulty was associated with a 0.023 (95% CI -0.034 to -0.012) decrease in utility. For application in the model, it was assumed that the pre-institutionalisation utility would increase by a magnitude equivalent to the reduction in IADLs observed in those receiving the PRIDE intervention compared to treatment as usual, with respect to the estimated utility coefficient.

Quality of Life Impact of Comorbidities

To estimate the effect of the quality of care indicators on quality of life, long-term morbidity decrements for failing to meet the indicators were estimated. For the QALY

impact associated with 'Hypertension Treatment' and 'Osteoporosis Supplements', utility multipliers were applied to the events using the same sources as the models used to inform the event rates. The multipliers were applied in the cycle in which the event was modelled to occur (assuming a one-year duration of the event), using the approaches applied in the models in NG136 and TA464. In TA464, an annual average utility was derived based on a pre-fracture utility, two weeks following the fracture, and four- and twelve-months post-fracture. As well as to the utility multiplier applied to the events, both of the models also attributed a post-event multiplier reflecting a minor, prolonged health decrement in the years following the event. For simplicity, this future decrement is not included in this model, though given the low event rates and high mortality in the current model this is assumed to have a limited impact on QALYs attained. The utility multipliers for each event can be seen in Table 6.21.

To estimate the QALY loss associated with the 'Diabetes Foot Check' indicator, results from the health economic analysis of the prevention and management of diabetic foot problems (NICE Guidance 19) were leveraged.[294] In this analysis, diabetes patients were stratified by risk of ulceration, which could lead to minor or major amputations. The risk of ulceration could be reduced through the provision of bespoke orthotic shoes and inserts. The analysis was intended to determine the cost-effectiveness of the provision of orthotic footwear by patient risk level of ulceration, to derive optimal intervention strategies. The results were used to inform the subsequent clinical indicators in the QOF regarding diabetes foot inspections. The guidance from NG19 recommends that patients with moderate or high risk of developing diabetic foot problems should be referred to the foot protection service for the provision of specialist footwear or orthoses.[295] For the purposes of this model, it was assumed that if patients in ELSA had reported receiving an annual foot check, then those in need of orthotic products would receive them (i.e., no deviation from clinical guidelines on the part of the treating physician or decision by the patient).

Table 6.21. Utility multipliers for cardiovascular and osteoporotic events

Cardiovascular Event	Utility Multiplier (Std Err)	Source
Stable Angina	0.81 (0.038)	Melsop 2003[296]
Unstable Angina	0.77 (0.038)	Goodacre 2004[297]/ Ward 2005[270]
Myocardial Infarction	0.76 (0.018)	Goodacre 2004[297] / Ward 2005[270]
Transient Ischaemic Attack	0.90 (0.025)	Lavender 1998[298]
Stroke	0.63 (0.040)	Tengs 2003[299] / Youman 2003[300]
Heart Failure	0.68 (0.020)	Davies 2006[301]
Hip Fracture	0.69 (NR)	Strom 2008[302]
Vertebral Fracture	0.57 (NR)	Strom 2008[302]
Proximal Humerus Fracture	0.86 (NR)	Zethraeus 2002[303]
Wrist Fracture	0.88 (NR)	Strom 2008[302]

Notes: If standard errors are not reported (NR), these are assumed to be 20% of the mean.

The results of the analysis for NG19 suggested that providing bespoke shoes, orthotic inserts, and education on their use to patients with diabetes at moderate or high risk of ulceration was associated with 0.15 more QALYs after discounting than not providing any bespoke orthotics (regardless of risk level). The results of their model assume a baseline age of 60 years and a lifetime horizon, accounting for diabetes-related mortality alongside background mortality. Given the advanced age of dementia patients, the lifetime health gains of treatment may not be as substantial in those with a higher risk of mortality. In addition, the diabetes foot checks should be conducted annually and therefore the benefits accrued via treatment would need to reflect those at risk in each year. To alleviate some of these concerns, a mean annual QALY gain of providing bespoke orthotics to those at moderate or high risk was estimated. Based on the reported model parameters, I estimated that the mean discounted survival in the NG19 model was 12.8, which permitted the calculation of a naïve estimate of 0.012 additional QALYs per year attributable to the morbidity reductions due to providing appropriate foot care and meeting the quality indicator. It was then assumed that this could be subtracted from QALY gains for the proportion of patients failing to meet the indicator in each model cycle. Although this approach is highly naïve in its estimation of the QALY losses associated with diabetic foot care, in that it does not account for the time disparity between the intervention and the potential benefits, where amputation is likely to occur after several years, given that less than a quarter of the cohort have diabetes and over 70% meet the indicator in any arm, the QALY losses will be limited. However, to account for the uncertainty, confidence intervals assuming limited benefit were applied in sensitivity analyses.

To estimate the benefits of diabetes training and the development of knowledge for managing diabetes, the QALY gains were estimated from the published study reporting on the cost-effectiveness of a self-management intervention for people with type 2 diabetes.[304] This analysis aimed to assess the long-term cost-effectiveness of "diabetes education and self-management for ongoing and newly diagnosed" (DESMOND) compared with usual care, based on a 12 month, multicentre, cluster randomised controlled trial, which was then extrapolated using a validated model for long-term outcomes in diabetes (the Sheffield type 2 diabetes model). Results were reported in terms of the incremental QALYs gained attributable to different aspects of morbidity and mortality in diabetes. Specific results that were extracted for application in this model were those QALYs gained during the first 12 months of the intervention (0.0070), those related to complications of diabetes (0.0002), and those due to weight-related changes in diabetes (0.0037). Those QALYs attributable to improvements in

diabetes-related survival were not included as these were assumed to be captured by the model. As for the QALYs gained due to Diabetes Training, these totals reflect a population with type 2 diabetes and not one with dementia and comorbid diabetes. Accordingly, the annual QALY gain due to training was calculated by deriving the estimated mean discounted survival in the published model. This was estimated to be 11.5 years based on the reported model parameters, and therefore the annual incremental QALY gain due to diabetes training was estimated at 0.002 QALYs.

Although the analysis published by Gillett and colleagues estimated the benefit of training, for application in the model two scenarios were considered: applying the QALY gain to the proportion of patients meeting the Diabetes Training indicator or to the Diabetes Knowledge indicator. The latter is justified by the assumption that all those who report having the knowledge to manage their diabetes would avoid the ill effects associated with a lack of diabetes training. In the base case, it was assumed that all those failing to meet the 'Diabetes Knowledge' indicator would be at risk for diabetes- or weight-related complications. As the diabetes knowledge indicator declines with time as cognitive function deteriorates at it was deemed reasonable that as the dementia patient's condition worsens, they would be less capable of self-management compared to all patients who had ever received training.

As part of the assessment of QOF indicators for smoking cessation, a cost-effectiveness analysis was conducted on offering support and treatment for current smokers.[245] Within the assessment of the cost-effectiveness of the potential indicator they used a previously developed model to estimate the uptake and efficacy of smoking cessation advice and treatments to derive an aggregate lifetime cost and benefit of providing care meeting the quality indicator or not. This analysis was considered directly comparable to that needed for the model. For a sample of the UK smokers, averaged by age and sex, the estimated average lifetime QALYs were 12.43 for those not receiving smoking cessation advice and 12.47 for those who do. To apply the potential losses in the model due to failure to provide smoking cessation advice, it was assumed that those eligible for the indicator was the proportion of current smokers over time, and respondents who continue to smoke should continue to be offered smoking cessation advice each model cycle. From this, the estimated proportion of patients who would meet the indicator over time and accrue the benefits of the indicator can be derived. The QALY gain from the previously developed model was estimated to be accumulated over a discounted mean survival of 18.5 years for an annual mean QALY gain of 0.002 QALYs, and so those modelled patients who received smoking cessation advice in the first cycle of the new cost-effectiveness

model could accrue this benefit each year over their whole modelled survival, whereas those receiving advice in subsequent years would only gain limited benefits.

6.7. Costs & Healthcare Resource Use

Costs in the model were considered in terms of those directly attributable to the strategies for improving care quality (the PRIDE intervention or expanded QOF scheme), ongoing health and social care for the management of dementia, care attributable to consequences of the provision of care, or lack thereof, related to the quality indicators, and end of life care.

Pride Intervention

Microcosting of the PRIDE intervention is being conducted as part of the feasibility trial. For the purposes of this analysis, a provisional estimate of the cost of the intervention was required.

In the feasibility trial for the PRIDE intervention, the intervention is largely captured within a manual which is used to guide participants during three facilitated sessions. The facilitator of the sessions is trained in the delivery of the sessions. The costs of the intervention were therefore assumed to be the time used to deliver the sessions, the materials needed by each participant, and training costs for facilitators. The estimated provisional per patient cost of the PRIDE intervention is shown in Table 6.22.

The PRIDE manual is available to participants in a paper or electronic (web-based) version, and participants can select which version to use. It was assumed that for the purposes of costing, all participants would receive a paper version at an estimated price of £5. The facilitated sessions are expected to be of between 60 and 90 minutes and held over 2 months. It was assumed that all patients would receive all three facilitated sessions (no discontinuations). Sessions are assumed to be delivered by health care professionals providing services for patients with dementia (occupational therapists or mental health nurses), and so hourly costs of these health care staff were obtained from the Unit Costs of Health and Social Care.[305] For costing purposes, all sessions were assumed to take 90 minutes and that the session facilitator would require an additional hour per session for preparation and travel, and have travel costs reimbursed. It was also assumed that up to one hour of time of administrative staff would be required per patient in order to arrange and coordinate the facilitated sessions.

Facilitators of the PRIDE intervention for the feasibility trial must attend a 1-day standardised training session. As training costs are not likely to be attributable to an

Table 6.22. Provisional microcosting of the PRIDE intervention

Cost Category / Item	Cost	Rationale	Source
Course to Train Facilitators			
Course Educators	£ 1,307.92	One day (8 hours) for the course, plus 4 hours of preparation and travel for two researchers as per feasibility trial. Hourly cost of community-based scientific and professional staff (band 7) was considered as a proxy	PSSRU 2019 [305]
New Facilitators	£ 3,200.90	Assumed 5 community-based mental health nurses (band 5) and 5 community-based occupational therapists (scientific and professional staff, band 5) would attend each 8-hour course (with one hour of travel)	PSSRU 2019 [305]
Travel	£ 108.00	Reimbursed travel costs assuming an average 20-mile return journey at 45p per mile for all 12 attendees per course	GOV.UK [306]
Venue	£ 25.00	Based on a published estimate of venue costs from feedback from Primary Care Trusts (note this can vary substantially by region)	Gillett 2010 [304]
Administration & Organisation	£ 75.18	Assumed 4 hours for one NHS administrator (band 4) to coordinate organisation of a course, including oncosts and capital costs	PSSRU 2019 [305]
Subtotal	£ 4,717.00		
Patients per Facilitator	935	Based on potential resource availability	Estimate
Training Costs per Patient	£ 0.50		
Delivery of the Intervention			
Session Facilitators	£ 106.69	Average cost of community-based mental health nurse (band 5) or community-based occupational therapist (scientific and professional staff, band 5) to provide three 90-minute sessions with one hour of preparation and travel per session	PSSRU 2019 [305]
Travel	£ 20.25	Assumption on an average 15-mile return journey per session at 45p per mile	GOV.UK [306]
PRIDE Manual	£ 5.00	Printing of manual	Assumption
Administration & Organisation	£ 18.79	One hour of NHS administrator (band 4) per patient, including costs, to arrange sessions	PSSRU 2019 [305]
Subtotal	£ 150.74		
Total Cost per Patient	**£ 151.24**		

individual patient, an estimate of how broadly these costs will be distributed in practice is required.

There were an estimated 297,700 older adults living in the community with mild or moderate dementia in England in 2015, with 171,000 new cases each year.[307] If 75% of these cases were eligible for the PRIDE intervention, then to ensure all eligible prevalent cases and future cases received the intervention over the next three years, over 600,000 facilitated sessions would have to be delivered each year, potentially taking 1.5 million hours requiring over 950 new full-time equivalent (FTE) workers. As this is a somewhat unrealistic expectation, instead a threshold analysis for uptake considering the feasibility with current NHS resources was conducted. The quality-

adjusted productivity growth in the NHS was 2.01% from the 2015/16 financial year to 2016/17, and for community mental health services this was 5.34%.[308] For the purposes of this analysis is was assumed that time resources for mental health services would increase by 5.34% each year, of which 5% of those could be attributed to delivering the PRIDE intervention. In the feasibility trial, part of the responsibility for recruitment lies with selected NHS mental health trusts providing services for people with dementia, as well as an aim of the trial being to assess the ability of NHS sites to deliver the intervention.[227] It is therefore assumed that responsibility for the delivery of the PRIDE intervention will lie with the 51 NHS mental health trusts and their employed occupational therapists or mental health nurses. Based on the reported number of FTE nurses and scientific, technical, and therapeutic staff employed in these trusts,[309] estimates of the proportion of mental health and occupational therapy trained staff,[310 311] and reported annual working hours,[305] it was determined that 115,000 hours per year could be dedicated nationally to delivering the PRIDE intervention. This equates to approximately 15,300 patients receiving the intervention per year, and 72.7 FTE requiring training (approximately 82 people based on the current FTE to headcount ratio). Whilst uptake may be lower in earlier years, it was assumed the 82:15,300 facilitator-to-patient ratio would be fairly consistent over time but that facilitators may require "refresher" training every five years, should the manual or practice be updated. Therefore, each facilitator should be able to treat 935 patients between trainings, and that 10 facilitators would attend each training session.

Training sessions take a full day and in the feasibility trial were delivered by two researchers. The costs of delivering the training programme in practice was assumed to be two full day rates for senior scientific staff (clinical psychologist, band 7) as well as a half-day of preparation and travel, along with the opportunity cost of the new facilitators attending the course rather than providing care services. In addition, estimates of the travel costs, venue hire, and administration requirements to organise the course were included.

QOF & Pay-for-Performance

The costs of improving care quality through pay-for-performance were considered within an expansion of the QOF framework. As mentioned above, points were attributable to each indicator which had some impact on the quality of care received, but also determined the level of cost associated with the indicator. Table 6.23 shows the points available for each quality indicator in the model. The value of a QOF point in the 2019/20 financial year was £187.74.[71] However, the number of points only reflects the maximum reimbursement available. Actual reimbursement is adjusted for

Table 6.23. Points available for each quality indicator in the model

ELSA Quality Indicator	QOF Indicator 2019/20	Current QOF	Expanded P4P / Combined Scheme		
			New Points	Thresholds	Rationale
Diabetes Foot Check	DM012	4	4 + 3 (0 to 30)	50 to 90%	As per current QOF
Diabetes Training	N/A	0	11 + 3 (0 to 30)	40 to 90%	Value of training for incident DM (DM014)
Hypertension Treatment	HYP003 / HYP007	14 / 5†	14 / 5† + 3 (0 to 30)	40 to 77% / 40 to 80%	As per current QOF
Osteoporosis Supplements	N/A	0	3 + 3 (0 to 30)	30 to 60%	Equal to past indicator for use of bone sparing agents in patients with previous fragility fracture (OST002 / OST003)[248]
Smoking Cessation	SMOK005	25	25 + 3 (0 to 30)	56 to 96%	As per current QOF

In the expanded QOF scheme, quality indicators are associated with additional for meeting the indicator in patients with dementia compared to none for those without a cognitive impairment. † In the current QOF, blood pressure control is valued at different levels for those age under or over 80 years, with different points for each group awarded.

disease prevalence and practice list size, within upper and lower limits of a defined pass rate.[71] As the model reflects a national perspective, it was assumed that disease prevalence would reflect national averages and were not considered. With regards to payment limits, when a practice's performance rate (pass rate of the indicator) is below the lower limit of the payment threshold, they receive no reimbursement for that indicator. Above the upper limit, they achieve the full reimbursement for that indicator. Between the limits, the payments are scaled. Therefore, to estimate the reimbursement attainable for each indicator the following formula is used:

$$£ = \left(\frac{\% - LT}{UT - LT}\right) * Points * Value * \frac{n}{\overline{N}}$$

where LT reflects the lower payment threshold, UT reflects the upper threshold, % is the achievement level by the practice, and n is the practice list size compared to the national average list size $\overline{N}$.

For indicators that are already included in the QOF, the achievement rate of the indicator should also reflect the quality of care in those patients without dementia for whom the indicator applies to. It was assumed that published achievement rates in the QOF in previous years reflected a mix of the modelled care quality for patients with dementia in the treatment as usual arm, plus the quality of care for patients without dementia. From this, the average care quality for those without dementia could be derived if the number of patients with and without dementia who were eligible to the indicator (the weightings) could be derived.

Table 6.24. Average patient sizes per GP practice for each comorbidity included in the QOF

Patient Group	Population Size	Diabetes	Hypertension	Smoking
All Severities				
Dementia	112	22	49	9
Non-Dementia	8,528	537	1,143	1,228
Total	8,640	560	1,192	1,237
Mild or Moderate Dementia				
Mild or Moderate Dementia	98	20	43	8
Other	8,542	540	1,149	1,229
Total	8,640	560	1,192	1,237

In 2018/19 the average practice list size was 8,640.[312] The population prevalence of dementia has been estimated at 1.3% and that 12.5% of those patients have severe dementia.[44] In patients with dementia, 44% have hypertension and 20% have diabetes compared to 13.4% and 6.3% of the general population,[313] and the prevalence of smoking in older adults is estimated at 8% compared to 14.4% in the overall population.[314] Based on these estimates, the weightings for dementia patients in each comorbidity were estimated for both those with all severities and those with mild or moderate dementia (Table 6.24). It was determined that care quality for the modelled patients with dementia would reflect 4.0% of the total quality estimate for diabetes indicators, 4.1% of hypertension, and 0.7% of smoking indicators in the sample for all dementia severities. In patients with mild or moderate dementia, their modelled care quality would contribute to 3.5%, 3.6%, and 0.6% of total care quality on diabetes, hypertension, and smoking QOF indicators, respectively.

In the published indicator pass rates in the 2018/19 year, the average pass rate per GP practice was 89.5% for indicators related to foot inspections in diabetes, 83.1% for blood pressure control in hypertension, and 96.7% for smoking cessation. Based on the estimated weightings and the modelled care quality for patients with dementia in the first cycle, the care quality for patients not captured by the model was estimated and assumed to be consistent over time.

For application in the model, all reimbursement (and therefore health care costs) at the practice level needs to be matched to the health gains of the modelled cohort. Therefore, the increase in the practice level reimbursement for the QOF compared to treatment as usual for that quality indicator at any given model cycle was attributed to the estimated average number of patients with dementia eligible for the indicator per GP practice. Thus, all additional reimbursement at the practice-level associated with expanding greater reimbursement and care quality for diabetes would be divisible by the 22 patients with dementia and comorbid diabetes at the GP practice, on top of the current per patient costs of the QOF for diabetes care (irrespective of dementia

diagnosis). Thereby, the costs of the QOF directly attributable to the average dementia patient was derived.

Note that as the PRIDE intervention would also be expected to lead to improvements in care quality, the QOF costs would increase for this regimen. Even if the reimbursement for quality is not increased, as pass rates for indicators at a practice level would be expected to increase as more patients with dementia meet the indicators the level of reimbursement per practice would increase.

Drug Costs

Medications directly attributable to the intervention strategies were those for which uptake may increase due to meeting quality indicators, namely treatments for hypertension and supplements for osteoporosis, for which further details can be found below. In addition, drugs for the treatment of dementia or Alzheimer's disease were also included. Whilst the intervention strategies were not considered to affect the uptake of use of dementia drugs, the prolongation of survival with improved care quality may mean that overall time on treatment is prolonged, increasing lifetime costs, and was therefore considered a potential differentiating factor.

Drugs for dementia and Alzheimer's disease were only captured in terms of cost and had no influence on survival or cognitive function beyond the already modelled effects as it was assumed patients would already have initiated treatment with relevant drugs in the prevalent cohort and effects of which would be equal between interventions.

The NICE guidance on the management of dementia recommends three AChEIs for managing mild to moderate Alzheimer's disease, namely donepezil, galantamine and rivastigmine.[34] It also states that treatment should normally be initiated with the drug with the lowest acquisition cost. Based on 2019 data from the drugs and pharmaceutical electronic market information tool (eMIT),[315] donepezil has the lowest cost considering the recommended daily dose. In addition, memantine is recommended as a treatment option for patients with severe Alzheimer's disease and for those patients who are already taking an AChEI, memantine can be offered as an adjunct therapy for those with severe disease.[34] The guidance also states that AChEIs should not be discontinued due to disease severity alone. It was therefore assumed in the model that at baseline all patients were taking donepezil, and that the proportion of the cohort with severe disease would also receive memantine, and would continue

Table 6.25. Dementia-related drug costs applied in the model

Drug	Tablet Dose	Pack Size	Cost per Pack	Source
Donepezil	10 mg	28	£ 0.58	eMIT
Memantine	20 mg	28	£ 2.79	eMIT

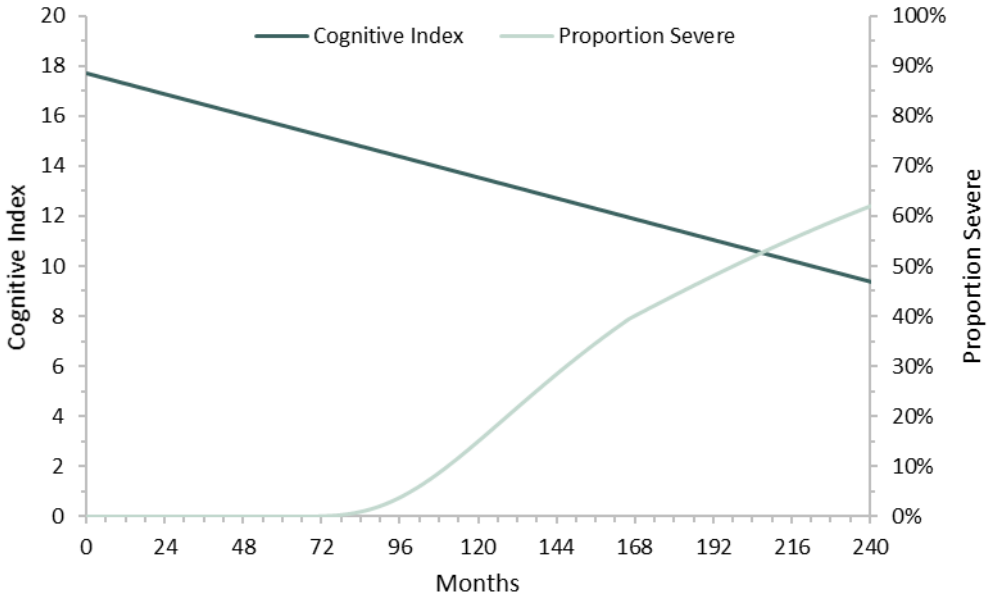

Figure 6.13. Estimated proportion of patients with severe dementia over time based on modelled cognitive index scores in patients with mild or moderate dementia.

on these treatments until death or treatment discontinuation. Treatment discontinuation was considered at a fixed rate of 4% per month for both donepezil and memantine, as applied in NICE TA217. The proportion of the modelled cohort with severe dementia was derived from the extrapolated cognitive function curve, determining those proportion with a score of less than 10 using the prediction intervals.

An example of the estimation of the proportion of patients with severe dementia under treatment as usual in the cohort with mild or moderate dementia at baseline is shown in Figure 6.13. The additional patients developing severe dementia each cycle were assumed to initiate memantine. Acquisition costs for donepezil and memantine are shown in Table 6.25. No administration costs were considered as therapies are taken orally, and drug wastage (unused tablets) was not accounted for as the impact was expected to be limited given the relatively low acquisition costs.

Whilst the economic evidence from TA217 and the product labels for donepezil and memantine refer to patients with Alzheimer's disease, the cohort of patients in ELSA may have other forms of dementia. For costing purposes, it was conservatively assumed that all patients would be receiving some form of pharmacological treatment and therefore the costs of donepezil and memantine were considered proxies for other drug costs for those with potentially other causes of dementia. This is somewhat supported for the NICE guidance for the pharmacological management of other forms of dementia, which states that people with dementia with Lewy bodies can be offered

donepezil or rivastigmine, and memantine can be considered for those unable to tolerate AChEIs.[34]

Health & Social Care

Dementia-Related Care

Most costs related to the management of dementia pre- and post-institutionalisation were derived from the model in NICE TA217. Their analyses used patient-level data on the number and duration of acute hospitalisations and respite care, number of outpatient visits, day care and home attendances by nurses and other care assistants, and the number of general practitioner visits to estimate total care costs over time.[228]

For care pre-institutionalisation, this was assumed to be a function of time as patients in this health state were not considered to be homogenous given that health care costs may increase as the patient's condition deteriorates prior to institutionalisation. The Assessment Group developed a linear mixed-effects model, with a cubic equation for the time to the end of pre-institutionalisation as a fixed effect and patient as a random intercept. Estimates were provided for both patients with mild or moderate Alzheimer's disease at baseline, or moderate to severe Alzheimer's disease. As patients with severe dementia only constituted 12.9% of the ELSA sample at baseline in the group with all severities, and poor cognitive function is associated with worse survival, it was assumed these patients would not contribute substantially to long-term costs, and so only the cost model for the mild/moderate group was considered. Costs for this group in their model were estimated as:

$$Monthly\ Cost\ (£) = 2877 - 1122t + 194t^2 - 10.9t^3$$

where *t* is the years before the end of pre-institutionalisation (either institutionalisation or pre-institutionalisation death). Costs were inflated from 2009 to 2019 values and annualised for use in the model. In the patient-level data, costs were demonstrated to stabilise approximately six years prior to institutionalisation and therefore were considered in categories of less than one year (£32,813), one to two years (£22,130), two to three years (£15,471), three to four years (£11,930), four to five years (£10,598), five to six years (£10,567), and over six years (£10,929) in the model, with costs estimated at the mid-point of each yearly interval. This is aligned with the approach used in TA217.

As care quality and social isolation were demonstrated to have an association with the number of IADLs receiving help with from nurses and social workers, and cognitive function and exercise were associated with reducing the overall number of self-reported difficulties with performing IADLs, social care needed to be costed

separately. As the annual costs of care above already include social care and domiciliary help, these were adjusted accordingly. In the patient-level data used to inform the regression model, domiciliary help constituted 21.1% of the total costs of care outside of the institutional setting.[316] Therefore, the modelled costs of care pre-institutionalisation were estimated at 78.9% of the costs of care reported above.

To estimate the costs of social care, a three-step process was taken: first the number of IADLs respondents reported difficulties performing was estimated, then the number of IADLs respondents received help performing was estimated, and finally this was used to estimate hours of social care respondents received. A baseline level of the number of self-reported difficulties with IADLs was estimated using a negative binomial mixed model with age as a fixed effect and respondent as a random effect (see Figure 6.14). For those patients receiving the PRIDE intervention (including in the combined scheme) where cognitive function and the level of exercise engaging in may be improved, the modelled number of difficulties was lower using the incidence rate ratios shown in Table 6.14. The volume of help received with IADLs from nurses or social workers was also considered to potentially be associated with time, independent of the number of IADLs reporting difficulties with, as the patient's situation may change, with increased comorbidities, or moving from a reliance on informal carers to formal support due to widowing or loss of social contacts.

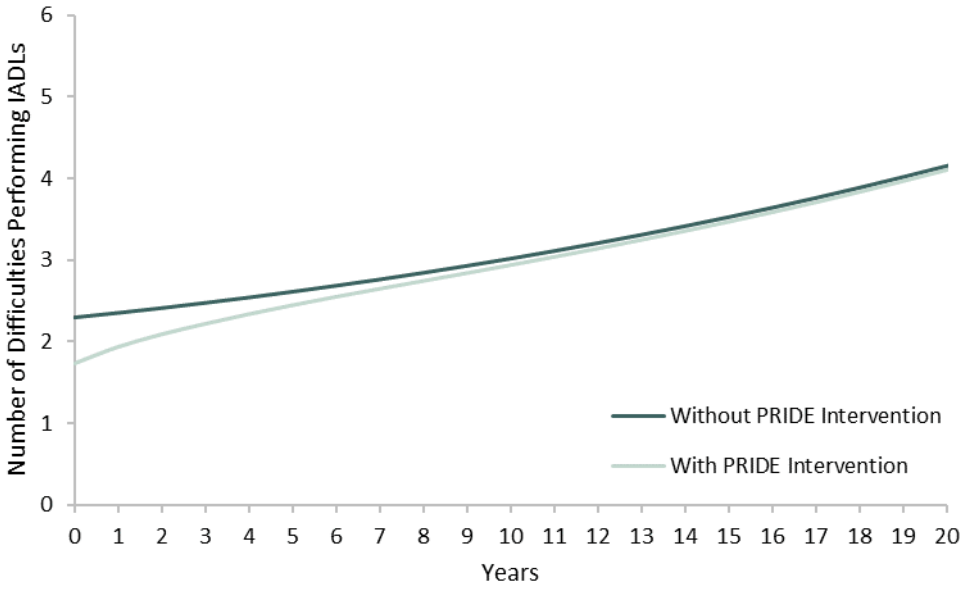

Figure 6.14. Modelled number of reported difficulties performing instrumental activities of daily living (maximum of 6) for those receiving the PRIDE intervention or not. Only the population with mild or moderate dementia at baseline and currently resident in the community shown.

Accordingly, a negative binomial regression model was developed with age as a fixed effect (including analyses with an additional age squared term), respondent as a random effect, and cognitive function, social isolation, physical activity, and quality of care as covariates, and number of reported difficulties with IADLs as the exposure variable. A model including both age and age squared provided the best fit, with statistically significant predictors, and so was included in the model, though total number of IADLs receiving help from social services with was low (0.7% of estimated IADL difficulties at baseline, up to 5.4% after 20 years), however respondents may be receiving domiciliary help for other factors.

Accordingly, whilst these factors could be used to determine how care quality and other aspects of the PRIDE intervention could influence how social care was delivered to patients, an estimated baseline level of care was required. Therefore, a mapping algorithm was defined to derive the association between the number of IADL difficulties respondents received help with, and the frequency of visits from social workers. At Wave 4 of ELSA respondents were asked how often they received help from the local authority or social services in the past month, rated between "every day or nearly every day", "two or three times a week", "once a week", "less often", or "not at all". An ordered logistic regression model in patients resident in the community with the number of IADLs assisted with by nurses or social services as a predictor was used to derive the mapping algorithm. The number of self-reported difficulties in performing IADLs was also considered as a predictor, though this was not statistically significant. A higher number of IADLs helped with was significantly associated with greater odds of receiving more frequent care (OR 3.08, 95% CI 1.73 to 5.48). In the treatment as usual arm, at baseline 17% of patients were modelled to receive no care from social workers and 23% received some care nearly every day, but after 20 years these proportions were 14% and 27%.

As the frequency of social worker visits does not explicitly denote hours of care utilised for costing purposes, certain assumptions were applied. It was assumed each visit from a social worker was approximately two and a half hours in duration including travel time (ranging between one hour and five hours). The cost of social care was estimated at £51 per hour, based on a social worker (adult services) from the Unit Costs of Health and Social Care 2019.[305] With regards to the actual frequency of visits, this was probabilistically sampled from the ranges reported in Table 6.26.

Table 6.26. Estimated frequency of social care help

Frequency of Social Care Visits	Estimated Visits per Week	Sampled Range
Not at All	0	N/A (Never)
Less Than Once a Week	0.5	0.23 (Once a Month) to 0.69 (Three Times a Month)
Once a Week	1	0.70 to 1.49
Two or Three Times a Week	2.5	1.50 to 3.49
Every Day or Nearly Every Day	5	3.50 to 7.00 (Every Day)

For the costs of care following institutionalisation, the estimates on the annual costs of care for people living with dementia living in residual care were extracted from the Alzheimer's Society estimated costs of dementia.[44] In 2014, it was estimated that patients with dementia living in residential care used £8,542 of healthcare each year, and £25,610 of social care (of which 35% is publicly paid). Inflated to 2019 values, this equated to £18,940 per year for health and social care funded by the NHS or PSS. These cost estimates are assumed to include all primary, community, and secondary healthcare services used, as well as the public costs of assessment and social care management and residential care.

Diabetes-Related Care

In addition to the QOF costs associated with diabetes indicators, there are also the costs associated with delivering the care captured within the indicators. Costs of care were obtained from the same sources as for the QALY gains associated with each indicator.

For 'Diabetes Foot Check' this is assumed to include the costs of annual foot inspections, the costs of orthotic footwear (where needed), and the costs of follow-up care for patients who receive annual check-ups and for those who do not.[294] For the estimated proportion of patients meeting the quality indicator, the foot inspection itself was assumed to cost the equivalent of one GP consultation. Of those patients receiving inspections, patients deemed at moderate or high risk of diabetic foot complications (36.1% of patients in NG19) were assumed to receive orthotic footwear. In NG19, the Guideline Development Group estimated that footwear would cost on average £525 per patient, including the cost of fitting the shoes. In their model it was assumed that patients would receive a new pair of shoes every year (or similarly expensive repair and maintenance) and therefore this cost is applied to 36.1% of surviving diabetic patients meeting the indicator throughout the model horizon.

For the ongoing costs of care related to foot inspections or the lack thereof, such as that related to the costs of ulceration or amputation, results of the model were used to

Table 6.27. Derived annual costs of care with and without annual diabetes foot checks

	Variable	No Bespoke Orthotics	Bespoke Footwear for Moderate/High-Risk Patients
A	Lifetime Discounted Total Costs	£ 4,677.53	£ 5,486.33
B	Estimated Discounted Survival	12.8 years	12.8 years
C	Proportion Moderate to High Risk	36.1%	36.1%
D	Bespoke Orthotics: Annual Cost	£ 0.00	£ 525.00
E	Bespoke Orthotics: Lifetime Cost (B*C*D)	£ 0.00	£ 2,429.88
F	Lifetime Discounted Care Costs (A-E)	£ 4,677.53	£ 3,056.45
G	Estimated Annual Care Costs (F÷B)	£ 364.87	£ 238.42
H	Inflated to 2019 Values	**£ 390.47**	**£ 255.14**

back calculate an approximate annual cost of meeting the indicator or not. Based on the estimated discounted survival, the discounted lifetime cost of providing bespoke footwear to moderate or high-risk patients each year was estimated. After excluding the costs of orthotic footwear, all other costs would be related to the ongoing care and management of diabetic foot complications based on the modelling approach in NG19. From this, the mean cost per year was derived. As with the QALY estimates, this may be a biased approach as the risk of higher cost events (e.g., amputation) and quality of life detrimental events are likely to be further into the future. However, as the approach is conservative (both short-term costs and short-term QALY detriments are overestimated) it was deemed acceptable for this preliminary analysis of cost-effectiveness.

For the costs related to diabetes training, these were considered in terms of the actual costs of the self-management intervention, as well as the increased risk of having diabetic complications due to a lack of knowledge on how to manage the condition.

The costs of the DESMOND intervention for diabetes were applied in the model to align with the QALY gains applied.[304] In this study the authors estimated the real world lifetime costs of delivering the intervention in the UK, including drug costs, ongoing care and monitoring, and management of diabetic complications. The estimates were derived separately for the first year (those captured during the clinical trial, including the intervention costs) and for the remaining lifetime by extrapolating treatment effects (Table 6.28). As the training quality indicator was assumed to apply to a prevalent cohort, the costs from the first year of the DESMOND intervention were applied in the first model cycle for those additional patients who met the training indicator due to interventions (those in the treatment as usual arm were assumed to accrue no additional training costs). Other patients were assigned the cost of "Usual Care". As with the QALYs associated with this indicator, I considered that those patients who reported to have the knowledge to manage their diabetes (the 'Diabetes

Table 6.28. Estimated costs of delivering a self-management intervention for diabetes and follow-up

	Variable	Usual Care	Self-Management Intervention
	Initial Costs (During Intervention Year)		
A	Intervention Costs	£ 0	£ 76
B	Healthcare Resource Use	£ 244	£ 260
C	Total Costs: Year 1 (A+B)	£ 244	£ 336
D	Inflated to 2019 values	**£ 295**	**£ 406**
	Remaining Lifetime Costs (Year 2+)		
E	Therapy & Monitoring	£ 5,286	£ 5,302
F	Diabetic Complications	£ 10,445	£ 10,419
G	Adverse Events	£ 105	£ 104
H	Total Costs: Year 2+ (E+F+G)	£ 15,836	£ 15,826
	Annualised Costs Estimates (Year 2+)		
I	Discounted Survival: Year 2+	10.68	10.71
J	Estimated Cost per Year (H÷I)	£ 1,483	£ 1,478
K	Inflated to 2019 values	**£ 1,793**	**£ 1,787**

Knowledge' indicator) at a lower risk of complications and care needs, aligned with those who had received the self-management intervention. Accordingly, from year 2 onwards those patients meeting the 'Diabetes Knowledge' indicator had the follow-up costs associated with the DESMOND intervention applied, whereas those not meeting the indicator had the annual costs of usual care applied. As with the QALYs, a scenario was considered with costs matched to the training quality indicator only.

Hypertension & Cardiovascular Care

The cost of drugs related to the Hypertension Treatment indicator were informed using the same method and approach as applied in the model for NICE Guideline 136 for the management of hypertension.[266] Drug costs were applied to all living patients with hypertension who met the quality indicator, not just those who had not yet experienced a cardiovascular event. Drug costs were calculated by age and sex, with consideration to the number and type of antihypertensive agents. The distributions were obtained from UK registry data from 27 GP practices in patients receiving antihypertensive drugs. Three classes of medication were considered: angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blockers (ARB), calcium channel blockers (CCB), and diuretics. The drug in each class was based on the NICE guidelines as per NG136. In the ACE inhibitor/ARB class, 10mg per day of ramipril was used, the chosen CCB was 10 mg per day of amlodipine, and the diuretic was 2.5mg per day of indapamide. Costs of the drugs were obtained from eMIT for 2019. Table 6.29 shows the distribution of drugs applied in the model.

As all drugs for hypertension are administered orally, no administration costs were included. However, these drugs are associated with ongoing monitoring and testing. In NG136, patients taking one antihypertensive medicine were assumed to have two

Table 6.29. Calculated costs for the treatment of hypertension

Age	Treatment	Males				Females			
		1	2	3	Average	1	2	3	Average
50 to 54	No. of Drugs	53%	33%	14%		58%	32%	10%	
	Ramipril	100%	100%	100%		100%	100%	100%	
	Amlodipine	0%	50%	100%		0%	50%	100%	
	Indapamide	0%	50%	100%		0%	50%	100%	
	Avg. Drug Cost	£ 4.49	£ 9.54	£ 14.60	**£ 7.57**	£ 4.49	£ 9.54	£ 14.60	**£ 7.11**
	GP Visits (Y1)	£ 78.46	£117.69	£156.92	**£102.39**	£ 78.46	£117.69	£156.92	**£102.39**
	GP Visits (Y2+)	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**
	Tests (Y1)	£ 20.32	£ 28.08	£ 35.83	**£ 25.05**	£ 20.32	£ 28.08	£ 35.83	**£ 24.35**
	Tests (Y2+)	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**
55 to 64	No. of Drugs	44%	38%	18%		51%	35%	13%	
	Ramipril	0%	100%	100%		0%	100%	100%	
	Amlodipine	50%	50%	100%		50%	50%	100%	
	Indapamide	50%	50%	100%		50%	50%	100%	
	Avg. Drug Cost	£ 5.05	£ 9.54	£ 14.60	**£ 8.48**	£ 5.05	£ 9.54	£ 14.60	**£ 7.91**
	GP Visits (Y1)	£ 78.46	£117.69	£156.92	**£102.39**	£ 78.46	£117.69	£156.92	**£102.39**
	GP Visits (Y2+)	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**
	Tests (Y1)	£ 7.76	£ 28.08	£ 35.83	**£ 20.53**	£ 7.76	£ 28.08	£ 35.83	**£ 18.68**
	Tests (Y2+)	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**
65 to 74	No. of Drugs	39%	39%	22%		44%	38%	18%	
	Ramipril	0%	100%	100%		0%	100%	100%	
	Amlodipine	50%	50%	100%		50%	50%	100%	
	Indapamide	50%	50%	100%		50%	50%	100%	
	Avg. Drug Cost	£ 5.05	£ 9.54	£ 14.60	**£ 8.90**	£ 5.05	£ 9.54	£ 14.60	**£ 8.48**
	GP Visits (Y1)	£ 78.46	£117.69	£156.92	**£102.39**	£ 78.46	£117.69	£156.92	**£102.39**
	GP Visits (Y2+)	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**
	Tests (Y1)	£ 7.76	£ 28.08	£ 35.83	**£ 21.86**	£ 7.76	£ 28.08	£ 35.83	**£ 20.53**
	Tests (Y2+)	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**
75+	No. of Drugs	38%	40%	22%		41%	39%	20%	
	Ramipril	0%	100%	100%		0%	100%	100%	
	Amlodipine	50%	50%	100%		50%	50%	100%	
	Indapamide	50%	50%	100%		50%	50%	100%	
	Avg. Drug Cost	£ 5.05	£ 9.54	£ 14.60	**£ 8.95**	£ 5.05	£ 9.54	£ 14.60	**£ 8.71**
	GP Visits (Y1)	£ 78.46	£117.69	£156.92	**£102.39**	£ 78.46	£117.69	£156.92	**£102.39**
	GP Visits (Y2+)	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**	£ 73.36	£ 73.36	£ 73.36	**£ 73.36**
	Tests (Y1)	£ 7.76	£ 28.08	£ 35.83	**£ 22.06**	£ 7.76	£ 28.08	£ 35.83	**£ 21.30**
	Tests (Y2+)	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**	£ 5.02	£ 5.02	£ 5.02	**£ 5.02**

Replicated from NG136, updated with new costs obtained from eMIT 2019, PSSRU 2019, and NHS Reference Costs 2018/19. Average costs are reported per year (model cycle).

GP visits in the first year for medication monitoring, and those taking two or three medications were assumed to have three or four GP visits, respectively, during the first year. In subsequent years, all patients taking antihypertensive medications were assumed to have an average of 1.87 GP visits per year to monitor medication. The cost of a GP visit is £39.23, based on the Unit Costs of Health and Social Care.[305] In addition to the GP visits, testing costs to monitor for adverse events were also included. The tests included clinical biochemistry of urea and electrolyte testing, as well as the urinary albumin-to-creatinine ratio. In the first year of drug use, testing levels were separated by the type of drugs taken as some classes of drug require more

Table 6.30. Unit costs of care associated with hypertension treatment

Resource	Cost	Source
Ramipril Tablets x 28 (10 mg)	£ 0.34	eMIT 2019
Amlodipine Tablets x 28 (10 mg)	£ 0.21	eMIT 2019
Indapamide Tablets x 28 (2.5 mg)	£ 0.56	eMIT 2019
GP Consultation (Ongoing Monitoring)	£ 39.23	PSSRU 2019
Clinical Biochemistry: Urea & Electrolyte Testing	£ 4.80	National Schedule of NHS Costs (2018/19): DAPS08 (Direct Access Phlebotomy) + DAPS04 (Direct Access Clinical Biochemistry)
Albumin-to-Creatinine Ratio	£ 1.10	National Schedule of NHS Costs (2018/19): DAPS04 (Direct Access Clinical Biochemistry)
Stroke Care	£ 5,963.59	Danese (2016),[317] inflated to 2019 values
TIA Care	£ 2,750.50	Danese (2016),[317] inflated to 2019 values
Myocardial Infarction Care	£ 6,775.10	Danese (2016),[317] inflated to 2019 values
Heart Failure Care	£ 1,778.27	Danese (2016),[317] inflated to 2019 values
Stable Angina Care	£ 3,726.09	Initial event costs derived from weighted average of National Schedule of NHS Costs (2018/19): EB13A-D (Angina with CC Score 0-12+) with follow-up care assumed equal to unstable angina
Unstable Angina Care	£ 3,944.85	Danese (2016),[317] inflated to 2019 values

testing than others. ACE inhibitors and ARB drugs require four biochemistry tests in the first year as well as one albumin-to-creatinine ratio test. CCBs required only one clinical biochemistry and diuretics required two clinical biochemistries and one albumin-to-creatinine ratio test. All estimates were the same as included in NG136. The estimated average GP visit and testing costs across age groups are also shown in Table 6.29, and the unit costs of drugs, visits, and tests are shown in Table 6.30.

The costs associated with each of the cardiovascular events were derived from the same sources at the health state costs applied in NG136. For stroke, transient ischaemic attack (TIA), myocardial infarction, unstable angina, and heart failure, evidence from a single study was used. Here the costs of care were reported to be related to the initial event (up to six months after the index date), as well as an estimate of the annual cost for follow-up care derived from data from month seven to 36 after the index date. To estimate the total cost for each of these events, a total of two years of care was assumed for each event as an approximation for the average care those who die shortly after the initial event and those who require prolonged care. The total costs for the initial six months were added to six months of estimated follow-up care, as well as a further 12 months of follow-up care discounted at 3.5%. All costs from the initial study were inflated to 2019 values using the NHS Cost Inflation Index.[305]

Osteoporosis & Fracture Care

Those patients meeting the 'Osteoporosis Supplements' indicator were assumed to have been prescribed calcium and vitamin D supplements. Based on recommendations

Table 6.31. Unit costs of care associated with osteoporosis and fracture treatment

Resource	Cost	Source
Cholecalciferol/Calcium Carbonate x 30 (800IU/1g)	£ 6.75	BNF
Hip Fracture	£ 8.922.32	NICE TA464, inflated to 2019 values
Vertebral Fracture	£ 4,809.03	NICE TA464, inflated to 2019 values
Proximal Humerus Fracture	£ 1,468.93	NICE TA464, inflated to 2019 values
Wrist Fracture	£ 993.78	NICE TA464, inflated to 2019 values

and guidelines,[318 319] it was assumed that patients with osteoporosis would take the equivalent of 800 IU (international units) of vitamin D per day, along with 1000mg of calcium carbonate. The cost of a combined tablet containing both supplements was obtained from the British National Formulary (BNF) at a cost of £6.75 per 30 tablet pack. As reported in §6.5 above, patients were assumed to stay on supplements for an average of three years taking one tablet per day with no wastage.

The costs of fracture were taken from NICE TA464, which were estimated from UK registry data with regards to hospitalisation costs, A&E (accident and emergency) admissions, GP visits, referrals, subsequent prescriptions and medications, as well as home help. Aggregate costs for each fracture type accounting for up to two years of follow-up care, inflated to 2019 values, are shown in Table 6.31. As per the model for TA464, no costs of ongoing care or monitoring of osteoporosis were included.

Smoking-Related Care

For costing care related to smoking cessation advice, aggregate results from the estimate of the cost-effectiveness of the QOF indicator were utilised. In this analysis, the lifetime costs of providing brief opportunistic support and treatment to smokers was valued at £6,453, compared to £6,377 if smoking cessation advice and support was not offered. As with the QALY decrements from smoking estimated above, the costs were assumed to be distributed across the lifetime. Therefore, the estimated annual cost of care in 2019 values was assumed to be £399 for those who were not offered smoking cessation advice, or £403 per year for the group with a higher proportion of ex-smokers as a result of offering advice and treatment.

6.8. Analyses

Given the various uncertainties in model inputs and approach, and the preliminary nature of the analysis, a probabilistic base case is adopted on the grounds that a single point estimate is not especially informative to the potential scale and range of cost and QALY differences. Alongside this, two additional scenarios are considered to have comparable weight to the base case in assessing the potential cost-effectiveness: an optimistic and a conservative scenario. Table 6.32 and Table 6.33 show the differences

Table 6.32. Key assumptions for main scenarios in all patients with dementia

Parameter	Base Case	Optimistic Scenario	Conservative Scenario
OS Distribution	Gompertz	Gompertz	Loglogistic
IFS Distribution	Generalised Gamma	Weibull	Generalised Gamma
All-cause mortality adjusted applied from:	Median Follow-Up (70 months)	75th Percentile (97 months)	From Baseline
Include QoC Benefit on IFS	No	Yes	No
Additional QOF points for comorbid dementia	3	1	5
Benefits of diabetes training are applied to patients meeting:	'Diabetes Knowledge' indicator	'Diabetes Knowledge' indicator	'Diabetes Training' indicator
Cognitive function score for severe dementia	10	12	7

in assumptions between the three scenarios. Results for all three scenarios are presented probabilistically, including mean sampled values and credible intervals, as well as cost-effectiveness acceptability curves (CEAC). Deterministic (one-way) sensitivity analyses (DSA) have also been conducted for all three scenarios, with results presented on tornado plots, to assess the influence of uncertainty in individual parameter estimates on the cost-effectiveness.

In addition, several further scenarios were considered in deterministic analyses, as mentioned throughout this chapter. In summary, these were:

- Time horizons of 5 and 30 years
- Discount rates of 1.5% for costs, outcomes, or both
- ELSA data to inform the utility value for in the institutionalised health state
- Using utility values from Anderson *et al.* (2004)[291] to inform both health states
- Using the loglogistic distribution for overall survival
- Using the Weibull distribution for institutionalisation-free survival
- Including a benefit of care quality on institutionalisation-free survival
- Assuming a higher baseline rate of diabetes training due to its current inclusion in the QOF for incident cases
- Assuming on 80% of patients improve their knowledge about managing their diabetes as a result of receiving self-management training
- Considering different numbers of QOF points for the comorbidity reimbursement for patients with dementia (0, 1, 3, 5, 10, 20, or 30)
- Awarding half the points for the new indicators not currently included in the QOF (i.e., five points for Diabetes Training instead of 11, and one point for Osteoporosis Supplements instead of three)

Table 6.33. Key assumptions for main scenarios in patients with mild or moderate dementia

Parameter	Base Case	Optimistic Scenario	Conservative Scenario
OS Distribution	Gompertz	Loglogistic	Gompertz
IFS Distribution	Generalised Gamma	Generalised Gamma	Weibull
All-cause mortality adjusted applied from:	Median Follow-Up (70 months)	75th Percentile (97 months)	From Baseline
Include QoC Benefit on IFS	No	Yes	No
Additional QOF points for comorbid dementia	3	1	5
Benefits of diabetes training are applied to patients meeting:	'Diabetes Knowledge' indicator	'Diabetes Knowledge' indicator	'Diabetes Training' indicator
Cognitive function score for severe dementia	10	7	12
PRIDE Intervention: duration of accumulating benefits of cognitive stimulation	6	12	2
PRIDE Intervention: duration of effect from cognitive stimulation	3	3	2
PRIDE Intervention: duration of convergence period from cognitive stimulation benefit	6	15	1
PRIDE Intervention: initial uptake in exercise	75%	95%	40%
PRIDE Intervention: annual exercise discontinuation rate	12.5	0%	25%
PRIDE Intervention: patients increasing social engagement	85%	100%	60%
PRIDE Intervention: magnitude of social engagement increase	1	1.5	1

Additional scenarios were explored related to the efficacy of the PRIDE intervention, namely:

- Optimistic benefits of the "keeping mentally active" component in that the intervention period (duration of improving cognitive function) was 12 months long, the follow-up phase was still three months, but the convergence phase lasted nine months (benefits reduced to null by month 24)
- Conservative benefits of the "keeping mentally active" component in that the intervention period was two months (duration of follow-up with facilitator), the follow-up phase was also two months, and the convergence phase was only one month (benefits reduced to null by month five)
- Optimistic benefits of the "keeping physically active" component in that 95% of patients receiving the intervention engage in regular physical activity and only discontinue this due to age/frailty and not due to lack of motivation
- Conservative benefits of the "keeping physically active" component where only 40% engage in regular physical activity, with a surplus discontinuation rate over age-related causes of 25% per year
- Optimistic benefits of the "keeping socially active" component where 100% of respondents reduce their social isolation (increase social engagement) by

1.5 points (e.g., by 100% joining a club or society, and 50% having regular contact with friends), which is sustained until the respondent reaches a cognitive index score of 7

- Conservative benefits of the "keeping socially active" component where 60% of respondents increase their social engagement by just one points, which is sustained until the respondent reaches a cognitive index score of 12

In the population with mild or moderate dementia, a fully incremental analysis has been conducted to ascertain whether, based on this early evidence, certain strategies show more promise of being cost-effective through dominating or extendedly dominating others.

Despite one of the potential objectives and use of these results to be to determine whether further research should be conducted, value of information analyses are not included in the results. Value of information analyses are often used to quantify the potential financial loss of imperfect information which may lead to an incorrect reimbursement decision being made, and thereby estimate the value of conducting additional research. The expected value of perfect information (EVPI) is now a recommended reporting requirement for health technology assessment in the Netherlands.[320] Whilst the EVPI or EVPPI (expected value of partial perfect information – the value of uncertainty associated with a subset of parameters, for example treatment effects) can establish a cost of information, and can further be used to estimate the value of collecting further data (the expected value of sampling; EVSI) they are limited by their inputs. Value of information analyses are informed by the probabilistic sensitivity analysis. The EVPI is estimated as the difference between the expected net monetary benefit from the modelled "best" intervention in each iteration of the PSA and the expected net monetary benefit of the "best" overall treatment (which treatment is cost-effective in most iterations). Therefore, results are contingent on the amount of parameter uncertainty captured within the PSA. In previous work I have demonstrated that inferences from probabilistic analyses, such as the CEAC, can be influenced as much by structural uncertainty as by parameter uncertainty. Models that do not explicitly capture the correlation between intermediate endpoints and long-term outcomes, or include two endpoints extrapolated independently of each other, can overinflate the sampled uncertainty in the model leading to a lower probability of being cost-effective (and an increased EVPI) compared to model structures that explicitly account for correlation between inputs.[321] Therefore, a single estimate of the value of uncertainty is likely to be practically uninformative. Given that, due to the data restrictions, this model includes various factors which are not explicitly correlated

in their extrapolation (e.g., institutionalisation, survival, cognitive function, IADLs), the EVPI would not reflect parameter uncertainty alone and would not express the value of improving information in a practical sense. However, more data may permit alternative model structures (e.g., discrete event simulation) which could more accurately reflect the parameter uncertainty and therefore benefits of data collection may be two-fold.

A full list of parameter values and the ranges sampled in sensitivity analyses, along with assumptions on parameter values, can be found in Appendix 6.2.

6.9. Results

All Dementia Severities

Main Results

Due to the many assumptions associated with the parameter estimates in the model, a representation of the uncertainty is considered as a core part of the analysis. As a result, the main analyses presented are those from probabilistic sampling of the parameter values. The cost-effectiveness results of the base case, optimistic, and conservative scenarios though 5,000 simulations each are presented in Table 6.34 and Table 6.35.

Expanding the QOF scheme to include reimbursement for specific targets in patients with dementia is likely to improve survival and QALY gains for patients with dementia. In all three scenarios health outcomes were improved, with the credible intervals not crossing the zero. Costs were also increased on average, with the largest

Table 6.34. Modelled discounted outcomes for all patients with dementia for the base case analysis

Outcome	Treatment as Usual	Expanded QOF Scheme
Life Years	7.32	7.44
Incremental Life Years (95% CrI) vs. TAU	-	0.12 (0.02 to 0.26)
QALYs, Pre-Institutionalisation	4.35	4.38
QALYs, Living in Institution	0.16	0.18
QALYs, Comorbid Condition-Related Morbidity	-0.08	-0.08
Total QALYs	4.43	4.48
Incremental QALYs (95% CrI) vs. TAU	-	0.05 (0.00 to 0.14)
Average QOF Cost per Dementia Patient	£ 52	£ 693
Costs of Comorbidity-Related Care	£ 7,340	£ 7,325
Costs of Dementia-Related Care	£ 86,666	£ 88,500
Other Home Help / Social Care Costs	£ 1,865	£ 1,868
Total Costs (95% CrI)	£ 100,715	£ 103,144
Incremental Costs (95% CrI) vs. TAU	-	£ 2,429 (387 to 5,562)
Incremental Cost-Effectiveness Ratio vs. TAU (95% CrI)	**-**	**£ 49,460 (8,760 to 268,884)**

Abbreviations: CrI, credible interval; QALYs, quality-adjusted life years; TAU, treatment as usual

Table 6.35. Comparison of base case, optimistic, and conservative scenarios for an expanded QOF scheme for all patients dementia showing mean incremental results and 95% credible intervals compared to treatment as usual

Outcome	Base Case	Optimistic Scenario	Conservative Scenario
Incremental Life Years (95% CrI) vs. TAU	0.12 (0.02 to 0.26)	0.14 (0.03 to 0.30)	0.11 (0.02 to 0.26)
Incremental QALYs (95% CrI) vs. TAU	0.05 (0.00 to 0.14)	0.06 (0.01 to 0.15)	0.04 (0.00 to 0.13)
Incremental Costs (95% CrI) vs. TAU	£ 2,429 (387 to 5,562)	£ 2,093 (-182 to 5,512)	£ 2,776 (688 to 5,970)
ICER vs. TAU† (95% CrI)	£ 49,460 (8,760 to 268,884)	£ 32,644 (-10,398 to 162,818)	£ 62,758 (14,468 to 335,934)
Probability Cost-Effective at £20,000 per QALY	11.1%	27.3%	4.6%
Probability Cost-Effective at £30,000 per QALY	22.5%	48.1%	11.3%

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years; TAU, treatment as usual.

† ICER derived from posterior means of the sampled costs and QALYs, with credible intervals reported from percentiles of individually sampled ICERs.

proportion of additional costs being attributable to the care of dementia (health and social care) accrued with the additional survival. In the optimistic scenario, it was identified that there may be the potential for the intervention to be cost saving. However, across all three scenarios the modelled mean incremental cost-effectiveness ratio (ICER) was typically above levels considered cost-effective in England (£20,000 to £30,000 per QALY). As can be seen from the CEACs in Figure 6.15, the expanded QOF scheme only has the highest probability of being cost-effective above a willingness-to-pay (WTP) for one additional QALY of between approximately £30,000 to £75,000, depending on the scenario.

Deterministic Sensitivity Analyses

The results for the 12 variables with the greater impact on the net monetary benefit in the deterministic sensitivity analyses for the base case, optimistic scenario, and conservative scenario are shown in Figure 6.16. Out of the variables shown, those which consistently have a large impact on the results were the benefit of care quality on survival, the utility for the post-institutionalisation health state and the longer-term costs of care for those who had received training to self-manage their diabetes. A lower cost of care for these patients was the only variable shown to make the broader QOF scheme cost-effective at £30,000 per QALY in the base case. The parameter uncertainty associated with the benefits of inclusion in the QOF scheme or the points attributable to the indicator on care quality were not associated with substantial variation in results.

Figure 6.15. Cost-effectiveness acceptability curve for the base case scenario for all patients with dementia in the base case (top), optimistic scenario (middle), and conservative scenario (bottom)

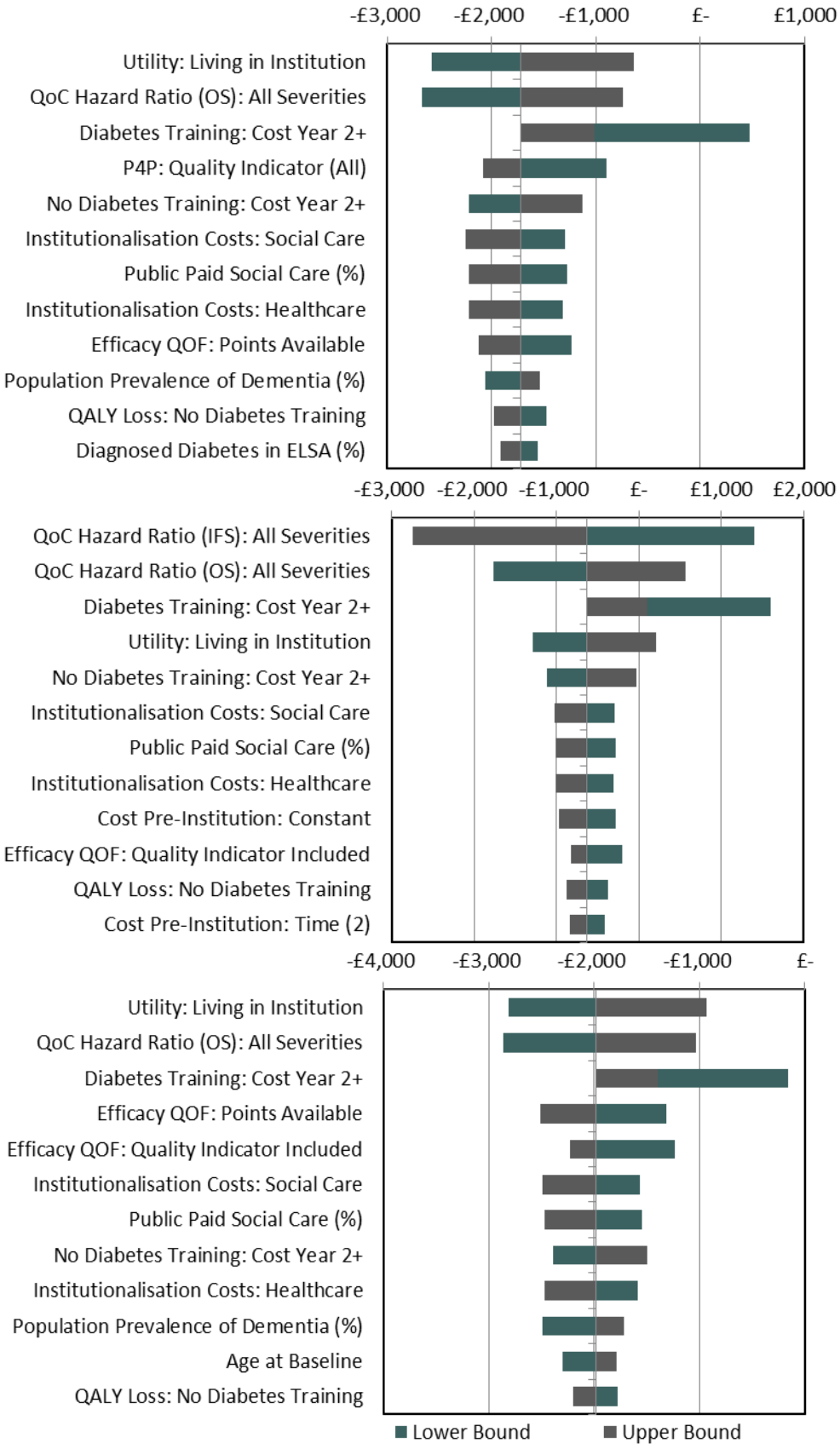

Figure 6.16. Tornado plots showing the impact of individual parameter uncertainty on the incremental net monetary benefit (at £30,000 per QALY) of an expanded QOF scheme for all patients with dementia in the base case (top), the optimistic scenario (middle), and the conservative scenario (bottom)

Scenario Analyses

In the additional scenarios considered, only four were considered to have a substantial impact on the ICER. Two of these were related to utilities, consistent with the findings of the DSA. A higher utility post-institutionalisation using the ELSA data improved the ICER given the survival benefits associated with care quality. In addition, using utilities from the literature that were lower overall, but had less difference between the pre- and post-institutionalisation health states served to reduce the ICER. Given the higher utility in the pre-institutionalisation state, extending the time in this health state also reduces the ICER, and therefore including a benefit of care quality on institutionalisation-free survival lowered the ICER by 37%. Improving overall care quality in the treatment as usual arm by assuming that more patients had previously received training to self-manage their diabetes due to the indicator currently in the QOF increased the ICER. Other scenarios, except changing the discount rates, had limited impact on the results. Note that the deterministic ICER for the base case is greater than the probabilistic ICER as the relationship between costs and effects is non-linear and mean values are lower.

Table 6.36. Deterministic scenario analyses assessing the impact on the ICER of an expanded pay-for-performance scheme for all patients with dementia

Scenario	QALYs		Costs		ICER	Difference
	TAU	P4P	TAU	P4P		vs. Base Case
Base Case	4.41	4.45	£ 100,569	£ 103,505	£ 72,669	-
Time Horizon: 5 years	2.25	2.27	£ 48,167	£ 49,031	£ 72,875	+0%
Time Horizon: 30 years	4.45	4.49	£ 102,816	£ 105,819	£ 72,988	+0%
Discount Rate (Costs): 1.5%	4.41	4.45	£ 113,245	£ 116,648	£ 84,203	+16%
Discount Rate (Health Effects): 1.5%	4.91	4.96	£ 100,789	£ 103,731	£ 62,835	-14%
Discount Rate (Costs & Effects): 1.5%	4.91	4.96	£ 113,488	£ 116,896	£ 72,801	+0%
Utility (Institutionalised): ELSA	4.57	4.65	£ 100,569	£ 103,505	£ 38,181	-47%
Utilities: Andersen 2004	4.21	4.27	£ 100,569	£ 103,505	£ 44,963	-38%
OS Distribution: Loglogistic	4.44	4.48	£ 102,751	£ 105,443	£ 73,287	+1%
IFS Distribution: Gompertz	4.40	4.44	£ 100,628	£ 103,561	£ 72,596	-0%
QoC Benefit on IFS	4.41	4.46	£ 100,569	£ 103,034	£ 45,492	-37%
Diabetes Training in Current QOF	4.43	4.45	£ 102,156	£ 103,472	£ 91,993	+27%
Diabetes Benefits Only for Those Receiving Training	4.40	4.44	£ 100,571	£ 103,509	£ 73,135	+1%
Knowledge Conversion of Training: 80%	4.41	4.44	£ 100,569	£ 103,341	£ 73,966	+2%
Half Points Available for New Indicators	4.41	4.44	£ 100,569	£ 103,281	£ 70,095	-4%

Abbreviations: ICER, incremental cost-effectiveness ratio; IFS, institutionalisation-free survival; OS, overall survival; P4P, pay-for-performance (the Quality and Outcomes Framework [QOF]); QALYs, quality-adjusted life years; QoC, quality of care; TAU, treatment as usual.

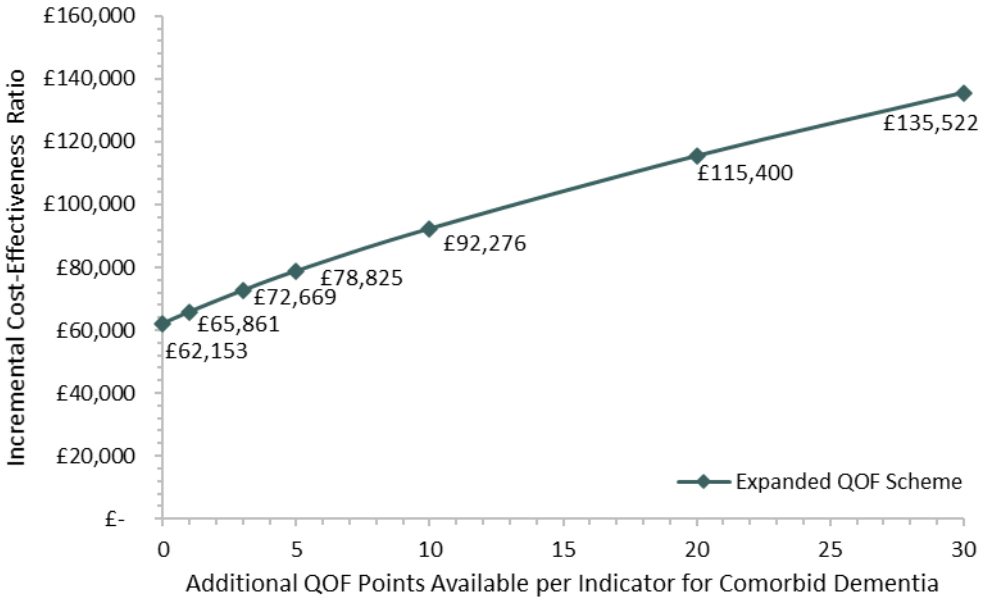

Figure 6.17. Association between the number of additional points (and reimbursement attainable) added to QOF indicators for managing comorbidities in all patients with dementia

The number of points available, and therefore the reimbursement attainable, for comorbid dementia for each quality indicator include in the QOF was positively correlated with the ICER. Lower number of points available decrease the ICER, though the marginal benefits exceed the marginal costs as the number of points increase, hence the declining gradient in Figure 6.17.

Mild or Moderate Dementia

Main Results

The results for patients with mild or moderate dementia are also presented as the mean values of probabilistic sampling of 5,000 simulations for the base case, optimistic, and conservative scenarios in Table 6.37 and Table 6.38. All three intervention strategies improved survival and QALYs gained, with the 95% credible intervals of the incremental gains for all treatments not crossing zero. Costs and QALY detriments due to morbidity associated with comorbidities were not reduced with the interventions as prolonged survival increased the overall lifetime probability of an event. Again, overall costs were increased due to the health and social care associated with dementia accrued with the additional survival.

There was evidence in the optimistic scenario that both the expanded QOF scheme and the PRIDE intervention had the potential to be cost saving, but not when combined, though all three interventions may be cost-effective compared to treatment as usual at £20,000 per QALY in the optimistic scenario. The PRIDE intervention was

considered cost-effective in all three scenarios. Interestingly, the lowest observed ICER for this intervention was in the conservative scenario. Although benefits were minimised in this scenario, with a limited impact on cognitive function, the high costs avoided with prolonged survival made these small short-term gains cost-effective.

In the base case, fully incremental analysis shows that whilst the expanded QOF scheme is the cheapest of the new intervention strategies, it is extendedly dominated by the PRIDE intervention (see Table 6.39 and Figure 6.18). In this analysis, it is also demonstrated that were the PRIDE intervention available, combining this with an expanded QOF scheme for patients with dementia would produce ICERs above what are typically considered cost-effective in the UK. However, in the optimistic scenario the combined scheme may still be cost-effective. In all three scenarios, an expanded QOF scheme was extendedly dominated. This is supported by the CEACs in **Error! R eference source not found.**, where between a willingness-to-pay of £20,000 to £30,000 per QALY, the PRIDE intervention has the highest probability of being cost-effective.

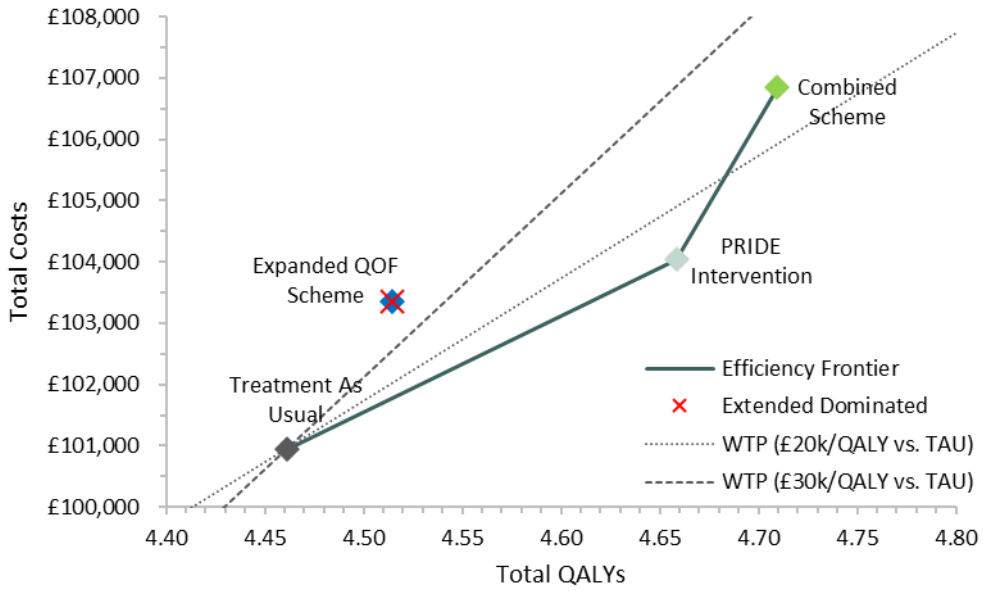

Figure 6.18. Fully incremental cost-effectiveness plane showing intervention and policy options for patients with mild or moderate dementia and at least one comorbid condition (base case)

Table 6.37. Modelled discounted outcomes for patients with mild or moderate dementia showing probabilistic means and 95% credible intervals for the base case analysis

Outcome	Treatment as Usual	Expanded QOF Scheme	PRIDE Intervention	Combined Scheme
Life Years	7.51	7.63	7.78	7.90
Incremental Life Years (95% CrI) vs. TAU	-	0.12 (0.02 to 0.26)	0.27 (0.07 to 0.52)	0.39 (0.16 to 0.67)
QALYs, Pre-Institution	4.43	4.46	4.61	4.63
QALYs, Living in Institution	0.12	0.14	0.14	0.16
QALYs, Comorbidity-Related	-0.08	-0.08	-0.09	-0.09
Total QALYs	4.46	4.51	4.66	4.71
Incremental QALYs (95% CrI) vs. TAU	-	0.05 (0.01 to 0.14)	0.20 (0.07 to 0.37)	0.25 (0.10 to 0.45)
Average QOF Cost per Dementia Patient	£ 53	£ 792	£ 56	£ 949
PRIDE Intervention Costs	£ 0	£ 0	£ 151	£ 151
Costs of Comorbidity-Related Care	£ 7,676	£ 7,667	£ 7,834	£ 7,984
Costs of Dementia-Related Care	£ 86,556	£ 88,272	£ 89,391	£ 91,180
Other Home Help / Social Care Costs	£ 1,917	£ 1,925	£ 1,942	£ 1,951
Total Costs	£ 100,942	£ 103,360	£ 104,036	£ 106,843
Incremental Costs (95% CrI) vs. TAU	-	£ 2,418 (645 to 5,203)	£ 3,095 (2 to 7,453)	£ 5,901 (2,154 to 11,131)
Incremental Cost-Effectiveness Ratio vs. TAU[†] (95% CrI)	**-**	**£ 45,109 (18,245 to 255,947)**	**£ 15,658 (131 to 40,752)**	**£ 23,728 (11,369 to 58,369)**

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years; TAU, treatment as usual.

[†] ICER derived from posterior means of the sampled costs and QALYs, with credible intervals reported from percentiles of individually sampled ICERs.

Table 6.38. Comparison of base case, optimistic, and conservative scenarios for patients with mild or moderate dementia showing mean incremental results and 95% credible intervals compared to treatment as usual

Outcome	Expanded QOF Scheme			PRIDE Intervention			Combined Scheme		
	Base Case	Optimistic	Conservative	Base Case	Optimistic	Conservative	Base Case	Optimistic	Conservative
Incremental Life Years	0.12 (0.02 to 0.26)	0.13 (0.02 to 0.28)	0.12 (0.02 to 0.28)	0.27 (0.07 to 0.52)	0.48 (0.16 to 0.85)	0.04 (0.00 to 0.13)	0.39 (0.16 to 0.67)	0.59 (0.26 to 0.99)	0.18 (0.04 to 0.39)
Incremental QALYs	0.05 (0.01 to 0.14)	0.07 (0.01 to 0.16)	0.05 (0.00 to 0.14)	0.20 (0.07 to 0.37)	0.36 (0.16 to 0.61)	0.05 (0.00 to 0.11)	0.25 (0.10 to 0.45)	0.42 (0.21 to 0.68)	0.10 (0.03 to 0.23)
Incremental Costs	£ 2,418 (645 to 5,203)	£ 1,631 (-106 to 5,042)	£ 2,136 (425 to 5,064)	£ 3,095 (2 to 7,453)	£ 4,784 (-752 to 10,757)	£ 194 (-988 to 1,561)	£ 5,901 (2,154 to 11,131)	£ 6,528 (630 to 13,082)	£ 3,735 (1,025 to 7,692)
ICER†	£ 32,901 (14,973 to 212,783)	£ 19,545 (-16,680 to 99,524)	£ 33,656 (16,343 to 319,602)	£ 15,658 (131 to 40,752)	£ 13,228 (-2,415 to 32,996)	£ 4,078 (-28,978 to 37,357)	£ 23,728 (11,369 to 58,369)	£ 15,472 (1,732 to 36,098)	£ 36,116 (13,263 to 110,441)

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years; TAU, treatment as usual.

† ICER derived from posterior means of the sampled costs and QALYs, with credible intervals reported from percentiles of individually sampled ICERs.

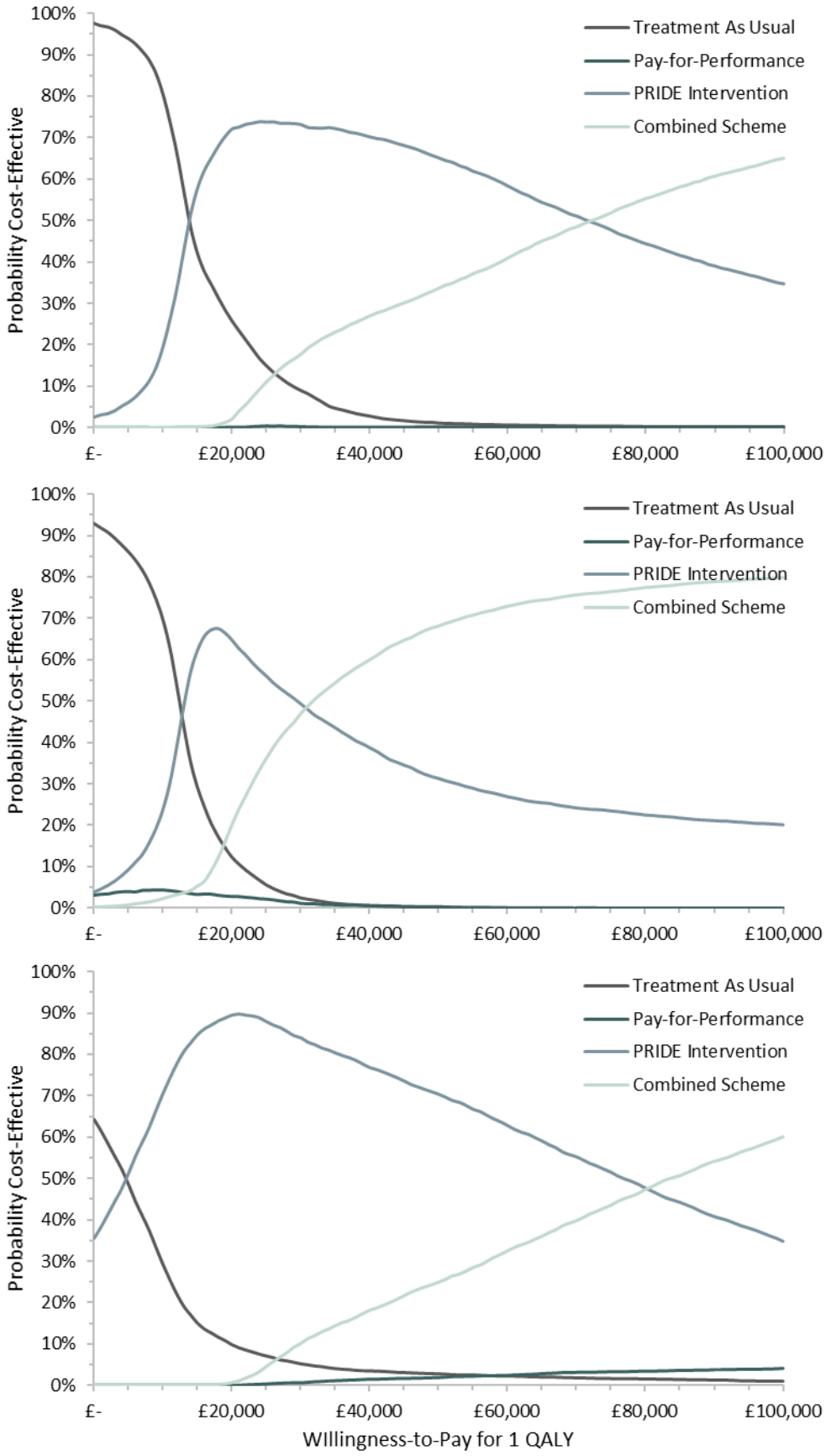

Figure 6.19. Cost-effectiveness acceptability curve for the base case scenario for patients with mild or moderate dementia in the base case (top), optimistic (middle), and conservative scenarios (bottom)

Table 6.39. Fully incremental cost-effectiveness analysis for patients with mild or moderate dementia and at least one comorbid condition

Intervention	Total Costs	Total QALYs	Incremental Costs	Incremental QALYs	ICER
Base Case					
Treatment as Usual	£ 100,942	4.46			
Expanded QOF Scheme	£ 103,360	4.51	£ 2,418	0.05	Extended Dominated
PRIDE Intervention	£ 104,036	4.66	£ 3,095	0.20	£ 15,658
Combined Scheme	£ 106,843	4.71	£ 2,806	0.05	£ 54,984
Optimistic Scenario					
Treatment as Usual	£ 104,692	4.63			
Expanded QOF Scheme	£ 106,323	4.70	£ 1,631	0.07	Extended Dominated
PRIDE Intervention	£ 109,476	5.00	£ 4,784	0.36	£ 13,228
Combined Scheme	£ 111,219	5.06	£ 1,743	0.06	£ 28,961
Conservative Scenario					
Treatment as Usual	£ 101,792	4.40			
PRIDE Intervention	£ 101,986	4.44	£ 194	0.05	£ 4,078
Expanded QOF Scheme	£ 104,743	4.44	£ 2,758	0.00	Extended Dominated
Combined Scheme	£ 105,527	4.50	£ 3,541	0.06	£ 63,369

Notes: Where a treatment is dominated or extended dominated, interventions lower in the table are compared to the last included intervention.

Deterministic Sensitivity Analyses

Figure 6.20 to 6.22 show the variables with greatest impact on the net monetary benefit for each intervention in the base case, optimistic scenario, and conservative scenario. As with the population irrespective of severity, the post-institutionalisation utility and the survival benefit associated with care quality had a significant impact on the results for the expanded QOF scheme. The impact of factors of the QOF scheme also had a large impact on results. Factors influencing the estimation of the per patient cost of the QOF, such as prevalence in patients with comorbid diabetes in dementia versus the prevalence of diabetes in the general population, also had a noticeable impact on the net monetary benefit of the QOF.

For the PRIDE intervention and the combined scheme, the impact of cognitive function on institutionalisation-free survival and care quality were key drivers of results, as well as factors associated with the magnitude of gains in cognitive function. Utilities were also a key driver for these interventions.

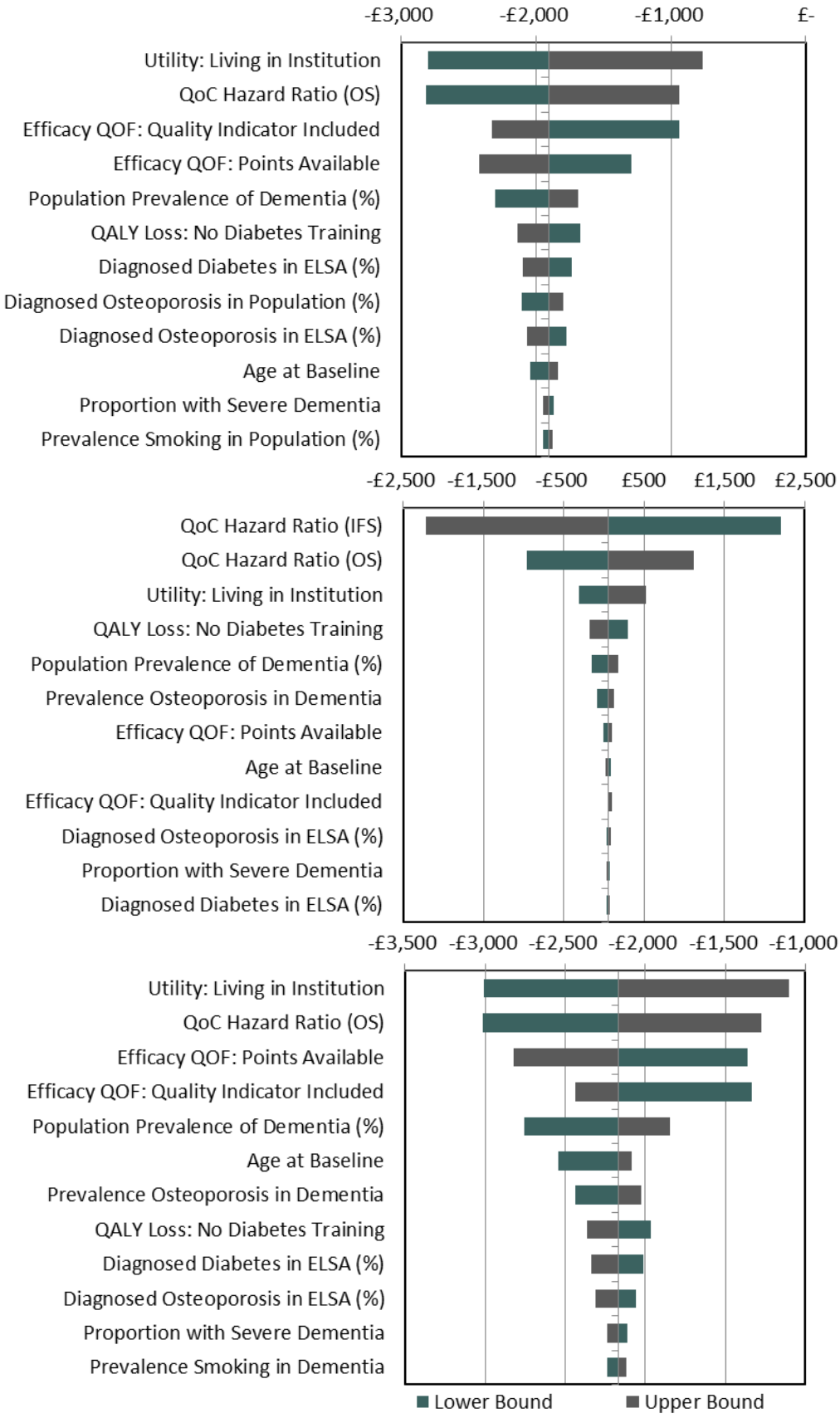

Figure 6.20. Tornado plots showing the impact of individual parameter uncertainty on the incremental net monetary benefit (at £30,000 per QALY) of an expanded QOF scheme for patients with mild or moderate dementia in the base case (top), the optimistic scenario (middle), and the conservative scenario (bottom)

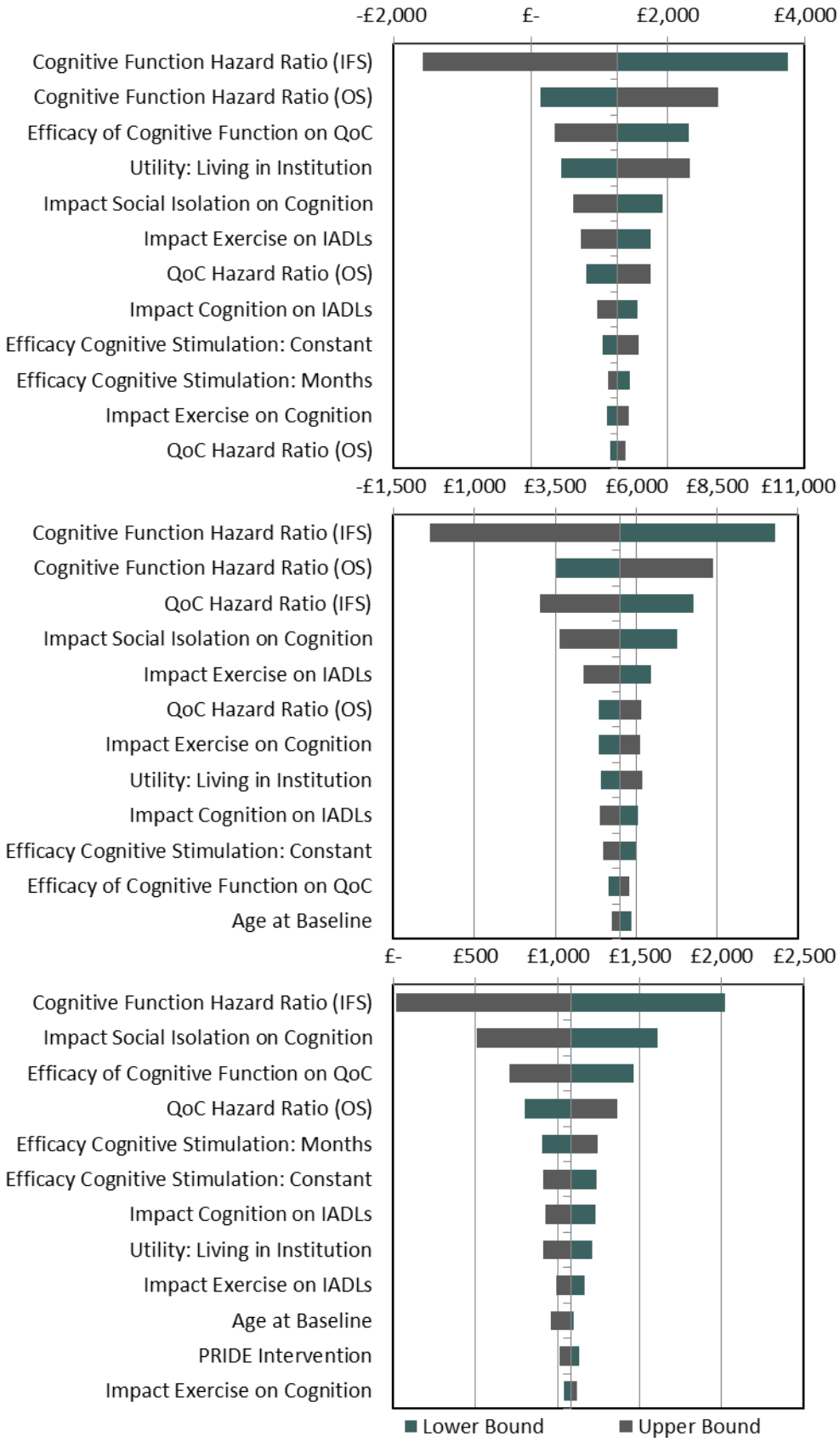

Figure 6.21. Tornado plots showing the impact of individual parameter uncertainty on the incremental net monetary benefit (at £30,000 per QALY) of the PRIDE intervention for patients with mild or moderate dementia in the base case (top), the optimistic scenario (middle), and the conservative scenario (bottom)

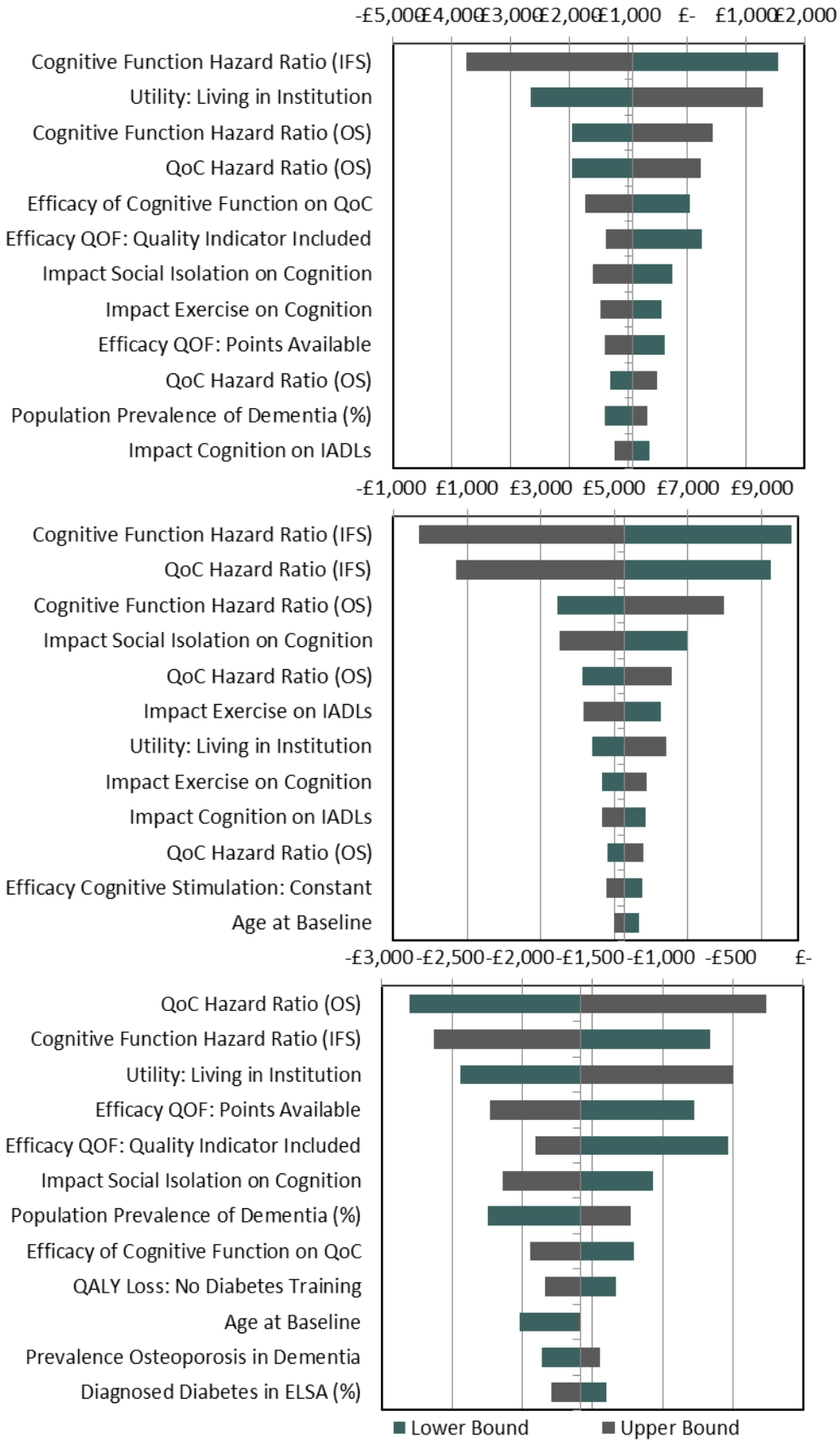

Figure 6.22. Tornado plots showing the impact of individual parameter uncertainty on the incremental net monetary benefit (at £30,000 per QALY) of the PRIDE intervention combined with an expanded QOF scheme for patients with mild or moderate dementia in the base case (top), the optimistic scenario (middle), and the conservative scenario (bottom)

Scenario Analyses

The results from the additional scenario analyses for patients with mild or moderate dementia are presented in Table 6.40. For the expanded QOF scheme, the same four scenarios showed the greatest impact on results as in the population with all dementia severities. The different utility scenarios and including an improvement in institutionalisation-free survival associated with care quality were also observed to have quite a substantial effect on the results for the PRIDE intervention as well as the combined scheme. Those interventions including the PRIDE programme were also sensitive to the parameters used to define the benefits, such as the durations of the intervention, follow-up, and convergence phases of cognitive stimulation training, and the parameters defining physical activity uptake and maintenance. Shorter time horizons also benefitted the PRIDE intervention given the relative magnitude of the short-term gains in institutionalisation-free survival, without accruing the costs associated with long-term survival in advanced dementia.

The number of QOF points attributable to comorbid dementia for each quality indicator was positively correlated with the ICER for both the combined scheme and the QOF scheme alone. As can be seen from Figure 6.23, the addition of the PRIDE intervention to the QOF scheme alone reduces the ICER. At least 24 comorbidity points would have to be awarded in conjunction with the PRIDE intervention before it would be more cost-effective to have a low or zero-point QOF scheme as the sole intervention.

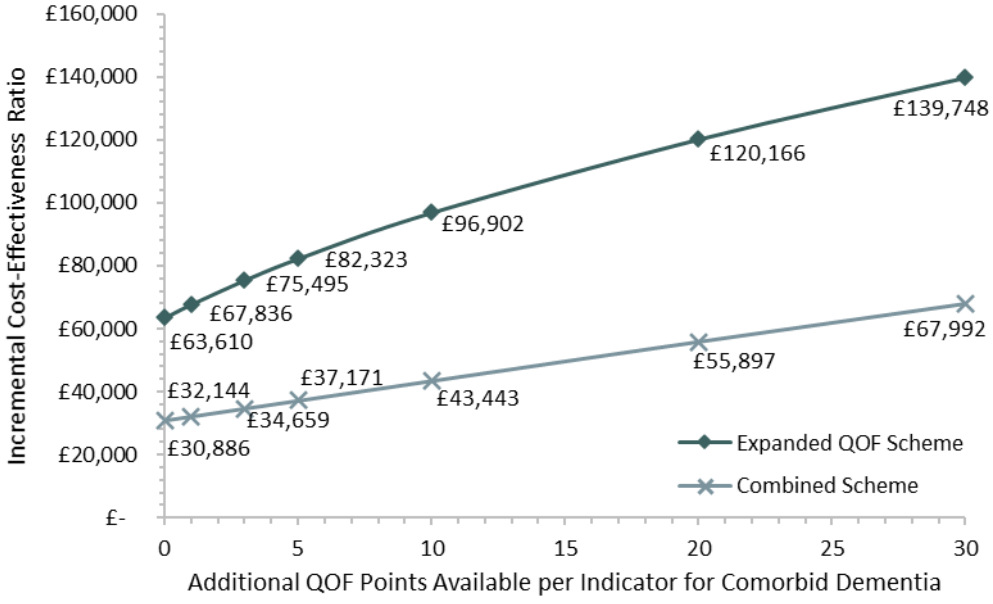

Figure 6.23. Association between the number of additional points (and reimbursement attainable) added to QOF indicators for managing comorbidities in patients with mild or moderate dementia

Table 6.40. Deterministic scenario analyses assessing the impact on the ICER of an expanded pay-for-performance scheme for patients with mild or moderate dementia

Scenario	Treatment as Usual		Expanded QOF Scheme				PRIDE Intervention				Combined Scheme			
	QALYs	Costs	QALYs	Costs	ICER	ΔICER	QALYs	Costs	ICER	ΔICER	QALYs	Costs	ICER	ΔICER
Base Case	4.45	£ 100,450	4.49	£ 103,622	£ 75,164	-	4.62	£ 104,241	£ 22,473	-	4.66	£ 107,733	£ 34,377	-
Time Horizon: 5 years	2.24	£ 46,959	2.25	£ 47,909	£ 76,243	+1%	2.32	£ 47,834	£ 11,690	-48%	2.33	£ 48,910	£ 22,436	-35%
Time Horizon: 30 years	4.50	£ 102,767	4.54	£ 106,011	£ 75,492	+0%	4.67	£ 106,670	£ 22,861	+2%	4.71	£ 110,241	£ 34,806	+1%
Discount Rate (Costs): 1.5%	4.45	£ 113,339	4.49	£ 117,012	£ 87,026	+16%	4.62	£ 117,795	£ 26,413	+18%	4.66	£ 121,830	£ 40,080	+17%
Discount Rate (Health Effects): 1.5%	4.97	£ 100,690	5.02	£ 103,868	£ 65,011	-14%	5.16	£ 104,492	£ 19,965	-11%	5.21	£ 107,990	£ 30,346	-12%
Discount Rate (Costs & Effects): 1.5%	4.97	£ 113,604	5.02	£ 117,282	£ 75,264	+0%	5.16	£ 118,071	£ 23,461	+4%	5.21	£ 122,113	£ 35,375	+3%
Utility (Institutionalised): ELSA	4.55	£ 100,450	4.63	£ 103,622	£ 40,456	-46%	4.75	£ 104,241	£ 18,748	-17%	4.83	£ 107,733	£ 25,826	-25%
Utilities: Andersen 2004	4.31	£ 100,450	4.38	£ 103,622	£ 46,435	-38%	4.50	£ 104,241	£ 20,171	-10%	4.57	£ 107,733	£ 28,283	-18%
OS Distribution: Loglogistic	4.49	£ 103,011	4.52	£ 105,828	£ 76,481	+2%	4.64	£ 105,906	£ 18,724	-17%	4.68	£ 109,046	£ 31,368	-9%
IFS Distribution: Gompertz	4.44	£ 100,539	4.48	£ 103,708	£ 75,085	-0%	4.61	£ 104,357	£ 22,752	+1%	4.65	£ 107,845	£ 34,630	+1%
QoC Benefit on IFS	4.45	£ 100,450	4.51	£ 102,874	£ 38,487	-49%	4.63	£ 103,673	£ 17,480	-22%	4.70	£ 106,419	£ 24,004	-30%
Diabetes Training in Current QOF	4.48	£ 102,137	4.49	£ 103,586	£ 98,899	+32%	4.62	£ 104,235	£ 14,868	-34%	4.66	£ 107,666	£ 29,997	-13%
Diabetes Benefits Only for Those Receiving Training	4.45	£ 100,453	4.49	£ 103,626	£ 75,579	+1%	4.62	£ 104,243	£ 22,443	-0%	4.66	£ 107,736	£ 34,382	+0%
Knowledge Conversion of Training: 80%	4.45	£ 100,450	4.49	£ 103,450	£ 76,570	+2%	4.62	£ 104,216	£ 22,382	-0%	4.66	£ 107,725	£ 34,363	-0%
Half Points Available for New Indicators	4.45	£ 100,450	4.49	£ 103,369	£ 72,368	-4%	4.62	£ 104,241	£ 22,473	-	4.66	£ 107,497	£ 33,443	-3%
Optimistic Cognitive Stimulation Gains	4.45	£ 100,450	4.49	£ 103,622	£75,164	-	4.69	£ 107,172	£ 27,491	+22%	4.73	£ 110,343	£ 35,029	+2%
Conservative Cognitive Stimulation Gains	4.45	£ 100,450	4.49	£ 103,622	£75,164	-	4.54	£ 100,593	£ 1,564	-93%	4.59	£ 104,379	£ 28,239	-18%
Optimistic Physical Activity Uptake	4.45	£ 100,450	4.49	£ 103,622	£75,164	-	4.66	£ 104,442	£ 18,703	-17%	4.70	£ 107,886	£ 29,101	-15%
Conservative Physical Activity Uptake	4.45	£ 100,450	4.49	£ 103,622	£75,164	-	4.57	£ 103,795	£ 26,680	+19%	4.62	£ 107,357	£ 40,646	+18%
Optimistic Social Isolation Reductions	4.45	£ 100,438	4.49	£ 103,610	£75,164	-	4.65	£ 104,534	£ 20,592	-8%	4.69	£ 107,971	£ 31,299	-9%
Conservative Social Isolation Reductions	4.45	£ 100,459	4.49	£ 103,631	£75,164	-	4.61	£ 104,158	£ 23,482	+4%	4.65	£ 107,669	£ 35,832	+4%

Abbreviations: ICER, incremental cost-effectiveness ratio; IFS, institutionalisation-free survival; OS, overall survival; P4P, pay-for-performance (the Quality and Outcomes Framework [QOF]); QALYs, quality-adjusted life years; QoC, quality of care; TAU, treatment as usual.

6.10. VALIDATION

The model was validated through a multistep process to verify the structure and underlying modelling and economic assumptions. This involved debugging and a quality check, along with a comparison of results with external data and models.

A technical validation of model functionalities and calculations upon completion of the final model. This involved checking inputs into the model against sources, ensuring the first three rows of any columns of formulae were correctly inputted and appropriately copied down to the rest of the column, and line-by-line debugging of any code programmed in Visual Basic for Applications (VBA), as well as running a series of logical checks on the deterministic base case. Any errors or discrepancies were rectified. The logical checks included:

- Setting the discount rates to 0% to see if discounted results equate to undiscounted results
- Setting all hazard ratios equal to 1 to ensure survival outcomes are equal between arms
- Setting all odds ratios for care quality equal to 1 to ensure care quality is equal between arms
- Setting all utilities equal to 1 and disutilities due to comorbidities to 0 to ensure QALYs gained equal life years gained
- Setting costs in each category to null to ensure calculated totals for each category are also zero
- Manually calculate upper and lower bound results for parameters shown in Tornado diagrams to ensure results align with those calculated in the DSA

With regards to cross validation of results with previous models, given that no previous models have evaluated the same interventions in the same population making comparisons is challenging. The key previous model utilising time to institutionalisation and survival as the efficacy parameters was NICE TA217. As can been seen from Table 6.41, despite a marginally shorter time since diagnosis in the ELSA data, the overall survival and institutionalisation-free survival free estimates in

Table 6.41. Comparison of survival estimates between treatment as usual in patients with mild or moderate dementia and those from NICE TA217

Model Results	NICE TA217	Treatment as Usual
Time Since Diagnosis, Mean (years)	4.9	4.3
Institutionalisation-Free Survival, Mean (years)	2.7[†]	7.1
Overall Survival, Mean (years)	3.5	7.5

[†] Results reported as 29.2 months, however only 90% of cohort started the model in the pre-institutionalisation health state and so this was uprated accordingly for the comparison.

the current model are still substantially longer. The model in TA217 aimed to appraise the cost-effectiveness of AChEIs for Alzheimer's disease but didn't include a benefit on survival for treatment, however studies on the survival in dementia since the availability of AChEIs have demonstrated increases in survival that are not purely attributable to time and general health improvements.[322] Therefore, survival may be longer than in TA217, though it is unclear if the extent of increase is valid. Whilst extrapolation methods are appropriate given the ELSA data, this casts doubt on the generalisability of results to other patients with dementia.

Other comparisons can be drawn on conclusions of model as opposed to raw results. For example, in the model noted at the start of this chapter which was developed to assess the cost-effectiveness of continuing the QOF, the results assessed the national scheme with a focus on patients with or at risk of cardiovascular disease aged between 40 and 74 years.[158] Whilst the approach and population do not align with this analysis, the authors also found QOF to not be cost-effective. In their analysis, care quality is associated with modest survival gains and morbidity reductions, but substantial costs, aligned with a similar conclusion reached here.

With regards to validation of the assumptions regarding the PRIDE intervention, Knapp and colleagues conducted a cost-effectiveness analysis alongside a clinical trial of a cognitive stimulation intervention.[323] As part of this a costing study was conducted which estimated providing sessions to patients with dementia at £90 per four-hour session, which equates to a similar cost per 90-minute session for delivery of the PRIDE intervention. They also demonstrated small reductions in social care costs in the group receiving the intervention, with modest increases in hospital and community health care costs, in line with the current model, which may be attributable to better access to care and care quality as an indirect effect of cognition.

A previous model has evaluated the cost-effectiveness of antihypertensive treatment for patients aged 80 or over in Switzerland.[324] To validate the approach used to estimate the rates of cardiovascular events, results were compared between models. They reported rates of any cardiovascular event of 33.7 per 1,000 person years at risk (PYAR) for those receiving antihypertensive treatment, or 50.6 per 1,000 PYAR for those receiving placebo. Their analysis only included stroke, myocardial infarction, or heart failure and so aggregate estimates of these events were calculated for the current model. The findings in Table 6.42 show comparable rates of events between the studies. The authors also found hypertension treatment to be cost saving across the first two years, at around 35 CHF saved per patient (~£18 at 2019 values). This is in

Table 6.42. Comparison of cardiovascular event rates between the model and Scucz *et al.* (2010)

Treatment	Total CV Events per 1,000 PYAR	Stroke, MI, or Heart Failure per 1,000 PYAR	Proportion Meeting Indicator	Szucs 2010: Weighted Average
Treatment as Usual	53.0	38.1	60.2%	40.4
Expanded QOF Scheme	53.0	38.1	61.3%	40.2
PRIDE Intervention	52.7	37.9	68.5%	39.0
Combined Scheme	52.7	37.9	70.2%	38.7

Abbreviations: CV, cardiovascular; MI, myocardial infarction; PRIDE, PRomoting Independence in DEmentia; PYAR, person-years at risk; QOF, quality and outcomes framework

line with the results observed here, where lifetime costs of hypertension treatment and complications were marginally lower than treatment as usual (between £13 and £113) for the intervention strategies where more patients were receiving antihypertensive treatment.

For patients with osteoporosis, supplementation with calcium and vitamin D has previously been modelled to show small lifetime cost increases in patients aged 70 years at baseline, and modest cost savings for those aged over 80.[278] Given the age at baseline and the prevalence of osteoporosis in this model, the small cost increases observed are somewhat in line with previous results. Likewise, the QALY gains from supplements for osteoporosis were between 0.013 and 0.021 in the previously published model.[278] As only 7% of the modelled cohort here had osteoporosis, and that the maximal increase in uptake of supplements was 48.5% higher than treatment as usual, differences between arms in this model would be expected to be between 0.000 and 0.001 QALYs, as is observed.

6.11. Discussion

Interpretation of the Evidence

Of the evaluated interventions and scenarios, the PRIDE intervention seems the most promising in terms of potential cost-effectiveness. The provisional estimates of the outcomes show that improvements in cognition and health demonstrate gains in survival and prolong the milder phase of dementia where costs of care are lower. Interestingly, the conservative benefit scenario reported the most favourable ICER of the three. It is postulated that given the lower survival benefit associated with cognition and care quality in this scenario, it meant that any extension to life in the most severe state was not modelled to the same extent and the high costs of care associated withs severe dementia were largely avoided. Even in the scenario with the most conversative QALY gains, the PRIDE intervention could have a cost of up to

£908 per patient and still be cost-effective at a WTP of £20,000 per QALY, or over £2,600 per patient in the most optimistic scenario.

Given the extent of the assumptions applied to the costing and efficacy of the PRIDE intervention, the base case, optimistic, and conservative scenarios should all carry equal weight when considering the potential cost-effectiveness. In all three scenarios, the PRIDE intervention had the highest probability of being cost-effective at WTP thresholds for the UK and therefore it is perhaps the preferred target for conducting additional research to validate the assumptions in the model. Should further research be conducted, it is potentially best focussed on how the PRIDE intervention and improvements in cognition and health could delay institutionalisation and increase survival, including these as endpoints for long-term follow-up in the definitive trial of the intervention. In addition, during follow-up, care reviews should be conducted to assess access to services, care quality, and how patients are involved in the care of their comorbidities to validate assumptions on improvements in care quality, and indeed whether cognition can increase demand for health care services.

Irrespective of the patient population, expanding the QOF scheme to improve care quality specifically for patients with dementia does not seem like it would be a cost-effective option. Different point allocations and payment schemes for points, whether that be those attributed to the main indicators or those for the dementia comorbidity, had little impact on the ICER. Reducing the reimbursement attainable for Diabetes Training or Osteoporosis Supplements by half only reduced the ICER by 4%, and excluding a dementia comorbidity payment still sustained ICERs above £60,000 per QALY. Whilst the scheme could be optimised so that points attainable for each indicator are targeted for maximum cost-effectiveness, this is still unlikely to be below standard WTP thresholds.

For the expanded QOF scheme to be cost-effective, it needs to be determined if care quality alone can delay institutionalisation. As can be seen from the scenario and sensitivity analyses, this appears to be the key driver for improving its cost-effectiveness. However, whilst this can bring the ICER within a range in line with the stated WTP in the NHS, it is possible that the WTP in practice for the QOF is higher than in other aspects of care delivery. Pandya *et al* estimated that the QOF as an overall scheme is not cost-effective,[158] but other research has shown individual indicators within the QOF are.[325] A substantial proportion of the QOF reimburses practices for domains without a direct measurable effect on health outcomes such as quality improvement,[71] and previously organisational practices were included, and therefore the scheme as a whole is unlikely to be cost-effective given the volume of payments

compared to health outcomes. In which case, the WTP for the QOF may be higher than in other health domains and establishing the true opportunity cost of investing in the QOF and which activities in general practice are displaced on a local basis is of interest.

For the patient group with all dementia severities, it is also important to consider whether providing reimbursement for referral to diabetes self-management programmes is appropriate if those prevalent patients with severe dementia could meaningfully benefit from it. In which case, there may be no improvement on this indicator with the QOF.

The cost-effectiveness results for the QOF in patients with mild or moderate dementia were slightly more favourable, however it is perhaps not appropriate to consider the expanded QOF scheme in this subgroup as this would be excluding severe patients, unless these were considered for exception reporting. For fully incremental analyses including the PRIDE intervention, it may be better to think on a population level of scenarios of a world with or without these interventions, considered as part of a basket of treatments. In a full prevalent population of patients with dementia, those with severe dementia would receive treatment as usual, whereas those milder patients may receive the PRIDE intervention. In this case, would the PRIDE intervention appear less cost-effective than it does when only considering it within a subgroup of patients with milder dementia? As was demonstrated in the calculations of feasibility of the scale of the programme above, only a limited number of patients would be able to receive the PRIDE intervention each year. Therefore, within the group of patients with mild or moderate dementia, as well as being cost-effective, the budget impact of the PRIDE intervention would also be low. However, the population-level health gains would also be limited, and it is therefore questionable as to if it is the best course of action. The expansion of the QOF could be initiated immediately and present an opportunity to impact care quality and survival for a vast number of patients and increase the QALYs gained by the national dementia population. The population level cost-effectiveness focussed on achieving large scale health gains for all patients with dementia could alter conclusions, especially if considering sunk costs of developing intervention programmes and recruiting staff.

Within the wider framework of the thesis, improving care quality for patients with dementia, and thereby potentially reducing inequalities in care quality compared to those without a cognitive impairment, may be a cost-effective strategy when targeting cognitive function as the mechanism to improve quality, given its additional benefits on the wider health of patients with dementia. Both supply-side and demand-side

targeted interventions for quality appear to improve health outcomes whilst increasing costs, in that no quality improving strategy appears to dominate treatment as usual. This therefore means that in introducing either of these interventions, care may be displaced due to funding and resource availability, and it is not unrealistic to consider that these displaced resources may be those currently provided to patients with dementia given the limited supply of resources and the demands of this complex patient group. Care quality may therefore be hampered in other domains by targeting comorbidity care.

Strengths & Limitations

The model structure utilised captured many of the patient relevant aspects of dementia identified in previous models, with regards to the progression of disease across the life course, the cost impacts, quality of life drivers, and the care and complications of comorbidities. However, the model should still be considered as exploratory for assessing the cost-effectiveness of interventions with complex implications in a complex disease area. Whilst a partitioned survival approach using cohort data was selected for this model, given the available data and usefulness for the decision problem, were future models to be developed from more comprehensive or targeted evidence sources focussing on the PRIDE intervention or other cognitive factors at a patient level, then individual patient-level simulation models could, and potentially should, be used. Whilst the dataset used does not provide the most comprehensive source for informing key patient transitions and quality of life driving factors in dementia, ELSA is a preferred data source for this initial model given the ability to derive the underlying progression of disease and time to event data, along with information on the associations with care quality measures for a cohort of English patients which is not attainable from many other cohort studies.

The current model structure is limited by its ability to demonstrate how cognition and IADLs are related, and how each of these parameters jointly define care quality, and how all of these can influence institutionalisation and survival, considering correlations and the predictive influence of each parameter. In the same consideration, the morbidity burden of comorbid conditions is naively linked to outcomes. For example, it is assumed that fatal cardiovascular events would be indirectly related to the modelled non-fatal cardiovascular events despite the cause of death not being explicitly modelled. For the smoking, diabetes training, and diabetes foot check indicators, the costing and QALY loss assumptions are also highly naïve. As mentioned above, most of the main health consequences are likely to be in the future

and therefore assuming an equal impact each year does not necessarily reflect the true results in this patient population.

More advanced modelling approaches may also better describe the true uncertainty in the parameter estimates and better highlight the weaknesses of the data to decision makers. As noted above, the uncertainty in the current model may be "artificially" increased as the correlation between interventions, indicators, short-term morbidity, and long-term mortality were not explicitly accounted for. This may therefore overestimate the joint parameter uncertainty, and consequently the EVPI or other value of information analyses were not conducted.

Consideration should also be given to the assumptions regarding equality of impact of effect estimates in the model. There is potentially a major limitation in assuming that the interventions increase care quality to an equal extent for each indicator, as well as increases in care quality on each indicator having an equal effect on health outcomes. There was insufficient data in ELSA to determine if inclusion in the QOF or cognitive function had the same impact on all included quality indicators, or whether the odds ratios differed between indicators. Likewise, it was not possible to estimate if care quality regarding treatment for osteoporosis had an equal effect on survival as treatment for hypertension. Whilst all included quality indicators are plausibly linked to survival, such as smoking cessation reducing the risk of conditions leading to death, lower risk of death following fracture in treated osteoporosis, or reduced cardiovascular disease risk, these effects may not all be equal. An additional year of survival is valued higher than a year of restoring health-related quality of life at the utility values used in the model. Therefore, any uncertainty on the magnitude or morbidity or mortality gains is uncertain by assuming the equality of impact of intervention and it is not possible to tell if costs or QALYs gained have been under- or overestimated. However, since this early model aims to assume average population effects, the current data is likely to be sufficient to inform decision making with regards to further evidence generation, but perhaps not sufficient to inform future policy and health practice. Future studies should consider the gains for each comorbidity separately, but on a patient-level given the potential combined benefits of an intervention on multiple comorbidities. This would require more complex modelling approaches and more comprehensive datasets.

The analysis has also only focussed on quality indicators areas where care quality is significantly lower for patients with dementia. It is within reason that whilst a pay-for-performance scheme could be targeted at reducing these inequalities, a cognitive intervention such as PRIDE would improve care quality across all comorbidity

domains. Therefore, future work would benefit at looking at care for all comorbidities with the greatest impact on survival and quality of life in this patient group.

The effect estimates also assumed that the quality indicators included in ELSA are suitable proxies for those in the QOF. Whilst there are significant similarities in their definitions, QOF records are based on recorded care processes based on a physician's perceived need for care and include exception reporting in the overall estimates for those patients deemed potentially inappropriate for inclusion from the perspective of the treating practitioner. Conversely, the ELSA indicators are derived from the self-reported receipt of care from patients with potentially impaired cognition, where the need is determined by an algorithm based typically on age and diagnosis alone. Therefore, the estimated practice-level care quality estimates and QOF payments are not without the possibility of bias.

The costs of the QOF also did not consider a dynamic cohort. When costing the QOF this is done at a practice level and should account for deaths, additions or removals from the practice list, and newly eligible patients in the overall quality estimates. For the modelled patients with dementia, care quality is assumed to be for a static cohort whose condition progresses, and care quality may deteriorate as a consequence, given the predictors. Therefore, aggregate costs may not be entirely accurate. The impact of this may be limited, however, as taking the average national QOF costs on a per-patient level does not vary much with the limited variation in national average care quality. Though this does mean that the results may be of limited applicability to a single GP practice with QOF achievement scores that deviate from the norm.

With regards to the cohort, the model evaluates outcomes in a prevalent cohort of patients with dementia with over four years elapsed since their dementia diagnosis. It is therefore unclear how the findings would be altered considering future incident patients if these patients are younger with potentially longer survival. Modelled outcomes at baseline may also differ from those collected in the ELSA dataset given the changing landscape of treatment for dementia and Alzheimer's disease, with newer pharmaceuticals being reimbursed for this patient population in England and Wales since 2011,[326] changes to the funding and management of primary healthcare,[194] and continuous updates to the QOF, where most quality of care measures in ELSA were collected over 10 years ago.

As noted above, the validity of the survival estimates does come into question. Both the OS and IFS estimates appear substantially longer than the model developed for TA217. Despite a trend for improved OS since the introduction of AChEIs, the

modelled gain here seems like a substantial increase. Up to the median follow-up of 70 months in the ELSA data, and therefore at a time where uncertainty in the extrapolation is relatively low, survival is between 58% and 60%. This is still much greater than in the model from TA217, where survival was approximately 20% at this time. If survival is longer, this would also support an extension to IFS compared to the previous values to some extent, especially if there is a trend to keep patients with dementia resident in the community for longer. However, I have identified no UK data that would permit the assumption that institutionalisation practices have substantially changed between the mid-1990s and late 2000s, when the two different data sources were developed.

Clinical & Research Implications

One of the main uncertainties driving results was utility values. Valuing health in dementia remains a huge challenge. Previous research has shown disparities between patient and proxy rated utility values,[58] and scales such of the EQ-5D used for measuring utilities have not been validated in patients with dementia, nor do they necessarily measure pertinent aspects of quality of life for this patient group.[228] The modelled utilities prior to institutionalisation were lower for patients with mild or moderate dementia than the group with all severities. Whilst other previous studies have shown a slight inverse relationship between disease severity and self-reported utility,[327] it does not necessarily confirm its validity given the lack of logic. Considering the difference in results obtained with the different utility value sources, it is challenging to make robust inferences on the potential cost-effectiveness of the appraised interventions without further research. Therefore, a key priority in future assessments of the cost-effective of the PRIDE intervention, care quality, or other interventions in dementia should look at deriving the best way to quantify quality of life in patients with dementia within a framework that can be compared to utilities derived from metrics such as the EQ-5D for comparison to other disease areas for reimbursement purposes and value assessments. Thought should be given as to whether dementia-related quality of life measures (e.g., the DEMQOL) can capture the relevant benefits to patients and their caregivers and if WTP thresholds can be defined for these to align with current QALY thresholds.

The importance of capturing care quality within the cost-effectiveness assessment is subject to further consideration. A well-designed study with sufficient follow-up would capture any indirect effects of improvement in cognition on survival or institutionalisation which were mediated by care quality, without the need to explicitly capture the association between care quality and outcomes. In which case, only the

health effects of non-fatal events related to care quality would not directly be captured within the data and require additional modelling, as well as the costs associated with the care and management of comorbidities. Considering the base case results of the PRIDE intervention, if modelled survival would remain largely unchanged as indirect effects were captured, but the costs and QALY loss due to comorbidities were excluded, the cost-effectiveness results would remain largely unchanged (see Table 6.43). However, if the pivotal study was unable to capture the lifetime benefits on survival, including all indirect effects, due to design or loss to follow-up, then the modelling techniques to include the benefits of care quality are important to capture as the lifetime survival gains may be underestimated.

The question therefore remains for future research to evaluate whether models, both in dementia or other conditions where cognition, health literacy, or the general ability to improve the self-management of care could be improved as a result of intervention, should include indirect effects of improvement in care quality and outcomes. These factors may be directly related to the intervention but not an endpoint of the studies. The NICE reference case states that the perspective on health outcomes should include "all direct health effects",[171] however there may be a debate as to whether a direct impact on wider care quality could be interpreted as having a direct impact on health outcomes in other domains mediated by care quality. This would presumably require evidence of a causal association between care quality and outcomes in other domains, with the intervention as the instrumental variable. However, as effect sizes could be expected to be smaller, statistical power would be lower with the same sample sizes used for the primary endpoints of the study. Therefore, the costs of research may be inflated in order to demonstrate the wider benefits, which may not be a priority or feasible for researchers to achieve.

One of the more immediate and direct considerations of this work is how it may affect the development programme of the PRIDE intervention. Endpoints in the feasibility trial focus on patient-reported outcomes (PRO) and quality of life measures up to six

Table 6.43. Estimated results excluding comorbidity care costs and outcomes

	Treatment as Usual	PRIDE Intervention
Costs of QOF & Comorbidity-Related Care	£ 7,728	£ 7,890
All Other Costs	£ 88,473	£ 91,484
QALYs, Comorbidity -Related	-0.08	-0.09
All Other QALYs	4.54	4.74
ICER Including Comorbidity-Related Care & Outcomes		**£ 15,658**
ICER Excluding Comorbidity-Related Care & Outcomes		**£ 15,044**

months after randomisation. Whilst PROs and utility analyses are a substantial limitation in the current model, estimating or confirming the benefits on institutionalisation and survival may be pertinent, as these were the key factors increasing cost-effectiveness in this model. Follow-up across the lifetime, either within the trial programme or linking to existing healthcare registries may also permit analysis of future care delivery and complications due to comorbidities to better defined parameter inputs into the model. In addition, it is also worth considering how to best optimise each of the modules in term of keeping physically, mentally, and socially active. As can be seen from **Error! Reference source not found.** above, the k eeping mentally active component in the analysis was estimated to provide the biggest short-term gains in cognition, but the social and physical domains sustained improvements for the longest. Therefore, understanding the duration and uptake of key activities and educating patients accordingly to engage and sustain the right activities for maintaining cognitive function may optimise the effectiveness and cost-effectiveness of the intervention.

Conclusions

The provisional cost-effectiveness estimates developed in this model suggest that there may be clinical benefits of expanding the QOF scheme for patients with dementia and for promoting independence and physical, mental, and social activities in patients with milder cases of dementia. Much of the benefit of these interventions on survival are considered to be mediated by improvements in care quality, though additional benefits could potentially be gained from the PRIDE intervention. However, both strategies are likely to be subject to increased costs across the patient lifetime, most notably with the high costs of managing dementia care in severe cases with prolonged survival. Given that, the PRIDE intervention represents the strategy that is most likely to be an efficient use of healthcare resources given its multifaceted effects. However, the cost-effectiveness estimates are provisional and require further evidence generation to be better estimated. That said, if resources are limited for conducting future research with the goal of improving care quality and outcomes for patients with dementia, the development programme for the PRIDE intervention is probably the preferred investment. Research should also focus on how to best value health and quality of life in patients with dementia in a comparable framework to the QALY used for decision-making in other domains. The uncertainty in the value of health can mean that irrespective of the clinical data and quality of the modelling methods, results may not appropriately reflect the value of investing in care for patient with dementia.

CHAPTER 7

SUMMARY, CONCLUSIONS, & IMPLICATIONS

7.1. INTRODUCTION

In this thesis, I explored whether there are differences in the quality of health care services provided to patients with dementia for non-dementia conditions when compared to patients without a cognitive impairment, as well factors which potentially drive these differences, and strategies which could be used to reduce inequalities in an economically efficient manner. Utilising health economic and econometric methods, I identified and began to evaluate potential strategies for improving care quality for patients living with dementia by determining if they have a clinically meaningful effect on outcomes.

The rationale for exploring these factors stemmed from the hypothesis that patients living with dementia may have difficulty in accessing high quality health care services as a consequence of changes in the supply or demand for quality due to their dementia diagnosis. Demand for care could be reduced based on a decline in cognitive function which limits understanding of their health status. This may reduce help seeking behaviour, as well as lead to functional limitations which may hinder access to care. Supply of care processes could be restricted in patients with dementia as physicians optimise their available resources to provide care. The physician's decisions on how to deliver care could be informed by the perceived marginal benefit to the patient, which may not focus on comorbidity care for those with dementia, whilst maximising their own personal agenda in each healthcare transaction, based on profit maximisation, efficiency of time spent, and satisfaction derived from clinical or interpersonal facets of care. Dividing resources appropriately between all patients in a manner advocated by policy or practice guidelines may also limit the supply of care to an individual patient or group of patients. This framework was used throughout the thesis with the aim of developing evidence to support the derivation of an optimal treatment paradigm for patients with dementia that maximises patient and provider utility within the resource constraints.

The topics in this thesis also have external justification, as the National Institute for Health and Care Excellence (NICE) guidance on the care and management of

dementia states that people living with dementia should have "equivalent access to diagnosis, treatment and care services for comorbidities to people who do not have dementia".[34] Therefore, understanding if this is the case in current practice and if strategies can be implemented to alleviate this was pertinent. The PRIDE (PRomoting Independence in DEmentia) programme, via which this PhD was funded, also provides rationale for these topics. Independence could take the form of keeping patients out of residential care whilst this remains appropriate for them or having greater control over their health care. With the impetus to give patients with dementia more independence, understanding the dynamics of the interactions in managing their comorbidities is important in order to provide appropriate training and support to maximise outcomes.

7.2. Main Findings

At the outset, four separate facets of the relationship between care quality and dementia aimed to be evaluated:

- The extent of current differences in the quality of care processes received between patients with dementia and those without cognitive impairments in the management of their comorbidities;
- Whether any observed differences in care quality have a meaningful impact on patient health or payer-relevant economic outcomes;
- What patient or health policy factors could be used to stimulate improvements in care quality, or reduce inequalities in care; and,
- What are the clinical and economic implications of introducing potential interventions to improve care quality for patients with dementia and where are the evidence gaps?

In the first study of this thesis, reported in Chapter 2, a systematic review and meta-analysis of 37 studies showed that there is a significant trend in published literature for patients with comorbid dementia to be less likely to receive care meeting quality metrics. The included metrics identified in studies that were incorporated into the meta-analysis considered care quality with respect to indicators or care needs in a range of conditions. However, several the indicators included in the analysis were not specific to older adults. These may not reflect what are considered appropriate care goals for patients with dementia, given a reduced marginal benefit due to poor prognosis or a desire to avoid discomfort in these patients. Incorporating study results that included statistical adjustments in their estimates, such as for age, sex, comorbidities, and other factors that may reflect care needs or heterogeneity in

practice, served to slightly attenuate differences between patients with dementia or cognitive impairment and those without.

Following the analyses in Chapter 2, questions remained about the differences in care quality for patients with comorbid dementia when keeping in mind the care goals specific to older adults. With age, and the various health aspects that come with it such as multimorbidity and polypharmacy, older patients may have different care goals, whether they have dementia or not. Therefore, comparisons of care quality in health domains that are more relevant to an ageing population, accounting for patient-level characteristics like comorbidity burden, frailty, and access to care, may serve to alleviate these differences. These questions were addressed in Chapter 3.

In Chapter 3, it was found that there were still significant differences in care quality for patients with dementia. The analyses in this chapter used a range of indicators that were specifically designed to assess care quality in vulnerable elders and selected for their relevance to a UK population. Data were derived from the English Longitudinal Study of Ageing (ELSA) – a longitudinal study of a representative sample of middle-aged and older adults in England, collected between 2004 and 2010, evaluating a range of health, social, and economic factors in an ageing population, which provided data on care quality measures, cognitive function, and health outcomes. The statistical adjustments applied based on health burden and sociodemographic factors which may limit access to high quality care also served to marginally exacerbate the differences between patients with dementia and those with cognitive impairments, contrary to the findings from Chapter 2.

Patients with lower cognitive function within their age group, at a level which was found to be highly accurate at correctly identifying diagnosed dementia, were not subject to worse quality care compared to those who were not identified to have a cognitive impairment. This would therefore suggest that there is some other component of the dementia condition beyond cognitive function, or which coexists with poor cognitive function, that influences care quality. This could either be on the patient-level, in factors which reduce demand for care such as functional ability, or on external factors, such as stigma or a differential perception of need and benefit which prevent informal caregivers assisting in accessing care or health care practitioners providing it.

The findings of Chapters 2 and 3 suggest that having a diagnosis of comorbid dementia is associated with receiving worse quality care for a range of conditions based on quality indicators. As noted above, this could be down to the goals of care for patients

with dementia not aligning with those within the indicators, and a desire to maximise comfort during cognitive decline rather than treating a condition in the hope of providing some longer-term benefits is preferred. However, assessing what impact care quality has on relevant and desirable outcomes for patients with dementia and their caregivers, such as survival or independence may change the goals of care.

In Chapter 4, the aim therefore was to ascertain if failure to meet quality indicators in patients with dementia was associated with worse health outcomes or hindered the goals of promoting independence. A subset of the quality indicators from ELSA included in Chapter 3 were considered, in which patients with dementia were observed to meet less often. The rationale for this was to assess whether the inequalities in care quality observed over the previous chapters could be leading to a health inequity in the failure to provide care. The results suggest that higher quality care was associated with improved survival and may be associated with greater independence by reducing the volume of IADLs helped with by social services, whilst showing a trend for prolonging time to institutionalisation without hampering several assessed aspects of quality of life. It was therefore concluded that it could be beneficial to increase care quality on these domains for patients with dementia.

Considering how health technologies and policies are evaluated by NICE, the extended survival and sustained quality of life could increase quality-adjusted life years gained by patients with dementia by improving the quality of care for comorbidities. Therefore, care goals for these patients should perhaps be updated to focus on meeting selected indicators where there is currently an underperformance. Accordingly, in Chapter 5 two potential intervention strategies were considered with regards to methods to improve care quality for patients with dementia, and potentially reduce the inequality in care observed. One of these potential interventions focussed on the supply of quality care based on the assumption that physicians can be stimulated to provide care meeting indicators in targeted domains by awarding specific reimbursement (pay-for-performance). On the demand side, it was postulated that within the economic framework outlined in Chapter 1, a decline in cognitive function combined with the depreciation in health in dementia leads to a reduced demand for high quality health care. Therefore, could interventions which improve cognitive function lead to higher quality care for these patients?

To assess these hypotheses, the quality indicators from ELSA were compared to those captured in the Quality and Outcomes Framework (QOF) – the world's largest health related pay-for-performance scheme which has formed part of the reimbursement to general practitioners in the UK since 2004. It was found that where care quality

indicators provided a basis for reimbursement in the QOF, the quality of care received by patients with dementia was significantly higher. However, the results also show that improvements in care quality are also achieved for patients without a cognitive impairment and so, whilst pay-for-performance can improve care quality for patients with dementia, schemes applying to the full population cannot reduce inequalities in care quality. Therefore, it was assumed that for pay-for-performance schemes to reduce inequalities in care these would have to provide reimbursement specifically for care for patients with dementia. Within the economic framework outlined in Chapter 1, this is considered plausible as several of the factors deemed to influence the supply of care are not specific to patients with dementia. For example, the utility function of the health care practitioner incorporating both profit maximisation and non-financial incentives could be applicable to all health care transactions, particularly when reimbursement is contingent on quality in a heterogenous group of patients at the practice level.

The analysis showed that higher cognitive function was associated with higher quality care. However, a threshold is reached in the most severe patients where cognitive function is no longer associated with care quality. The economic framework I developed for this thesis hypothesised that as cognition declines in patients with dementia, the demand for care is reduced but may be largely sustained in the early stages of the disease. By developing interventions to improve cognition in milder dementia, this could prolong benefits by increasing care demand and maintaining health in other domains.

Having identified some patient and policy level factors that are predictive of care quality, these need to be formalised into intervention strategies. For interventions to be introduced and reimbursed, they should provide value within a resource constrained health care system. In Chapter 6, the potential cost-effectiveness of strategies based on these exposures was assessed to inform targets for future evidence generation. Two potential strategies were considered: expanding the QOF specifically to target care quality for patients with dementia, and the PRIDE intervention – an intervention being evaluated in a feasibility randomised controlled trial that provides patients with dementia with training to boost their independence through cognitive, physical, and social activity. The results suggest that a targeted expansion of the QOF for patients with dementia is unlikely to be cost-effective, whereas the PRIDE intervention had a high probability of being cost-effective given the compound benefits of improving survival and delaying institutionalisation as a result of cognitive and physical health gains, as well as improving care quality.

It is worth noting that these results are based on very provisional data and conclusions are limited by the range of assumptions applied. However, targets for future research to support and validate these assumptions were defined. The first of these is to capture the long-term benefits of the PRIDE intervention in the definitive trial, including the potential impact on care quality, institutionalisation, and survival. The second is to ascertain how utilities and quality of life should be measured for economic evaluations in patients with dementia, given this was a key driver of uncertainty.

7.3. Potential Implications

Practice & Policy Implications

In the Health and Social Care Act 2012, it is noted that health care providers should "reduce inequalities between patients with respect to their ability to access health services" as well as "reduce inequalities between patients with respect to the outcomes achieved for them by the provision of health services".[194] This thesis has provided some evidence to suggest that these are potentially one and the same thing in certain domains of care for patients with dementia – unequal access to high quality care services may be associated with poorer health outcomes for these patients. Whilst current policy theoretically provides patients equal access to care, the delivery as such is inequitable. Therefore, policy and practice should change in order to provide patients with equality of outcomes rather than equality of opportunity.

With this in mind, the immediate thought on practice implications is to whether physicians should consider the potential addition health gains to patients when treating comorbidities, if time and resources permit. There is an existing school of thought that as many medical interventions may cause some discomfort to patients with dementia, and the therapeutic benefit of treatment may be limited due to reduced life expectancy, that treatment of comorbidities should be reserved to the very early stages of dementia.[12] Assuming rational treatment choices are being made, balancing of benefits and harms or discomforts to patients with dementia with regards to the treatment of comorbidities, then the results of Chapter 4 provide reason to further consider potential survival benefits. This thesis has provided some evidence that the therapeutic benefits associated with selected care quality indicators are not necessarily limited, and providing such treatment could potentially be cost-effective. Therefore, further research and dissemination of the benefits of treatment of hypertension, osteoporosis, diabetes, and smoking in patients with dementia should be used to inform future clinical decision making. However, this recommendation is subject to limitations given the early evidence of the benefits of high-quality comorbidity care in this

population. It also fails to account for the perspective of GPs in clinical practice with regards to their experience in the clinic in optimising interactions on a patient level.

The work in this thesis also provides some evidence that policy interventions, reimbursement, and availability of resources are associated with better quality care. If the supply of care through the recruitment of more staff cannot be realistically or efficiently increased, then policy and reimbursement decisions can be used to redirect the focus of resources to improve care quality on domains of interest. Including clinical domains in the QOF is associated with higher quality care in the areas reimbursed. Therefore, redesigning the scheme to be orientated more towards personalised medicine or care of a homogenous group (e.g., patients with dementia and comorbid hypertension) rather than the overall population may be a Pareto improvement if further research can ascertain which disease areas and treatment processes provide the greatest health gains within these subgroups. Policymakers may be receptive to this approach, as the NHS in their review of the QOF concluded it would be desirable to take onboard different definitions of high-quality care and recognise changes in clinical evidence and practice.[220]

Research & Methodological Implications

Despite the PRIDE intervention being the most likely evaluated intervention to be cost-effective within the framework used, it is worth considering how conclusions would change if a different perspective was considered. In order to deliver the PRIDE intervention to all patients with dementia, thousands of care staff would have to be trained in facilitating the sessions, requiring additional recruitment. Using currently available resources, only a limited number of the dementia population in the UK would be able to receive the PRIDE intervention. Conversely, an expansion of the QOF could be initiated nationally using the resources already in place for providing care and reimbursing general practices for this care. Therefore, it could provide health gains to the broadest population within the shortest time frame, without the sunk costs associated with the PRIDE intervention. If the cost-effectiveness framework was changed to evaluate benefits at a population level, costs of introducing a scheme, and consider discounting of future health outcomes with respect to the time taken to initiate the scheme, train staff, and roll out the intervention nationally, rather than from an arbitrary model baseline time, inferences on the results could change. Novel methods of economic assessment evaluating the population-level and time-limited budget consequences considering the health gains to be made in all patients with dementia in the UK, versus a patient-level cost-effectiveness analysis could change conclusions.

The current reimbursement framework of evaluating cost-effectiveness at a patient-level and budget impact at a population level only considers a narrow perspective of maximising outcomes for a specific patient within a framework of economic feasibility. When making substantial policy decisions as opposed to reimbursing a single technology, using a borderline welfarist/extra-welfarist perspective that maximises the welfare function within the healthcare system may be a better framework to provide overall improvements to the population. Such an approach may produce different conclusions on the most economically efficient intervention to improve outcomes mediated by care quality for patients with dementia. In this context, the PRIDE intervention or a similar cognition and independence boosting programme, may be hindered by training and rollout times and limited resources to provide care.

With regards to further changes to the frameworks for economic assessment, one should consider as to whether future cost-effectiveness analyses should include the influence of interventions on other disease areas or outcomes that may be considered out of direct scope. With potential disease-modifying therapies for Alzheimer's disease on the horizon,[328] would the fact that cognitive function may be sustained or improved in the long-term have compound implications in terms of health benefits for patients with comorbidities? It could be argued that these are direct consequences of treatment and therefore would be in scope for health technology assessment, however further research is needed to confirm the hypothesis of this thesis as to whether care quality is a mediating factor in the relationship between cognition and health outcomes, and whether these indirect effects could be sufficiently captured within trials.

In both of these potentially novel methodological approaches, a cost per health outcome framework would still be utilised. As was identified in the model in Chapter 6, valuing health and the use of utilities is an area of key uncertainty in the cost-effectiveness of interventions in dementia. Further research should be conducted to determine how valuations of health and quality of life can be conducted in patients with dementia. These would be required to value health in a way that is directly comparable to that of other diseases to ensure fairness in reimbursement decisions, and so the use of questionnaires measuring dementia-specific symptoms may not be the correct avenue to follow. The EQ-5D is the preferred metric for estimating utilities in the UK because of its simplicity and the broad domains of health-related quality of life that it captures means that it is assumed to reflect key changes in health in all conditions to some degree, without tackling the nuances of individual conditions. The challenge with patients with dementia is, as noted by the Technology Assessment Group in TA217, there is no evidence to suggest that patients with dementia can

reliably value their own health.[228] Proxy-rated values are commonly used as an alternative to this, but these are subject to their own limitations in that it is unclear if ratings are correct, if some of the indirect impact on the carer's quality of life is captured, or even if the health experienced by the patient compared to the perceptions of the health they experience is the correct thing to measure. For appraisals of health technologies for use in children, where validated utility weights are not available, NICE permit the use of alternative metrics.[171] Perhaps a dementia-specific utility metric is required for when cognitive function limitations do not permit the assessment of utilities using traditional methods. Whilst I cannot comment what the correct method for valuing health is in patients with dementia, to ensure the fair reimbursement of health technologies in this patient group compared to others, a greater understanding is required.

With regards to research for the development of the PRIDE programme, estimates of the current survival and time to institutionalisation for patients with dementia are required. There was a disparity in the estimates developed in the model in Chapter 6 compared to that in NICE TA217, and further differences in the published literature. To quantify how various treatments for dementia, whether pharmacological or psychosocial, can improve survival and increase independence, understanding and validating baseline estimates is required. These data, along with the results from the ongoing feasibility RCT for the PRIDE intervention, could be used to update the existing model to provide further evidence to inform the design of the definitive RCT for the PRIDE intervention by identifying the key evidence gaps in the cost-effectiveness assessment.

7.4. Shortfalls & Limitations

Throughout this thesis, various limitations have been acknowledged within the individual analyses. Several of these have stemmed from the restrictions in the available data and the analysis methods that were consequently required. Below is a summary of the main themes identified.

In econometrics, endogeneity refers to situations when an independent variable is correlated with the error term in the analysis.[329] The three main reasons for endogeneity to arise are when variables are omitted from the analysis that affect both the dependent and independent variable, when there is reverse causality, or when there is measurement error. All three of these factors may have arisen in this thesis.

When confounding variables are omitted from the analysis, for example due to data availability, this can lead to the incorrect estimation of effect sizes. Directed acyclic

graphs (DAG) were developed for each analysis in this thesis to determine which of the available variables should be adjusted for the determine the direct effects of independent variables on dependent variables. The preferred solution would be to conduct a randomised controlled trial (RCT) on the assumption that this would eliminate selection bias and confounding variables. Whilst observational data was necessary for certain aspects of this thesis, in that patients cannot be randomised to have a dementia diagnosis for assessing differences in care quality, for others it would be preferred. For example, conducting a trial where patients were randomised to receive care meeting quality indicators or not would be preferred to avoid endogeneity.

Simultaneity or reverse causality is the second source of endogeneity. Within all the analyses included in this thesis, there has been an underlying assumption of a unidirectional effect. However, with the exception of the time to event analyses, regression models have focussed on cross-sectional methods and therefore it is not possible to reliably determine whether exposure preceded outcome or vice-versa, casting doubt on the feasibility of causality. Patients with dementia were observed to receive lower quality care than those without, though it is plausible that patients who have previously received and continue to receive low quality care are at greater risk of dementia and cognitive decline. Cardiovascular conditions, including hypertension and diabetes, are prognostic of dementia diagnoses,[141] and therefore those patients with poorer care for these conditions in the past may be the patients subsequently developing dementia who were identified as having low quality care on these domains.

The final source of endogeneity is measurement error, where for some reason we include an imperfect measure of a predictor in the regression equation. The implication of this is that because the observed value of the independent variable x_i contains some error v_i, the actual regression model follows the equation:

$$y_i = \alpha + \beta(x_i - v_i) + \varepsilon_i$$

which can also be written as:

$$y_i = \alpha + \beta x_i + (\varepsilon_i - \beta v_i)$$

Therefore, since both the independent variable and the compounded error term are dependent on the measurement error they are correlated, and so the estimation of β will be biased downwards.

Why this presents itself as an issue in this thesis is all variables in ELSA were based on self-reported measures, except for the cognition function measures. All respondents, including patients with dementia, could have a family member or

caregiver present during the interview but this does not guarantee accuracy of the recorded responses. Previous research has demonstrated strong correlations between self-reported processes using quality indicators and processes recorded in medical records in the general population,[145 159] however this cannot be guaranteed in patients with dementia and memory impairments. Several of the included quality indicators required respondents to comment on whether some process of care was conducted over the past 12 months, and so recorded responses may be based on care patients thought they received but did not or vice versa. It has also been noted above that patients with dementia may not be able to reliably provide responses to quality of life measures. It is therefore possible that there was some form of measurement error in several of the included variables.

Another key challenge in using self-report measures is missing data. A not insignificant proportion of patients with dementia in ELSA had missing data on either cognitive function measures, quality of care indicators, quality of life measures, or selected covariates, which were imputed for use in analyses. Early analyses suggested that missingness was correlated with dementia, poor cognition, age, and frailty, and therefore the data were considered to be missing at random under the definitions by Rubin.[137] Multiple imputation can reduce bias in effect estimates when data are missing at random compared to only using a complete cases analysis.[138 163 164] Best practice methods were followed in order to impute data, considering the multilevel structure of responses from participants in ELSA, and key variables were included in the imputation model to ensure all analyses were based on the same imputed dataset. However, this is potentially still not a substitute for a complete and high-quality sample and estimated effect sizes may differ in other studies.

The final key limitation may be ignored heterogeneity. As noted in Chapter 4, it is questionable as to whether better quality care for hypertension would improve survival outcomes to the same extent as advising on smoking cessation. The assumption of the transferability of effects on outcome between the evaluated comorbid conditions is uncertain. The same is true of the analyses in Chapter 5, where it was not evaluated if better cognitive function or pay-for-performance influenced care quality to a different extent on different indicators. Whilst this was a necessity for methodological reasons as observations across conditions had to be combined due to small number of patients with diagnosed dementia being eligible for these quality indicators in ELSA, uncertainties in the conclusions remain.

7.5. Contributions of the Thesis

As noted above, this thesis had four key aims. The thesis has met the first of these in that the extent of the differences in care quality between patients with dementia and those without a cognitive impairment were quantified in both a meta-analysis and a novel analysis on the ELSA data. It is with reasonable certainty that one can conclude that patients with dementia are less likely to meet quality indicators for the management of certain comorbid conditions which may have implications for clinical practice, irrespective of whether these differences are specifically caused by a diagnosis of dementia. However, these implications for clinical practice are contingent on the second aim in assessing whether the observed differences in care quality have a meaningful impact on patient outcomes. Whilst the thesis has provided some evidence to suggest that high quality care can improve survival which may be stimulus enough to change practices and re-evaluate current care decisions, the limitations of the methods and the use of observational data is not sufficient to soundly confirm this.

Nevertheless, the thesis has started to lay the groundwork for methods to improve care quality for patients with dementia and assess the value of reducing inequalities in care quality. In aiming to determine what patient or policy factors could be used to improve care quality some evidence has been presented that pay-for-performance schemes are a mechanism which can stimulate physicians to provide care in targeted areas, including for patients with dementia. Whilst higher cognitive function is associated with better quality care, whether improvements in cognitive function in response to treatment, or being able to prolong the milder phase of the disease can lead to long-term improvements in care quality would require randomised evidence. Some of the key evidence gaps in determining the clinical and economic implications of introducing potential interventions to improve care quality for patients with dementia have also been defined, notably how interventions can impact institutionalisation and how to value health.

With regards to the contributions to theory, the results of this thesis provide some empirical support to the economic framework outlined in Chapter 1. The quality of care received in healthcare transactions, perhaps particularly for patients with dementia, can be considered in terms of supply and demand. Grossman's human capital for health model can be extended to not only consider demand for health but demand for high quality healthcare as, assuming an evidence basis to quality indicators, these are processes for providing and improving health. Consciousness of the health state, or the decrements to health and the increased depreciation rate in health, at a certain level can stimulate demand for health. Higher cognitive function in

patients with dementia was associated with better quality healthcare for these patients and so may be a factor in driving demand. However, including the most severe patients in analyses serves to eliminate the observed associations. Therefore, severe dementia itself is not a predictor of care quality and is perhaps supplemented by access to care, such as through support from informal caregivers. It is therefore concluded that demand for care can be modulated through a range of avenues, and the promotion of independence and increased cognition to stimulate demand may be the preferred avenue in the early phases of dementia. Evidence has also suggested that the supply of care is modifiable by motivating physicians to provide care using reimbursement mechanisms to increase care quality in targeted areas. Wealth and financial motivations appear to form part of the utility function of the physician, as proposed in Chapter 1, though potentially not the main driver as the actual volume of reimbursement was not significantly associated with quality of care received after adjustment for the burden of disease. Therefore, burden of disease and clinical need also forms part of the supply side of the equation and so evidence-based medicine and physician education could be another motivator to provide care (i.e., the knowledge and satisfaction of doing the right thing).

Finally, to my knowledge, this is the first study to fully quantify and discuss the associations and impacts of dementia on care quality. The work conducted provides a framework for future researchers to develop studies in the hope of improve outcomes for patients with dementia.

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Appendices and Supplementary Materials

Chapter 2

Appendix 2.1: MEDLINE Search Strategy for Systematic Review

1. dementia/
2. dement*.mp.
3. alzheimer disease/
4. alzheimer*.mp.
5. mild cognitive impairment/
6. (cogniti* adj2 impair*).mp.
7. (cogniti* adj2 declin*).mp.
8. (cogniti* adj2 function*).mp.
9. (cerebr* adj2 deteriorat*).mp.
10. cognitive aging/
11. or/(1-10)
12. quality of health care/
13. quality indicators, health care/
14. quality assurance, health care/
15. delivery of health care/
16. standard of care/
17. process assessment (health care)/
18. primary health care/
19. general practice/
20. health services accessibility/
21. health equity/
22. or/(12-21)
23. 11 and 22
24. limit to (year = "1990 – Current" and (Middle Aged (45 plus years) or All Aged (65 and over) or Aged (80 and over)))

Appendix 2.2: Characteristics of Included Studies

Author (Year)	Country	Main Treatment Setting	Impairment Measure	Disease/Area	Quality Indicator
Banach (2012)	USA	Community Care	Diagnosed Dementia	Influenza	Receipt of seasonal influenza vaccination
Béjot (2015)	France	Secondary Care	Diagnosed Dementia	Stroke	Receipt of comprehensive diagnostic assessment (including brain imaging, ECG, Doppler ultrasound, and echocardiography)
Bravo (1999)	Canada	Residential Care	Modified Mini-Mental State Examination	Various	Total score on the QUALCARE Scale (a multidimensional instrument comprising 54 items that assess care in six areas: environmental, physical, medical management, psychosocial, human rights, and financial)
Byers (2017)	USA	Community Care	World Health Organization's Disability Assessment Schedule (score >0 on cognitive subscale)	Mood & Anxiety Disorders	Use of specialty mental health or general medical services for "emotions, nerves, mental health, or use of alcohol or drugs" in the past 12 months
Cancian (2013)	Italy	Community Care	Diagnosed Dementia	Cardiovascular Disease	Treatment with beta-blockers
Christensen (2017)	Denmark	Community Care	Diagnosed Dementia	Various	Whether a preventative home visit had been conducted within the preceding year
Connolly (2013)	United Kingdom	Community Care	Diagnosed Dementia	Atrial Fibrillation	Currently treated with anticoagulation/anti-platelet therapy
				Cardiovascular Disease	Patients who smoke whose notes have a record of smoking cessation advice/referral to specialist offered
				Coronary Heart Disease	Patient with a history of myocardial infarction currently treated with an ACE inhibitor or angiotensin II antagonist
					Blood pressure recorded
					Total cholesterol level recorded
					Record of influenza immunization over previous winter
				Diabetes Mellitus	Blood pressure recorded

Author (Year)	Country	Main Treatment Setting	Impairment Measure	Disease/Area	Quality Indicator
					Total cholesterol level recorded
					HbA1c recorded
					Neuropathy testing conducted
					Retinal screening conducted
					eGFR or serum creatinine testing conducted
				Hypertension	Blood pressure recorded
				Stroke	Blood pressure recorded
					Total cholesterol level recorded
					Record of influenza immunization over previous winter
Dreischulte (2014)	United Kingdom	Community Care	Diagnosed Dementia	Atrial Fibrillation	Prescription of oral anticoagulants
Fleming (2017)	USA	Secondary Care	Diagnosed Dementia	Colorectal Cancer	Receipt of chemotherapy after metastasis
Fung (2016)	USA	Community Care	Diagnosed Dementia	Chronic Kidney Disease	Outpatient visit to a nephrology provider within a 12-month period from an index eGFR measurement ≤ 30mL/min/1.73m^2 body surface area
Gershon (2014)	Canada	Community Care	Diagnosed Dementia	Chronic Obstructive Pulmonary Disease	Receipt of pulmonary function testing
Giangregorio (2009)	Canada	Residential Care	Cognitive Performance Scale (score ≥2)	Osteoporosis	Current use of an osteoporosis therapy amongst long-term care residents with a diagnosis of osteoporosis, hip fracture, or recent fracture
Grant (2013)	United Kingdom	Community Care	Diagnosed Dementia	Incontinence	Received drug treatment for urinary incontinence The rates of prolonged use of indwelling urinary catheters
Han (2007)	USA	Secondary Care	Diagnosed Dementia	Acute Coronary Syndrome	Receipt of cardiac catheterization in ACS with high-risk features
Hoffmann (2014)	Germany	Community Care	Diagnosed Dementia	Pain Management	Prescription of analgesic drug
Holt (2012)	United Kingdom	Community Care	Diagnosed Dementia	Atrial Fibrillation	Prescription of anticoagulant or antiplatelet drug within the last 6 months
Huang (2013)	United Kingdom	Community Care	Diagnosed Dementia	Smoking Cessation	Receipt of prescription for smoking cessation medication

Author (Year)	Country	Main Treatment Setting	Impairment Measure	Disease/Area	Quality Indicator
Kimmick (2014)	USA	Secondary Care	Diagnosed Dementia	Breast Cancer	Receipt of guideline-concordant care
Klarin (2003)	Sweden	Community Care	Mini Mental State Examination (score <24)	Cardiovascular Disease	Use of antithrombotic agents regularly and/or as needed
					Use of agents acting on the renin-angiotensin system regularly and/or as needed
					Use of beta-blocking agents regularly and/or as needed
					Use of calcium-channel blockers regularly and/or as needed
					Use of cardiac therapy regularly and/or as needed
					Use of diuretics regularly and/or as needed
Klop (2015)	United Kingdom	Community Care	Diagnosed Dementia	Hip Fracture	The initiation of anti-osteoporosis drug prescribing after hip fracture
Lin (2012)	Taiwan	Secondary Care	Diagnosed Dementia	Acute Coronary Syndrome	Use of guideline-recommended medications (including aspirin, beta-blockers, ACE inhibitors, or angiotensin receptor blockers, statins, or clopidogrel) for at least 30 days or for at least 180 days within 35 days after the first ACS event
Müther (2010)	Germany	Community Care	Diagnosed Dementia	Diabetes Mellitus	Prescribed medication for diabetes
				Hypertension	Prescribed antihypertensive medication
				High Cholesterol	Prescribed medication for hyperlipidaemia
Nilsson (2011)	Sweden	Secondary Care	Diagnosed Dementia	Hip Fracture	Receipt of occupational therapy following hip fracture
Nygaard (2005)	Norway	Residential Care	Diagnosed Dementia	Pain Management	Prescribed as well as administered analgesic drugs 'as needed'
			Abbreviated Mental Test (score ≤7)		
Pileggi (2014)	Italy	Residential Care	Short Portable Mental Status Questionnaire	Various	Adherence to the ACOVE quality indicators pertaining to screening and prevention, diagnosis, and treatment
Preuss (2016)	Germany	Community Care	Diagnosed Dementia	Atrial Fibrillation	Received oral anticoagulants

Author (Year)	Country	Main Treatment Setting	Impairment Measure	Disease/Area	Quality Indicator
Quinn (2009)	USA	Community Care	Diagnosed Dementia	Diabetes Mellitus	Glycated haemoglobin tests
					Fasting glucose tests
					Retinal screening
					Cholesterol tests
					Serum creatinine tests
		Residential Care			Glycated haemoglobin tests
					Fasting glucose tests
					Retinal screening
					Cholesterol tests
					Serum creatinine tests
Raijmakers (2018)	Netherlands	Secondary Care	Diagnosed Dementia	Death	Whether patient dies in their preferred place of death
					Whether patient dies at home if that is their preferred place of death
Saposnik (2011)	Canada	Secondary Care	Diagnosed Dementia	Stroke	Admission to designated stroke unit
					Antihypertensive therapy at discharge
					Carotid imaging during hospital stay
					Dysphagia screening
					Thrombolytic therapy for eligible patients
					Antithrombotics at discharge
					Patients with atrial fibrillation discharged on warfarin
Scowcroft (2013)	United Kingdom	Community Care	Diagnosed Dementia	Atrial Fibrillation	Initiation of warfarin in the first year following diagnosis
Shah (2012)	United Kingdom	Community Care Residential Care	Diagnosed Dementia	Influenza	Receipt of influenza vaccination
Thorpe (2012)	USA	Community Care	Diagnosed Dementia	Diabetes Mellitus	Receipt of one or more LDL-C tests
					Receipt of one or more HbA1c tests
					Receipt of one or more eye examinations

Author (Year)	Country	Main Treatment Setting	Impairment Measure	Disease/Area	Quality Indicator
Tjia (2012)	USA	Residential Care	Diagnosed Dementia	Atrial Fibrillation	Receipt of INR tests whilst treated with warfarin
Vitagliano (2004)	USA	Secondary Care	Diagnosed Dementia	Cardiovascular Disease	Prescription of beta-blockers at hospital discharge for myocardial infarction survivors
Wachterman (2016)	USA	Secondary Care	Diagnosed Dementia	Death/Palliative Care	Whether patient received a palliative care consultation
					Whether family member(s) of the deceased rated palliative care received as excellent
Wargny (2018)	France	Community Care	Diagnosed Dementia	Diabetes Mellitus	Rates of diabetic monitoring (glycated haemoglobin, LDL-cholesterol, microalbuminuria screening, and retinal screening)
					Rates of hospitalisations for acute diabetic complications
Zinn (2004)	USA	Secondary Care	Mini Mental State Examination (<2 standard deviations below the mean, standardized by level of educational attainment)	Stroke	Acute rehabilitation: speech therapy evaluation
					Acute rehabilitation: occupational therapy evaluation
					Acute rehabilitation: diagnostic CT/MRI performed
					Post-acute inpatient rehabilitation: communication evaluation
					Post-acute inpatient rehabilitation: depression evaluation
					Post-acute inpatient rehabilitation: social functioning evaluation
					Post-acute inpatient rehabilitation: cognitive evaluation
					Post-acute inpatient rehabilitation: cognitive goals listed
					Post-acute inpatient rehabilitation: physical goals listed

Abbreviations: ACE, angiotensin-converting-enzyme; ECG, electrocardiograph; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; LDL-C, low-density lipoprotein cholesterol

Appendix 2.3: Risk of Bias Assessment

Question	Banach (2021)	Bilgic (2015)	Bravo (1999)	Byers (2017)	Candan (2013)	Christensen (2017)	Connelly (2013)	Dreinhofer (2004)	Fleming (2016)	Fung (2017)	Gershon (2014)	Giangregorio (2009)	Grant (2013)	Han (2007)	Hoffmann (2011)	Hoh (2012)	Huang (2013)	Kimmick (2014)	Kurin (2020)	Mop (2015)	Lin (2021)	Mather (2010)	Nilsson (2011)	Nyggard (2005)	Pilegi (2014)	Preiss (2016)	Quinn (2009)	Rajmakers (2018)	Saposnik (2011)	Seaworth (2013)	Shah (2012)	Thorpe (2012)	Tjia (2012)	Villagomez (2004)	Wachterman (2016)	Wanjiru (2008)	Zinn (2004)
Q1: Do the inclusion/exclusion criteria vary across the comparison groups?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Q2: Does the strategy for recruiting participants differ across groups?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Q3: Is the selection of the comparison group inappropriate?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Q6: Were valid and reliable measures, implemented consistently across all study participants?	Unsure	Yes	Yes	Yes	Yes	Unsure	Unsure	Yes	Yes	Yes	Unsure	No	Unsure	Yes	Yes	Yes	Unsure	Yes	Yes	Unsure	Yes	Yes	Unsure	Yes	Yes	Unsure	Yes	Yes	Yes	Yes	Yes	Yes	Unsure	Yes	Yes	Yes	Yes
Q7: Was the length of follow-up different across study groups?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Yes/ Unsure	N/A	N/A	N/A	Yes/ Unsure	N/A	N/A	N/A	N/A	N/A	No	N/A	N/A	Yes/ Unsure	N/A	N/A	N/A	No	N/A	Yes/ Unsure	No	N/A	N/A	Yes/ Unsure	N/A	N/A	Yes/ Unsure	No
Q8: In cases of high loss to follow-up (or differential loss to follow-up), was the impact assessed?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Unsure	N/A	N/A	N/A	Unsure	N/A	N/A	N/A	N/A	N/A	Unsure	N/A	N/A	Unsure	N/A	N/A	N/A	Unsure	N/A	Yes	No	N/A	N/A	Unsure	N/A	N/A	Unsure	N/A
Q9: Are any important primary outcomes missing from the results?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Unsure	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No
Q11: Are results believable taking study limitations into consideration?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q12: Any attempt to balance the allocation between the groups or match groups?	Yes	Yes	Yes	Yes	No/ Unsure	Yes	No/ Unsure	Yes	Yes	Yes	Yes	Yes	Yes	No/ Unsure	Yes	No/ Unsure	Yes	Yes	Yes	Yes	Yes	Yes	No/ Unsure	Yes	Yes	No/ Unsure	Yes	Yes	No/ Unsure	Yes	Yes	Yes	Yes	No/ Unsure	Yes	Yes	No/ Unsure
Q13: Were important confounding variables not taken into account in the design and/or analysis?	No	Partially	No	Partially	Yes	No	Yes	No	No	No	No	No	Partially	Yes	No	Yes	Unsure	Unsure	No	No	No	Unsure	Yes	Unsure	No	Yes	No	Unsure	Yes	Partially	Partially	Unsure	Yes	Yes	Unsure	No	Yes
Q15: Are the statistical methods used to assess the primary outcomes inadequate?	No	No	No	No	Partially	No	Partially	No	No	No	No	No	No	Partially	No	Partially	No	No	No	No	No	No	Partially	No	No	Unsure	No	No	No	No	No	No	Partially	Partially	No	No

Appendix 2.4: Subgroup Analysis & Meta-Regression using Multilevel Meta-Analysis

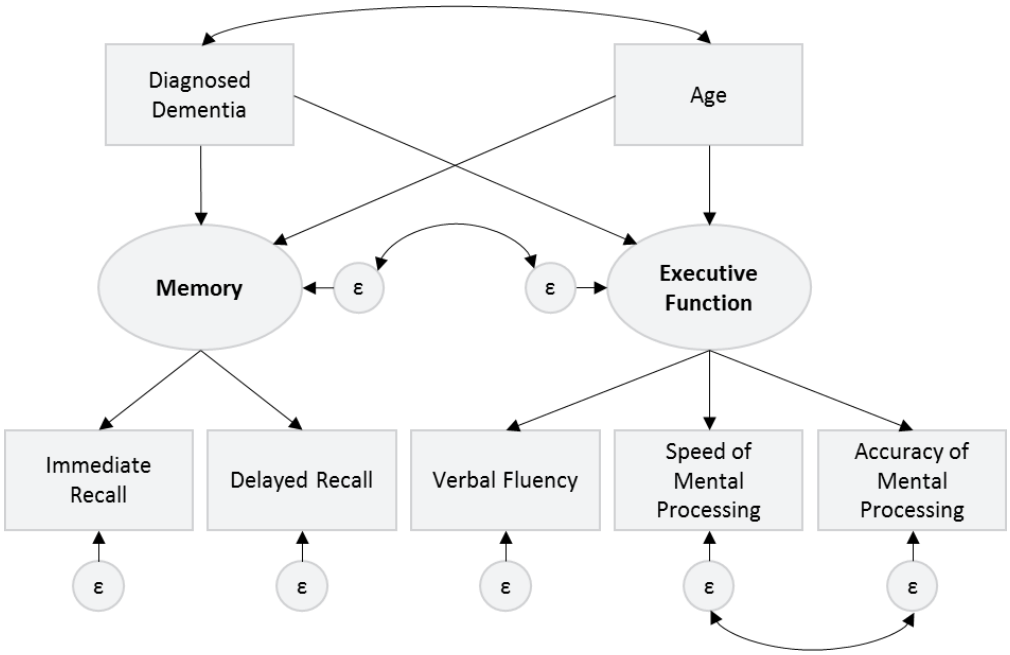
Appendix 2.4.1. Multilevel meta-regression subgroup analyses on the impact of dementia or cognitive impairment on care quality

Subgroup Analysis	Odds Ratio (95% CI)	Test for Residual Heterogeneity				Test for Moderators		
		Q	df	*p*	σ^2	Q	df	*p*
Disease Area		965.2	53	<0.001	0.357	63.3	20	<0.001
ACS	0.55 (0.22 to 1.40)							
Atrial Fibrillation	0.64 (0.42 to 0.99)							
CVD	0.36 (0.22 to 0.60)							
CHD	0.70 (0.46 to 1.06)							
Diabetes	0.50 (0.34 to 0.74)							
Hypertension	0.78 (0.51 to 1.19)							
High Cholesterol	0.82 (0.36 to 1.82)							
Stroke	0.86 (0.59 to 1.27)							
Cancer	0.43 (0.16 to 1.13)							
CKD	0.71 (0.22 to 2.30)							
COPD	0.73 (0.23 to 2.36)							
Influenza	1.22 (0.52 to 2.88)							
Osteoporosis	0.71 (0.21 to 2.35)							
Fractures	0.20 (0.05 to 0.83)							
Incontinence	0.76 (0.24 to 2.46)							
Anxiety	2.23 (0.59 to 8.42)							
Pain	0.62 (0.25 to 1.55)							
Smoking	0.17 (0.05 to 0.60)							
Various	1.60 (0.87 to 2.94)							
End of Life	1.34 (0.42 to 4.34)							
Country		1955.2	62	<0.001	0.307	30.4	11	0.001
Canada	0.72 (0.38 to 1.37)							
Denmark	3.35 (1.06 to 10.64)							
France	0.62 (0.19 to 2.00)							
Germany	0.73 (0.38 to 1.40)							
Italy	0.87 (0.28 to 2.67)							
Netherlands	0.80 (0.20 to 3.25)							
Norway	0.45 (0.12 to 1.76)							
Sweden	0.48 (0.21 to 1.13)							
UK	0.40 (0.26 to 0.61)							
USA	0.85 (0.58 to 1.23)							
Taiwan	0.78 (0.26 to 2.33)							
Indicator Type		1447.3	68	<0.001	0.323	58.9	5	<0.001
Patient-Centred	1.28 (0.77 to 2.13)							
Drug Therapy	0.70 (0.56 to 0.88)							
Rehabilitation	0.60 (0.46 to 0.78)							
Surgery	0.45 (0.13 to 1.61)							
Testing	0.47 (0.37 to 0.59)							
Main Treatment Setting		1784.0	70	<0.001	0.407	41.0	3	<0.001
Community Care	0.59 (0.46 to 0.75)							
Inpatient Care	0.83 (0.64 to 1.06)							
Residential Care	0.59 (0.22 to 1.55)							
Cognitive Impairment		2039.8	71	<0.001	0.360	16.7	2	<0.001
Dementia	0.61 (0.48 to 0.78)							
Assessment	1.15 (0.66 to 2.03)							

Appendix 2.4.2. Cross-category multilevel meta-regression model on the impact of dementia or cognitive impairment on care quality

Subgroup Analysis	Odds Ratio (95% CI)	Test for Residual Heterogeneity				Test for Moderators		
		Q	df	*p*	σ^2	Q	df	*p*
Atrial Fibrillation	0.75 (0.50 to 1.11)	964.7	60	<0.001	0.251	117.5	12	<0.001
CVD	0.42 (0.27 to 0.66)							
Diabetes	0.73 (0.60 to 0.89)							
Fractures	0.22 (0.06 to 0.80)							
Smoking	0.30 (0.09 to 0.99)							
Denmark	4.05 (1.26 to 13.05)							
UK	0.72 (0.43 to 1.20)							
Drug Therapy	0.95 (0.57 to 1.57)							
Rehabilitation	0.82 (0.49 to 1.36)							
Testing	0.62 (0.37 to 1.03)							
Community Care	0.74 (0.65 to 0.83)							
Dementia	0.65 (0.37 to 1.12)							
Constant	1.73 (0.88 to 3.43)							

APPENDIX 3.1: CONFIRMATORY FACTOR ANALYSIS OF COGNITIVE FUNCTION SCORES



Note: Model includes a multilevel latent variable (not shown) at the respondent level to account for correlation between waves. Variables in boxes represent those observed in ELSA, and the appending epsilons *ε* the measurement error in those variables. Ellipses represent the latent variables measured by the model.

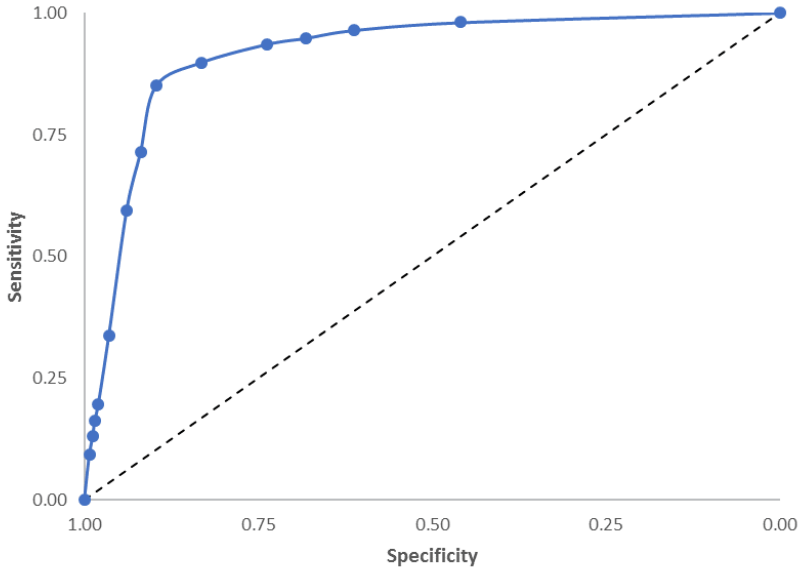
APPENDIX 3.2: CORRELATES OF THE ESTIMATED COGNITIVE FUNCTION SCORE

The table below shows the coefficients for selected known predictors of cognitive impairment on the latent scores developed for memory and executive function, estimated using multilevel regression models with a random intercept at the respondent level. Also shown are the odds ratios for having a cognitive impairment based on the index generated from the latent variable using a multilevel logistic regression with a random intercept at the respondent level.

Predictor	Memory Score		Executive Function Score		Cognitive Impairment	
	β	*p*-value	*β*	*p*-value	OR	*p*-value
Age	-0.071	<0.001	-0.252	<0.001	1.024	<0.001
Ethnicity						
▪ Non-White	*Ref*		*Ref*		*Ref*	
▪ White	0.515	<0.001	1.393	<0.001	0.094	<0.001
Educational Attainment						
▪ Degree or Equivalent	*Ref*		*Ref*		*Ref*	
▪ Other Higher Education	-0.401	<0.001	-1.062	<0.001	1.961	<0.001
▪ A-Level or Equivalent	-0.322	<0.001	-0.869	<0.001	2.232	<0.001
▪ O-Level or Equivalent	-0.484	<0.001	-1.319	<0.001	2.233	<0.001
▪ CSE or Equivalent	-1.230	<0.001	-3.331	<0.001	6.775	<0.001
▪ Foreign/Other	-0.907	<0.001	-2.593	<0.001	4.019	<0.001
▪ No Qualifications	-1.372	<0.001	-3.695	<0.001	11.146	<0.001
Diabetes	-0.375	<0.001	-0.992	<0.001	1.802	<0.001
Hypertension	-0.174	<0.001	-0.479	<0.001	1.246	<0.001
High Cholesterol	-0.028	0.057	-0.144	<0.001	0.941	0.333
Body Mass Index						
▪ < 18.5 (Underweight)	-0.399	<0.001	-1.110	<0.001	2.112	0.001
▪ 18.5 to 25 (Normal)	*Ref*		*Ref*		*Ref*	
▪ 25 to 30 (Overweight)	-0.022	0.424	0.002	0.980	1.039	0.570
▪ ≥ 30 (Obese)	-0.073	0.020	-0.066	0.418	1.311	<0.001

Appendix 3.3: Receiver Operating Characteristic Analysis

Appendix 3.3.1. ROC analysis curve



Appendix 3.3.2. Sensitivity and specificity of the cognitive impairment indicator for identifying cases of diagnosed dementia

Standard Deviation	*z*-score Percentile	TP	FP	FN	TN	Sensitivity	Specificity	Youden Index
0.00	50.0%	549	21,001	11	17,797	0.980	0.459	0.439
-0.33	36.9%	540	15,036	20	23,762	0.964	0.612	0.577
-0.50	30.9%	531	12,376	29	26,422	0.948	0.681	0.629
-0.67	25.2%	524	10,194	36	28,604	0.936	0.737	0.673
-1.00	15.9%	503	6,516	57	32,282	0.898	0.832	0.730
-1.33	**9.1%**	**476**	**3,996**	**84**	**34,802**	**0.850**	**0.897**	**0.747**
-1.50	6.7%	400	3,138	160	35,660	0.714	0.919	0.633
-1.67	4.8%	333	2,362	227	36,436	0.595	0.939	0.534
-2.00	2.3%	189	1,369	371	37,429	0.338	0.965	0.302
-2.33	1.0%	110	779	450	38,019	0.196	0.980	0.176
-2.50	0.6%	91	579	469	38,219	0.163	0.985	0.148
-2.67	0.4%	73	469	487	38,329	0.130	0.988	0.118
-3.00	0.1%	52	280	508	38,518	0.093	0.993	0.086

Abbreviations: FN, false negative; FP, false positive; TN, true negative; TP, true positive

Appendix 3.4: Quality of Care Indicators in the English Longitudinal Study of Ageing

Indicator	Clinical	Process	Disease
Stroke Antihypertensives: If a person aged ≥ 50 years has had a previous stroke, then the patient should be offered antihypertensive medication	General Medical	Treatment (Pharmacotherapy)	Cerebrovascular Disease
Depression Suicide: If a person aged ≥ 50 years receives a diagnosis of a new depressive episode, then the diagnosing physician should ask on the day of diagnosis if the person had any thoughts about suicide	General Medical	Diagnosis	Depression
Depression Treatment: If a person aged ≥ 50 years is diagnosed with clinical depression, then antidepressant treatment, talking treatment, or electroconvulsive therapy should be offered within 2 weeks after diagnosis unless within that period the patient has improved, or unless the patient has substance abuse or dependence, in which case treatment may wait until 8 weeks after the patient is in a drug- or alcohol-free state	General Medical	Treatment (Pharmacotherapy)	
Depression Review: If a person aged ≥ 50 years has no meaningful symptom response after 6 weeks of treatment, then one of the following treatment options should be initiated by the eighth week of treatment: medication dose should be optimised (if initial treatment was medication), or medication should be initiated (if initial treatment was psychotherapy alone), or referral to a psychiatrist should be offered	General Medical	Prognosis & Monitoring	
Diabetes HbA_{1c}: If a person aged ≥ 50 years has diabetes, then his or her glycosylated haemoglobin or fructosamine level should be measured at least annually	General Medical	Prognosis & Monitoring	Diabetes Mellitus
Diabetes Proteinuria: If a diabetic person aged ≥ 50 years does not have established renal disease and is not receiving an ACE inhibitor or angiotensin II receptor blocker, then he or she should receive an annual test for proteinuria	General Medical	Prognosis & Monitoring	
Diabetes Cholesterol: If a diabetic person aged ≥ 50 years has a fasting total cholesterol level of ≥ 5 mmol/l, then he or she should be offered an intervention to lower cholesterol.	General Medical	Treatment (Pharmacotherapy)	

Indicator	Clinical	Process	Disease
Diabetes ACE Inhibitor: If a diabetic person aged ≥ 50 years has one additional cardiac risk factor (i.e., smoking, hypertension, hypercholesterolemia, or renal insufficiency/microalbuminuria), then he/she should be offered an ACE inhibitor or receptor blocker	General Medical	Treatment (Pharmacotherapy)	Diabetes Mellitus
Diabetes Foot Check: All diabetic persons aged ≥ 50 years should have an annual examination of his or her feet	General Medical	Prognosis & Monitoring	
Diabetes Training: People with diabetes may receive training to help manage their diabetes themselves	General Medical	Patient-Centred Care	
Diabetes Knowledge: People with diabetes should know about managing their diabetes	General Medical	Patient-Centred Care	
Fall History: If a person aged ≥ 65 years reported two or more falls in the past year, or a single fall with injury requiring treatment, then the physician should take a basic fall history	Geriatric	Diagnosis	Falls
Fall Assessment: If a person aged ≥ 65 years reported two or more falls in the past year, or a single fall with injury requiring treatment, then the patient should be offered a multidisciplinary falls assessment	Geriatric	Diagnosis	
Hearing Evaluation: If a person aged ≥ 65 years has a problem with hearing, then he or she should be offered a formal audiological evaluation within 3 months	Geriatric	Diagnosis	Hearing Problems
Hearing Rehabilitation: If a person aged ≥ 65 years is a hearing aid candidate, then he or she should be offered hearing rehabilitation	Geriatric	Treatment (Rehabilitative)	
Cholesterol Explanation: Patients with high cholesterol should have it explained to them what it means	General Medical	Patient-Centred Care	High Cholesterol
Cholesterol Preferences: Patients should have their preferences considered when treating high cholesterol	General Medical	Patient-Centred Care	

Indicator	Clinical	Process	Disease
Hypertension Treatment: If a person aged ≥ 50 years remains hypertensive after non-pharmacological intervention, then pharmacological antihypertensive treatment should be initiated	General Medical	Treatment (Pharmacotherapy)	Hypertension
Blood Pressure Explanation: Patients with hypertension should have it explained to them what it means	General Medical	Patient-Centred Care	
Blood Pressure Choice: Patients may be offered choices in their treatment for high blood pressure	General Medical	Patient-Centred Care	
IHD Cholesterol: If a person aged ≥ 50 years has established CHD and LDL cholesterol > 3 mmol/l, then he or she should be offered an intervention to lower cholesterol	General Medical	Treatment (Pharmacotherapy)	Ischaemic Heart Disease
IHD Antiplatelets: If a person aged ≥ 50 years has established CHD and is not on warfarin, then he or she should be offered antiplatelet therapy	General Medical	Treatment (Pharmacotherapy)	
IHD Smoking: If a person aged ≥ 50 years has established CHD smokes, then he or she should be offered counselling for smoking cessation	General Medical	Treatment (Rehabilitative)	
MI Beta Blockers: If a person aged ≥ 50 years has had a recent myocardial infarction, then he or she should be offered a beta-blocker	General Medical	Treatment (Pharmacotherapy)	
INR Test: If a person aged ≥ 50 years is prescribed warfarin, then an INR should be determined at least every 12 weeks	General Medical	Prognosis & Monitoring	
Osteoarthritis Exercise: If an ambulatory person aged ≥ 50 years has had a diagnosis of symptomatic osteoarthritis of the knee for longer than 3 months and has no contraindications to exercise and is physically and mentally able to exercise, then a directed or supervised strengthening or aerobic exercise programme should have been prescribed at least once	Geriatric	Treatment (Rehabilitative)	Osteoarthritis
Osteoarthritis Education: If an ambulatory person aged ≥ 50 years has a diagnosis of symptomatic osteoarthritis, then education regarding the natural history, treatment and self-management of the disease should be offered at least once	Geriatric	Patient-Centred Care	

Indicator	Clinical	Process	Disease
Osteoarthritis Paracetamol: If oral pharmacological therapy is initiated to treat osteoarthritis among people aged ≥ 50 years, then paracetamol should be the first drug used, unless there is a contraindication to use	Geriatric	Treatment (Pharmacotherapy)	Osteoarthritis
Osteoarthritis Referral: If a person aged ≥ 50 years with severe symptomatic osteoarthritis of the knee or hip has failed to respond to non-pharmacological and pharmacological therapy, then the patient should be offered referral to an orthopaedic surgeon to be evaluated for total joint replacement within 6 months unless surgery is contraindicated	Geriatric	Treatment (Surgical)	
Osteoarthritis Treatment Purpose: If a patient is being treated for osteoarthritis, then they should be informed to the purpose, as well as the nature, of their treatment	Geriatric	Patient-Centred Care	
Osteoporosis Supplements: If a person aged ≥ 50 years has untreated osteoporosis, then calcium and vitamin D supplements should be recommended at least once	Geriatric	Treatment (Pharmacotherapy)	Osteoporosis
Osteoporosis Treatment: If a woman aged ≥ 50 years is newly diagnosed with osteoporosis, then the patient should be offered treatment with hormone replacement therapy, SERMs, bisphosphonates, calcitonin, or calcium and vitamin D within 3 months of diagnosis	Geriatric	Treatment (Pharmacotherapy)	
Pain Treatment: If a person aged ≥ 50 years has a newly reported chronic painful condition, then treatment should be offered	General Medical	Treatment (Pharmacotherapy)	Pain Management
Smoking Cessation: If a person aged ≥ 50 years uses tobacco regularly, then he or she should be offered advice and/or pharmacological therapy to stop tobacco use at least once	General Medical	Treatment (Rehabilitative)	Smoking
Incontinence History: If a person aged ≥ 65 years has new UI that persists for over one month or UI at the time of a new evaluation, then a targeted history should be obtained about each of the following: (1) characteristics of voiding, (2) ability to get	Geriatric	Diagnosis	Urinary Incontinence

Indicator	Clinical	Process	Disease
to the toilet, (3) prior treatment for urinary incontinence, (4) importance of the problem to the patient, and (5) mental status			
Incontinence Examination: If a person aged ≥ 65 years has new UI that persists for over one month after consulting a doctor, then a targeted physical exam should be performed that includes (1) a rectal exam and (2) a genital system exam (including a pelvic exam for women)	Geriatric	Diagnosis	Urinary Incontinence
Incontinence Treatment: If a person aged ≥ 65 years has new UI or UI at the time of a new evaluation, then treatment options should be discussed	Geriatric	Patient-Centred Care	
Urinalysis: If a person aged ≥ 65 years has new UI that persists for over one month or UI at the time of a new evaluation, then a dipstick urinalysis and/or mid-stream urine sample should be obtained	Geriatric	Diagnosis	
Cataracts Surgery: If a person aged ≥ 50 years is diagnosed with a cataract that limits the patient's ability to carry out needed or desired activities, then cataract extraction should be offered	Geriatric	Treatment (Surgical)	Vision Problems

APPENDIX 3.5: MISSING DATA ON QUALITY INDICATORS

Quality Indicator	No Impairment		Non-Dementia Impairment		Diagnosed Dementia		*p*-value
	N	Missing	*N*	Missing	*N*	Missing	
Stroke Antihypertensives	372	8.6%	96	17.7%	20	10.0%	0.034
Depression Suicide	668	4.8%	106	3.8%	25	40.0%	< 0.001
Depression Treatment	468	1.3%	90	3.3%	11	0.0%	0.329
Depression Review	29	0.0%	5	0.0%	1	0.0%	N/A
Diabetes HbA1c	2,725	5.4%	495	7.3%	48	14.6%	0.009
Diabetes Proteinuria	1,088	3.2%	208	6.7%	17	5.9%	0.048
Diabetes Cholesterol	196	0.0%	39	0.0%	4	0.0%	N/A
Diabetes ACE Inhibitor	1,618	2.0%	306	1.6%	49	14.3%	< 0.001
Diabetes Foot Check	2,875	5.4%	497	0.8%	75	36.0%	< 0.001
Diabetes Training	1,956	4.5%	360	0.6%	52	36.5%	< 0.001
Diabetes Knowledge	1,956	4.7%	360	1.1%	52	40.4%	< 0.001
Falls History	247	0.0%	54	3.7%	8	0.0%	0.009
Falls Assessment	247	0.0%	54	1.9%	8	0.0%	0.094
Hearing Evaluation	890	0.1%	143	0.0%	15	0.0%	0.915
Hearing Rehabilitation	584	0.2%	94	0.0%	9	0.0%	0.915
Cholesterol Explanation	1,489	0.9%	219	0.0%	10	16.7%	< 0.001
Cholesterol Preferences	1,489	1.9%	219	0.9%	11	8.3%	0.143
Hypertension Treatment	11,540	10.6%	1507	11.1%	129	41.4%	< 0.001
Blood Pressure Explanation	1,430	0.2%	220	0.0%	11	8.3%	< 0.001
Blood Pressure Choice	1,430	1.9%	220	3.2%	12	0.0%	0.398
IHD Cholesterol	221	0.0%	45	0.0%	5	0.0%	N/A
IHD Antiplatelets	767	0.0%	118	0.0%	16	0.0%	N/A
IHD Smoking	186	4.8%	58	0.0%	6	14.3%	0.095
MI Beta Blockers	172	0.0%	32	3.1%	2	0.0%	0.065
INR Test	140	4.3%	19	0.0%	4	0.0%	0.599
Osteoarthritis Exercise	1,305	0.0%	135	0.0%	12	0.0%	N/A
Osteoarthritis Education	6,475	1.7%	681	0.4%	77	33.0%	< 0.001
Osteoarthritis Paracetamol	1,445	1.0%	166	0.6%	5	0.0%	0.844
Osteoarthritis Referral	566	0.2%	114	0.0%	9	10.0%	< 0.001
OA Treatment Purpose	1,619	0.1%	173	0.0%	13	0.0%	0.891
Osteoporosis Supplements	802	2.9%	103	2.9%	11	26.7%	< 0.001
Osteoporosis Treatment	172	2.3%	14	7.1%	1	0.0%	0.554
Pain Treatment	524	0.0%	102	0.0%	5	0.0%	N/A
Smoking Cessation	2,217	2.4%	455	0.0%	21	27.6%	< 0.001
Incontinence History	269	1.1%	56	3.6%	8	0.0%	0.365
Incontinence Examination	269	1.5%	56	1.8%	8	0.0%	0.926
Incontinence Treatment	269	0.7%	56	0.0%	8	0.0%	0.787
Urinalysis	269	0.7%	56	0.0%	8	0.0%	0.787
Cataracts Surgery	1,090	4.1%	162	1.9%	24	29.4%	< 0.001
Overall	**52,074**	**4.2%**	**7,893**	**3.6%**	**716**	**26.0%**	**< 0.001**

Notes: *p*-value denotes the statistical significance of the distribution of missingness by type of cognitive impairment as determined by the χ^2 test. Values less than 0.05 suggest a significant association between cognitive function and missingness.

Appendix 3.6: Summary Statistics on Sample From ELSA by Wave

	Wave 2				Wave 3			
	No Impairment	Non-Dementia Impairment	Diagnosed Dementia	*p*-value	No Impairment	Non-Dementia Impairment	Diagnosed Dementia	*p*-value
N	5,056	823	56		4,024	541	77	
Age, Mean (SD)	67.8 (10.1)	67.5 (9.4)	76.2 (10.1)	< 0.001	67.7 (10.5)	66.1 (9.7)	78.1 (9.9)	< 0.001
▪ 50 - 54	471 (9.3%)	58 (7.0%)	2 (3.6%)		431 (10.7%)	70 (12.9%)	1 (1.3%)	
▪ 55 - 59	876 (17.3%)	151 (18.3%)	5 (8.9%)		656 (16.3%)	98 (18.1%)	6 (7.8%)	
▪ 60 - 64	705 (13.9%)	146 (17.7%)	1 (1.8%)		630 (15.7%)	89 (16.5%)	3 (3.9%)	
▪ 65 - 69	840 (16.6%)	138 (16.8%)	4 (7.1%)		550 (13.7%)	83 (15.3%)	1 (1.3%)	
▪ 70 - 74	765 (15.1%)	134 (16.3%)	11 (19.6%)		593 (14.7%)	81 (15.0%)	12 (15.6%)	
▪ 75 - 79	632 (12.5%)	104 (12.6%)	8 (14.3%)		515 (12.8%)	75 (13.9%)	9 (11.7%)	
▪ 80 - 84	471 (9.3%)	57 (6.9%)	11 (19.6%)		360 (8.9%)	32 (5.9%)	19 (24.7%)	
▪ 85 - 89	222 (4.4%)	26 (3.2%)	11 (19.6%)		222 (5.5%)	10 (1.8%)	23 (29.9%)	
▪ ≥ 90	74 (1.5%)	9 (1.1%)	3 (5.4%)	< 0.001	67 (1.7%)	3 (0.6%)	3 (3.9%)	< 0.001
Female	2,887 (57.1%)	396 (48.1%)	16 (28.6%)	< 0.001	2,325 (57.8%)	269 (49.7%)	44 (57.1%)	0.002
Married and/or Cohabiting	3,396 (67.2%)	504 (61.2%)	39 (69.6%)	0.003	2,677 (66.5%)	328 (60.6%)	42 (54.5%)	0.003
№ Chronic Conditions, Mean (SD)	0.60 (0.80)	0.63 (0.81)	0.57 (0.74)	0.433	1.12 (0.96)	1.23 (1.03)	1.49 (1.19)	< 0.001
№ Cardiovascular Conditions, Mean (SD)	1.13 (1.04)	1.17 (1.11)	1.43 (1.17)	0.055	1.46 (1.06)	1.63 (1.16)	1.74 (1.21)	< 0.001
Net Non-Pension Wealth, Mean (SD)	£ 244,298 (356,216)	£ 141,623 (175,720)	£ 202,496 (260,786)	< 0.001	£ 283,436 (548,007)	£ 167,840 (208,477)	£ 169,596 (166,781)	< 0.001
Eligible Quality Indicators, Mean (SD)	3.62 (2.79)	4.06 (3.18)	4.61 (3.59)	< 0.001	2.11 (1.68)	2.31 (1.99)	2.04 (1.73)	0.033
GPs per 1,000 Patients, Mean (SD)	0.54 (0.04)	0.54 (0.04)	0.54 (0.04)	0.019	0.59 (0.07)	0.58 (0.06)	0.58 (0.05)	0.020
QOF Organisational Domain, Mean (SD)	88.9% (0.04)	88.3% (0.04)	88.9% (0.04)	0.002	93.7% (0.03)	93.3% (0.03)	93.7% (0.03)	0.006
QOF Patient Experience Domain, Mean (SD)	94.6% (0.03)	94.1% (0.04)	94.9% (0.03)	0.001	97.1% (0.02)	96.8% (0.02)	97.0% (0.02)	0.011

Notes: Values are *n* (%) unless otherwise stated

p-values for differences between cognitive groups were calculated using ANOVA for continuous variables and χ^2 tests for categorical variables

	Wave 4				Wave 5			
	No Impairment	Non-Dementia Impairment	Diagnosed Dementia	*p*-value	No Impairment	Non-Dementia Impairment	Diagnosed Dementia	*p*-value
N	5,226	602	97		5,708	635	118	
Age, Mean (SD)	67.5 (9.7)	67.0 (9.7)	77.1 (10.3)	< 0.001	68.1 (9.1)	67.0 (9.1)	75.9 (9.6)	< 0.001
▪ 50 - 54	406 (7.8%)	74 (12.3%)	1 (1.0%)		209 (3.7%)	38 (6.0%)	1 (0.8%)	
▪ 55 - 59	857 (16.4%)	88 (14.6%)	6 (6.2%)		931 (16.3%)	123 (19.4%)	5 (4.2%)	
▪ 60 - 64	1,021 (19.5%)	100 (16.6%)	8 (8.2%)		1,169 (20.5%)	126 (19.8%)	16 (13.6%)	
▪ 65 - 69	798 (15.3%)	97 (16.1%)	10 (10.3%)		978 (17.1%)	102 (16.1%)	12 (10.2%)	
▪ 70 - 74	849 (16.2%)	102 (16.9%)	10 (10.3%)		927 (16.2%)	110 (17.3%)	9 (7.6%)	
▪ 75 - 79	602 (11.5%)	79 (13.1%)	11 (11.3%)		737 (12.9%)	69 (10.9%)	28 (23.7%)	
▪ 80 - 84	395 (7.6%)	37 (6.1%)	25 (25.8%)		498 (8.7%)	48 (7.6%)	18 (15.3%)	
▪ 85 - 89	226 (4.3%)	22 (3.7%)	16 (16.5%)		259 (4.5%)	19 (3.0%)	29 (24.6%)	
▪ ≥ 90	72 (1.4%)	3 (0.5%)	10 (10.3%)	< 0.001	0 (0.0%)	0 (0.0%)	0 (0.0%)	< 0.001
Female	2,957 (56.6%)	313 (52.0%)	51 (52.6%)	0.078	3,226 (56.5%)	329 (51.8%)	61 (51.7%)	0.049
Married and/or Cohabiting	3,573 (68.4%)	352 (58.5%)	57 (58.8%)	< 0.001	3,963 (69.4%)	389 (61.3%)	72 (61.0%)	< 0.001
№ Chronic Conditions, Mean (SD)	0.98 (0.88)	1.08 (0.98)	1.23 (0.97)	0.002	0.97 (0.91)	1.07 (1.01)	1.25 (1.03)	< 0.001
№ Cardiovascular Conditions, Mean (SD)	1.44 (1.12)	1.59 (1.18)	2.06 (1.31)	< 0.001	1.40 (1.13)	1.44 (1.22)	1.93 (1.48)	< 0.001
Net Non-Pension Wealth, Mean (SD)	£ 306,424 (552,000)	£ 168,439 (230,656)	£ 187,329 (260,102)	< 0.001	£ 309,724 (451,170)	£ 185,712 (293,415)	£ 184,304 (171,926)	< 0.001
Eligible Quality Indicators, Mean (SD)	2.52 (2.02)	2.89 (2.34)	2.80 (2.16)	< 0.001	2.13 (1.49)	2.46 (1.73)	2.37 (1.51)	< 0.001
GPs per 1,000 Patients, Mean (SD)	0.58 (0.06)	0.57 (0.06)	0.57 (0.05)	0.282	0.58 (0.05)	0.57 (0.05)	0.58 (0.06)	0.453
QOF Organisational Domain, Mean (SD)	95.7% (0.02)	95.4% (0.02)	95.7% (0.02)	< 0.001	97.3% (0.01)	97.1 (0.01)	97.4% (0.01)	< 0.001
QOF Patient Experience Domain, Mean (SD)	91.3% (0.07)	90.6% (0.08)	90.3% (0.08)	0.029	73.4% (0.07)	73.4% (0.06)	73.4% (0.07)	> 0.999

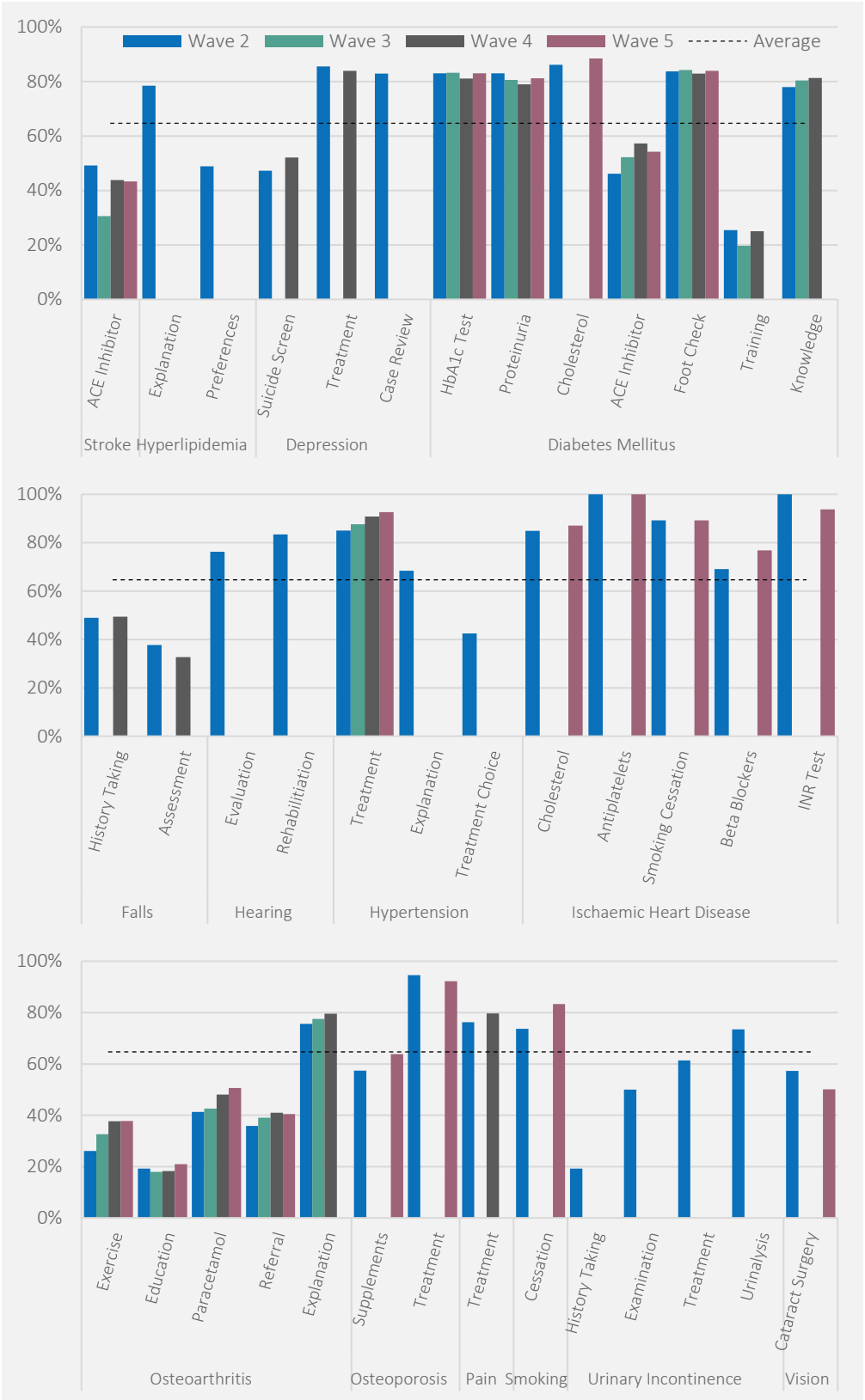
Notes: Values are *n* (%) unless otherwise stated

p-values for differences between cognitive groups were calculated using ANOVA for continuous variables and χ^2 tests for categorical variables

Appendix 3.7: Summary of Outcomes on Individual Quality Indicators

The table below summarises the overall proportion of respondents claiming to have met the quality indicator across all observed waves, whereas the figures overleaf show the proportion passing each indicator at each wave.

Disease Area	Quality Indicator	Proportion Met	Standard Deviation	ELSA Wave(s)	Observations
Cerebrovascular	Stroke Antihypertensives	40.7%	0.492	2 – 5	437
Depression	Depression Suicide	51.1%	0.500	2 & 4	753
	Depression Treatment	84.3%	0.364	2 & 4	560
	Depression Review	82.9%	0.382	2	35
Diabetes	Diabetes HbA1c	82.5%	0.380	2 – 5	3,077
	Diabetes Proteinuria	80.9%	0.393	2 – 5	1,263
	Diabetes Cholesterol	87.0%	0.337	2 & 5	239
	Diabetes ACE Inhibitor	52.6%	0.499	2 – 5	1,928
	Diabetes Foot Check	83.7%	0.370	2 – 5	3,260
	Diabetes Training	23.7%	0.426	2 – 4	2,259
	Diabetes Knowledge	80.0%	0.400	2 – 4	2,252
Falls	Falls History	49.2%	0.501	2 & 4	307
	Falls Assessment	35.1%	0.478	2 & 4	308
Hearing Problems	Hearing Evaluation	76.3%	0.425	2	1,047
	Hearing Rehabilitation	83.4%	0.373	2	686
Hyperlipidaemia	Cholesterol Explanation	78.5%	0.411	2	1,705
	Cholesterol Preferences	48.9%	0.500	2	1,688
Hypertension	Hypertension Treatment	89.7%	0.304	2 – 5	11,783
	Blood Pressure Explanation	68.5%	0.465	2	1,658
	Blood Pressure Choice	42.4%	0.494	2	1,628
Ischaemic Heart Disease	IHD Cholesterol	85.6%	0.352	2 & 5	271
	IHD Antiplatelets	100.0%	0.000	2 & 5	901
	IHD Smoking	89.2%	0.311	2 & 5	241
	MI Beta Blockers	72.2%	0.449	2 & 5	205
	INR Test	95.5%	0.207	2 & 5	157
Osteoarthritis	Osteoarthritis Exercise	34.0%	0.474	2 – 5	1,452
	Osteoarthritis Education	19.2%	0.394	2 – 5	7,119
	Osteoarthritis Paracetamol	46.1%	0.499	2 – 5	1,600
	Osteoarthritis Referral	39.2%	0.489	2 – 5	688
	Treatment Purpose	78.4%	0.411	2 – 4	1,803
Osteoporosis	Osteoporosis Supplements	62.4%	0.485	2 & 5	890
	Osteoporosis Treatment	93.4%	0.249	2 & 5	182
Pain	Pain Treatment	78.1%	0.414	2 & 4	631
Smoking	Smoking Cessation	78.1%	0.413	2 & 5	2,640
Urinary Incontinence	Incontinence History	19.2%	0.395	2	328
	Incontinence Examination	50.0%	0.501	2	328
	Incontinence Treatment	61.3%	0.488	2	331
	Urinalysis	73.4%	0.442	2	331
Vision	Cataracts Surgery	53.6%	0.499	2 & 5	1,228


100%
80%
60%
40%
20%
0%
Wave 2
Wave 3
Wave 4
Wave 5
Average
ACE Inhibitor
Explanation
Preferences
Suicide Screen
Treatment
Case Review
HbA1c Test
Proteinuria
Cholesterol
ACE Inhibitor
Foot Check
Training
Knowledge
Stroke
Hyperlipidemia
Depression
Diabetes Mellitus
History Taking
Assessment
Evaluation
Rehabilitiation
Treatment
Explanation
Treatment Choice
Cholesterol
Antiplatelets
Smoking Cessation
Beta Blockers
INR Test
Falls
Hearing
Hypertension
Ischaemic Heart Disease
Exercise
Education
Paracetamol
Referral
Explanation
Supplements
Treatment
Treatment
Cessation
History Taking
Examination
Treatment
Urinalysis
Cataract Surgery
Osteoarthritis
Osteoporosis
Pain
Smoking
Urinary Incontinence
Vision

Appendix 3.8: Sensitivity Analysis Using Observed Data Only

Predictor	Overall QoC		General Medical		Geriatric	
	OR	95% CI	OR	95% CI	OR	95% CI
Observations (Respondents)	57,194 (10,060)		38,863 (8,475)		18,331 (5,422)	
Univariate Analyses						
Cognitive Impairment						
▪ No Impairment	*Ref*		*Ref*		*Ref*	
▪ Non-Dementia Impairment	1.03	0.91 – 1.17	0.78***	0.68 – 0.90	1.29***	1.07 – 1.56
▪ Diagnosed Dementia	1.13	0.76 – 1.70	1.00	0.63 – 1.60	1.23	0.69 – 2.20
Multivariate Analyses						
Cognitive Impairment						
▪ No Impairment	*Ref*		*Ref*		*Ref*	
▪ Non-Dementia Impairment	1.01	0.90 – 1.14	0.85**	0.74 – 0.99	1.19*	0.99 – 1.43
▪ Diagnosed Dementia	0.94	0.63 – 1.38	0.78	0.48 – 1.25	1.12	0.64 – 1.97
Age (years)						
▪ 50 - 54	*Ref*		*Ref*		*Ref*	
▪ 55 - 59	1.20**	1.01 – 1.44	1.38***	1.12 – 1.70	0.95	0.71 – 1.27
▪ 60 - 64	1.11	0.92 – 1.34	1.37***	1.10 – 1.72	0.95	0.71 – 1.29
▪ 65 - 69	1.12	0.92 – 1.35	1.55***	1.23 – 1.96	1.07	0.79 – 1.44
▪ 70 - 74	1.10	0.90 – 1.33	1.54***	1.22 – 1.94	1.20	0.89 – 1.62
▪ 75 - 79	1.14	0.93 – 1.39	1.47***	1.15 – 1.87	1.43**	1.05 – 1.95
▪ 80 - 84	1.08	0.87 – 1.35	1.31**	1.00 – 1.71	1.65***	1.19 – 2.28
▪ 85 - 89	1.23	0.94 – 1.59	1.35*	0.97 – 1.89	2.03***	1.41 – 2.92
▪ ≥ 90	0.71	0.45 – 1.14	0.63	0.33 – 1.22	1.35	0.77 – 2.36
Female	0.74***	0.66 – 0.82	0.84***	0.74 – 0.96	1.06	0.92 – 1.23
Married and/or Cohabiting	1.19***	1.07 – 1.34	1.33***	1.16 – 1.53	1.19**	1.02 – 1.38
Chronic Comorbidity Index						
▪ None	*Ref*		*Ref*		*Ref*	
▪ 1	0.49***	0.44 – 0.54	1.12*	0.99 – 1.26	0.44***	0.36 – 0.54
▪ 2 or 3	0.39***	0.34 – 0.44	1.02	0.87 – 1.19	0.47***	0.38 – 0.59
▪ 4 or More	0.30***	0.22 – 0.42	0.82	0.52 – 1.29	0.49***	0.32 – 0.75
Cardiovascular Comorbidities						
▪ None	*Ref*		*Ref*		*Ref*	
▪ 1	2.22***	1.95 – 2.52	1.38***	1.12 – 1.68	0.95	0.82 – 1.10
▪ 2 or 3	3.42***	3.01 – 3.90	1.60***	1.31 – 1.95	1.06	0.91 – 1.24
▪ 4 or More	4.37***	3.58 – 5.32	1.95***	1.50 – 2.53	1.03	0.75 – 1.41
Net Non-Pension Wealth						
▪ 1st Quintile (Least Wealthy)	*Ref*		*Ref*		*Ref*	
▪ 2nd Quintile	0.88**	0.77 – 1.00	0.95	0.81 – 1.11	0.91	0.76 – 1.09
▪ 3rd Quintile	0.96	0.83 – 1.10	1.05	0.88 – 1.24	0.96	0.79 – 1.17
▪ 4th Quintile	0.91	0.79 – 1.06	1.07	0.89 – 1.28	0.94	0.76 – 1.15
▪ 5th Quintile (Wealthiest)	0.84**	0.71 – 0.98	1.07	0.88 – 1.31	0.88	0.70 – 1.09
GPs per 1,000 Patients	1.28	0.53 – 3.07	0.87	0.29 – 2.63	2.57	0.78 – 8.49
QOF Organisation Domain (%)	1.03***	1.02 – 1.04	1.10***	1.09 – 1.11	0.00***	0.00 – 0.00

Notes: * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

CHAPTER 4

APPENDIX 4.1: PREDICTING PREFERENCE-BASED QUALITY OF LIFE UTILITIES FROM HEALTH & DEMOGRAPHIC VARIABLES

Background

For health technology assessments where an economic analysis of the new technology is required, assessments of its cost-effectiveness using a cost per quality-adjusted life year (QALY) framework are commonly used. The NICE Guide to the Methods of Technology Appraisals states the three-level version of the EQ-5D, using utilities measured in a time trade-off exercise in the UK, is the preferred method for deriving utilities to estimate QALYs in model.[i] However, these guidelines recognise that EQ-5D data may not have been collected or be directly available to inform analyses and presents options for alternative options for measuring and valuing health effects, which includes mapping other dimensions of health to the EQ-5D. Mapping is the use of an algorithm to estimate or predict utilities using other measures of health or indicators of quality of life.[ii] A vast number of mapping algorithms have been developed for both disease-specific quality of life measures or clinical indicators of disease severity to predict EQ-5D scores,[iii] however most of the scales used in these algorithms were not routinely collected in the English Longitudinal Study of Ageing (ELSA) – the dataset used to inform most analyses in this thesis. The exception to this is the Satisfaction with Life Scale (SWLS),[iv] for which a mapping algorithm to the EQ-5D is published,[v] however as this was considered conceptually different from health-related quality of life due to the lack of health and functional measures captured in the scale, an alternative was sought to inform analyses on health-related quality of life. In addition, despite a significant association between SWLS scores and utilities derived from the EQ-5D, this correlation is weak, and the mapping model provided a poor fit to the data.[v]

The aim of this analysis is to assess the relationship between metrics of general physical and mental health, functional limitations, and demographic factors, and the EQ-5D-3L, and develop a mapping algorithm between the measures. This algorithm can be used to determine the changes in utility associated with effects or exposures for respondents in ELSA, where the utility measures were not collected.

Methods

The EQ-5D is a self-administered questionnaire in which respondents are asked to rate problems on five dimensions associated with health or function: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. On the three-level version,

response options are (1) no problems, (2) some problems, and (3) extreme problems, meaning 243 health states are possible. Perfect health is defined as no problems on all five dimensions (11111), and the worst possible health state is with extreme problems on all dimensions (33333). Utility values for each of the 243 health states have been derived from a time trade-off study obtained from a sample of the general population in the UK, whereby a generalised least-squares regression model was used to estimate decrements in utility associated with each derivation from perfect health (i.e., specific decrements for some problems and extreme problems on each dimension).[vi]

In addition, decrements were included for any deviation from perfect health (all health states apart from 11111) and for having extreme problems (a score of three) on any domain. The resulting EQ-5D utilities range from 1 (perfect health) to -0.594 (state 33333). The regression model defined for utilities in the UK is:

$$Y = 1 - 0.081L_1 - 0.069MO_2 - 0.314MO_3 - 0.104SC_2 - 0.214SC_3 - 0.036UA_2 - 0.094UA_3 - 0.123PD_2 - 0.386PD_3 - 0.071AD_2 - 0.236AD_3 - 0.269N_3,$$

where *L* represents the deviation from perfect health, *N* is a response of extreme problems (3) on any dimensions, the numbers in subscript represent some problems (2) and extreme problems (3) with each of the dimensions of mobility *MO*, self-care *SC*, usual activities *UA*, pain/discomfort *PD*, or anxiety/depression *AD*. Therefore, a respondent with a response of 11213 would have a utility of

$$1 - 0.081 - 0.036 - 0.236 - 0.269 = 0.378,$$

accounting for the decrements associated with a deviation from perfect health, the level 2 response on usual activities, the level 3 response on anxiety/depression, and the fact that a level 3 response had be included at all.

To acquire data on the EQ-5D on a representative UK population in order to derive a mapping algorithm, the Health Survey for England (HSE) was used. The HSE is an annual cross-sectional survey of private households in England and the data are freely available from the UK Data Service for academic purposes. In 2003, 2004, 2005, 2006 and 2008, EQ-5D data were collected in the HSE and these datasets were combined for the purpose of developing the mapping algorithm.[vii viii ix x xi] Only respondents who had complete data on the EQ-5D were retained, as were those respondents aged over 50 years and therefore eligible for enrolment in ELSA.

Demographic and socioeconomic variables, as well as questions to assess general physical and mental health, diagnosed conditions, and other health related variables

collected in ELSA were compared to those collected in the included waves of the HSE to identify those measuring the same constructs. These were further filtered based on comparability of the wording of the question or the reporting of responses to derive a list of relevant variables included in both studies. Results from the identified variables were then compared on the population level between studies to determine if any other differences needed to be accounted for. For example, data on income and equivalised income were collected in both studies, but values reported between studies were inexplicably different and therefore the method of calculation was assumed to differ meaning that it could not be included as a variable.

A previous analysis of health-related quality of life and utilities in HSE has identified age, age-squared, sex, highest level of education attained, and self-reported general health as predictors of health-related quality of life,[xii] and so were considered to inclusion here. For consistency between the studies, educational attainment was categorised as degree or equivalent, higher education below degree level, A level or equivalent, O level or equivalent, other (includes other educational level or foreign qualifications), and no qualifications. Self-rated general health was categorised as excellent/very good, good, fair, or bad/very bad. Whether the respondent had any longstanding illness, and specific diagnosed conditions were also considered. Diagnosed conditions recorded in both HSE and ELSE were angina, myocardial infarction, or stroke, arrhythmia or heart murmur, arthritis, other heart problems, asthma, bronchitis or emphysema, cancer, diabetes, hypertension, psychiatric diagnoses, hearing problems, vision problems, and urinary incontinence. Given the conceptual links to the dimensions of the EQ-5D, whether the respondent had been recently feeling depressed and whether any of the longstanding illnesses limited their mobility or ability to conduct activities of daily living were also considered. No appropriate metrics of pain were found to be applicable to both the ELSA and HSE datasets.

As the UK value set for the EQ-5D includes an additional decrement if respondents have extreme problems on any domain, two metrics of severity were developed for assessment in the analysis. The first of these was the effect of multimorbidity, accounting for the number of diagnosed conditions included grouped into three categories: none or one, two or three, and four or more. The second was the combined impact of diagnoses and overall health, again grouped into three categories: general health rated poor and respondent is diagnosed with a longstanding illness which limits activities of daily living, poor self-rated health and a longstanding illness which does not limit activities of daily living, and good or fair health. In addition, given the

decrement for a deviation from perfect health included in the utility estimation algorithm, a dummy variable for having no longstanding illnesses was also included.

A linear model for predicting EQ-5D utilities was defined using an ordinary least squares regression including all explanatory variables in the first instance. Explanatory variables were backwards eliminated one-by-one in order of *p*-value to derive a model composed of variables that were statistically significant predictors at the 5% level of the format:

$$Y = \alpha + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_n x_n + \varepsilon$$

where Y represents the utility derived from the EQ-5D, α represents the constant, ε the error term in estimation, and β the coefficients to be estimated associated with explanatory variables x. Models and the impact of excluding variables was evaluated for goodness-of-fit using the R^2 and root mean squared error (RMSE).

Appendix 4.1.1. Summary of respondent characteristics

	HSE Estimation Sample	HSE Validation Sample	ELSA Sample
N	20,448	6,816	22,963
Age, Mean (SD)	65.7 (10.3)	65.7 (10.3)	67.8 (9.8)
Age Groups			
▪ 50 - 54	3,294 (16.1%)	1,087 (16.0%)	1,762 (7.7%)
▪ 55 - 59	3,589 (17.6%)	1,202 (17.6%)	3,802 (16.6%)
▪ 60 - 64	3,227 (15.8%)	1,061 (15.6%)	4,014 (17.5%)
▪ 65 - 69	3,093 (15.1%)	1,062 (15.6%)	3,613 (15.7%)
▪ 70 - 74	2,711 (13.3%)	898 (13.2%)	3,603 (15.7%)
▪ 75 - 79	2,169 (10.6%)	690 (10.1%)	2,869 (12.5%)
▪ 80 - 84	1,437 (7.0%)	495 (7.3%)	1,971 (8.6%)
▪ 85 - 89	683 (3.3%)	239 (3.5%)	1,085 (4.7%)
▪ ≥ 90	245 (1.2%)	82 (1.2%)	244 (1.1%)
Female	11,248 (55.0%)	3,769 (55.3%)	12,874 (56.1%)
Highest Educational Qualification			
▪ Degree or Equivalent	2,642 (12.9%)	831 (12.2%)	3,144 (13.8%)
▪ Higher Education Below Degree	2,314 (11.3%)	755 (11.1%)	3,070 (13.5%)
▪ A-Level or Equivalent	1,327 (6.5%)	480 (7.0%)	1,623 (7.1%)
▪ O-Level or Equivalent	3,519 (17.2%)	1,126 (16.5%)	4,011 (17,6%)
▪ Other	1,857 (9.1%)	637 (9.4%)	2,960 (13.0%)
▪ No Qualifications	8,789 (43.0%)	2,987 (43.8%)	7,926 (34.9%)
Self-Rated Health			
▪ Excellent or Very Good	5,104 (25.0%)	1,658 (24.3%)	6,048 (27.1%)
▪ Good	8,065 (39.4%)	2,768 (40.6%)	8,024 (35.9%)
▪ Fair	5,191 (25.4%)	1,674 (24.6%)	5,932 (26.5%)
▪ Bad or Very Bad	2,088 (10.2%)	716 (10.5%)	2,350 (10.5%)
Recently Felt Depressed	2,516 (12.3%)	867 (12.7%)	4,050 (17.8%)
Longstanding Illnesses			
▪ None	7,428 (36.3%)	2,479 (36.4%)	3,663 (16.1%)
▪ 1	8,176 (40.0%)	2,712 (39.8%)	3,812 16.7%)
▪ 2 - 3	4,327 (21.2%)	1,452 (21.3%)	11,210 (49.2%)
▪ ≥ 4	517 (2.5%)	173 (2.5%)	4,114 (18.0%)
Whether Longstanding Illness(es) Limit ADLs			
▪ No	12,862 (62.9%)	4,300 (63.1%)	12,544 (55.0%)
▪ Yes	7,586 (37.1%)	2,516 (36.9%)	10,255 (45%)
EQ-5D Utility Weight, Mean (SD)	0.795 (0.263)	0.795 (0.265)	N/A

Numbers reported are *n* (%) unless otherwise stated.

The sample from HSE was split randomly into two groups representing 75% and 25% of the total sample. The larger group was defined as the estimation sample from which to derive the mapping algorithm, and the smaller group the validation sample on which to test the predictive ability of the algorithm. Predicted utility values were derived for the validation sample based on the mapping algorithm derived in the estimation sample. Predicted values were adjusted for implausible values (any scores higher than

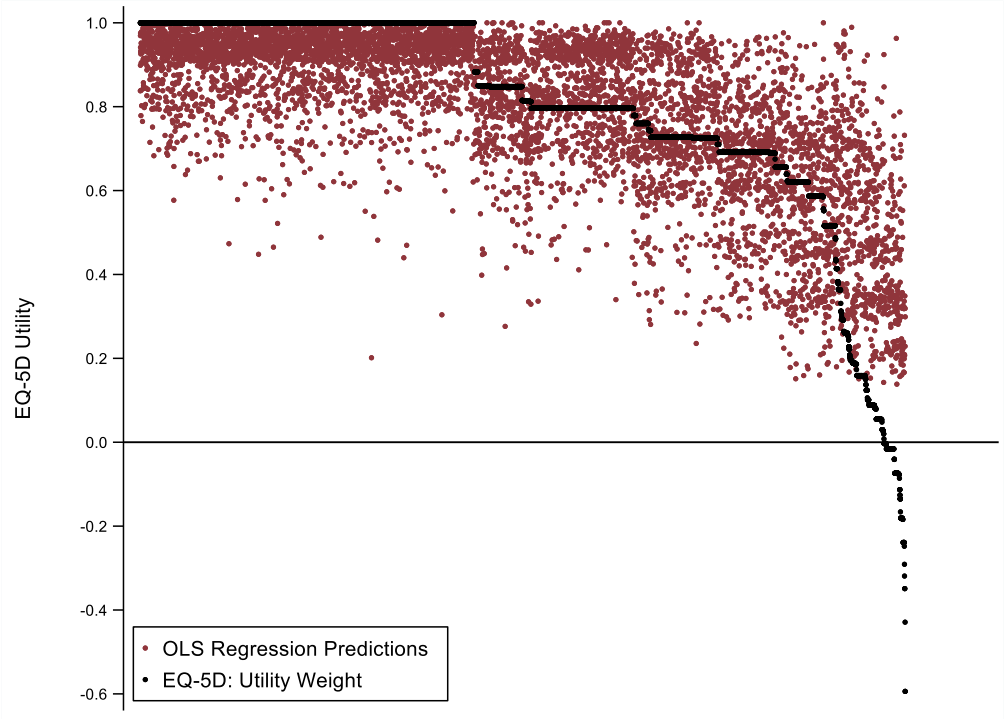
Appendix 4.1.2. Model coefficients for the algorithms containing all variables and after elimination of non-significant variables

	All Variables			Restricted Model		
Adjusted R^2	0.5204			0.5169		
RMSE	0.1828			0.1830		
	β	SE	*p*-value	β	SE	*p*-value
Age	0.0116	0.0014	< 0.001	0.0112	0.0016	< 0.001
Age^2	-0.0001	0.0000	< 0.001	-0.0001	0.0000	< 0.001
Female	-0.0176	0.0023	< 0.001	-0.0184	0.0026	< 0.001
Highest Educational Qualification						
▪ Degree or Equivalent	*Ref*			*Ref*		
▪ Higher Education Below Degree	-0.0184	0.0046	< 0.001	-0.0183	0.0052	< 0.001
▪ A-Level or Equivalent	-0.0194	0.0053	< 0.001	-0.0202	0.0062	0.001
▪ O-Level or Equivalent	-0.0154	0.0041	< 0.001	-0.0154	0.0048	0.001
▪ Other	-0.0320	0.0049	< 0.001	-0.0343	0.0057	< 0.001
▪ No Qualifications	-0.0360	0.0038	< 0.001	-0.0352	0.0043	< 0.001
Self-Rated Health						
▪ Excellent or Very Good	*Ref*			*Ref*		
▪ Good	-0.0338	0.0029	< 0.001	-0.0353	0.0034	< 0.001
▪ Fair	-0.1099	0.0037	< 0.001	-0.1126	0.0043	< 0.001
▪ Bad or Very Bad	-0.3493	0.0244	< 0.001	-0.3704	0.0059	< 0.001
Recently Felt Depressed	-0.1405	0.0036	< 0.001	-0.1382	0.0041	< 0.001
No Longstanding Illnesses	0.0119	0.0032	< 0.001	0.0108	0.0036	0.003
Longstanding Illnesses						
▪ Angina, Heart Attack, or Stroke	-0.0052	0.0054	0.340	-	-	-
▪ Arrythmia or Heart Murmur	0.0143	0.0054	0.008	0.0148	0.0060	0.014
▪ Other Heart Problems	0.0230	0.0055	< 0.001	0.0243	0.0061	< 0.001
▪ Arthritis	-0.0947	0.0039	< 0.001	-0.0940	0.0042	< 0.001
▪ Asthma	0.0285	0.0054	< 0.001	0.0342	0.0059	< 0.001
▪ Bronchitis or Emphysema	0.0203	0.0093	0.029	0.0249	0.0107	0.020
▪ Cancer	0.0208	0.0064	0.001	0.0177	0.0073	0.015
▪ Diabetes	0.0173	0.0054	0.001	0.0176	0.0061	0.004
▪ Hypertension	0.0115	0.0033	< 0.001	0.0115	0.0036	0.001
▪ Psychiatric Diagnoses	-0.0293	0.0070	< 0.001	-0.0282	0.0080	< 0.001
▪ Poor Hearing or Deafness	0.0101	0.0075	0.180	-	-	-
▪ Cataracts, Poor Eyesight, or Blindness	0.0161	0.0080	0.045	0.0238	0.0092	0.009
▪ Bladder Problems or Incontinence	-0.0103	0.0154	0.503	-	-	-
Longstanding Illness(es) Limit ADLs	-0.1252	0.0033	< 0.001	-0.1262	0.0037	< 0.001
Multimorbidity Index						
▪ 0 - 1 Longstanding Illnesses	*Ref*			*Ref*		
▪ 2 - 3 Longstanding Illnesses	-0.0125	0.0052	0.015	-0.0149	0.0052	0.004
▪ ≥ 4 Longstanding Illness	-0.0481	0.0122	< 0.001	-0.0451	0.0121	< 0.001
Severity Index						
▪ Fair or Good Health	*Ref*			-	-	-
▪ Bad Health and Longstanding Illnesses	0.0385	0.0283	0.175	-	-	-
▪ Bad Health and Limiting Illness	-0.0223	0.0247	0.368	-	-	-
Constant	0.6382	0.0465	< 0.001	0.6522	0.0537	< 0.001

one, representing better than perfect health). The ability of the model to predict EQ-5D scores was assessed using the mean absolute errors (MAE) and RMSE. Summary statistics on actual and predicted EQ-5D utilities are also presented. All validation statistics are presented for the sample overall, and in subsets across the range of scores on the EQ-5D (EQ-5D < 0, 0 ≤ EQ-5D < 0.25, 0.25 ≤ EQ-5D < 0.5, 0.5 ≤ EQ-5D < 0.75, 0.75 ≤ EQ-5D ≤ 1), as well as a plot of the observed and predicted values, as recommended by the NICE DSU in developing mapping algorithms.[ii] Capacity checking of the model was performed by calculating Pearson correlation between the observed and predicted utility values. All analyses were conducted in Stata/SE 15.1.

Results

Descriptive information regarding the estimation sample, validation sample, and the population in ELSA for which utilities are intended to be derived are provided in Appendix 4.1.1. Respondent characteristics were largely comparable between the estimation and validation samples in the HSE, though respondents in ELSA were slightly older and had a greater number of longstanding illness or incidence of depression. The number of diagnosed conditions may be higher in the ELSA sample due to this reflecting only respondents who were eligible for a quality of care indicator and most of these indicators are associated with a diagnosed condition. Individual EQ-5D utility weights covered the full range (-0.594 to 1) is both the estimation and validation samples, and the mean values were comparable.



Appendix 4.1.3. Plot of observed and predicted EQ-5D utility weights in the validation sample

Appendix 4.1.4. Comparison of actual and predicted EQ-5D utility weights

EQ-5D Utility Range	*n*	Observed Mean (SD)	Observed Range	Predicted Mean (SD)	Predicted Range	MAE	RMSE
Overall	6,816	0.795 (0.265)	-0.594 to 1.000	0.792 (0.191)	0.138 to 1.000	0.129	0.183
EQ-5D < 0	191	-0.085 (0.098)	-0.594 to -0.003	0.385 (0.157)	0.138 to 0.963	0.470	0.499
0 ≤ EQ-5D < 0.25	319	0.127 (0.057)	0.008 to 0.244	0.502 (0.184)	0.143 to 0.989	0.375	0.417
0.25 ≤ EQ-5D < 0.5	126	0.328 (0.070)	0.251 to 0.487	0.610 (0.198)	0.180 to 0.980	0.293	0.343
0.5 ≤ EQ-5D < 0.75	1,629	0.672 (0.061)	0.516 to 0.746	0.664 (0.176)	0.151 to 1.000	0.128	0.161
0.75 ≤ EQ-5D ≤ 1	4,551	0.936 (0.092)	0.760 to 1.000	0.880 (0.107)	0.201 to 1.000	0.093	0.121

The results for the mapping algorithms from the estimation sample are presented in Appendix 4.1.2, including both the model with all identified variables and the final model after stepwise elimination of all explanatory variables that were not significant at the 5% level. Most variables in the first model were statistically significant and with the expected sign, except for selected diagnosed conditions and the severity index. After adjustment for self-rated health, multimorbidity, depression, functional limitations, and demographics, some diagnoses are associated with a slight increase in health-related quality of life. After elimination of non-significant variables from the model there was minimal loss in the proportion of variance explained by the model, as described by the R^2 statistic, and a negligible impact on the RMSE, whilst reducing model complexity. Predicted utilities were derived from the restricted model for the validation sample.

The Pearson correlation between the observed and predicted values in the validation sample was 0.721 ($p < 0.0001$) and is supported by the associations observed in the plot of observed and predicted utilities (Appendix 4.1.3). The model was accurate in predicting the overall mean, though underestimated dispersion overall (see Appendix 4.1.4). The predictions covered a much smaller range overall, however covered a much broader range within each range of observed utilities but did not predict any negative scores. The errors in the predicted values were substantially smaller for those with better health-related quality of life.

Discussion

The developed algorithm provides a reasonable prediction of utility weights derived from the EQ-5D-3L using the UK value set, showing a strong and significant correlation between predicted and observed values. The algorithm also gains some content validity in that two of the strongest predictors of reduced quality of life were

recent feelings of depression or having a longstanding illness which limits mobility or the ability to conduct (instrumental) activities of daily living, which are both strong predictors of lower utilities on the EQ-5D. Based on the MAE and RMSE, model fit is comparable to previous mapping algorithm based on demographics, acute illness and general health with the HSE dataset,[xii] and one based on self-rated health and psychiatry morbidity conducted on a Swedish population.[xiii] The new algorithm also shows an improvement in fit compared to the only other algorithm available for ELSA data based on the SWLS, which has a Pearson's correlation coefficient of 0.361 with the EQ-5D.[v]

However, there are limitations with the mapping algorithm. For patients with the lowest observed utilities on the EQ-5D, the algorithm overestimates these utilities to the extent that patients would gain nearly half an additional QALY over the course of a year, and therefore any study to estimate gains in health-related quality of life from the worst health states to better ones will underestimate the incremental gain of that effect. In addition, none of the included measures in the mapping algorithm are explicitly preference-based and therefore cannot be considered a metric of utility, and most included explanatory variables do not involve the ranking of health states as is used on the EQ-5D questionnaire, apart from the self-complete response to perceived general health. However, the algorithm does capture the influence of health, patient perceptions of their health, and the severity of their condition on quality of life and shows comparable errors in prediction to other mapping algorithms published and used in economic evaluations.

In addition, there are some limitations associated with the use of the HSE. Respondents in the HSE are not recruited from residential or nursing homes, or hospitals, and therefore the observed EQ-5D scores may represent those who are less impaired by their diagnosed conditions. Whilst this is reflective of the majority of patients in ELSA, who are resident in the community at the time of recruitment, as these patients age or their health deteriorates, the algorithm may no longer be a representative method for deriving utilities. In addition, many of the longstanding illnesses in the HSE are self-reported and not necessarily clinically diagnosed, in response to the question "what is the matter with you?" This may introduce some bias where respondents in the HSE may have self-diagnosed. Whilst this risk is also present in ELSA, many questions on longstanding illness in ELSA are phrased as "has a doctor ever diagnosed you with…?" and so the framing of the question may limit this risk. Conditions are also very broadly defined, and therefore the impact of the diagnosis on quality of life may not be homogenous. For example, the impact of different cancers

can have a substantial difference in utilities, where patients with an early-stage basal cell carcinoma have near perfect health-related quality of life,[xiv] but those with relapsed metastatic non-small cell lung cancer have a utility of around 0.6.[xv]

As a formal multi-attribute utility instrument is not used to estimate health-related quality of life, the algorithm should be considered as a second-best solution for deriving utilities for an economic evaluation, but potentially the best available tool for use in analyses on the ELSA data. The current analysis has demonstrated some internal validity of the mapping algorithm and is supported by the large sample size, but external validation is still required. Given that the algorithm provides the best estimate for predicting utilities for the ELSA dataset known to date, it may help support inferences or hypothesis generation on improvement in health-related quality of life in English older adults.

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Appendix 4.2: The Association Between Care Quality and Outcomes

Appendix 4.2.1. Overall survival

Minimum Survival Time	HR	90% CI
Observations (Respondents)	263 (176)	
Events	68	
Quality of Care, per 10% increase	0.93**	0.88 to 0.98
Age	1.10***	1.07 to 1.13
Female	0.57**	0.37 to 0.88
GPs per 1,000 Patients	1.31	0.01 to 116.82
QOF Organisational Domain (%)	0.92**	0.87 to 0.98
Maximum Survival Time	HR	90% CI
Quality of Care, per 10% increase	0.92***	0.26 to 0.71
Age	1.10***	1.08 to 1.15
Female	0.54**	0.29 to 0.72
GPs per 1,000 Patients	4.45	0.01 to 139.28
QOF Organisational Domain (%)	0.88**	0.83 to 0.94

Notes: CI, confidence intervals; HR, hazard ratio. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.2.2. Health-related quality of life (EQ-5D)

	β	90% CI
Observations (Respondents)	263 (176)	
Quality of Care, per 10% increase	0.002	-0.002 to 0.007
Age	0.002*	0.000 to 0.004
Female	0.037	-0.004 to 0.079
Married and/or Cohabiting	0.009	-0.030 to 0.049
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	-0.114***	-0.155 to -0.072
▪ 2 or 3	-0.193***	-0.240 to -0.145
▪ 4 or more	-0.232***	-0.334 to -0.129
Cardiovascular Comorbidities		
▪ None	*Ref*	
▪ 1	-0.055	-0.136 to 0.025
▪ 2 or 3	-0.139***	-0.217 to -0.061
▪ 4 or more	-0.149***	-0.236 to -0.062
№ Challenges with Mobility	-0.024***	-0.036 to -0.013

Notes: CI, confidence intervals. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.2.3. CASP-19

	β	90% CI
Observations (Respondents)	263 (176)	
Quality of Care, per 10% increase	-0.046	-0.304 – 0.212
Age	0.113	-0.015 – 0.241
Female	2.347	-0.445 – 5.140
Married and/or Cohabiting	2.013	-0.528 – 4.555
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	-2.068	-4.768 – 0.632
▪ 2 or 3	-4.750***	-7.687 – -1.813
▪ 4 or more	-9.641**	-16.47 – -2.812

Notes: CI, confidence intervals. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.2.4. Self-rated health

	OR	90% CI
Observations (Respondents)	263 (176)	
Quality of Care, per 10% increase	1.04	0.97 to 1.11
Age	1.06**	1.02 to 1.10
Female	2.31*	1.12 to 4.78
Married and/or Cohabiting	0.92	0.50 to 1.71
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	0.51	0.24 to 1.07
▪ 2 or 3	0.22***	0.10 to 0.50
▪ 4 or more	0.09*	0.01 to 0.79
Cardiovascular Comorbidities		
▪ None	*Ref*	
▪ 1	0.62	0.15 to 2.54
▪ 2 or 3	0.27	0.07 to 1.09
▪ 4 or more	0.27	0.05 to 1.39
№ Challenges with Mobility	0.67***	0.55 to 0.81

Notes: CI, confidence intervals; OR, odds ratio. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.2.5. Satisfaction with Life Scale

	β	90% CI
Observations (Respondents)	263 (176)	
Quality of Care, per 10% increase	0.000	-0.006 to 0.006
Age	0.005***	0.002 to 0.008
Female	0.033	-0.023 to 0.088
Married and/or Cohabiting	0.068*	0.004 to 0.131
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	-0.032	-0.097 to 0.033
▪ 2 or 3	-0.078**	-0.143 to -0.014
▪ 4 or more	-0.059	-0.218 to 0.100
Cardiovascular Comorbidities		
▪ None	*Ref*	
▪ 1	0.015	-0.097 to 0.127
▪ 2 or 3	-0.031	-0.135 to 0.073
▪ 4 or more	-0.028	-0.136 to 0.080
№ Challenges with Mobility	-0.013	-0.032 to 0.005
№ Challenges with IADLs	0.005	-0.008 to 0.018
Net Non-Pension Wealth		
▪ 1st Quintile (Least Wealthy)	*Ref*	
▪ 2nd Quintile	-0.020	-0.098 to 0.058
▪ 3rd Quintile	0.030	-0.037 to 0.097
▪ 4th Quintile	0.001	-0.077 to 0.078
▪ 5th Quintile (Wealthiest)	0.061	-0.031 to 0.152

Notes: CI, confidence intervals; IADLs, instrumental activities of daily living. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.3.6. Number of IADLs helped with by local authority worker, nurse, or social services (does not include privately paid help)

	IRR	90% CI
Observations (Respondents)	200 (145)	
Quality of Care, per 10% increase	0.92***	0.88 – 0.97
Age	1.01	0.98 – 1.04
Female	1.17	0.69 – 1.97
Married and/or Cohabiting	0.40***	0.24 – 0.65
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	0.73	0.44 – 1.21
▪ 2 or 3	0.61	0.34 – 1.10
▪ 4 or more	0.58	0.15 – 2.20
QOF Organisational Domain (%)	1.06	0.99 – 1.12

Notes: CI, confidence intervals; IRR, incidence rate ratio. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.3.7. Time to institutionalisation

Minimum Time to Institutionalisation	HR	90% CI
Observations (Respondents)	214 (150)	
Events	20	
Quality of Care, per 10% increase	0.85	0.68 – 1.07
Age	1.07	0.96 – 1.18
Female	0.96	0.17 – 5.38
Married and/or Cohabiting	5.49	0.72 – 41.81
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	2.59	0.45 – 14.75
▪ 2 or 3	0.69	0.05 – 10.06
▪ 4 or more	NE	NE
№ Challenges with IADLs	0.81	0.57 – 1.17
Maximum Time to Institutionalisation	HR	90% CI
Quality of Care, per 10% increase	0.74	0.49 – 1.11
Age	1.05	0.93 – 1.20
Female	1.05	0.19 – 5.93
Married and/or Cohabiting	14.53	0.61 – 348.24
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	0.78	0.13 – 4.79
▪ 2 or 3	0.86	0.07 – 10.65
▪ 4 or more	NE	NE
№ Challenges with IADLs	0.66	0.35 – 1.23

Notes: CI, confidence intervals; HR, hazard ratio; NE, not estimatable (insufficient observations). * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

Appendix 4.3.8. Institutionalisation-free survival

Minimum Institutionalisation-Free Survival	HR	90% CI
Observations (Respondents)	215 (150)	
Events	57	
Quality of Care, per 10% increase	0.86*	0.75 – 0.99
Age	1.21***	1.09 – 1.34
Female	0.14**	0.04 – 0.58
Married and/or Cohabiting	0.71	0.26 – 1.93
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	4.51*	1.06 – 19.17
▪ 2 or 3	5.35*	1.10 – 26.14
▪ 4 or more	NE	NE
№ Challenges with IADLs	0.71**	0.56 – 0.90
GPs per 1,000 Patients	0.00	0.00 – 1782.37
QOF Organisational Domain (%)	0.68**	0.53 – 0.88
Maximum Institutionalisation-Free Survival	HR	90% CI
Quality of Care, per 10% increase	0.84	0.66 – 1.08
Age	1.30***	1.11 – 1.52
Female	0.08**	0.01 – 0.56
Married and/or Cohabiting	0.59	0.19 – 1.82
Chronic Comorbidity Index		
▪ None	*Ref*	
▪ 1	3.58	0.54 – 23.51
▪ 2 or 3	4.16	0.57 – 30.36
▪ 4 or more	812.67***	16.99 – 38871
№ Challenges with IADLs	0.62**	0.43 – 0.89
GPs per 1,000 Patients	0.00	0.00 – 13.92
QOF Organisational Domain (%)	0.61**	0.43 – 0.86

Notes: CI, confidence intervals; HR, hazard ratio; NE, not estimatable (insufficient observations). * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

APPENDIX 5.1: PROBABILITY OF MEETING THE INCLUDED QUALITY OF CARE INDICATORS IN THE OVERALL POPULATION WITHOUT INTERVENTION EFFECTS

Predictor	OR	95% CI	*p*-value
Cognitive Impairment			
▪ No Impairment	*Ref*		
▪ Diagnosed Dementia	0.25	0.15 to 0.40	< 0.001
Age (years)			
▪ 50 - 54	*Ref*		
▪ 55 - 59	1.56	1.21 to 2.01	0.001
▪ 60 - 64	2.21	1.69 to 2.90	< 0.001
▪ 65 - 69	2.79	2.10 to 3.71	< 0.001
▪ 70 - 74	2.84	2.14 to 3.76	< 0.001
▪ 75 - 79	3.12	2.32 to 4.20	< 0.001
▪ 80 - 84	2.06	1.50 to 2.83	< 0.001
▪ 85 - 89	2.32	1.58 to 3.42	< 0.001
▪ ≥ 90	1.28	0.63 to 2.60	0.502
Female	0.98	0.84 to 1.14	0.787
Married and/or Cohabiting	1.03	0.87 to 1.21	0.753
Number of Close Relationships			
▪ 0 or 1	*Ref*		
▪ 2 or 3	3.32	2.58 to 4.26	< 0.001
▪ 4 or 5	3.52	2.85 to 4.35	< 0.001
▪ 6 to 9	3.42	2.83 to 4.13	< 0.001
▪ 10 or more	3.36	2.72 to 4.15	< 0.001
Diagnosed Chronic Conditions			
▪ None	*Ref*		
▪ 1	1.53	1.33 to 1.77	< 0.001
▪ 2 or 3	1.32	1.10 to 1.59	0.003
▪ 4 or more	1.12	0.64 to 1.96	0.685
Diagnosed Cardiovascular Conditions			
▪ None	*Ref*		
▪ 1	1.37	1.08 to 1.75	0.010
▪ 2 or 3	2.05	1.62 to 2.60	< 0.001
▪ 4 or more	1.92	1.39 to 2.65	< 0.001
Net Non-Pension Wealth			
▪ 1st Quintile (Least Wealthy)	*Ref*		
▪ 2nd Quintile	1.01	0.83 to 1.24	0.892
▪ 3rd Quintile	1.13	0.92 to 1.39	0.236
▪ 4th Quintile	1.02	0.82 to 1.27	0.855
▪ 5th Quintile (Wealthiest)	0.95	0.74 to 1.21	0.661
GPs per 1,000 Patients	37.05	10.90 to 125.94	< 0.001

Abbreviations: CI, confidence intervals; OR, odds ratio.

APPENDIX 6.1: MEDLINE SEARCH STRATEGY FOR TARGETED LITERATURE SEARCH

1. Cost-Benefit Analysis/
2. exp models, economic/
3. (cost$ adj2 (effective$ or utility$ or benefit$ or minimis$)).ab.
4. economic$ model$.tw.
5. or/(1-4)
6. dementia/
7. dement$.tw.
8. alzheimer disease/
9. alzheimer*.tw.
10. or/(6-9)
11. limit 10 to (English language and full text and yr= “2010 – Current”)
12. exp Reimbursement Mechanisms/
13. (pay adj2 perform$).tw.
14. (pay for performance).tw.
15. (quality and outcomes framework).tw.
16. QOF.tw.
17. quality indicators, health care/
18. or/(12-17)
19. limit 18 to (English language and full text and yr= “2002 – Current”)
20. (cognit$ adj2 stimulat$).tw.
21. cognitive rehabilitation.tw.
22. reality orientation.tw.
23. (cogniti* adj2 impair*).tw.
24. (cogniti* adj2 function*).tw.
25. or/(20-24)
26. limit 25 to (English language and full text)
27. 11 or 18 or 26
28. 5 and 27
29. remove duplicates from 28
30. (letter or editorial or comment or note).pt.
31. 30 not 31

Searches were conducted in May 2020. Searches for dementia models were limited to 2010 onwards given the systematic literature review conducted as part of NICE TA217 (Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease) which was completed in 2010 and was assumed to capture all relevant studies prior to this date with regards to determining appropriate cost-effectiveness modelling methods in patients with dementia. Searches on pay-for-

performance mechanisms were limited to 2002 onwards given the QOF was launched in the 2004/05 fiscal year and represents the most relevant pay-for-performance framework for our analyses, and so a two-year lead in buffer was included. No date restriction was applied to studies on cognitive stimulation. Given the targeted nature of the review, only full-text articles (no conference abstracts) were considered, and only English language papers were reviewed. The systematic review and meta-analysis by Huntley and colleagues on cognitive interventions for improving cognition in dementia demonstrated that only cognitive stimulation was shown to have a significant effect on cognition, and so search terms were focussed on those used in their identified publications to describe cognitive stimulation interventions. Only original publications were considered, with editorials, notes, letters, and comments being excluded from the search. Further systematic reviews were also not included, though were screened for additional relevant publications.

Appendix 6.2: List of Model Parameters & Uncertainty Ranges

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Structural Parameters & Assumptions					
Cycle Length (Days)	365.25	N/A	N/A	N/A	Assumption
Time Horizon (Years)	20	5	30	N/A	Assumption
Discount Rate: Costs	3.5%	1.5%	N/A	N/A	NICE PMG9
Discount Rate: Outcomes	3.5%	1.5%	N/A	N/A	NICE PMG9
Population Parameters: All Dementia Severities					
Age at Baseline	76.2	74.5	77.8	Normal	ELSA (Data on File)
Proportion Female	51.0%	43.0%	59.0%	Beta	ELSA (Data on File)
Diagnosed Diabetes	23.8%	17.3%	31.0%	Beta	ELSA (Data on File)
Diagnosed Hypertension	83.7%	77.9%	88.7%	Beta	ELSA (Data on File)
Diagnosed Osteoporosis	7.5%	4.1%	11.8%	Beta	ELSA (Data on File)
Current Smoker	8.2%	4.6%	12.6%	Beta	ELSA (Data on File)
Population Parameters: Mild or Moderate Dementia					
Age at Baseline	75.5	73.8	77.2	Normal	ELSA (Data on File)
Proportion Female	49.2%	40.6%	57.8%	Beta	ELSA (Data on File)
Diagnosed Diabetes	24.2%	17.7%	31.4%	Beta	ELSA (Data on File)
Diagnosed Hypertension	84.4%	78.7%	89.3%	Beta	ELSA (Data on File)
Diagnosed Osteoporosis	7.0%	3.8%	11.2%	Beta	ELSA (Data on File)
Current Smoker	8.6%	4.9%	13.1%	Beta	ELSA (Data on File)
Current Quality of Care (QOC): All Dementia Severities					
Diabetes Foot Check: Community	71.2%	50.9%	85.5%	Logit	ELSA (Data on File)
Diabetes Foot Check: Institutionalised	7.9%	0.4%	65.2%	Logit	ELSA (Data on File)
Diabetes Training: Baseline	15.8%	7.3%	31.0%	Logit	ELSA (Data on File)
Hypertension Treatment: Community	64.4%	55.1%	72.6%	Logit	ELSA (Data on File)
Osteoporosis Supplements: Community	28.6%	11.1%	56.1%	Logit	ELSA (Data on File)
Smoking Cessation: Community	73.5%	53.5%	87.0%	Logit	ELSA (Data on File)
Smoking Cessation: Institutionalised	0.0%	0.0%	0.0%	N/A	ELSA (Data on File)
Current Quality of Care (QOC): Mild or Moderate Dementia					
Diabetes Foot Check: Community	70.4%	51.9%	84.0%	Logit	ELSA (Data on File)
Diabetes Foot Check: Institutionalised	9.3%	0.6%	64.7%	Logit	ELSA (Data on File)
Diabetes Training: Baseline	18.2%	8.4%	35.0%	Logit	ELSA (Data on File)
Hypertension Treatment: Community	60.2%	50.3%	69.3%	Logit	ELSA (Data on File)
Osteoporosis Supplements: Community	33.3%	13.1%	62.4%	Logit	ELSA (Data on File)
Smoking Cessation: Community	72.4%	52.0%	86.4%	Logit	ELSA (Data on File)
Smoking Cessation: Institutionalised	0.0%	0.0%	0.0%	N/A	ELSA (Data on File)

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Survival Parameters: All Dementia Severities					
Overall Survival: Shape	-0.02	-0.03	-0.01	Multivariate	ELSA (Data on File)
Overall Survival: Rate	-4.43	-4.85	-4.01	Normal	
Institutionalisation-Free Survival: Mu	5.69	4.92	6.46	Multivariate Normal	ELSA (Data on File)
Institutionalisation-Free Survival: Sigma	0.38	-0.69	1.45		
Institutionalisation-Free Survival: Q	1.74	-0.27	3.75		
Survival Parameters: Mild or Moderate Dementia					
Overall Survival: Shape	-0.02	-0.03	-0.01	Multivariate	ELSA (Data on File)
Overall Survival: Rate	-4.41	-4.87	-3.96	Normal	
Institutionalisation-Free Survival: Mu	6.03	5.11	6.95	Multivariate Normal	ELSA (Data on File)
Institutionalisation-Free Survival: Sigma	0.45	-0.88	1.78		
Institutionalisation-Free Survival: Q	1.69	-0.72	4.09		
Hazard Ratios: All Dementia Severities					
Overall Survival: QoC	0.44	0.23	0.82	Lognormal	ELSA (Data on File)
Institutionalisation-Free Survival: QoC	0.70	0.34	1.42	Lognormal	ELSA (Data on File)
Hazard Ratios: Mild or Moderate Dementia					
Overall Survival: QoC	0.36	0.17	0.74	Lognormal	ELSA (Data on File)
Overall Survival: Cognitive Function	0.89	0.81	0.99	Lognormal	ELSA (Data on File)
Institutionalisation-Free Survival: QoC	0.49	0.20	1.23	Lognormal	ELSA (Data on File)
Institutionalisation-Free Survival: Cognitive Function	0.93	0.87	1.00	Lognormal	ELSA (Data on File)
Cognitive Function Parameters: All Dementia Severities					
Cognitive Index: Constant	16.82	15.95	17.69	Multivariate	ELSA (Data on File)
Cognitive Index: Years	-0.43	-0.51	-0.34	Normal	ELSA (Data on File)
Cognitive Function Parameters: Mild or Moderate Dementia					
Cognitive Index: Constant	17.73	16.98	18.49	Multivariate	ELSA (Data on File)
Cognitive Index: Years	-0.42	-0.49	-0.34	Normal	
Help with IADLs: All Dementia Severities					
No. of IADLs: Constant	3.37	1.05	5.69	Multivariate	ELSA (Data on File)
No. of IADLs: $Age^{0.5}$	-2.39	-4.80	0.03	Normal	
No. of IADLs: $Age^{0.5}$	0.97	0.04	1.90		
IADLs Helped With: Constant	-3.15	-6.14	-0.17	Multivariate Normal	ELSA (Data on File)
IADLs Helped With: Age	-1.32	-2.80	0.17		
IADLs Helped With: Age^2	0.32	0.00	0.63		
Incidence Rate Ratio for Help: QoC	0.38	0.21	1.07	Lognormal	ELSA (Data on File)
Help with IADLs: Mild or Moderate Dementia					
No. of IADLs: Constant	3.46	1.05	5.87	Multivariate	ELSA (Data on File)
No. of IADLs: $Age^{0.5}$	-2.79	-5.13	-0.44	Normal	
No. of IADLs: $Age^{0.5}$	1.19	0.28	2.11		

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Incidence Rate Ratio for IADLs: Cognitive Function	0.96	0.94	0.99	Lognormal	ELSA (Data on File)
Incidence Rate Ratio for IADLs: Exercise	0.72	0.54	0.96	Lognormal	ELSA (Data on File)
IADLs Helped With: Constant	-5.37	-8.12	-2.61	Multivariate Normal	ELSA (Data on File)
IADLs Helped With: Age	0.02	0.00	0.05		
Incidence Rate Ratio for Help: QoC	0.35	0.19	0.66	Lognormal	ELSA (Data on File)
Incidence Rate Ratio for Help: Social Isolation	1.68	1.25	2.27	Lognormal	ELSA (Data on File)
Frequency of Visits from Social Worker Mapping Algorithm					
IADLs Help With	1.12	0.55	1.70	Multivariate Normal	ELSA (Data on File)
Cut-Off: Not at All	-1.57	-2.79	-0.35		
Cut-Off: Less Than Once a Week	-0.64	-1.63	0.36		
Cut-Off: Once a Week	0.38	-0.54	1.31		
Cut-Off: Two or Three Times a Week	1.21	0.26	2.16		
Cardiovascular Event Parameters					
QRISK2 Score (Male): Constant	8.44	7.09	9.79	Multivariate Normal	Estimated from ELSA parameters (Data on File)
QRISK2 Score (Male): $Age^{-0.5}$	-24.10	-27.73	-20.47		
QRISK2 Score (Female): Constant	-2.61	-2.91	-2.30	Multivariate Normal	Estimated from ELSA parameters (Data on File)
QRISK2 Score (Female): Age^{3}	0.00	0.00	0.00		
Distribution of Cardiovascular Events by Age & Sex	See Table 6.15			Dirichlet	NICE NG136
CHD RR: QoC	0.86	0.76	0.96	Lognormal	Brunström 2018
Stroke RR: QoC	0.86	0.72	1.01	Lognormal	Brunström 2018
Heart Failure RR: QoC	0.87	0.73	1.04	Lognormal	Brunström 2018
Age & Sex Adjustments to Relative Risks	See Table 6.16 for estimated values			Lognormal	Law 2009 (as used in NICE NG136)
Osteoporotic Fracture Parameters					
Baseline Hazard of Fracture per Cycle	0.001	0.001	0.001	Normal	Fitted to QFracture baseline hazard curve
QFracture HR: Age^{2}	1.15	1.11	1.20	Lognormal	Hippisley-Cox J, et al. BMJ. 2012;344:e3427
QFracture HR: Age^{3}	0.99	0.99	0.99	Lognormal	
QFracture HR: Ex-Smoker	1.04	1.01	1.07	Lognormal	
QFracture HR: CVD	1.21	1.21	1.26	Lognormal	
QFracture HR: Falls	1.57	1.47	1.68	Lognormal	
QFracture HR: Previous Fracture	1.08	1.03	1.13	Lognormal	
Distribution of Fractures by Age	See Table 6.17			Dirichlet	Kanis JA, et al. Osteoporosis Int. 2001;12:417-27
Fracture Multipliers for Other Sides	See Table 6.18	-20%	+20%	Lognormal	Kanis JA, et al. Osteoporosis Int. 2001;12:417-27

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Hip Fracture RR: QoC	0.82	0.71	0.94	Lognormal	Boonen S, et al. J Clin Endocrinol Metab. 2007;92(4):1415-23
Vertebral Fracture RR: QoC	0.87	0.75	1.01	Lognormal	Tang BM, et al. Lancet. 2007;370(6):57-66
Other Fracture RR: QoC	0.80	0.72	0.89	Lognormal	Bischoff-Ferrari HA, et al. Arch Intern Med. 2009;169(5):51-61
Time on Osteoporosis Supplements (Years)	3	1	10	Gamma	Hiligsmann M, et al. Eur J Public Health. 2014;25(1):20-5
Smoking Cessation Parameters					
Background Quit Rate	2.0%	1.2%	2.8%	Beta	Coleman T, et al. Health Technology Assessment. 2010;14(49).
Cessation RR: QoC	1.78	-20%	+20%	Lognormal	NICE NM40
PRIDE Intervention Parameters					
Efficacy Cognitive Stimulation: Constant	-4.05	-6.58	-1.52	Multivariate Normal	Meta-regression reanalysis of: Huntley JD, et al. BMJ Open. 2014;5(4):e005247.
Efficacy Cognitive Stimulation: Months	-4.17	-7.82	-0.52		
Time to Maximum Effect of Cognitive Stimulation	6	2	12	N/A	Assumption
Duration of Follow-Up Period	3	2	3	N/A	Garcia-Casal 2017
Duration of Convergence Period	6	1	9	N/A	NICE NG97
Impact of Exercise on Cognitive Function Score	1.58	0.31	2.84	Multivariate Normal	ELSA (Data on File)
Impact of Social Isolation on Cognitive Function	-0.76	-1.45	-0.07		
Baseline Exercise Level: Constant	-0.27	-2.08	1.53	Multivariate Normal	ELSA (Data on File)
Baseline Exercise Level: Age^{-2}	-1.11	-2.72	0.51		
Baseline Exercise Level: Age^{3}	-0.08	-0.14	-0.01		
Initial Uptake in Exercise	75%	40%	95%	Beta	Steinberg 2009
Surplus Exercise Discontinuation Rate	12.5%	0%	25%	Beta	Machado 2020
Baseline Social Isolation Level: Constant	2.53	2.31	2.75	Multivariate Normal	ELSA (Data on File)
Baseline Social Isolation Level: Years	0.04	0.02	0.06		
Proportion Increasing Social Engagement	85%	60%	100%	Beta	Theurer 2014
Magnitude of Increase in Social Engagement	1	1	1.5	N/A	Assumption
QoC OR: Cognitive Function	1.13	1.00	1.28	Lognormal	ELSA (Data on File)

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
QOF Efficacy Parameters					
QoC OR: Indicator Included	5.70	1.72	18.81	Multivariate Normal	ELSA (Data on File)
QoC OR: Points Available	1.02	0.98	1.05		
Health State Utilities: All Dementia Severities					
Utility: Constant	0.44	0.33	0.54	Multivariate Normal	ELSA (Data on File)
Utility: Age^2	0.08	0.03	0.13		
Utility: Age^2	-0.05	-0.08	-0.01		
Utility: Institutionalised	-0.02	-0.11	0.08		
Health State Utilities: Mild or Moderate Dementia					
Utility: Constant	0.46	0.35	0.56	Multivariate Normal	ELSA (Data on File)
Utility: Age^2	0.07	0.01	0.12		
Utility: Age^2	-0.04	-0.08	0.00		
Utility: Institutionalised	0.34	-0.12	0.09		
Other Utilities					
Institutionalised	0.34	0.09	0.65	Beta	Jönsson L, et al. Alzheimer Dis Assoc Disord. 2006;20(1):49-55.
Reduction in IADLs	0.02	0.01	0.03	Beta	ELSA (Data on File)
Stable Angina	0.81	0.73	0.88	Beta	NICE NG136
Unstable Angina	0.77	0.69	0.84	Beta	NICE NG136
Myocardial Infarction	0.76	0.72	0.79	Beta	NICE NG136
Transient Ischaemic Attack	0.90	0.85	0.94	Beta	NICE NG136
Stroke	0.63	0.55	0.70	Beta	NICE NG136
Heart Failure	0.68	0.64	0.72	Beta	NICE NG136
Hip Fracture	0.69	0.39	0.92	Beta	NICE TA464
Vertebral Fracture	0.57	0.34	0.78	Beta	NICE TA464
Should Fracture	0.86	0.38	1.00	Beta	NICE TA464
Wrist Fracture	0.88	0.36	1.00	Beta	NICE TA464
Not Receiving Diabetic Foot Care (per year)	-0.01	-0.10	-0.21	Normal	NICE NG19
Not Receiving Diabetes Training (per year)	-0.00	-0.13	0.09	Normal	Gillett M, et al. BMJ. 2010;341:c4093.
Not Receiving Smoking Cessation Tx (per year)	-0.00	-0.02	0.02	Normal	NICE QOF Indicator NM40 Cost-Effectiveness Analysis
Dementia Care Costs					
Pre-Institution: Constant	2877	2842	2912	Multivariate Normal	NICE TA217
Pre-Institution: Time	-1122	-1146	-1098		
Pre-Institution: Time^2	194	186	202		
Pre-Institution: Time^3	-10.9	-12.4	-9.4		
Proportion Non-Domiciliary Help	78.9%	40.8%	98.9%	Beta	Wolstenholme J. Br J Psychiatry. 2002;181:36-42.
Institutionalisation: Healthcare	8542	5528	12201	Gamma	Alzheimer's Society (2014): Dementia UK Update
Institutionalisation: Social Care	25610	16573	36581	Gamma	Alzheimer's Society (2014): Dementia UK Update
Public Paid Social Care	35.0%	22.0%	49.3%	Beta	Alzheimer's Society (2014): Dementia UK Update
Donepezil Tablets x 28	0.58	0.30	0.95	Gamma	eMIT 2019
Memantine Tablets x 28	2.79	0.96	5.57	Gamma	eMIT 2019

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Annual Drug Discontinuation Rate	38.7%	24.4%	50.6%	Beta	NICE TA217
Social Worker (per hour)	51	33	73	Gamma	PSSRU 2019 (Social Worker: Adult Services)
Hours per Visit	2.5	1	5	Gamma	Assumption
Average Visits: < Once per Week	0.50	0.23	0.69	Uniform	Assumption
Average Visits: Once per Week	1.00	0.70	1.49	Uniform	Assumption
Average Visits: 2/3 Times per Week	2.50	1.50	3.49	Uniform	Assumption
Average Visits: Nearly Every Day	5.00	3.50	7.00	Uniform	Assumption
End of Life Care	6780	4388	9685	Gamma	Wittenberg R, et al. Int J Geriatr Psychiatry. 2019;34(7):1095-1103.
PRIDE Intervention Costs					
PRIDE Intervention	151.24	97.88	216.03	Gamma	Assumption
Current QOF Costs					
Value of a QOF Point	187.74	N/A	N/A	N/A	2019/20 GMS Contract QOF
Diabetes Foot Check: Points	4	N/A	N/A	N/A	2019/20 GMS Contract QOF
Diabetes Foot Check: Minimum Threshold	50%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Diabetes Foot Check: Maximum Threshold	90%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Diabetes Foot Check: Current Achievement	89.5%	67.7%	99.4%	Beta	QOF 2018-19: Prevalence, Achievements & Exceptions at GP Practice Level
Hypertension Treatment (Under 80 Years): Points	14	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment (Under 80 Years): Minimum Threshold	40%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment (Under 80 Years): Maximum Threshold	77%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment (Over 80 Years): Points	5	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment (Over 80 Years): Minimum Threshold	40%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment (Over 80 Years): Maximum Threshold	80%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Hypertension Treatment: Current Achievement	83.1%	70.9%	92.5%	Beta	QOF 2018-19: Prevalence, Achievements & Exceptions at GP Practice Level

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Smoking Cessation: Points	25	N/A	N/A	N/A	2019/20 GMS Contract QOF
Smoking Cessation: Minimum Threshold	56%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Smoking Cessation: Maximum Threshold	96%	N/A	N/A	N/A	2019/20 GMS Contract QOF
Smoking Cessation: Current Achievement	96.7%	76.3%	100.0%	Beta	QOF 2018-19: Prevalence, Achievements & Exceptions at GP Practice Level
Average Practice List Size	8640	1376	22440	Gamma	QOF 2018-19: Prevalence, Achievements & Exceptions at GP Practice Level
Population Prevalence of Dementia	1.3%	0.8%	1.9%	Beta	Alzheimer's Society (2014): Dementia UK Update
Proportion Severe Dementia	12.5%	8.0%	17.8%	Beta	Alzheimer's Society (2014): Dementia UK Update
Population Prevalence of Diabetes	6.2%	6.3%	6.4%	Beta	Public Health England (2019)
Population Prevalence of Hypertension	13.4%	13.3%	13.5%	Beta	Public Health England (2019)
Population Prevalence of Osteoporosis	3.5%	2.8%	4.2%	Beta	Gauthier A, et al. Archive Osteo. 2011;6:179-88.
Population Prevalence of Smoking	14.4%	13.0%	15.8%	Beta	NHS Digital (2019)
Dementia Comorbidity Payment: Points	3	0	30	N/A	Assumption
Diabetes Training: Points	11	5	N/A	N/A	Assumption
Diabetes Training: Minimum Threshold	40%	N/A	N/A	N/A	Threshold for diabetes training for incident cases
Diabetes Training: Maximum Threshold	90%	N/A	N/A	N/A	Threshold for diabetes training for incident cases
Osteoporosis Supplements: Points	3	1	N/A	N/A	Assumption
Osteoporosis Supplements: Minimum Threshold	30%	N/A	N/A	N/A	Threshold for previous indicator for osteoporosis treatment
Osteoporosis Supplements: Maximum Threshold	60%	N/A	N/A	N/A	Threshold for previous indicator for osteoporosis treatment
Comorbidity Care Costs					
Diabetes Foot Check: Annual Care (Not Met)	390	253	558	Gamma	NICE NG19 (Economic Model Results)
Diabetes Foot Check: Annual Care (Met)	484	281	709	Gamma	NICE NG19 (Economic Model Results)
Diabetes Training: Year 1 (Not Met)	244	158	349	Gamma	Gillett M, et al. BMJ. 2010;341:c4093.
Diabetes Training: Year 2+ (Not Met)	1793	1161	2562	Gamma	Gillett M, et al. BMJ. 2010;341:c4093.
Diabetes Training: Year 1 (Met)	336	109 210	481	Gamma	Gillett M, et al. BMJ. 2010;341:c4093.

Parameter	Estimate	Lower Bound	Upper Bound	Distribution	Source
Diabetes Training: Year 2+ (Met)	1787	218	3461	Gamma	Gillett M, et al. BMJ. 2010;341:c4093.
Hypertension Treatment: Annual Care (Not Met)	39.23	25.39	56.04	Gamma	PSSRU 2019 (GP Consultation)
Ramipril x 28	0.34	0.15	0.62	Gamma	eMIT 2019
Amlodipine x 28	0.21	0.09	0.39	Gamma	eMIT 2019
Indapamide x 28	0.56	0.07	1.59	Gamma	eMIT 2019
Stroke	5964	4493	8279	Gamma	Danese MD, et al. BMJ Open. 2016;6:e011805.
Transient Ischaemic Attack	2750	2202	3396	Gamma	Danese MD, et al. BMJ Open. 2016;6:e011805.
Myocardial Infarction	6775	4637	9782	Gamma	Danese MD, et al. BMJ Open. 2016;6:e011805.
Stable Angina	1778	849	3099	Gamma	National Schedule of NHS Costs (2018-19): EB13A-D
Unstable Angina	3726	2779	5025	Gamma	Danese MD, et al. BMJ Open. 2016;6:e011805.
Heart Failure	3945	3100	5011	Gamma	Danese MD, et al. BMJ Open. 2016;6:e011805.
Cholecalciferol/Calcium Carbonate x 30	6.75	4.37	9.64	Gamma	BNF
Hip Fracture	8922	5774	12745	Gamma	NICE TA464
Vertebral Fracture	4809	3112	6869	Gamma	NICE TA464
Shoulder Fracture	1469	951	2098	Gamma	NICE TA464
Wrist Fracture	994	643	1420	Gamma	NICE TA464
Smoking Cessation: Annual Care (Not Met)	399	258	569	Gamma	NICE QOF Indicator NM40 Cost-Effectiveness Analysis
Smoking Cessation: Annual Care (Met)	403	261	576	Gamma	NICE QOF Indicator NM40 Cost-Effectiveness Analysis