BROADENING THE PERSPECTIVE OF ECONOMIC EVALUATION IN HEALTH CARE – A CASE STUDY IN DEMENTIA CARE IN THE UK

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A thesis submitted in partial fulfilment of the requirements for

the degree of Doctor of Philosophy

Date of submission: July 2017

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ACKNOWLEDGEMENTS

I would like to thank many people who have helped me to complete this thesis. Without their support, this thesis would not have been possible. First, it is my sincere gratitude to my supervisors, John Brazier and Praveen Thokala, for their excellent advice and support. They have always been there for me and their knowledge and experience have been invaluable. John has been a kind and tremendously supportive lead supervisor. His wisdom, experience, and vision were very helpful in many occasions. Praveen has also been very kind and hugely supportive. They both have been a great source of help and encouragement for me in the production of this thesis.

This research would not have been possible without the participants who took part in my research, and many individuals and organisations who assisted in discussion, identification, and recruitment. My thanks go to the Sheffield Clinical Commissioning Group (CCG), Sheffield City Council, the two Sheffield memory clinics, Northern General Hospital, and the Alzheimer’s Society. I would also like to acknowledge my PhD friends and broader colleagues in ScHARR who have provided me such a welcoming and friendly place to work and study. Everyone has been so kind and helpful. I would like to thank Alan Brennan and Donna Rowen who kindly acted as examiners for my upgrade from MPhil to PhD. I have been lucky to spend my time here with these wonderful people.

On the production side of the thesis, I am very grateful to a number of friends and families for their assistance. Thank you Edward, Anh Tho, Hannah for helping proof read the thesis. Especially I would like to thank my wife, Tam, for all her support and assistance (and proofreading skills) throughout this journey. And also to other members in my family for their patience, love, and care; without their support I would not have even started this journey. There are many other people who have supported me in various ways to complete this thesis. Thank you Wayne and Emma for being excellent neighbours who would go out of their way to help us with whatever they can. Thank you Rajesh, Pratistha, and Shraddha for teaching me how to be strong and resilient through difficult times during the PhD. My special thanks go to Sridhar Rana Rinpoche for his wisdom and encouragement that helped me greatly.
Finally, I must thank the Department of Health’s Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU) for their financial support that made it possible for me to enrol in the PhD. The views expressed in this thesis are solely those of the author.
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<tr>
<td>6CIT</td>
<td>6-item Cognitive Impairment Test</td>
</tr>
<tr>
<td>AcHEI</td>
<td>Acetylcholinesterase Inhibitor</td>
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<tr>
<td>AD</td>
<td>Alzheimer’s Disease</td>
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<tr>
<td>ADAS</td>
<td>Alzheimer’s Disease Assessment Scale</td>
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<td>ADL</td>
<td>Activities of Daily Living</td>
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<td>AHP</td>
<td>Analytic Hierarchy Process</td>
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<td>ASCOT</td>
<td>Adult Social Care Outcomes Toolkit</td>
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<tr>
<td>CBA</td>
<td>Cost Benefit Analysis</td>
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<td>CCA</td>
<td>Cost Consequences Analysis</td>
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<td>CCG</td>
<td>Clinical Commissioning Group</td>
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<td>CEA</td>
<td>Cost Effectiveness Analysis</td>
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<td>CUA</td>
<td>Cost Utility Analysis</td>
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<tr>
<td>CV</td>
<td>Contingent Valuation</td>
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<tr>
<td>DCE</td>
<td>Discrete Choice Experiment</td>
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<tr>
<td>DH</td>
<td>Department of Health</td>
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<tr>
<td>DM</td>
<td>Decision Maker</td>
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<tr>
<td>DSA</td>
<td>Deterministic Sensitivity Analysis</td>
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<tr>
<td>EEACT</td>
<td>Economic Evaluation Alongside Clinical Trial</td>
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<tr>
<td>EQ5D</td>
<td>EuroQol five dimensions</td>
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<tr>
<td>EUT</td>
<td>Expected Utility Theory</td>
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<tr>
<td>FTC</td>
<td>Full-Time Care</td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
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<td>GPCOG</td>
<td>General Practitioner assessment of Cognition</td>
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<td>HRQOL</td>
<td>Health Related Quality Of Life</td>
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<td>HTA</td>
<td>Health Technology Appraisal</td>
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<td>HUI</td>
<td>Health Utility Index</td>
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<td>HYE</td>
<td>Healthy Year Equivalent</td>
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<td>IADL</td>
<td>Instrumental Activities of Daily Living</td>
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<td>ICECAP</td>
<td>ICEpop CAPability measure</td>
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<td>ICER</td>
<td>Incremental Cost Effectiveness Ratio</td>
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<td>Abbreviation</td>
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<td>ISPOR</td>
<td>International Society For Pharmacoeconomics and Outcomes Research</td>
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<td>MCDA</td>
<td>Multi-Criteria Decision Analysis</td>
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<td>MCI</td>
<td>Mild Cognitive Impairment</td>
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<td>MMSE</td>
<td>Mini-Mental State Examination</td>
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<tr>
<td>NHB</td>
<td>Net Health Benefit</td>
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<tr>
<td>NHS</td>
<td>National Health Services</td>
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<td>NICE</td>
<td>The National Institute for Health and Care Excellence</td>
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<td>NMB</td>
<td>Net Monetary Benefit</td>
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<tr>
<td>NPI</td>
<td>Neuropsychiatric Inventory</td>
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<td>PSA</td>
<td>Probabilistic Sensitivity Analysis</td>
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<tr>
<td>PSS</td>
<td>Personal Social Services</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality-Adjusted Life Year</td>
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<tr>
<td>RCT</td>
<td>Randomised Clinical Trial</td>
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<td>RP</td>
<td>Revealed Preference</td>
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<tr>
<td>SF6D</td>
<td>Short-Form Six-Dimension</td>
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<tr>
<td>SP</td>
<td>Stated Preference</td>
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<tr>
<td>VaD</td>
<td>Vascular Dementia</td>
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<td>VBA</td>
<td>Value Based Assessment</td>
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<tr>
<td>VBP</td>
<td>Value Based Pricing</td>
</tr>
<tr>
<td>WTA</td>
<td>Willingness To Accept</td>
</tr>
<tr>
<td>WTP</td>
<td>Willingness To Pay</td>
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PUBLICATIONS AND PRESENTATIONS

Papers


Conference presentations

1. “Value engineering and multi-criteria decision making as a part of health technology assessment in medical devices – A discussion”. Oral presentation at the Health Economists’ Study Group (HESG) conference in Sheffield, UK, 8 – 10 Jan 2014


3. “Incorporating multiple criteria in health technology assessment (HTA): a case study of dementia”. Oral Presentation (by my second supervisor, Dr. Praveen Thokala) at the International Health Economics Association (iHEA) conference in Milan, Italy, 12 – 15 July 2015


SUMMARY

Introduction

There is always a constraint on how much we can spend on health care. A new health care intervention often means additional costs besides its benefits. A decision to fund a new health care intervention needs to consider whether the benefits outweigh the costs. Such a decision is usually informed by an economic evaluation.

Methods of economic evaluation in health care have developed rapidly in the last three decades. In 1987, Drummond et al. published the first ‘textbook’ in the United Kingdom (UK) providing guidance on methods for the economic evaluation of health care programmes (Drummond et al., 1987). It discussed in detail the methods used in cost-effectiveness, cost-benefit, and cost-utility studies. The book became a successful textbook that has been referred to by health economists worldwide. In the subsequent years, the book has gone through four editions (1987, 1997, 2005, and 2015) reflecting the advancement in the field of health economics.

On the other hand, in 1996, the first United States (US) Panel on Cost-Effectiveness in Health and Medicine made the first attempt to establish a set of standards for conducting Cost-Effectiveness Analysis in health care (Gold et al., 1996). Their report was well received and quickly became a standard internationally. Twenty years later, given substantial advances in the field, the second US Panel on Cost-Effectiveness in Health and Medicine was convened to update the original report (Neumann et al., 2017).

Despite advances, the controversy surrounding which perspective is appropriate for economic evaluation of health care interventions remains. Drummond et al. lend support to the adoption of a societal perspective. The first Panel on Cost-Effectiveness in Health and Medicine (1996) also recommended a societal perspective for conducting CEAs. However, most economic evaluation studies did not adopt a societal perspective; the payer perspective was a more pragmatic choice (Claxton et al., 2010). One of the main challenges is the lack of a methodological framework to account for wider elements in a societal perspective. The second Panel on Cost-Effectiveness in Health and Medicine acknowledged this gap in the current methods (Neumann et al., 2017). Nonetheless, they still emphasised the importance of a societal perspective. The second Panel went on to recommend a reference case that reports the results from both perspectives: one is based on a healthcare sector perspective and the other is
based on a societal perspective. Whilst the methods for a healthcare sector perspective are straightforward, it is not clear how a societal perspective should be implemented and how its results could inform decision-making. For the healthcare sector Reference Case, the second Panel recommended that the results be summarised as an Incremental Cost-Effectiveness Ratio (ICER). For the societal perspective Reference Case, what the second Panel recommended is presenting an ‘Impact Inventory’ table where all costs and consequences are reported, which is basically a Cost Consequences Analysis (CCA) where the results are presented in the form of disaggregated consequences across different sectors. However, there was no suggestion on how decision makers are supposed to use the disaggregated results to make a decision.

**Summary of main thesis**

Inspired by this challenge, this PhD research set out to investigate methodological approaches that can be used to implement a societal perspective in economic evaluation of health care interventions. It started by reviewing all economic evaluation techniques (Chapter 2): Cost-Benefit Analysis (CBA), Cost-Effectiveness Analysis (CEA), Cost-Utility Analysis (CUA), and Cost-Consequences Analysis (CCA). The definition of CCA was expanded to incorporate Multiple-Criteria Decision Analysis (MCDA) which is an approach commonly used in decision science to help decision makers systematically understand the evidence and quantify their judgement. The extended definition of CCA was termed CCA-MCDA to differentiate it from more general definitions of CCA and MCDA separately. CCA-MCDA is an extension of CCA because it does not stop at presenting costs and consequences in a disaggregated format to decision makers; it uses MCDA techniques to elicit and use views and judgements from decision makers for aggregating costs and consequences.

The PhD research then reviewed the arguments for and against a societal perspective for economic evaluation of health care interventions (Chapter 3). The arguments for a societal perspective outweighed the arguments against it. However, there are important challenges that make implementing a societal perspective difficult such as the specification of a complete social welfare function or the lack of widely agreed upon methods for quantifying and valuing some broader impacts. In terms of approaches to implement a societal perspective, the thesis proposed two approaches for further investigation based on the review of economic evaluation techniques in Chapter 2: the extended cost-per-QALY (or a CUA approach) and the CCA-MCDA. Whilst there are other approaches that could be used for implementing a societal perspective such as a Welfarist CBA approach suggested by the Green Book or a Value Based
Assessment/Valued Based Pricing approach (DH, 2010, Roberts, 2015), these approaches were not investigated due to time and resource constraint.

The proposed approaches, the extended cost-per-QALY and the CCA-MCDA, were investigated by applying them in a case study of dementia. The case study of dementia interventions was chosen because of wider costs and consequences from their impacts. Dementia is also the area where there has been an increasing interest from policy makers. This made it relevant and worthwhile.

The main research was conducted in five studies. The first study (Chapter 4) was a systematic review of previous economic evaluation studies in dementia. This review included all types of economic evaluation. Its objective was to understand the current state of knowledge regarding dementia, dementia care, and applied methods of economic evaluation in dementia care. The review focused on understanding the following aspects of methods in previous studies: type of economic evaluation, stated perspectives, identification, measurement and inclusion of costs, identification, measurement and inclusion of benefits, and how value for money was calculated. This study found more than half of previous studies stated their adoption of a societal perspective. This confirms the importance of a broader societal perspective for economic evaluation of dementia care. The review identified a range of relevant costs and benefits of dementia care and how they were measured and valued in previous studies. There was no agreement among previous studies on how a societal perspective should be implemented. This review highlighted the limitations in the methods of economic evaluation when it was applied in dementia.

Based on the findings of the review, it was decided that research was needed for approaches to implement a broader societal perspective for economic evaluation of dementia interventions. The case study was specified in more details. Four alternative options for early detection of dementia in primary care were evaluated: (1) GP’s unassisted clinical judgement, or GPs administer either the MMSE (2), the 6CIT (3) or the GPCOG (4). Costs included health care, government social care, private payment for care, and informal care. Benefits included patient QALYs and carer QALYs. A new cost-effectiveness model was required to provide estimates for these costs and benefits. The development of the cost-effectiveness model was conducted in two studies: a systematic review to inform the model development and the development of the model itself.
The second study (Chapter 5) was another systematic review with a narrower scope that focused only on previous model-based economic evaluation studies. Its objective was to inform the development of a cost-effectiveness model for evaluating different interventions for early detection of dementia in primary care. It provided a summary of methods and potential data sources for developing the cost-effectiveness model. The review found key aspects of modelling dementia progression that included modelling the cognitive decline, behavioural symptoms, deterioration in functioning, institutionalisation, and death. The majority of previous models only modelled the cognitive decline. Four modelling approaches were identified: (A) decision tree models, (B) traditional state-transition models, (C) transition to Full-Time-Care (FTC) models, and (D) models that directly simulate progression rates of specific clinical measures. Given the availability of data from previous studies, the need for the model to address a wide range of costs and benefits from a societal perspective, and the need for the model to be flexible, approach (D) was considered as the most appropriate approach.

The third study (Chapter 6) involved the development of a new cost-effectiveness model for evaluating four alternative interventions for early detection of dementia in primary care (Tong et al., 2016). The model was a patient-level simulation in which patients were followed over their life-time period. This model only examined dementia in the Alzheimer’s disease (AD) form. The model simulated the dementia pathway from pre-diagnosis to post-diagnosis, disease progression and death. The simulated population represented the English population 65 years and older. Benefits were measured in terms of QALYs gained for both patients and their informal caregivers. The benefit of GP-based diagnostic interventions came from improving HRQOL over the patients’ life. Costs included government health and social care, private payment for social care, and unpaid informal care.

The model provided estimates for costs and benefits of the interventions in the case study. The results suggested that using either the MMSE or the GPCOG saved resources and delivered more QALYs compared to the baseline option (the GP’s unassisted judgement). The 6CIT option was estimated to incur a small health care cost but save resources in the social care and the informal care compared to the baseline option. The 6CIT option was estimated to deliver the highest number of QALYs gained among all options considered due to it having the highest sensitivity. The GPCOG option was estimated to make the most saving for health care resources due to it having the highest specificity. The health care cost was estimated (per patient) at £80,144 for the baseline option (the GP’s unassisted judgment), £80,077 for the
MMSE, £79,957 for the GPCOG, and £80,139 for the 6CIT. The total number of QALYs for the patients were estimated at 12.00886 for the baseline option, 12.008976 for the MMSE option, 12.009246 for the GPCOG option, and 12.013143 for the 6CIT option. If only considering the health care cost and the patient QALYs, the incremental analysis showed that the GPCOG option clearly dominated the baseline option and the MMSE option, and the ICER between the 6CIT option and the GPCOG option was £59,453 per QALY. The PSA results showed that at cost-effectiveness thresholds lower than £52,000 per QALY, the GPCOG had the highest probability of being the best option.

The model estimates were used as the initial basis to operationalise a broader societal perspective using the two proposed economic evaluation approaches. The operationalisation of the extended cost-per-QALY did not require further data collection. The operationalisation of the CCA-MCDA required a further step of organising a facilitated decision-making workshop in which the views and values of the local decision makers were elicited and recorded. The objective of the research was to gain an understanding of strengths and limitations of each approach when they were applied.

The fourth study (Chapter 7) implemented the extended cost-per-QALY approach in the case study. The extended cost-per-QALY approach used sector-specific thresholds and a societal value of a QALY to derive weights that were attached to the wider costs falling on different sectors. The wider costs were then aggregated to the healthcare cost to derive a single aggregated cost that was compared with the aggregated benefit measured in QALYs. Once costs and benefits were aggregated, the economic evaluation became similar to a conventional cost-per-QALY analysis. In the case study implementation, the best option was mainly a choice between the 6CIT and the GPCOG. The two perspectives gave two different cost-effectiveness results. The healthcare-perspective cost-per-QALY analysis resulted in an ICER (the 6CIT vs the GPCOG) of £59,453 per QALY, whereas the extended cost-per-QALY analysis gave an ICER (the 6CIT vs the GPCOG) of £41,355. This study showed that the key aspect to implement a broader societal perspective in an extended cost-per-QALY approach was the aggregation of costs falling on different sectors, the aggregation of benefits across sectors and groups of individuals, and the sector-specific threshold values. This study highlighted the key operational steps in implementing the extended cost-per-QALY approach and opportunities for future research.
The fifth study (Chapter 8) implemented the CCA-MCDA approach in the case study. This approach used views and values elicited from local decision makers to aggregate costs and benefits. The general approach included the development of a simple system to be used for weighting costs and weighting benefits. The MCDA techniques were used in a facilitated decision-making workshop to elicit views and values. The workshop was audio-recorded and a qualitative analysis was performed on the recorded data to understand the participants’ views and experiences. The operationalisation used the same model estimates from the third study (Chapter 6). It should be noted that this CCA-MCDA study was not the implementation of a full standard MCDA with all its steps (Dodgson et al., 2009, Thokala et al., 2016, Marsh et al., 2016). There was no attempt to identify and develop a comprehensive list of decision criteria from the decision makers. Only MCDA weighting techniques were used in a facilitated decision-making workshop to elicit views and values from decision makers for a pre-specified list of costs and benefits in the case study. The research found that the main difficulty in implementing this approach was to get the participants to think about the problem consistently with the economic evaluation framework. Understanding the problem was key to engagement. The participants voiced difficulties in understanding the approach and the weighting of different costs and different benefits. However, with more explanations and examples provided, their understanding improved and they could state their views and values. Implementing the values in the case study, the best option was still a choice between the 6CIT and the GPCOG. The CCA-MCDA resulted in a higher ICER (the 6CIT vs the GPCOG) at £46,799 per QALY compared to the extended cost-per-QALY (£41,355 per QALY). This was due to the different weights attached to costs and benefits when they were aggregated.

Chapter 9 (the final chapter) provides a recap of the main themes of the thesis. The key findings and contributions from each study in the thesis are summarised along with the implications for methods of economic evaluation and policy. The limitations of the thesis are also discussed before presenting future research directions based on the work in this thesis.

**Contributions**

The findings from this thesis make contributions to knowledge and policy in a number of ways. Each study makes its own contribution. The key contribution to knowledge of the first study (Chapter 4) is a description of applied economic evaluation methods in dementia; there has not been any published review of economic evaluation methods in dementia. The contribution to knowledge of the second study (Chapter 5) is a description of the key components in
developing a cost-effectiveness model for evaluating dementia interventions. Previous reviews (Green, 2007, Cohen and Neumann, 2008, Green et al., 2011) covered the literature up to March 2010. This study has extended the coverage of the literature up to October 2015.

The third study (Chapter 6) makes contributions to both knowledge and policy making, and has been published in the International Journal of Geriatric Psychiatry (Tong et al., 2016). A key contribution of this study is the more detailed modelling of the pathway from normal cognition to presenting at GPs, being assessed and referred to memory services. This feature of the model makes it possible to evaluate different screening tests that could be used by GPs. To policy, this study contributes to the understanding and evidence of the cost-effectiveness of early detection and interventions in dementia care. Even with the modest effectiveness of current dementia treatments, interventions to improve the accuracy of GPs in detecting and referring patients with dementia are likely to be cost-effective. Any of the three commonly used screening tests (the MMSE, the GPCOG, the 6CIT) was shown to be better than the GPs’ unassisted judgement. With a cost-effectiveness threshold range between £20,000 per QALY and £30,000 per QALY, the GPCOG was the most cost-effective option. It is important to keep in mind the caveats (the model’s assumptions) regarding the model’s estimates. To our knowledge, this is the first screening/diagnostic model to have looked at the effects of interventions for early detection of cognitive impairment in primary care.

The fourth (Chapter 7) and fifth (Chapter 8) studies make contributions to the methods of economic evaluation taking a broader societal perspective. These are the first studies which investigate methodological approaches for implementing a societal perspective in economic evaluation in health care. Manuscripts for two papers arising from these two studies have been submitted to be considered for peer-review publication. As mentioned at the beginning, there has not been a widely agreed method to implement a societal perspective in economic evaluation. The two proposed approaches in this thesis found a starting point for future research with the conduct of a broader societal perspective. The extended cost-per-QALY study broadens the knowledge regarding the method of conducting a Cost-Utility Analysis. Taking a societal perspective, it is important to recognise the opportunity costs of resources in different sectors. There are different sector-specific cost-effectiveness thresholds which can be used to weight sector-specific costs for their aggregation. Taking a societal perspective also requires a broader perspective on benefits. The development of a generic outcome measure that can be
used across sectors (in future research) will complement this extended cost-per-QALY approach.

On the other hand, the CCA-MCDA study broadens the knowledge for both CCA and MCDA methods. Stopping the analysis at just presenting costs and consequences in disaggregated format (as in CCA) is not enough and there is a need to provide decision makers with analytical tools that can help them process the results and to make decisions based on their views and judgements. Such tools are readily available in the field of operational research; a useful set of tools is offered by MCDA. As found in this thesis, MCDA methods can take CCA further. In a CCA-MCDA approach, decision makers are engaged in a structured decision-making process in which their views and values are quantified and used to inform the final economic evaluation results. There have been discussions in the literature surrounding the role of MCDA in a HTA process (Devlin and Sussex, 2011, Thokala and Duenas, 2012, Thokala et al., 2016, Marsh et al., 2016). The CCA-MCDA study in this thesis contributes to the evidence and current debate regarding the role of MCDA methods in HTA. This is the first study that attempted to apply MCDA methods to implement a Cost-Effectiveness Analysis taking a broader societal perspective. Challenges have been identified and discussed for the application of MCDA techniques which include the identification and construction of the decision-making group, the specification of costs and benefits, the conduct of the facilitated workshop(s), and the value elicitation tasks.

Discussion and conclusion

Through the implementation of the extended cost-per-QALY and the CCA-MCDA, it has become apparent that these two approaches could be complementary: one is more appropriate for decisions at a national level and the other has the flexibility to allow for local variations in decision making. Healthcare resource allocation decisions take place at different levels from national to local regions to individuals. For example, NICE makes recommendations nationally on which health care interventions should be provided by the NHS. Locally, Clinical Commissioning Groups (CCGs) need to decide how much they should spend on different health care programmes. Individually, clinicians need to decide whether to give a particular health care intervention to a patient. Going from individually to nationally, decisions become more complex and involve a broader range of different aspects and stakeholders; the quality and quantity of information required for decision-making also increases.
The extended cost-per-QALY is recommended for healthcare resource allocation decisions at the national level when a broader societal perspective is required. This is because decisions at the national level deal with things that are shared by all local regions within the national system. Evidence to inform decisions at the national level requires a high level of consistency, quality and quantity. Subjective judgement from a specific group of individuals may not represent national interests and it leaves too much room for bias and inconsistency. The extended cost-per-QALY approach can satisfy the evidence requirement at national level since it only uses ‘objective’ evidence.

On the other hand, the CCA-MCDA is recommended for decision-making at the local level. The implementation at the local level may diverge from the national values, as found in this thesis. Local decisions deal with some aspects that can be only relevant to the local areas where ‘objective’ evidence is not always available (or it is not practical to conduct research to collect data). In this case, subjective judgment from local decision makers can be useful when elicited in a transparent and accountable manner. With the CCA-MCDA approach, local values can be used directly in an economic evaluation and local decision makers can be involved in the decision-making process in a transparent, accountable and structured manner.

All in all, implementing a societal perspective remains a challenging task. This thesis only managed to deal with one aspect of the problem. Nonetheless, it is an aspiration to move a societal perspective closer to practice.
CHAPTER 1. INTRODUCTION

“The societal perspective does not represent the situation from the viewpoint of particular agents in society, but it is the only perspective that never counts as a gain what is really someone else’s loss.”

(Gold et al., 1996) - page 7.

The first Panel on Cost-Effectiveness in Health and Medicine (1996) recommended a reference case to set the methodological standard for Cost-Effectiveness Analysis. They recommended a societal perspective. However, in the following decades, most economic evaluation studies did not adopt a societal perspective (Claxton et al., 2010, Neumann et al., 2017). Methodological challenges with a societal perspective make it impractical in real practice despite its theoretical advantages. This thesis aims to tackle some of the methodological challenges regarding the implementation of a societal perspective in economic evaluation.

1.1 Background

Economic evaluation is ‘the comparative analysis of alternative courses of action in terms of both their costs and consequences’ (Drummond et al., 2005) – page 9. In conducting economic evaluation, the perspective of analysis implies the point of view of the users of the analysis who are often the decision makers. The perspective of an economic evaluation sets the boundary of what types of costs and benefits should be included in the analysis. For example, different perspectives in economic evaluation can be placed from narrow to broad as following: patients, providers, payers, and society.

The societal perspective is the broadest perspective which considers ‘all costs and benefits associated with an intervention, no matter who bears the costs and who gains the benefits’ – quoted in (Currie et al., 1999) from (Boyle et al., 1983). The payer’s perspective is narrower; it restricts the analysis to only the costs and consequences that are relevant to the payers (Drummond et al., 2015).

The reference case recommended by the first Panel on Cost-Effectiveness in Health and Medicine was based on a societal perspective (Gold et al., 1996). Other textbooks in health economics also lend support to the adoption of a societal perspective in economic evaluation.
The second Panel on Cost-Effectiveness in Health and Medicine recently published their recommendations on the methods of economic evaluation in health care (Neumann et al., 2017). The societal perspective still stands firmly as the desirable perspective for economic evaluation.

Despite the theoretical appeal of a societal perspective, methodological challenges make it difficult to implement in practice. Most economic evaluation studies did not adopt a societal perspective. The perspective of the health system is a more pragmatic choice. The National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) adopts a health system perspective (only including costs falling on health and social care) for economic evaluation of health technologies (NICE, 2013a). Outside the UK, Claxton et al. reviewed guidelines from 24 other countries and found that eleven guidelines require a health system perspective, six recommend both health and societal perspectives as separate analyses, and one has no preference (Claxton et al., 2010). None of the guidelines offered a methodological framework or a reference case to implement the societal perspective.

There is a demand from both policy makers and academics for a methodological framework to address the societal perspective in economic evaluations. In 2010, the Department of Health (DH) in the UK proposed a Value Based Pricing (VBP) approach to incorporate wider considerations into the current cost-per-QALY approach recommended in the NICE guidance (DH, 2010). In September 2014, NICE issued a consultation paper regarding the use of VBP and it received more than 900 responses but found no agreement in the responses to the proposed changes (Houses of Parliament, 2015). Methodological and ethical issues with the VBP were raised during the consultation process (Miners et al., 2013b, Miners et al., 2013a).

At the end, the VBP approach was not adopted and the NICE framework remained unchanged (Houses of Parliament, 2015). On the other hand, NICE published the social care guidance for economic evaluation of social care interventions that recognises the importance of including costs falling on all relevant public sectors and costs falling on non-public sectors such as family funding and informal care (NICE, 2013b). However, methods to include wider costs in economic evaluation are rarely used and there is no agreement on how to do it (Brazier and Tsuchiya, 2015).

There is an increasingly governmental interest in being able to do a comparative Cost-Effectiveness Analysis of interventions across sectors. The Five Year Forward View (2014) aims for a future in which the individual is the centre of networks of care, and new models of
care emphasises integration across acute, primary, mental, specialist and social care services (NHS England, 2014). With this emphasis on coordination between sectors, there is a need to understand how Cost-Effectiveness Analysis can be conducted to account for effects across sectors.

Given the gap in methods to implement a societal perspective in economic evaluation, this thesis set out to investigate potential approaches that can help implement the societal perspective. In doing so, it hopes to contribute to the current state of knowledge for economic evaluation and implications on policy in health care.

1.2 The case study

A specific disease area was selected for the focus of the investigation. This thesis chose dementia and the rationale is as follows.

Dementia care is the area where evidence suggests that there are substantial wider effects that fall outside the healthcare sector, however, their considerations have little to no impact on decision making (Garau et al., 2016). The substantial wider effects of dementia care include impacts on informal caregivers, impacts on social care, and spill-over effects on other non-health sectors such as police, fire brigade, and so on (Prince et al., 2014). Garau et al. (2016) interviewed decision makers and experts in eight countries including the UK and found several barriers to incorporating wider effects into decision making; among them are the issues with methods and practical issues due to added complexity when the wider effects are included.

Only one case study could be carried out in this thesis due to time and resource constraints. Whilst there could be other disease areas that needed to be investigated for generalisation of the methodological approaches, the focus of this thesis was in the area of dementia care. The conduct of other case studies was reserved for future research after this PhD.

1.3 Methods of research

1.3.1 Aim, objectives and research questions

This thesis aims to investigate methodological approaches for implementing a societal perspective in economic evaluation. A review of economic evaluation techniques (Chapter 2) led the research to focus on two approaches: the extended cost-per-QALY and the CCA-
MCDA. Taking dementia care as the case study, the objectives and research questions are as follows.

**Objective 1:** To review the methods of economic evaluation in previous studies of dementia:
- What type of economic evaluation was performed?
- What perspective was stated?
- Which costs were included and how were they measured and valued?
- Which benefits were included and how were they measured and valued?
- How were costs and benefits aggregated to support the decision?
- Which decision problem should be used in the case study to explore the application of the methodological approaches?

**Objective 2:** To review previous modelling studies in dementia:
- What modelling technique was utilised?
- What data sources were used?
- How were relationships between health and disease progression/interventions modelled?
- How were relationships between costs and disease progression/interventions modelled?
- Which outputs were reported?

**Objective 3:** To develop a cost-effectiveness model for the decision problem chosen in the case study:
- Which model structure should be used?
- How can the model be populated (input data)?
- How can uncertainty be addressed?
- What are the model results for costs, benefits and their uncertainty?

**Objective 4:** To explore the operationalisation of the extended cost-per-QALY:
- How are costs aggregated?
- How are benefits aggregated?
- How to calculate and present the economic evaluation results?
- How to address and present uncertainty?
- What are the lessons for future research?
Objective 5: To explore the operationalisation of the CCA-MCDA:

- How to establish the decision context?
- How to conduct facilitated decision-making workshops?
- How to apply the MCDA model in the economic evaluation?
- How to present and interpret the results?
- How to conduct sensitivity analysis?
- What are the lessons for future research?

1.3.2 Methodology

To achieve the aim and objectives, the investigation included five tasks (undertaken in five studies). The first task (Chapter 4) was a systematic review of previous economic evaluation studies in dementia. The second task (Chapter 5) was a systematic review of previous models and other potential sources for model inputs. The third task (Chapter 6) was the development of a cost-effectiveness model for the decision problem in the case study. Using the model’s estimates, the fourth task (Chapter 7) was to explore the operationalisation of the extended cost-per-QALY and the fifth task (Chapter 8) was to explore the CCA-MCDA in the case study. This section describes the methodology employed and rationale for its use to undertake the tasks.

1.3.2.1 Study 1: Review methods of economic evaluation in previous studies

It was important to understand the current state of economic evaluation methods which had been applied for evaluating dementia interventions. Although evidence suggested the existence of substantial wider costs and benefits of dementia interventions, we did not know how these wider effects had been addressed in previous studies. Therefore, the first study set out to provide the evidence base for subsequent studies.

This study aimed to answer the research questions for the first objective of the thesis. It had a broader scope than the second systematic review in study two. The review included all types of economic evaluation (both model-based and non-model based). Its purpose was to understand the current state of knowledge regarding dementia, dementia care, and applied methods of economic evaluation in dementia care. The review focused on understanding the following aspects of methods in previous studies: types of economic evaluation; stated
perspectives; identification, measurement and inclusion of costs; identification, measurement and inclusion of benefits; and how value for money was calculated.

Based on the understanding from previous studies, a new decision problem was proposed for the case study. This decision problem needed to be topical so that its investigation would make contributions to the current evidence base for the cost-effectiveness of dementia interventions and therefore, make the research worthwhile.

1.3.2.2 Study 2: Review for the model development

A new cost-effectiveness model was needed to synthesize and extrapolate the evidence for the costs and benefits of interventions in the case study. To develop the model, a systematic review of previous models and the data sources they used was conducted. This review looked at previous models in terms of how they modelled the disease progression, how they modelled the interventions, how they linked the progression and intervention with costs, how they linked the progression and intervention with QALYs, and what potential data sources to populate the model were. The findings of this study informed the model structure and provided data sources for the model input in Study three. Compared to Study one, the systematic review in this study had a narrower scope that focused only on modelling aspects in previous model-based economic evaluation studies.

1.3.2.3 Study 3: Developing the cost-effectiveness model

The third study developed a new cost-effectiveness model for the decision problem in the case study. The model was a patient-level simulation in which patients that represent the elderly population in England (65 years and older) were followed over their life-time period. The model’s conceptual structure was developed based on the review of previous models and validated by clinicians and professionals in dementia care. The model parameters were informed by available data from the literature. Uncertainty with the model estimates was assessed in both Deterministic Sensitivity Analyses (DSA) and Probability Sensitivity Analyses (PSA). The model results were reported for costs and benefits of dementia interventions in the case study.
1.3.2.4 Study 4: Implementing the extended cost-per-QALY

Given the model estimates, the healthcare-perspective cost-per-QALY analysis only included costs falling on the healthcare budget and benefits measured in terms of patient QALYs. The societal-perspective cost-per-QALY analysis, on the other hand, needed to include wider costs and benefits. Study four was the implementation of the extended cost-per-QALY in the case study. Using the model estimates from Study three as the initial basis, this study first demonstrated how the healthcare-perspective cost-per-QALY analysis was conducted. It then demonstrated the conduct of an extended cost-per-QALY analysis for the societal perspective. This approach did not require the involvement of decision makers for its development and implementation. Lessons for future research were drawn from the experience conducting this study.

1.3.2.5 Study 5: Implementing the CCA-MCDA

Another approach to implement the societal perspective in economic evaluation was through the CCA-MCDA. Unlike the extended cost-per-QALY, this approach relies on the judgement from a decision-making group to aggregate costs, aggregate benefits, and arrive at a judgement for cost-effectiveness of alternative decision options. This approach requires the identification of a decision-making group and the organisation of facilitated decision-making workshops.

Study five was the implementation of the CCA-MCDA. Local decision makers and stakeholders in dementia care were identified and recruited to form a hypothetical decision-making group for the case study. A decision-making workshop was organised. The workshop was audio recorded. Values (weights) and views about the costs and benefits in the case study were elicited from the decision makers and stakeholders. The elicited weights were used to demonstrate the calculation of aggregated cost, aggregated benefit, and value-for-money (cost-effectiveness) of alternative decision options in the case study. The recorded data were analysed qualitatively to understand the views and experiences of the workshop participants.

It should be emphasised that this was not the implementation of a full standard MCDA with all its steps because there was no attempt to identify and include all possible decision criteria from the decision makers (more details about the standard practice of MCDA are referred to (Thokala et al., 2016, Marsh et al., 2016)). This study focused on the use of MCDA weighting
techniques to elicit views and values from local decision makers for use in economic evaluation.

1.4 Structure of the thesis

This thesis has nine chapters. The next chapter (Chapter 2) provides an overview and critique of the techniques of economic evaluation in health care. The chapter outlines the key features and criticisms of Cost-Benefit Analysis (CBA), Cost-Effectiveness Analysis (CEA), Cost-Utility Analysis, and Cost-Consequence Analysis (CCA). The definition of CCA was expanded to incorporate Multiple-Criteria Decision Analysis (MCDA). The extended definition of CCA was termed CCA-MCDA to differentiate from more general definitions of CCA and MCDA.

Chapter 3 goes into more details on the implementation of a broader societal perspective in economic evaluation. It starts by reviewing the arguments for and against a societal perspective in economic evaluation. The challenges in implementing a societal perspective are discussed in this chapter. This is followed by a proposal of two approaches for implementing a broader societal perspective in this thesis: the extended cost-per-QALY, and the CCA-MCDA.

Chapters 4 to 8 report the main research conducted in this thesis. These includes five original studies. Chapter 4 reports the systematic review of applied economic evaluation methods in previous studies in dementia. It then introduces the decision problem for the case study. The decision problem concerned the cost-effectiveness of four alternative options for early detection of dementia in primary care: (1) GP’s unassisted judgement, (2) GPs using the MMSE, (3) GPs using the 6CIT, and (4) GPs using the GPCOG. Chapter 5 reports another systematic review to support the development of a new cost-effectiveness model for the case study. This review had a different purpose and a narrower scope compared to the review in Chapter 4. Chapter 6 reports the development of a new cost-effectiveness model and its results. The model provided estimates for costs and benefits in the case study. Chapter 7 reports the investigation of the operationalisation of the extended cost-per-QALY. It reports how the approach was implemented given the model estimates. It also highlights issues and challenges in the operationalisation. Chapter 8 reports the investigation of the operationalisation of the CCA-MCDA. The chapter reports the results of the operationalisation and the results of the qualitative analysis that looked at the views and experiences of the workshop participants.
The concluding chapter (Chapter 9) summarises and discusses the key findings, contributions, and implications of this PhD research. Recommendations for further research are made at the end of the chapter.
CHAPTER 2. ECONOMIC EVALUATION TECHNIQUES

This chapter provides an overview and critique of the techniques for economic evaluation in health care. This includes Cost-Benefit Analysis (CBA), Cost-Effectiveness Analysis (CEA), Cost-Utility Analysis (CUA), and Cost-Consequence Analysis (CCA). These techniques are different in terms of how costs and consequences of alternative decision options are identified, measured, valued, and used in decision making (Drummond et al., 2015).
2.1 Cost Benefit Analysis

2.1.1 Definition

In Cost Benefit Analysis (CBA), all costs and benefits of alternative options are measured, valued and expressed in monetary units (Drummond et al., 2015). The monetary valuation is either revealed in markets (through prices) or stated by the individuals through their willingness-to-pay (WTP) or willingness-to-accept (WTA). The net monetary benefit (NMB) is calculated by subtracting the monetary value of costs from the monetary value of benefits. An intervention is considered more cost-effective than its comparator if its incremental NMB is positive. These principles are illustrated in the equations below.

\[
\text{Equation 2.1} \quad NMB_i = V_i^E (\text{benefits}) - V_i^E (\text{costs})
\]

\[
\text{Equation 2.2} \quad \Delta NMB_i = NMB_i - NMB_o > 0
\]

The practice of CBA has a long record of practice in areas outside health such as transport and environment (Drummond et al., 2015).

2.1.2 Theoretical foundation

CBA has been claimed to be consistent with welfare economics (Birch and Donaldson, 2003). CBA is the practical implementation of the Welfarist view (in contrast to the Non-welfarist view of Cost Utility Analysis). In social decision making, the social decision makers need to judge how a decision option would change the current welfare of the society. The Welfarist view states that social welfare should be judged solely on the sum of individual utilities revealed through choices that they make especially in markets, and individuals are the best judges of their welfare (Brouwer et al., 2008b). Since utility is an abstract concept, the monetary amount that an individual is willing and able to pay for an item is used as an indicator (Arrow et al., 1993).
Pareto said that if at least one individual is made better off and no one is made worse off, then the action definitely increases social welfare (McGuire, 2001). However, we often face situations where some individuals are made better off and some other individuals are made worse off. In those cases, Hicks and Kaldor suggested a solution that assumes we can compensate individuals who are made worse off (McGuire, 2001). If worse-off individuals agree a compensation value (in monetary units), then we can determine whether a positive net benefit is possible by subtracting the compensation amount from the utility gained. Thus, using the Pareto principle and Hicks-Kaldor assumption, a decision option can be judged on whether it would increase social welfare.

CBA is operated on that foundation to determine whether an intervention would increase social welfare measured by individuals’ utilities. Thus, we can see that CBA inherits the following assumptions from the Welfarist view:

- Individuals’ utilities are perfectly reflected by market prices or their stated monetary values from WTP or WTA. This utility is the only thing that matters in social welfare.
- It is always possible to compensate individuals who are made worse-off by asking them how much (money) they would accept for their losses.

2.1.3 Criticisms

2.1.3.1 Criticisms on the theoretical ground:

On the theoretical ground, the criticism points at the assumptions made by the Welfarist view. First, it is argued that individuals’ utilities are not perfectly reflected by market prices or their stated monetary values in WTP or WTA. This is particularly true for health care. On the one hand, the health care market is not a perfect market. It is heavily regulated by the government. Therefore, market prices are not good indicators of utilities for users of health care. On the other hand, health care is a special commodity. The consumers (patients) cannot choose health care for themselves but must rely on doctors. In addition, they consume health care not for the pleasure of consumption but for restoring or maintaining their health.

Second, it is argued that the kind of utility arising from consumption should not be the sole basis on which to judge social welfare (Sen, 1987). The well-being (welfare) of a person should go beyond the conventional concept of utility (i.e. willingness to pay for commodities) to
include other aspects of their life such as how they function (physically and mentally) or what they are capable of doing. Commodities are one of the means to achieve wellbeing but they cannot be the wellbeing themselves (Sen, 1987). Culyer (1991) emphasised this to be highly relevant in the health care area where more attention is given to individual health rather than to health care as a commodity:

“Since, in the Welfarist approach, the basis of social welfare – or diswelfare – is only the utility got from goods and services (including labour services), an important class of ‘extra’ welfare sources is the non-goods characteristics of individuals (like whether they are happy, out of pain, free to choose, physically mobile, honest). Extra-welfarism thus transcends traditional welfare: it does not exclude individual welfares from the judgement about the social state, but it does supplement them with other aspects of individuals (including even the quality of the relationships between individuals, groups and social classes).” (Culyer, 1991).

The third criticism concerns the Hicks-Kaldor compensation test. The Hicks-Kaldor principle assumes that it is possible to pay worse-off individuals for their losses. This does not seem appropriate for health care. We would have ethical concerns when asking to pay individuals for the loss of their health. We do not want to allocate health care resources based on how much individuals can pay for their health. This distributional implication is one of the reasons that health economists do not welcome CBA in health care resources allocation (Boadway and Bruce, 1984, Brazier et al., 2007).

2.1.3.2 Criticisms on the practical ground:

The criticisms on the practical ground mainly concern the techniques for monetarily valuing health effects in CBA. These techniques are broadly grouped into two categories: revealed preference (RP) methods and stated preference (SP) methods.

2.1.3.2.1 Revealed Preference methods:

Revealed preference (RP) methods estimate the monetary value of an item from the preferences revealed by consumer behaviour (Kroes and Sheldon, 1988). Usually, the market price of an item is a good indicator of its value; it reflects consumers’ preferences through their behaviours in the market. However, for prices to truly reflect values, the market needs to meet certain conditions such as being perfectly competitive, no externalities, no distorting incentives, etc.
Such conditions do not often exist in health care: patients are often ignorant of existing treatments and their health outcomes; patients have to rely on doctors in the consumption of health care, and patients rarely pay the full market price for health care but their health care consumption is often funded by medical insurance or Government budget (Brazier et al., 2007).

When the item does not have a market (e.g. an intangible item such as a health risk), RP methods can still monetarily value such an item by attaching it to another commodity for which there is a market. For example, by looking at the difference in average salaries between a job with an increased risk of death (e.g. a researcher who works in a radioactive environment) and a similar job with less risk of death (e.g. a research who works in a normal lab), we can estimate a monetary value associated with the difference in health risk. Nonetheless, one major problem is the difficulty to control for the confounding factors as these wage rates depend on many other factors besides the health risk and it is almost impossible to identify and isolate them (Drummond et al., 2005). This might result in wide variation in the estimation according to the contexts (e.g. kind of jobs). A more serious drawback as mentioned by Drummond et al. (2005, p.219) is that ‘the observed risk-money trade-offs may not reflect the kind of rational choice revealing preferences that economists believe, because of many imperfections intervening in labour markets and limitation in how individuals perceive occupational risks’.

2.1.3.2.2 Stated Preference methods:

Stated preference (SP) methods value an item by presenting individuals with hypothetical scenarios and asking them to directly state the value they would place on the item (contingent valuation) or make choices between scenarios so that the value of the item can be inferred based on their preferences (conjoint analysis). Stated preference methods are often performed through surveys or experiments.

Historically, SP methods were first mentioned and applied in the field of natural resource and environmental economics to elicit market valuation of non-market good (Portney, 1994). Economists proposed SP methods because they recognised the existence of some benefits of environmental interventions that were difficult or impossible to value using markets; one way to obtain the value is to ask individuals directly how much they would be willing to pay (Portney, 1994).

The main assumption that underpins the validity of SP methods is that people are assumed to make the kind of rational choice in the hypothetical scenarios as in their real world, and people
would make the same decision if the hypothetical scenarios became real situations that they were to encounter (Morris et al., 2007). In practice, there might be non-market factors such as moods or emotions that might influence a person’s reasoning and decision-making process in a psychological experiment that causes the assumptions of SP to not hold.

The techniques from SP methods include contingent valuation (WTP/WTA) and conjoint analysis. In contingent valuation (CV), respondents are asked to state their maximum WTP for receiving a good or minimum WTA for a good being taken away. In addition to the issue with presenting unfamiliar hypothetical scenarios to respondents and asking them some tasks that they would never encounter in their real life, the practice of WTP/WTA in health care suffers other major pragmatic measurement issues such as: issues with non-response, protest response or strategic response, framing effects (e.g. starting point bias), absence of a meaningful budget constraint consideration, or appropriate amount of information provided for the hypothetical scenarios. These issues can possibly be resolved by improving the methods (Donaldson, 1995b, Dixon, 2008). However, there remain two important unresolved concerns with WTP/WTA: insensitivity to scope is the issue with evidence showing that people gave same WTP regardless of the scale of the effect (e.g. same WTP to save 2,000 birds, 20,000 birds or 200,000 birds in an oil spill), and ‘warm glow’ effect is the observation that people might give small WTP to indicate their approval of a cause rather than giving their true WTP (Arrow et al., 1993, Donaldson, 1995b, Dixon, 2008).

On the other hand, conjoint analysis is a de-compositional approach to analyse the structure of a person’s preferences for an object (Green and Srinivasan, 1978). Methods using conjoint analysis are different in terms of their elicitation techniques such as ranking (ordinal values from best to worst scenarios), rating (giving cardinal values on a numeric or semantic scale) or discrete choice modelling/experiment (DCE). DCEs are often preferred by economists and they are becoming more and more popular (Drummond et al., 2005). Despite advantages of DCE (compared to CV) such as it can provide insights about the relative importance of various attributes of a health care intervention, or it can avoid asking respondents directly about the monetary value of their health outcomes, there are unresolved issues with DCEs that require cautions in their application (Drummond et al., 2005). One major issue concerns the inclusion of a cost attribute to estimate WTP for CBA because there is evidence showing the levels for a cost attribute can affect the WTP estimates (Drummond et al., 2005). Another limitation of DCE is the burden it might incur on respondents due to the amount of valuation tasks (van den Berg et al., 2005).
2.2 Cost Effectiveness Analysis

2.2.1 Definition

In Cost Effectiveness Analysis (CEA), costs are measured and valued in monetary units and benefits are a single effect measured in natural units (Drummond et al., 2015). The single effect of interest needs to be common to all alternative decision options (but are achieved to different degrees). Examples of a single effect of interest are life-years gained, days of independence, number of accurate diagnoses, etc. The results are presented in terms of cost per unit of effect. An intervention is compared to its comparator in an incremental analysis and the result is presented in terms of an Incremental Cost Effectiveness Ratio (ICER). The graphical presentation of the comparison is a Cost-Effectiveness plane (Figure 2.1 – comparing intervention (A) with its comparator (O)).

Figure 2.1: The Cost Effectiveness plane.

Source: adapted from (Black, 1990).

The comparison is straightforward in quadrants II or IV: the intervention is rejected when its ICER is in quadrant IV; it is accepted when its ICER is in quadrant II. It is more complicated when the ICER is in quadrant I or III. In quadrant I, the intervention incurs more costs (positive incremental costs) but also more effective. In quadrant III, the intervention makes savings but also less effective. If there isn’t a constraint on the budget, the solution is simple, we just care about the effectiveness of the intervention: we reject the intervention if its ICER is in quadrant
III, and we accept the intervention if its ICER is in quadrant I. However, if there is a budget constraint (fixed budget), we need to estimate the effect of the incremental cost (or savings) in terms of their opportunity costs. For example, an incremental cost can be translated to an equivalent amount of effect (loss) by estimating the effect of imposing that cost on the fixed budget. This results in a cost-effectiveness (CE) threshold which describes the equivalent effect lost or gained when adding the incremental cost or savings on the fixed budget. Then, the comparison becomes a calculation of the incremental net effect. If the incremental net effect is positive, we accept the intervention. If it is negative, we reject the intervention. This principle is illustrated in the equations below. We can see that through mathematical transformation, the comparison is to compare the ICER with the threshold (k).

Equation 2.3

\[
\text{Incremental Net Effect} = \Delta E - \frac{\Delta C}{k} > 0
\]

Equation 2.4

\[
\text{ICER} = \frac{\Delta C}{\Delta E} < k
\]

It should be noted that CEA can only compare interventions with similar effectiveness measures. Because it uses a specific measure for effectiveness in a natural unit, we cannot generalise the results to other interventions where a different measure of effectiveness is required.

2.2.2 Theoretical foundation

CEA is based on the theory of production efficiency: for any given level of resources available, CEA can identify the choices within a limited range of options that can maximise a single effect that can be produced (Morris et al., 2007). CEA is appropriate for situations where decision makers evaluate a limited range of options within a given field and a given budget (Drummond et al., 2015). This is similar to the production of a specific good in a factory and the factory manager needs to choose the combination of machines and materials that can maximise the number of good produced. The CEA technique is not able to make a statement about the impact on social welfare because the outcome is left unvalued (in natural units).
2.2.3 Criticisms

CEA is mainly criticised for its limited use in health care resource allocation (Drummond et al., 2015). Due to the specific measure of a single effect for outcome in the CEA technique, we cannot make a comparison across programmes covered by the same budget if each programme produces a different effect. For example, it is difficult to compare an intervention to increase the diagnosis rate of dementia and an intervention to reduce blood pressure. Furthermore, it is difficult to use the CEA technique to compare programmes that produce multiple health effects. For example, to compare interventions that increase the diagnosis rate of dementia, the number of accurate diagnoses is only one effect beside other effects on patients such as their experience of the process. However, these limitations can be addressed by using a general measure of effectiveness in CEA as described in the next section.

2.3 Cost Utility Analysis

2.3.1 Definition

In Cost Utility Analysis (CUA), costs are measured and valued in monetary units and benefits are measured and valued in healthy years expressed in quality-adjusted life years (QALYs) (Drummond et al., 2015). The QALY is a measure of health benefit that captures both impacts on morbidity (health-related quality of life) and where relevant mortality (length of life in life years). It does this by assigning each year of life a value on a scale where full health is one and states as bad as being dead zero (Brazier et al., 2007).

The decision rules for CUA are like those for CEA. If the ICER is in quadrants II or IV, the comparison is straightforward (reject the intervention in quadrant IV and accept it in quadrant II). If the ICER is in quadrant I or III, we need to use a cost-effectiveness threshold to judge the cost-effectiveness of the intervention (see 2.2.1).

The cost-effectiveness (CE) threshold describes the estimated equivalent QALYs lost or gained when adding the incremental cost or savings on the fixed budget. When an incremental cost is imposed on the fixed budget, some existing services would be displaced. The displaced services would have a negative health effect. This negative health effect can be expressed as an amount of QALYs lost for individuals. The challenge is that we do not know exactly which existing activities will be displaced and who will be affected.
Claxton et al. (2015) conducted research to empirically estimate the CE threshold based on the relationship between the overall NHS expenditure and mortality. It is assumed that there is a relationship between the NHS budget and QALYs such that there is a point of equilibrium where:

Equation 2.5

\[
\frac{\Delta b}{\Delta q} = \text{a constant } (k) \ (\text{£ per QALY})
\]

\(\Delta b\): a unit increase on the budget (at the margin)
\(\Delta q\): the increase in QALYs (at the margin) for a unit increase of the budget

For an additional cost (\(\Delta C\)) from the intervention, its effect on the budget is assumed to be marginal. In other words, the additional cost is insignificant compared to the budget that it does not change the point of equilibrium. Therefore, the constant rate (k) is the cost-effectiveness threshold and it can be estimated empirically. Claxton et al. (2015)’s central estimate of the threshold was £ 12,936 per QALY. This value is lower than the cost-effectiveness threshold range specified by NICE (£20,000 per QALY and £30,000 per QALY).

2.3.2 Theoretical foundation

CUA is often seen as a practical implementation of the Extra-welfarist or Non-welfarist view (in contrast to the Welfarist view in CBA). Brouwer et al. (2008) set out four features that distinguish Extra-welfarism from Welfarism: ‘(i) it permits the use of outcomes other than utility, (ii) it permits the use of sources of valuation other than the affected individuals, (iii) it permits the weighting of outcomes (whether utility or other) according to principles that need not be preference-based and (iv) it permits interpersonal comparisons of wellbeing in a variety of dimensions’.

Extra-welfarism is widely accepted in health care and maximising health has become the main objective (if not the only objective) of economic evaluation in health care. Health, often measured as Quality Adjusted Life Years (QALYs), has become the central focus and has been treated as both a maximand and a distribuendum of a healthcare system (Brouwer et al., 2008a). The impact of a health technology is judged on the aggregation of health gained and lost by individuals. The gain of health is due to the health benefits of the health care technology for a
certain group of patients who would receive the treatment. The loss of health is due to the costs of the health care technology that would ultimately take away some other health care activities due to scarce resources. If the net health is positive, the technology is considered to have a positive impact on the society and hence is approved.

2.3.3 Criticisms

2.3.3.1 Health as the only source of benefit from health care

Current application of CUA focuses on the health benefit of health care to the exclusion of non-health benefits. Health measured in terms of QALY has become the only argument to represent individual utility functions, assuming other non-health arguments are insignificant in health care. As it will be argued below, this position is too narrow in many circumstances in health care.

First, we need to be clear about the definitions for utility, health, and non-health. Their definitions have always been ambiguous. There are two prominent ways to understand utility: preference orderings of different states, and desirability of a state of consciousness in terms of happiness, enjoyment or pleasure. In the first interpretation, utility is the strength of an individual preference. If an individual prefers state A to state B, we know utility of state A is higher than utility of state B. Thus, the level of utility can only be revealed by choices made by an individual. Utility only makes sense when an individual compares one state to another. Utility in this sense cannot be measured directly in cardinal units (Brazier, 1997). However, we can measure utility indirectly using monetary units (WTP or WTA). For example, if an individual is willing to pay £1 for an orange and £2 for an apple, we know the utility of consuming an apple is twice the utility of consuming an orange for that person. In the second interpretation, utility is the desirability of an individual for a state of consciousness (Dolan and Kahneman, 2008). The utility of a state reflects how happy or how well a person would be in that state. In this sense, we measure the utility of a state in terms of happiness or wellbeing. It is the first interpretation of utility which is applied in the Welfarist CBA.

The definition of health, on the other hand, can lie on a broad spectrum from a narrow view which confines health to the absence of disease to a broad view which brings health towards a “state of complete physical, mental and social well-being”, such as the WHO definition of health (World Health Organization, 2006). This diversity is reflected in the wide range of health
status measures ranging from disease-specific measures to broader well-being measures. We can see that there is an overlap between health and the second interpretation of utility.

The current application of CUA uses a definition of health somewhere between the narrow view for the absence of disability and the broader view of wellbeing. For example, the EQ-5D recommended by NICE for use in the measurement of HRQOL in the QALY describes health in terms of five dimensions: mobility (how well you can walk about), self-care (how well you can wash and dress yourself), usual activities (how well you can do your usual activities), pain/discomfort (how much pain you have), and anxiety/depression (how much anxiety/depression you have). As a result, non-health aspects are other effects that are not captured in the definition of health by a specific HRQOL measure.

One area where the significance of non-health benefits is highlighted is in evaluating public health programmes. Although cost-per-QALY analysis has been established and widely accepted in methods for evaluating ‘clinical’ interventions, such as drugs, medical devices, it encounters substantial challenges when applied in public health (Drummond et al., 2007). The main reason for this is the existence of a broad range of benefits generated by public health interventions. Indeed, NICE’s reference case for public health interventions has broadened its perspective on outcomes by adding: ‘non-health benefits may also be included’ (NICE, 2012b), but it is not clear how.

Another area where the sole focus on health seems to be inappropriate is in social care. NICE’s reference case for assessing social care services has broadened its perspective on outcomes to include all effects on service users or carers (NICE, 2013b). The EQ-5D, a preference-based generic measure commonly used in evaluating clinical interventions, is not recommended in social care. Instead, broader measures such as the ASCOT (Netten et al., 2012) and ICECAP (Grewal et al., 2006, Coast et al., 2008, Al-Janabi et al., 2012) are recommended to accommodate the calculation of social-care related QALYs (NICE, 2013b). In such measures, aspects considered beyond health such as humanness, dignity and autonomy are explicitly included.

There are non-health benefits in health care such as the value of knowing about one’s condition in screening and diagnostic interventions (Grosse et al., 2008), and process utility (Donaldson and Shackley, 1997, Brouwer et al., 2005). The value of knowing is the perceived value of information which can be independent of health outcomes; this value is particularly relevant in
areas such as genetic testing. The process utility is the value derived not from outcomes but from the way the outcome is accomplished (Brouwer et al., 2005). Brouwer et al. (2005) tested the hypothesis that informal caregivers derive utility not only from the outcome of information care but also from the process of providing informal care. They conducted a survey on a large sample of Dutch caregivers (n=950). Their results confirm the existence and substantiality of process utility in the context of informal care.

Given the existence of non-health benefits as discussed above, they are relevant and should be addressed in health care resource allocation decisions. If these non-health benefits are valued significantly by individuals but not addressed in the valuation of health care, it will lead to health care resource allocation being sub-optimal because such benefits are not counted. Health is the main, but not the only source of benefits of health care. The influence of excluding non-health benefits in resource allocation decisions in health care depends on the substantiality of non-health benefits and whether individuals are willing/prepared to make trade-offs between health benefits and non-health benefits.

2.3.3.2 Limitations of the QALY model and its alternatives

For the QALY to be a model of preferences, it needs to be linked to the expected utility theory (EUT). EUT was initiated by Daniel Bernoulli (1738) and was further developed by von Neumann and Morgenstern (1947) and Savage (1954) (Tversky, 1975). Pliskin et al. (1980) identified three conditions for the validity of the QALY model: mutual utility independence between life years and health status, a constant proportional trade-off of life years for health status, and a constant risk attitude (Brazier et al., 2007).

The main criticisms of the QALY model concern the restrictions it places on health state values and time, its handling of risk attitude, and the violation of the axioms of EUT. Nonetheless, there is little evidence regarding their significance (Brazier et al., 2007). Alternative measures to overcome the limitations of the QALY model are the Healthy Year Equivalents (HYE) and ‘ex ante QALYs’ (Brazier et al., 2007). However, these measures are more difficult or too infeasible and inflexible to apply in practice due to more complex and lengthy valuation tasks (Brazier et al., 2007). Prevailing belief among health economists still seems to support the QALY measure continuing to be the preferred measure for capturing the health benefits of health care interventions (Gold et al., 1996, Brazier et al., 2007, Drummond et al., 2015).
2.4 Cost Consequences Analysis

2.4.1 Current definition:

CCA is loosely defined as a technique of economic evaluation where costs and consequences of the alternatives are computed separately and listed but not aggregated (Gold et al., 1996). Gold et al. (1996) explained:

“The analysis itself does not combine these components, nor does indicate the relative importance of the various outcomes. This option is left to the user of the study ... CCA is based on the premise that users of the study can and should make the value judgement trade-offs necessary to integrate a disparate list of pros and cons of the various alternatives and reach a final decision.” (p59)

CCA aims to systematically identify and measure a broad set of attributes/decision criteria that should be considered when making decisions. The attributes can be measured in any relevant units and presented to the decision makers. With this definition, there is a completely black box after the presentation of costs and consequences to the final decision. This makes CCA un-scientific and opaque.

2.4.2 Expanding the current definition to include MCDA

The current definition is not helpful in distinguishing CCA as a separate technique for economic evaluation from CBA, CEA, and CUA. However, with more specification on how decision makers can apply their judgements on the disparate list of costs and consequences to make decisions, CCA can be linked to the vast area of decision science which is often applied more flexibly in other policy areas (Jensen, 2012). CCA can be a special case of Multiple-Criteria Decision Analysis (MCDA) where the decision criteria are the costs and benefits of alternative health care interventions.

MCDA\(^1\), which arose from decision analysis and found its home in operational research (Raiffa, 1968, Phillips and Stock, 2003), is still relatively new to the field of health economics. As a result, there is some confusion/ misunderstanding regarding what MCDA is and how it

\(^1\) The literature also refers to this same term as Multiple Criteria Analysis (MCA), Multi-attribute decision analysis (MADA) and Multiple Criteria Decision Making (MCDM)
can be applied in economic evaluation. For example, it can be argued that all types of economic evaluation are also forms of MCDA because they deal with multiple criteria. This view generalises MCDA to include all forms of decision analyses that deal with multiple criteria. Another view is one that restricts MCDA to a strictly mechanistic process which always imposes weights and scores on the criteria (Devlin and Sussex, 2011).

It is important to be clear about the definition of MCDA in this thesis. There are several ways to define MCDA from the literature (Keeney and Raiffa, 1976, Belton and Stewart, 2002, Dodgson et al., 2009, Devlin and Sussex, 2011). In general, the definitions agree on aspects of MCDA such as the involvement of a complex problem, multiple criteria, conflicting criteria, and multiple objectives. The definitions also agree on the process of MCDA that breaks a complex problem into more manageable pieces or criteria to allow data and judgements to be brought to bear on the criteria. However, the definitions differ in terms of whether the data and judgements on the criteria need to be aggregated and how they support the decision-making process. Keeney and Raiffa’s definition (1976) necessitates the aggregation of data and judgements on the criteria into a single expression of value, whereas others allow the use of MCDA to support deliberation without the necessity to aggregate the criteria (Devlin and Sussex, 2011, Thokala et al., 2016). It should be noted that, in contrast to the more unified body of techniques for economic evaluation such as CBA, CEA or CUA, the approaches in MCDA often involve the direct participation of a group of decision makers and stakeholders; the MCDA approaches support the decision makers’ value judgements to let them decide the outcomes of the analysis.

In this thesis, the term MCDA is used to imply a set of methods and techniques to facilitate a structured decision-making process which directly involves the participation of the decision makers and stakeholders: the process explicitly breaks the decision problem into more manageable well-defined criteria to allow data and the decision makers’ judgements to be brought to bear on the criteria, then it presents the results to the decision makers and stakeholders for them to make a decision with or without an explicit aggregation of the data and judgements.

We can see the difference between MCDA as an approach arising from operations research and economic evaluation methods in health care. The objective of economic evaluation concerns the best use of resources. The objective of MCDA, on the other hand, is to help decision makers make a decision. That is why it is all about supporting the decision makers to
identify the criteria, structure the criteria, and assess the criteria. The direct and explicit involvement of a group of specific decision makers is a distinctive feature of MCDA that distinguishes it from CBA/CUA. MCDA is all about facilitating the decision-making process for specific decision makers, whereas CBA/CUA is often considered as evidence which is provided independently to the decision-making process. The set of analytical tools employed in MCDA is very different from those employed in CBA/CUA. More details on different MCDA methods are discussed in the next section.

Incorporating MCDA to CCA, the approach needs to include an explicit participatory decision-making process which requires decision makers and other relevant participants to discuss and address their value judgement for costs and benefits. This is termed CCA-MCDA to distinguish it from the more general definitions of CCA and MCDA separately. In CCA-MCDA, all costs and benefits are computed separately and presented to the decision makers (an individual or a group of individuals); then MCDA methods are applied to help the decision makers compare between the alternatives and make the final decision.

2.4.3 MCDA methods

The full conduct of an MCDA involves a specific group of decision makers and includes eight steps (Dodgson et al., 2009):

- Establish the decision context
- Identify the options to be appraised
- Identify objectives and criteria
- Assessing and valuing the options: this varies between different MCDA approaches. However, for the most commonly used MCDA approach (value measurement model), the sub-steps include:
  - Scoring: assess the expected performance of each option within a criterion and assign the value (score) associated with it.
  - Weighting: assess the relative importance between the criteria and assign the value (weight) associated with it.
- Deriving and assessing the overall value of each option
- Examining and interpreting the results
- Sensitivity analysis
The core components of an MCDA include a group of decision makers (and stakeholders), decision options, a set of decision criteria for the appraisal, a table of information for the performance of the decision options (the performance matrix), facilitated decision-making workshop(s) to elicit the views and values from decision makers, and an analytical framework to assess the mixed data (performance, views, and values).

Different MCDA approaches are distinguished from each other in terms of how they conduct the decision-making workshops and the analytical framework to assess the mixed data. The ISPOR MCDA task force categorised MCDA approaches into two groups: methods based on formal modelling, and methods not based on formal modelling (Thokala et al., 2016).

MCDA methods not based on formal modelling simply present the performance matrix to the decision makers and let them use simple rules to find the best decision option. For example, the decision makers can simply identify the best option as the one which performs at least as well as others on all criteria and strictly better than the others on at least one criterion.

MCDA methods based on formal modelling can be further divided into three categories: value measurement models, outranking methods, and goal programming models (Thokala and Duenas, 2012). Among those models, value measurement models are the most widely used in the public sectors (Dodgson et al., 2009, Thokala et al., 2016). An introduction to these models is provided below.

**Value measurement model MCDA**

The aim of approaches based on value measurement models is to construct a single overall value for each decision option in order to establish a preference order of all decision options (Thokala and Duenas, 2012). The general principle is to develop mathematical equations and operational procedures to calculate a single overall value for each decision option based on its performance on different decision criteria and the decision makers’ judgement.

The most common approach for value measurement models is to assume the function to calculate overall value perceived by decision makers takes the following linear additive form:

**Equation 2.6**

\[ V_i = \sum_{j=1}^{n} W_j S_{ij} = W_1 S_{i1} + W_2 S_{i2} + \cdots + W_n S_{in} \]
Where:

\( V_i \) is the overall value perceived by the decision makers for option i.

\( S_{ij} \) is the preference score regarding the performance level of option i on criterion j.

\( W_j \) is the relative weight of criterion j.

The linear additive form of the overall value requires the assumption for mutual independence of preference between decision criteria/attributes (Keeney and Raiffa, 1976). This means the trade-off (in terms of preferences) between any two criteria/attributes is independent of the values of all the other criteria. For example, there are three criteria A, B, and C. These three criteria are mutually preference-independent if the trade-off between any pair (i.e. 1 unit in A can compensate 3 units in B) is independent of the values of the other criterion (i.e. values in C do not matter). More theoretical details can be found in the book written by Keeney and Raiffa (1976).

The operational procedure includes two stages: scoring and weighting. Scoring is the process to elicit the single-attribute preference scores \( (S_{ij}) \), whereas weighting is the process to elicit the weights \( (W_j) \) of the criteria. Different techniques can be used for the preference elicitation tasks. Two commonly used techniques in applied MCDA include multi-attribute rating technique with swing weighting (SMARTS) and the analytical hierarchy process (AHP).

SMARTS was developed by Ward Edwards (Edwards, 1971). For scoring, the decision makers can rate the preference score for the performance of a decision option regarding a single decision criterion on a standardised preference scale (e.g. between 0 and 100 where 0 is the score for the least preferred performance and 100 is the score for the most preferred performance). For weighting, the decision makers need to compare the full swing of preference in one criterion (e.g. from the worst level to the best level) with the full swing of preference in another criterion. The relative weight between two criteria are then elicited and normalised on a standardised scale. Finally, the weights and scores are used in equation (3) to calculate the overall value of a decision option.

On the other hand, the analytical hierarchy process (AHP) was originally developed by Thomas Saaty (Saaty, 1980). The principal difference of AHP (compared to SMARTS) is that it uses pair-wise comparisons to elicit scores and weights instead of using rating techniques. The decision makers are asked to give their answers to a series of pairwise comparison questions of the following general form: ‘how important is A relative to B?’ The measure for pairwise
comparison has both verbal orders and an equivalent nine-point intensity scale (Table 2.1). The numbers elicited from pairwise comparisons are then entered a comparison matrix which describes all possible pairs of alternatives (see example in Table 2.2). Saaty used matrix algebra to calculate the values of the scores/weights from the pairwise expressions in the matrix. The weights/scores are the elements in the eigenvector associated with the maximum eigenvalue of the matrix (Dodgson et al., 2009) – see example in Table 2.2. Because the calculations could be complex, they are often undertaken by AHP computer packages such as Expert Choice, HIPRE 3+, etc.

Table 2.1: The scale for pairwise comparisons in AHP

<table>
<thead>
<tr>
<th>How important is A relative to B?</th>
<th>Intensity of importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equally important</td>
<td>1</td>
</tr>
<tr>
<td>Moderately more important</td>
<td>3</td>
</tr>
<tr>
<td>Strongly more important</td>
<td>5</td>
</tr>
<tr>
<td>Very strongly more important</td>
<td>7</td>
</tr>
<tr>
<td>Overwhelmingly more important</td>
<td>9</td>
</tr>
</tbody>
</table>

(Source: (Dodgson et al., 2009))

Table 2.2: Example of the comparison matrix and calculation of relative scores/weights

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>scores/weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>¼</td>
<td>4</td>
<td>0.217</td>
</tr>
<tr>
<td>B</td>
<td>3</td>
<td>1</td>
<td>9</td>
<td>0.717</td>
</tr>
<tr>
<td>C</td>
<td>¼</td>
<td>1/9</td>
<td>1</td>
<td>0.066</td>
</tr>
</tbody>
</table>

Despite the attractions of the AHP for its simplicity in implementation (i.e. pairwise comparisons), there are several issues related to the application of the AHP which should be noted:

- The nine-point scale with its verbal descriptions lacks a theoretical foundation. This raises doubts regarding its validity and consistency in measuring preferences (Dodgson et al., 2009).
- Rank reversal phenomenon: introducing a new option can change the relative ranking of some of the original options (Belton and Gear, 1983).
The underlying theoretical model on which the AHP is based is not sufficiently clear or well explained (Dodgson et al., 2009).

Outranking methods

The concept for outranking methods originated from the work of Bernard Roy and colleagues in France in the mid-1960s (Dodgson et al., 2009). The basic principles of outranking methods are as follows:

- Preparing the performance matrix/ consequences table (the same as other MCDA methods)
- Eliciting the weights of the decision criteria in terms of their relative importance.
- Conducting pairwise comparisons for all pairs of decision options across the criteria to identify the dominances (outranking).
- Further fine-tuning procedures to determine a smaller set of dominant options (even down to just one option).

The key point of outranking methods is the procedure to identify the dominances at the level of pairwise comparison between every pair of decision options being considered. The idea is that option A outranks option B (hence A is the dominance) if there is sufficient evidence or arguments to justify that A is at least as good as B, while the evidence or arguments to refute that statement is not good enough.

The fundamental difference of outranking methods compared to value measurement models is that they do not need to assume a function to aggregate preferences such as the one described in Equation 2.6. Outranking methods seek to make fewer assumptions about the nature of the underlying preference model (e.g. mutual preference independence) by introducing more interactive process between the decision makers and the model. Examples of outranking procedures can be seen in the literature for the ELECTRE methods (ELECTRE I, II, III, IV, TRI), the PROMETHEE method, or the GAIA method; they are not discussed in detail here.

Goal programming models

Goal programming is based on the concept of ‘satisficing’ (a combination of satisfy and suffice) (Simon, 1997). The idea is that the decision makers would be satisfied with the options which achieve at least some minimum level of performances (goals); they would not necessarily seek to maximise utility. Thus, the principle of goal programming models is to
attain satisfactory levels of performance; they use linear programming techniques to build the optimisation models (Thokala et al., 2016). The basic steps of goal programming are as follows:

- Preparing the performance matrix
- Setting satisficing/aspiration levels (goals) for the criteria
- Specifying the optimisation model (linear programming model)
- Determining the degree of attainment of the goals for each option: the difference between the option’s performances and the goals are goal deviations.
- Choosing the options to minimise the goal deviations

2.4.4 Theoretical foundation of CCA-MCDA

The normative foundation of CCA-MCDA is more inclined towards the Non-welfarist view. It allows welfare to be judged by criteria other than utilities. In addition, the source of value judgement is not necessarily the affected individuals but it can be a legitimate group of decision makers and stakeholders. In fact, the role of the decision makers is very much emphasised and centralised in CCA-MCDA.

However, for economic evaluation of health care interventions, the identification of legitimate decision makers and stakeholders is not always straightforward. The legitimate decision makers could be any individual or group of individuals who have been authorised or elected by the society through a democratic process to make decisions on behalf of the society. The social decision makers are supposed to perfectly act on behalf of the society. This means they make the decisions according to society’s best interests; their utility function when making social decisions is assumed to be a valid social welfare function. On the other hand, the legitimate decision makers could be argued to be the whole society; the society preferences need to be brought into the social decision. In real practice, a mixture of both is often used in resource allocation decision making in health care. We use social preferences in constructing the values for QALYs however, preferences from specific decision makers (e.g. NICE, DH, patient groups) are often brought in when an intervention concerns end-of-life treatment.

In theory, CCA-MCDA could facilitate a structured decision-making process for the whole society (e.g. through a big online survey). However, it would be impractical to do so for every economic evaluation problem. Indeed, the usual application of MCDA only involves a small
(manageable) group of decision makers and stakeholders. Thus, this raises the question of who should be the legitimate group of decision makers and stakeholders for resource allocation decision making in health care.

2.4.5 Criticisms of CCA-MCDA

The main criticisms of CCA-MCDA concern the direct involvement of the decision makers in a ‘scientific analysis’, the burden it would impose on the decision makers, the potential inconsistency with the decision being made, and whether the analysis can address health opportunity costs of resources.

First, the direct involvement of the decision makers attracts criticisms which question the scientific quality of the technique. Claxton et al. (2005) commented that if there are some social values not captured in current analysis (CUA), we should establish what these social values should be and fully reflect them in subsequent analyses, rather than letting the decision makers to do what they want (Claxton et al., 2005). Outside of the health economics area, researchers in decision science, however, already accept and support the participatory decision-making process where the involvement of the decision makers is made transparent and explicit. The approach which explicitly involves the decision makers in scientific analysis is called Post-Normal Science (PNS) by Funtowicz and Ravetz (1993) to distinguish it from the conventional applied social science.

When the decision problem is not complex (e.g. simple and straightforward) and the decision stake is low, conventional applied science is an appropriate problem-solving strategy to prescribe a rational course of action. However, when the decision problem is more complex (e.g. involving large uncertainty, conflicts of interest, ethical issues) and the decision stake is higher, subjective judgments might be required to adjust the knowledge from applied science to specific contexts; this is called professional consultancy, and in further complex situations, post-normal science (Funtowicz and Ravetz, 1993). The resource allocation situation in health care seems to fall into the areas which require professional consultancy and/or post-normal science.
The second criticism is about the burden the approach would impose on the decision makers. Brazier et al. (2005) raised the concern that the approach would present substantial difficulties to the decision makers in terms of understanding, interpreting and applying their value judgement on the scientific information from the analysis (Brazier et al., 2005). For example, it is not easy for decision makers without some health economics background to understand and interpret the QALY measure correctly, not to mention applying their preferences to make a trade-off between QALYs and other outcomes. Brazier et al. (2005) also cited evidence from the psychological literature suggesting that people struggle to process around seven pieces of information simultaneously. The decision makers would struggle to apply their value judgements when information is presented to them in many disparate types in CCA. This criticism of the technique is reasonable when it is left without MCDA. However, the problem could be overcome in with the help of MCDA techniques.

The third criticism concerns with inconsistency regarding the decision being made. Since the technique allows decision makers’ judgements to affect the decision outcomes directly, it can be argued that it also allows the decision being made to be inconsistent when changing the decision-making board (i.e. replacing a member).

Finally, it could be argued that CCA-MCDA can only rank the options/interventions within a specific decision problem. It cannot make a statement about the cost-effectiveness of the best option. CCA-MCDA deals with each decision problem in separation from the broader system. The criteria and the decision-making board could be considered specific for each decision problem therefore, the result can only be a ranking of the options within that decision problem. CCA-MCDA cannot generalise the result of one decision problem to the broader system of other interventions and disease areas.

2.5 Conclusion

This chapter reviewed and discussed different techniques for economic evaluation in health care. CBA with monetary measures of benefit has a long record of practice in areas outside health such as transport and environment however, many health economists oppose the use of monetary measures of benefit in economic evaluation of healthcare interventions (Brazier et al., 2017, Brooks, 1995, Culyer, 1991, Feeny and Torrance, 1989). The alternative approaches, which use non-monetary measures of benefit, include CUA/CEA and CCA-MCDA.
CUA (cost-per-QALY analysis) has been the dominant technique for economic evaluation in health care. The QALY model has been proven to be useful and flexible as a composite measure of health benefits for use in economic evaluation; it continues to be the preferred measure for economic evaluation of health care interventions (Drummond et al., 2015, Neumann et al., 2017, Brazier et al., 2017). However, the current application of cost-per-QALY analysis that focuses on health measured in terms of QALYs to the exclusion of other non-health benefits of health care is not justified. Evidence suggests the existence of other social values which are not captured in the QALY. If the society values these non-health effects of health care interventions, research needs to look at how the cost-per-QALY analysis can capture them.

CCA-MCDA is relatively new to the field of health economics. The loose definition of CCA (without MCDA) is limited because it leaves the decision-making process undefined. When defined in a combination with MCDA, CCA-MCDA emphasises and centralises the role of the decision makers in the economic evaluation analysis; it uses MCDA methods to help the decision makers structure and quantify their preferences.

To conclude, the QALY model remains the main component of economic evaluations whether from the healthcare sector perspective or the societal perspective. Regarding the implementation of the societal perspective in economic evaluation, two potential approaches appear to be worth further investigation: one is to extend the conventional cost-per-QALY analysis and the other is to explore the use of MCDA in a societal-perspective economic evaluation.
CHAPTER 3. A SOCIETAL PERSPECTIVE IN ECONOMIC EVALUATION

This chapter starts by reviewing the arguments for and against a societal perspective in economic evaluation. The societal perspective was argued to be more favourable in theory but it encountered substantial challenges in implementation. The challenges in implementing a societal perspective are also discussed in this Chapter (the reasons why a societal perspective is not adopted despite its advantages). This is followed by the proposal of two approaches for implementing a broader societal perspective: the extended cost-per-QALY, and the CCA-MCDA. The chapter concludes by emphasising the need to investigate further into the methods for implementing a broader perspective in economic evaluation.
3.1 Arguments for and against a societal perspective

3.1.1 Arguments for a restricted perspective

(1) The chosen perspective should fit the need of the target audience

A common reason for choosing a restricted perspective is that the chosen perspective should fit the need of the target audience of the analysis (Claxton et al., 2010). When the target audience of the analysis is the decision makers in health care who are responsible for allocating their constrained budget to maximise health gain, the analysis’s scope should focus on an efficient use of available health care resources.

For example, CUA is carried out because payers want to know which intervention among the alternatives will be the best to produce the greatest health outcome at the least cost because they face a budget constraint. Therefore, it is reasonable to limit the economic analysis to costs and consequences that are within their remit and that matter to their budget. Payers do not want to include factors that they do not have a control over. This can be compared to the situation where individuals consider buying a healthcare intervention for themselves. They would only consider costs of the health care intervention that have a direct impact on their budget and benefits that matter to them. They would not consider costs that fall on others such as someone else might have to drive them to the clinic and they would not consider some spill-over health benefits/dis-benefits that fall on others.

(2) The objective of the health care sector is to maximise the population health using its allocated budget (available resources).

In England and Wales, NICE is legally obliged to conform to its Establishment Order to adopt a restricted perspective for economic evaluation of health care intervention. It includes only costs that fall on the NHS or PSS while health outcomes are measured and valued in terms of QALYs. NICE reasoned its perspective as consistent with the objective of the health service sector to maximise health gain from available health care resources. The health service sector receives a fixed budget from the government for the NHS and PSS resources. As an agent of the society, the health service sector needs to justify how it would spend its fixed allocated budget to ensure an efficient use of available resources (to maximise the population health gain). To do so, NICE argues that an investment should be judged based on its impact only on the health service budget with an aim to maximise population health gain in terms of QALYs.
Adopting a restricted perspective is a pragmatist view.

Devlin and colleagues commented on a restricted perspective for NICE stating that: “a wider perspective on costs would require NICE to extend its remit to optimising resource use in the public sector generally, not just health care, and indeed in the economy as a whole... Decisions made from this broader perspective might maximise society’s welfare but would not maximise health gain from the NHS budget.” (Devlin et al., 2003)

Claxton et al. (2010) pointed out a practical problem with adopting a broader societal perspective for NICE. It was not clear how a broader societal perspective could be implemented while the fixed healthcare budget was set by the government and transfers between sectors were not possible. There are many conceptual and methodological issues around the measurement, valuation, and aggregation of the wider effects in a societal perspective for economic evaluation. Moreover, implementing a societal perspective requires additional information, time, and resources compared to a more restricted perspective. This means additional administrative costs to the system and raises the question whether it is worth doing a societal perspective while a restricted perspective might just do the job.

The results from a restricted perspective and a societal perspective for economic evaluation could be identical in many cases (Claxton et al., 2010). For example, if improvement in health is strongly associated with improvement in overall welfare, interventions which are already regarded as cost-effective from a health service perspective would also be more likely to offer a positive net welfare benefit under a societal perspective. Hence, appropriate decisions can be made based on a health service perspective and a broader societal perspective seems unnecessary.

3.1.2 Arguments for a societal perspective

(1) A restricted perspective would miss important social values in resource allocation decision making, therefore, lead to sub-optimal decisions or even wrong decisions.

In decision making, one always needs to check whether one has not considered some crucial factors. Completely failing to account for an important factor that has a significant impact on the decision result would lead to sub-optimal or even wrong decisions being made. For example, imagine a decision maker is choosing between two alternative interventions for his
population. Intervention A has a budget cost of £10,000 to provide an additional QALY but requires a substantial amount of patients’ time and informal caregivers’ time. Intervention B that has a budget cost of £11,000 to provide an additional QALY and does not require patients’ time and informal caregivers’ time. According to the health service perspective, intervention A is adopted. However, after one year, the decision maker collects the real data and realises that many people have not received the intended treatment because of the time requirement. In addition, for those who have received the treatment, a significant amount of productivity loss is reported due to their absence from work. The actual QALY gain for the population is only 0.5 QALYs. Thus, the decision that was made based on a health service perspective is sub-optimal. Indeed empirical evidence has shown that dementia, multiple sclerosis and rheumatoid arthritis are examples of disease areas where significant benefits of interventions are in terms of improvements in productivity and reductions in informal care time (Jonsson, 2009).

Another example, NICE’s decisions only consider the QALY production process within the boundary of the health and social care system (NHS and PSS) by restricting the costs to only those that fall on the NHS or PSS. However, producing health is a process that involves the wider society. For example, besides formal care, patients also receive informal care which is provided by their family and friends. If NICE only focuses on the government health and social care system, other inputs to produce health such as informal/unpaid labours (e.g. informal carers) or private capitals (e.g. co-payment by patients and families) will be actively ignored. If these ignored inputs contribute significantly to the production of QALYs as in some cases such as Alzheimer’s disease, the exclusion of them will not guarantee the validity of the results. For example, the costs of informal care and co-payment are not included in the analysis but the total number of QALYs is still counted for the NHS/PSS even though some of them should be credited to informal care and private co-payment.

Furthermore, the measurement of outcome in a restricted perspective will miss other important social values because health intervention can have substantial non-health effects on a society. There is value in the process of care, for example, other things being equal, people may prefer less invasive, painful, and more convenient services. There is also evidence of other values beyond health from health care such as consumption benefits (e.g. information from screening processes) and more general benefits, such as option value and externalities (Wailoo, 2002). Coast criticised a health care budget cost-per-QALY approach on the basis that maximising health output would not be the only objective that our society or authorised decision makers
would wish to allocate scarce healthcare resources (Coast, 2004). There is empirical evidence showing cost-per-QALY results are a good predictor of decision for HTA. However, this only confirms the predominance of the cost-per-QALY approach as a standard in the current decision-making process but does not address the relevance of the decision; for example, the extent to which they align with society’s preferences.

It was argued that a health service perspective is likely to be sufficient in many cases for NICE assuming an association between health benefit and wider welfare benefit (Claxton et al., 2010). In exceptional circumstances (identified by and referred to by the Department of Health) where this assumption does not hold, it is suggested that a deliberative approach might be adopted by NICE to handle the impacts of wider benefits in the analysis (NICE, 2013a). However, this might not be a rigorous solution for wider effects in economic evaluation because the decision-making process may not be transparent and consistent. If the existence of wider effects in economic evaluation in health care has been recognised and their importance has been admitted, attempts should be made to change the decision-making approach and broaden the restricted perspective.

(2) Wider costs should be included to give a more meaningful interpretation for QALYs.

The quality adjustment component in QALYs is supposed to be health related only, however preference-based measures such as the EQ-5D also include a dimension for usual activities that describes whether people have some problems doing their usual activities such as work, study, housework, family, or leisure activities. It could be argued that wider costs such as productivity have already been captured in QALYs. Thus, a restricted perspective is not consistent between the numerator (costs) and denominator (QALYs). For this reason, to make the assessment more transparent and consistent, wider costs should be explicitly recognised and included in the analysis under a societal perspective.

(3) A societal perspective is fairer and more acceptable.

A societal perspective represents the interest and viewpoint of the public but not any particular group. Therefore, it is fairer and more acceptable for social decision making.

‘Some people would not get everything they want. But neither would anyone categorically be excluded’. (Gold et al., 1996)
While a restricted perspective is more likely to lead to suboptimal allocation decisions due to failing to capture important social values, a societal perspective that explicitly prescribes all important social values to be included is more likely to produce optimal social decisions. A societal perspective implies the scarcity of all social resources among which health care resource is a part. It does not ignore many other values that are important for other sectors such as education, transportation, or criminal justice. It also does not make health to be of such dominance that its interventions always displace interventions in other sectors. A societal perspective is ‘the only perspective that never counts as a gain for what is really someone else’s loss’ (Gold et al., 1996, p.7). Adopting a societal perspective is a standard approach for assessing interventions in other public sectors such as environment and transportation, so it seems odd for economic evaluations of interventions in the healthcare sector to deviate from this standard (Jonsson, 2009). Morris et al. (2007, p.306) emphasised:

“An important advantage of the societal perspective on costs in CEA is that it avoids the possibility of identifying as cost-effective options that appear so merely because they shift costs between sectors or groups.” (Morris et al., 2007)

(5) A societal perspective promotes comparability among studies

To help resource allocation decisions in general, CEA studies needs to be carried out in a way to produce comparable results among them. It is argued that a common perspective is the foundation for comparability among studies (Gold et al., 1996). While it is difficult to consistently define a restricted perspective, a societal perspective often has mutual understandings across many situations. Hence, a societal perspective is recommended as the appropriate perspective for the reference case to promote comparability among economic evaluation studies (Gold et al., 1996). Improving comparability of studies through the adoption of a societal perspective can also facilitate international collaboration in assessing medical interventions (Jonsson, 2009)

(6) A societal perspective can be a benchmark to assess results from other perspectives

A restricted perspective can be useful to address and investigate the interest of a specific group of stakeholders. They can be the payers who actually have the power to make a decision to allocate their budget to alternative interventions and after all, it is them who will make the
decision in many cases, not the public. Nevertheless, ‘there is value in beginning with a perspective that includes all costs and effects because it provides background against which to assess results from other perspectives’ (Gold et al., 1996, p.7). Indeed, the decision-making process would be more transparent and comprehensive if a restricted perspective is related or compared to a societal perspective. A reference to a societal perspective would also be beneficial for the decision makers when they want to explain and communicate their spending decisions to the public. It provides the authorised decision makers a valid rationale to justify their public spending.

(7) A societal perspective would support the consistency, validity, and interpretation of economic evaluation results.

Under a societal perspective, health-related QALYs can be interpreted in a meaningful way beside other social values. As discussed above, the quality of life component in QALYs can include different things from health to broader wellbeing. It is not easy to have a clear definition of the health that should be captured in health-related QALYs while excluding non-health factors. Therefore, a restricted perspective would not be applied consistently for both costs and benefits in CEA but a societal perspective would make sure the interpretation of benefits and costs is consistent and meaningful in CEA. Since transparency and consistency of CEA are improved with a societal perspective, it also increases the validity of its results.

(8) A societal perspective can improve democracy and engage public discussion and scrutiny in social decision making.

Because economic evaluation taking a societal perspective accounts for everyone who is under the impact of the intervention, it would have the interest of many different groups of individuals from the public. People are interested in getting involved in and discussing decisions that would directly impact on their lives. Analyses taking a societal perspective would provide a common ground for discussion between the health care authorities and the public as well as among the public themselves. Since the perspective is the viewpoint of the public, it enables them to scrutinise the decision-making process as well. Therefore, a societal perspective has the potential to involve the public in the decision-making process and promote democracy.
An approach that is more likely to produce the right result is better

Although a restricted perspective for economic evaluation in health care can still work in many situations (e.g. NICE in the UK), it should be noted that CEA is not the only criterion for resource allocation decision making in health care. Indeed, jurisdictions such as NICE have to carefully consider other evidence such as clinical effectiveness before they can recommend a specific intervention. There are also special cases where a deliberative approach is required to judge the appropriateness of economic evaluation results. In addition, it is difficult or almost impossible to prove that decisions based on such economic evaluation results such as NICE’s decisions are wrong because of the uncertainty in the analysis and in the cost effectiveness threshold. CEA can only provide a basis for decision making in resource allocation but it cannot prescribe a definite answer for the decision problem. There is no guarantee that interventions that have been approved by NICE are cost effective. Even if an intervention that has been approved by NICE is not cost effective, there is no motivation for performing research to check and confirm this hypothesis, whereas there is more incentive for companies to appeal NICE’s decision when it does not approve an intervention. There is a chance that the system is still working well with many interventions that are not cost-effective. Hence, it is argued that we should rather work with an approach that is more likely to produce right results than stay with the comfort of a restricted perspective.

3.1.3 Conclusion

Arguments for and against a societal perspective have been reviewed and discussed. The arguments for taking the societal perspective are strong however, there are substantial challenges that make the implementation of the societal perspective difficult.

3.2 Challenges with a societal perspective

3.2.1 The specification of a social welfare function

When a societal perspective is concerned, the list of possible costs and benefits becomes much broader. In addition to healthcare costs, wider costs can include costs falling on other government sectors (e.g. social care, fire rescue, police, education), productivity costs, informal care time, patient time to receive care, costs of private consumption (e.g. food, clothing, travelling). In addition to health, wider benefits can include sector-specific outcomes (e.g.
educational outcomes, environmental outcomes), non-health generic outcomes such as other aspects of well-being (e.g. satisfaction, friendship, empowerment), process utility, altruistic utility, and the value of knowing (e.g. diagnostic interventions). Furthermore, equity also needs to be addressed in the societal perspective: society might want to give preference to an allocation of resources that increases fairness.

Given this list of many possible costs and benefits, the question is whether it is possible to specify such a social welfare function which would describe all implied social arguments and their trade-offs. Claxton et al. (2010) discussed two approaches: a formal prescription of the social welfare function, and a deliberative approach.

**A formal prescription of the social welfare**

A formal prescription of social welfare is often seen in the application of the traditional Welfarist CBA (see 2.1). Claxton et al. (2010) contemplates that for economic analysis in health care, the full formalisation of the social welfare function is very difficult because it poses fundamental questions about social value. This requires a comprehensive review of all social choice and public policy (not just health) to identify a social welfare function which captures all social arguments and their interactions, and to carry some broad consensus and social legitimacy (Claxton et al., 2010). The task is extremely arduous.

Even if we could find an acceptable welfare function, other fundamental problems still remain (Claxton et al., 2010). Detailed description of these problems is presented in Claxton et al. (2010). Among them, important challenges include:

- Different social arguments are often not separable in production although they can be separable in social preferences. For example, there can be important interaction in the production of health and education which makes trading off between health and education not simple.
- We cannot ignore budget constraints imposed on each sector. Therefore, opportunity costs must always be fully accounted for.

**A deliberative approach**

Alternatively, we can limit the role for economic analysis to only inform social decisions in health, rather than to prescribe them. Economic analysis just provides a useful starting point
for deliberation, rather than making claims about social welfare. This position is often seen in the application of CEA/CUA in health technology appraisal. A health authority such as NICE in the UK can be regarded as the agent of a socially legitimate higher authority (e.g. the government). The agent is given a fixed budget by the government and tasked with a set of specific objectives (e.g. maximising health given the fixed budget). The government allocation of resources (budget) between different sectors such as health and education is a partial expression of an unknown underlying welfare function. Assuming this process is socially legitimate, the role of economic analysis then simply concerns the best use of the allocated healthcare budget given the objectives.

If the objective is only to maximise health given the allocated healthcare budget, there are two scenarios. First, if all costs fall on the healthcare budget, the healthcare perspective is the same as the societal perspective. Second, if there are wider costs falling on other sectors, the healthcare perspective becomes inadequate because it ignores opportunity costs in other sectors. In this case, we need to identify where the opportunity costs fall on other sectors and value them appropriately (Claxton et al., 2010).

If there are multiple objectives such as maximising health and increasing fairness in health, the analysis becomes more complicated. The healthcare perspective cannot be applied because of its limited scope. To implement a societal perspective, we need to find out the trade-offs between the objectives and how they can be reflected in opportunity costs. One issue is deciding whose preferences should be counted when making the trade-offs and how. A mixture of public preferences and individual preferences has been used in the current practice. Preferences of the public have been used in the aggregation of various aspects of HRQOL to calculate QALYs in the cost-per-QALY analysis (e.g. the EQ-5D tariff for the UK). On the other hand, NICE has been using preferences from a specific group including decision makers, clinicians, and patients when end-of-life conditions are concerned. While the public preferences used in the QALY measure is formally modelled and explicitly included, the use of other individual preferences is relatively informal and implicit.

3.2.2 Additional informational requirements from the societal perspective

NICE appraisal requires the incremental health benefits to be measured in QALYs and the incremental costs to be measured in £ for costs falling on the NHS and Personal Social Services
Implementing a societal perspective raises several empirical questions and requires additional information.

First, wider costs and benefits need to be measured and valued appropriately. Examples of the wider costs include informal care time, patient time, private payment for care, and productivity costs. The measurement and valuation of private payment for care are straightforward (e.g., monetary payment). The measurement and valuation of informal care are more complicated but their methods have been developed. Details of this development are reported in a review conducted by van den Berg et al. (2004). The authors conclude that informal care should be included in economic evaluation from a societal perspective and provide guidance on appropriate methods to do so (van den Berg et al., 2004). However, the measurement and valuation of the other wider costs are not clear. For example, health economists still debate between two different approaches for measuring and valuing productivity costs: the human capital approach (Weisbrod, 1961) and the friction cost method (Koopmanschap and van Ineveld, 1992, Koopmanschap et al., 1995). Despite a significant amount of empirical research for measuring and valuing productivity costs, consensus has not been reached on whether and how productivity costs should be included in economic evaluations (Krol et al., 2013).

The identification, measurement, and valuation of wider benefits are more challenging. Little is known about important non-health (not captured in the QALY measure) outcomes of healthcare interventions. For example, impacts of dementia on other sectors such as police or fire rescue are well recognised but we do not know how they can be measured and valued for use in economic evaluation. Research is still on-going looking at the methods to measure and value other beyond-health aspects of well-being, process utility, altruistic utility, and the value of knowing. Furthermore, equity consideration emphasises the importance of equitable distribution of health care resources in addition to efficiency. Although equity has received substantial discussion in the health economics literature, its definition, measurement, valuation, and inclusion in economic evaluation are still matters of debate (Culyer and Wagstaff, 1993, Williams, 1997, Nord et al., 1999, Wagstaff and van Doorslaer, 2000, Drummond et al., 2007, NICE, 2012a, Linley and Hughes, 2013, Miners et al., 2013a, Asaria et al., 2013).

Second, a societal perspective needs to consider opportunity costs of costs falling on different budget constraints in different sectors. It is likely that costs falling on non-health budgets would have different opportunity costs compared to those falling on the healthcare budget. In other words, there are sector-specific cost-effectiveness thresholds and that need to be accounted for.
in the societal perspective. Much discussion and research have looked at the threshold for the healthcare budget, however little is known about the opportunity costs of costs falling on the budget constraints of other sectors. Even the threshold in the healthcare sector is still a matter of debate. NICE has been using a threshold range between £20,000 and £30,000 per QALY. However, this range is arbitrary and not evidence-based. Recent research to empirically estimate the healthcare threshold tends to support a lower threshold range (e.g. £13000 per QALY).

3.2.3 Discussion and conclusion

Implementing a societal perspective is challenging and requires substantially more information than the current practice that takes a narrower healthcare perspective. Nevertheless, policy makers are more aware of wider costs of health care such as informal care. They have an increasing interest in broadening the measure of health outcome that can be used across sectors. The field of health economics has advanced remarkably in measuring and valuing these impacts of health care interventions. Thus, it is imperative to investigate methodological approaches to implement a societal perspective. From the review of economic evaluation techniques in Chapter 2, there are three possible approaches that can be used to implement a societal perspective: the CBA approach, the extended CUA or extended cost-per-QALY analysis, and the CCA-MCDA.

The CBA approach is a natural candidate for a societal perspective (Donaldson et al., 2002, Birch and Donaldson, 2003, Currie et al., 1999). In fact, the societal perspective is considered the correct perspective for CBA. A CBA requires all costs and benefits of interventions to be included in the analysis regardless of where or on whom they fall (Boardman et al., 2010). The CBA approach supports a Welfarist view and relies heavily on Willingness-To-Pay and Willingness-To-Accept exercises. On the other hand, the extended cost-per-QALY approach retains the central role of the QALY measure. To accommodate a societal perspective, the extended cost-per-QALY approach would find ways to measure and exchange wider impacts to QALYs equivalence. The CCA-MCDA approach is relatively new to the field of health economics. It has the flexibility of a CCA that can accommodate the inclusion of any costs and consequences in the analysis. However, it does not stop at presenting the results in disaggregated format to decision makers. It uses MCDA techniques to help decision makers quantify their judgement and come to a decision. The CCA-MCDA approach is a good
candidate for implementing a societal perspective due to its flexibility. Due to time and resource constraints, only two approaches were chosen for further investigation: the extended cost-per-QALY and the CCA-MCDA. The next section will discuss this in more details.

3.3 Extending the cost-per-QALY analysis

3.3.1 Healthcare-perspective cost-per-QALY analysis

Taking the healthcare perspective, costs only include those falling on the healthcare budget; benefits are measured in terms of patient QALYs gained. Maximising patient QALYs gained is the objective. The healthcare budget faces an exogenous constraint. The healthcare cost-effectiveness threshold \((k_h)\) is the reciprocal of the shadow price of the budget constraint. The threshold describes the amount of patient QALYs that would be forgone given an incremental amount of costs imposed on the budget. The incremental patient QALYs gained from the new intervention is denoted \(\Delta Q_p\). The patient QALYs that would be forgone due to the incremental costs are calculated as follows.

Equation 3.1

\[
\Delta Q_{\text{forgone healthcare cost}} = \frac{\Delta C_h}{k_h}
\]

The net QALYs gained from the new intervention can be calculated and the decision rule is to approve the intervention if the net QALYs gained is positive.

Equation 3.2

\[
\Delta Q_{\text{net}} = \Delta Q_{\text{gained patient}} - \Delta Q_{\text{forgone patient}} = \Delta Q_{\text{gained patient}} - \frac{\Delta C_h}{k_h} > 0
\]

Equation 3.3

\[
ICER = \frac{\Delta C_h}{\Delta Q_{\text{gained patient}}} < k_h
\]
3.3.2 Societal-perspective cost-per-QALY analysis

Taking a societal perspective, Claxton et al. presented a general case where a health care intervention generated costs to both the health sector ($\Delta C_h$) and the wider non-health economy ($\Delta C_c$); the benefit of the intervention is improvement in health ($\Delta Q$). When the cost to the wider non-health economy is included, the decision can be described as ‘a comparison of the net health gained in the health sector with the health equivalent of the net consumption costs falling on the wider economy’ (Claxton et al., 2010). This is illustrated in the equation below.

Equation 3.4

$$\Delta Q_{\text{net}}^\text{net} = \left[\Delta Q_{\text{patient}}^{\text{gained}} - \frac{\Delta C_h}{k_h}\right] - \frac{\Delta C_c}{\nu} > 0$$

Where ‘$\nu$’ is the social consumption value of health which represents the amount of consumption that is equivalent to one unit of health. The authors noted that ‘Health must inevitably be traded-off against other aspects of social value, most notably consumption, by social decision makers: whether this is done implicitly by a higher authority setting the budget constraints or more explicitly using some specified social welfare function. This trade-off becomes particularly apparent once effects outside the health sector are acknowledged.’ (Claxton et al., 2010)

The following assumptions need to hold, quoted below from (Claxton et al., 2010):

1. If transfers between sectors are not possible, then $\Delta C_h$ must be marginal with respect to the health budget, i.e. incurring these costs will not change the cost-effectiveness threshold.
2. $\Delta C_c$ must be marginal with respect to total consumption in the wider economy so that incurring $\Delta C_c$ will not change $\nu$.
3. The value of $\nu$ must be a complete and socially legitimate value of health – this assumption requires that health and consumption are the only arguments of social value, or that they are separable from all other potential arguments in some more complex and complete welfare function.

This general framework is a good start to look at the implementation of a societal perspective using cost-per-QALY analysis. To develop further, it is argued that costs falling on government
non-health sectors need to be included and distinguished from the costs falling on patients and their families. Since other government sectors face their own budget constraints, there could be different sector-specific thresholds. One example is the existence of costs falling on the government social care sector. The social care activities are different from the health care activities and the social care budget is different from the healthcare budget. Health care activities focus on restoring functioning lost due to diseases, whereas social care activities focus on compensating functioning and maintaining independence. In England, health care costs are mostly covered by the National Health Services (NHS), whereas social care costs are shared between patients and the government. Thus, these two budget constraints are different and we need to recognise their differences in a societal perspective.

This thesis proposes some improvements for a societal-perspective cost-per-QALY analysis. Three general groups of costs are distinguished: health care costs ($\Delta C_h$), costs falling on other government non-health sectors ($\Delta C_{gov}^i$), and costs falling on patients and their families ($\Delta C_c$). Benefits are measured in QALYs and we need to allow for possible weighting between different types of QALYs. This proposal for a generic approach to implement a societal-perspective cost-per-QALY analysis is illustrated in the following equations.

**Equation 3.5**

\[
\Delta Q_{net} = \Delta Q_{gained} - \Delta Q_{forgone} = \sum_{i=1}^{n} \Delta Q_{i}^{gained} - \sum_{j=1}^{m} \Delta Q_{j}^{forgone}
\]

\[
= \sum_{i=1}^{n} \Delta Q_{i}^{gained} - \left[ \frac{\Delta C_h}{h} + \sum_{j=1}^{m} \frac{\Delta C_i}{k_i} + \frac{\Delta C_c}{v} \right] > 0
\]

**Equation 3.5** can be transformed:

**Equation 3.6**

\[
\Delta Q_{net} = \sum_{i=1}^{n} \frac{\Delta Q_{i}^{gained}}{k_h} - \left[ \frac{\Delta C_h}{h} + \sum_{i=1}^{m} \frac{k_h * \Delta C_i}{k_i} + \frac{k_h * \Delta C_c}{v} \right] > 0
\]
Comparing Equation 3.6 of a societal-perspective with Equation 3.2 of a healthcare-perspective, we can see that the inclusion of wider costs could be implemented by weighting and aggregating them with the health care cost:

Equation 3.7

\[
\Delta C_{\text{total aggregated}} = \Delta C_h + \sum_{i=1}^{m} \frac{k_h}{k_i} \Delta C_i + \frac{k_h}{v} \Delta C_c
\]

Looking at Equation 3.7, the relative weight of a specific wider cost (compared to health care cost) is reflected by the comparison between the healthcare threshold and the sector-specific threshold for the sector of the wider cost. In the case of costs falling on patients and their family, the relative weight is the comparison between the healthcare threshold and the consumption value of health (v). When wider costs are weighted and aggregated with healthcare cost in this way, the rest of the implementation of the societal-perspective cost-per-QALY analysis looks like the healthcare-perspective cost-per-QALY analysis.

Equation 3.8

\[
\Delta Q_{\text{net}} = \sum_{i=1}^{n} \Delta Q_{i}^{\text{gained}} - \frac{\Delta C_{\text{total aggregated}}}{k_h} > 0
\]

Equation 3.9

\[
ICE_R = \frac{\Delta C_{\text{total aggregated}}}{\sum_{i=1}^{n} \Delta Q_{i}^{\text{gained}}} < k_h
\]

3.4 CCA-MCDA

3.4.1 Application of MCDA in economic evaluation

MCDA methods have been widely used to support the decision-making process in many areas including healthcare (Wallenius et al., 2008, Adunlin et al., 2015, Thokala et al., 2016).
Nevertheless, the application of MCDA in economic evaluation of health care interventions is still unclear (Devlin and Sussex, 2011, Drummond et al., 2015).

Regarding the application of MCDA in the UK, Dodgson et al. (2009) provided a comprehensive review of MCDA approaches and methods for the Department for the Environment, Transport, and the Regions. The document is the principal central government guidance on the application of MCDA techniques. In the report, the authors presented three case studies for the application of MCDA in economic evaluation. The first is an evaluation of overseas trade services. The second is an evaluation of potential UK sites that could be suitable as radioactive waste repositories. The third is an evaluation of social care options for the management of social care budgets by local authorities. All of them followed the full conduct of value measurement model MCDA (see Chapter 2, section 2.4.3). The main components of the MCDA in the first case study are discussed below. The other case studies are similar in their nature regarding the methods to apply MCDA in economic evaluation.

**Case study: evaluation of overseas trade services:**

The evaluation concerned services offered by Overseas Trade Services. Four one-day working meetings attended by decision makers and other key players were organised over several months in 1995 to implement an MCDA to determine the impact and relative cost-effectiveness of the services.

The objectives and criteria were identified and organised in a hierarchical diagram (a value tree). Figure 3.1 reproduces the value tree reported for the case study from Dodgson et al. (2009).
Figure 3.1: Example of hierarchical presentation of objectives and criteria

The overall value of a decision option (left side of the diagram) is a combined assessment of benefits and costs. Within the benefit criterion, there are multiple sub-criteria such as export outputs, market knowledge, etc. Within each sub-criterion, there are bottom-level criteria (right side of the diagram) which could be measured. Similarly, for the cost criterion, there are sub-criteria and bottom-level criteria.

Data were collected for the performance of each decision option on each bottom-level criterion (measurable criteria). The performance data for each bottom-level criterion were then scored by the decision makers and stakeholders on a preference scale between 0 and 100 where 0 is

(Source: Dodgson et al., 2009)
the score for the worst performance level (among the evaluation options) and 100 is the score for the best performance level (among the evaluation options). Dodgson et al. (2009) did not present the full data in the case study but only a subset of the criteria and decision options for demonstrative purposes. This example of performance data and their scores is presented in Table 3.1 below.
Table 3.1: Example of data in a performance matrix

<table>
<thead>
<tr>
<th></th>
<th>COSTS</th>
<th>BENEFITS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monetary costs</td>
<td>Awareness</td>
</tr>
<tr>
<td></td>
<td>Non-monetary costs</td>
<td>% of firms aware of the service</td>
</tr>
<tr>
<td>Programme Costs</td>
<td>Number of changes to services</td>
<td>Perform (1)</td>
</tr>
<tr>
<td>AAGs</td>
<td>1.70</td>
<td>25.0</td>
</tr>
<tr>
<td>EP</td>
<td>3.40</td>
<td>40.0</td>
</tr>
<tr>
<td>DT</td>
<td>0.00</td>
<td>5.0</td>
</tr>
<tr>
<td>MIE</td>
<td>0.05</td>
<td>26.0</td>
</tr>
<tr>
<td>EIS</td>
<td>1.00</td>
<td>45.0</td>
</tr>
<tr>
<td>OM</td>
<td>1.60</td>
<td>43.0</td>
</tr>
<tr>
<td>TF</td>
<td>24.20</td>
<td>48.0</td>
</tr>
</tbody>
</table>
(1) The direct yearly costs of the services net income per programme, expressed in millions of pounds sterling.

(2) The average number of times annually that the service delivery arrangements were changed significantly.

(3) The percentage of those businesses surveyed who reported they were aware of the service.

(4) The average rating awarded by companies surveyed for the importance of the service in assisting their market entry into foreign countries.

(5) The extent to which the service improves the image of UK companies and products abroad. No quantitative data were available for this criterion. The MCDA team had to ask embassies and export promoters for their views of the relative merits of the services on this criterion. The decision makers then directly judged the scores based on the elicited views.

(6) Some measure of the UK added value of contracts was required. However, no direct measures were available. Instead, the performance was calculated by multiplying the number of commissions by the following factors:

- The percentage of those businesses who won contracts following the use of an OTS service and who said that the service played some part in the winning of those contracts,
  and
- The average value of the contracts per successful survey respondent set out under the 'number of contracts' criterion.

At this stage, a unit of preference on one scale is not the same as a unit of preference on any other scale. ‘Swing weighting’ (see Chapter 2, section 2.4.3) was performed to elicit the relative weights of the preference scales of different bottom-level criteria. In this case study, the swing weighting of bottom-level criteria was performed separately for COST criteria and BENEFIT criteria. There were 20 bottom-level criteria within BENEFITS. The weight for a criterion in comparison to other criteria was elicited by asking the decision makers to consider at the same time two aspects of the preference scale of that criterion: how different are the most and least preferred options (100 score and 0 score), and how important is that difference on this scale as compared to another one for another criterion. For example, within the BENEFIT objective, the decision makers judged the most important bottom-level criterion was ‘Number of new exporters’ accounting for both the swing of its scale and how important it is compared to other scales. This criterion was assigned a weight of 100 and became the standard against which
other criteria were judged. If a swing in preference on another criterion was judged half that of the standard, it was assigned a weight of 50. Table 3.2 illustrates the results of this example about swing weighting in the case study.

Table 3.2: Example of swing weighting results

<table>
<thead>
<tr>
<th>Sub-criteria</th>
<th>Bottom-level criteria</th>
<th>Relative Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Export Outputs</td>
<td>Number of new exporters</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Value of export contracts</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Number of export contracts</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>% of firms winning export contracts</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>Number of agents appointed</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>% of firms appointing agents</td>
<td>32</td>
</tr>
</tbody>
</table>

Source: Dodgson et al., 2009 – example results for the six bottom-level criteria under the Export Outputs sub-criteria.

The seven bottom-level criteria within the COST objective were weighted in a similar manner. Consistency checks were performed regularly during the weighting process. Any anomalies or inconsistencies which arose were addressed and the decision makers revised their values until they felt that the weights accurately reflected their views.

At the highest level concerning the trade-off between COST and BENEFIT, the decision makers were asked to consider how different the services were, overall, on costs and benefits. The decision makers were then asked to state the weight for costs and benefits in terms of how important it is regarding the evaluation of the services. Dodgson et al. (2009) said that ‘the group felt that the Export Benefits were about twice as important as the Costs, so weights of 100 and 50 were assigned at this level’.

To calculate the overall value of an option, the preference scores for different attributes of costs were aggregated. The aggregated score of costs is the weighted average of its bottom-level attributes (7 attributes). Similarly, the aggregated score of benefits is the weighted average of its bottom-level attributes (20 attributes). Then, the weighted score for costs was aggregated
with the weighted score for benefits to derive the overall value of an option. Table 3.3 illustrates the example results.

Table 3.3: Example of final results

<table>
<thead>
<tr>
<th></th>
<th>Options (Services)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>AAGs</td>
<td>EP</td>
<td>DT</td>
<td>MIE</td>
<td>EIS</td>
<td>OM</td>
</tr>
<tr>
<td>COSTS</td>
<td>0.33</td>
<td>93</td>
<td>85</td>
<td>100</td>
<td>70</td>
<td>87</td>
</tr>
<tr>
<td>BENEFITS</td>
<td>0.67</td>
<td>28</td>
<td>54</td>
<td>36</td>
<td>50</td>
<td>36</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1</td>
<td>50</td>
<td>65</td>
<td>57</td>
<td>57</td>
<td>53</td>
</tr>
</tbody>
</table>

The interpretation of the results is as follows. For costs, higher preference scores mean lower costs. The option with highest costs is TF (aggregated score 22) and the option with the lowest costs is DT (aggregated score 100). For benefits, higher preference scores mean more benefits. With the aggregated score for benefits judged to be twice as important as the aggregated score for costs, the overall value was the weighted average of the aggregated score for costs and the aggregated score for benefits. Higher preference scores mean higher overall value. Thus, the option with highest overall value is OM (overall score 77) and the option with lowest overall value is AAGs (overall score 50). The results could also be presented on a cost-benefit plane (Figure 3.2) which looks similar to the cost-effectiveness plane in a Cost-Effectiveness Analysis.
**Critique/discussion:**

MCDA has already been applied in economic evaluation in non-health sectors. The demonstration from the case study above shows the potentiality of MCDA in helping economic evaluation taking a societal perspective where there are many attributes within costs and benefits. However, regarding whether this can be applied in a HTA process, the following important issues with the method should be considered.

First, it only addresses the ranking of options in a specific decision problem. The preference score is only meaningful in comparing the options within the decision problem. If the list of options is complete, the overall preference scores actually represent the cost-effectiveness (value for money) of the options. If the list of options is not complete, the overall preference scores cannot make a statement about the cost-effectiveness of the options. For example, let’s imagine the case study above was for seven alternative treatments of cancer. We found that OM was the best treatment because it had the highest overall score. However, we could not make any statement about whether OM was cost-effective because such a cost-effectiveness statement requires more information about the healthcare budget and other healthcare activities in the budget. The score of costs for OM was 85 and the score of its benefits was 73. We could not relate them to a similar concept of Incremental Cost-Effectiveness Ratio and Cost-Effectiveness Threshold. The overall score becomes meaningless when cost-effectiveness is concerned.
Second, the full implementation of an MCDA requires several facilitated meetings/workshops with decision makers and stakeholders. This would add extra costs to the appraisal and might not be practical for HTA. However, future research can look at ways to simplify the process. For example, an online platform and teleconference can be used instead of a face-to-face meeting.

3.4.2 Proposing the CCA-MCDA approach:

This sub-section presents the proposal of an approach for applying MCDA in economic evaluation of healthcare interventions taking a societal perspective. The approach is termed CCA-MCDA to emphasise its nature. The CCA-MCDA approach relies on a value measurement model MCDA (see section 2.4.3 for other alternative MCDA approaches). The criteria are structured/grouped into ‘costs’ and ‘benefits’. Regarding costs, they are only differentiated in terms of the sector/budget where they fall (e.g. health care versus social care). Regarding benefits, only health benefits measured in QALYs are considered. However, they are differentiated in terms the HRQOL measure (e.g. healthcare QALY with EQ5D versus social care QALY with ASCOT). In addition, they are differentiated in terms of the characteristics of their recipients (e.g. patients versus caregivers, end-of-life versus normal). Details of the approach are described below.

3.4.2.1 The MCDA steps

This section presents an overview of the steps in the approach. The steps are based on the description from the MCDA manual by Dodgson et al. (2009) with some adjustments for the HTA process.

Step 1: The decision context

This is the context of the appraisal. The economic evaluation concerns the choice of alternative healthcare interventions. First, we need to establish the population for the assessment (e.g. adults with Alzheimer’s Disease). Second, we need to specify whether the decision problem is at national level, regional level, or local level. For example, NICE only concerns decision problems at the national level, whereas local decision makers such as Clinical Commissioning Groups (CCGs) or local authorities need to consider decision problems at their local levels.
Third, we need to identify and establish the healthcare interventions (decision options) in the appraisal. And finally, besides the decision makers who are directly responsible for solving the decision problem, we need to identify other stakeholders (key players) and decide who should be included for participation in the analysis; this forms the decision-making group for the analysis.

**Step 2: Specifying the criteria for costs and benefits**

In terms of costs, the decision-making group needs to discuss and identify which sectors/budgets the costs of the healthcare interventions would fall upon. In terms of benefits, the decision-making group needs to discuss and identify which groups of individuals would receive the health benefit measured in QALYs. For example, a distinction might need to be made between patients and their caregivers, or between those who are in poor health and those who are in good health. In addition, there might be different measures of quality of life in different sectors and this needs to be recognised in the sub-criteria for benefits.

**Step 3: Data collection for performance of alternative options**

Once costs and benefits are specified, the next task is to collect the data for the comparative performance of alternative options. Data can be collected from various sources and they can be synthesised and extrapolated with the help of a cost-effectiveness model. This task has always been required in current HTA process. The only difference is that in CCA-MCDA approach, more data might be required for wider costs and benefits than are required from the current narrow perspective.

**Step 4: Aggregating costs and aggregating benefits**

This is similar to the scoring and weighting stages in an MCDA approach. However, as discussed in the case study in section 3.4.1, it is necessary to simplify the scoring and weighting process for applying MCDA in HTA. In CCA-MCDA approach, costs falling on different sectors are measured in a monetary unit (£) and health benefits are measured in QALYs. These measures (£ and QALYs) already reflect preferences: less cost is always preferred and more QALYs is always preferred.
In CCA-MCDA, the scoring stage is not performed. Different costs are kept in monetary measure (£) and different benefits are kept in QALYs. The weighting stage is performed separately for costs and benefits. Costs falling on different sectors/budgets are aggregated using the values (weights) elicited from the decision makers. For example, the decision makers could be asked to state the weight between a £ falling on the healthcare sector with a £ falling on the social care sector. This results in a single aggregated value (in £) for costs. Similarly, different benefits are also aggregated using the values (weights) elicited from the decision makers. This results in a single aggregated value (in QALYs) for benefits.

**Step 5: Calculating value for money/cost-effectiveness**

This is similar to the stage to calculate the overall weighted scores for alternative options in MCDA. However, in CCA-MCDA, more emphasis is given to the trade-off between the aggregated cost and the aggregated benefit.

In CCA-MCDA, since costs are aggregated in a single value in pound sterling (£) and benefits are aggregated in a single value in QALYs, the value for money of an option is the ratio between the aggregated cost (£) and the aggregated benefit. This is comparable to the concept of a cost-effectiveness ratio. Value for money depends on the acceptable trade-off ratio between the aggregated cost (£) and the aggregated benefit (QALYs). This is similar to the concept of a cost-effectiveness threshold in a conventional cost-per-QALY analysis. The decision-making group needs to determine a Willingness-To-Pay (WTP) in terms of the aggregated cost and the aggregated benefit. For example, how much they would be willing to trade the aggregated cost (£) with the aggregated benefit (QALYs). Using this WTP, the cost-effectiveness of alternative options can be assessed.

**Step 6: Presenting/interpreting the results**

The results are presented to the decision-making group for examination, validation, and formulating proposals/recommendations for the way forward. In addition to the use of tables to present details of the results, graphical presentation is useful in helping the decision makers to understand the results, their meaning, and how they are calculated. There can be discrepancies between the results from the MCDA model and people’s intuitions. The decision-making group can decide to revise areas where there are inconsistencies or anomalous values.
Step 7: Sensitivity Analyses

The last step in the approach is to conduct sensitivity analyses.

3.4.2.2 The decision makers

The CCA-MCDA approach requires the involvement of decision makers and other key players. This is a group of individuals. This group first includes those who are directly responsible for making the decision (the decision makers). Then it can be expanded to include other individuals (stakeholders and key players) from the wider decision-making circle such as those who would be affected by the decision. For example, NICE is considering whether they should approve donepezil for the treatment of mild Alzheimer’s disease (AD) in the NHS. First, the decision makers are a group of individuals from NICE who are directly responsible for making the decision. Then, these individuals can decide whether to expand their decision-making group to include, for example, clinicians, patients, and/or members of the public.

3.4.2.3 The MCDA model

Another component of the approach is the MCDA model. The decision makers consider a list of alternative healthcare interventions. The performance of an option is assessed in terms of its costs and benefits.

Equation 3.10

\[ \text{Per}_{\text{overall}}^i = (C_1^i, C_2^i, ..., C_n^i, B_1^i, B_1^i, ..., B_m^i) \]

A value measurement MCDA model is employed. The aim of the MCDA model is to describe how the performance of a decision option is rationally translated to values perceived by the decision-making group.

Equation 3.11

\[ V(\text{Per}_{\text{overall}}^i) = V(C_1^i, C_2^i, ..., C_n^i, B_1^i, B_1^i, ..., B_m^i) \]

Given their costs and benefits, option (A) is preferred to option (B) if and only if:

Equation 3.12
The overall value is assumed to follow a linear additive function that describes the aggregated value of costs and benefits (Equation 3.13).

**Equation 3.13**

\[ V(\text{Per}_{\text{overall}}^A) > V(\text{Per}_{\text{overall}}^B) \]

Where \( V_2^i \) is the aggregated value for costs for option (i); \( V_1^i \) is the aggregated value for benefits for option (i); \( W_1 \) and \( W_2 \) are the relative weights that describe the exchange or trade-off between the aggregated value for costs and the aggregated value for benefits.

**Aggregating benefits:**

Different benefits are aggregated by a valuation function \( (V_1) \). The aggregated benefit (in QALYs) is the weighted average of all benefits (Equation 3.14).

**Equation 3.14**

\[ B_{\text{aggregated}}^i = \sum_{y=1}^{m} w'_y * B_y^i \text{ (QALYs)} \]

Where \( B_y^i \) is the benefit (y) (measured in QALYs) of option (i); \( w'_y \) is the relative weight for benefit (y) in a comparison to other benefits. The weights are elicited from the decision-making group.

**Aggregating COSTS:**

Costs falling on different sectors are aggregated by a value function \( (V_2) \). The aggregated cost (in £) is the weighted average of all costs (Equation 3.15).

**Equation 3.15**

\[ C_{\text{aggregated}}^i = \sum_{j=1}^{n} w_j * C_j^i \]
Where \( C^j_i \) is the cost falling on sector \((j)\) of option \((i)\); \( w_i \) is the relative weight for cost falling on sector \((j)\) in a comparison to costs falling on other sectors. The relative weights are elicited directly from the decision-making group.

**Value for money/cost-effectiveness**

Costs have been aggregated into a single value in (£) and benefits have been aggregated into a single value in (QALYs). The overall value is the value for money or cost-effectiveness perceived by the decision-making group. This is the weighted average of the aggregated value for COSTS and the aggregated value for BENEFITs.

Equation 3.16

\[
V_{total}^i = -W_1 \times C_{aggregated}^i + W_2 \times B_{aggregated}^i
\]

\( W_1 \) and \( W_2 \) are the relative weights that reflect the trade-off between the aggregated cost (in £) and the aggregated benefit (in QALYs). Denote \( K \) as the amount of £ (in the aggregated cost) the decision-making group is willing to pay for one QALY in the aggregated benefit (e.g. £20,000 per QALY):

\[
K = \frac{W_2}{W_1}
\]

The overall value of option \((i)\) can be expressed in QALYs.

Equation 3.17

\[
V_{total}^i = B_{aggregated}^i - \frac{C_{aggregated}^i}{K} \text{ (QALYs)}
\]

3.4.2.4 The decision-making workshops

The CCA-MCDA approach requires the conduct of a series of facilitated decision-making workshops. This is a platform for the decision-making group to express and discuss their judgements. The workshops are often lively with much exchange of information between participants and are guided by a facilitator who is a specialist in MCDA (Dodgson et al., 2009). The amount of time required for facilitated workshops depends on how complex the decision
is: for relatively straightforward decisions, it could be only a few hours; for complex decisions, it could be between two days and several months (Dodgson et al., 2009). For CCA-MCDA, the workshops need to be simple and convenient so that it can be incorporated into routine decision making in HTA.

3.5 Conclusion

This chapter has reviewed the argument for and against a societal perspective in economic evaluation of healthcare interventions. A societal perspective is theoretically more advantageous than a restricted perspective. In cases where the existence of wider costs and benefits is significant, the healthcare perspective can distort the economic results and lead to sub-optimal decisions. However, implementing a societal perspective faces substantial challenges in terms of its demand for more information and the lack of a methodological approach to address multiple aspects of a broad perspective.

The chapter proposed two approaches for implementing a societal perspective in economic evaluation: the extended cost-per-QALY and the CCA-MCDA. This forms the basis for the research in this thesis. The thesis aims to investigate the operationalisation of these two approaches in a case study in dementia care. The next chapter will report a systematic review of previous economic evaluation studies in dementia. Its purpose is to provide an initial understanding of different costs and benefits considered in previous economic evaluation studies of dementia.
CHAPTER 4. REVIEW OF ECONOMIC EVALUATION METHODS IN PREVIOUS STUDIES IN DEMENTIA

This chapter reports a systematic review of economic evaluation methods in previous studies in dementia. Through the review, the current state of applied economic evaluation methods in dementia was exposed and described. Evidence from the review was used to inform the subsequent investigations.

The chapter is divided into five sections. The first section gives an introduction and background information about dementia and dementia care. The second section describes the methods of the review. The third section describes the search results and included studies. The fourth section presents result of the review. The fifth section concludes the chapter.
4.1 Background

4.1.1 Dementia

“Dementia is a clinical syndrome with the development of impairment in multiple cognitive functions (including memory), severe enough to interfere with activities of daily living” (Brunnstrom, 2011). Dementia is caused by structural and chemical changes taking place in the brain due to brain diseases (Knapp et al., 2007). It is a progressive condition where advanced age is one of the main risk factors. Dementia is most common in older people (over 65) (Knapp et al., 2007).

Dementia includes different sub-types. The most common sub-type of dementia is Alzheimer’s disease (62%), followed by vascular dementia (17%) and mixed dementia (10%) (Prince et al., 2014, Brunnstrom, 2011).

4.1.2 Dementia care in the UK

One common feature of dementia is the presence of informal caregivers throughout the journey of people with dementia. Figure 4.1 illustrates an example of a map of different services and the journey that people with dementia and their caregivers go through from pre-diagnosis to post-diagnosis and end of life (UK context).
Figure 4.1: Services and the journey of dementia in the UK

(Expert opinions – from the local CCGs, memory services, clinicians, and the AD society)

The dementia journey starts with the identification of dementia symptoms during disease onset and symptomatic progression. Dementia symptoms are first noticed by people who are close to the patients or the patients themselves. Afterwards, patients and caregivers would seek advice from their GPs. This would trigger the initial assessment for dementia by GPs. If GPs suspect patients have dementia but cannot reach a firm conclusion, they would refer the cases to memory services where patients will receive a formal assessment by specialists.

After receiving a formal diagnosis of dementia, patients and their caregivers would be officially on the dementia pathway for post-diagnosis. Health care and social care needs from patients and caregivers will be assessed regularly. If the level of independence is still high (usually in early stages of dementia), patients and caregivers would still live in their own homes in their
community. There are different services from health care, social care, and the voluntary sector available to patients and their caregivers according to their needs.

As dementia progresses, patients will become more and more dependent up to a point where they need to move to a care home. The movement to a care home is an important milestone in the dementia journey. The transition marks a substantial change in the quality of life of both patients and their caregivers, and in the costs to the government social care services and the private budget (mainly the cost of the placement).

For the most common sub-type of dementia, Alzheimer’s disease, a cure (disease-modifying treatment) has not been found (Ghezzi et al., 2013). The current health care interventions can only slow down the progression of dementia symptoms. Early diagnosis of dementia has been recognised as an important strategy besides the research effort to find a cure: the earlier the intervention in the illness the better the outcomes (McKhann, 2011, Banerjee and Wittenberg, 2009).

In general, interventions for dementia can be categorised into three groups: pharmaceutical interventions, non-pharmacological interventions, and diagnostic interventions. The currently available medications for people with Alzheimer’s disease (AD) includes cognitive enhancers (acetylcholinesterase inhibitors and memantine), and antipsychotic medications (e.g. olanzapine, clozapine). These are only symptomatic treatments. Research is still on the way to find a disease-modifying drug for AD (Siemers et al., 2016).

Non-pharmacological interventions include interventions such as group-based cognitive stimulation, physical exercise programmes, tailored activity programmes (TAPs), occupational therapy, and psychosocial interventions. There is a lack of evidence for both the effectiveness and the cost-effectiveness of non-pharmaceutical interventions for people with dementia (Knapp et al., 2013). Diagnostic interventions are interventions that aim to improve the accuracy of dementia diagnosis and/or the timeliness of the diagnosis in the disease development.
4.1.3 Costs of dementia care

Table 4.1 outlines an example of a list of the possible costs for those involved in caring for people with dementia in England.

Table 4.1: Possible costs in dementia care

<table>
<thead>
<tr>
<th>Funder(s)</th>
<th>Expenditure item</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCGs/ NHS England</td>
<td>• Assessment (screening and diagnosis)</td>
</tr>
<tr>
<td></td>
<td>• Treatments</td>
</tr>
<tr>
<td></td>
<td>• Hospital inpatient services</td>
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<td></td>
<td>• Hospital outpatient services</td>
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<tr>
<td></td>
<td>• Day hospital (also provides respite care)</td>
</tr>
<tr>
<td></td>
<td>• Domiciliary visit (GP or consultant)</td>
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<tr>
<td></td>
<td>• Community health visits: nurses, therapists, etc.</td>
</tr>
<tr>
<td>Local authorities</td>
<td>• Assessment for support need</td>
</tr>
<tr>
<td></td>
<td>• Meals on wheels</td>
</tr>
<tr>
<td></td>
<td>• Social services (social workers, bathing and dressing)</td>
</tr>
<tr>
<td></td>
<td>• Home care</td>
</tr>
<tr>
<td></td>
<td>• Day care (to provide respite care)</td>
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<tr>
<td></td>
<td>• Sitter services (respite care)</td>
</tr>
<tr>
<td></td>
<td>• Long-term residential care</td>
</tr>
<tr>
<td></td>
<td>• Transport</td>
</tr>
<tr>
<td>Private (patients and</td>
<td>• Meals on wheels</td>
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<tr>
<td>family)</td>
<td>• bathing/dressing</td>
</tr>
<tr>
<td></td>
<td>• Home care</td>
</tr>
<tr>
<td></td>
<td>• Long-term residential care</td>
</tr>
<tr>
<td></td>
<td>• Day care and respite care</td>
</tr>
<tr>
<td></td>
<td>• Drug costs</td>
</tr>
<tr>
<td></td>
<td>• Travelling/parking</td>
</tr>
<tr>
<td></td>
<td>• Other out-of-pocket payments (patients and carers)</td>
</tr>
<tr>
<td></td>
<td>• Informal care time</td>
</tr>
<tr>
<td></td>
<td>• Patient’s time (receiving care)</td>
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<td></td>
<td>• Productivity losses (due to health)</td>
</tr>
<tr>
<td>Voluntary Organisations</td>
<td>• Meals on wheels</td>
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<tr>
<td></td>
<td>• Home care</td>
</tr>
<tr>
<td></td>
<td>• Transport</td>
</tr>
<tr>
<td></td>
<td>• Long-term residential care</td>
</tr>
<tr>
<td></td>
<td>• Respite care</td>
</tr>
</tbody>
</table>

(Expert opinions from the local CCGs, memory services, clinicians, and the AD society)
The care for people with dementia involves several different funding sectors: the NHS is the main source of funding for health care expenditure; local authorities are in charge of funding social services and some social community support; voluntary organisations can contribute by providing support for people with dementia and their caregivers in the community as well as in nursing homes. Patients and family are affected directly by the costs of private paid care, unpaid informal care, other out-of-pocket expenses, and the cost of time involved in seeking and receiving care. Figure 4.2 illustrates the main components of the organisational financial structure of the health care system in England in 2013.

Figure 4.2: The structure of the English health and social care system (2013)

Health services in England are mainly funded by the government. The Department of Health (DH) is the government body responsible for allocating the funds to the NHS, public health, and adult social care. Direct responsibility for commissioning health care services lies with two groups of bodies – the NHS England (including 4 regional teams) and clinical commissioning groups (CCGs) (including 211 groups). The CCGs are supported by and accountable to the NHS England. The commissioning of pharmaceutical treatments is influenced by NICE at the national level. This means for pharmaceutical treatments that have been approved by NICE
based on their cost-effectiveness, the NHS is obliged to provide those for people in need. Responsibility for commissioning adult social care services and public health services rests with local authorities (county councils and unitary authorities). Local authorities receive support, advice, and guidance from Public Health England on how to improve health.

4.1.4 Benefits of dementia care

Broadly speaking, the main benefits of dementia care are the wellbeing of people with dementia and their caregivers. Although the health economics literature mentions the existence of altruistic utility (caring externality – people gain more happiness because of seeing others happy) (Jacobsson et al., 2005, Brouwer et al., 2009), that utility would not be significant for people other than the informal caregivers.

People with dementia receive the direct benefits of dementia care. They gain improvement in their health and wellbeing. On the other hand, the health and wellbeing of informal caregivers can be affected by the act of informal care giving, the relationship between the carer and the patient, and health care interventions which target patients, informal caregivers or both of them.

Regarding the impact of informal care on the health and wellbeing of carers, two points should be noted: there are both positive aspects (i.e. enjoying caring for your loved one) and negative aspects (i.e. burden, stressors) (Hirst, 2004, Brouwer et al., 2005, Hoefman et al., 2011), and the causal relationship between providing informal care and carers’ health is not clear (van den Berg et al., 2004).

Regarding the relationship between the carer and the patient, there can be altruistic utility that is the effect of caring externality on the carer: carer might feel better just because the patient’s health is improved (Basu and Meltzer, 2005, Jacobsson et al., 2005, Bobinac et al., 2010). There can also be direct health and wellbeing benefits for informal caregivers that are purely from the effects of care interventions.

4.2 Review methods

The following databases were searched for in October 2015: Medline, PsycINFO, EconLit, CINAHL, and the Cochrane Library (Cochrane reviews, DARE, NHS EED, Trials, and HTA). Full details of the search strategy are given in Appendix 1.
First, the titles and abstracts of articles retrieved in the search were screened. Articles were retained for the full-text assessment stage if they met the following criteria:

- Complete economic evaluation studies of pharmaceutical, diagnostic, or screening interventions.
- Systematic reviews of economic evaluation studies for pharmaceutical, diagnostic, or screening interventions.
- HTA reports of pharmaceutical, diagnostic or screening interventions in dementia.

Articles which were commentaries, letters, methods papers, abstracts, and reviews but not systematic reviews were excluded. The review focused only on pharmacological, diagnostic, and screening interventions. These areas of focus were considered sufficient to capture the evolution as well as important issues regarding the methods of economic evaluation in dementia. Thus, studies which were about non-pharmacological interventions (e.g. cognitive stimulation therapies), and carer interventions were excluded.

At the full-text assessment stage, the entire body of the text of an article was reviewed to see whether they met the inclusion and exclusion criteria. Only CUA, CEA and CCA were included. Cost analysis studies and CBA were excluded. If two papers reported the same economic evaluation study (i.e. a HTA report and another journal article paper), only the paper which provided more detailed information was retained (i.e. only the HTA report).

All previous systematic review studies were checked to see whether their included papers overlap with one another. If included papers in a systematic review study were fully covered in a newer study, only the newer study was retained. Data extraction was first performed to identify and extract the included papers from previous systematic reviews. Details of data extraction of previous systematic reviews are also provided in Appendix 1.

Papers identified from previous systematic reviews were then combined with economic evaluation studies identified in the search above to create the final list of economic evaluation studies for the final review. Information of these economic evaluation studies was extracted using a data extraction form (Table 4.2).
Table 4.2: Data extraction form for economic evaluations

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</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Year</td>
<td>9</td>
<td>What were costs included?</td>
</tr>
<tr>
<td>3</td>
<td>Country of the evaluation</td>
<td>10</td>
<td>How were costs measured, valued, and aggregated?</td>
</tr>
<tr>
<td>4</td>
<td>Intervention (s)</td>
<td>11</td>
<td>What benefits were included?</td>
</tr>
<tr>
<td>5</td>
<td>Comparator</td>
<td>12</td>
<td>How were benefits measured, valued, and aggregated?</td>
</tr>
<tr>
<td>6</td>
<td>Population</td>
<td>13</td>
<td>How were costs and benefits aggregated?</td>
</tr>
<tr>
<td>7</td>
<td>Economic evaluation type</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Narrative analysis was used to synthesise the evidence base, supported by the data extraction form.

4.3 Included studies

In brief, 837 citations were identified from the searches. 132 of which were ordered for full-text. Of the 132 that came to the full-text assessment stage, 75 were excluded using the exclusion criteria. 5 systematic reviews and 55 economic evaluation studies were included.

Data extraction from 5 systematic reviews helped identify 7 economic evaluation studies in addition to those already identified from the searches. A total of 62 economic evaluation studies were included in the final review (Figure 4.3). Table 4.3 provides a brief summary of included studies.
Figure 4.3: Flow chart for study identification and selection

1. Papers for screening (n = 827)
   - Excluded by title/abstract (n = 705)
2. Full-text assessment (n = 132)
   - Excluded by full-text (n = 75)
3. Economic evaluation studies (n = 55)
4. Systematic reviews (n = 5)
   - Additional economic evaluation studies (n = 7)
5. Total included economic evaluation studies (n = 62)
6. Screening/diagnostic interventions (n = 15)
7. Pharmacological interventions (n = 47)
<table>
<thead>
<tr>
<th>No</th>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Population</th>
<th>Intervention</th>
<th>Reference</th>
</tr>
</thead>
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<td>Spain</td>
<td>AD</td>
<td>Pharmacological</td>
<td>(Antonanzas et al., 2006)</td>
</tr>
<tr>
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<td>2000</td>
<td>Canada</td>
<td>AD/VaD</td>
<td>Pharmacological</td>
<td>(Bachynsky et al., 2000)</td>
</tr>
<tr>
<td>3</td>
<td>Bermingham</td>
<td>2014</td>
<td>Canada</td>
<td>Dementia</td>
<td>Diagnostics</td>
<td>(Bermingham, 2014)</td>
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<td>France</td>
<td>Old people</td>
<td>Screening and Diagnostics</td>
<td>(Biasutti et al., 2012)</td>
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<td>AD</td>
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<td>(Bond et al., 2012a)</td>
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<td>(Courtney et al., 2004)</td>
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<td>(Francois et al., 2004)</td>
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<td></td>
<td>Name</td>
<td>Year</td>
<td>Location</td>
<td>Diagnosis</td>
<td>Method</td>
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<td>UK</td>
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<td>2007</td>
<td>Germany</td>
<td>AD</td>
<td>Pharmacological</td>
<td></td>
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<tr>
<td>54</td>
<td>Touchon</td>
<td>2014</td>
<td>France</td>
<td>AD</td>
<td>Pharmacological</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>Valcarcel-Nazco</td>
<td>2014</td>
<td>Spain</td>
<td>MCI and dementia</td>
<td>Diagnostics</td>
<td></td>
</tr>
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<td>56</td>
<td>Ward</td>
<td>2003</td>
<td>UK</td>
<td>AD</td>
<td>Pharmacological</td>
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</tr>
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<td>57</td>
<td>Weimer</td>
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<td>US</td>
<td>Old people (65+)</td>
<td>Screening</td>
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<td>58</td>
<td>Weycker</td>
<td>2007</td>
<td>US</td>
<td>AD</td>
<td>Pharmacological</td>
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<td>Willan</td>
<td>2006</td>
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<td>Parkinson Dementia</td>
<td>Pharmacological</td>
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<td>2009</td>
<td>Netherlands</td>
<td>Dementia</td>
<td>Diagnostics</td>
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<td>61</td>
<td>Wong</td>
<td>2009</td>
<td>Canada</td>
<td>VaD</td>
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<tr>
<td>62</td>
<td>Yu</td>
<td>2015</td>
<td>Korea</td>
<td>Old people (60+)</td>
<td>Screening</td>
<td></td>
</tr>
</tbody>
</table>

### 4.4 Results

#### 4.4.1 What type of economic evaluation was performed?

89% (55) economic evaluation studies were performed as secondary research (using data from the literature with the aid of modelling or simple calculation). Only 11% (7) of the studies were performed alongside a clinical trial (primary research).

71% (44) of the studies were Cost Utility Analysis (CUA) where all health benefit was measured and valued in terms of Quality Adjusted Life Years (QALYs). 26% (16) of the studies were Cost Effectiveness Analysis (CEA) where a health benefit was measured in natural units.
such as life years gained, time spent in non-severe states, clinical score improvement, etc. 3% (2) of the studies were Cost Consequence Analysis (CCA) where multiple health benefits were reported in their natural clinical units and the results were reported in a disaggregated format (i.e. no ratio for costs and benefits was calculated).

4.4.2 What perspective was stated?

52% (32) of the studies clearly stated the adoption of a societal perspective. 31% (19) of the studies stated the adoption of a restricted perspective which was often the perspective of the health care system (including social care) or the payer perspective. 6% (4) of the studies stated that they adopted a perspective which was broader than the health care system (to include informal care). 11% (7) of the studies did not state the perspective of their economic evaluation.

4.4.3 What costs were included and how were they measured and valued?

4.4.3.1 Inclusion of costs in economic evaluations:

The inclusion of different costs depended on the perspective of the evaluation. It was clear and highly consistent in terms of what costs were included in economic evaluation studies taking a restricted perspective (i.e. payer perspective), whereas the inclusion of costs in economic evaluation studies stating the adoption of a societal perspective varied substantially between studies.

For studies stating the adoption of a restricted perspective (usually the payer perspective), they consistently included costs falling on the payer’s budget such as government health and social care, and excluded wider costs that fell on other parts of society such as informal care, private payment for care, or patient out-of-pocket expenses.

For studies stating the adoption of a ‘societal perspective’ (32 studies), in addition to the inclusion of the costs falling on the payer (e.g. government health and social care), informal care was included in 94% (30) of the studies; private payment for care was explicitly included in 23% (7) of the studies; patient out-of-pocket expenses for seeking and receiving treatments were included in 19% (6) of the studies; patient time in seeking and receiving treatments was explicitly included in 6.5% (2) of the studies; patient productivity loss was explicitly included
in 9.7% (3) of the studies; cost to the voluntary sector was included in 3% (1) of the studies; and costs to the transportation sector and legal system were included in 3% (1) of the studies.

Table 4.4: Frequency of wider costs being included

<table>
<thead>
<tr>
<th>Type of cost</th>
<th>Number of ‘societal perspective’ studies that included the cost</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informal care</td>
<td>30</td>
<td>94 (%)</td>
</tr>
<tr>
<td>Private co-payment for care</td>
<td>7</td>
<td>22 (%)</td>
</tr>
<tr>
<td>Patient out-of-pocket expenses for seeking and receiving treatments</td>
<td>6</td>
<td>19 (%)</td>
</tr>
<tr>
<td>Patient time in seeking and receiving treatments</td>
<td>2</td>
<td>6 (%)</td>
</tr>
<tr>
<td>Patient productivity loss</td>
<td>3</td>
<td>9 (%)</td>
</tr>
<tr>
<td>Costs to the voluntary sector</td>
<td>1</td>
<td>3 (%)</td>
</tr>
<tr>
<td>Costs to the transportation sector</td>
<td>1</td>
<td>3 (%)</td>
</tr>
</tbody>
</table>

Regarding the costs of health and social care, the majority of studies only included the health and social care resources consumed by patients. Three studies included the health care resources consumed by the informal caregivers. They all stated the adoption of a societal perspective. Antonanzas et al. (2006) assessed the cost-effectiveness of Memantine in community-based AD patients in Spain; they included the cost of caregiver medication in health care costs (€4 per month). Gagnon et al. (2007) evaluated the cost-effectiveness of Memantine in AD in Canada; they included the cost of caregiver use of counselling or support groups. Biasutti et al. (2012) evaluated the use of Magnetic Resonance Imaging (MRI) with a new contrast agent for the early diagnosis of AD in France; they included the costs of psychiatrist consultation and antidepressant treatment for informal caregivers. It was also noted that one study did not include the costs of social care although it stated the adoption of a societal perspective. Fuh and Wang (2008) evaluated the use of donepezil for AD; they only included medical expenses (paid by National Health Insurance), out-of-pocket co-payments, and unpaid informal care.
Regarding the costs of informal care, two studies did not include informal care although they clearly stated the adoption of a societal perspective in their evaluation. Wong et al. (2009) evaluated the use of AcHEIs and memantine for vascular dementia in Canada; they only included the costs of pharmaceuticals and physician services in their analysis. Retchin and Hillner (1994) evaluated a screening programme for dementia among older drivers in the US; the cost of informal care was not included in their analysis.

Private co-payment for care by patients and family was included in seven out of 32 societal-perspective studies. None of the studies were from the UK. The cost was in the form of co-payment for health and social care which were already covered partly by the government or a third-party payer. Francois et al. (2004) evaluated the use of memantine for AD in Finland; they included private payment for care for patients living in the community. Fuh and Wang (2008) included co-payments by patients and family to the Taiwan’s National Health Insurance system. Lopez-Bastida et al. (2009) evaluated the cost-effectiveness of donepezil for AD in Spain; they included private payment for care for services such as medical visits and domestic cleaners. Neumann et al. (1999) assessed the cost effectiveness of donepezil for AD in the US; they included costs of ‘self-pay’ (private payment) for health and social care for patients in both community and institutional care. Suh et al. (2008) evaluated the use of galantamine for AD in South Korea; they included the private purchase of paid caregivers, paid home helpers and other private health care expenses. Teipel et al. (2007) assessed the cost effectiveness of donepezil for the treatment of AD in Germany; they included co-payments for care by families. Touchon et al. (2014) evaluated the use of memantine in combination with AcHEIs for AD in France; they included the amount of family contributions in the costs of community care.

Patient out-of-pocket expenses in seeking and receiving treatments were included in six out of 32 societal-perspective studies. This often included the costs of travelling, food, telephone, and personal alarms. Hoogveldt et al. (2011) assessed the cost effectiveness of memantine for AD in the Netherlands; they included the travelling expenses incurred to patients to travel to day-care centres. Rive et al. (2012) evaluated the use of memantine for AD in Norway; they included the travelling expenses and personal alarms incurred to patients. Handels et al. (2015) evaluated the use of cerebrospinal fluid (CSF) AD biomarkers for early detection of AD in MCI and treatment with a hypothetical disease-modifying treatment; they included patient and family out-of-pocket costs. In two economic evaluation studies which evaluated different diagnostic work-up strategies for AD in the US, McMahon et al. included travelling expenses
incurred to patients to travel to the diagnostic centre (petrol, parking, and lunch) (McMahon et al., 2000, McMahon et al., 2003). Wolfs et al. (2009) conducted an economic evaluation alongside a RCT to evaluate the use of an integrated multidisciplinary diagnostic facility for diagnosing dementia in ambulatory psychogeriatric patients; they included the costs of travelling to different health care locations and other out-of-pocket expenses for patients and caregivers.

Patients’s time spent seeking and receiving treatments was included in two (same first author) out of 32 societal-perspective studies. McMahon et al. (2000) and McMahon et al. (2003) included patient time to travel to a health care centre and to receive a diagnostic assessment.

Patient productivity loss was included in three out of 32 societal-perspective studies. Biasutti et al. (2012) argued that although most AD patients are retired, they can still perform volunteer activities within non-profit organisations (NPOs) as well as perform domestic productive activities (i.e. childcare); thus they included these productivity costs in their evaluation. Retchin and Hillner (1994) (US) included the cost of lost productivity resulting from motor vehicle injury and death. Yu et al. (2015) assessed the cost effectiveness of a nationwide opportunistic screening programme for dementia in South Korea; they included productivity loss for people with dementia in addition to other costs.

The cost to the voluntary sector was included in one out of 32 societal-perspective studies. Lopez-Bastida et al. (2009) used the direct health care and non-health care costs reported in a Spanish cost study (Lopez-Bastida et al., 2006). Thus, they included the costs of voluntary services.

We found one study that included costs falling on the transportation sectors and the legal system. Retchin and Hillner (1994) presented an interesting case about a screening programme to detect people with dementia among older drivers. The benefit of the programme came from a reduction in the number of motor vehicle crashes when demented drivers were identified and discontinued driving. Thus, they included costs falling on the transportation sector and legal costs per motor vehicle crash.

Overall, for the inclusion of wider costs in economic evaluation studies that clearly stated the adoption of a societal perspective, we found that there was a high level of consistency in including informal care. However, the inclusion of other wider costs such as private co-
payment for care, out-of-pocket expenses in seeking and receiving care, time seeking and receiving care, as well as productivity costs were not consistent between studies.

4.4.3.2 Measuring and valuing costs:

**Health and social care**

The measurement and valuation of costs were straightforward for the costs of formal health and social care which fell on third-party payers (i.e. the governments, insurance companies). It was generally agreed that the more severe the disease, the more health and social care were required by patients. These costs were valued in monetary units with reference unit costs from health and social care providers.

**Informal care**

The measurement and valuation of informal care are not straightforward in theory (van den Berg et al., 2004) and this was reflected in the reported estimates from economic evaluation studies in this review.

Informal care was included in 34 studies (among all 62 studies): 30 studies stated the adoption of a societal perspective, three studies stated the adoption of a perspective that was broader than the healthcare perspective, and one study stated the adoption of the US health system perspective (Kirbach et al., 2008). Among these studies, six studies were EEACTs and 28 studies were model-based evaluation studies.

All EEACTs used the recall method (van den Berg et al., 2004) to measure the amount of informal care in clinical trials. The primary informal caregiver was asked to complete a survey which asked about the amount of informal care time spent over a certain recall period. The Caregiver’s Activity Time Survey (Clipp and Moore, 1995) was used in two studies (Bachynsky et al., 2000, Courtney et al., 2004). The Client Service Receipt Inventory (CSRI) (Beecham and Knapp, 2001) was adapted in two studies (Suh et al., 2008, Romeo et al., 2013). The other two studies (Willan et al., 2006, Wolfs et al., 2009) used surveys developed in their clinical trials.
Model-based studies, on the other hand, used primary data from other studies for the measurement and valuation of informal care. It was generally agreed that informal care increased with disease severity or dependency and reduced significantly when the patient moved to institutionalisation. The specific amount of informal care used in the models varied depending on the particular context (i.e. country), and the population being researched.

Regarding the valuation of informal care, four studies did not report the method used for valuing informal care; one study reported informal care without valuation (in hours); and the rest (29 studies) used revealed preference methods (van den Berg et al., 2004) to value informal care. Among the 29 studies which reported the use of revealed preference methods for the valuation of informal care, eight studies used the proxy good (replacement cost) method; one study used a mix of both the proxy good method and the opportunity cost method (average value); and 20 studies used the opportunity cost method (the majority of them used the national average wage rate). The majority of studies applied a single rate for the value of an hour of informal care regardless of specific informal care tasks. Few studies applied different values for basic ADL tasks and IADL tasks. For example, McMahon et al. (2000) used the average wage of professional personal care attendants for basic ADL tasks, whereas the average wage of homemakers was applied for IADL tasks.

**Private co-payment for care**

Among seven studies which included private co-payment for care, six studies were model-based evaluation studies and only one study was EEACT.

The EEACT (Suh et al., 2008) (Korea) used the adapted version of the Client Service Receipt Inventory (CSRI) (Beecham and Knapp, 2001) to ask primary caregivers about their purchase of private hire of a paid caregiver or home helper, health food and supplement, etc.

Model-based studies used primary data from other studies for the measurement and valuation of private co-payment for care. Francois (2004) (Finland) used the estimates from the Kuopio 75+ study (Rahkonen et al., 2003) for the measurement of the private health and social care consumed compared with the government-funded ones. Fuh and Wang (2008) (Taiwan) used the estimates from a previous cost study (the publication was in Chinese only) on 106 AD patients in Taiwan for the private co-payment for care. Lopez-Bastida et al. (2009) (Spain) used
the estimates from a previous cost study on a sample of 237 patients with AD in Spain (Lopez-Bastida et al., 2006) for the private purchase of medical visits and domestic cleaners. Neumann et al. (1999) (US) used the estimates from a previous cost study (Rice et al., 1993) on 180 AD patients in the US for the private co-payment for care; Rice et al. (1993) reported the total care costs according to type of payers: Medicare, Medicaid, private insurance, HMO, self-pay, and other. Teipel et al. (2007) (Germany) used the estimates from a previous cost survey (the publication was in German only) on 1682 German AD patients for the amount of outpatient care purchased by families. Touchon et al. (2014) (France) used the estimates obtained from a 2005 national report of the French Assembly on AD (French parliamentary report) for the family contributions to care costs.

**Out-of-pocket expenses in seeking and receiving treatments**

Among six studies which included out-of-pocket expenses for seeking and receiving treatments, five studies were model-based evaluation studies and only one study was EEACT.

The EEACT (Wolfs et al., 2009) (The Netherlands) used cost diaries completed by the proxy (e.g. informal caregiver) of the patient to measure the amount of out-of-pocket expenses incurred to them including travelling expenses, meals, telephone, petrol, etc. Various sources for unit costs were used for the valuation of out-of-pocket expenses.

Three model-based studies used primary data from other studies for the measurement and valuation of out-of-pocket expenses for seeking and receiving treatments. Handels et al. (2015) (The Netherlands) used the estimates from an EEACT (Wolfs et al., 2009) for the out-of-pocket expenses. Hoogveldt et al. (2011) (The Netherlands) used the estimates from a previous cost study (van der Roer et al., 2000) for the measurement of travelling costs (to the day-care centres) incurred to patients; the valuation of this cost was derived from the Dutch guidelines. Rive et al. (2012) (Norway) used the estimates from a previous cost study (Jonsson et al., 2006b) on 272 AD patients in Scandinavia for the measurement of out-of-pocket expenses such as transportation or meals; the unit costs of these resources were derived from various Norwegian sources. McMahon et al. (2000,2003) estimated the travel expenses (gas, parking, and lunch) for a patient at $40 per day based on their own opinion. Out-of-pocket expenses for seeking and receiving treatments were mainly travel expenses when they were included in
previous economic evaluation studies. This was often a very small amount compared to the total costs of care.

**Patient time in seeking and receiving treatments**

The cost of patient time in seeking and receiving care was only mentioned briefly in two model-based studies (McMahon et al., 2000, McMahon et al., 2003). Nonetheless, the authors just assumed the amount of time incurred to patients (based on their own opinion); there was no empirical evidence. For example, they estimated that the completion of a standard diagnostic work-up would take 1 day (8 hours, including travelling time). This time was valued by using the median income of persons aged 65 years and older at $50 per day (McMahon et al., 2000).

**Patient productivity loss**

All three studies which included patient productivity loss were model-based studies.

Biasutti et al. (2012) (France) used data from previous French studies (the publication was in French) to estimate that 60 to 75 year-old individuals performed on average 63.8 hours of informal volunteering activities (e.g. childcare) and 36 hours of volunteer activities with non-profit organisations (NPO) over a 6-month period. This production was adjusted by an efficiency coefficient of 0.7 to account for the reduced productivity in older individuals. The production of informal volunteering activities was valued at €7.7 per hour (the minimum wage in France in 2009), whereas the production of NPO volunteering activities was valued slightly higher at €7.9 per hour.

Retchin and Hillner (1994) (US) used the data provided by the Insurance Institute for Highway Safety to measure the cost of lost productivity resulting from motor vehicle injury and death; the valuation was derived on the basis of the human capital approach.

Yu et al. (2015) (Korea) measured lost productivity using data from 2,564 subjects who responded to their survey. However, methods and detailed information about the survey were not reported. The method for the valuation of lost productivity was also not reported. The authors just reported the monetary values of lost productivity per year used in their model. The
value of lost productivity was reported to increase with dementia severity and decrease with age (Yu et al., 2015).

**Costs to the voluntary sector**

This review only found one study (Lopez-Bastida et al., 2009) which included the cost of voluntary services. Lopez-Bastida et al. (2009) (Spain) included the cost of voluntary services in the category for direct non-health care costs. The measurement and valuation of this cost was taken from another study (Lopez-Bastida et al., 2006). None of the studies reported how the cost of voluntary services was measured and valued. The reported figure for the cost of voluntary services was €234 per year, whereas the figure for the total direct cost per year was €23,902 (Lopez-Bastida et al., 2006); the cost of voluntary services was just 0.1% of the total direct costs.

**Costs to the transportation sector and the legal system**

The costs to the transportation sector and the legal system were mentioned in one study (Retchin and Hillner, 1994). However, it should be noted that this study evaluated the cost-effectiveness of a dementia screening programme for older drivers in the US. Thus, the screening programme was paid by the transportation sector and the effects were assessed in terms of a reduction in the number of deaths and injuries resulting from motor vehicle crashes. The legal system and the health care system were just naturally involved as spill-over effects of motor vehicle crash cases. This is different from the evaluation of other conventional health care programmes where the health care sector is the main decision maker and the initiator of the intervention. Retchin and Hillner (1994) used estimates from other sources provided by the industries such as the American Automobile Association or The Alliance of American Insurers for the measurement and valuation of these costs.

4.4.4 What benefits were included and how were they measured and valued?

4.4.4.1 Inclusion of benefits in economic evaluations

There were only two types of benefits which were included in previous economic evaluation studies: patient health benefit and caregiver health benefit. None of the studies included
benefits which were beyond health or benefits received by those other than the patients and their informal caregivers.

All studies (62) included patient health benefit, whereas only five studies (8%) included caregiver health benefit in their base-case analyses and one study (1.6%) addressed caregiver health benefit in their sensitivity analyses. Among the five studies that included caregiver health benefit in their base-case analysis, four of them stated the adoption of a societal perspective and one stated the adoption of a perspective that was broader than health and social care. One study which included caregiver health benefit in their sensitivity analyses was the HTA of AD medications in the UK (Bond et al., 2012b). This study stated the adoption of a health and social care perspective following the NICE guidance for HTA (NICE, 2013a).

A review by van den Berg et al. (2004) concludes that it is necessary to include the health impacts on informal caregivers if informal care costs are included and valued using revealed preference methods such as proxy good method or opportunity cost method. However, in this review, we found that among 33 studies that included informal care costs and measured them using revealed preference methods (see above); only six of them included the impacts on the health of informal caregivers.

4.4.4.2 Measuring and valuing benefits:

4.4.4.2.1 Patient health benefits

Measurement

The measures of patient health benefits used in previous EEA CTs (7 studies) were categorised into four groups: dementia domain-specific measures, global dementia staging measures, dementia-specific health-related quality of life (HRQOL) measures, and generic HRQOL measures. Table 4.5 provides a summary for the use of these measures in previous EEA CTs.

The domain-specific measures were further categorised to include cognitive measures, measures of activities of daily living, measures of behavioural and psychological problems, and measures of depression symptoms. The Mini-Mental State Examination (MMSE) (Folstein et al., 1975) was the only cognitive measure mentioned in previous EEA CTs. Measures of Activities of Daily Living included the Bristol Activities of Daily Living Scale (BADLS)
(Bucks et al., 1996), the Alzheimer’s Disease Cooperative Study Activities of Daily Living Scale (ADCS-ADL) (Galasko et al., 1997), and the Disability Assessment for Dementia (DAD) scale (Gelinas et al., 1999). Measures of behavioural and psychological symptoms included the Neuropsychiatric Inventory (NPI) (Cummings et al., 1994), and the Behaviour Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD) (Reisberg et al., 1987). The Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos et al., 1988) was the only measure used for depression symptoms in previous EEACTs.

Global dementia staging measures included The Clinical Global Impressions (CGI) (Busner and Targum, 2007) and The Global Deterioration Scale (GDS) (Reisberg et al., 1982). Dementia-specific HRQOL measures included the Alzheimer’s Disease Related Quality of Life Scale (Kasper et al., 2009) and the AD Dependence Scale (Stern et al., 1994). Generic HRQOL measures included the EQ5D (The EuroQoL Group, 1990) and Health Utility Index Mark 3 (HUI3) (Feeny et al., 2002).

Table 4.5: Summary of measures of patient health benefits in EEACTs

<table>
<thead>
<tr>
<th>First author, year, and country</th>
<th>Intervention</th>
<th>Measures of patient health benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bachynsky, 2000, Canada</td>
<td>Propentofylline</td>
<td>CGI and GDS</td>
</tr>
<tr>
<td>Courtney, 2004, UK</td>
<td>Donepezil</td>
<td>BADLS, NPI, and MMSE</td>
</tr>
<tr>
<td>Romeo, 2013, UK</td>
<td>Antidepressants</td>
<td>CSDD and EQ5D</td>
</tr>
<tr>
<td>Rosenheck, 2007, US</td>
<td>Antipsychotics</td>
<td>HUI3, the AD Related QOL Scale, and the AD Dependence Scale</td>
</tr>
<tr>
<td>Suh, 2008, Korea</td>
<td>Galantamine</td>
<td>DAD scale, ADAS-cog, BEHAVE-AD, and GDS</td>
</tr>
<tr>
<td>Willan, 2006, Canada</td>
<td>Rivastigmine</td>
<td>MMSE</td>
</tr>
<tr>
<td>Wolfs, 2009, The Netherlands</td>
<td>A new memory service</td>
<td>EQ5D, MMSE, and NPI</td>
</tr>
</tbody>
</table>

On the other hand, previous model-based economic evaluations (55 studies) measured patient health benefits by modelling/extrapolating the estimates from primary research (e.g. clinical trials). Patient health benefits were described in terms of the following outcomes: quality-
adjusted life years (QALYs) (40 studies), years of independence or without the need of Full-Time Care (FTC) (4 studies), years or days in non-severe stages (5 studies), life years (1 study), number of accurate diagnoses (3 studies), number of surgically treatable dementia cases identified (1 study), and improvement in ADAS-cog score (1 study).

Among 40 model-based studies which used the QALY as the measure for patient health benefits, the EQ-5D was mentioned in 13 studies (33%). The HUI mark 2 was mentioned in 17 studies (43%). The HUI mark 3 was mentioned in five studies (13%). The Index of Health Related Quality of Life (IHQOL) (Rosser et al., 1992) was mentioned in two studies (5%). The Clinical Dementia Rating (CDR) (Berg, 1988, Morris, 1993) was mentioned in one study (3%), and two studies (5%) mentioned the use of both the EQ5D (for some health states) and HUI (for some other health states) in their models.

There could be an issue with model-based studies that used values derived from the EQ5D for some health states and values derived from the HUI for some other health states (in the same model). Bermingham (2014) evaluated the cost effectiveness of different diagnostic work-up strategies for diagnosing dementia in Canada. For the utilities of patients in AD states (e.g. mild, moderate, severe), their model used values derived from the HUI2 (Neumann et al., 1999b), whereas for the dis-utilities caused by strokes, their model used values derived from the EQ5D (Sullivan and Ghushchyan, 2006). Hornberger et al. (2015) assessed the cost-effectiveness of Florbetapir-PET for diagnosing AD in Spain. Their model used utilities values derived from the EQ5D (Wimo et al., 2013) for health states when patients were in the community, whereas utilities values derived from the HUI2 (Neumann et al., 1999b) were used for health states when patients were in nursing homes.

**Valuation**

The preference-based measures used in previous studies included the EQ5D, HUI2, HUI3, and the Clinical Dementia Rating with Time-Trade-Off. Model-based studies used the values reported from other utility studies, whereas EEACTs valued the health states in their study using provided tariff values for each preference-based measure.

Only three EEACTs in our review used preference-based measures. Romeo et al. (2013) assessed the cost-effectiveness of antidepressants (mirtazapine and sertraline) for dementia in the UK. The EQ-5D was the preference-based measure used for patient health benefits. The
authors used the tariff values for the UK population (Dolan et al., 1995). The same tariff values were used in the EEACT by Wolfs et al. (2009). Rosenheck et al. (2007) evaluated second-generation antipsychotics for AD in the US and they used the HUI3 for the patient health benefits. The tariff values from the Canadian population (Feeny et al., 2002) were used for the HUI3.

For model-based studies that used preference-based measures (40 studies), Table 4.6 summarises all utility studies that were cited in those model-based studies for the valuation of patient health states.

Table 4.6: Studies that were cited in model-based studies for utility values

<table>
<thead>
<tr>
<th>HRQOL measure</th>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Number…*</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ5D</td>
<td>Jonsson</td>
<td>2006</td>
<td>Sweden, Denmark, Finland, Norway</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Andersen</td>
<td>2004</td>
<td>Denmark</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lopez-Bastida</td>
<td>2006</td>
<td>Spain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wolfs</td>
<td>2009</td>
<td>The Netherlands</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Livingston</td>
<td>2004</td>
<td>UK</td>
<td>3</td>
<td>Publication in Korean</td>
</tr>
<tr>
<td></td>
<td>Kang</td>
<td>2006</td>
<td>Korea</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>HUI</td>
<td>Neumann</td>
<td>1999/2000</td>
<td>US</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Murman and Colenda</td>
<td>2005</td>
<td>US</td>
<td>1</td>
<td>Unpublished source</td>
</tr>
<tr>
<td></td>
<td>Brazier</td>
<td>2001</td>
<td>-</td>
<td>1</td>
<td>Mapping from clinical trial data</td>
</tr>
<tr>
<td>CDR TTO</td>
<td>Ekman</td>
<td>2007</td>
<td>Sweden</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>IHQOL</td>
<td>Stein</td>
<td>1997</td>
<td>UK</td>
<td>1</td>
<td>Purely speculative**</td>
</tr>
<tr>
<td></td>
<td>Stein</td>
<td>1998</td>
<td>UK</td>
<td>1</td>
<td>Purely speculative**</td>
</tr>
</tbody>
</table>

* (number of model-based studies citing this source)

** (the author just assumed the values without any evidence)
Informal caregiver health benefits were included in seven studies: six of them were model-based and one of them was an EEACT. The EEACT (Courtney et al., 2004) assessed the cost-effectiveness of long-term donepezil treatment in 565 patients with AD in the UK. They measured the psychological health of the principal caregiver with the General Health Questionnaire (GHQ)-30 (Goldberg and Williams, 1988). They found no significant improvement in caregiver GHQ score for the treated group. However, it should be noted that this trial also found no significant improvement in patient health for the treated group.

Six model-based studies used the estimates from two sources for the measurement and valuation of caregiver health benefits in their models: a cross-sectional study of 679 AD patient/caregiver pairs in the US by Neumann et al. (1999b), and an analysis of caregiver health data from donepezil trials by Getsios et al. (2010).

Neumann et al. (1999b) measured and valued caregiver health using the HUI2 with the Canadian population tariff values. They found that the caregiver utility scores did not change with patients’ Alzheimer’s disease stage and setting. Nonetheless, when this study was cited in subsequent model-based studies, the results were interpreted slightly differently in different studies. The models by Neumann et al. (1999a) and Weimer and Sager (2009) used the estimates from Neumann et al. (1999b): they used the same utility value for caregivers regardless of patient dementia severity however, they assumed a small increase in utility of caregivers when patients with severe dementia moved to a nursing home. The model by Bond et al. (2012) (UK HTA) also cited the study by Neumann et al., 1999b but their reported utility values for caregivers showed a steady decrease in caregiver utility when patient with dementia became more severe; noted that Bond et al. (2012) only included caregiver health in their sensitivity analyses.

Getsios et al. (2010) mapped caregiver’s SF-36 scores collected in donepezil trials onto a preference-based measure (the SF6D) (Brazier et al., 2002). The authors then used regression models to develop an equation that describes the relationship between the caregiver utility and other variables such as patient MMSE score, age, gender, etc. However, statistical information about their regression models and details about their methods were not published. Their
equation was cited in three model-based studies (Getsios et al., 2010, Getsios et al., 2012, Hartz et al., 2012) in this review.

4.4.5 How were costs and benefits aggregated?

To understand how costs and benefits were aggregated to make the decision, previous economic evaluation studies were grouped by the country where the evaluation was intended to serve. Afterwards, each study was examined to see how it came to conclusions about the cost-effectiveness of the intervention. Table 4.7 reports the distribution of studies according to their countries.
Table 4.7: Distribution of societal perspective studies by country of evaluation

<table>
<thead>
<tr>
<th>Country of the evaluation</th>
<th>Number of studies</th>
<th>% of total 62 studies</th>
<th>Studies stating a societal perspective</th>
<th>% of ‘societal perspective’ studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>14</td>
<td>23%</td>
<td>3</td>
<td>21%</td>
</tr>
<tr>
<td>US</td>
<td>12</td>
<td>19%</td>
<td>5</td>
<td>42%</td>
</tr>
<tr>
<td>Canada</td>
<td>10</td>
<td>16%</td>
<td>7</td>
<td>70%</td>
</tr>
<tr>
<td>Spain</td>
<td>4</td>
<td>6%</td>
<td>3</td>
<td>75%</td>
</tr>
<tr>
<td>Sweden</td>
<td>4</td>
<td>6%</td>
<td>1</td>
<td>25%</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>4</td>
<td>6%</td>
<td>3</td>
<td>75%</td>
</tr>
<tr>
<td>France</td>
<td>2</td>
<td>3%</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>Germany</td>
<td>2</td>
<td>3%</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>Japan</td>
<td>2</td>
<td>3%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Korea</td>
<td>2</td>
<td>3%</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>Belgium</td>
<td>1</td>
<td>2%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Finland</td>
<td>1</td>
<td>2%</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Norway</td>
<td>1</td>
<td>2%</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1</td>
<td>2%</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1</td>
<td>2%</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Multiple countries</td>
<td>1</td>
<td>2%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>100%</td>
<td>32</td>
<td>52%</td>
</tr>
</tbody>
</table>

Seven UK studies stated the adoption of a government health and social care perspective. Only four of them (57%) mentioned the range for cost-effectiveness thresholds (between £ 20,000 per QALY and £ 30,000 per QALY). One study (Jones et al., 2004) did not need a threshold because the intervention was found to save resources and produce more health benefits. The other two studies (Gustavsson et al., 2009, Ward et al., 2003) reached a conclusion about the
cost-effectiveness of their interventions without mentioning any threshold value although the interventions were estimated to bring more health benefits at additional costs.

Three UK studies stated the adoption of a societal perspective. They all reached conclusions in the base-case without the need for a threshold. Courtney et al. (2004) reached the conclusion without the need for a threshold because there was no difference in terms of costs or effectiveness between the intervention (donepezil) and the placebo. Getsios et al. (2010, 2012) concluded the intervention cost-effective because it saved costs and delivered more health benefits. Nevertheless, Getsios et al. (2010, 2012) still mentioned the cost-effectiveness threshold (£30,000 per QALY) when they reported Probability Sensitivity Analysis (PSA).

One UK study (Romeo et al., 2013) stated the adoption of both a government health and social care perspective and a broader perspective to include unpaid care (only patient health benefits were included). In the broader perspective, the incremental aggregated costs (including informal care) per QALY was compared with the same cost-effectiveness threshold (£30,000 per QALY). The other three UK studies (Stein, 1997, Stein, 1998b, Stewart et al., 1998) did not state a perspective. They did not provide conclusions about the cost-effectiveness of the interventions but just reported costs and effectiveness separately.

Among the 12 US studies, three studies adopted a payer perspective (excluding informal care), two studies adopted a broader perspective (including informal care beside health and social care), five studies stated the adoption of a societal perspective, and two studies did not state their perspective. For US studies in which a payer perspective was stated, two of them were Cost-Effectiveness Analysis and did not use any cost-effectiveness threshold (Migliaccio-Walle et al., 2003, Silverman et al., 2002). One study (Rosenheck et al., 2007) used two different estimated values of a QALY to compare health benefits with costs: $US 50,000 per QALY and $US 100,000 per QALY.

For US studies in which a broader perspective (including informal care) was stated, Kirbach et al. (2008) used the same threshold at $US 50,000 per QALY to determine the cost-effectiveness of the intervention when informal care cost was included and when it was not. Weimer and Sager (2009) on the other hand used the statistical value of a life year between $US 93,500 and $US 187,000 to compare the benefit of additional QALYs with costs.
For US studies in which a societal perspective was stated, two studies did not mention the use of any threshold (McMahon et al., 2000, Retchin and Hillner, 1994); two studies mentioned the threshold at $US 50,000 per QALY (Neumann et al., 1999a, Weycker et al., 2007); and one study mentioned the threshold at $US 100,000 per QALY (McMahon et al., 2003).

For the two US studies in which a perspective was not stated, one (Hauber et al., 2000b) did not mention the use of any threshold and the other (Simon and Lubin, 1985) mentioned the use of the threshold at $US 50,000 per QALY.

Among the 10 Canadian studies, two studies adopted the payer perspective; one study adopted a broader perspective (including informal care in addition to health and social care); and seven studies stated the adoption of a societal perspective. For studies in which a payer perspective was stated, Caro et al. (2003) just compared between different dementia drugs but did not specify any value for the CE threshold, whereas Getsios et al. (2001) mentioned a CE threshold of $US 30,000 per QALY. For the study in which a broader perspective was stated (Bermingham, 2014), study interventions were compared with one another based on their ICERs; no CE threshold was mentioned to determine the cost-effectiveness of interventions. For studies in which a societal perspective was stated, four studies (Bachynsky et al., 2000, Lachaine et al., 2011, O'Brien et al., 1999, Wong et al., 2009) did not mention the use of any threshold for cost-effectiveness; Hauber et al. (2000) and Gagnon et al. (2007) mentioned two values for a gain of 1 QALY: Can$20,000 and Can$ 100,000; Willan et al. (2006) used the range of thresholds between Can$ 50,000 per QALY and Can$ 100,000 per QALY when the Canadian price weights were applied and another range between £20,000 per QALY and £40,000 per QALY when the UK price weights were applied.

4.5 Discussion and conclusion

4.5.1 Summary of main findings

This chapter reviewed the methods of economic evaluation in 62 economic evaluation studies of pharmacological and diagnostic interventions in dementia. The review found most studies were model-based cost per QALY analysis. Very few studies were Cost Consequence Analysis and none of them reported the decision-making process after costs and consequences were presented to the decision makers. Adopting a societal perspective was considered necessary for
economic evaluation of dementia interventions. This was reflected in the majority of studies stating the adoption of a societal perspective and/or including informal care in their main analyses. However, the methods for economic evaluation taking a broader perspective were not clear.

A wide range of different costs were identified from the review. This included government (or third-party payer) healthcare, government (or third-party payer) social care, informal care, private payment for care, patient out-of-pocket expenses for seeking and receiving treatments, patient time in seeking and receiving treatments, patient productivity loss, costs to the voluntary sector, costs to the transportation sector, and costs to the legal sector. Their inclusion in societal-perspective studies varied substantially. There was no agreement on what wider costs should be included from a societal perspective. The most significant wider costs seemed to be informal care and private co-payment for care. They were also the wider costs that had evidence for their measurement and valuation. Other wider costs were either insignificant, specific to the intervention or their measurement and valuation were controversial. For example, dementia patients are often retired (65 years or older). Thus, their productivity loss due to dementia would not be significant in terms of paid income. It could be argued that they could still be productive in terms of unpaid work and voluntary work (Biasutti et al., 2012) however, the methods for measuring and valuing such unpaid work for productivity costs were still underdeveloped (Krol et al., 2013).

The review only identified two types of benefits mentioned in previous studies: patient health benefit and caregiver health benefit. Patient health benefit was measured by a wide range of different measures from health measures (e.g. clinical measures, dementia-specific HRQOL measures, and generic HRQOL measures) to accurate diagnoses, surgically treatable dementia cases identified, life years, years of independence, and QALYs. The QALY was the most commonly used measure for patient health. Among studies that used the QALY measure for patient health, the HUI (mark 2 or mark 3) was the most commonly used preference-based measure of HRQOL (56% of studies); the EQ5D was the second most commonly used (33% of studies).

In theory, the inclusion of caregiver health in benefits depends on how informal care is valued (van den Berg et al., 2004). Stated preference methods capture both the cost of informal care and the health benefit of the informal caregivers, whereas revealed preference methods only capture the cost of informal care (van den Berg et al., 2004). All studies in this review used
value of informal care that was derived from revealed preference methods, therefore it was necessary for them to include caregiver health benefit in their economic evaluation. However, the evidence of informal caregiver health benefit was limited. This review only found three studies (Neumann et al., 1999b, Courtney et al., 2004, Getsios et al., 2010) that provided the evidence for the caregiver health benefits.

In terms of aggregating costs and benefits to arrive at the final cost-effectiveness decision, this review found that equal weights were used for the aggregation of different costs when wider costs were included. The same was applied for benefits: equal weights were used when the health benefit of informal caregivers was included together with the patient health benefit. Furthermore, the aggregated cost and the aggregated benefit were compared by means of a cost-effectiveness threshold to determine the cost-effectiveness of an intervention. The value of the threshold was unfounded and arbitrary. It was often interpreted in previous studies as the Willingness-To-Pay for a unit of health rather than the opportunity costs of imposing the additional costs on the fixed budgets.

4.5.2 The decision problem for the case study

4.5.2.1 The selection of the problem

Early detection of dementia is a topical issue in dementia care. Timely diagnosis has consistently been a top priority in recent policies for dementia care in the United Kingdom (UK) (DH, 2015) and around the world (Prince et al., 2011, World Health Organisation, 2012).

The National Dementia Strategy (NDS) was launched in England in 2009 highlighting the issue of under-diagnosis in dementia and setting the objective to improve dementia diagnosis rates (Health & Social Care Information Centre, 2014). As a result of the NDS, more and more people have been diagnosed with dementia (Mukadam et al., 2014). This implied an increase in the number of cognitive-impairment cases assessed and referred by GPs. Timely diagnosis for people with dementia in England is related to the performance of primary care teams detecting people with dementia with a degree of accuracy and referring them to memory services. However, evidence suggests that it was difficult for GPs to identify those with Mild Cognitive Impairment (MCI) and mild dementia (Mitchell et al., 2011). In their meta-analysis, Mitchell et al. (2011) found that the accuracy of GP clinical judgement (unassisted) was low.
in detecting dementia, especially those in the early stages of dementia or those with pre-dementia MCI.

A recent survey\(^2\) found 29% of GPs in the UK used the 6CIT, 26% used the MMSE, and 21% used the GPCOG to assess patients with cognitive impairment. However, there has not been any economic evaluation study comparing the cost-effectiveness of GPs using different cognitive screening tests in the UK. Hence, this evaluation problem was chosen for the case study in this thesis. The case study compares the cost-effectiveness of alternative options for GPs in assessing patients with cognitive impairment: (1) GP unassisted judgement, (2) GP using the MMSE, (3) GP using the 6CIT, and (4) GP using the GPCOG.

4.5.2.2 Included costs and benefits

Based on the review in this chapter, a list of costs and benefits was specified for the decision problem. Costs included health care, social care, private payment for care, and informal care. Benefits included patient health and caregiver health. Productivity costs were not included because the methods for their measurement and valuation were controversial (Krol et al., 2013). In addition, productivity costs would not be significant in dementia given the high proportion of retired age (65+) in the cohort (Knapp et al., 2007). Other wider costs were not included because they were either insignificant or the evidence for their measurement and valuation was not readily available. Non-health benefits were also not included because of the lack of available data. The QALY was chosen to be measure health benefit for patients and their caregivers. Regarding the HRQOL measure used for calculating the QALY, the EQ-5D was preferred over the HUI as recommended by NICE (NICE, 2013a).

4.5.3 Conclusion

The importance of adopting a societal perspective for economic evaluation of interventions in dementia care was confirmed by the review in this chapter. There was a gap in the methods for economic evaluation taking a societal perspective in dementia care. It was not clear how a societal perspective could be implemented in economic evaluation. To proceed with the case study in dementia, a decision problem was specified. The decision problem concerns with the cost-effectiveness of alternative options for GPs in assessing patients with cognitive

\(^2\) The survey was conducted by us in the GP section of an online forum for doctors in the UK (www.doctors.net.uk)
impairment. Costs include health care, social care, private payment for care and informal care. Benefits include health benefit for patients and health benefit for informal caregivers. A new cost-effectiveness model was required to provide estimates for the costs and benefits for alternative options. The next Chapter (Chapter 5) reports another systematic review to support the model development and Chapter 6 reports the development of the model itself and its estimates for costs and benefits of alternative decision options.
CHAPTER 5. SYSTEMATIC REVIEW TO SUPPORT THE DEVELOPMENT OF A DEMENTIA MODEL

The aim of this study was to review previous model-based economic evaluation studies to inform the development of a new cost-effectiveness model for evaluating alternative options for GPs to detect patients with cognitive impairment early. Compared to the review in Chapter 4, this systematic review had a narrower scope that focused only on modelling aspects in previous model-based economic evaluation studies.

The chapter is divided into four sections. Section one gives background information for cost-effectiveness modelling in dementia in general. Section two describes the methods of the review. Section three reports the results. Section four discusses and concludes the chapter.
5.1 Background

5.1.1 Natural disease of dementia

The main feature of the natural clinical progression of dementia is a progressive cognitive decline (Prince et al., 2011). This is illustrated in Figure 5.1.

Figure 5.1: Natural disease progression in dementia

The progressive cognitive decline is caused by structural and chemical changes in the brain (Knapp et al., 2007). When this happens, patients start losing their ability in memory, reasoning, communication skills, and other skills needed to perform daily activities. Finally, they lose their independence and may have to move to a nursing home.

The development and progression of dementia in general can be described in four clinical stages: mild cognitive impairment (MCI), mild dementia, moderate dementia, and severe dementia. After the onset of brain pathology, symptoms and signs of cognitive impairment start appearing. As the brain pathology develops, symptoms and signs of cognitive impairment also progress. MCI requires the presence of subjective memory impairment and cognitive impairment that does not meet dementia diagnostic criteria (i.e. with no impairment on core activities of daily living) (Prince et al., 2011). When cognitive impairment meets dementia diagnostic criteria, depending on the level of severity, the dementia condition can be categorised into stages such as mild, moderate, or severe.
5.1.2 Cost-effectiveness modelling for dementia interventions

The nature of the modelling task is to develop algorithms/equations that can describe how the disease(s) and interventions affect individuals (patients and other people) and resources (public and/or private). Taking the example of dementia, the first step is to understand the natural disease progression of dementia and describe that using mathematical equations. We want to know the relationship between the disease severity and time.

For dementia, ideally we want to model the biological/pathological changes in the brain that leads to the clinical deterioration of symptoms in dementia. However, this approach is too ambitious. It requires a confirmed pathology of the disease and available data linking the pathology with clinical symptoms. This is not yet available in dementia.

An alternative modelling approach is to model the clinical manifestation of the underlying pathological changes for dementia. This includes the cognitive functioning of the brain, the behavioural functioning of the brain, the abilities to perform activities, and the overall/global health. We want to model how they change with time given characteristics such as age, gender, and the presence of other diseases.

The second step is to identify, understand and include important/relevant events that would change the natural disease progression and resources. For example, important events in a dementia model would include having a diagnosis, receiving treatments/interventions, admitted to hospitals, moving to a care home, or death. The third step is to link the natural disease progression and events with outcomes. Then, the model is able to produce estimates of costs and benefits for different intervened scenarios. The following sections report a systematic review looking at these aspects of modelling in previous model-based economic evaluation studies in dementia.
5.2 Review methods

5.2.1 Identification and selection of studies

The systematic search in Chapter 4 identified 62 economic evaluation studies: 53 model-based studies; two studies were just simple calculations and seven studies were EEACTs. The 53 model-based studies were included for the review in this chapter.

5.2.2 Data extraction

The extraction of information from previous model-based studies focused on the following aspects in developing a cost-effectiveness model:

- Modelling disease progression
- Modelling interventions
- Linking the disease progression and the interventions with costs
- Linking the disease progression and the interventions with QALYs

Information was extracted using a data extraction form (Table 5.1).

Table 5.1: Data extraction form

<table>
<thead>
<tr>
<th></th>
<th>First author</th>
<th>1</th>
<th>Year</th>
<th>2</th>
<th>Country of the evaluation</th>
<th>3</th>
<th>Intervention (s)</th>
<th>4</th>
<th>Patient population</th>
<th>5</th>
<th>Are caregivers modelled? And how?</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First author</td>
<td>6</td>
<td>Year</td>
<td>7</td>
<td>Country of the evaluation</td>
<td>8</td>
<td>Intervention (s)</td>
<td>9</td>
<td>Patient population</td>
<td>10</td>
<td>Are caregivers modelled? And how?</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Year</td>
<td>7</td>
<td>Country of the evaluation</td>
<td>8</td>
<td>Intervention (s)</td>
<td>9</td>
<td>Patient population</td>
<td>10</td>
<td>Are caregivers modelled? And how?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Country of the evaluation</td>
<td>8</td>
<td>Intervention (s)</td>
<td>9</td>
<td>Patient population</td>
<td>10</td>
<td>Are caregivers modelled? And how?</td>
<td></td>
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<tr>
<td>4</td>
<td>Intervention (s)</td>
<td>9</td>
<td>Patient population</td>
<td>10</td>
<td>Are caregivers modelled? And how?</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5</td>
<td>Patient population</td>
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<td>Are caregivers modelled? And how?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

5.2.3 Synthesis of extracted evidence

Although there were 53 model-based economic evaluation studies, many of them were adaptations of an original model. Many studies just re-applied a previous model in different settings. For example, the AHEAD model (Caro et al., 2001) was used in seven economic
evaluation studies in the Netherlands, Australia, Canada, Sweden, the US, and the UK. Overall, there were 21 different models that were used in 53 model-based economic evaluation studies: 17 models were for economic evaluations of pharmaceutical interventions and four models were for economic evaluations of screening or diagnostic interventions. If the model in a study was an adaptation of a previous model, only the information about the original model was extracted and analysed (not the adapted model). Narrative analysis was used to synthesise the evidence base, supported by the data extraction form and previous systematic reviews.

5.3 Results

5.3.1 Modelling disease progression

Due to the nature of the problem, the disease progression was modelled differently in models that looked at diagnostic or screening interventions compared with those looked at pharmaceutical interventions. The models for diagnostic and screening interventions needed a broader scope for the intervened population and the disease progression. Therefore, this review dealt with two groups of models separately: models for pharmaceutical interventions (39 studies) and models for diagnostic/screening interventions (14 studies).

5.3.1.1 Models for pharmaceutical interventions

Previous models for pharmaceutical interventions were categorised into four groups: decision tree models, traditional state-transition models, transition to Full-Time-Care (FTC)/institutionalisation models, and models that directly simulated the declining rates of specific clinical measures. The categorisation of 39 model-based studies for pharmaceutical intervention is illustrated in Table 5.2. Note that Gustavsson et al. (2009) developed three different models in their study, therefore their study appeared in three modelling groups.
Table 5.2: Previous model-based studies for pharmaceutical interventions

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<th>Model Group</th>
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<td>2004</td>
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<tr>
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<td>2010</td>
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<td>2012</td>
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<td>Nagy</td>
<td>2011</td>
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</table>
a) Decision Tree:

At the simplest level, decision tree models were used to describe the outcomes of the disease over a certain period of time. Only one study (Wong et al., 2009) used this approach. The model was very basic looking at adverse events when treating vascular dementia with medication over a period of 24-28 weeks. The adverse events included discontinuation, nausea, vomiting, diarrhoea, anorexia, and insomnia.

b) Traditional State-Transition Models:

The traditional state-transition models described the natural disease progression in terms of the movement between mutually exclusive health states. The simulated patient could only be in one health state at a time. There were 21 studies that belonged to this group of modelling method however, many of them were just the adaptation of an original model in different contexts (see Table 5.2)

The health states that were used in these models included transition states between different levels of disease severity (e.g. mild, moderate, and severe), dependency transitions, and institutionalisation transitions. Severity transitions described the movement from one disease severity level to another. Dependency transitions described the movement from being independent to being dependent. Institutionalisation transitions described the movement from community to care homes.

Stewart et al. (1998) described the disease severity progression in four states corresponding to patient MMSE scores: minimal (MMSE > 21), mild (MMSE between 15 and 20), moderate (MMSE between 10 and 14), and severe (MMSE <10). Dependency transitions and institutionalisation transitions were not modelled. Six-month transition probabilities were based on observations from a 24-week RCT of donepezil in patients with AD (Rogers et al., 1998). The annual probability of death was estimated based on previous research on long-term survival among AD patients in England (Burns, 1996, Burns and Förstl, 1996).

Neumann et al. (1999) described the disease severity progression in three states corresponding to the Clinical Dementia Rating (CDR) scale: mild, moderate, and severe. For each severity state, the authors also modelled the transition from community to nursing homes (institutionalisation transitions). Dependency transitions were not modelled. Annual transition probabilities including probability of death were estimated using data from the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD), a longitudinal database of 1,145
dementia patients in the US between 1986 and 1995. The model used 6-week transition probabilities which were calculated by taking the 6/52 root of the annual probabilities (Neumann et al., 1999a).

Jonsson et al. (1999) described the disease severity progression in five states corresponding to patient MMSE scores: state 1 (MMSE score between 30 and 27), state 2 (MMSE score between 26 and 21), state 3 (MMSE score between 20 and 15), state 4 (MMSE score between 14 and 10), and state 5 (MMSE score between 9 and 0). Dependency transitions and institutionalisation transitions were not modelled. The 3.32-year transition probabilities (including probability of death) were estimated using data from the Kungsholmen project, a longitudinal observational study of 1810 persons aged 75 years or older living in Sweden between 1987 and 1992. The model itself used half-year transition probabilities calculated from the 3.32-year transition probabilities.

Similar to the Jonsson (1999) model, O’Brien (1999) also described the disease severity progression in five states corresponding to patient MMSE scores: MMSE 27-30, MMSE 21-26, MMSE 15-20, MMSE 10-14, and MMSE <10. Dependency transitions and institutionalisation transitions were not modelled. Six-month transition probabilities were based on observations from the same 24-week RCT of donepezil (Rogers et al., 1998) as used in the Stewart’s model. Probability of death was assumed to be independent of a person’s MMSE score and treatment; the rate was estimated based on a 5-year survival rate reported in previous research in Canada (Hogan et al., 1994).

Focusing on the moderately severe to severe AD population, Jones et al. (2004) described the disease severity progression in three states corresponding to patient MMSE scores: moderate (MMSE >14), moderately severe (MMSE between 10 and 14), and severe (MMSE<10). The 6-month severity transition probabilities were estimated based on observations from a 28 weeks RCT of memantine (Reisberg et al., 2003). Dependency transitions were modelled to depend on disease severity, dependency at the beginning of the cycle, and treatment. The dependency level was defined as the ability to perform daily tasks as measured by the ADCS-ADL scores. The dependency transition probabilities were estimated based on two sources of data: the memantine RCT (Reisberg et al., 2003) and the London and South-East Region (LASER) Study, a longitudinal study of AD patients and their caregivers in the UK over a 6-month period (Livingston et al., 2004). Institutionalisation transitions were modelled to depend on disease severity and treatment; the transition probabilities were estimated from the LASER study and
the memantine RCT. Death probabilities were assumed to be dependent on disease severity and independent of treatments; the rates were estimated based on data from the UK epidemiological study (Livingston et al., 2004).

Lachaine et al. (2011) did not model severity transitions or dependency transitions. Their model only specified two health states: non-institutionalised and institutionalised. The annual transition probabilities were estimated from an observational study comparing admission to a nursing home between a patient group who received a ChEI alone (n=289) and a patient group who received a ChEI plus memantine (n=140) over a period of up to 7 years (Lopez et al., 2009). Probability of death was estimated using the Canadian life tables adjusted for death specifically caused by AD.

Skoldunger et al. (2013) described the disease severity progression in four states corresponding to patient MMSE scores: MCI, mild (MMSE between 18 and 23), moderate (MMSE between 10 and 17), and severe (MMSE between zero and 9). Dependency transitions and institutionalisation transitions were not modelled. The transition probabilities including mortality were estimated based on data from the Kungsholmen project in Sweden (Fratiglioni et al., 1992).

Gustavsson et al. (2009) in their Markov model described the disease severity progression in four states corresponding to patient MMSE scores: MMSE between 30-21, MMSE between 20-15, MMSE between 14-10, and MMSE between 9-0. Transition probabilities were estimated from the Swedish Alzheimer Treatment Study (SATS) (Wallin et al., 2007). The annual risk of death was assumed to be a constant (11.2%) following the NICE model in 2006 (Loveman et al., 2006). This figure (11.2%) was based on a historic prospective study in the US of 202 patients with dementia matched with 202 non-demented controls (Martin et al., 1987).

c) Transition To Full-Time-Care (FTC)/institutionalisation Models:
Three models belonged to this group: the first one was the AHEAD model developed by Caro et al. (2001), the second one was developed by Rive et al. (2010) using the same concept but different predictive equations, and the third one was the NICE model (Bond et al., 2012b).

AHEAD stands for Assessment of Health Economics in Alzheimer’s Disease. The original framework for developing an AHEAD model was reported in 2001 by the AHEAD Study Group at Caro Research Institute, Canada (Caro et al., 2001). This modelling framework was
proposed given the limitations of previous modelling methods as noted by the authors: the difficulty of translating a change in score (i.e. MMSE) into a meaningful outcome, and previous models relied only on changes in cognitive function for disease progression and ignored some important patient characteristics and other measures of functioning (i.e. behavioural symptoms, activities of daily living) (Caro et al., 2001).

In the AHEAD modelling framework, the patient natural disease progression was described as a transition from not requiring Full Time Care (FTC) to requiring FTC. Patients also had a risk of death at any point. The authors stressed that the need for FTC was not the same as institutionalisation; patients who progressed to the FTC stage could still be cared for in community setting. The move to FTC was assumed to be irreversible (similar to being dead). The transition to FTC was modelled as a function of time and several patient characteristics including the presence of psychotic symptoms, duration of illness, a young age at disease onset (<65 years old), extrapyramidal symptoms (EPS), and cognitive function measured by the modified Mini-Mental State Examination (mMMS) score. The risk of death was dependent on sex, EPS, mMMS, duration of illness, and age. For each set of patient characteristics, an index was computed; based on this index, the hazard function over time was estimated for the risk of requiring FTC and the risk of death. The monthly hazard rate was then used to model the monthly transition probability from pre-FTC to FTC and the death transition for the patient cohort. The main data source for the predictive equations used in the AHEAD model was from a published study (Stern et al., 1997) that predicted time to nursing home care and death based on observation of a cohort of 236 patients with AD in the US over a period of up to 7 years. Institutionalisation transition was not modelled as a separate state. Instead, distribution of location of care was integrated into the main health states. For example, 85% of patients in the FTC state was assumed to live in nursing homes.

Caro et al. (2001) only reported the modelling framework for the AHEAD model. Our review here identified nine subsequent studies that applied the model to real populations (see Table 5.2); three of them (Ward et al., 2003, Loveman et al., 2006, Gustavsson et al., 2009) were UK studies.

Despite using the same concept of modelling the natural disease progression in terms of the transition from pre-FTC to FTC, Rive et al. (2010) developed different predictive equations for transition probabilities from a different source of data. They predicted the monthly probabilities of reaching FTC state from cognitive measure (ADAS_cog), functioning measure
(ADCS_ADL) and behavioural measure (NPI). The data source was from the LASER-AD, a UK longitudinal epidemiological study of 117 patients over 54 month follow-up period (Livingston et al., 2004). The monthly death probability only depended on the time since the model started; it was also estimated based on data from the LASER-AD study. The same model was adapted for the population in Norway in another study by the same author (Rive et al., 2012).

In the NICE cost-effectiveness model for the appraisal of AD medications, Bond et al. (2012) used a similar structure that models the disease progression in terms of the transition from pre-institutionalisation to institutionalisation. They used the concept of institutionalisation defined as ‘living in a residential home or a nursing home (not as short respite care) or in hospital on a long-term or permanent basis’; this was different from the concept of FTC above. The transition from pre-institutionalisation to institutionalisation of the cohort was modelled using an equation that describes time to end of pre-institutionalisation. The transition to death was modelled using an equation that describes time to death. Both time to end pre-institutionalisation and time to death were dependent on MMSE score at entry, Barthel ADL Index score at entry, and age at entry. The equation was estimated from patient-level data of 92 individuals from a longitudinal observational study in the UK (Wolstenholme et al., 2002).

d) Models that simulate the declining rates of specific clinical measures

In this group of models, the natural disease progression was described directly by how its clinical measures changed over time. For example, how patient MMSE scores (reflecting their cognitive function) changed with time.

In 1999, Fenn and Gray used survival analysis to predict how patient MMSE score changes with time (Fenn and Gray, 1999). For example, we could model time to a reduction in MMSE score of x points (x could be 1,2,3,4 or 5) using data from clinical trials or observations studies. Fenn and Gray (1999) used patient-level data from two 26-week clinical trials of rivastigmine (Corey-Bloom et al., 1998, Rosler et al., 1999) to estimate the hazard functions for a drop in MMSE score at a given point in time for a patient with their age and baseline MMSE score.

Hauber et al. (2000) applied the Fenn and Gray method to describe the cognitive progression in their model however, they added another statistical model to estimate the probability of institutionalisation for each MMSE score using data from the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) (Hauber et al., 2000b). Mortality was not modelled
since the authors limited their study to 2-year time horizon. The same model was used again in another study in Canada by the same author (Hauber et al., 2000a).

Weycker et al. (2007) described the disease progression in moderate-to-severe AD using a statistical model that predicted change over time in cognitive function measured by the Severe Impairment Battery (SIB) (Weycker et al., 2007). The SIB is a 40-item measure of cognitive function with score range between 0 and 100 where lower scores representing worse levels of cognitive function. The authors used data from a US observational study of 180 moderate-severe AD patients over a 1-year period (Schmitt et al., 1997). In order to link the change in SIB score with other data for costs and HRQOL which were based on MMSE, they mapped from SIB to MMSE using the same data from (Schmitt et al., 1997). For the risk of institutionalisation, Weycker et al. (2007) adapted the data from Neumann model (Neumann et al., 1999a) for the relationship between disease severity and the probability of institutionalisation. Risk of death for AD patients was estimated by multiplying age- and sex-probabilities of death for the general population by relative risk of death for people with AD (compared with no AD). The risk of death for the general population was estimated from the US life tables, whereas the relative risk of death for people with AD was taken from a previous study in the US (Evans et al., 1991).

Gustavsson et al. (2009) in their micro-simulation model described the disease progression in terms of the decline over time in cognitive function and functional ability. The predictive equations were derived from data from the Swedish Alzheimer Treatment Study. Cognitive decline was found to be conditional on previous progression. Functional ability was found to be conditional on present cognitive function, six-month cognitive decline duration of illness, and gender. The risk of institutionalisation was estimated from the Kungsolmen project (KHP) (Fratiglioni et al., 1992) dependent on cognitive function, functional ability, and age. The paper did not give details about the particular analyses or developed equations; it just mentioned “data on file”.

Getsios et al. (2010) in a discrete event simulation (DES) described the disease progression in three clinical aspects of AD: Cognitive function (measured by MMSE); behavioural symptoms (measured by the Neuropsychiatric Inventory (NPI)); and functional ability (measured by ADL and IADL. The predictive equations were developed using data from the CERAD study and donepezil’s clinical trials (Getsios et al., 2010). The cognitive declining rate was dependent on the previous declining rate, the previous MMSE score, age, and treatment. The rate of change
for NPI was dependent on treatment, weeks of follow-up in the simulation, baseline NPI, previous NPI, race (black or white), presence of psychiatric medications at baseline, baseline MMSE, previous MMSE, and age. The rate of change for ADL was dependent on treatment, weeks of follow-up in the simulation, presence of psychiatric medications at baseline, race, baseline ADL, previous ADL, baseline MMSE, previous MMSE, and age. The rate of change for IADL was dependent on treatment, weeks of follow-up in the simulation, presence of psychiatric medications at baseline, race, baseline IADL, previous IADL, baseline MMSE, previous MMSE, and gender. The authors used age and sex-specific survival data from the MRC CFAS (Medical Research Council Cognitive Function and Aging Study) (Xie et al., 2008) to construct an equation to predict time to death for people with dementia according to their age and gender.

Nagy et al. (2011) modelled the disease progression in terms of the decline over time of patient cognitive function measured by the MMSE. For the short-term decline (first 12 months), they used data from the IDEAL (Investigation of transdermal Exelon in Alzheimer’s Disease) study (Winblad et al., 2007, Grossberg et al., 2009). For the longer-term decline (after 12 months) they used a published equation by Mendiondo et al. (2000) who used the CERAD database of 719 AD patients (up to 7 years follow-up) to estimate a predictive equation for the time to 1-point MMSE decline (in years); the quadric equation showed the MMSE score declined in a non-linear fashion dependent on previous MMSE score. Nagy et al. (2011) also integrated a probability of institutionalisation into the disease progression. They specified and applied two different equations for the probability of institutionalisation: one being dependent only on MMSE score using UK data from (Martin et al., 1987), the other being dependent on MMSE score and ADCS-ADL using a UK published equation (McNamee et al., 2001) and a mapping equation between the Townsend-ADL and ADCS-ADL (Rozsa et al., 2009). The authors used a constant risk of death (11.2%) in their model; the figure was from a US study (Martin et al., 1987).

5.3.1.2 Models for diagnostic/screening interventions

This review identified 14 model-based studies that looked at the evaluation of diagnosis or/screening interventions. These models were categorised into three groups: decision tree cohort models, state-transition/Markov cohort modes, and individual-level simulation models. The categorisation of these model-based studies is illustrated in Table 5.3.
**Table 5.3: Previous model-based studies for diagnostic/screening interventions**

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<th>Year</th>
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<th>Original Model</th>
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<td>Spain</td>
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</table>

*a) Decision tree cohort models:*

Simon and Lubin (1985) evaluated different diagnostic interventions for a hypothetical cohort of individuals aged 60, 70, or 80 presenting with a dementing illness but without the historical, physical, and laboratory findings. The diagnostic examination was one-time/one-off only (i.e. not repeated). They used a decision tree to describe different outcomes of a diagnostic intervention (e.g. false negative, positive primary brain tumour, irreversible dementia, etc.) followed by long-term outcomes of the disease (e.g. survive, die, continued dementia, etc.).

Silverman et al. (2002) evaluated the fiscal outcomes of different diagnostic strategies using decision tree analysis with the help of the software Data 3.0 (TreeAge Software, Inc., Williamstown, MA, US). It was not clear from their paper whether the diagnostic examination was repeated or just one-off. The structure for modelling long-term disease progression was also not clear. The same model was applied again in (Moulin-Romsee et al., 2005).
Valcarcel-Nazco et al. (2014) also used a simple decision tree model to assess the cost-effectiveness of the use of cerebrospinal fluid (CSF) biomarkers to diagnose AD in MCI and dementia patients. The treatment for diagnosed AD was donepezil. The authors assumed the same health outcomes (QALYs) of the two scenarios (with and without the early diagnosis) stating the reason that donepezil did not have any impact on patient survival; thus, they ignored the impact of treatments on patient quality of life. Based on that assumption, the authors only compared the costs and number of accurate diagnosis between the two scenarios. Their decision tree model simply described outcomes of AD diagnosis in terms of positive (true or false) and negative (true or false) AD diagnosis: positive diagnosis was treated as AD and negative diagnosis was treated as not AD. No other features of disease progression were mentioned.

b) State-transition/Markov cohort models:

Retchin (1994) evaluated different repeated screening programmes to detect dementia in older drivers in the US. The author used a Markov cohort modelling approach. The cohort included elderly drivers 65 years old being followed until death or reached age 90. Each Markov cycle was one year. The cohort started in a ‘well state’ and full driving privileges. They had a probability of developing dementia in each year depending on their age. They also had a probability of motor vehicle crash per year depending on their dementia status, and a probability of death per motor vehicle crash depending on their age.

McMahon et al. (2000) evaluated different diagnostic strategies for a cohort of patients suspected to have AD and referred to a tertiary AD clinic in the US. The diagnostic examination was one-time only. They used and extended the Markov model developed by Neumann et al. (1999) for describing the diagnostic outcomes and disease progression. Four disease states were specified: no AD, mild AD, moderate AD, and severe AD. The transition probabilities between mild AD, moderate AD, and severe AD were taken from Neumann et al. (1999). Institutionalisation transition (from community to nursing home) was also modelled in the same way as Neumman et al. (1999). The ‘no AD’ state was added due to the broader scope of the diagnostic interventions however, there was no transition from the ‘no AD’ state to AD states. The probabilities of death for mild AD, moderate AD, and severe AD were taken from Neumann et al. (1999), whereas the probability of death for no AD was estimated from the US Life Tables. All patients went through the diagnostic strategies at the beginning. Depending on the sensitivity and specificity of the diagnostic strategy, they received a diagnosis of probable
AD. All patients with a diagnosis of AD received treatment, whereas those without a diagnosis did not. The same model was applied again in (McMahon et al., 2003).

Biasutti et al. (2012) evaluated different screening and diagnostic strategies for early diagnosis of AD. They also used an extended version of the Markov model developed by Neumann et al. (1999) for describing the disease progression. Five disease states were specified: no AD, early AD (asymptomatic), mild AD, moderate AD, and severe AD. The transition probabilities between mild AD, moderate AD, and severe AD were taken from Neumann et al. (1999). The transition probabilities from ‘no AD’ to AD were estimated based on combined evidence from previous studies (Helmer et al., 2001, Bowen et al., 1997, Drago et al., 2011). Transitions from ‘no AD’ to ‘early AD’ and from ‘early AD’ to AD were estimated based on the authors’ personal communication with an expert in the field. Institutionalisation transition probabilities for diagnosed AD (mild, moderate, and severe) were taken from Neumann et al. (1999), whereas the data for diagnosed ‘no or early AD’ or undiagnosed individuals were from a study that reported the transition into a nursing home in old age using survey data from Germany and US (Himes et al., 2000). The probabilities of death for mild AD, moderate AD, and severe AD were taken from Neumann et al. (1999), whereas the probability of death for ‘no AD’ and ‘early AD’ was estimated from the French Life Tables.

Bermingham (2014) developed a Markov model to assess the cost-effectiveness of different imaging strategies for the diagnosis of people with suspected dementia who had already been assessed by standard criteria (without imaging) in Canada. The hypothetical population for the model included people with mild to moderate dementia as diagnosed by standard criteria. It should be noted that the Bermingham model was the only model identified in this review that modelled multiple types of possible diagnostic outcomes for dementia: Alzheimer’s disease (AD), vascular dementia (VaD), mixed dementia (AD and VaD), normal-pressure hydrocephalus, subdural hematoma, and brain tumour. Only the aspects for AD, VaD, and mixed dementia are discussed here. The natural progression for each disease was different, therefore, it was described in different state-transition structures. For the natural progression of AD, the author used the Neumann model (Neumann et al., 1999a). For the natural progression of VaD and mixed dementia, the additional feature of this disease compared to AD was the risk of stroke and recurrent stroke. Thus, the author integrated more states to the AD model to account for strokes: past stroke, recurrence of stroke, and post-stroke. The institutionalisation transition was accounted for in both models by assuming 50% moderate dementia, and 86%
severe dementia patients stay in nursing homes (all mild dementia was assumed to be in community). The risk of death in the AD model was taken from the Neumann model. The risks of death in the VaD and mixed dementia model were estimated based on the relative risk of death in people with VaD/mixed dementia compared with AD; the impact of recurrent stroke on death was accounted for by adding the 90-day mortality following a stroke in the model.

Yu et al. (2015) extended the Markov model developed by Neumann et al. (1999) for the evaluation of a one-off national opportunistic screening programme for dementia in Korea. The extension was the inclusion of people without dementia in the cohort. Without the screening programme, people with undiagnosed dementia would be diagnosed 2 years after they enter the model, whereas people without dementia would have their dementia onset according to data about incidence rate and then have their diagnosis 2 years after onset. With the screening programme at the beginning of the model, people without a diagnosis would be diagnosed earlier (before 2 years). Individuals were given AD treatment (donepezil) once they had been diagnosed.

Hornberger et al. (2015) developed a Markov model to assess the cost-effectiveness of adding florbetapir-PET to the standard clinical evaluation of AD in Spain. Since the intervention had better sensitivity and specificity compared to the comparator, it led to earlier diagnosis of AD and hence earlier initiation of treatments (AD medications). Early treatments would deliver more benefits to patients in terms of cognitive improvement and delay time to care home. The disease progression was described in health states characterised by levels of cognitive function measured by the MMSE (mild, moderate, severe) and location of care (community or nursing home). The relative risk of death for AD patients in community was from a French study (Helmer et al., 2001), whereas the figure for AD patients in nursing home was from another study in Australia (Harris et al., 2010).

c) Individual-level simulation models:
Weimer and Sager (2009) evaluated the costs and benefits of early identification and treatment of AD for a hypothetical cohort of patients in the US. The cohort was modelled to start by going through a screening and diagnosis programme for early identification (Boustani et al., 2005). The identification of AD patients was based on the results from a study by Boustani et al. (2005) who screened 3,340 patients aged 65 and older receiving primary care services in a health service centre in the US. Weimer and Sager described the natural disease progression by assigning a random annual MMSE decline to patient MMSE score. For example, the annual
MMSE decline without treatment for a patient was drawn from a normal distribution with a mean of 3.5 and a standard deviation of 1.5 with negative truncation. The authors claimed the figures consistent with findings from (Matthews et al., 2000, Small et al., 2005, Sabbagh et al., 2006). Institutionalisation was modelled using an annual institutionalisation risk by MMSE, sex, age, and marital status based on estimated models by Hauber et al. (2000). Death was modelled using an annual survival probability by age and sex based on the US life tables; for AD patients, a 2.1 hazard rate was applied based on a previous study (Fitzpatrick et al., 2005).

Getsios et al. (2012) extended their previous Discrete Event Simulation (DES) model (Getsios et al., 2010) to evaluate the cost-effectiveness of early assessment for AD in the UK. The early assessment intervention was an annual assessment of patients reporting memory complaints and aged 65 to 100 years. The assessment was assumed to be 100% accurate. In terms of the natural disease progression, patients were assumed to enter the model after onset of disease. Each patient was assigned a time to assessment which determines when they would have their assessment for AD. Other details about the disease progression were similar to their model in 2010 (Getsios et al., 2010) which has been reviewed above.

Handels et al. (2015) developed an individual-level simulation model to assess the cost effectiveness of using cerebrospinal fluid-specific AD biomarkers in MCI. The simulated cohort included 2000 incident MCI patients in a memory clinic setting. Each individual in the cohort was quadruplicated for four diagnostic scenarios: one was the current practice strategy, the other three were different intervention strategies. Once a patient had been diagnosed with AD, they were given a hypothetical Disease Modifying Treatment (DMT) that would delay dementia progression. There were two types of disease progression in the model. The first one was the progression from MCI to dementia (time from MCI dementia). The second one was the progression in dementia which was described by the annual change in cognition measured by the MMSE and activity of daily living measured by Katz score. The authors used data from the Kungsholmen Project (Handels et al., 2013) to construct an equation to predict time from MCI to dementia, and two other equations to predict the progression of MMSE and the progression of the Katz score. Time from MCI to dementia was dependent on gender. The progression of MMSE was dependent on age. The progression of Katz score was dependent on MMSE score, age, and years of formal education. Institutionalisation transition was not modelled. The risk of death was estimated from the Dutch life tables. The risk of death was not
adjusted in the event of receiving a dementia diagnosis to avoid lead-time bias (Handels et al., 2015).

5.3.2 Modelling interventions

This review looked at the modelling aspects of two types of interventions: screening/diagnostic interventions, and pharmacological interventions.

5.3.2.1 Modelling screening and diagnostic interventions:

The detection of dementia often involves two stages of assessment: a screening stage and a more comprehensive examination stage. The screening stage can be initiated by a screening programme or by patients who present themselves with symptoms of dementia. The screening stage involves initial/basic clinical assessment and/or screening tests (including gene testing) which can be performed by normal healthcare staff, whereas the more comprehensive examination needs to be performed by specialists and involves more diagnostic tests to identify dementia and its causes more accurately. Only when patients receive a formal diagnosis of dementia, they can start receiving dementia-specific treatments and benefiting from them.

Screening and diagnostic interventions aim at improving the accuracy of dementia diagnosis. The accuracy of a diagnostic tool is described by its sensitivity and specificity. They are the two important parameters in modelling screening and diagnostic interventions. The main health benefit of screening/diagnostic interventions is due to early access to treatments.

This review identified nine studies (Simon and Lubin, 1985, McMahon et al., 2000, McMahon et al., 2003, Moulin-Romsee et al., 2005, Bermingham, 2014, Valcarcel-Nazco et al., 2014, Hornberger et al., 2015, Handels et al., 2015) that looked at specific diagnostic interventions and five studies that looked at screening interventions or non-specific diagnostic interventions.

Regarding the nine studies assessing specific diagnostic interventions, the intervention was specific including CT scan, MRI scan, CSF test, diagnostic guidelines, etc. The population included people in a clinic setting. The interventions were distinguished in terms of their sensitivity and specificity in detecting the disease.

Regarding the five studies assessing screening interventions or non-specific diagnostic interventions, the way they modelled the intervention is discussed below.
Retchin and Hillner (1998) looked at a repeated screening programme (using the MMSE) by the department of motor vehicles for dementia among older drivers (65 years or older) in the US; people with positive screened results were referred to have a comprehensive examination by specialists. The screening programme was assumed to have the sensitivity and specificity of the MMSE: sensitivity (0.85) and specificity (0.85). The specificity of the comprehensive evaluation was (0.995). The authors also assumed a 5% probability of finding a reversible component to a dementing illness.

Yu et al. (2015) looked at a one-off national screening programme (using the MMSE) for people aged 60 years or older in Korea; people with positive screened results were referred to have a comprehensive examination by specialists. The sensitivity and specificity of the screening programme (MMSE) were 0.818 and 0.805 respectively, whereas those of the comprehensive examination were 0.9 and 0.9 respectively. The authors assumed 100% of positive screening results were referred for the comprehensive examination.

Weimer and Sager (2009) did not actually assess any specific screening or diagnostic interventions. They looked at the cost-effectiveness of diagnosing AD patients earlier. Thus, the intervention was a hypothetical one. With the intervention, they assumed all AD patients in the model immediately had their diagnoses from the beginning. Without the intervention, they assumed AD patients would receive their diagnosis later at an MMSE score of 19.

Getsios et al. (2012) modelled the annual assessment of patients reporting memory complains. The assessment was assumed to be 100% accurate. Diagnosed patients were assumed to receive donepezil as the only treatment; treatment was restricted to patients with MMSE scores between 10 and 26. The effectiveness of the early assessment was modelled to shorten the time patients received treatment before their disease progressed further.

Biasutti et al. (2012) modelled a scenario where there was a national screening programme for people aged 60 years or older before the diagnostic workups but they did not actually model the effectiveness of the screening programme. The model only started from the point patients came for the diagnostic workups. The only effect of the screening programme was to introduce a new group called early AD to the clinic population.
Modelling pharmaceutical interventions:

Among 39 previous model-based studies concerning pharmaceutical interventions, 37 studies looked at AD medications (AcHEIs and memantine), one study looked at antipsychotics, and one study looked at a hypothetical AD disease-modifying drug. Regarding AD medications, ten studies looked at donepezil, six studies looked at galantamine, three studies looked at rivastigmine, eight studies looked at memantine, and ten studies looked at multiple of them at the same time.

Bond et al. (2012) provided a comprehensive systematic review and meta-analysis of the evidence from clinical trials for the clinical effectiveness of AD medications as part of a NICE HTA. The conclusions from the NICE HTA were reproduced here:

- “Donepezil was shown to provide gains on cognitive, functional and global outcomes when compared with placebo.

- Similar pooling of data from galantamine studies was conducted, showing clear benefits from cognitive, functional and global outcomes. Additionally, results favouring treatment were seen for behavioural outcomes at later (6-month) follow-up.

- Pooled estimates of cognitive benefits from rivastigmine were favourable, but were shown to be dose dependent as in the previous review in 2004. The results from functional and global outcomes also showed significant gains. However, results from individual trials of behavioural outcomes were mixed (pooling was not possible owing to heterogeneity). The lower dose transdermal patch (9.5 mg/day) was shown to be as effective as the capsule (12 mg/day), but with fewer side effects.

- The meta-analysis of memantine versus placebo showed benefit from memantine at 12 weeks’ follow-up on the SIB. However, treatment gain, measured by functional outcome, depended on the type of instrument used, and no benefit on behavioural outcomes was seen. Nevertheless, pooled estimates of global outcomes showed a benefit from taking memantine.

- Pooling data from trials combining memantine plus an AChEI versus an AChEI failed to show any additional benefit from combination therapy”.

(Bond et al., 2012, p. 126)

In terms of modelling, the effectiveness of AD medications was incorporated in two ways: for decision tree/state transition models, the probabilities were adjusted for the treated group to account for treatment effects; for models that directly simulated the declining rates of clinical
measures, treatment effects were added directly for the treated groups in terms of improvement in clinical scores (e.g. MMSE score, ADL scores, NPI scores). When the modelling time was beyond the clinical trial period, a decision was needed for an assumption regarding whether treatment effects maintain. A common assumption among previous models was that AD medications would have no survival effect on people with dementia. Treatment discontinuation was another point that should be taken when modelling treatment effectiveness. Bond et al. (2012) noted that many RCTs did not report an Intention-To-Treat (ITT) analysis. Not accounting for drug discontinuation was likely to overestimate any treatment effects in the decision model.

Only one model-based study (Kirbach et al., 2008) looked at antipsychotics. They developed a state-transition model to assess the cost-effectiveness of olanzapine for treating agitation and psychosis in AD in the US. The clinical effectiveness of olanzapine was measured in terms of improvement in behavioural symptoms. Thus, the authors incorporated the intervention into the model by specifying the transitions between states with high and low levels of behavioural problems in addition to the AD states (mild AD, moderate AD, and severe AD). For the treated group, the transition probabilities between high and low levels of behavioural problems were adjusted.

5.3.3 Linking disease progression and intervention to health

This aspect of modelling concerns the methods that connect the simulated clinical progression and intervention with health measured in terms of QALYs. This is done by linking the patient pathway in the model with HRQOL. This review identified nine model-based studies that evaluated interventions in the UK and used the QALY measure for benefits (Table 5.4).
Table 5.4: UK model-based studies that used the QALY measure for benefits

<table>
<thead>
<tr>
<th>Studies</th>
<th>Source for patient utility values</th>
<th>Source of carer utility values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Ward</td>
<td>Neumann et al., 1999</td>
<td>None</td>
</tr>
<tr>
<td>2 Jones</td>
<td>Andersen et al. (1999, 2003)</td>
<td>None</td>
</tr>
<tr>
<td>3 Loveman</td>
<td>Neumann et al., 1999</td>
<td>None</td>
</tr>
<tr>
<td>4 Gustavsson</td>
<td>Ward and Brazier equation,</td>
<td>None</td>
</tr>
<tr>
<td>5 Rive</td>
<td>LAZER-AD study, equations</td>
<td>None</td>
</tr>
<tr>
<td>6 Getsios</td>
<td>Jonsson et al. 2006</td>
<td>Donepezil Clinical Trials</td>
</tr>
<tr>
<td>7 Getsios</td>
<td>Jonsson et al 2006</td>
<td>Donepezil Clinical Trials</td>
</tr>
<tr>
<td>8 Nagy</td>
<td>Brazier equation</td>
<td>None</td>
</tr>
<tr>
<td>9 Bond</td>
<td>Jonsson et al 2006</td>
<td>Neumann et al., 1999</td>
</tr>
</tbody>
</table>

Ward et al. (2003) in their state-transition (AHEAD type) model assigned a patient utility weight of 0.60 for the pre-FTC state and 0.34 for the FTC state. The utility values were derived from data reported by Neumann et al. (1999b, 2000). Neumann et al. (1999b, 2000) conducted a cross-sectional study of 679 pairs of AD patient and their caregivers in the US. They reported HUI II and HUI III scores for both patients and caregivers in different dementia stages and care settings; the HUI preference tariff was based on a population sample in Ontario, Canada. The same patient utility weights were used again in the NICE HTA model in 2006 (Loveman et al., 2006) and in the Gustavsson’s implementation of the NICE model in 2009 (Gustavsson et al., 2009).

Jones et al. (2004) in their state-transition model specified 12 disease states based on disease severity (three levels), dependency (two levels), and location of care (two locations) however, they only differentiated patient utility weights in terms of dependency levels based on the findings from the Odense study (Andersen et al., 1999, Andersen et al., 2003). This study found dependency was the main factor influencing QALYs. Thus, Jones et al. (2004) assigned a utility
weight (EQ5D) of 0.6511 (SD: 0.1981) for being in the independent states and 0.3207 (SD: 0.3084) for being in the dependent states.

Nagy et al. (2011) modelled disease progression by directly simulating the MMSE declining rate. They then linked the disease progression in terms of MMSE score to utility weight using a published equation by Brazier (2001):

\[ \text{Utility}_{HUI3} = 0.0982 + 0.0298 \times \text{MMSE} \quad (R^2 = 0.52) \]

The equation was developed based on rivastigmine clinical trial data (Brazier, 2001). The same equation was used in Gustavsson’s micro-simulation model and state-transition model.

Rive et al. (2010) in their state-transition model (AHEAD type) developed an equation to estimate patient utility weight (EQ-5D) for the pre-FTC state based on ADCS-ADL score and simulation time:

\[ \text{Utility}_{\text{Pre-FTC}}^{\text{EQ5D}} = 0.202 + 0.008 \times \text{ADCS. ADL}_{\text{baseline total score}} + \text{month}(i) \times \text{ADL}_{\text{slope total score}} \]

The FTC state was assigned a utility weight of 0.336 (SD = 0.043). These were based on analyses of data from the LASER-AD study in the UK (Livingston et al., 2004).

Getsios et al. (2010, 2012) modelled disease progression by directly simulating the declining rates of MMSE score, ADL scores, and NPI score. The authors then adapted a published regression equation (Jonsson et al., 2006a) to link the disease progression to patient utility weight (EQ5D):

\[ \text{Utility}_{\text{patient}}^{\text{EQ5D}} = 0.408 + 0.010 \times \text{MMSE} - 0.004 \times \text{NPI} - 0.159 \times \text{Institutionalised} + 0.051 \times \text{Caregiver} \]
This published equation was developed based on data from a prospective observational study of 272 patients and their primary caregivers in Sweden, Denmark, Finland and Norway (Jonsson et al., 2006a). The study reported EQ-5D scores for different MMSE groups and care settings. The study results were also used for patient utility weights in the most recent NICE HTA state-transition model (Bond et al., 2012b). Bond et al. (2012) assigned different patient utility weights (EQ5D) according to MMSE category: 0.33 for MMSE 0-9 and/or institutionalisation, 0.49 for MMSE 10-14 (pre-institutionalisation), 0.5 for MMSE 15-20 (pre-institutionalisation), 0.49 for MMSE 21-25 (pre-institutionalisation), and 0.69 for MMSE 26-30 (pre-institutionalisation).

Only three studies (Getsios et al., 2010, Getsios et al., 2012, Bond et al., 2012b) addressed caregiver utility weights. Getsios et al. (2010, 2012) developed an equation that estimates caregiver utility (SF-6D) using data from donepezil clinical trials where caregivers completed the SF-36:

**Equation 5.4**

\[
\text{Carer Utility (SF6D)} = 0.9 - 0.003\text{Age}_{\text{caregiver}} + 0.03\text{Male}_{\text{caregiver}} + 0.001 \times \text{Male}_{\text{patient}} + 0.00 \times \text{MMSE} - 0.001\text{NPI} - 0.001\text{ADL} - 0.0004\text{IADL} + 0.01\text{Psymed}
\]

Bond et al. (2012) used data from the Neumann study (Neumann et al., 1999b, Neumann et al., 2000) to assign carer utility weights (HUI2) for different MMSE ranges: 0.88 for MMSE 26-29, 0.87 for MMSE 21-25, 0.87 for MMSE 11-20, and 0.86 for MMSE 0-10.

### 5.3.4 Linking disease progression and intervention to costs

This aspect of modelling concerns the methods that connect the simulated clinical progression and intervention with resources used and costs. This review identified ten model-based studies that evaluated interventions in the UK context (Table 5.5).
Table 5.5: UK model-based studies for costs

<table>
<thead>
<tr>
<th></th>
<th>Studies</th>
<th>Including informal care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Stewart</td>
<td>1998 No</td>
</tr>
<tr>
<td>2</td>
<td>Ward</td>
<td>2003 No</td>
</tr>
<tr>
<td>3</td>
<td>Jones</td>
<td>2004 No</td>
</tr>
<tr>
<td>4</td>
<td>Loveman</td>
<td>2006 No</td>
</tr>
<tr>
<td>5</td>
<td>Gustavsson</td>
<td>2009 No</td>
</tr>
<tr>
<td>6</td>
<td>Rive</td>
<td>2010 No</td>
</tr>
<tr>
<td>7</td>
<td>Getsios</td>
<td>2010 Yes</td>
</tr>
<tr>
<td>8</td>
<td>Getsios</td>
<td>2012 Yes</td>
</tr>
<tr>
<td>9</td>
<td>Nagy</td>
<td>2011 Yes</td>
</tr>
<tr>
<td>10</td>
<td>Bond</td>
<td>2012 No</td>
</tr>
</tbody>
</table>

Stewart et al. (1998) calculated the costs for the dementia states (minimal, mild, moderate, and severe) in their model using the earlier work on costs of care packages for elderly people with dementia from the PSSRU (Kavanagh et al., 1995). Their paper and references did not provide much information about the estimates.

Ward et al. (2003) calculated direct costs (in 2001, £) in terms of medical and social services in their model. They assigned the monthly cost of £238 for the pre-FTC state, £433 for the FTC in community state, and £1,878 for the FTC in an institutional setting. For services in community, 46% of the costs were inpatient services, 4% were outpatient services, 5% were private care, 13% were GP services, and 32% were social services. For patients in institutional settings, the costs included placement costs and services provided externally to the institution. The estimates were calculated by determining the amount of resources used and multiplying them with unit costs. Resources used estimates based on two national surveys conducted by the Office of Population Census Survey during 1985 and 1986 (Martin et al., 1988). Unit costs
were from published sources (Netten et al., 1998). The average daily cost for treatment was estimated to be £2.44 for galantamine 16mg and £3.00 for galantamine 24 mg (no reference was mentioned).

Jones et al. (2004) calculated direct costs (in 2003, £) in terms of medical and social services in their model. They assigned the six-month costs of £5,670 (SD = 7,223) for a dependent patient in community, £2,234 (SD = 4,712) for an independent patient in community, £32,919 (SD = 25,952) for a dependent patient in institution, and £21,102 (SD=17,141) for an independent patient in institution. Data for resource use were from the LASER-AD study for a London population (Livingston et al., 2004). Unit costs were from published sources (Netten and Curtis, 2000). The treatment cost (memantine) was estimated based on the UK price (without VAT) at £2.65 for memantine per defined daily dose of 20 mg.

Loveman et al. (2006) calculated direct costs (in 2002/03, £) in terms of medical and social services in their model (NICE HTA model). They assigned the monthly costs of £328 (SD = £164) for a patient in pre-FTC state based on previous studies (Stewart, 1997, Kavanagh et al., 1995) and £937.30 (SD = £468) for a patient in FTC state. The figure for FTC state was the weighted average of FCT in community and FTC in institutional setting. For FTC in community, the authors used the figure in Ward et al. (2003) of £5,196 per year. For FTC in institutional setting, the authors distinguished between institutional costs (placement costs) and other health and social care costs. Total institutional (placement) costs were estimated to be £18,471 per year based on a previous study in England (Netten et al., 2001). However, Loveman et al. (2006) only included the amount of institutional costs that were funded publicly; the proportion was 70% of the total institutional costs based on the study by Netten et al. (2001). Other health and social care costs for institutionalised patients were estimated to be £4,874 per year (all publicly funded) based on Ward et al. (2003). Treatment costs included drug costs and a monitoring cost of 2 outpatient visits per year. The annual drug costs were based on prices reported in the British National Formulary, No.49 (2005): £828.29 for donepezil 5mg per day, £1,160.96 for donepezil 10mg per day, £886.95 for rivastigmine 3-12 mg per day, £890.60 for galantamine 16mg per day, £1,095 for galantamine 24mg per day, £449.77 for memantine 10mg per day, and £899.53 for memantine 20mg per day. The monitoring costs were based on the cost of £ 108 (SD = 25) per outpatient visit based on the NHS reference cost (2002).

Gustavsson et al. (2009) calculated direct costs (in 2005, £) in terms of medical and social services in their models. In their SHTAC model (using the same method from Loveman et al.
(2006)), the authors used the same cost inputs from Loveman et al. (2006). In the micro-
simulation model, the authors assigned a constant annual cost of £24,669 for an
institutionalised patient based on Loveman et al. (2006). For non-institutionalised patients, the
authors used a previous cross-sectional study on non-institutionalised patients and their
caregivers in the UK (Souetre et al., 1999) to assign £9,202 per year for a non-institutionalised
patient with MMSE above 17, £20,648 per year for a non-institutionalised patient with MMSE
between 17 and 10, and £23,299 per year for a non-institutionalised patient with MMSE below
10. In their Markov model, the authors used data from a previous study on a cohort of 100 AD
patients in the UK (Wolstenholme et al., 2002) to assign 6-month costs of £4,826 for a patient
with MMSE 30-21, £6,760 for a patient with MMSE 20-15, £9,105 for a patient with MMSE
14-10, and £12,929 for a patient with MMSE 9-0. The authors set the costs of medical treatment
in all models at £1,464 per year with an additional cost of £488 for the first four months prior
to the start of the simulation; this estimate was based on the model by Loveman et al. (2006).

Rive et al. (2010) calculated direct costs (in 2009, £) in terms of medical and social services in
their models. They assigned a cost of £724 (SE=217) per month for a patient in pre-FTC state
and £3267 (SE=284) for a patient in FTC state. These figures were estimated based on resource
use data from the LASER-AD study (Livingston et al., 2004) and the published unit costs of
health and social care (2009). Treatment costs included drug costs for memantine and
monitoring costs. The drug costs for memantine was estimated to be £2.16 per defined daily
dose based on the reported price from the British National Formulary 58 (2009). The
monitoring costs included an initial visit to a psychiatrist (£124.28 per visit) followed by visits
to the GP (£36 per visit) every six months (no reference was mentioned).

Getsios et al. (2010) calculated not only the costs for medical and social care but also informal
care in their model. For medical and social care costs, the authors used the data from the
Dementia UK report (Knapp et al., 2007). They assigned a fixed monthly cost of £2,645 for an
institutionalised patient. For a non-institutionalised patient, the monthly cost was £649 with
MMSE ≥ 25, £701 with MMSE between 20 and 25, £754 with MMSE between 15 and 20,
£829 with MMSE between 10 and 15, and £904 with MMSE< 10. Treatment costs included
drug costs for donepezil and monitoring costs. The drug costs for donepezil was estimated to
be £3.18 per daily dose of 10mg based on the reported price from the British National
Formulary at that time. The monitoring costs included two visits per year to a GP at £50 per
visit based on the Unit Costs of Health and Social Care 2007. For the cost of informal care,
the authors used data from donepezil clinical trials to develop an equation that predicts the amount of informal care in minutes per day from other variables (Caregiver time was valued at the UK minimum wage of £5.30 per hour):

**Equation 5.5**

Care Minutes Per Day

\[
= 76.41 + 1.8 \times \text{Age}_{\text{care}} + 93.02 \times \text{Male}_{\text{care}} \\
+ 85.56 \times \text{Male}_{\text{patient}} - 6.47 \times \text{MMSE} + 0.58 \times \text{NPI} \\
+ 2.66 \times \text{ADL} + 2.61 \times \text{IADL} + 20.55 \times \text{PsyMed}
\]

Getsios et al. (2012) extended their previous model (Getsios et al., 2010) to evaluate the cost-effectiveness of early assessment. Thus, they only added the costs for early assessment in the extended model; other costs were the same as in Getsios et al., 2010. The early assessment cost components (in 2007, £) included a GP visit (£50), first visit to specialist (£245), second visit to specialist (£140), a full blood count (£2.91), erythrocytes sedimentation rate/C-reactive protein (£5.26), biochemistry (£1.52), an average cost of MRI/CT scan in 5% of cases (£5.11). These estimates were based on the following sources: the Unit Costs of Health and Social Care 2007, the Department of Health NHS reference costs 2005-06 and 2006-07.

Nagy et al. (2011) also calculated both the costs for medical and social care and informal care (for sensitivity analyses) in their model. For medical and social care costs, they assigned a fixed annual cost of £29,948 for an institutionalised patient and £14,300 for a non-institutionalised patient based on The Unit Costs of Health and Social Care 2007. Treatment costs included drug costs for rivastigmine transdermal patch and monitoring costs. The drug costs for rivastigmine was estimated to be £1020 per year based on basic NHS prices in 2009 (excluding VAT). The monitoring costs included two outpatient visits per year (£264 per year) based on NICE clinical guideline 42 (NICE, 2006). The estimates of informal care time (included in sensitivity analyses) were taken from a previous study in the US (Bell et al., 2001) which reports hours of informal care required per week according to disease severity and care setting. Caregiver time was then valued at the UK minimum wage of £5.52 per hour.

Bond et al. (2012) calculated the costs for medical and social care in their model (the most recent NICE HTA model). They used patient-level data for resources used and costs from the
Oxfordshire study of 100 AD patients (Wolstenholme et al., 2002). For patients in pre-institutionalisation, the cost per month was distinguished for mild-to-moderate AD and moderate-to-severe AD and was dependent on time before the end of pre-institutionalisation (in years):

Equation 5.6

\[
\text{Monthly Inflated Cost}^{\text{mild-to-moderate AD}}_{\text{pre-institutionalisation}} = 2877 - 1122 \times t + 194 \times t^2 - 10.9 \times t^3
\]

Equation 5.7

\[
\text{Monthly Inflated Cost}^{\text{moderate-to-severe AD}}_{\text{pre-institutionalisation}} = 3363 - 1117 \times t + 191 \times t^2 - 10.7 \times t^3
\]

Where t is time before end of pre-institutionalisation in years.

For patients in institutional care, the overall monthly cost was £2,941 but the authors assumed only 72% of it was funded publicly hence the monthly cost for a patient in institutional care in their model was £2,117. Treatment costs included drug costs and monitoring costs. The monthly drug cost was estimated based on prices reported in BNF 58 (fourth quarter 2009): £97 for donepezil 10mg per day, £83 for galantamine 16-24 mg per day, £72 for rivastigmine capsules 9-12 mg per day, £79 for rivastigmine patches 9.5mg per day, £71 for memantine 15-20mg per day. The monitoring cost included one outpatient visit every six months per (£158 per visit) based on NICE Reference Costs 2008-09.

5.4 Discussion and conclusion

This chapter reviewed modelling aspects in previous studies to support the development of a new cost-effectiveness model for the case study. The aspects of modelling included the modelling of disease progression, the modelling of interventions, the modelling of relationships between disease progression and interventions and health, and the modelling of relationships between disease progression and interventions and costs.
First, for modelling disease progression, the review found that it was not yet possible to model the biological/pathological changes in the brain for economic evaluation models in dementia. Current methods could only model disease progression in terms of the clinical manifestation of dementia. The key clinical aspects of dementia progression were cognitive decline, behavioural symptom progression, and deterioration in functioning. These three aspects needed to be modelled simultaneously to describe the disease progression in dementia (Green et al., 2011) however, most of the studies only modelled the cognitive progression. Other key aspects in modelling dementia progression were institutionalisation and mortality. Institutionalisation reflects the transition of patients from community care to institutional care due to patients losing their ability to be independent. All previous models agreed that dementia had a negative impact on mortality (compared with normal cognition), whereas mortality for people with MCI was often assumed to be the same as the general population. None of the previous models addressed the interaction between patients and their informal caregivers although this was an important feature in dementia.

Based on this review, we had a choice of several approaches for modelling disease progression in our dementia model: (A) decision tree models, (B) traditional state-transition models, (C) transition to Full-Time-Care (FTC) models, and (D) models that directly simulate progression rates of specific clinical measures. Given the availability of data from previous studies, the need for the model to address a wide range of costs and benefits from a societal perspective, and the need for the model to be flexible, approach (D) was considered the most appropriate. Since our case study concerned interventions for early detection and diagnosis of dementia, the model needed to incorporate the disease progression before the clinical manifestation of dementia. None of the previous models for diagnosis/screening interventions explicitly modelled this.

Second, for modelling interventions, two groups of interventions were reviewed: screening/diagnostic interventions, and pharmaceutical interventions. The benefit of screening/diagnostic interventions came from the health benefit (and potential resources saving) from giving patients early access to post-diagnostic treatments and care. Their effect was modelled in terms of sensitivity and specificity in detecting people with dementia and people without dementia. Pharmaceutical treatments (AD medications for treating cognitive symptoms) were those that had the most evidence for their clinical effectiveness and cost-effectiveness. Following approach (D) in modelling disease progression, the effects of
pharmaceutical treatments were modelled by adding their symptomatic improvement from clinical trial data. When extrapolating beyond the clinical trial period, assumptions were needed. The common assumption in previous models was that symptomatic improvement was only counted for treated patients in the first year (where most evidence from clinical trials was available); beyond that time treatments were assumed to add no further symptomatic improvement and patients were assumed to resume to normal disease progression. Furthermore, a proportion of treated patients was often modelled to discontinue their treatments.

Third, for linking disease progression and interventions to health (calculating QALYs), it was done by assigning utility scores to different health states in the progression. Two most commonly cited patient utility measures from previous models were the HUI (2 and 3) and the EQ5D. Most commonly cited data source for HUI values was from the US study by Neumann et al. (1999b, 2000). Most commonly cited data source for EQ5D value was from the study by Jonsson et al. (2006) who researched the population in Sweden, Denmark, Finland, and Norway; this source was used in the NICE HTA model (Bond et al., 2012b). For HRQOL of informal caregivers, only few studies addressed this. Two sources for modelling the HRQOL of informal caregivers were identified in this review: one was data from the US study by Neumann et al. (1999b, 2000) and the other was the regression equation developed by Getsios et al. (2010) using clinical trial data.

Fourth, for linking disease progression and interventions to costs, the majority of previous UK studies only calculated costs in terms of medical and social care funded by the government (i.e. NHS and PSS). Only three UK studies (Getsios et al., 2010, Getsios et al., 2012, Nagy et al., 2011) addressed the cost of informal care. Although there were many different sources for estimates of resources used and costs, the dementia UK report (Knapp et al., 2007) was identified as the most comprehensive and robust source for estimating costs of dementia care in the UK; this was used in the study by Getsios et al. (2010). The report was prepared by the Personal Social Services Research Unit (PSSRU) at the London School of Economics and the Institute of Psychiatry at King’s College London for the Alzheimer’s Society. The report was updated in 2014 (Prince et al., 2014).

Given the findings from this review, the next chapter reports the development of a new cost-effectiveness model for evaluating alternative options for GPs in assessing patients with cognitive impairment.
CHAPTER 6. COST-EFFECTIVENESS MODEL FOR EVALUATING THE USE OF DIFFERENT COGNITIVE SCREENING TESTS IN PRIMARY CARE

This chapter reports the development of a new cost-effectiveness model for evaluating the use of different cognitive screening tests in primary care. The model is an important component for operationalising the economic evaluation approaches proposed. The model development was informed by a systematic review of previous model-based economic evaluation studies in dementia reported in Chapter 5.

This chapter is divided into three sections. The first section describes the methods for the development of the model. It provides details for the model structure, input data, and analyses. The second section then reports the results of the model estimates. The final section discusses the results and concludes the chapter. The work from this chapter is also published in the International Journal of Geriatric Psychiatry (Tong et al., 2016).
6.1 Methods

A patient-level cost-effectiveness model was developed to include the dementia pathway from pre-diagnosis to post-diagnosis, disease progression and death. The clinical disease and service pathway were developed by reviewing previous model-based studies and interviews with experts in dementia care.

This model only examined dementia in the Alzheimer’s disease (AD) form. The simulated population represented the English population 65 years and older. Each patient was tracked over his/her life time (i.e. until the patient dies or reaches 100 years of age). Benefits were measured in terms of QALYs gained for both patients and their informal caregivers. The benefit of GP-based diagnostic interventions comes from improving HRQOL over the patients’ lives. Costs include government health and social care, private payment for social care, and unpaid informal care. A detailed input data table is provided in Appendix 2. All costs were reported in pounds sterling at year 2016 prices, and all outcomes were discounted at 3.5% per year. The simulation software SIMUL8® (SIMUL8, 2014) was used to implement the model.

6.1.1 Model structure

The conceptual models are illustrated in Figure 6.1 and Figure 6.2.

**Figure 6.1: The conceptual model: patient health states and disease progression**

<table>
<thead>
<tr>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Declining cognition (MMSE)</td>
</tr>
<tr>
<td>o Worsening in ADL and IADL</td>
</tr>
<tr>
<td>o Worsening in behaviour (NPI)</td>
</tr>
<tr>
<td>o Moving to a nursing home</td>
</tr>
</tbody>
</table>
Figure 6.2: The conceptual model: health care events

1 Patient

Start a year

Diagnosed dementia?

No

Diagnosed MCI and being followed up?

No

Assessed by GPs for dementia?

No

Outcomes of GP assessment

Yes

Assessment by memory services

Yes

Refer to memory service

No

Not refer to memory service

Assessed by GPs for dementia?

Diagnosed dementia

Diagnosed MCI

Following up for 2 years

Confmed non-cases

THE COHORT
- Normal cognition
- MCI
- Dementia

UPDATE PATIENT CHARACTERISTICS (age, disease status, disease progression, institutionalisation)

Move to next year

Die this year?

Yes

Exit the model

No

Receive dementia treatment
The model starts by simulating a cohort of patients and assigning each patient a set of unique characteristics (e.g. age, gender, disease status, etc.). The cohort includes a representative sample of the general population 65 years and older in England. The same cohort is analysed for four assessment scenarios: (1) GP’s unassisted clinical judgement, (2) GPs using MMSE, (3) GPs using GPCOG, and (4) GPs using 6CIT.

Patients are followed up with their characteristics updated every year until they die. Patients move between four health states as described in Figure 6.1: normal cognition (not having dementia or MCI), MCI, dementia, and death. For patients in the dementia state, their dementia progresses every year in terms of worsening cognition (measured by MMSE score), behaviours (measured by Neuro Psychiatric Inventory (NPI) score), and functioning in activities of daily living (measured by Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scores). Due to dementia symptoms, patients in the dementia state also have an increased risk of being institutionalised.

Figure 6.2 describes the health care events in the model. The model annually checks the status of patients to see whether they have already had a dementia diagnosis; whether they have already been diagnosed with MCI and are currently being followed up by memory services; and whether they would receive an assessment for cognitive impairment by GPs this year. Depending on the outcome, the model will send the patient to the relevant route (see Figure 6.2). Since the focus of the evaluation is on interventions for GP-based assessment of cognitive impairment, memory services were assumed to be able to diagnose all cases with 100% accuracy. Newly diagnosed dementia will receive dementia medications. Newly diagnosed MCI will be followed up by memory services for two years. Confirmed non-cases (not dementia or MCI) will just return to the population.

The model updates characteristics of a patient at the end of the year. All patients face an annual mortality rate based on their age, gender and dementia status. If a patient survives the year, the model will send him/her to another cycle of events for the next year. If a patient dies, he/she will exit the model and have his/her total costs and QALYs calculated. The Simul8 schematic for the model is illustrated in Figure 6.3.
6.1.2 Input Data

6.1.2.1 The cohort

Characteristics of patients in the cohort were assigned to represent the general population in England. The distributions of age and gender for the cohort were based on the mid-2013 data from the Office for National Statistics (ONS, 2015). The prevalence of dementia and dementia severity according to age and gender was based on the recent dementia UK report (Prince et al., 2014). The prevalence of MCI was based on a UK study (Fish et al., 2008).

6.1.2.2 Parameters relating to the GP assessment for cognitive impairment:

a. Annual probability of having a GP assessment for cognitive impairment:

If a patient has not had a diagnosis of dementia or is not followed up by memory services, they can be assessed by GPs for dementia within any given year. Since a national dementia screening programme was not implemented in England, the annual probability for a 65+ patient to receive a dementia assessment by GPs should be less than 100%.

For patients with dementia, the health and social care information centre reported the recorded dementia register (total number of people with dementia) and diagnosis rates in England between 2009/10 and 2013/14 (Health & Social Care Information Centre, 2014). Using those data, the number of new dementia diagnoses per year and the proportion of undiagnosed dementia cases diagnosed per year were estimated. Using the average sensitivity of GPs for
assessing dementia, the proportion of undiagnosed dementia who had a GP assessment for dementia per year was estimated at 21.63% (range: 13.00% - 27.26%).

Abdel-Aziz and Larner (2015) reported the diagnostic outcomes of patients who were referred to a memory clinic in England in one year. Of 245 new patient referrals, 48 (20%) were diagnosed with dementia and 67 (27%) were diagnosed with MCI (Abdel-Aziz and Larner, 2015). Using those figures, the relative numbers of referred cases for MCI and referred non-cases (not dementia or MCI) from the number of new diagnoses of dementia per year were estimated. Knowing the prevalence of dementia and MCI in the simulated cohort, the relative proportions of MCI and non-cases who were diagnosed by memory services per year were estimated. Then, using the average sensitivity of GPs for MCI and the average specificity of GPs for non-case, the proportions of MCI and non-cases who would have a GP assessment for cognitive impairment per year were estimated: 10.53% (range: 6.33% - 13.27%) for MCI, and 18.17% (range: 10.92% - 22.89%) for non-cases (not impaired).

b. Sensitivity and specificity of different assessment strategies:

It was assumed that severe dementia was always detected with 100% sensitivity by GPs regardless of the assessment strategy. This assumption was similar to the one used in a published diagnostic model for AD (Biasutti et al., 2012). Thus, the effect of GP-based interventions only came into play in detecting mild dementia, moderate dementia, MCI and non-cases. Table 6.1 shows the sensitivity and specificity of each assessment strategy.
Table 6.1: Sensitivity and specificity of assessment strategies

<table>
<thead>
<tr>
<th></th>
<th>Mean and Range (95% CI)</th>
<th>Data source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (dementia)</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Sensitivity (MCI)</td>
<td>Specificity (no dementia)</td>
</tr>
<tr>
<td>GP unassisted</td>
<td>0.58 (0.38 – 0.78)</td>
<td>0.75 (0.66 – 0.80)</td>
</tr>
<tr>
<td>judgement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td>0.59 (0.39 – 0.80)</td>
<td>0.85 (0.79 – 0.91)</td>
</tr>
<tr>
<td>6CIT</td>
<td>0.88 (0.78 – 0.97)</td>
<td>0.78 (0.72 – 0.84)</td>
</tr>
<tr>
<td>GPCOG</td>
<td>0.60 (0.39 – 0.81)</td>
<td>0.93 (0.82 – 0.99)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data from three studies were used to derive the relative sensitivity and specificity for each option. The first one was an UK pragmatic diagnostic accuracy study of the use of 6CIT in primary care settings (Abdel-Aziz and Larner, 2015). The authors studied consecutive patients (N=245) referred over the course of one year to a memory clinic. The performance of using 6CIT in detecting dementia and MCI was compared to that of the simultaneously administered MMSE. The comparative results for sensitivity and specificity of 6CIT and MMSE were reported for both dementia and MCI.

In order to derive the relative sensitivity and specificity for the GPCOG option, data from an Australian study (Brodaty et al., 2002) were used. Brodaty et al. (2002) compared the performance of the GPCOG with the MMSE in primary care settings. The study included sixty-seven GPs and 283 patients. The comparative results for sensitivity and specificity of GPCOG and MMSE were reported. Using the reported results, the relative rates comparing the performance (in terms of sensitivity and specificity) of GPCOG with MMSE were calculated and these were used to derive the relative sensitivity and specificity for the GPCOG strategy in the model.
In order to derive the relative sensitivity and specificity for the unassisted strategy (no screening test), data from another UK study (O’Connor et al., 1988) were used. O’Connor et al. (1988) studied 2889 elderly people aged 75 years or older listed in the registers of six group practices in Cambridge city, England. 2616 patients were screened by the MMSE. 657 patients were then screened positive and invited to have a more comprehensive investigation (specialist diagnosis). Among them, 125 patients did not have the comprehensive investigation and a further 88 patients were excluded; this left 444 patients available for the analysis. After that, the authors asked GPs to look at this list of 444 patients and state which ones they considered to be definitely not demented, possibly demented, or definitely demented. Table 6.2 presents the results from their study.

**Table 6.2: Diagnostic outcomes from O’Connor study**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>General practitioners ratings</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not demented</td>
<td>Possibly demented</td>
</tr>
<tr>
<td>Not demented</td>
<td>185</td>
<td>40</td>
</tr>
<tr>
<td>Dementia</td>
<td>87</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>272</td>
<td>91</td>
</tr>
</tbody>
</table>

(Adapted from (O’Connor et al., 1988))

Using the dementia prevalence rate of 19.8% for the age group 75+ as reported in the dementia UK report (Prince et al., 2014), the sensitivity and specificity of the MMSE used in the O’connor study were calculated (0.59 for sensitivity and 0.89 for specificity), whereas the sensitivity and specificity of the GP unassisted judgement were calculated from Table 6.2 (0.58 for sensitivity and 0.78 for specificity). Then, the relative rates comparing the performance (in terms of sensitivity and specificity) of the GP unassisted judgement with MMSE were calculated. Using these rates, the relative sensitivity and specificity for the GP unassisted judgement were calculated for the model input.

c. **Costs per assessment for different strategies:**

The base cost per assessment for each strategy included one GP consultation, one practice nurse consultation and laboratory tests (NICE, 2010). Regarding the use of cognitive screening tests, the MMSE was associated with a small license fee of £ 0.96 per test (PAR, 2016), whereas the
6CIT and GPCOG were free. Furthermore, their administration time per assessment was different (Cordell et al., 2013): the MMSE required 7-10 minutes/8.5 minutes; GPCOG required 2-5 minutes/3.5 minutes; and 6CIT required 4-6 minutes/5 minutes. This difference in administered time was converted to health care costs by multiplying the time by the cost per minute of a GP in a surgery. Sensitivity analyses explored the use of time of a practice nurse instead.

6.1.2.3 Parameters for the transitions between health states

Transition from normal cognition to MCI was described in the model as an annual probability of having MCI for normal cognition patients. Ward et al. (2012) performed a systematic review of estimates for MCI prevalence and incidence. They found 13 studies reporting the incidence of MCI; among them, five studies reporting age-stratified rates (none of the study was for the UK) (Ward et al., 2012). The annual probability in our base-case analysis was derived from the pooled data of those five studies which reported MCI incidence rates in Italy, Germany, Sweden, and France (Ward et al., 2012).

The annual probability of having dementia for patients with normal cognition was derived from data for dementia incidence rates in England and Wales (Matthews and Brayne, 2005). It was assumed that all new incident dementia was modelled as undiagnosed mild dementia in the community. In other words, when a person with normal cognition has the onset of dementia, the model will change their disease status (in the simulation) to undiagnosed mild dementia.

MCI patients were modelled to have two types of transitions: some of them progressed to dementia, and some of them reverted to normal cognition. The data for the annual conversion rate from MCI to dementia was from a meta-analysis of 41 robust inception cohort studies (Mitchell and Shiri-Feshki, 2009). For people with MCI who reverted to normal cognition, the annual rate was derived from a UK study on 3,020 individuals diagnosed with MCI (Koepsell and Monsell, 2012).

6.1.2.4 Parameters for the dementia progression

The review in Chapter 5 found that the most appropriate method for modelling dementia progression was to directly simulate the progression rates of specific clinical measures. In particular, the equations developed by Getsios et al. (2010) were good sources for modelling
the dementia progression. Using the Getsios’ equations, progression was described in terms of annual worsening rates for MMSE, NPI, ADL and IADL measures.

For the progression of cognitive symptoms, Getsios et al. (2010) described the annual change in MMSE score as a function of previous MMSE score, last known rate of decline, and patients’ age at baseline (Equation 6.1). This equation was derived from a large longitudinal database, the CERAD (Consortium to Establish A Registry for Alzheimer’s Disease) registry. The CERAD data were obtained on 1,094 American patients with AD and on 463 non-demented controls; many were observed for periods as long as seven years.

Equation 6.1

\[ \Delta \text{MMSE}_{i}^{\text{annual}} = 5.4663 - 0.4299 \times \min(\text{PrevMMSE}, 9) - 0.0042 \times \max(0, \min(\text{PrevMMSE} - 9, 9)) + 0.1415 \]
\[ \times \max(0, \min(\text{PrevMMSE} - 18, 12)) - 0.0791 \times \text{Prev}\Delta\text{MMSE} + 0.0747 \times \text{Age} + \delta_{i}^{\text{MMSE}} \]

PrevMMSE represents a patient’s previous MMSE score; PrevΔMMSE is the patient’s last known rate of decline; Age represents the patient’s age at baseline (years); and \( \delta_{i} \) represents a random intercept parameter allowing the pattern of decline to vary between patients. In the simulation, \( \delta_{i} \) for MMSE was implemented as a normal distribution (0, 0.5) (Getsios et al., 2010, Bond et al., 2012b).

For the progression of performance in Activities of Daily Living (ADL), one issue was that different studies used different measures of ADL. Getsios et al. (2010) selected data from donepezil clinical trials which used the most similar scales to measure ADL. Then, they created standardised scales ranging from 0 (best function) to 100 (worst function) for ADL measure (toileting, feeding, dressing, grooming, ambulation, and bathing), and for IADL measure (phone, shopping, food preparation, house tasks, and finance). Data for ADL and IADL from 5 different donepezil trials were then mapped onto the standardised scales and pulled to provide inputs for the development of equations predicting their annual changes (on standardised scales) (Equation 6.2 and Equation 6.3)
\[ \Delta ADL_{i}^{\text{annual}} = 1.35 + 0.06 \times \text{weeks} - 0.79 \times ADL_{\text{base}} + 0.71 \times ADL_{\text{previous}} + 0.12 \times MMSE_{\text{base}} + 0.09 \times \text{Age} + 0.81 \times \text{PsyMed} - 3.05 \times \text{Black} - 0.49 \times MMSE_{\text{previous}} + \delta_{i}^{\text{ADL}} \]

\[ \Delta IADL_{i}^{\text{annual}} = 1.27 + 0.17 \times \text{weeks} - 0.84 \times IADL_{\text{base}} + 0.002 \times IADL_{\text{base}} \times \text{weeks} + 0.84 \times IADL_{\text{previous}} - 0.67 \times \text{Male} + 0.20 \times MMSE_{\text{base}} - 0.28 \times MMSE_{\text{previous}} - 0.16 \times ADL_{\text{base}} + 0.18 \times ADL_{\text{recent}} + \delta_{i}^{\text{IADL}} \]

‘Weeks’ represents weeks of follow-up in the simulation; ADL/IADL/MMSE base is the patient’s baseline ADL/IADL/MMSE score; ADL/IADL/MMSE previous is the patient’s last ADL/IADL/MMSE score; ‘Black’ is a dummy variable for race; and PsyMed is a dummy variable for patients on psychiatric medications at baseline. Regarding the random intercept, \( \delta_i \) for ADL was implemented as a normal distribution \((0, 2.48)\), whereas \( \delta_i \) for IADL was implemented as a normal distribution \((0, 1.9)\) (Getsios et al., 2010, Bond et al., 2012b).

For the progression of behavioural symptoms, the annual rate of change for NPI score was described in Equation 6.4. The prediction was based on data from donepezil trials where NPI was measured. It should be noted that the original scale for NPI has a range between 0 and 144 with higher scores indicating worse symptoms. However, Getsios et al. (2010) derived the equation for NPI progression based on a normalised scale between 0 and 100; hence they applied a multiplier of 1.44 to re-scale it to the standard range.

\[ \Delta NPI_{i}^{\text{annual}} = \left( 5.74 + 0.03 \times \text{weeks} - 0.59 \times NPI_{\text{base}} - 0.0012 \times NPI_{\text{base}} \times \text{weeks} + 0.24 \times NPI_{\text{previous}} - 1.74 \times \text{White} - 3.82 \times \text{Black} + 2.34 \times \text{PsyMed} + 0.12 \times MMSE_{\text{base}} - 0.22 \times MMSE_{\text{previous}} + \delta_{i}^{\text{NPI}} \right) \times 1.44 \]
NPI\textsubscript{base} represents the patient’s baseline NPI score; NPI\textsubscript{previous} is the patient’s last NPI score; ‘White’ is a dummy variable for race. Regarding the random intercept, $\delta_i$ for NPI was implemented as a normal distribution $(0, 3.75)$ (Getsios et al., 2010, Bond et al., 2012b).

For people with dementia living in community, they had an annual probability of institutionalisation based on their MMSE score. The probability was calculated based on an equation estimated by Nagy et al. (2011) using data from a UK-based study (Stewart, 1997).

**Equation 6.5**

\[
\text{Probability of institutionalisation} = 0.512 - 0.016 \times \text{MMSE}
\]

### 6.1.2.5 Effectiveness of dementia medications:

The main benefit of early detection and diagnosis of dementia was the additional health benefit (and potential resources saving) from giving patients timely access to treatments (see the review in Chapter 5). Although there were many different potential treatments for dementia, all of them were symptomatic treatments. Only medications for AD were modelled as dementia treatments since they had the most concrete evidence for clinical effectiveness (Knapp et al., 2013, Bond et al., 2012b). NICE recommended the three AChEIs (Donepezil, Rivastigmine, and Galatamine) for mild to moderate AD, whereas memantine was recommended for severe AD, or moderate AD who were intolerant of or had a contraindication to AChEIs (NICE, 2015). It was assumed that all with diagnosed mild to moderate dementia were given donepezil 10 mg once daily whereas those with diagnosed severe dementia were given memantine 10 mg once daily.

The effectiveness of dementia medication came into play through symptomatic improvements in several aspects of dementia progression: MMSE score, ADL score, and NPI score. It also helped increase the time staying in the community (before moving to institutionalisation) due to the improvement in the MMSE score.

Only people with diagnosed dementia received treatments. Newly treated patients were modelled to have their clinical scores (MMSE, ADL, NPI) improved immediately. Due to the lack of effectiveness data for long-term benefits of treatments from clinical trials (beyond one year), it was assumed that after the immediate improvement in the first year, treated patients would not gain any further improvement; they would still progress at the same rate as untreated
patients (continuing treatments after one year only help to maintain the initial improvement). This assumption was consistent with previous models in AD (see the review in Chapter 5). The improvement in clinical scores for donepezil and memantine was based on the meta-analysis results reported in the recent HTA report (Bond et al., 2012b).

6.1.2.6 Mortality

From the review in Chapter 5, it was agreed that dementia had a negative impact on mortality, whereas MCI did not. The 2011-2013 national life tables for England by the Office for National Statistics (ONS) provided the age-specific mortality rate (qx) (http://www.ons.gov.uk). This rate is the conditional probability of dying before age (x + 1) provided the individual has survived to age x. The age-specific annual mortality rates from the national life tables were applied for people with normal cognition and people with MCI in the model. For people with dementia, a relative risk of death was used to adjust their annual mortality rates. The relative risk of death after developing dementia was estimated to be 1.82 (95% CI: 1.77 – 2.68), adjusted for sociodemographic variables (Helmer et al., 2001).

6.1.2.7 Costs

The review in Chapter 5 identified an existing source for cost data: the largest cost study for dementia in the UK (Knapp et al., 2007) which was updated in 2014 (Prince et al., 2014). This study provided estimates for the annual figures for the UK for 2013 using the best currently available information. According to this report, health care costs were met entirely by the National Health Service (NHS), whereas social care costs were met partly by local authorities and partly by people with dementia themselves through self-funding. The same ratios reported in (Prince et al., 2014) were used in the model to separate the social care costs falling on the government from the private social care.

Prince et al. (2014) used data from a number of UK trials and other studies to identify the detailed patterns of care and support for people with dementia in the community. The pooled dataset provided detailed information on about 1400 people with dementia and on more than 200 carers. The services covered in those studies included (but were not confined to) inpatient stays, outpatient attendances, day hospital treatment, visits to social clubs, meals at lunch clubs, day care visits, hours spent in contact with community-based professionals such as community teams for older people, community psychologists, community psychiatrists, general
practitioners, nurses (either practice, district or community psychiatric), social workers, occupational therapists, paid home help or care workers, and physiotherapists. Those studies also provided information about hours of unpaid/informal care. The authors noted that data on the costs of services used by carers were not included because of the paucity of data on carers’ service use patterns and the difficulty of dis-entangling the services used by carers that stem exclusively from their roles as carers and that stem from their own needs.

Prince et al. (2014) converted resources consumed to cost estimates using UK unit costs. The data sources mainly came from the annual PSSRU volumes on unit costs, the National Health Service Schedule of Reference Costs for inpatient and outpatient costs. The authors used local authority data on care home fees from the official Health and Social Care Information Centre report (2014) on expenditure and unit costs in 2012/13 to calculate the cost of institutionalisation for people in care homes.

Regarding the valuation of informal care, Prince et al. (2014) argued that the opportunity cost method taking carer age and employment status into account was considered to be more appropriate for valuing informal care compared to the replacement cost method – see (van den Berg et al., 2004) for definitions. Thus, for carers whose employment was known, the authors valued their informal care at the average wage for the relevant job category (by gender and age band). For carers who reported that they were not employed, the authors valued their informal care at the national minimum wage rate for those 65 years or older; and at national average wage (according to gender and age band) rate for those 64 years or younger.

The cost of medications (donepezil and memantine) for diagnosed dementia were from the British National Formulary (BNF) accessed in 2016 (BNF, 2016). Patients receiving medications were assumed to incur costs associated with biannual visits to a physician (Getsios et al., 2010). All costs were inflated to 2015/16 prices for input in our model.

6.1.2.8 Health utilities

The review in Chapter 5 identified few sources for utility values for people with dementia. Two most commonly cited patient utility measures from previous models are the HUI and the EQ5D. The most commonly cited data source for HUI values was from the US study (Neumann et al., 1999b, Neumann et al., 2000). The most commonly cited data source for EQ5D value was from the study by Jonsson et al. (2006) who researched the population in Sweden, Denmark, Finland,
and Norway; this source was used in the NICE HTA model (Bond et al., 2012b). Getsios et al. (2010) used the published regression equation for EQ-5D utilities of AD patients from Jonsson et al. (2006) with a slight modification for the NPI term: the coefficient for the NPI term was modified to correspond to the full NPI scale because Jonsson et al. (2006) used the brief version of the NPI. The same equation reported in (Getsios et al., 2010) was used in our model. For people with dementia, their utility value (EQ-5D) was calculated based on their MMSE score, NPI score, and institutionalisation status:

**Equation 6.6**

$$\text{Utility (EQ5D)} = 0.408 + 0.010 \times \text{MMSE} - 0.004 \times \text{NPI} - 0.159 \times \text{Institutionalised} + 0.051 \times \text{Caregiver}$$

‘Institutionalised’ and ‘Caregiver’ are dummy variables for whether the patient is institutionalised or lives with their caregiver in the community.

For HRQOL of informal caregivers, the evidence was limited. The review in Chapter 5 only identified two sources for modelling the HRQOL of informal caregivers: one was data from the US study by Neumann et al. (1999b, 2000) and the other was the regression equation developed by Getsios et al. (2010) based on clinical trial data. The Getsios equation was used in our model for utilities of informal caregivers. The utility of the informal caregivers was measured in terms of the SF6D score and was dependent on other characteristics of the carer and the patient (Equation 6.7):

**Equation 6.7**

$$\text{Carer Utility (SF6D)}$$

$$= 0.9 - 0.003 \times \text{Age}_{\text{caregiver}} + 0.03 \times \text{Male}_{\text{caregiver}} + 0.001 \times \text{Male}_{\text{patient}} + 0.00 \times \text{MMSE} - 0.001 \times \text{NPI} - 0.001 \times \text{ADL} - 0.0004 \times \text{IADL} + 0.01 \times \text{Psymed}$$

### 6.1.3 Analyses

The model’s conceptual structure was validated by checking with three experts in dementia care: a neurologist, a dementia lead, and a GP. The model codes were verified internally throughout the model implementation. Simulated patients were checked to make sure they behaved logically as expected, i.e. their characteristics were changing and they followed expected routes. The outputs for costs and health utility were checked against the patient’s
other characteristics. The model estimates were also checked to see if they agreed with the input data.

Base-case analyses were based on simulation of 5,000 patients. For each simulated patient, four identical copies were created corresponding to four decision options/scenarios. The simulation took each patient through their pathway and reported the results in terms of accumulated costs and QALYs for each individual. The overall results were expressed as the average (per patient) of the cohort. Uncertainty in key inputs into the model were examined in sensitivity analyses. Deterministic Sensitivity Analyses (DSA) were undertaken where the impact of changing important inputs was examined one at a time. A more sophisticated probability sensitivity analysis (PSA) was undertaken where all key variables were varied at the same time and the values were sampled from a distribution of values given to each variable. 1000 simulations were run for the PSA.
6.2 Results

6.2.1 Base-case results

Table 6.3 presents the base-case results from the model.

Table 6.3: Base-case results

<table>
<thead>
<tr>
<th>Per patient</th>
<th>Absolute</th>
<th>Incremental from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>MMSE</td>
</tr>
<tr>
<td><strong>COSTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnostic costs, GPs</td>
<td>£88</td>
<td>+£42.4</td>
</tr>
<tr>
<td>Diagnostic costs, memory services</td>
<td>£509</td>
<td>-£108.0</td>
</tr>
<tr>
<td>Medications</td>
<td>£402</td>
<td>+£1.7</td>
</tr>
<tr>
<td>Other health care</td>
<td>£27,833</td>
<td>-£1.7</td>
</tr>
<tr>
<td>Total health care</td>
<td>£28,834</td>
<td>-£65.62</td>
</tr>
<tr>
<td>Government-funded social care</td>
<td>£26,035</td>
<td>-£0.1</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>£36,832</td>
<td>-£0.25</td>
</tr>
<tr>
<td>Informal care</td>
<td>£10,433</td>
<td>-£0.56</td>
</tr>
<tr>
<td><strong>BENEFITS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Years</td>
<td>12.042</td>
<td></td>
</tr>
<tr>
<td>QALYs (patient)</td>
<td>5.99830</td>
<td>+0.000103</td>
</tr>
<tr>
<td>QALYs (carers)</td>
<td>6.98902</td>
<td>+0.000018</td>
</tr>
</tbody>
</table>

The performance of the baseline option (the GP unassisted judgement) is presented in absolute values and the performances of the intervened options are presented in incremental values (compared with the baseline). For costs, a negative incremental value means that the intervened option saves resources compared with the baseline option.

In terms of the healthcare cost, the MMSE and the GPCOG saved health care resources, whereas the 6CIT incurred a small cost (+£3.2 per patient). Looking more closely at the
components of the healthcare cost, all intervened options consumed more healthcare resources in terms of the GP assessment for cognitive impairment and the dementia medications however, they saved the healthcare resources in terms of the memory services and the other health care.

In terms of the government-funded social care costs, the private payment for care, and the informal care, all intervened options saved resources. The government-funded social care, the private payment for care, and the informal care for the baseline option were £26,035 per patient, £36,832 per patient, and £10,433 per patient in absolute values respectively. The cost of informal care was quite small because it was assumed that only people with dementia in our model would require informal care. The incremental government care for the MMSE, the 6CIT, and the GPCOG were -£0.1, -£2.5, and -£0.3 per patient respectively. The incremental private payment for care for the MMSE, the 6CIT, and the GPCOG were -£0.25, -£3.8, and -£0.49 per patient respectively. The incremental informal care for the MMSE, the 6CIT, and the GPCOG were -£0.56, -£4.38, and -£0.72 per patient respectively. The costs for the government-funded social care, the private payment for care, and the informal care were reduced in intervened scenarios compared to the baseline because of early diagnosis and early access to medications for people with dementia. Overall, these incremental costs were relatively smaller than the incremental cost for the health care; the 6CIT was the best performer regarding the incremental costs for the government-funded social care, the private payment for care, and the informal care.

For QALYs, a positive incremental value means that the intervened option delivers more QALYs compared with the baseline option. All intervened options delivered more QALYs (both patients and caregivers) than the baseline option. QALYs were gained because of early diagnosis and early access to medications for people with dementia. Overall, the GPCOG was the best performer in terms of saving resources, especially healthcare resources, due to it having the highest specificity. The 6CIT was the best performer in terms of delivering more QALYs due to it having the highest sensitivity.

6.2.2 DSA and PSA results

6.2.2.1 Deterministic Sensitivity Analysis

A summary for the deterministic sensitivity analysis results from the model is presented in Table 6.4, Table 6.5, Table 6.6 (each table presents the results for an intervened option).
Table 6.4: DSA results for the MMSE option

<table>
<thead>
<tr>
<th>Results for the MMSE option (compared to the baseline option)</th>
<th>Incremental costs</th>
<th>Incremental QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>Base case</td>
<td>-£65.62</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Medication effectiveness duration increased to 2 years</td>
<td>-£66.62</td>
<td>-£0.25</td>
</tr>
<tr>
<td>Medication effectiveness Upper 95% CI value</td>
<td>-£65.62</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Medication effectiveness Lower 95% CI value</td>
<td>-£65.62</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Annual medication costs (including monitoring costs) ▲+25%</td>
<td>-£65.20</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Annual medication costs (including monitoring costs) ▼-25%</td>
<td>-£66.04</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Annual probability of being assessed by GP Upper range value</td>
<td>-£82.09</td>
<td>-£0.14</td>
</tr>
<tr>
<td>Annual probability of being assessed by GP Lower range value</td>
<td>-£38.16</td>
<td>-£0.07</td>
</tr>
<tr>
<td>No license fee for using MMSE</td>
<td>-£66.92</td>
<td>-£0.13</td>
</tr>
<tr>
<td>Nurse administering the test</td>
<td>-£106.73</td>
<td>-£0.13</td>
</tr>
</tbody>
</table>

(1) health care, (2) government-funded social care, (3) private payment for care, (4) informal care, (5) patient QALYs, and (6) carer QALYs
Table 6.5: DSA results for the 6CIT option

<table>
<thead>
<tr>
<th>Results for the 6CIT option (compared to the baseline option)</th>
<th>Incremental costs</th>
<th>Incremental QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>Base case</td>
<td>+£3.17</td>
<td>-£2.48</td>
</tr>
<tr>
<td>Medication effectiveness duration increased to 2 years</td>
<td>-£23.73</td>
<td>-£5.21</td>
</tr>
<tr>
<td>Medication effectiveness</td>
<td>Upper 95% CI value</td>
<td>-£3.00</td>
</tr>
<tr>
<td></td>
<td>Lower 95% CI value</td>
<td>+ £8.33</td>
</tr>
<tr>
<td>Annual medication costs (including monitoring costs)</td>
<td>▲+25%</td>
<td>+ £12.96</td>
</tr>
<tr>
<td></td>
<td>▼-25%</td>
<td>-£6.62</td>
</tr>
<tr>
<td>Annual probability of being assessed by GP</td>
<td>Upper range value</td>
<td>-£2.96</td>
</tr>
<tr>
<td></td>
<td>Lower range value</td>
<td>+ £3.83</td>
</tr>
<tr>
<td>No license fee for using MMSE</td>
<td>+ £3.17</td>
<td>-£2.48</td>
</tr>
<tr>
<td>Nurse administering the test</td>
<td>-£20.81</td>
<td>-£2.48</td>
</tr>
</tbody>
</table>

(1) health care, (2) government-funded social care, (3) private payment for care, (4) informal care, (5) patient QALYs, and (6) carer QALYs
Table 6.6: DSA results for the GPCOG option

<table>
<thead>
<tr>
<th>Results for the GPCOG option (compared to the baseline option)</th>
<th>Incremental costs</th>
<th>Incremental QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>Base case</td>
<td>-£185.54</td>
<td>-£0.31</td>
</tr>
<tr>
<td>Medication effectiveness duration increased to 2 years</td>
<td>-£187.45</td>
<td>-£0.54</td>
</tr>
<tr>
<td>Medication effectiveness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper 95% CI value</td>
<td>-£185.99</td>
<td>-£0.38</td>
</tr>
<tr>
<td>Lower 95% CI value</td>
<td>-£185.18</td>
<td>-£0.25</td>
</tr>
<tr>
<td>Annual medication costs (including monitoring costs)</td>
<td>▲+25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-£184.55</td>
<td>-£0.31</td>
</tr>
<tr>
<td></td>
<td>▼-25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-£186.52</td>
<td>-£0.31</td>
</tr>
<tr>
<td>Annual probability of being assessed by GP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper range value</td>
<td>-£234.83</td>
<td>-£0.44</td>
</tr>
<tr>
<td>Lower range value</td>
<td>-£113.37</td>
<td>-£0.25</td>
</tr>
<tr>
<td>No license fee for using MMSE</td>
<td>-£185.54</td>
<td>-£0.31</td>
</tr>
<tr>
<td>Nurse administering the test</td>
<td>-£202.45</td>
<td>-£0.31</td>
</tr>
</tbody>
</table>

(1) health care, (2) government-funded social care, (3) private payment for care, (4) informal care, (5) patient QALYs, and (6) carer QALYs
For the MMSE option, its incremental costs and QALYs were robust in all DSA scenarios. The health care cost was the most sensitive outcome, especially with the change in the monetary valuation of administration time. For the 6CIT option, DSA results showed that its incremental costs and QALYs were sensitive to the effectiveness of the dementia medications. This was due to the high sensitivity of the 6CIT since it helped detect people with dementia earlier in the model. The more effective the post-diagnostic treatments for dementia, the more benefit the 6CIT would deliver. For the GPCOG option, its incremental costs and QALYs were robust in all DSA scenarios. Its incremental health care cost was sensitive to the annual probability of being assessed by GPs. This was because the savings in health care resources for the GPCOG came from its high specificity. The GPCOG reduced the number of false positive patients referred by GPs to memory services, hence, saved memory service resources. This was again sensitive to the number of patients who present themselves at GPs.

### Probabilistic Sensitivity Analysis

A summary for the PSA results from the model is presented in Table 6.7, Table 6.8, and Table 6.9 (each table presents the results for an intervened option).

#### Table 6.7: PSA results for the MMSE option

<table>
<thead>
<tr>
<th>Results for the MMSE option</th>
<th>Range of values from the PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental value per patient</td>
<td>Minimum</td>
</tr>
<tr>
<td>Health care</td>
<td>- £215.21</td>
</tr>
<tr>
<td>Government-funded social care</td>
<td>- £1.31</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>- £1.70</td>
</tr>
<tr>
<td>Informal care</td>
<td>- £12.73</td>
</tr>
<tr>
<td>Patient QALYs</td>
<td>0.00000</td>
</tr>
<tr>
<td>Carer QALYs</td>
<td>0.00000</td>
</tr>
</tbody>
</table>
Table 6.8: PSA results for the 6CIT option

<table>
<thead>
<tr>
<th>Results for the 6CIT option</th>
<th>Range of values from the PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental value per patient</td>
<td>Minimum</td>
</tr>
<tr>
<td>Health care</td>
<td>- £76.15</td>
</tr>
<tr>
<td>Government social-funded care</td>
<td>- £7.19</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>- £12.22</td>
</tr>
<tr>
<td>Informal care</td>
<td>- £41.49</td>
</tr>
<tr>
<td>Patient QALYs</td>
<td>0.00000</td>
</tr>
<tr>
<td>Carer QALYs</td>
<td>0.00000</td>
</tr>
</tbody>
</table>

Table 6.9: PSA results for the GPCOG option

<table>
<thead>
<tr>
<th>Results for the GPCOG option</th>
<th>Range of values from the PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental value per patient</td>
<td>Minimum</td>
</tr>
<tr>
<td>Health care</td>
<td>- £530.66</td>
</tr>
<tr>
<td>Government-funded social care</td>
<td>- £1.34</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>- £2.32</td>
</tr>
<tr>
<td>Informal care</td>
<td>- £19.57</td>
</tr>
<tr>
<td>Patient QALYs</td>
<td>0.00000</td>
</tr>
<tr>
<td>Carer QALYs</td>
<td>0.00000</td>
</tr>
</tbody>
</table>
6.3 Discussion and conclusion

6.3.1 Limitations of the model

First, the model assumed all dementia followed the pattern of the AD sub-type. However, there are other dementia sub-types which can have some different features in addition to the common characteristics of dementia. For example, people with vascular dementia can have higher risk of recurrent strokes which can significantly reduce their quality of life and chance of survival (Bermingham, 2014).

Second, memory services were assumed to always be able to correctly diagnose dementia, MCI, and non-cases. However, in reality, there might be false negatives and false positives made by memory services. False positive diagnoses could have a negative impact on the patient quality of life but the evidence is limited. Our model can be improved in the future by relaxing that assumption when more data are available.

Third, the model assumed the treatment for diagnosed dementia was only the current AD medications however, in practice, there is a wide range of different treatment options and support for diagnosed dementia. The evidence for the effectiveness of those interventions is limited although some of them could improve the quality of life for patients and caregivers (Knapp et al., 2013).

Finally, data were not available to accurately estimate all model parameters. This study had to combine the best available evidence from different sources to estimate the model inputs. Nevertheless, these were addressed in DSA and PSA. The DSA results showed that model results were sensitive to changes in some inputs such as the medication effectiveness, the probability of being assessed by GPs, and the cost of administering the test. The results in this study were specific for the situation in England. The model structure and logic can be generalised to similar health care systems, though the input estimates would need to be adjusted to reflect the situation in other countries.
6.3.2 Discussion on the issue of heterogeneity in the cost-effectiveness results

Cost-effectiveness analyses estimate the cost and benefit of an intervention compared with relevant comparators. These estimates can be average (i.e. a mean estimate) across a heterogeneous population. However, there can be important variations between individuals that result in substantial differences in the sub-group estimated benefit and cost (Sculpher, 2008). Some of this variation can be explained by certain sociodemographic or clinical characteristics of patients (Sculpher, 2008). This type of heterogeneity in cost-effectiveness analysis has been recognised (Sculpher, 2008, Espinoza et al., 2014) and the use of subgroup analyses in cost-effectiveness analysis has been recommended by several national health care agencies including NICE (Espinoza et al., 2014).

Chapter 6 of the thesis reports the results of a patient-level cost-effectiveness model which was used to evaluate four diagnostic strategies to identify patients with cognitive impairment in a primary care setting: (1) GPs’ unassisted judgement, (2) GPs using the MMSE; (3) GPs using the 6CIT; (4) GPs using the GPCOG. The modelled cohort was a heterogeneous cohort which was a representative sample of the general population 65 years and older in England. The cost-effectiveness results were the average estimates for the cohort. Given the decision problem, the possible forms of subgroup and heterogeneity could include the following factors:

- Age groups (for example, the results could be stratified for different age groups at the baseline: 65 – 75 years old, 75 – 85 years old, and above 85 years old)
- Gender (male versus female)
- Educational level of the patient (for example, by years of education)
- ‘At-risk’ individuals (NHS, 2015):
  - Patients 60+ years old who had cardiovascular disease (CVD), stroke, peripheral vascular disease or diabetes.
  - Patients 60+ years old and had a ‘high-risk’ of CVD (e.g. smoking, alcohol consumption or obesity)
  - Patients 60+ years old with a COPD diagnosis
  - Patients 40+ years old with Down's syndrome
  - Patients 50+ years old with learning disabilities
  - Patients with a long-term neurological disorder that has a known neurodegenerative element (e.g. Parkinson’s disease).
These factors could influence the diagnostic strategies and the cost-effectiveness results. For example, the prevalence of cognitive impairment and dementia is one of the key factors that drives the effectiveness of different diagnostic strategies. This prevalence varies by age group (higher prevalence among older individuals) and gender (higher prevalence among older female) (Knapp et al., 2007, Prince et al., 2014). Educational level and age of the patient could also influence the sensitivity and specificity of the diagnostic strategies (Crum et al., 1993).

This heterogeneity in the cost-effectiveness could be relevant to policy. The results based on the average estimates favoured the use of the GPCOG to screen individuals 65 years and older. However, taking into account the heterogeneity in the cost-effectiveness results, the results could be different (for example, the 6CIT could be more cost-effective than the GPCOG for certain sub-groups of patients), which could result in a different recommendations (i.e. different diagnostic strategies) for different sub-groups of patients. Nonetheless, there could be significant challenges regarding the required data for the subgroup analyses and addressing the subsequent uncertainty. This heterogeneity was not considered in the analysis. The average results from the mixed cohort were used instead of more stratified results from homogenous subgroups.

6.3.3 Discussion on the possibility of missing one or more options in the analysis

The economic analysis reported in this chapter concerned four diagnostic/opportunistic screening strategies that could be adopted by GPs to early identify patients with cognitive impairment in a primary care setting: (1) GPs’ unassisted judgement, (2) GPs using the MMSE; (3) GPs using the 6CIT; (4) GPs using the GPCOG. The key part of the care pathway that these interventions involved was described with three important events:

- A patient came to the GP
- The GP assessed the patient to see whether the patient was suspected with cognitive impairment. If the assessment was positive, the GP then referred the patient to have a confirmative diagnosis at a memory service. The memory service was assumed to be able to confirm the disease status with 100% accuracy.
- If the patient was confirmed with dementia, he/she was given the post-diagnostic care. Here it was assumed that the post-diagnostic care was simply the dementia medication that would give the patient some temporary improvement in their cognitive function.
It could be argued that the list of the four options was not comprehensive. In particular, the option whereby GPs perform no opportunistic screening was not considered in the analysis. In other words, GPs could be asked to stop the whole opportunistic screening and only refer patients to memory services if they come with obvious symptoms. This is a potential option to be included in the economic evaluation. However, there could be a couple of issues in specifying and differentiating this option from the current baseline option (GPs’ unassisted judgement). The ‘no-screening’ strategy would vary substantially between different GPs (e.g. GPs have different opinions about obvious symptoms of cognitive impairment) and it does not guarantee that all cases referred by GPs are accurate. This would look similar to the current baseline option (GPs’ unassisted judgment) but perhaps with less patients being referred to memory services. In principles we could assume that without opportunistic screening, GPs would only refer patients with moderate or severe cognitive impairment to memory services.

In other words, patients with cognitive impairment would not be detected until they progressed to moderate dementia. This would result in later access (compared to other scenarios) to treatments and care for patients and their caregivers but more savings in terms of the diagnostic cost for the NHS. However, it could be argued that this assumption would not be realistic and it would make the strategy look quite unethical (i.e. delaying patients and caregivers’ access to post-diagnostic treatment and care). Furthermore, at the time when this research was conducted, GPs had already been incentivised to carry out an opportunistic screening strategy (NHS, 2015). Given early detection of dementia is a big policy issue, it was realistic to assume GPs performing opportunistic screening.

The current ‘standard of care’ in this analysis (GPs’ unassisted judgement scenario) is of questionable effectiveness and cost-effectiveness. This was mentioned quite often in conversations with local commissioners and clinicians. More could be done to improve GPs’ performance in assessing and referring people suspected with cognitive impairment. Given the pressure from the government to increase the diagnosis rate in dementia, it was important to make sure GPs are efficient in identifying people with cognitive impairment. Nonetheless, the question of how was not easy to answer. More systematic options (e.g. using screening tools) in this thesis looked more cost-effective compared to the standard of care but there could be other options that could be even more cost-effective to improve the current situation.
6.3.4 Why the particular interventions were chosen in the first instance and the pathways that they involve

These particular interventions were selected in consultation with dementia experts, commissioners, clinicians and based on the results of online survey of GPs in UK.

First, from the literature review, conversations with local experts in dementia, and by attending various conferences about dementia and dementia care (in 2014 and 2015) I was informed that early detection of dementia was a topical issue of interest to current policy making. Although a cure for dementia (a disease-modifying treatment) had not been found, the main argument for early detection of dementia was that the current post-diagnostic care includes a wide range of different types of therapies and supports which could be helpful for patients and their caregivers; and the earlier the patients and their caregivers were put on the care pathway, the better it would be. Thus, I was interested in looking at the interventions for early detection of dementia.

In further conversations with local commissioners and clinicians in Sheffield, one issue which was raised quite often by memory services was that GPs were not doing a good job in referring people suspected with cognitive impairment to memory services. Memory services received cases which shouldn’t be referred to them. Because it was quite expensive for memory services to perform the confirmative diagnosis for dementia, we should look at strategies to make GPs more effective in screening people with cognitive impairment and referring them to memory services. This issue was discussed with a local GP. We found that GPs could have different strategies in screening and identifying people with dementia.

We then conducted a brief survey on an online forum for GPs in the UK. We asked GPs on the forum what cognitive test they often used in screening for dementia and cognitive impairment. We received 102 responses from the forum suggesting three most frequently used screening tests: the MMSE (26% of responses), the 6CIT (29% of responses), and the GPCOG (21% of responses). These tests were different in terms of their performances (sensitivity and specificity) and the time needed to perform the test. After consulting with the GP, I decided to finalise the evaluation decision problem looking at the four options as described above.

The pathway that they involved was developed during the development of the conceptual model. It went through several stages and it was discussed and validated by local clinicians.
6.3.5 Decision making based on the results

The model in this chapter provided estimates for costs and QALYs of different (mutually exclusive) decision options regarding the use of cognitive screening tests in a primary care setting. All three screening tests were estimated to deliver more QALYs (for both patients and caregivers) and make savings across different sectors including health care, social care, and informal care. Given the estimates from the model, questions remain about which option is the best and whether the interventions are cost-effective. As discussed in previous chapters, the answers of these questions are not simple since there are multiple criteria to be considered and we need to understand the exchanges/trade-offs between different costs and benefits. Costs include the health care, the government-funded social care, the private payment for care, and the informal care. Benefits include the patient QALYs and the carer QALYs. How should we exchange one to another? How can we judge the cost-effectiveness of them given our budget? The next two chapters will report and discuss the operationalisation of the extended cost-per-QALY approach and the CCA-MCDA approach to address the above questions.
CHAPTER 7. THE EXTENDED COST-PER-QALY APPROACH

This chapter reports the implementation of the extended cost-per-QALY approach in the case study. The chapter is divided into four sections. The first section summarises the case study. Section two presents the implementation of the healthcare-perspective cost-per-QALY analysis. Section three describes the implementation of the extended cost per QALY approach. Section four discusses the limitations, lessons learned, and concludes the chapter.
7.1 The case study

The case study looked at the evaluation of four interventions for early detecting dementia in primary care: (1) GP’s unassisted judgement, (2) GPs using the MMSE, (3) GPs using the 6CIT, and (4) GPs using the GPCOG. The baseline option was GP’s unassisted judgement. Decision makers could only choose one of the four options. A cost-effectiveness model was developed in Chapter 6 to estimate the costs and benefits for each decision option. Costs of the interventions fell on three sectors: the NHS, the government social care, and the patients and families. Benefits of the interventions were measured in terms of QALYs for patients and for informal caregivers. A brief description of the absolute costs and benefits estimated by the model for each decision option is presented in Table 7.1.
Table 7.1: Costs (£) and benefits (QALYs) of interventions

<table>
<thead>
<tr>
<th></th>
<th>Note</th>
<th>Unit</th>
<th>Perspective</th>
<th>Decision options</th>
</tr>
</thead>
<tbody>
<tr>
<td>BENEFITS</td>
<td></td>
<td></td>
<td>(1) (2)</td>
<td>Baseline</td>
</tr>
<tr>
<td>Patients</td>
<td>Q1</td>
<td>QALYs</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Caregivers</td>
<td>Q2</td>
<td>QALYs</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>COSTS</td>
<td></td>
<td></td>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>Health care (NHS)</td>
<td>Ch</td>
<td>£</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Government-funded social care</td>
<td>Cs</td>
<td>£</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Private payment and informal care</td>
<td>Cc</td>
<td>£</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

(1) Health care perspective
(2) Societal perspective

(Source: the estimates were produced from the model developed in Chapter 6. The table structure was adapted from the inventory table recommended by Neumann et al. (2017))
Evidence for the cost-effectiveness thresholds in different sectors

As discussed in Chapter 3 (section 3.3.2), the extended cost-per-QALY approach aimed to aggregate wider costs and health care cost using sector-specific cost-effectiveness thresholds. Regarding the threshold values for different sectors, there was evidence for the use of threshold in the healthcare sector but no threshold has been established for the social care sector. For the threshold in the healthcare sector, there are two sources of values. First, it is the policy-based value which is used by NICE: the value ranges between £20,000 per QALY and £30,000 per QALY (NICE, 2013a). These values can be interpreted as the WTP for a unit of health by NICE given its knowledge about the national healthcare system. Second, there has been an empirical estimate of the threshold in the healthcare sector: the central estimate is £12,936 per QALY (Claxton et al., 2015). This value is argued to reflect the QALYs forgone as other NHS activities are displaced to accommodate the additional costs of new health care interventions. For the social care sector, no threshold has been established although expert opinion suggested that the social care cost-effectiveness threshold was similar to the one in the health care sector (Private correspondence with Professor Julien Forder, University of Kent).

The evidence for the consumption value (v) of a QALY is mixed. The Department of Health uses the value of £60,000 per QALY (Glover and Henderson, 2010). However, a systematic review by Rowen et al. (2017) found that this value did not reflect UK general population values reported in the existing literature. The value (£60,000 per QALY) was estimated based on the WTP value of a prevented fatality in road traffic accident from a research in the Department of Transport. The value of a prevented fatality was divided by the average discounted expected number of remaining QALYs for those who died in road traffic accident to produce the £60,000 per QALY. Rowen et al. (2017) found four studies that elicited monetary values of a QALY from members of the UK general population. The mean values from the studies ranged from £1,765 to billions in 2009 prices. The extremely large and implausible values (billions) were only found using in one study for a specific method. When excluding the implausible values, the mean values ranged from £1,765 to £28,729 (Rowen et al., 2017).
7.2 The healthcare-perspective implementation

The healthcare perspective implementation only included the health care cost and the patient QALYs in the analysis. The economic evaluation principle is described by the following equation (more details are referred to Chapter 3, section 3.3.1):

\[
ICER = \frac{\Delta C_h}{\Delta Q_{\text{patient}}} < k_h
\]

Base-case implementation

Table 7.2 presents the economic evaluation results from a healthcare perspective (only the patient QALYs and the health care cost were considered).

<table>
<thead>
<tr>
<th>Option</th>
<th>Ch</th>
<th>H</th>
<th>ΔCh</th>
<th>ΔQ</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>28,834</td>
<td>12.00886</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MMSE</td>
<td>28,768</td>
<td>12.008976</td>
<td>-66</td>
<td>0.0001</td>
<td>MMSE dominates baseline</td>
</tr>
<tr>
<td>GPCOG</td>
<td>28,648</td>
<td>12.009246</td>
<td>-120</td>
<td>0.0002</td>
<td>GPCOG dominates MMSE</td>
</tr>
<tr>
<td>6CIT</td>
<td>28,837</td>
<td>12.013143</td>
<td>189</td>
<td>0.00318</td>
<td>£59,453 per QALY</td>
</tr>
</tbody>
</table>

The incremental analysis showed that at thresholds less than £59,453 per QALY, the most cost-effective option was the GPCOG. At thresholds more than £59,453 per QALY, the most cost-effective option was the 6CIT.

Probability Sensitivity Analysis (PSA) was run with 2000 samples of the input parameters. Each sample of the input parameters gave an estimate for health care cost and patient QALYs gained. The cost-effectiveness acceptability curve (CEAC) is shown in Figure 7.1.
The best option was a choice between the 6CIT and the GPCOG. At cost-effectiveness thresholds lower than £52,000 per QALY, the GPCOG had the highest probability of being the best option. However, at thresholds higher than £52,000 per QALY, the 6CIT had the highest probability of being the best option.

7.3 The extended cost-per-QALY

In the extended cost-per-QALY, all costs and benefits were included: the health care, the government-funded social care cost, the private payment for care, the patient QALYs, and the carer QALYs. The economic evaluation principle is described by the following equation (more details are referred to Chapter 3, section 3.3.2):

\[
ICER = \frac{\Delta C_{\text{aggregated}}^{\text{total}}}{\sum_{i=1}^{n} \Delta Q_i^{\text{gained}}} < k_h
\]
Aggregating costs falling on different sectors:

Costs falling on the three sectors were aggregated as follows (see Chapter 3, section 3.3.2 for more details):

$$\Delta C_{\text{total}}^{\text{aggregated}} = \Delta C_h + \frac{k_h}{k_s} \cdot \Delta C_{ss} + \frac{k_h}{v} \cdot \Delta C_c$$

To implement this equation, we needed to have estimates for the two ratios: the ratio between the cost-effectiveness thresholds in the healthcare sector and the social care sector ($k_h/k_s$), and the ratio between the cost-effectiveness threshold in the healthcare sector and the consumption value of a QALY ($k_h/v$). Theoretically, these ratios can lie anywhere between zero and infinity.

For the ratio between the healthcare sector and the social care sector thresholds ($R_1 = k_h/k_s$), expert opinion suggested that the social care cost-effectiveness threshold was similar to the one in the healthcare sector (Private correspondence with Professor Julien Forder, University of Kent). Thus, for the demonstration in this case study, we chose the ratio $k_h/k_s$ to be one in the base case, but different values were explored in sensitivity analyses.

For the ratio between the healthcare sector threshold and the social value of a QALY ($R_2 = k_h/v$), there was no evidence suggesting whether one was higher, lower, or equal to the other. Table 7.3 presents various possible values for the ratio given available evidence. For the healthcare threshold, the values recommended by NICE were used (£20,000 per QALY and £30,000 per QALY). For the value of a QALY for patients and families, all reported mean values from the four studies identified in the systematic review by Rowen et al. (2017) and the DH recommended value (£60,000 per QALY) were used.
Table 7.3: Possible values for the ratio $R_2 (k_i/v)$

<table>
<thead>
<tr>
<th>Values for the ratio $R_2$</th>
<th>The healthcare threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20000</td>
</tr>
<tr>
<td>The value of a QALY for patients and their families</td>
<td></td>
</tr>
<tr>
<td>1765</td>
<td>11.3</td>
</tr>
<tr>
<td>6140</td>
<td>3.3</td>
</tr>
<tr>
<td>8636</td>
<td>2.3</td>
</tr>
<tr>
<td>19056</td>
<td>1.0</td>
</tr>
<tr>
<td>19134</td>
<td>1.0</td>
</tr>
<tr>
<td>21197</td>
<td>0.9</td>
</tr>
<tr>
<td>28729</td>
<td>0.7</td>
</tr>
<tr>
<td>40273</td>
<td>0.5</td>
</tr>
<tr>
<td>60000</td>
<td>0.3</td>
</tr>
</tbody>
</table>

(Source: Rowen et al., 2017)

Given available evidence, the ratio ($R_2$) lied between 0.3 and 17 (mean = 3.0). The mean (3.0) was chosen in our base case, and the variation was explored in sensitivity analyses.

**Aggregating benefits**

Benefits were aggregated as following assuming patient QALYs and carer QALYs could be aggregated with equal weights:

$$\Delta Q^{\text{aggregated}}_{\text{total}} = \Delta Q^{\text{gained}}_{\text{patient}} + \Delta Q^{\text{gained}}_{\text{carer}}$$

This assumed the only benefit of spending in social care was the same health measured in QALYs (with health-related quality of life) as in the healthcare sector. This may not be the case. In the healthcare sector, the EQ-5D is recommended to be used for HRQOL. However, the EQ-5D is too narrow for social care benefits (NICE, 2013b). For the social care, the outcomes of care are broader to include other aspects of quality of life of the individuals (e.g. accommodation, relationships, independence) and their informal carers. In the social care, other measures have been suggested such as the Adult Social Care Outcomes Toolkit (ASCOT) and the capability measure ICECAP (NICE, 2013b). Nevertheless, it has been shown that health and social care QALYs are commensurate in value (Brazier et al., 2016).
**Base-case results**

*Table 7.4* presents the base-case results for the economic evaluation from the societal perspective. *Table 7.5* presents the incremental analysis.
Table 7.4: Base-case results for the societal perspective from the extended cost-per-QALY approach

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>MMSE</th>
<th>GPCOG</th>
<th>6CIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEALTH BENEFITS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (patients)</td>
<td>5.9983</td>
<td>5.998403</td>
<td>5.998606</td>
<td>6.001785</td>
</tr>
<tr>
<td>Q2 (carers)</td>
<td>6.98902</td>
<td>6.989038</td>
<td>6.989116</td>
<td>6.989951</td>
</tr>
<tr>
<td>Total health</td>
<td>12.98732</td>
<td>12.98744</td>
<td>12.98772</td>
<td>12.99174</td>
</tr>
<tr>
<td>COSTS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weighting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ch (health care)</td>
<td>1</td>
<td>1</td>
<td>28,834</td>
<td>28,848</td>
</tr>
<tr>
<td>Cs (social care)</td>
<td>R₁ = K₁/K₅</td>
<td>1</td>
<td>26,035</td>
<td>26,035</td>
</tr>
<tr>
<td>Cc (private)</td>
<td>R₂ = K₂/V</td>
<td>3</td>
<td>47,266</td>
<td>141,798</td>
</tr>
<tr>
<td>Aggregated Cost</td>
<td></td>
<td></td>
<td>196,667</td>
<td>196,598</td>
</tr>
</tbody>
</table>

Note: The table presents the base-case results for the societal perspective using the extended cost-per-QALY approach. The table includes health benefits and costs for different scenarios (Q1, Q2, Total health, Ch, Cs, Cc, Aggregated Cost) with original and weighted values.
Using the extended cost-per-QALY analysis for a societal perspective, the incremental analysis showed that at healthcare thresholds less than £41,355 per QALY, the most cost-effective option was the GPCOG. At healthcare thresholds more than £41,355 per QALY, the most cost-effective option was the 6CIT. Compared to the evaluation from the healthcare perspective only, the incorporation of wider costs and carer QALYs gained brought the critical point of the threshold from £59,453 to £41,355 per QALY.

**Deterministic Sensitivity Analysis (DSA) with the ratios**

The impact of the two ratios ($R_1$ and $R_2$) on the results was assessed in one-way sensitivity analyses. First, $R_1$ was varied from 0 to 30 (with a step of 0.5) while keeping $R_2$ fixed at 3. The ICER for the comparison between the 6CIT and the GPCOG were calculated for each value of $R_1$. Figure 7.2 presents the results.
Figure 7.2: One-way sensitivity for changes in the ratio $R_1$ (between $k_s$ and $k_h$)

As can be seen, the value of the ratio $R_1$ could change the cost-effectiveness ranking of the options. The impact was mainly on the cost-effectiveness ranking of the 6CIT option because the 6CIT option had the highest estimate in terms of saving for the government-funded social care. The higher the value of $R_1$, the more cost-effective ranking the 6CIT option became. At the healthcare threshold of £30,000 per QALY, the 6CIT became the best option when $R_1$ was increased to 30. However, it should be noted that the value of $R_1$ is the ratio between £ per QALY in the healthcare sector and in the social care sector reflecting the comparison between the two sectors in terms of the efficiency of their resources. It is unlikely for $R_1$ to reach a high value such as 30; this would mean, for example, for $k_h = £30,000$ per QALY, $k_s$ (for social care) = £1,000 per QALY.

Figure 7.3 presents the results for the one-way sensitivity analysis on $R_2$ at different healthcare thresholds (keeping $R_1$ fixed at 1).
The value of $R_2$ could also change the cost-effectiveness ranking of the options. The impact was mainly on the cost-effectiveness ranking of the 6CIT option because the 6CIT option had the highest estimate in terms of savings for the private payment for care and the informal care. The higher the value of $R_2$, the more cost-effective ranking the 6CIT option gained. Compared to the change in value of $R_1$ in the sensitivity analysis above, the value of $R_2$ only needed to increase to a relatively lower value to change the cost-effectiveness ranking of the options.

**Probabilistic Sensitivity Analysis**

In conducting Probabilistic Sensitivity Analysis (PSA), in addition to the usual parameters for costs and QALYs, we needed to incorporate the uncertainty around the estimates for the two ratios ($R_1$, $R_2$). For the ratio between the health care and the social care ($R_1$), a beta distribution with a mean of 1 was used to describe the uncertainty: Beta distribution (min = 0, max =3, alpha = 1.5, beta = 3.0). For the ratio between the health care and the private costs ($R_2$), a beta distribution with a mean of 3 was used: Beta distribution (min = 0, max = 9, alpha = 1.5, beta = 3.0). The values of $R_1$ and $R_2$ were sampled from their distributions together with other usual parameters for costs and QALYs in the PSA runs. PSA was run with 2000 samples of the input parameters. The Cost-Effectiveness Acceptability Curve (CEAC) was shown in Figure 7.4.
As can be seen, the best option was still mainly a choice between the 6CIT and the GPCOG from the societal perspective. However, the critical point of the cost-effectiveness threshold (where the decision changes) was different from the healthcare perspective. The critical point was now at £29,000 per QALY (compared to £52,000 per QALY in the healthcare perspective).

7.4 Discussion and conclusion

7.4.1 Summary

This study investigated the use of sector-specific cost-effectiveness thresholds and a social value of health to aggregate costs falling on different sectors in an extended cost-per-QALY analysis. The results were compared with a conventional cost-per-QALY analysis from the healthcare perspective. The healthcare perspective only included the health care cost and the patient QALYs. The best option was the choice between the 6CIT and the GPCOG. The ICER for the 6CIT when compared with the GPCOG was £59,453 per QALY. The broader societal perspective included the wider costs (the government-funded social care, the private payment for care, and the informal care) in addition to the health care cost; the carer QALYs were included with equal weight to the patient QALYs. The extended cost per QALY approach
aggregated costs falling on different sectors with different weights based on sector-specific thresholds and a societal value of health. Taking a broader societal perspective in an extended cost-per-QALY, the ICER for the 6CIT when compared with the GPCOG was £41,355 per QALY. We can see that the decision could change between the healthcare perspective and the societal perspective. With thresholds less than £41,355 per QALY or more than £59,453 per QALY, the decision did not change between the two perspectives. However, with thresholds between £41,355 per QALY and £59,453 per QALY, the decision was different between the two perspectives.

We found that costs falling on different sectors could be weighted and aggregated based on the sector-specific cost-effectiveness thresholds and the social value of health. This way, wider costs were aggregated to health care cost to derive a single aggregated cost which was compared with QALYs gained similarly to a conventional cost-per-QALY analysis. A full incremental analysis could be performed. PSA needed to explicitly sample the estimates for the ratios between different sector-specific thresholds. Although the demonstration was performed for a case study of dementia, the approach can potentially be generalised to other interventions, conditions, and sectors.

7.4.2 Limitations of the case study

There are some limitations associated with our study. First, the case study was not comprehensive; it was only illustrative as an exploration of methods. The case study only showed one way to operationalise the extended cost-per-QALY approach; there are other ways such as the Value-Based Pricing approach in the UK (DH, 2010, Roberts, 2015).

Second, the case study was limited to dementia care only. The case study only included government funded social care, private social care and informal care as the wider costs. The case study only accounted for patient QALYs and carer QALYs for health benefits. However, from a societal perspective, there could be other costs such as costs falling on the police sector, costs falling on the housing sector, etc. and there could be other benefits beyond the health-related QALY measure such as process utility, well-being, etc. Thus, the case study was not truly the implementation of a full societal perspective.
Third, the evidence for thresholds in non-health sectors is very limited. The case study had to make several assumptions regarding the values of the threshold ratios. Although these were tested in sensitivity analyses, their values were still controversial.

Fourth, the case study only showed the aggregation of patient QALYs and carer QALYs with equal weights. In practice, they could be argued to be aggregated with different weights. However, the method for weighting QALYs and incorporating them in a Cost-Effectiveness Analysis is not well developed (Rowen et al., 2014). Further research is needed to see how we can account for QALYs weighting in both costs and benefits in an extended cost-per-QALY approach.

Finally, taking a broader perspective in costs also needs a broader perspective in benefits. This case study assumed health benefit was measured the same across sectors. Although this may not be the case with the current practice in health and social care, future research is expected to develop a broader quality of life measure for use across the sectors of health care, social care, and public health (Brazier et al., 2016).

7.4.3 Discussion on the inclusion of carer QALYs under a ‘health care perspective’

In the healthcare-perspective implementation, only the patient QALYs gained were included in the cost-effectiveness calculation. It is recognised that this is not really the case for a real-life implementation of the healthcare perspective. The common position that national health care agencies often take is to include all health gained regardless of who receive them. For example, the NICE’s reference case for the method of health technology appraisal (2013) states that ‘all direct health effects, whether for patients or, when relevant, carers’ should be the perspective on outcomes in economic evaluation.

Nonetheless, given the objective of the thesis was to demonstrate the implementation of the two perspectives (healthcare perspective and societal perspective), caregiver QALYs were not included under the healthcare-perspective demonstration to give more emphasis on the complexity of aggregating different types of benefits in the societal perspective. It is worth noting that that carer QALYs were not considered in the base case analyses in the NICE appraisal of medications for Alzheimer’s disease (Bond et al., 2012) even though some companies submitted evidence on carer QALYs. Please see the text “Total QALYs are also estimated to be greater from the Eisai/Pfizer model compared with the PenTAG model;
however, Eisai/Pfizer include both patient and carer QALYs in their base case (whereas the PenTAG base-case model includes only patient QALYs).” in page 234 of the report (Bond et al., 2012b)

7.4.4 Conclusion

This study shows that it is possible to weight and aggregate costs falling on different sectors in an extended cost-per-QALY approach. This can help implement a societal perspective in economic evaluation of health care interventions. More evidence for the thresholds in other non-health sectors is needed, however, the method to measure them can be challenging. Further research is needed to understand the relationship between opportunity costs of resources in different sectors. On the other hand, a broader societal perspective also needs a broader measure of health that can be used across sectors. The development a broader QALY measure will complement and make this extended cost-per-QALY approach easier to implement. The next chapter describes the implementation of CCA-MCDA approach.
CHAPTER 8. THE CCA-MCDA APPROACH

This chapter reports the implementation of the CCA-MCDA approach in the case study.

The chapter is divided into six sections. The first section summarises the evaluation problem and the decision context. The following sections (section two to section five) describe the operationalisation of the approach in details. Section two describes the identification and recruitment of a hypothetical decision-making group. Section three describes the customisation of the general approach to the problem in the case study. Section four describes the facilitated decision-making workshop and reports the results from the workshop (including the results from a qualitative analysis of the workshop recording). Section five describes the calculation and presentation of the results. The final section (section six) summarises, discusses and concludes the chapter.
8.1 The decision problem

The cost-effectiveness model (Chapter 6) provided estimates for costs and benefits of alternative interventions in early detection of dementia in primary care: (1) GP’s unassisted judgement, (2) GPs using the MMSE, (3) GPs using the 6CIT, and (4) GPs using the GPCOG. The baseline option was GP’s unassisted judgement. Decision makers could only choose one of the four options based on their costs and benefits. Costs included health care, government-funded social care, private payment for care, and informal care. Benefits included patient health and caregiver health measured in QALYs. A brief description of the absolute costs and benefits estimated by the model for each decision option is presented in Table 8.1.
Table 8.1: Costs (£) and Benefits (QALYs) of interventions (per patient)

<table>
<thead>
<tr>
<th></th>
<th>Note</th>
<th>Unit</th>
<th>Perspective</th>
<th>Decision options</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1)</td>
<td>(2) Baseline</td>
</tr>
<tr>
<td>BENEFITS</td>
<td></td>
<td></td>
<td></td>
<td>MMSE</td>
</tr>
<tr>
<td>Patients</td>
<td>Q1</td>
<td>QALYs</td>
<td>x</td>
<td>5.9983</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.998403</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>5.998606</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.001785</td>
</tr>
<tr>
<td>Caregivers</td>
<td>Q2</td>
<td>QALYs</td>
<td>x</td>
<td>6.98902</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.989038</td>
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<tr>
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<td>6.989116</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.989951</td>
</tr>
<tr>
<td>COSTS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health care (NHS)</td>
<td>C1</td>
<td>£</td>
<td>x</td>
<td>28,834</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28,768</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28,648</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28,837</td>
</tr>
<tr>
<td>Government-funded social care</td>
<td>C2</td>
<td>£</td>
<td>x</td>
<td>26,035</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26,035</td>
</tr>
<tr>
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<td>26,035</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26,033</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>C3</td>
<td>£</td>
<td>x</td>
<td>36,832</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36,832</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td>36,832</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36,828</td>
</tr>
<tr>
<td>Informal care</td>
<td>C4</td>
<td>£</td>
<td>x</td>
<td>10,434</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10,433</td>
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<td>10,433</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10,430</td>
</tr>
</tbody>
</table>

(1) Health care perspective  
(2) Societal perspective

(Source: the estimates were produced from the model developed in Chapter 6. the Table structure was adapted from the inventory table recommended by Neumann et al. (2017))
Health services in England are mainly funded by government. The Department of Health (DH) is the government body responsible for allocating the fund on the NHS, public health, and adult social care. Direct responsibility for commissioning health care services lies with two groups of bodies – the NHS England and clinical commissioning groups (CCGs). The CCGs are supported by and held accountable to the NHS England. Health care services are commissioned by CCGs at the local level. The responsibility for commissioning adult social care services and public health services rests with local authorities (county councils and unitary authorities). The appraisal in this case study was assumed to be at the local level concerning the local Clinical Commissioning Group (CCG).

8.2 The hypothetical decision-making group

This approach is designed to support the local decision makers. The local decision-making group includes those who are directly responsible for making the decision (primary decision makers). It can be expanded to include other individuals from the wider decision-making circle such as those who would be affected by the decision (stakeholders). In our study, the primary decision makers were members of a local Clinical Commissioning Group (CCG) who were responsible for commissioning health care. The stakeholders included members of the local authority (the social care and public health department), members of the local memory services, members of the local General Practices (GP), and members of the local hospitals.

First, the local CCG was approached. The aim, objectives, and methods of this study were presented and discussed with a commissioning manager and a clinical director who were responsible for commissioning dementia care. These two individuals agreed to take part in the study and thus became the decision makers for the evaluation problem in the case study. The evaluation problem was hypothetical because it was not a problem that the local CCG was facing and considering at the time. This study imposed the problem on the decision makers although technically it was still within their commissioning remit.

Four main sectors which were involved in the care of dementia were identified: the NHS (providing health care), the city council (providing social care), the Alzheimer’s society (a voluntary organisation which supports people with AD and their informal caregivers), and the private sector (including patients, their informal caregivers, and the public). Other sectors affected by dementia included the police and the fire brigade.
In addition to the local CCG, three other organisations from the NHS were approached: the local memory services were responsible for diagnosing dementia, the local hospitals were responsible for providing secondary care for dementia, and the local GPs were responsible for providing primary care for dementia. They were all considered to be the stakeholders and were invited to take part in the study.

The social care and public health department from the local city council was approached. They were also considered to be the stakeholders and were invited to take part in the study.

The Alzheimer’s society was approached. The aim, objectives and methods of the study were presented and discussed with an officer from the society. After careful consideration, the study decided not to include the Alzheimer’s society or the private sector (patients and their informal caregivers). Due to the conduct of a decision-making workshop later in this study, including them could make the study become unmanageable. The same reason was applied for excluding the police and the fire brigade. This issue will be discussed later in the limitations of this study.

As the result, fifteen individuals were invited to join this study. Two individuals were commissioning manager and clinical director from the local CCG. Four individuals were commissioning manager, commissioning officer, and public health principals from the city council. Four individuals were clinicians and managers from the local memory services. Four individuals were clinicians who were involved with dementia care from the local hospitals. And one individual was a GP. Ten individuals agreed to take part in the study and came to the decision-making workshop (Table 8.2)

Table 8.2: The decision makers

<table>
<thead>
<tr>
<th>The decision makers</th>
<th>Organisation</th>
<th>Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary decision</td>
<td>The local CCG</td>
<td>• 1 commissioning manager&lt;br&gt;• 1 clinical director</td>
</tr>
<tr>
<td>makers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stakeholders</td>
<td>The NHS</td>
<td>• 2 representing memory services&lt;br&gt;• 1 representing hospitals&lt;br&gt;• 1 representing GP</td>
</tr>
<tr>
<td></td>
<td>The city council</td>
<td>• 1 commissioning manager&lt;br&gt;• 1 commissioning officer&lt;br&gt;• 2 public health principals</td>
</tr>
</tbody>
</table>
8.3 Applying the CCA-MCDA approach

The generic MCDA model was presented in Chapter 3 (section 3.4.2.3). The principle is described in the following equation (see details in section 3.4.2.3):

\[ V_{total}^i = B_{aggregated}^i - \frac{C_{aggregated}^i}{K} \ (QALYs) \]

The overall value of a decision option (option i) is described by a weighted sum of single-attribute values for its aggregated cost and aggregated benefit. In this case study, the decision options were assessed in terms of four different costs (C1, C2, C3, C4) and the two different benefits (Q1, Q2). K is the exchange rate between a unit of aggregated cost and a unit of aggregated benefit. In other words, K is the WTP for a unit of aggregated benefit.

**Aggregating benefits:**

The generic principle (see Chapter 3, section 3.4.2.3) was applied in the case study as follows.

\[ B_{aggregated}^i = V_1^i (B_1^i, B_2^i, ..., B_m^i) = \sum_{y=1}^{m} w'_y \ast B_y^i \ (QALYs) \]

Applying to the two types of QALYs gained in the case study:

\[ \text{Benefit}_{aggregated}^i = (Q_1^i, Q_2^i) = \sum_{j=1}^{2} w_j \ast Q_j^i \]

All benefit was measured in terms of QALYs. Q_j^i is the amount of QALYs gained for group (j) by implementing the decision option (i), and w_j is the relative weight of a QALY gained between different groups. We assumed that the decision makers accepted the legitimacy and validity of the public preferences used in the calculation of QALYs.

To elicit the relative weights between the different benefits, a weighting system was used. The decision makers’ value for one QALY gained for the patients may be different from one QALY gained for the caregivers. First, one QALY gained for the patient was chosen to be the reference.
to weight other benefits i.e. the patient QALY gained was assigned a weight of one. Then, the relative weights for the other benefits were elicited from the decision makers by asking them to compare a QALY gained for another group to a QALY gained for the patients. For example, if the decision makers think the QALYs gained for carers should receive less weight than QALYs gained for patients, they give it a weight of less than one. The smaller the weight, the less that benefit is counted when it is aggregated with the patient QALYs gained. It is possible to give a weight of zero so that the benefit is not counted at all. The range of the relative weight is between zero and infinity. Table 8.3 illustrates the weighting system for benefits.

Table 8.3: The weighting system for benefits

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient QALYs gained (Q₁)</td>
<td>+ 1 QALY per patient</td>
</tr>
<tr>
<td>Carer QALYs gained (Q₂)</td>
<td>+ 1 QALY per carer</td>
</tr>
</tbody>
</table>

This weighting system was developed based on the principles of ‘swing’ weighting in MCDA (Dodgson et al., 2009). It was simple and generic so that the approach could be generalised and applied in other situations. This weighting system could be extended to QALYs falling on other different groups of individuals. This process aggregated different benefits into a single value in patient QALYs gained using the weights elicited from the decision makers:

\[
\text{Benefit}^i_{\text{aggregated}} = (Q^i_1, Q^i_2) = \sum_{j=1}^{2} w_j \cdot Q^i_j = (Q^i_1 + W_2 Q^i_2) \text{ (QALYs)}
\]  

\[
(3)
\]

**Aggregating costs falling on different sectors:**

The general principle (see Chapter 3, section 3.4.2.3) was applied in the case study as follows.

\[
C^i_{\text{aggregated}} = \sum_{j=1}^{n} w_j \cdot C^i_j
\]

Applying to the four different costs in the case study:
\[
\text{Cost}^i_{\text{aggregated}} = (C_1^i, C_2^i, C_3^i, C_4^i) = \sum_{j=1}^{4} w_j \times C_j^i
\]

All cost was measured in a monetary unit (£). \(C_j^i\) is the cost in monetary unit of option (i) falling on sector (j). \(W_j\) is the relative weight of a £ falling on different sectors. We assumed resources in different sectors would have different opportunity costs. For example, a £ spent in health care would not give the same amount of health as a £ spent in social care or in informal care. When there is no evidence regarding the opportunity costs in different sectors, the relative weights can be used to reflect the judgements of the decision makers for these differences between sectors.

To elicit the relative weights between different costs, the following weighting system was used. The underlying assumption was that the decision makers’ preference for £1 of costs in the healthcare sector is different from £1 of costs in the other sectors. The cost falling on the healthcare sector was chosen to be the reference to weight the costs falling on the other sectors. Although it is possible to choose any other group to be the reference, it is better to start with the healthcare sector because it is the sector that will provide the interventions. Thus, £1 falling on the healthcare sector was assigned a weight of 1. The relative weights for the costs falling on other sectors were elicited from the decision makers by asking them to compare a £1 falling on another sector to a £1 falling on the healthcare sector. The smaller the weight, the less that cost is counted when it is aggregated with the health care cost. It is possible to give a weight of zero so that the cost is not counted at all. The range of a relative weight is between zero and infinity.

For example, the decision makers were asked to compare £1 falling on the government social care budget with £1 falling on the healthcare budget. The rationale was that which sector would be more efficient in producing health benefit (having higher health opportunity cost of resources). If they thought £1 falling on the government social care should receive less weight than £1 falling on the healthcare sector, they would give it a weight of less than 1. Table 8.4 illustrates the weighting system for costs.
Table 8.4: The weighting system for costs

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS (C₁)</td>
<td>+ £1 per patient</td>
</tr>
<tr>
<td>Government social care (C₂)</td>
<td>+ £1 per patient</td>
</tr>
<tr>
<td>Private payment for care (C₃)</td>
<td>+ £1 per patient</td>
</tr>
<tr>
<td>Informal care (C₄)</td>
<td>+ £1 per patient</td>
</tr>
</tbody>
</table>

This process aggregated different costs into a single value in healthcare £ using the weights elicited from the decision makers.

\[
\text{Cost}^i_{\text{aggregated}} = (C₁^i, C₂^i, C₃^i, C₄^i) = (C₁^i + W₂C₂^i + W₃C₃^i + W₄C₄^i) \text{ (£ health care)}
\]

*Estimating value for money:*

With costs aggregated in health care £ and benefits aggregated in patient QALYs gained, the net value of a decision option depends on the amount of health care £ that decision makers are willing to pay for a patient QALY gained. This exchange ratio was denoted as K. The net value of a decision option \(i\) can be calculated in terms of patient QALY gained:

\[
\text{NHB}^i = \frac{\text{Benefit}^i_{\text{aggregated}}}{K} \text{ (patient QALYs)} \tag{7}
\]

The difference between the net health benefit calculated here and the net health benefit in a conventional cost-per-QALY analysis is the involvement of the decision makers’ judgement. In a conventional cost-per-QALY analysis, there is no involvement of the decision makers in calculating the cost-effectiveness of an intervention.

### 8.4 The facilitated decision-making workshop

#### 8.4.1 Conducting the workshop

The workshop took place over half a day and was organised in four sections. The first section was an introduction to the decision problem and the CCA-MCDA approach. The second section was the weighting for different costs. The third section was the weighting for different
benefits. And the last section was a discussion about general issues with the approach and the weighting tasks.

The workshop was planned three months in advance and took place in September 2015 in Sheffield. The workshop structure and content had been piloted with a group of PhD students and with the local CCG. The workshop agenda and study description were sent to the participants one week before they came to the workshop. The workshop was conducted in a conference room where the participants were arranged to sit in a U-shape arrangement. The PhD researcher was the main conductor of the workshop. He explained the evaluation problem and talked the participants through the elicitation tasks for generating the MCDA weights. Two supervisors of this thesis (Professor John Brazier and Dr Praveen Thokala) also joined the workshop as observers. They helped explain difficult tasks to the participants. There was an assistant who took notes and helped with any emergency during the workshop. At the end of the workshop, the participants were asked to discuss about what they thought about the approach.

There were two weight elicitation sessions in the workshop: one for aggregating costs and the other for aggregating benefits (see the specification of the MCDA model above).

For aggregating costs, the decision makers were first asked to discuss the ranking of different costs in terms of how important their sectors were comparing to the healthcare sector regarding the evaluation problem. For example, they were asked to consider whether the cost falling on the government-funded social care was more important than, less important than, or as important as the cost falling on the health care regarding the care of dementia. They were then asked to state the specific weight to each non-health care cost which should be consistent with their ranking. The workshop did not seek consensus among the participants. The decision makers were asked to explain why they thought one cost was more important than the other.

For QALYs, the decision makers were asked to discuss the ranking of the patient QALY and the carer QALY. They were asked to consider whether the carer QALY was more important than, less important than, or as important as the patient QALY regarding the care of dementia. The decision makers had to explain their rationale for their ranking although they did not have to agree with each other. They were then asked to state the relative weight for the carer QALY.
The discussion section at the end of the workshop asked the decision makers if they thought the approach could be generalised to other health conditions, any other important criteria they would consider for the evaluation, and any other concerns they had regarding the approach.

The workshop used a computer and a projector to present information in PowerPoint slides. The participants were given pens, papers, and questionnaires to record their values. The workshop was audio-recorded. After the workshop, each participant was followed up by emails if there was any further question that needed their answer. The study protocol, ethics documents and approval, workshop presentation slides, questionnaires are provided in Appendix 3 and Appendix 4.

8.4.2 Data collection and analysis

Two sets of data were collected in the workshop: the quantitative data included the decision makers’ weights for costs and benefits; the qualitative data included the audio recording and the notes taken from the observation of the participants. The weights were used to aggregate costs and benefits in the CCA-MCDA approach.

A qualitative analysis was conducted on the qualitative data. The aim of the qualitative analysis was to understand views of the participants and identify difficulties experienced by the participants during the workshop. The qualitative analysis was descriptive; it did not seek an explanatory account. The framework method (Ritchie and Spencer, 1994, Spencer et al., 2003) was used for the qualitative analysis. The procedure for the framework method includes the following stages (Ritchie and Spencer, 1994, Ritchie et al., 2003): familiarising with the data, identifying a thematic framework, indexing, charting and mapping, and interpreting the data.

The audio recording was transcribed verbatim by the PhD researcher. In the familiarisation stage, the PhD researcher became familiar with the data by listening to the recorded tape and reading the transcript and the workshop note. Due to the pre-specified structure of the workshop, the following three main themes were used as the basis for conducting a detailed thematic analysis: (1) general difficulties in following the CCA-MCDA approach, (2) difficulties and issues in weighting between different costs, and (3) difficulties in issues in weighting between different benefits. Within each main theme, a list of sub-themes and key ideas was identified from the data. The thematic framework was developed based on the three main themes and their sub-themes. The transcript was indexed based on the thematic framework. This means each section of the transcript that relates to a sub-theme (and its parent
theme) was marked and labelled. This process was done in an iterative manner (repeated several times).

In the charting and mapping stage, a table of all themes, sub-themes and participants was created: the columns listed the themes/subthemes and the rows listed the participants. The relevant quotation, if made, from a participant on a sub-theme was entered into its designated cell. Finally, the descriptive analysis was conducted using the mapping table above. The descriptive results were interpreted by the PhD researcher.

8.4.3 Results

8.4.3.1 The participants

The workshop was attended by ten individuals who represented the decision makers and stakeholders (Table 8.5).

Table 8.5: The workshop participants

<table>
<thead>
<tr>
<th>Code</th>
<th>Profession</th>
<th>Organisation</th>
<th>Role in the workshop</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CCG_1 Commissioning Manager</td>
<td>CCG</td>
<td>Decision maker</td>
</tr>
<tr>
<td>2</td>
<td>CCG_2 Clinical Director</td>
<td>CCG</td>
<td>Decision maker</td>
</tr>
<tr>
<td>3</td>
<td>NHS_1 Psychologist</td>
<td>Memory services</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>4</td>
<td>NHS_2 Manager</td>
<td>Memory services</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>5</td>
<td>NHS_3 Clinician/Geriatrician</td>
<td>Hospitals</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>6</td>
<td>NHS_4 General Practitioner</td>
<td>General Practice</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>7</td>
<td>CC_1 Commissioning Manager</td>
<td>City Council/ Social Care</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>8</td>
<td>CC_2 Commissioning Officer</td>
<td>Care</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>9</td>
<td>CC_3 Public health principal</td>
<td>City Council/ Public Health</td>
<td>Stakeholder</td>
</tr>
<tr>
<td>10</td>
<td>CC_4 Public health principal</td>
<td>City Council/ Public Health</td>
<td>Stakeholder</td>
</tr>
</tbody>
</table>

8.4.3.2 Views of the participants about the tasks (qualitative analysis results)

8.4.3.2.1 Theme 1: Following the CCA-MCDA

The main difficulty in implementing CCA-MCDA was to get the participants to think about the problem consistent with the economic evaluation framework. From our observation, initially the participants were not engaged with the problem. For example, they wanted to understand why they should be interested in including the government-funded social care, the
private payment for care, and the informal care in the economic evaluation. Once they started understanding the problem, they began to engage better. The participants voiced difficulties in understanding and following the CCA-MCDA approach. The thematic framework analysis identified three related sub-themes within this:

- The difficulty in understanding what it means by the importance of an attribute
- The difficulty in understanding how weighting influences the decision
- The difficulty in imagining the view taken in making judgements

First, different attributes (different costs or different benefits) were weighted in terms of how important they were considered by the decision makers regarding the evaluation problem in dementia care. However, the concept of ‘importance’ was not clear. In particular, the link between the importance of an attribute and the evaluation problem was not understood clearly. For example, in thinking how important the government-funded social care cost was compared to the health care cost, there seemed to be no common logic or principle behind it which should have been explained to the decision makers. Examples of this difficulty are given in the following quotes:

“…by importance? So whenever you talk about importance, is that important to policy makers or important to patients or carers; whom it is important to?”

(NHS_4)

“It just seems that the importance and cost effectiveness are being sort of conflated and they are two different things. I don't really get it.”

(NHS_4)

Second, at the beginning, some participants were struggling to understand how weighting influences the decision in the CCA-MCDA approach. The examples are given in the following quotes:

“I don't really understand why some weight being more important will be less likely to get funded. I think I just need that to be explained to me a bit more.”

(NHS_4)

“I think I would probably rate the unpaid/informal care highest to all of those four in
some ways. And in many ways I'll be seeing, you know, part of our responsibility in the NHS and local authority to support carers; continue doing that, do that more or do it for longer which presumably in this formula would be more costly and something that we would be seeking to avoid. So I equally struggle a bit really.”

(NHS_1)

“…picking up carers, actually the cost is quite small possibly in comparison to what we spend but actually we weight it much more important so that actually, you know, maybe, it is the formula isn't it?”

(NHS_1)

Third, some participants were struggling to understand how they should make judgements purely from the perspective of a professional doing their jobs. One of the main concerns was that they did not know how to account for the view from the direct users of the health care (patients and their caregivers). There was a confusion regarding how to separate their own view as decision makers and the view of the patients and the view of the informal caregivers. Examples of this difficulty are given in the following quotes:

“But still, coming back to importance to who as well because that would influence your weighting, so if it’s important to the person with dementia you might look at things in a different way. But if it is important to me, I might look at it in a different way. I think that I am still struggling with that bit you raised before.”

(CC_4)

“But what values should I use in my decision making? Because if I am decision making with the person with dementia, it is my most valuable person in my head, I would look at it in a different way.”

(CC_4)

“I am struggling in thinking on which perspective am I going to take in terms of how I answer this and in sense who am I speaking for... I know you are saying as a decision maker or professional … I suppose I was just curious really: are you asking these questions or versions of these questions to people with dementia and their carers? I think I would find it much easier that I was just talking as a psychologist if part of your process included actually discussing and
consulting with people who use dementia services and if in a sense they had a space to put their own opinion forward in this process.”

(NHS_1)

Lesson:

Based on the reflections above, the following lesson has been suggested for the operationalisation of the CCA-MCDA approach. For the decision makers who are not familiar with the approach, there needs to be a warm-up session with a simplified example to help them understand the concepts and principles thoroughly. The rationale for weighting needs to be explained and discussed clearly with decision makers at the beginning. For example, to weight costs falling on different sectors they could consider how efficient each sector is in terms of producing health. To weight benefits, they could consider how each benefit should be prioritised and whether there is any other equity consideration they would like to include. The decision makers should also be explained clearly about their role and the view they take. They need to be instructed to think as decision makers who are in charge of the resources and prioritisation in their sector.

8.4.3.2.2 Theme 2: Weighting costs

The thematic framework analysis identified five related sub-themes within this theme:

- The issue with the integration (overlaps) of budgets for health and social care
- The difficulty in correctly understanding a cost and what to consider in weighting costs
- The issue with other costs not included
- The issue with monetarily valuing informal care

First, there was an issue with the integration (overlaps) of budgets for health and social care which made the separation of costs difficult. This is reflected in the following quotes:

“I suppose the first comment I would like to make is that the NHS costs are not necessarily confined to the things that people traditionally think health spend is spent on and I think increasingly we are spending more around public health and social care in order to minimise the clinical impact on the high end-cost within health. So I think the lines are slightly blurred in terms of NHS spend in terms of what we would traditionally class as health and what we would traditionally class as social care spend. I am sorry that it just makes things a bit more
complicated but I am just conscious of where the CCG budget does not necessarily just go on memory service and hospital beds and things like that.”

(CCG_1)

“We ((health and social care)) are integrating …”

(CC_2)

**Lesson:** The integration of the budgets for health and social care means transfers between these two sectors are possible. If the two sectors are completely integrated, the two costs (health care and social care) should be treated as one cost. Further research is warranted to look at the effect of the integration of health care and social care.

Second, the participants were struggling to understand what to consider in weighting costs. At the beginning, some of them misunderstood the purpose of weighting costs. They were supposed to think about costs in terms of their funders (the sectors that would pay for those costs) and how efficient the sectors were in terms of producing health. However, they got into thinking about the services and the providers (provision) of the services, and this made them confused. The following quotes are examples:

“…even though you split NHS and local authority even in this sort of how things have been changing over the last year to 18 months with integrated commissioning with the health and social care budget is the broad, sort of, more together. Actually even if you unpick the NHS costs, there would be things like prevention and early intervention that would be sort of diagnostic and then the immediate post-diagnostic service. There would be then elements of where does carers, health of those who are caring, fit into the cost of delivering care to those who are suffering with dementia. Where would co-morbid mental health costs sit with those that person who has a dementia diagnosis. And where would also the on-going costs of those people with a dementia diagnosis that are probably living with four, sometimes up to seven, of the long-term conditions that are physical health related, that are actually affecting their dementia trajectory as well, as well as then the long-term care so the CHC budget that is blurred between health and social care. So it is incredibly complex even within one line saying NHS.”

(CCG_2)
The misunderstanding even led to the confusion among some participants about private payment for care. They thought private payment for care was about private care providers. This had to be clarified with them several times during the workshop. The examples of this confusion can be seen in the following quotes:

“I don't know how you read the equation, for the private care providers to not really get a look-in, to in a sense to not be needed …”

(NHS_1)

“I'd be tempted to rate private health care as the highest importance because I don't want shareholders to get any NHS money”

(NHS_4)

**Lesson:** The reflections from this sub-theme give more emphasis on the need of a warm-up session which takes the decision makers through a simplified example so that they can thoroughly understand the concepts. Clear instruction needs to be given for the definition of each cost and what to consider in weighting them. The comment from CCG_1 about considering who is paying is an interesting point. It suggests that in addition to the consideration of how efficient a sector is in producing health, we may want to consider the budget which would directly fund the implementation of the intervention.

Third, some participants mentioned the existence of other sectors where costs of dementia care could fall but which were not included in the criteria.

“I don't know whether it is relevant or it is something which does happen is we, emergency services report, and I don't mean just ambulance service ((NHS)), I mean police and fire brigade are often … we find that before the breakdown happens, there's been a period where 27 calls to police 101 number and … I don't know whether you would treat that for costs but it's a bigger cost. So we talk to colleagues in housing and they all said that they have been dealing with somebody constantly fall several months before we even got involved trying to … so it's kind of, I don't know, I suppose it comes under other costs doesn't it? … They are outside this and I don't know if you are wanting to put on a price against it.”

(CC_2)

“…my other question around benefits and employment … because that individual is not being
productive, I mean bear in mind that many people in the age of 65 will have dementia and if they stop being economically productive within the context of their own life…”

(CCG_2)

**Lesson:** as presented in previous chapters, the PhD researcher had been aware of the issue with other wider costs in dementia which were excluded (see the review in Chapter 3). The reason for the exclusion of those costs was mainly due to their data unavailability and/or the lack of methods in measuring them. As it was raised again during the workshop, further research is warranted to look into the measurement of those costs in dementia care.

Fourth, it was raised during the workshop that the method of monetary valuation of informal care could influence in its weighting. The participants were instructed to consider informal care valued by a revealed preference method (using the UK minimum wage rate) and they were instructed to consider that in the way they weight informal care costs with other costs. One of the participants expressed concerns about the appropriateness of this method in valuing informal care.

“… my point is that what if the informal carer was a professional and had stepped out of their work, were no longer economically productive in their environment, either in producing and providing the services that they would provide and also the outcomes that their service would have been provided if they had remained ((in work)) I appreciate that there is a lot of complexity. But I just wonder about the simplicity of using the minimum wage in that way or whether or not we just have to do it because we have to start somewhere.”

(CCG_2)

“I think there is something about the economics; not so much about the patients but actually about the carers because actually while … carer is caring, they are not contributing economically and they are possibly receiving benefits from another pot of the public purse because they are in that situation and that possibly doesn't … you know... what could they have been producing for the economy. We have a lot of evidence that carers either reduce the hours or give up work completely.”

(CCG_2)
Lesson: van den Berg et al. (2004) reviewed the methods to measure and value informal care. Two groups of methods for valuing informal care include revealed preference methods and stated preference methods. One of the debates concerns which method should be used to generate the monetary value of informal care for use in economic evaluation. This issue is also important in the operationalisation of the CCA-MCDA approach. Further research is needed to look into the relationship between the valuation of informal care and its weight compared to other costs.

8.4.3.2.3 Theme 3: Weighting benefits

In the workshop, the participants were asked to compare a QALY gained for a caregiver with a QALY gained for a patient. The concept of a QALY and its measurement had been explained to the participants. The thematic framework analysis identified two sub-themes within this theme:

- Difficulty in understanding the QALY measure
- Issue with the rationale to weight different QALYs

First, there was some confusion about what was already considered in the QALY measure. Some participants expressed concerns about their views and values being dependent on how severe the dementia stage of the patient is.

“I am not sure that this is consistent across the dementia journey if you like. In the early disease, you might rank it one way and in the later disease, the severity and complexity might weight it entirely differently. And for me, there is kind of a tipping point at some point in the middle that where that change is. So to say which is more important relatively across the board is quite difficult because the severity and complexity ...”

(CCG_1)

“I slightly worry about that depends where you ((patients)) are in the condition that sort of you reach a point of no return, at which point we say it doesn't really matter what happens to you so much but it matters to the carers...we are more bothered perhaps now about how the carer ... I just want to be really careful about how we articulate it ... the idea that the course or the stage of disease might make a difference to this ...”

(NHS_1)
However, this is more like a confusion among the participants. They were confused between valuing the impact on a caregiver with the impact itself. It should be noted that the QALY measure should already capture the severity of the disease and any impact on health of the informal caregivers. This was not easily understood by the participants hence, they got confused.

Second, the participants were struggling to understand what rationales they should use in weighting between a patient QALY and a carer QALY. Although they had been instructed to consider in terms of priority (who should have more priority), it was not clear on what basis one group of individuals would have higher priority in terms of health than another group of individuals.

“We are assuming that all carers are as effective as each other. That's not an issue within this context because if somebody is giving better care and it is more effective caregiver keeping people out of secondary care, social health services, etc. That's not a variable in this part of what we are considering. We are considering everything is equal. Is that right? Does it matter?”

(CCG_2)

“I do think it is impossible to separate the two because they are so interconnected”

(NHS_4)

**Lesson:** To weight different benefits in the CCA-MCDA approach, there needs to be a clear guide on the principles or rationales for weighting. Through the weighting of patient QALYs and carer QALYs in this workshop, it emerged that there was not a clear rationale for weighting a patient QALY and a carer QALY differently.

**8.4.3.3 Values elicited from the participants for the weights for costs**

Before stating the weights, the meaning of each cost had been explained to the workshop participants. The healthcare cost was the impact on NHS resources (for example, medications, primary care services, memory services, etc). Healthcare resources were commissioned by the CCG. The government social care cost was the impact on the resources or services commissioned by the social care department within the local authority. The private payment for care was the payment by patients, informal caregivers and their families; examples of this
are payment for a care home. The informal care cost was the amount of caring time provided by an unpaid caregiver; this time was valued in £ using the UK minimum wage.

The ranking results for different costs are presented in Table 8.6.

Table 8.6: The ranking for costs

(Ranking 1 for the most important cost, ranking 4 for the least important cost)

<table>
<thead>
<tr>
<th>Code</th>
<th>Role</th>
<th>NHS health care</th>
<th>Government Social Care</th>
<th>Private payment for care</th>
<th>Informal care</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCG_1</td>
<td>DM</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>1243</td>
</tr>
<tr>
<td>CCG_2</td>
<td>DM</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>1243</td>
</tr>
<tr>
<td>NHS_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>1243</td>
</tr>
<tr>
<td>NHS_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>1342</td>
</tr>
<tr>
<td>NHS_3</td>
<td>Stakeholder</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2231</td>
</tr>
<tr>
<td>NHS_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>1243</td>
</tr>
<tr>
<td>CC_1</td>
<td>Stakeholder</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>3241</td>
</tr>
<tr>
<td>CC_2</td>
<td>Stakeholder</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2241</td>
</tr>
<tr>
<td>CC_3</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1132</td>
</tr>
<tr>
<td>CC_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1132</td>
</tr>
<tr>
<td>Average Ranking</td>
<td>1.40</td>
<td>1.90</td>
<td>3.70</td>
<td>2.10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Two individuals (CCG_1 and CCG_2) who were decision makers (DMs) gave the same ranking (1243) that suggested the healthcare cost was the most important cost, followed by the government funded social care as the second, the informal care cost as the third, and the least important cost was the private payment for care.

For the stakeholders, there were three ranking opinions:

- The first one agreed with the DMs ranking (1243 or 1132). Four individuals gave this ranking (NHS_1, NHS_4, CC_3, and CC_4).
• The second one (2231 or 2241 or 3241) suggested the informal care cost was the most important cost, followed by the healthcare cost and the government-funded social care as the second, and the least important cost was the private payment for care. Three individuals gave this ranking (NHS_3, CC_1 and CC_2).

• The third one (1342) suggested the healthcare cost was the most important cost, followed by the informal care as the second, the government-funded social care as the third, and the least important cost was the private payment for care. One individual gave this ranking (NHS_2).

On average (counting all participants), the average ranking agreed with the DMs’ opinion.

The weights for costs are presented in Table 8.7.

Table 8.7: The elicited weights for costs

<table>
<thead>
<tr>
<th>Code</th>
<th>Role</th>
<th>NHS healthcare</th>
<th>Government Social Care</th>
<th>Private payment for care</th>
<th>Informal care</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCG_1</td>
<td>DM</td>
<td>1</td>
<td>0.9</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>CCG_2*</td>
<td>DM</td>
<td>1</td>
<td>1</td>
<td>0.6</td>
<td>1.1</td>
</tr>
<tr>
<td>NHS_1*</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td>NHS_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>NHS_3*</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0.9</td>
<td>1.1</td>
</tr>
<tr>
<td>NHS_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>CC_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>CC_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>CC_3*</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>CC_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Mean weight 1.00 0.99 0.41 1.00
Max weight 1.00 1.00 0.90 1.10
Min weight 1.00 0.90 0.00 0.50

There were two individuals whose weights were not consistent with their rankings (CCG_2 and NHS_1). They changed their mind when coming to weighting. Their results are marked
with the symbol (#). This was addressed immediately after the workshop by follow-up emails. NHS_1 explained in their email: “I did change my mind as I went through. I think I should probably have ranked unpaid care 1, NHS 2, local authority 3 etc. I’m afraid I probably found myself a bit confused by trying to weight things in such a way to make it more likely that unpaid carers became the focus of more interventions!”

There were two other individuals who mistakenly gave wrong weights due to confusions (NHS_3 and CC_3). Their results are marked with the symbol (*). Their results given in Table 8.7 have already been corrected. The original results for NHS_3 were (1, 1, 1.1, and 0.9). They mistakenly gave the highest weight to the private payment for care although they had ranked it the least important. NHS_3 clarified in their email (after the workshop): “I suspect I got confused and gave the wrong weighting. I would go with unpaid care as 1.1 and the other as 0.9.” The original results for CC_3 were (1, 1, 2, and 2). They mistakenly gave the highest weight to the private payment for care and the informal care although they had ranked them the least important.

Regarding the results for weights, two individuals (CCG_1 and CCG_2) who were DMs gave different weights. CCG_1 was consistent with their ranking giving the highest weight to the healthcare cost (1), then the government funded social care (0.9), then the informal care cost (0.5), and finally the private payment for care (0.3). CCG_2 was not consistent with their ranking. When it came to weights, CCG_2 gave highest weight to the informal care cost (1.1), then the healthcare cost and the government funded social care (both had a weight of 1), and finally the private payment for care (0.6).

For the stakeholders, there was also no consensus in their weights. The main conflict/disagreement was whether the informal care cost should have a higher weight than the government funded social care and even the healthcare cost. The opinion to support the higher importance of the informal care cost all came from those who were clinicians (NHS_1, and NHS_3).

Overall (considering all participants), the weight for the government funded social care had a mean of 0.99 (0.90 – 1.00). The weight for the private payment for care had a mean of 0.41 (0.00 – 0.90). The weight for the informal care cost had a mean of 1.00 (0.50 – 1.10). Some rationales from the participants’ views for weighting costs are presented below.

CCG1 emphasized that the sector who was paying to implement the intervention should have its cost weighted more heavily.
“…one of the things that is in my head is who is paying for that intervention because if the NHS is paying, i.e. this is part of my budget, I might weight things slightly different than actually if I am holding the social care budget and the impact it has on health for example. So I think it sort of matters who might be paying for these things in the first place as to the relative weight.”

(CCG_1)

The relative weight for cost falling on the government-funded social care was thought to be as important as the healthcare cost. However, the rationale seemed to arise from the difficulty in separating social care from health care.

“I struggle to differentiate the NHS and local authority in a sense regardless of who is paying for it, because they're so incredibly interdependent and it really is just which pot of money has that come out of so I think they are on an even keel. I give those parity because the journey of dementia is so long and complex, and involves so much health and social care need at different points in the journey. I think it'll be very hard to weight one more strongly than the other…I almost think that if they could be just joined up so that we, professionals, and patients experience that as one service I think that would probably make far more sense…”

(NHS_1)

Regarding the cost of informal care in relation to the government funded health care and social care, the common view was that informal care was a crucial element of dementia care that could not be replaced by formal care. Thus, the informal care cost was weighted heavily, even higher than the healthcare cost (from three participants CCG2, NHS_1, and NHS_3).

“For me, still, I think probably unpaid/informal care would seem more important than those two in the sense that it is the glue the keeps dementia services running, and without it, and if carers stop working today, it'd be absolute chaos, the NHS and local authority would not be able to cope …”

(NHS_1)

“I think I would probably rate the unpaid/informal care highest to all of those four in some ways. And in many ways I'll be seeing, you know, part of our responsibility in the NHS and local authority to support carers, continue doing that, do that more or do it for longer…”

(NHS_1)
8.4.3.4 Values elicited from the participants for the weights for benefits

Before stating the weights, the meaning of each benefit had been explained to the workshop participants. The definition of the QALY measure was explained (e.g. combining HRQOL and length of life). The participants were asked to assume the patient QALYs and the carer QALYs were independent.

The ranking for different benefits is presented in Table 8.8.

Table 8.8: The ranking for benefits

(Ranking 1 for the most important benefit)

<table>
<thead>
<tr>
<th>Code</th>
<th>Role</th>
<th>Patient QALY</th>
<th>carer QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCG_1</td>
<td>DM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CCG_2</td>
<td>DM</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>NHS_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>NHS_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NHS_3</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>NHS_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>CC_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_3</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Average ranking</td>
<td></td>
<td><strong>1.00</strong></td>
<td><strong>1.50</strong></td>
</tr>
</tbody>
</table>

For the DMs, CCG_1 gave an equal ranking to the patient QALY and the carer QALY, whereas CCG_2 ranked the patient QALY higher than the carer QALY.

For the stakeholders, four individuals (NHS_2, CC_1, CC_2, and CC_3) gave equal rankings to the patient QALY and the carer QALY and four individuals (NHS_1, NHS_3, NHS_4, and CC_4) ranked the patient QALY higher than the carer QALY.
The weights for benefits are presented in Table 8.9.

Table 8.9: The elicited weights for benefits

<table>
<thead>
<tr>
<th>Code</th>
<th>Role</th>
<th>Patient QALY</th>
<th>Carer QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCG_1</td>
<td>DM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CCG_2</td>
<td>DM</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>NHS_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>NHS_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NHS_3</td>
<td>Stakeholder</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>NHS_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_1</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_2</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_3</td>
<td>Stakeholder</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CC_4</td>
<td>Stakeholder</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean weight</td>
<td></td>
<td><strong>1.00</strong></td>
<td><strong>0.86</strong></td>
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<tr>
<td>Max weight</td>
<td></td>
<td><strong>1.00</strong></td>
<td><strong>1.00</strong></td>
</tr>
<tr>
<td>Min weight</td>
<td></td>
<td><strong>1.00</strong></td>
<td><strong>0.00</strong></td>
</tr>
</tbody>
</table>

For the DMs, CCG_1 gave equal weights to the patient QALY and the carer QALYs, whereas CCG_2 gave a lower weight to the carer QALYs (0.9).

For the stakeholders, five individuals gave equal weights to the patient QALY and the carer QALY and three individuals gave a lower weight to the carer QALY. NHS_3 even gave a zero weight to the carer QALY that means the carer QALY should not be counted at all in the evaluation problem.

Overall (considering all participants), the weight for the carer QALY had a mean of 0.86 (0.00 – 1.00). The common view was that the carer QALY should have the same weight as the patient QALY. However, one of the participants (NHS_3) who gave a zero weight to caregiver QALY gave the following argument:
“So we do recognise that when carers suffer, patients suffer as well. But if you are talking about giving a drug to somebody then I need to think about what you would do to that person as a priority rather than thinking what you would do to somebody else because it is that person who is taking that drug; so they are taking on all the risks and all the side effects or whatever, and benefits may be for another person which yes, you could say that if that carers benefit therefore patients also benefit, but that is more like a secondary effect rather than a primary...”

(NHS_3)

This point was not agreed by other participants. For example:

“But with carers, the concern is that sometimes they become a secondary patient at which point do carers tip into patient themselves without ... clearly I do have a carer responsibility so my overwhelming thoughts are with the carers.”

(CC_1)

“I think it is difficult for the NHS and social care because in some respect, the patient is the most important thing and that is what we are ethically trained to do but for the authority, there is that wider context and actually the impact therefore it's probably on the authority anyway if you don't equally, you know, if it falls over we bear the brunt as well…”

(CCG_1)

8.5 The CCA-MCDA results

8.5.1 Base-case results

The mean weights were used to aggregate costs and aggregate benefits. The base-case results for the aggregated cost and QALYs are presented in Table 8.10.
### Table 8.10: The aggregated costs and QALYs using the decision-makers’ weights

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Mean weight</th>
<th>Value per patient</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>MMSE</td>
<td>GPCOG</td>
<td>6CIT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>unweighted</td>
<td>Weighted</td>
<td>unweighted</td>
<td>Weighted</td>
<td>unweighted</td>
<td>Weighted</td>
</tr>
<tr>
<td>Health care</td>
<td>1.00</td>
<td>28,834</td>
<td>28,768</td>
<td>28,648</td>
<td>28,837</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>28,834</td>
<td>28,768</td>
<td>28,648</td>
<td>28,837</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gov social care</td>
<td>0.99</td>
<td>26,035</td>
<td>25,775</td>
<td>25,775</td>
<td>25,774</td>
<td>25,772</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>26,035</td>
<td>25,775</td>
<td>25,775</td>
<td>25,774</td>
<td>25,772</td>
<td></td>
</tr>
<tr>
<td>Private payment</td>
<td>0.41</td>
<td>36,832</td>
<td>15,101</td>
<td>36,832</td>
<td>15,101</td>
<td>36,828</td>
<td>15,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15,101</td>
<td>15,101</td>
<td>15,101</td>
<td>15,101</td>
<td>15,100</td>
<td></td>
</tr>
<tr>
<td>Informal care</td>
<td>1.00</td>
<td>10,434</td>
<td>10,433</td>
<td>10,433</td>
<td>10,433</td>
<td>10,430</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>10,434</td>
<td>10,433</td>
<td>10,433</td>
<td>10,433</td>
<td>10,430</td>
<td></td>
</tr>
<tr>
<td>Aggregated cost</td>
<td></td>
<td><strong>80,144</strong></td>
<td><strong>80,077</strong></td>
<td><strong>79,957</strong></td>
<td><strong>80,139</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient QALYs</td>
<td>1.00</td>
<td>5.9983</td>
<td>5.998403</td>
<td>5.998403</td>
<td>5.998606</td>
<td>6.001785</td>
<td>6.001785</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.9983</td>
<td>5.998403</td>
<td>5.998403</td>
<td>5.998606</td>
<td>6.001785</td>
<td>6.001785</td>
</tr>
<tr>
<td>Carer QALYs</td>
<td>0.86</td>
<td>6.98902</td>
<td>6.01056</td>
<td>6.989038</td>
<td>6.989116</td>
<td>6.989951</td>
<td>6.989951</td>
</tr>
<tr>
<td>Aggregated QALY</td>
<td></td>
<td><strong>12.00886</strong></td>
<td><strong>12.0089757</strong></td>
<td><strong>12.009246</strong></td>
<td><strong>12.013143</strong></td>
<td><strong>12.013143</strong></td>
<td><strong>12.013143</strong></td>
</tr>
</tbody>
</table>
Using the aggregated cost and the aggregated benefit, the net health benefit was calculated for each decision option at two values of the exchange rate (K) between healthcare £ and a patient QALY: £20,000 per QALY and £30,000 per QALY. Table 8.11 presents the results.

**Table 8.11: The MCDA Net Health Benefit (per patient)**

<table>
<thead>
<tr>
<th>Option</th>
<th>Aggregated cost in healthcare £</th>
<th>Aggregated benefit in patient QALYs</th>
<th>NHB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>K= 20,000</td>
</tr>
<tr>
<td>Baseline</td>
<td>80,144</td>
<td>12.00886</td>
<td>8.0017</td>
</tr>
<tr>
<td>MMSE</td>
<td>80,077</td>
<td>12.008976</td>
<td>8.0051</td>
</tr>
<tr>
<td>GPCOG</td>
<td>79,957</td>
<td>12.009246</td>
<td><strong>8.0114</strong></td>
</tr>
<tr>
<td>6CIT</td>
<td>80,139</td>
<td>12.013143</td>
<td>8.0062</td>
</tr>
</tbody>
</table>

Looking at the ranking in terms of NHB, the GPCOG was the best option (with the highest NHB) at both values of K. Figure 8.1 presents the breakdown of the NHB value for each decision options for K at £30,000 per QALY.
A full incremental analysis was performed based on the aggregated cost and the aggregated benefit of the decision options. First, the decision options were ranked in terms of their increasing aggregated benefit (QALYs gained): the baseline option, the MMSE, the GPCOG and the 6CIT. Second, the incremental analysis was performed in pair-comparison as illustrated in Table 8.12.
Table 8.12: The incremental analysis results from the CCA-MCDA

<table>
<thead>
<tr>
<th>Option</th>
<th>Caggregated</th>
<th>H</th>
<th>ΔCagg</th>
<th>Δh</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>80,144</td>
<td>12.00886</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MMSE</td>
<td>80,077</td>
<td>12.008976</td>
<td>-67</td>
<td>0.000116</td>
<td>MMSE dominates</td>
</tr>
<tr>
<td>GPCOG</td>
<td>80,139</td>
<td>12.013143</td>
<td>-120</td>
<td>0.00027</td>
<td>GPCOG dominates</td>
</tr>
<tr>
<td>6CIT</td>
<td>79,957</td>
<td>12.009246</td>
<td>182</td>
<td>0.003897</td>
<td>£46,799 per QALY</td>
</tr>
</tbody>
</table>

As can be seen, the GPCOG was the best option at thresholds less than £46,799 per QALY. However, at thresholds more than £46,799 per QALY, the 6CIT becomes more cost-effective than the GPCOG. Compared to the implementation of the extended cost-per-QALY approach (Chapter 7, section 7.3), the critical point of the threshold in the CCA-MCDA approach was higher (£46,799 per QALY versus £41,355 per QALY). Thus, depending on the value of the threshold, the decision would change between the extended cost-per-QALY approach and the CCA-MCDA approach. With thresholds less than £41,355 per QALY or more than £46,799 per QALY, the decision did not change between the two approaches. However, with thresholds between £41,355 per QALY and £46,799 per QALY, the decision was different between the two approaches.

8.5.2 Deterministic Sensitivity Analysis (DSA)

The MCDA weights were elicited from the decision makers. There was variation in the MCDA weights between individuals in the decision-making group. The mean weights were used in the base-case analysis. This DSA looked at how the heterogeneity in the MCDA weights may influence the outcome of the decision. This was conducted through a series of one-way sensitivity analyses.

First, the minimum and maximum value of weights for each cost and benefit were tested to see how they affected the ICER between the 6CIT and the GPCOG. Table 8.13 presents the results from this one-way sensitivity analysis.
Table 8.13: The one-way sensitivity analysis results from the CCA-MCDA

<table>
<thead>
<tr>
<th>Scenario</th>
<th>6CIT vs GPCOG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ΔCagg</td>
</tr>
<tr>
<td>Base case (at mean weights)</td>
<td>£182</td>
</tr>
<tr>
<td>DSA 1 (at minimum weights)</td>
<td>£186</td>
</tr>
<tr>
<td>DSA 2 (at maximum weights)</td>
<td>£180</td>
</tr>
</tbody>
</table>

As can be seen, when the minimum values of all the weights were used, the ICER was increased to £58,415 per QALY. When the maximum values of all the weights were used, the ICER was decreased to £44,868 per QALY. In all DSA scenarios, the ICER was still higher than £30,000 per QALY.

Second, each MCDA weight was varied (one at a time) between minus 0.4 and plus 0.4 to see how it affected the ICER between the 6CIT and the GPCOG. When one weight was varied, other weights were kept fixed. Figure 8.2 presents the results of this one-way sensitivity analysis.

Figure 8.2: The one-way sensitivity analysis results for MCDA weights

We can see that the weight of the carer QALY was the most sensitive input. When this weight varied between minus 0.4 and plus 0.4, the range of change for the ICER (between the 6CIT and the GPCOG) was between £4,387 and £3,694 per QALY. The relationship between the weight of the carer QALY and the ICER was not linear, whereas the weights of the wider costs had a linear relationship with the ICER.
8.5.3 Probabilistic Sensitivity Analysis (PSA)

In conducting PSA, in addition to the usual parameters for costs and QALYs, we incorporated the variation in MCDA weights. For the relative weight of the government-funded social care, a beta distribution with mean of 0.99 was used: Beta distribution (min = 0.9, max = 1.0, alpha = 10, beta = 1.09). For the relative weight of the private payment for care, a beta distribution with mean of 0.41 was used: Beta distribution (min = 0, max = 0.9, alpha = 2.575, beta = 3.0). For the relative weight of the informal care, a beta distribution with a mean of 1 was used: Beta distribution (min = 0.5, max = 1.1, alpha = 10, beta = 1.981). For the relative weight of the carer QALY, a beta distribution with a mean of 1 was used: Beta distribution (min = 0, max = 1, alpha = 10, beta = 1.585). The values of the MCDA weights were sampled from their distributions together with other parameters in PSA runs. PSA was run with 2000 samples of the input parameters. The Cost-Effectiveness Acceptability Curve (CEAC) is shown in Figure 8.3. The best option was a choice between the 6CIT and the GPCOG from the societal perspective. The critical point of the threshold was £35,000 per QALY. At thresholds lower than £35,000 per QALY, the GPCOG had the highest probability of being the best option, whereas at thresholds higher than or equal £35,000 per QALY, the 6CIT had the highest probability of being the best option. This critical point was £29,000 per QALY in the extended cost per QALY approach (see Chapter 7, section 7.3).

Figure 8.3: The Cost-Effectiveness Acceptability Curve in CCA-MCDA
8.6 Discussion and conclusion

8.6.1 Summary

This chapter demonstrated the operationalisation of the CCA-MCDA approach in the case study. It took a more limited MCDA approach in which only MCDA weighting techniques were used in a facilitated decision-making workshop to elicit views and values from local decision makers for a pre-specified list of costs and benefits. The elicited values were used in a Cost-Effectiveness Analysis taking a broader societal perspective. This was not the implementation of a full standard MCDA with all its steps (see Dodgson et al., 2009, Thokala et al., 2016, Marsh et al., 2016). There was no attempt to identify and develop a comprehensive list of decision criteria from the decision makers.

To make a comparison with the extended cost-per-QALY in Chapter 7, the same decision problem and model estimates were used. The operationalisation of the CCA-MCDA was investigated in four stages: (1) forming a hypothetical decision-making group, (2) specifying the decision model, (3) conducting a facilitated decision-making workshop, and (4) analyses and results. Through the workshop, we found that the main difficulty in implementing this approach was to get the participants to think about the problem consistently with the economic evaluation framework. Understanding the problem was key to engagement. Using the mean weights elicited from the workshop, the costs were aggregated to a single aggregated cost in £ and the benefits were aggregated to a single aggregated benefit in QALYs. An incremental analysis was performed on the aggregated cost and the aggregated benefit to derive the ICER. Deterministic Sensitivity and Probabilistic Sensitivity Analyses were also conducted. Similar to the extended cost-per-QALY, the best option was still a choice between the 6CIT and the GPCOG in the CCA-MCDA approach. In the base-case, the ICER comparing the 6CIT versus the GPCOG was £46,799 per QALY. This value was higher than the ICER calculated by the extended cost-per-QALY (in Chapter 7) which was at £41,355 per QALY. In PSA, the critical point (where the probability of being cost-effective for the 6CIT was higher than the GPCOG) of the threshold was £35,000 per QALY in the CCA-MCDA approach, whereas it was £29,000 per QALY in the extended cost-per-QALY.

This is the first study that attempted to apply MCDA methods to implement a Cost-Effectiveness Analysis taking a broader societal perspective. A conventional application of MCDA ranks and scores a list of alternative decision options, therefore, it can only indicate
whether an option is better than other options within the list. In our approach demonstrated above, we used weights elicited from decision makers to aggregate costs to a single aggregated cost in £ and benefits to a single aggregated benefit in QALYs. Thus, it was possible to have an estimate of value for money for a decision option by comparing the aggregated cost with the aggregated QALY. A cost-effectiveness threshold could also be specified to indicate the cost-effectiveness of a decision option. The overall MCDA value of a decision option is similar to the concept of a net benefit in the extended cost-per-QALY. However, there remains theoretical issues around whether this approach can actually address opportunity costs of resources given the subjectivity of the weights attached to costs and benefits.

8.6.2 Limitations of the case study

There are some limitations associated with our study. First, it was only illustrative. The study had to impose the decision problem on the primary decision makers (a hypothetical decision problem) although technically it was still within their commissioning remit. Ideally, a real-life decision problem could have been identified and followed up to make the case study. Due to the time and resource constraint of the PhD project, this was not possible. The implication of this limitation could be that the values were given by the study participants without careful thinking hence, there was no validity in those values. The decision makers did not have the kind of responsibility that they would have in their real practice. In addition, the list of included costs and benefits was not comprehensive although it was informed by a systematic review. There were other significant costs which were not included. Their exclusion was justified either by the lack of evidence or their measurement methods were still controversial.

Second, although patients and their caregivers were identified as stakeholders, they were not included in the study due to concerns about their well-being during the workshop. This was justified given the case study was explorative. However, it could have important methodological implications and certainly for understanding feasibility of the approach.

Third, due to the time and resource constraints, only one facilitated workshop was conducted in the case study. As the result, the study did not have a chance to re-visit the issues arisen during the workshop and see whether they could be resolved. This also resulted in engaging the decision makers at later stage than usual – ideally they would be involved in setting the decision problem including identifying and selecting what costs/outcomes matter. With only one workshop, we found it challenging to make sure that the decision makers understood the approach and gave valid weights. Given the time constraints and the hypothetical nature of our
problem, we chose a pragmatic approach. However, future researchers should involve the
decision makers from an early stage to ensure their buy-in such approaches.

Fourth, the conduct of the facilitated workshop could be improved. Simplified examples should
be provided to the participants from the beginning to help them understand the approach and
the problem better. The questionnaires for eliciting the weights have some limitations. It was
difficult to ask the participants to directly state their weights for a patient QALY gained and a
care QALY gained. This weighting task could be put in a specific context to elicit the weight
indirectly. For example, the participants could be given two scenarios: one is a situation where
a health care intervention delivers health benefits for patients but it also puts more stress on
caregivers; the other is a situation where a health care intervention helps reduce stress on
caregivers but at a reduced HRQOL for patients. By asking the participants to choose between
the two scenarios, we could elicit their weights for patient QALYs and carer QALYs.

8.6.3 Lessons from the case study

First, in implementing the CCA-MCDA technique, the identification of the primary decision
makers and the stakeholders needs to be relevant and appropriate. It starts with the
identification of the primary decision makers who are the owner of the decision problem (e.g.
the one who needs to decide whether they should spend their money on the intervention). Then
it expands to include other stakeholders (from the view of the primary decision makers). At the
national level, we can start with members of NICE committee, then this can expand to include
other relevant stakeholders. At the local level, we can start with members of a local clinical
commissioning group and expand to include local authority, clinicians, patients, etc. The
expansion needs careful discussion and justification by the primary decision makers.

Second, the definition and measurement of costs and benefits need to be clear, sensible, and
presented to the decision makers in a way that they can easily understand. This is especially
important for non-market costs and benefits expressed in QALYs gained. For example, we
need to explain to the decision makers that the informal care cost only includes the labour value
of informal caregiving in terms of how many hours spent for caring and it has already been
valued in monetary units using the national minimum wage, and the impact on informal
caregivers’ health is accounted separately in benefits. How the informal care is valued is an
important information that needs to be clarified with the decision makers before any weight is
elicited. It is argued that the decision makers should decide how it should be valued. This would
make sure the decision makers understand correctly about what is included in the informal care cost so that they can give an appropriate weight for it.

Third, the weighting system for weighting costs and weighting benefits is an important component of the CCA-MCDA technique. The case study here has developed a simple weighting system that could be generalised for other situations.

Fourth, the facilitated decision-making workshop needs to be planned and conducted carefully. More than one workshop might be needed if the decision makers are not familiar with the evaluation problem and the approach. The facilitator(s) need to understand the approach, the evaluation problem and to be well trained in facilitating MCDA workshops. On-the-spot modelling might be helpful in simultaneously presenting the results and any conflicts or inconsistencies arising during the workshop. Regarding the structure of the workshop, a warm-up session with a simplified example is necessary for participants who are not familiar with the approach. The rationale for weighting costs and the rationale for weighting benefits need to be explained and discussed clearly before eliciting weights. When weighting costs, the first point is to think about how efficient each type of resources is in terms of producing health, then other factors might be considered such as who is directly paying for the implementation of the intervention. When weighting benefits, the participants need to agree on some ethical and equity principles: why would we give more priority to a group of individuals than the other?

8.6.4 Discussion on the use of experts’ judgements regarding forgone benefits

Consider more detail on the use of experts’ judgements regarding forgone benefits. How can this be done under MCDA?

One of the key issues in using the CCA-MCDA approach for health care resource allocation decisions is the question whether forgone benefits or opportunity costs could be addressed within the MCDA framework. In this thesis, it has been proposed that the judgements from the decision makers (experts) who know and understand both their budget and how it has been spent could be useful and could be used to address/adjust the local estimates of opportunity costs of costs falling on multiple sectors where the evidence for their local empirical estimates is not available or readily usable.

In the case study, costs were categorised into four groups: healthcare, government-funded social care, private payment for care, and informal care. The idea was that each cost would
have a different opportunity cost in terms of forgone benefits because they fell on different sectors and budgets. The services displaced due to the healthcare cost are different from the services displaced due to the government-funded social care cost; thus they should have different rates in terms of forgone benefits. The additional cost from private payment for care has a direct impact on the private budget of patients and their families. This would mean less consumption for them in terms of forgone benefits. The impact from the informal/unpaid care is more complicated (Hirst, 2004, Hoefman et al., 2011, van den Berg et al., 2004). It is not only just the amount of time that informal caregivers spending for caring that could not be used for something else but also the impact of the caring act on the well-being of both the caregivers and the patient (both positive and negative).

Evidence for the empirical estimates of some of these opportunity costs is available at the national level (Claxton et al., 2015). Nonetheless, even when evidence is available at the national level, it may not be appropriate to use at the local level (see the added discussion in the correction number 6 below). Because of local variation, disinvestment activities at the local level can deviate significantly from the national average. On the other hand, it could be possible to know specific potential disinvestment activities at the local level. More accurate estimates of opportunity costs at the local level could be possible. This would require working closely with the local decision makers and their judgements could be used directly in the analysis (see more discussion in the correction number 6 below). For these reasons, the CCA-MCDA approach was found to be more relevant and useful to support resource allocation decisions at the local level.

For decisions at the local level, the objective of the CCA-MCDA approach is to facilitate a decision-making exercise in which the decision makers could look and assess the possible forgone benefits resulting from a cost that falls on their fixed budget. For example, with the healthcare cost falling on a local healthcare budget, the decision makers need to look at their portfolio of currently funded services and also other potential services that they want to fund. They then need to consider possible disinvestments they may need to make or things they want to invest but they are not able to do so now due to the additional cost from the intervention under the current evaluation. After considering all this, they can come up with a judgement in their mind about the potential forgone benefit of a healthcare cost. Let’s say, for the sake of simplicity, they come up with the judgement of 0.5 forgone QALYs for every £10,000 healthcare cost.
The decision makers need to do the same for other costs. For example, after considering the social care portfolio, they come up with the judgement of 0.4 forgone QALYs for every £10,000 social care cost. After considering the private consumption budget, they come up with the judgement of 0.2 forgone QALYs for every £10,000 from private payment for care. After considering the consequences of the informal care hours, they come up with the judgement of 0.3 forgone QALYs for every £10,000 worth (or 1000 hours) of informal care.

In this example, the total forgone benefit from the different costs are calculated as follows from the decision makers’ judgements:

\[
Benefit^i_{\text{forgone}} = \left( 0.5 \times C^i_1 + 0.4 \times C^i_2 + 0.2 \times C^i_3 + 0.3 \times C^i_4 \right) \times \frac{1}{10000} \text{ (QALYs)}
\]

Is programme budgeting and marginal analysis a framework that could be helpful for this?

In the case study, experts’ judgements were used in the CCA-MCDA approach to address forgone benefits resulting from costs falling on different local budgets. However, rather than relying completely on experts’ judgements for estimating the opportunity costs, local data could be quantified and incorporated. The Programme Budgeting and Marginal Analysis (PBMA) framework (Donaldson, 1995a, Ratcliffe et al., 1996, Ruta et al., 2005, Peacock et al., 2010) could be helpful (complementary) for the implementation of the CCA-MCDA approach. Programme Budgeting is a process to look at and assess the current resource allocation in terms of meaningful programmes in order to see how the allocation could be improved for better. Marginal Analysis is a process to look at and incrementally assess a proposed investment (or disinvestment) in terms of added benefits and added costs in order to see whether it is worthwhile. The PBMA framework is a process in which local decision makers appraise proposed investments (or disinvestments) in terms of their added (incremental) benefits and added costs, together with an assessment of their impacts on the current resource allocation on existing programmes. The PBMA framework has eight steps (Charles et al., 2016):

- Choose a set of meaningful programmes: For example, a matrix of different factors could be created including disease areas (e.g. dementia, vascular, etc.), age groups (e.g. child, adults, and elders), economic groups, service groups, etc.
- Identify current activity and expenditure in those programmes
• Identify potential improvements: think of new investments and possible disinvestments, form a list of these options.
• Marginal (incremental) analysis of the potential improvements
  o Measure incremental costs and benefits of each option
  o Measure the impacts of incremental costs on existing programmes (opportunity costs)
  o Weigh up costs and benefits to prioritise the options
• Consult widely with other decision makers and stakeholders
• Decide on changes (final decision)
• Effect the change (making it happen)
• Evaluate the progress (checking that the actual anticipated costs/savings, benefits have actually materialised).

We can see that the PBMA framework lends support to the CCA-MCDA approach. Indeed, the PBMA should be incorporated/integrated to the CCA-MCDA to better handle the issue with local opportunity costs. With the integration of the PBMA, the CCA-MCDA stages (see 3.4.2.1 in the thesis – page 58) could be modified as follows:

Stage 1: specifying the decision problem and establishing the decision context
  o Specifying the current resource allocation in terms of meaningful programmes
  o Describing the proposed investments, identifying possible disinvestments, and specifying where they are within the programmes

Stage 2: identifying costs and benefits of the proposed options
  o Costs: identifying all costs falling on different sectors/budgets
  o Benefits: identifying all benefits
  o Identifying which sectors/groups are impacted. These are the stakeholders.

Stage 3: data collection
  o Data for activities, expenditure, and outcomes of current programmes
  o Data for added costs and benefits of the proposed options
  o Regarding the impacts on wider sectors/groups, additional data for their opportunity costs.

Stage 4: assessment of opportunity costs
  o Specify the possible consequences of cost falling on each sector/budget
  o Each sector/budget judges these consequences falling on them in terms of forgone benefits
Stage 5: decision-making workshops

- Workshops between decision makers and stakeholders to discuss and agree on the estimates/judgements of costs and benefits
- The decision options are appraised in terms of their benefits and forgone benefits. The cost-effectiveness of a decision option is determined by whether it creates net benefit.
- Results from sensitivity analyses are also discussed and assessed
- Making the final decision (what to invest and what to disinvest)
- Documenting the workshops, rationale for the judgements, and the expected changes.

Stage 6: effect the changes

Stage 7: evaluate the progress

8.6.5 Discussion on the issue of stakeholders for private consumption not being included

In Chapter 8, consumption costs were included in the analysis but patients and caregivers were not included as stakeholders in the decision-making board. This has been recognised as one of the limitations of the study and it could have some methodological implications and for understanding feasibility of the CCA-MCDA approach (Chapter 8, page 207). The reasons for dropping this type of stakeholders are presented below.

For our CCA-MCDA case study, it was felt important to include the private consumption costs to ensure consistency with the implementation of the extended cost per QALY approach (which does include these costs). Initially people with dementia and their caregivers were identified as stakeholders and planned to be invited to participate in the decision-making exercise. The Alzheimer’s Society was approached, and this was discussed with their staff. Further discussion with the main decision makers (members of the local Clinical Commissioning Group) identified the concern with the wellbeing of people with dementia and their caregivers and whether it was appropriate and necessary for them to take part in the exercise.

Given the discussions could be sensitive in nature and the fact that our study was at an exploratory stage, it was decided that patients and their caregivers should not be included in the decision-making workshop. However, it is recognised that the roles of patients and their caregivers are important in the implementation of the CCA-MCDA approach. After the experience and lessons learned from the study, the conduct of the decision-making exercise
could be improved much further and it would be possible to include patients and their caregivers in the future research.

8.6.6 Conclusion

This study showed how MCDA techniques could be used to implement a Cost-Effectiveness Analysis taking a broader societal perspective. Although it was conducted in a case study of dementia care, the application demonstrated in this study can potentially be generalised to other situations and conditions. There were limitations with the case study. If the CCA-MCDA study was conducted again, the work with the decision makers and stakeholders would be done differently. First, a real-life situation would be used in which the researcher would work closely with local health care commissioners to go through the seven stages of the CCA-MCDA with PBMA as described above. Second, the decision makers and stakeholders would be given more time to go through simplified examples so that they could understand the concepts properly. They would also be asked to spend more time thinking about the possible consequences of a cost falling on their budget and thus, coming up with an appropriate judgement in terms of forgone benefits. Third, local patients, caregivers, and/or members of the public would be included in the decision-making workshops so that their views and values could be included in the final decision.

CHAPTER 9. DISCUSSION AND CONCLUSION
This chapter begins by providing a summary of the main themes of the thesis. Section two discusses the key findings and contributions from each study in the thesis. Section three discusses the implications of the thesis for methods of economic evaluation and policy. Section four discusses the limitations of the thesis. Section five discusses future research from the work in this thesis. The final section concludes the chapter and the thesis.

9.1 Overview of the thesis

The aim of this PhD was to investigate methodological approaches that can be used to implement a societal perspective in economic evaluation of health care interventions. After the introduction Chapter, Chapter 2 started by reviewing all economic evaluation techniques: Cost-Benefit Analysis (CBA), Cost-Effectiveness Analysis (CEA), Cost-Utility Analysis (CUA), and Cost-Consequences Analysis (CCA). The definition of CCA was expanded to incorporate
Multiple-Criteria Decision Analysis (MCDA). The extended definition of CCA was termed CCA-MCDA to differentiate it from more general definitions of CCA and MCDA separately. In CCA-MCDA, all costs and benefits are computed separately and presented to the decision makers, then MCDA methods are applied to help the decision makers compare between the alternatives and make the final decision.

Chapter 3 reviewed the arguments for a societal perspective. It also discussed the known challenges of implementing a societal perspective in economic evaluation of health care interventions. These challenges include the difficulty or impossibility to specify a complete social welfare function and the additional information required in a societal perspective. There are three potential approaches that could be used to implement a societal perspective: the CBA approach, the extended CUA or cost-per-QALY analysis, and the CCA-MCDA. Due to time and resource constraint, only two approaches were chosen for investigation in the thesis: the extended cost-per-QALY and the CCA-MCDA. The investigation was conducted using a case study in dementia care. Dementia was chosen because of wider costs and consequences from their impacts. Dementia is also the area where there has been an increasing interest from policy makers. The main research in the case study was reported in Chapters four to eight.

The main research had five objectives that were specified to meet the aim. The first was to review the methods of economic evaluation in previous studies in dementia. The second was to systematically review previous model-based studies to inform the development of a new cost-effectiveness model in the case study. The third was to develop a cost-effectiveness model for evaluating the use of different cognitive screening tests in primary care. The fourth was to implement the extended cost-per-QALY approach given the model results and available information about the cost-effectiveness thresholds in different sectors. The fifth was to implement the CCA-MCDA approach.

The objectives were achieved by conducting five studies. First, a systematic review of previous economic evaluation studies in dementia was undertaken to understand the current state of methods applied in practice (Chapter 4). The findings of the first study confirmed the importance of taking a broader perspective in economic evaluation in dementia. The findings also informed the specification of a decision problem for the case study and the selection of costs and benefits included. To inform the development of a cost-effectiveness model for the evaluation problem in the case study, another systematic review was conducted in study two.
(Chapter 5). This review had a narrower scope than the first review. The second review focused only on modelling aspects in previous model-based economic evaluation studies. Study three (Chapter 6) was the development of a new cost-effectiveness model and its estimates for the costs and benefits of different interventions in the case study. Given the estimated costs and benefits from the model, study four (Chapter 7) first implemented a conventional cost-per-QALY analysis from the healthcare perspective only. It then implemented the extended cost-per-QALY. Study five (Chapter 8) was the implementation of the CCA-MCDA using the same estimated costs and benefits from the model in study three and weights elicited from a group of local decision makers and stakeholders. Note that this study was not the implementation of a full standard MCDA approach because there was no attempt to identify and include all possible decision criteria from the decision makers. In study five, the weights for costs and benefits were collected through a decision-making workshop where all participants were together in one room. A qualitative analysis was employed to analyse the data collected in the workshop. The qualitative analysis helped identify other challenges in implementing the CCA-MCDA.

In this discussion chapter (Chapter 9), the key findings of the five studies are summarised and discussed in the context of the existing literature. The contributions of this thesis to existing knowledge are highlighted. Then, the implications of the findings for the methods of economic evaluation taking a societal perspective are discussed. Finally, the chapter discusses the limitations of this thesis and make recommendations for further research.

9.2 Key findings and contributions

9.2.1 Study 1 (Chapter 4): Review economic evaluation methods in previous studies

The majority of economic evaluations in dementia were model-based cost-per-QALY analysis. The review found that more than half of previous economic evaluations stated the adoption of a societal perspective. The range of possible costs of dementia interventions included the government-funded health care, the government-funded social care, the informal care, the private payment for care, the patient out-of-pocket expenses for seeking and receiving treatments, the patient time in seeking and receiving treatments, the patient productivity loss, the costs to the voluntary sector, the costs to the transportation sector, and the costs to the legal sector. The range of possible benefits of dementia care included the health benefit for patients and the health benefit for informal caregivers. The inclusion of these costs and benefits in a
‘societal perspective’ varied substantially between the published studies. There was no agreement on what costs and benefits ought to be included from a societal perspective. In dementia care, this study found that the informal care, the informal caregivers and the private co-payment were significant wider impacts that always needed to be included in economic evaluation.

The key contribution to knowledge of this study is a description of applied economic evaluation methods in dementia. There had not been any published review of economic evaluation. Taking a societal perspective is important for economic evaluation of dementia interventions due to the existence of substantial wider costs and benefits. However, there was no agreement among previous studies on how a societal perspective should be implemented. The study highlighted the gap in the methods of economic evaluation when it was applied in dementia.

The findings of this study provided the evidence base for subsequent studies. A decision problem was specified for the case study. Four alternative options for early detection of dementia in primary care were evaluated: (1) GP’s unassisted clinical judgement, or GPs administer either the MMSE (2), the 6CIT (3) or the GPCOG (4). This problem was chosen because there was an interest from policy makers in interventions for early detection and intervention in dementia care. Costs included the health care cost, the government funded social care, the private payment for care, and the informal care. Benefits included the patient QALYs and the carer QALYs. A mathematical model was needed to provide estimates for these costs and benefits. To inform the development of the mathematical model, another systematic review was conducted in study two.

9.2.2 Study 2 (Chapter 5): Review previous model-based studies in dementia

This second study was designed to inform the development of the cost-effectiveness model for evaluating the use of alternative cognitive screening tests in primary care. A systematic review of previous model-based economic evaluation studies in dementia was performed. This review had a narrower scope (in terms of included studies) and a different focus compared to the review in the first study. This review only included model-based economic evaluations. It extracted the key components in developing a cost-effectiveness model for dementia interventions from previous models: modelling the disease progression, modelling the
intervention effects, linking disease progression and intervention to health, and linking disease progression and intervention to costs.

For modelling disease progression, all previous studies modelled the dementia progression in terms of its clinical manifestation. No model described the dementia progression in terms of the biological/pathological changes in the brain. The key aspects of the dementia progression included the modelling of cognitive decline, behavioural symptoms, deterioration in functioning, institutionalisation, and death. Although it was important to model the disease progression for cognitive decline, behavioural symptoms and functioning simultaneously (Green, 2007, Cohen and Neumann, 2008, Green et al., 2011), most studies only modelled the cognitive decline. Four modelling approaches were identified from previous studies: (A) decision tree models, (B) traditional state-transition models, (C) transition to Full-Time-Care (FTC) models, and (D) models that directly simulate progression rates of specific clinical measures. Approach (D) was considered the most appropriate approach for the development of the cost-effectiveness model in study three because of several reasons such as the flexibility in incorporating various aspects of the patient pathway and the wider impacts of interventions, and there were readily available data for modelling the disease progression.

For modelling interventions, two groups of interventions were reviewed: screening/diagnostic interventions, and pharmaceutical interventions. Regarding the screening/diagnostic interventions, their health benefits came from early access to post-diagnostic treatment and care. Regarding the pharmaceutical interventions, their effects were modelled through the symptomatic improvements based on clinical trial data. When extrapolating beyond the clinical trial period, assumptions were needed. The common assumption in previous models was that the symptomatic improvements were only counted for treated patients in the first year (where most evidence from clinical trial is available); beyond that time the treatments were assumed to add no further symptomatic improvement and patients were assumed to resume to the normal disease progression.

The disease progression and interventions were linked to health by assigning utility scores to different health states through the disease progression. The HUI and the EQ5D were the most commonly used measures for health utility. Various sources for utility values were identified from the literature. The disease progression and interventions were linked to costs by assigning costs to different health states through the progression. Sources for costs were also identified from the literature.
The contribution to knowledge in this study was a description of the key components in developing a cost-effectiveness model for evaluating dementia interventions. Previous reviews (Green et al., 2007, Cohen et al., 2008, Green et al., 2011) covered the literature up to March 2010. This study extended the coverage of the literature up to October 2015. The findings of this study informed the development a new cost-effectiveness model in study three.

9.2.3 Study 3 (Chapter 6): Developing a patient-level cost-effectiveness model for evaluating the use of different cognitive screening tests in primary care

The objective of the third study was to develop a cost-effectiveness model for evaluating the use of different cognitive screening tests in primary care. Four options for cognitive assessment in primary care were evaluated: (1) GP’s unassisted judgement, (2) GPs using the MMSE, (3) GPs using the 6CIT, and (4) GPs using the GPCOG. The baseline option was the GP’s unassisted judgement. The modelling strategy was informed by the systematic review in study two.

A patient-level simulation was developed. The choice of a patient-level simulation approach was informed by the systematic review in study two. The disease progression was described in three main states: normal cognition, Mild Cognitive Impairment (MCI), and dementia. Patients progressed from normal cognition to MCI or dementia. Patients with MCI had a higher rate to progress to dementia but a proportion of them reverted to normal cognition. The transition rates were estimated from data on annual incidents of dementia and MCI, and the annual rate of MCI reverting to normal cognition in the population. Once patients were in the dementia stage, they began having a steady decline in cognitive function, behavioural symptoms, and functioning. This progression was described directly by applying the annual rates of decline to the clinical measures in the model.

The screening interventions were modelled through their effectiveness in discriminating people with cognitive impairment (sensitivity and specificity), the prevalence of cognitive impairment, and the annual number of cases present at primary care. Positive cases were referred to memory services where it was assumed that dementia and MCI would be detected with 100% accuracy. Post-diagnostic treatments only considered dementia medication. The effects of dementia medication were modelled directly by adding their symptomatic improvements (for cognitive function, behavioural symptoms, and functioning) to the natural disease progression. Since
clinical trial data were mainly short-term, the effects were only applied for one year, and after the first year, patients were assumed to resume to the normal rates of decline.

Patient health utility values were estimated for normal cognition, MCI, and dementia. For the normal cognition and MCI, an average utility value was used. For the dementia stage, a utility function that describes utility value varying with cognitive measure, behavioural measure, and institutionalisation status was used. On the other hand, the caregiver utility was described by a function that describes their utility value varying with the patient behavioural measure, functioning measure, and the patient’s gender.

Costs were modelled by assigning costs to different states in the disease progression and costs to specific services and interventions. The different states included normal cognition, MCI, mild dementia, moderate dementia, severe dementia, and death.

The results suggested that using either the MMSE or the GPCOG would save resources and deliver more QALYs compared to the baseline option (the GP’s unassisted judgement). The 6CIT option was estimated to incur a small health care cost but save resources in the social care and the informal care compared to the baseline option. The 6CIT option was estimated to deliver the highest number of QALYs gained among all options due to it having the highest sensitivity. The GPCOG option was estimated to make the most savings for the health care resources due to it having the highest specificity. The health care cost of the interventions was estimated (per patient) at £80,144 for the baseline option (the GP’s unassisted clinical judgment), £80,077 for the MMSE, £79,957 for the GPCOG, and £80,139 for the 6CIT. The total number of QALYs for the patients were estimated at 12.00886 for the baseline option, 12.009246 for the GPCOG option, and 12.013143 for the 6CIT option. If only considering the health care cost and the patient QALYs, the incremental analysis showed that the GPCOG option clearly dominated the baseline option and the MMSE option, and the ICER between the 6CIT option and the GPCOG option was £59,453 per QALY. The PSA results (only considering the health care cost and the patient QALYs) showed that at cost-effectiveness thresholds lower than £52,000 per QALY, the GPCOG had the highest probability of being the best option.

This study makes contributions to both knowledge and policy making. To knowledge, a key contribution of this study is the more detailed modelling of the pathway from normal cognition to presenting at GPs, being assessed and referred to memory services. This feature of the model
makes it possible to evaluate different screening tests that could be used by GPs. To policy, this study contributes to the understanding of the cost-effectiveness of early detection and interventions in dementia. The model outputs (costs and QALYs of different interventions) provided the inputs for study four and five.

9.2.4 Study 4 (Chapter 7): Implementing the extended cost-per-QALY approach

The objective of the fourth study was to investigate the implementation of the extended cost-per-QALY in the case study. Starting with the estimates of costs and QALYs from the model in study three, the healthcare perspective cost-per-QALY analysis was implemented. This implementation only included the health care cost and the patient QALYs in the cost-effectiveness estimation. Then, taking a broader societal perspective (including the other wider costs and benefits), the generic extended cost-per-QALY approach was customised for a broad range of costs and QALYs in the case study. The key point for implementing the broader societal perspective was the aggregation of wider costs and wider benefits. For costs falling on different sectors, we used the ratios between the health care threshold and the thresholds in other sectors as weights attached to the wider costs. The total cost was then the weighted sum of all costs. For benefits, all benefits were measured and valued in terms of QALYs. The aggregated cost was compared with the aggregated QALYs in a similar way to the methods applied in a conventional cost-per-QALY analysis with incremental analysis, DSA, and PSA performed as usual. Although this demonstration was performed for a case study of dementia care, the approach can be generalised to other interventions, conditions, and sectors.

In the case study, the best option was a choice between the 6CIT and the GPCOG. The two perspectives (the healthcare perspective and the societal perspective) gave two different mean cost-effectiveness results. The healthcare-perspective cost-per-QALY analysis resulted in an ICER (6CIT vs GPCOG) of £59,453 per QALY, whereas the extended cost-per-QALY analysis gave an ICER (6CIT vs GPCOG) of £41,355.

The previous literature looked at other methods to implement a broader societal perspective in economic evaluation of health care interventions. The Value-Based Pricing (VBP) in the UK proposed to aggregate all wider resource impacts of an intervention into a single monetary measure called Wider Societal Impacts (WSIs) (Roberts, 2015). WSIs are calculated as the patient’s net contribution to society. It is the net difference between the amount of resources consumed and the amount of production for a patient. For production, these include paid
production and unpaid production. For consumption, these include social care, informal care, personal paid consumption, and personal unpaid consumption. These elements of WSIs are illustrated in Table 9.1.

Table 9.1: Elements of Wider Societal Impacts in the VBP

<table>
<thead>
<tr>
<th>Group</th>
<th>Sub-group</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumption</td>
<td>Formal care</td>
<td>Social care provided to the patient (except treatment for their health condition) that is paid for – either by the patient or their family, or by Government.</td>
</tr>
<tr>
<td></td>
<td>Informal care</td>
<td>Unpaid care provided by family or friends</td>
</tr>
<tr>
<td></td>
<td>Private paid consumption</td>
<td>Goods and services that are purchased for consumption in the course of normal life – such as food, clothing, accommodation, travel, communications and entertainment.</td>
</tr>
<tr>
<td></td>
<td>Consumption of unpaid</td>
<td>E.g., domestic works in the home, child care, volunteering</td>
</tr>
<tr>
<td></td>
<td>production (non-care)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consumption of Government</td>
<td>Services provided directly by Government excluding ‘public goods’ and ‘transfers of funds’, and ‘social care’ (measured in formal care).</td>
</tr>
<tr>
<td></td>
<td>services</td>
<td></td>
</tr>
<tr>
<td>Production</td>
<td>Paid production</td>
<td>Paid labour by patients</td>
</tr>
<tr>
<td></td>
<td>Unpaid production</td>
<td>Unpaid labour by patients</td>
</tr>
</tbody>
</table>

WSIs are converted to a QALY-worth equivalent by a constant exchange rate such as £60,000 per QALY. These are then added to both sides of a cost-per-QALY analysis: to adjust the QALYs displaced by costs falling on the healthcare budget, and to adjust the QALYs gained by an intervention. The main issue with this approach is the valuation of different components of WSIs (Miners et al., 2013b). The health care cost of an intervention is separated from wider costs and not included in WSIs. This health care cost is valued in terms of its impact on the constrained healthcare budget by estimating the QALYs loss due to displaced health care services (e.g. a healthcare cost-effectiveness threshold of £20,000 per QALY). On the other hand, other wider costs including social care, production, and other consumption are
aggregated with equal weights to calculate WSIs and WSIs are then converted to QALYs equivalent by an exchange rate that is different from the healthcare cost-effectiveness threshold (e.g. £60,000 per QALY). This assumes one value for the opportunity costs of resources in non-health sectors and this value is different from the healthcare sector. The appropriateness of this assumption is open for debate.

The important contribution to knowledge of this study is the development and investigation of the extended cost-per-QALY approach for implementing a societal perspective in economic evaluation. This approach focuses on the aggregation of wider costs and benefits to implement a societal perspective. It uses sector-specific thresholds and the societal value of a QALY for aggregating costs falling on different sectors. The study highlights the key operational steps in implementing the approach and the challenges for future research. This is the first study that investigates the operationalisation of a potential approach to extend the cost-per-QALY analysis for a societal perspective. A paper which arises from this research has been submitted to be considered for a peer-review publication.

9.2.5 Study 5 (Chapter 8): Implementing the CCA-MCDA approach

The objective of the fifth study was to investigate the implementation of the CCA-MCDA approach in the case study. The CCA-MCDA approach is defined as an extension of Cost-Consequences Analysis (CCA). The decision criteria in the CCA-MCDA approach are the costs and benefits that are included in the economic evaluation. The decision makers can be asked to select the most important costs and benefits and state their reasons why they are important. Going further than a conventional CCA, the CCA-MCDA does not stop at presenting costs and consequences in a disaggregated format to decision makers. It uses MCDA techniques to elicit and use views and judgements from decision makers regarding costs and consequences falling on different sectors and individuals. Note that due to time and resource constraints (and the explorative nature of the study), the implementation of the CCA-MCDA in this case study did not follow a full MCDA process. There was no attempt to engage the decision makers and stakeholders in identifying and selecting important costs and benefits to be included in the economic evaluation. The included costs and benefits were pre-specified by the analyst.

Starting with the estimates of different costs and QALYs from the model in study three (Chapter 6), a hypothetical decision-making group was formed. This group included members
of the local Clinical Commissioning Group (CCG), members of the social care department (city council), members of the public health department (city council), staff from the local memory services, a clinician from the local hospital, and a GP. The generic CCA-MCDA approach was customised for the specific costs and benefits in the case study. A simple weighting system was developed for weighting the different costs and weighting the different benefits using weights elicited from the local decision makers. A facilitated decision-making workshop was organised by the researcher. The decision-making group took part in a half-day workshop where they were presented the decision problem, the CCA-MCDA approach, and were asked to discuss and state their weights for the costs and the benefits. The MCDA weights were collected on questionnaires. The workshop was audio-recorded and the data were analysed qualitatively. The elicited weights were used to demonstrate the implementation of the CCA-MCDA approach. The aggregated cost was the weighted sum of different costs. The aggregated QALY was the weighted sum of different QALYs. The aggregated cost can be compared with the aggregated QALY in a similar way compared to the methods applied in a conventional cost-per-QALY analysis with incremental analysis, DSA, and PSA performed as usual.

The qualitative analysis of the workshop data showed that the main difficulty in implementing this approach was to get the participants to think about the problem consistently with the economic evaluation framework. Once they started understanding the problem, they began to engage better. The participants voiced difficulties in understanding the approach and the weighting of costs and the weighting of benefits. Regarding weighting the different costs, the challenges include the meaning of a cost and how to see one cost different from another cost, what rationale should be used in weighting costs, and how weights would influence the overall decision. The problem was emphasised with non-market costs such as the informal care costs since their measurement methods influenced how they were weighted against the other costs. Regarding weighting different benefits, the participants showed some difficulties in understanding the QALY measure and the rationale to weight the QALYs gained for carers compared to the QALYs gained for patients. The participants gained a better understanding as the workshop progressed, with more explanations and examples. At the end of the workshop, the participants could rank the items (costs and benefits) and state their weights.

In the case study for the CCA-MCDA approach, the best option was still a choice between the 6CIT and the GPCOG. The CCA-MCDA approach resulted in a higher ICER (the 6CIT vs the GPCOG) at £46,799 per QALY compared to the extended cost-per-QALY approach (£41,355
per QALY). This was due to the different weights attached to the costs and the benefits when they were aggregated.

There have been discussions about the possibility of using MCDA methods to support a HTA process from a broader societal perspective. Devlin and Sussex (2011) observed that HTA decisions such as the ones made by NICE in the UK are already based on multiple criteria including criteria other than the evidence from a cost-per-QALY analysis. The problem was that these wider criteria had not been made explicit in a formal MCDA approach. After reviewing the evidence, Devlin and Sussex (2011) concluded that MCDA methods could be useful for both national and local commissioners who need to make investment and disinvestment decisions in health care resource allocation. They suggested a future possibility that NICE could provide the evidence for the performance of new technologies in an agreed MCDA format and local commissioners could apply their own weights (to the criteria) to tailor the decisions to their local circumstances. Thokala and Duenas (2012) also came to a similar conclusion that the existing NICE appraisal process is already similar to an MCDA process but without formal modelling. The authors emphasised the importance of being aware of the wide range of different MCDA methods; each of them has its own strengths and limitations. Drummond et al. (2015) mentioned the possible use of MCDA to incorporate other aspects of value in economic evaluation of health care. In their opinion, MCDA could be used to incorporate and aggregate other attributes of benefits which go beyond health in CUA. Nonetheless, none of the previous empirical studies could provide a satisfactory method to incorporate MCDA techniques into the cost-per-QALY analysis. The main challenge is to address the issue with constrained budgets, subjectivity, legitimacy, and validity of decision makers’ weights, and consistency of decision outcomes.

Findings from this research add to the current debate about the potential role of MCDA to support a HTA process from a broader societal perspective. This is the first study that attempted to apply MCDA methods to implement a Cost-Effectiveness Analysis taking a broader societal perspective. A conventional application of MCDA ranks and scores a list of alternative decision options, therefore, it can only indicate whether an option is better than other options within the list. In our approach demonstrated above, we used weights elicited from decision makers to aggregate costs to a single aggregated cost in £ and benefits to a single aggregated benefit in QALYs. Thus, it was possible to have an estimate of value for money for a decision option by comparing the aggregated cost with the aggregated QALY. A cost-effectiveness threshold
could also be specified to indicate the cost-effectiveness of a decision option. However, there remains theoretical issues around whether this approach can address the opportunity costs of resources given the subjectivity of the weights attached to costs and benefits.

The important contribution to knowledge of this study is the development and investigation of a CCA-MCDA approach for implementing a broader societal perspective in economic evaluation. The approach emphasises the use of weighting techniques from MCDA to elicit views and weights from local decision makers for the aggregation of different costs and benefits. Local variation in HTA decisions is recognised and we need to provide a mechanism for local decision makers to be involved in the decision-making process in a transparent and structured manner. Although the demonstration was performed for a case study of dementia care, the approach could potentially be generalised to other interventions, conditions, and sectors. The study highlights the key operational steps in implementing the CCA-MCDA approach and the challenges for future research.

9.3 Implications

9.3.1 Implications for methods of economic evaluation

In early 2017, the second Panel on Cost Effectiveness in Health and Medicine reviewed the Reference Case for Cost-Effectiveness Analysis set out by the original Panel in 1996 (Neumann et al., 2017). The original Panel recommended a societal perspective to improve comparability and quality. However, experience since the original panel shows that most studies have not use a societal perspective. The main concern is with the practicality of a societal perspective. Recognising the strengths and limitations of both a societal perspective and a narrower healthcare perspective, the second Panel recommends analysts to present both a societal perspective and a healthcare perspective. For the Societal Reference Case, the second Panel’s recommendation is a Cost-Consequence Analysis (CCA). Costs and benefits are identified, measured, valued, and listed in a table as disaggregated consequences across different sectors. This table is termed an ‘Impact Inventory’. The report of summary measures (after the Impact Inventory) is also encouraged. The second Panel recommends the use of one or more summary measures such as an ICER, NMB, or NHB that include some or all of those listed in the Impact Inventory.
The findings from this thesis complement the Societal Reference Case set out by the second Panel. Starting with an Impact Inventory, there are different approaches to deal with a broad range of disaggregated consequences across different sectors. This thesis has provided an investigation of the two approaches: the extended cost-per-QALY and the CCA-MCDA. As demonstrated, these approaches can produce summary measures (i.e. ICER, NMB, NHB) that include all listed effects from an Impact Inventory, albeit with some caveats.

The extended cost-per-QALY study (Chapter 7) has the following implications for the methods of economic evaluation. First, taking a broader societal perspective, wider costs need to be valued in the same way as health care cost. The opportunity costs of consuming resources in other non-health sectors need to be recognised and measured. Similar to the healthcare sector, other sectors also have cost-effectiveness thresholds that reflect the opportunity costs of their resources. Sector-specific thresholds can be different due to different budget constraints and activities. Second, taking a broader perspective on costs needs a broader perspective on benefits. The extended cost-per-QALY approach assumes the measure of health benefit is the same across sectors. Although this is currently not the case, future research is expected to develop a broader quality of life measure for use across sectors. Example is the recent proposal by researchers at School of Health and Related Research (ScHARR), University of Sheffield, to develop a broad quality of life measure to calculate QALYs for use in economic evaluation by policy makers to inform decisions across the sectors of health care, social care, and public health (Brazier et al., 2016). Such a broader QALY measure would complement and make this extended cost-per-QALY approach easier to implement.

The implications of the CCA-MCDA study (Chapter 8) examined the potential role of MCDA in economic evaluation of health care interventions.

First, there is a concern about which criteria to be included when applying an MCDA for economic valuation. It should be noted that this is not a challenge faced by the MCDA approach. It is a common challenge for economic evaluation taking a broader societal perspective in general. A societal perspective requires all costs and consequences of interventions to be included regardless of where they fall or who receive them. However, it is not possible to identify and include all costs and consequences in practice. Claxton et al. (2010) note that it is impossible to have a complete social welfare function. One way to overcome the impossibility is to identify as many costs and consequences and select the most important ones. The question is that if an exhaustive list of costs and consequences cannot be established, who
has the legitimacy to identify and select the costs and consequences for a societal perspective. In this aspect, the MCDA approach can offer a practical solution although this was not tested in this thesis due to time and resource constraints. The MCDA approach can engage the decision makers and stakeholders of the decision problem to discuss, identify, and select important costs and consequences to be included in the economic evaluation.

Second, the CCA-MCDA approach can be applied flexibly. As demonstrated in this thesis, costs and benefits can be weighted and aggregated separately to derive an aggregated cost and an aggregated benefit. An incremental analysis can be performed and the value for money can be calculated within an MCDA approach. However, caution needs to be taken when conducting facilitated decision-making workshops for eliciting the weights. We need to make sure decision makers understand the approach and the evidence presented.

Third, regarding opportunity costs of resources, we can see that the CCA-MCDA approach could produce a measure of trade-off between the aggregated cost and the aggregated benefit. This is not the same as the concept of a cost-effectiveness threshold in a healthcare-perspective cost-per-QALY analysis. In a healthcare-perspective cost-per-QALY analysis, the additional cost is thought to result in displaced existing health care services due to a fixed healthcare budget. The health consequences of displaced services are the opportunity cost of the additional cost on the fixed budget. However, it can be argued that a fixed budget is only one of many constraints that are present in a sector. For examples, other constraints include capacity, demand, political strategy, etc. Thus, there are other factors affecting the consequences of an additional cost besides budget constraints. The potential advantage of an MCDA approach is that it could address multiple criteria revealed from the decision makers’ views and values. However, this is hypothetical at the moment and requires further research and development.

Fourth, another implication of the CCA-MCDA study (Chapter 8) is a method to weight QALYs received by different groups of individuals and incorporate the weights in an economic evaluation. The study suggests a simple weighting system that could be used to weight QALYs received by different groups of individuals. In principles, this could be extended to incorporate even non-health benefits. For non-health benefits, their inclusion in economic evaluation depends on how substantial they are and how much they are related to the health benefit. We do not need to include some non-health benefits which are closely linked to the health benefit to avoid double-counting. If we need to include non-health benefits, using a similar approach such as the one comparing a carer QALY to a patient QALY in this thesis, non-health benefits
can be compared to a patient QALY and their corresponding weights can be elicited from the decision makers and stakeholders. A weighted sum model can be used to aggregate non-health benefits to health benefits.

Through the implementation of the extended cost-per-QALY and the CCA-MCDA, it has been realised that there is a need to recognise the HTA decision setting. Healthcare resource allocation decisions take place at different levels from national to local regions to individuals. For example, NICE makes recommendations nationally on which health care interventions should be provided by the NHS. Locally, Clinical Commissioning Groups (CCGs) need to decide how much they should spend on different health care programmes. Individually, clinicians need to decide whether to give a particular health care intervention to a patient. Going from individually to nationally, decisions become more complex and involve a broader range of different aspects and stakeholders; the quality and quantity of information required for decision-making also increases. Economic evaluation often uses estimates and assumptions at the national level but local variation is inevitable. Different local areas might be different in terms of their local production functions, budgets and value judgements. Recommendations can be made nationally, but the implementation at the local level might be different. In this aspect, it is thought that the two approaches (the extended cost-per-QALY and the CCA-MCDA) proposed in this thesis could be complementary: one is more appropriate for decisions at national level and the other has the flexibility to allow for local variations in decision-making.

The extended cost-per-QALY is recommended for healthcare resource allocation decisions at the national level when a broader societal perspective is required. This is because decisions at the national level deal with things that are shared by all local regions within the national system. Evidence to inform decisions at the national level requires a high level of consistency, quality and quantity. Subjective judgement from a specific group of individuals might not represent national interests and it leaves too much room for bias and inconsistency. The extended cost-per-QALY approach can satisfy the evidence requirement at national level since it only uses ‘objective’ evidence.

The CCA-MCDA is recommended for decision-making at the local level. The implementation at the local level may diverge from national values, as found in this thesis. Local decisions deal with some aspects that can be only relevant to the local areas where ‘objective’ evidence is not always available (or it is not practical to conduct research to collect data). In this case,
subjective judgment from local decision makers and stakeholders can be useful. However, it is not often used in a transparent and accountable manner. With the CCA-MCDA approach, local values can be used directly in an economic evaluation and local decision makers can be involved in the decision-making process in a transparent, accountable and structured manner.

9.3.2 Implications for policy

This thesis has several implications for policy in health care. First, the results of the first review (Chapter 4) emphasise the existence of substantial wider costs and consequences of dementia care. These wider costs need to be recognised and included in economic evaluation studies to inform resource allocation decisions. Research in this thesis shows that excluding certain costs and consequences could lead to different decisions being made depending on the value of the healthcare cost-effectiveness threshold. It is important for policy to be aware of areas where wider costs and consequences of health care are significant.

Second, results of the cost-effectiveness model (Chapter 6) in this thesis showed that interventions to improve the accuracy of the cognitive assessment in primary care saved resources and brought additional health benefits to patients and their caregivers. The health benefits came from early diagnosis of dementia and early access to treatments. When people with dementia are diagnosed earlier, they have timely access to dementia treatments and receive more health benefits from the treatments. The health benefits of early diagnosis increase with more effective treatments. Savings in resources in health care came directly from less false-positive cases referred to memory services and indirectly from health improvement. Savings in resources in social care and informal care came indirectly from health improvement. Thus, health care policy in dementia should focus on early diagnosis of dementia, especially when more effective treatments become available.

Third, the extended cost-per-QALY study (Chapter 7) suggested an approach to broaden the perspective of economic evaluation of health care interventions at the national level. As discussed in Chapter 3 in this thesis, a broader societal perspective is needed to increase the validity and ‘cross-sector’ comparability of healthcare resource allocation decisions. It is even more important regarding our ambitions for a future in which health care, social care, and public health are integrated and managed around the individual (NHS England, 2014). With this greater policy emphasis on coordination between sectors, a restricted healthcare perspective for economic evaluation such as the one currently adopted by NICE will be
struggling to support national resource allocation decision making. The national HTA system needs to be ready for a change for a broader societal perspective. Research has already been started to develop a broad quality of life measure to calculate QALYs for use in economic evaluation by policy makers to inform decisions across the sectors of health care, social care, and public health (Brazier et al., 2016). When such a broader QALY measure is developed and used, moving to a broader perspective for economic evaluation of health care interventions is inevitable. The HTA system can start the change from now by following the two reference cases recommended by the second Panel on Cost Effectiveness in Health and Medicine (Neumann et al., 2017): one reference case for the healthcare perspective and the other reference case for a broader societal perspective. For now, the societal-perspective reference case can simply require all important costs and consequences identified, assessed, and presented in a disaggregated format. In the future, with the development of a broader measure for benefits across sectors and a more refined mechanism to aggregate costs falling on different sectors such as one discussed in this thesis, costs and consequences from a societal perspective can be formally aggregated to inform resource allocation decisions.

Fourth, the CCA-MCDA study (Chapter 8) explored the decision-making process at the local level regarding resource allocation in dementia care. NICE makes decisions and recommendations for health care interventions at the national level. However, the implementation at the local level does not always follow and this may be due to differences in local production functions, budget constraints, and value judgements. Local implementation requires more of a local decision-making and commissioning process. The implication for policy is that we need to engage local decision makers and stakeholders more in HTA decisions. There seems to be a gap between the national recommendations and the local implementation regarding HTA decisions. Local variation is inevitable and we need to make sure the local implementation is aligned with analyses at the national level. Given the wide variation between local areas and the lack of evidence at the local level, local decision makers’ judgement is a useful source of information for a local Cost-Effectiveness Analysis using an approach such as the CCA-MCDA. However, critical issues need to be resolved. The key issue lies with the identification and construction of the decision-making group, the interpretation of different costs, benefits, and their weights, the conduct of the facilitated workshop(s), and the value elicitation tasks.
9.4 Limitations

The key limitations of this thesis are the case study selection and the design of the selected case study. The research is mainly methodological. It would be preferable to investigate the operationalisation of the approaches in a range of different disease areas. Dementia is not the only disease area where the existence of wider costs and consequences is significant. The investigation should be extended to other disease areas where other disease characteristics might have some important implications on the operationalisation of the approaches. The typical characteristics of dementia care are the presence of the government-funded social care, the private payment for care and the important role of the informal caregivers. People with dementia are mostly retired. Other disease areas might require the inclusion of more costs and benefits. For example, looking at the impacts of autism on children, costs might need to expand to include those falling on the education sector and benefits might need to include beyond-health aspects such as learning outcomes. Since only one disease area was selected, the thesis is not able to investigate the comparability across disease areas.

We only examined two approaches to implement a societal perspective. The Welfarist Cost-Benefit Analysis approach was not included. The thesis would provide a more complete picture for the implementation of a societal perspective in economic evaluation if CBA was compared with the extended cost-per-QALY and the CCA-MCDA. Furthermore, the list of included costs and benefits in a broader societal perspective was limited to those identified in a systematic review of previous economic evaluation studies. This does not include all relevant costs and consequences of dementia care. The issue was also raised in the facilitated decision-making workshop with local decision makers. For example, other costs could include those falling on the fire brigade sector, the housing sector, and the voluntary sector.

The study design for implementing the extended cost-per-QALY approach (Chapter 7) could be improved. It only focused on the aggregation of costs falling on different sectors. The aggregation of benefits was not researched in depth. Patient QALYs gained and carer QALYs gained were aggregated with equal weights, however, there could be evidence to aggregate them with different weights. A QALY gained by patients could be different from a QALY gained by unpaid caregivers.

The study design for implementing the CCA-MCDA (Chapter 8) could also be improved. First, instead of a hypothetical decision-making group, we could engage with actual decision makers
and stakeholders using a decision problem that they currently need to solve. Second, we could implement a full MCDA process (A full MCDA was not implemented in the CCA-MCDA study). To implement a full MCDA, we would need at least two more facilitated workshops in addition to the one conducted in the case study. The first workshop would be to give decision makers and stakeholders an opportunity to discuss about all possible costs and consequences of the interventions, and how to measure and include them in the economic evaluation. Then, the second workshop would be the one conducted in this thesis for eliciting their views and weights for the aggregation of costs and benefits. The third workshop would be to present to them the base-case results and sensitivity analyses and let them arrive at the final decision. Due to limited time and resources, only one workshop was conducted. The case study did not assess the full application of an MCDA approach.

Furthermore, this thesis has not touched an important area which is the incorporation of equity in economic evaluation. This can be especially important in a societal perspective. One of the consequences of providing one health care intervention but not the other is the change in the distribution of health and health care in society. To that extent, equity considerations concern distributional objectives perceived by policy-makers and society.

9.5 Further discussion

9.5.1 Addressing opportunity cost in health care resource allocation decisions

To implement a broader societal perspective, this thesis has recommended the use of the extended cost-per-QALY approach at the national level (i.e. NICE) whereas the CCA-MCDA approach could be used at the local level (i.e. CCGs). The basic difference is in the understanding and estimation of opportunity costs of resources at the national level and at the local level. In both cases, additional costs would mean lost benefits due to forgone opportunities and our ultimate goal is to make a decision that creates a positive net benefit (i.e. gained benefit > lost benefit). Thus, accurate estimates of opportunity costs are important to make sure a positive net benefit of the decision being made.

*Opportunity costs at national level*

Let’s take an example of a new drug X that is evaluated by NICE nationally. Let’s assume the evidence suggests nationally approving drug X would bring 1000 QALYs and impose an additional cost of £20 million on the NHS budget (£20,000 per QALY). An empirical estimate
of the opportunity cost of £20 million on the NHS budget suggests a loss of 1546 QALYs (i.e. using the rate of £12,936 per QALY). Given the loss (1546 QALYs) is more than the gain (1000 QALYs), drug X should not be approved nationally.

However, it should be noted that the empirical estimate of the opportunity cost nationally assumed certain behaviour (in terms of disinvestment activities) of the whole system and that the same behaviour is expected to still be the same if drug X is approved. This is a second-best approach (Culyer, 2016) for the estimation of the opportunity cost. If this assumption does not hold, there are several implications. If the system behaviour is better now (compared to the data time of the empirical estimate), actually less health would be lost (i.e. less than 1546 QALYs) since the system would be more efficient in displacing least cost-effective existing services. On the other hand, if the system behaviour is worse now (compared to the data time of the empirical estimate), actually more health would be lost (i.e. more than 1546 QALYs) since the system would not be as efficient as before in displacing least cost-effective existing services. If this is the case, it suggests a necessary update for the empirical estimate.

**Opportunity costs at local level**

With the same rationale, the national estimate might not be true for a local area. This is because the investment and disinvestment activities/behaviour can deviate from the national average and there is no guarantee that they will be the same. If the disinvestment behaviour of a local area is believed to be better than the national average, then less health would be lost if the intervention is funded in that local area. In the example of drug X, it could still be funded in a local area if the local estimate of the opportunity cost suggests less QALYs lost than gained because the local system could identify least cost-effective services to displace.

So the idea is that local estimates of opportunity cost need to be accounted for in resource allocation decisions at the local level. In addition to the points discussed above, it should be noted that it could be possible to identify specific disinvestment activities, and disinvestment activities could be guided at the local level to improve efficiency. An optimisation approach could be adopted for the estimate of opportunity costs at the local level (Thokala et al., 2018). In principle, this would move the estimate of opportunity costs at the local level closer to a first-best estimate. It is also recognised that this cannot be done by an analyst alone like how it has been done at the national level.

**Role of local decision makers**
The role of local decision makers is key in identifying and implementing disinvestment activities. Through the research in this thesis, it has been recognised that we could directly involve the local decision makers in the framework using the CCA-MCDA approach.

The local decision makers in the framework using the CCA-MCDA approach can be used to estimate the opportunity costs in two different ways: a) eliciting an estimate of the opportunity cost based on their expert judgement, and b) empirical estimate of the opportunity cost using the local data. In this thesis, the former approach was used.

Much improvement is needed with the CCA-MCDA approach before it could be used in practice. As found in this thesis, just by asking the decision makers to think about the consequences of the costs of an intervention would not take us to the opportunity costs. The lesson learned from this thesis is that the CCA-MCDA approach needs to include/integrate the Programme Budgeting and Marginal Analysis (PBMA) framework (see the discussion earlier). Both national and local evidence/data could be presented to and judged by the decision makers in the decision-making exercise. It is better not to vaguely ask the decision makers to think about the opportunity costs of the costs but to ask them to look at the allocation of current services/programmes and appraise potential investment and disinvestment activities. By working closely with local decision makers, specific disinvestment activities could be identified and a local estimate of opportunity cost could be possible. However, there would be high uncertainty around this local estimate due to the lack of data. If this is the case, the decision makers’ judgement would be useful to mediate the estimates. This judgement can be brought into the analysis in terms of weights as demonstrated in the implementation of the CCA-MCDA approach in this thesis.

On the other hand, the same rationale could be used with the private consumption cost. The national estimate might not represent the willingness to pay of the local people. With the CCA-MCDA approach, local stakeholders could be asked to join the decision-making exercise. They could be presented with the national evidence and asked to state the value that they think would represent better what the local people want.

**Recommendations for estimating opportunity costs**

It is widely acknowledged that accurate estimates of opportunity costs are important for resource allocation decisions. At the national level, they can and should be empirically
estimated. At the local level, the national estimate might not hold true. Local deviation is natural and local adjustment could be necessary. In addition, local estimates of opportunity costs could be more accurate and specific with the involvement of local decision makers. Decision makers and stakeholders can come together to discuss and evaluate what to invest and what to disinvest. They can look at their different budgets and understand the lost benefits of forgone opportunities if they fund the new intervention. Local estimates would often have high uncertainty due to the lack of data and the judgement from the decision makers could be necessary to mediate these estimates.

9.5.2 The potential role of CBA as an alternative approach

Although CBA was identified as a potential approach that could be used to implement a societal perspective (3.2.3, page 45), it was not explored in this thesis due to the time and resource constraint. This subsection provides a more detailed discussion on the potential role of CBA as an alternative approach to the extended cost-per-QALY and the CCA-MCDA. Applied CBA in health care has already been considered by other researchers (Johannesson and Jonsson, 1991, Frew, 2010).

As mentioned earlier in 2.1, CBA aims to measure, value, and express all costs and benefits in monetary units. The societal perspective is the natural/default perspective of a CBA: all costs and benefits are included and valued in monetary units. If an item of costs or benefits has a perfect market, its price is the monetary valuation. If an item does not have a market or the market is not perfect, individuals’ willingness to pay (WTP) or willingness to accept (WTA) is used as a proxy of market value (see 2.1). At the heart of the CBA is the assumption that such market price could reflect opportunity costs. In other words, the net monetary value calculated from comparing monetarily valued costs and benefits is the actual gain (or loss) for the society if the intervention is funded. However, as shown below, this is not the case for a government funded health care system with the existence of budget constraints (such as the one in the UK).

Let’s take the example of a new drug X as described above: approving drug X would bring 1000 QALYs and impose an additional cost of £20 million on the NHS budget. As discussed earlier, the cost-per-QALY looks at the forgone benefit of the £20 million and compare that with the 1000 QALYs gained to determine whether a positive net benefit is achieved with X. The CBA, on the other hand, looks at the WTP of the 1000 QALYs gained and compare that with the cost of £20 million to determine whether a positive net monetary value is achieved. These would give very different results for the decision. For example, the empirical estimate
of the opportunity cost of the £20 million suggests a loss of 1546 QALYs (£12,936 per QALY) and thus, X should not be funded. However, the CBA can come up with a WTP of £30,000 per QALY and hence the monetary value of 1000 QALYs gained is £30 million which would create a positive net monetary value of £10 million compared to the cost which suggests X should be approved. As can be seen, the use of CBA would ignore the fact of budget constraints and opportunity costs.

Research has shown that the WTP for a QALY are often higher than the empirical estimate of the opportunity cost (Vallejo-Torres et al., 2016). Given the existence of fixed budgets in healthcare resource allocation, using the WTP to value health gained and comparing that to costs may lead to decisions that reduce rather than improve health overall. It could be argued that if the health care system is privately funded and there is not an explicit budget constraint, the WTP value could represent the opportunity cost of private consumption (Drummond et al., 2015). Given a fixed budget, this WTP value (consumption value of health) does not inform healthcare resource allocation decisions although it may guide decisions such as the level of the overall NHS budget (Claxton et al., 2015). The fact that the WTP value is higher than the empirical estimate of opportunity cost could suggest an increase in public budgets for healthcare.

To sum up, although in principles CBA is a potential approach to implement a societal perspective for economic evaluation in health care, the fact that its application tends to ignore opportunity costs in constrained budgets makes it less favourable compared to the other approaches. Given the government funded health care system and existence of fixed budgets, the other approaches that explicitly look at opportunity costs from forgone opportunities are more appropriate to support resource allocation decisions.

### 9.6 Further research

Further research is required to refine and extend the proposed approaches and findings from this thesis. The two studies regarding the implementation of the extended cost-per-QALY and the CCA-MCDA can be taken much further, especially with the CCA-MCDA. Given the limitations of this thesis, further studies can focus on addressing them. More case studies can be carried out in other disease areas and interventions.

From the investigation of the extended cost-per-QALY approach, more evidence is required on the cost-effectiveness thresholds across sectors similar to that undertaken in the healthcare
sector by Claxton et al. (2014). Research can look at the relationship between resources and outcomes in different sectors. This would provide insights regarding the impacts of cross-sectoral effects. Another area for further research is to look at the measure of health benefit across sectors and develop a broader measure that can be used across sectors. This research has already been started at ScHARR, University of Sheffield (Brazier et al., 2016). A broader measure of health that is used across sectors would complement the implementation of the extended cost-per-QALY.

From the investigation of the CCA-MCDA, further research should focus on understanding local variations in HTA decisions. Research should look at the implementation of a full MCDA approach to see how local decision makers and stakeholders interpret national recommendations and apply them in their local context. This can be done with actual decision makers and stakeholders using a decision problem that they currently need to solve. Further refinement and improvement can be developed for the weighting methods and the conduct of facilitated decision-making workshops. For example, an online platform could be developed to increase the practicality of MCDA. With an online platform, facilitated decision-making workshops could be conducted without the participants having to attend in person. Further research is also needed to look at the psychology and behaviours of decision makers and stakeholders when they are asked to engage in an MCDA approach. It is important to know the factors that influence the views and values of decision makers and stakeholders.

Another direction for future research is to investigate the use of CCA-MCDA to address equity issues in economic evaluation taking a societal perspective. This is not examined in this thesis.

9.7 Conclusion

Despite strong academic advocates for a broader societal perspective in economic evaluation, a societal-perspective in practice is not easy to implement. One of the major challenges is how to aggregate and incorporate wider costs and consequences. This thesis has proposed two approaches: the extended cost-per-QALY and CCA-MCDA. These approaches have been described and their operationalisation has been investigated in a case study of dementia interventions. Both approaches have the potential to be used in practice for implementing a broader societal perspective in economic evaluation. They can be complementary to each other. The extended cost-per-QALY is more relevant to inform decisions at the national level. The
CCA-MCDA is useful for engaging local decision makers and stakeholder, since it offers a method to allow local variations in resource-allocation decision making.

This thesis has extended the knowledge about the methods to implement a broader societal perspective in economic evaluation. The research focused on developing new approaches but has a number of limitations. The two approaches and their operational steps proposed in this thesis can be improved, refined, and extended to other conditions in future research.

REFERENCES


DH 2013. The health and care system explained (guidance). DH.


NICE 2010. Quality and Outcomes Framework Programme - NICE cost impact statement Indicator area: Dementia NICE.


APPENDIX 1 – SEARCH STRATEGY

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<td>EconLit (Ovid) since 1886</td>
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<td>PsycINFO (Ovid) since 1806</td>
<td></td>
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<tr>
<td>CINAHL (via EBSCO) since 1981</td>
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<td>Cochrane Library (Cochrane Reviews, NHS EED, DARE, Trial, and HTA)</td>
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The following search strategy was first run in Medline (Ovid) and then adapted for running in other databases:

1. Economic evaluation*. mp.
2. Cost benefit*. mp.
5. Cost utility. mp.
7. Cost per QALY*. mp.
8. Decision analys*.mp.
9. (1) OR (2) OR (3) OR (4) OR (5) OR (6) OR (7) OR (8)
10. Alzheimer*. ti.
12. (10) OR (11)
13. (9) AND (12)
14. Limit 13 to English language.
### Checked previous systematic reviews

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<td>Loveman et al.</td>
<td>2006</td>
<td>MEDLINE, EMBASE, Cochrane Library, DARE, NHS EED, ISI Web of Science Proceedings, National Research Register, Science Citation Index, BIOSIS, EconLit, Clinicaltrials.gov, Current Controlled Trials.</td>
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<td>Green</td>
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<td>2008</td>
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<td>Cohen and Neumann</td>
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## APPENDIX 2 – MODEL INPUT DATA

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<td>Other healthcare, community</td>
<td>Mild</td>
<td>per person/year</td>
<td>2751.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
<td></td>
</tr>
<tr>
<td>Other healthcare, institutionalisation</td>
<td>Mild</td>
<td>per person/year</td>
<td>4504.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
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<tr>
<td>Social care, community</td>
<td>Mild</td>
<td>per person/year</td>
<td>3121.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
<td></td>
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<tr>
<td>Social care, institutionalisation</td>
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<td>per person/year</td>
<td>24737.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
<td></td>
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<td>Informal care, community</td>
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<td>per person/year</td>
<td>19714.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
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<td>Informal care, residential care</td>
<td>Mild</td>
<td>per person/year</td>
<td>2901.0</td>
<td>£</td>
<td>2012</td>
<td>Prince, 2014</td>
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</tr>
<tr>
<td>% community social care funded privately</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.4</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>% residential social care funded privately</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.65</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Medication effectiveness</td>
<td>Effect</td>
<td>95% CI</td>
<td>Bond et al., 2012</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Donepezil vs placebo</td>
<td>On NPI</td>
<td>-2.683</td>
<td>-5.673</td>
<td>0.207</td>
<td></td>
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<tr>
<td>Donepezil vs placebo</td>
<td>On MMSE</td>
<td>-1.6</td>
<td>-4.762</td>
<td>1.54</td>
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<tr>
<td>Donepezil vs placebo</td>
<td>On ADCS-ADL</td>
<td>1.24</td>
<td>0.81</td>
<td>1.66</td>
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<td>Memantine vs placebo</td>
<td>On NPI</td>
<td>0.7</td>
<td>0.02</td>
<td>1.38</td>
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<td>Memantine vs placebo</td>
<td>On MMSE</td>
<td>2.02</td>
<td>1.09</td>
<td>3.28</td>
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</table>

<table>
<thead>
<tr>
<th>MCI incidence</th>
<th>Age group</th>
<th>Male incidence per 1,000 person-years</th>
<th>Ward et al., 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>65 to 69</td>
<td>12.30</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>70 to 74</td>
<td>17.75</td>
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</tr>
<tr>
<td>Severe</td>
<td>75 to 79</td>
<td>31.67</td>
<td></td>
</tr>
<tr>
<td>80 to 84</td>
<td>31.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>85+</td>
<td>31.67</td>
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</table>

<table>
<thead>
<tr>
<th>Dementia incidence</th>
<th>Age group</th>
<th>Female incidence per 1,000 person-years</th>
<th>Matthews and Brayne, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>65 to 69</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>70 to 74</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>75 to 79</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>80 to 84</td>
<td>31.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>85+</td>
<td>31.2</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Progressing from MCI to dementia</th>
<th>Annual rate</th>
<th>0.049</th>
<th>Mitchell and Shiri-Feshki, 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reverting from MCI to normal cognition</td>
<td>Annual rate</td>
<td>0.16</td>
<td>Koepfeli and Monsell, 2012</td>
</tr>
<tr>
<td>Relative risk of death for dementia</td>
<td>Mean 95% CI</td>
<td>1.82 1.77 2.68</td>
<td>Helmer et al., 2001</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-------------</td>
<td>-------</td>
<td>------------------------</td>
</tr>
</tbody>
</table>
APPENDIX 3 – DOCUMENTS RELATING TO ETHICS

APPROVAL STUDY 5 (CCA-MCDA)
Information Sheet

1. Research Project Title:

Broadening the perspective in economic evaluation in healthcare – A case study in dementia in the UK

2. Invitation paragraph

You are being invited to take part in a research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

3. What is the project’s purpose?

Economic evaluation of healthcare interventions often ignores external wider costs and consequences such as informal care, private payment for care, etc. This study aims to explore different methodological approaches that can be used to undertake economic evaluation in healthcare accounting for such wider costs and consequences. We have chosen a case study in dementia to demonstrate the methods.

We are looking to explore the various decision criteria for costs, benefits, and equity in evaluating alternative policy options in dementia. By organising a workshop with local decision makers and stakeholders, we would like to understand how they think about the criteria and how their preferences (value judgment) can be expressed in a transparent manner to make the final decision.

The whole project will contribute to the completion of a doctoral degree at School of Health and Related Research (ScHARR), University of Sheffield.

4. Why have I been chosen?

You are being invited to take part in our workshop because of your expertise in dementia care or you are a decision maker in health or social care.

5. Do I have to take part?

It is entirely up to you to decide whether or not to take part. If you decide to participate, you will be asked to sign a consent form. You can still withdraw at any time.

Date: 21st Jun 2015
Thatson Tong – Broadening the perspective in economic evaluation – a case study in dementia in the UK
6. **What will happen to me if I take part? And what do I have to do?**

If you decide to take part, please reply to my email at: snttong1@sheffield.ac.uk (full contact details are at the end of the sheet).

Before the workshop, you will be given 1 – 2 months notice about the date, time and venue. We will try to arrange the time and date based on your availability. The workshop will be held in Sheffield.

The workshop is expected to last about 3 hours. Refreshment and lunch will be provided to participants. You can request a reimbursement from us for your travel expense to the meeting venue by public transport.

<table>
<thead>
<tr>
<th>Activities</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Welcome&lt;br&gt;Consent forms collected&lt;br&gt;Introduction/ opening</td>
<td>20 minutes</td>
</tr>
<tr>
<td>2. Presenting the decision problem in dementia care&lt;br&gt;Presenting the evaluation framework:&lt;br&gt; Costs&lt;br&gt; Benefits&lt;br&gt; Equity&lt;br&gt; Discussing the framework</td>
<td>40 minutes</td>
</tr>
<tr>
<td>3. Discussing our judgments for different costs&lt;br&gt;Weighting different costs (individually)&lt;br&gt;Group consensus for the weights of different costs</td>
<td>40 minutes</td>
</tr>
<tr>
<td>4. Break</td>
<td>10 minutes</td>
</tr>
<tr>
<td>5. Discussing our judgments for different benefits&lt;br&gt;Weighting different benefits (individually).&lt;br&gt;Group consensus for the weights of different benefits.</td>
<td>40 minutes</td>
</tr>
<tr>
<td>6. Discussion&lt;br&gt;Summary, conclusion</td>
<td>30 minutes</td>
</tr>
</tbody>
</table>

*Date: 21st Jun 2015*

Thaison Tong – *Broadening the perspective in economic evaluation – a case study in dementia in the UK*
7. What are the possible disadvantages and risks of taking part?

You will have to spend time to travel to the meeting place and take part in the workshop.

8. What are the possible benefits of taking part?

Whilst there are no immediate benefits for you to participate in the project, it is hoped that this work will help policy makers from the Department of Health make better decisions regarding resources allocation for interventions in dementia.

9. What if something goes wrong?

If you would like to raise a complaint or your concern regarding this project or members of the research team, please contact either of my supervisors and their contact details can be found at the end of the sheet.

10. Will my taking part in this project be kept confidential?

All the information collected during the course of the research will be kept strictly confidential. The collected information and meeting transcriptions will be anonymised and stored securely within the project premises (locked room and drawers) and they will only accessible to the student investigator and his supervisors. We will make sure your personal data will not be used and you will not be identified in any reports or publications. We will use a code for your name and professional in each workshop. All recording files will be destroyed permanently immediately after transcription and your personal information, meeting records will be destroyed permanently at the end of the study.

11. What will happen to the results of the research project?

The results of this research project will be reported to the Department of Health and may also be presented at some relevant conferences, seminars, and scientific journal papers.

12. Who is organising and funding the research?

This project leading to a doctoral degree is sponsored by the Department of Health funded Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU).

13. Who has ethically reviewed the project?

This project has been ethically approved via SchARR ethics review procedure. The University’s Research Ethics Committee monitors the application and delivery of the University’s Ethics Review Procedure across the University.

Date: 21st Jun 2015
Thaison Tong – Broadening the perspective in economic evaluation – a case study in dementia in the UK
14. Will I be recorded, and how will the recorded media be used?

We will use audio recording for the workshops which will be transcribed. The recordings will be kept securely as encrypted and password protected files and they will be deleted permanently immediately after the transcription.

15. Contact Details of the research team:

- The PhD student:
  
  Mr Thaison Tong
  
  Office: Room 1.02, the Innovation Centre, Sheffield. S1 4DP
  
  Telephone: 0114 222 6381
  
  Mobile: 07868888858.
  
  Email: snttong1@sheffield.ac.uk

- Project supervisors:

  Professor John E. Brazier
  Lead Supervisor
  School of Health and Related Research
  The University of Sheffield, S1 4DA
  Telephone: 0114 222 0726
  Email: j.e.brazier@sheffield.ac.uk

  Dr Praveen Thokala
  Second Supervisor
  School of Health and Related Research
  The University of Sheffield, S1 4DA
  Telephone: 0114 222 0784
  Email: p.thokala@sheffield.ac.uk

THANK YOU VERY MUCH FOR READING THIS INFORMATION LETTER
Dear Sir/Madam,

Re: Broadening the perspective in economic evaluation in healthcare – a case study in dementia in the UK

My name is Thaison Tong, a PhD student at School of Health and Related Research (ScHARR), the University of Sheffield. I am conducting a research study in economic evaluation in healthcare for the completion of a doctoral degree under the supervision of Professor John Brazier. This study is sponsored by the Department of Health funded Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU).

This study aims to explore different methodological approaches that can be used to undertake economic evaluation in healthcare accounting for wider costs and consequences. We have chosen a case study in dementia to demonstrate the methods. We are looking to explore the various decision criteria for costs, benefits, and equity in evaluating alternative policy options in dementia. By organising a workshop with local decision makers and stakeholders, we would like to understand how they think about the criteria and how their preferences (value judgment) can be expressed in a transparent manner to make the final decision.

We would like to invite you to participate in the workshop to help us understand those issues. If you decide to participate, please reply to my email at: sntongl@sheffield.ac.uk. Before the workshop, you will be given 1 – 2 months notice about the date, time and venue. We will try to arrange the time and date based on your availability. The workshop will be held in Sheffield.

A detailed information sheet is enclosed for your consideration.

Yours faithfully,

Thaison Tong
Participant Consent Form

Title of Research Project: Broadening the perspective in economic evaluation in healthcare - A case study in dementia in the UK

Name of researcher: Mr Thai-Son Tong

Participant Identification Number for this project: Please initial box

1. I confirm that I have read and I understand the information letter dated 21st Jun 2015 explaining the above research project. I have had the opportunity to ask questions about the project.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative consequences. In addition, should I not wish to answer any particular question or questions, I am free to decline.

3. I understand that my responses will be kept strictly confidential. I give permission for members of the research team to have access to my anonymised responses. I understand that my name will not be linked with the research materials, and I will not be identified or identifiable in the report or reports that result from the research.

4. I agree for the data collected from me to be used in future related research.

5. I agree to be audio recorded during each workshop I participate.

6. I agree to take part in the above research project.

Would you like us to contact you about the study results and further research?

YES  ☐  NO  ☐

______________________________  ______________________  ______________________
Name of Participant                  Date                  Signature

______________________________  ______________________  ______________________
Name of person taking consent        Date                  Signature

Once this has been signed by all parties the participant will receive a copy of the signed and dated participant consent form by email.
Our ref: 0710KW
27 February 2014

Thaison Tong
ScHARR

Dear Thaison

Broadening the perspective in economic evaluation in healthcare – a case study in dementia in the UK.

Thank you for submitting the above research project for approval by the ScHARR Research Ethics Committee. On behalf of the University Chair of Ethics who reviewed your project, I am pleased to inform you that on 27 February 2014 the project was approved on ethics grounds, on the basis that you will adhere to the documents that you submitted for ethics review.

The research must be conducted within the requirements of the hosting/employing organisation or the organisation where the research is being undertaken. You are also required to ensure that you meet any research ethics and governance requirements in the country in which you are researching. It is your responsibility to find out what these are.

If during the course of the project you need to deviate significantly from the documents you submitted for review, please inform me since written approval will be required. Please also inform me should you decide to terminate the project prematurely.

Yours sincerely

Kirsty Woodhead
Ethics Committee Administrator
Our ref: 0710/KW

7th May 2014

Thaison Tong
SchARR

Dear Thaison

Broadening the perspective in economic evaluation in healthcare – a case study in dementia in the UK

Thank you for submitting the above amended research project for approval by the SchARR Research Ethics Committee. On behalf of the University, I am pleased to inform you that the project with changes was approved.

If during the course of the project you need to deviate significantly from the documents you submitted for review, please inform me since written approval will be required.

Yours sincerely

[Signature]

Kirsty Woodhead
Ethics Committee Administrator
4th September 2014

Mr Thaison N Tong
SchARR
30 Regent Street
Sheffield
S2 2TN

Dear Mr Tong

RDU ID: ZP99
Full Project Title: Broadening the perspective in economic evaluation in healthcare - a case study in dementia in the UK
REC No: n/a

I can confirm on behalf of Sheffield Health and Social Care NHS Foundation Trust that you now have NHS Permission to start research within that Trust.

We also advise you of the following conditions and guidance:

1. We are required to report on and request that you notify us of the following (as soon as they are available):
   - The actual start date of the study and an estimated end date
   - The date of the first participant’s first visit
   - The date of the last participant’s first visit
   - The date of the last participant’s last visit
   - The actual end date of the study
2. The study is to be conducted in accordance with the Research Governance Framework.
3. A favourable opinion must have been given by the REC
4. All amendments (including changes to the local research team) need to be submitted in accordance with guidance in IRAS. Please also notify us of any changes to the status of your project.
5. Please note that the NHS organisation is required to monitor research to ensure compliance with the Research Governance Framework and other legal and regulatory requirements. This is achieved by selected audit of research, usually chosen randomly.
6. We recommend the enclosed documents for maintenance of your project site file to ensure all documentation is readily accessible for our audit.
7. Permission has been granted based on the following documentation:
   1. Thaison_NHS R n D form signed dated.pdf 154507/629047/11/64
   2. Thaison_SSI form signed dated.pdf 154507/628048/7/220/244495/302715
   4. ThaisonParticipant information sheet.pdf
   5. ThaisonParticipant invitation letter.pdf
   6. Thaison_Consent Form.pdf
8. Thaison_evidence ethics approval.pdf
9. Thaison_evidence of scientific review.pdf
10. Thaison_evidence of funding.pdf
11. Evidence of indemnity_UniVrsity insurance cef.pdf
12. Evidence of indemnity_UoS_Insurance_arrangements_v2.pdf
Brazier CV 3 page.docx
Research CV BLACKBURN 2014.doc
Research Passport Algorithm v3.pdf
Thaison_Shef Uni Insurance Certificate.pdf

Yours sincerely

Nick Bell
Director

Enc  Site File Guidance
     Amendment Log

ecc:  Professor John Brazier
Thaison Tong  
c/o Professor John Brazier  
PhD Student  
ScHARR  

31 March 2014  

Research Ethics Administrator  
Miss Kirsty Woodhead  
School of Health and Related Research (ScHARR)  
Regent Court  
30 Regent Street  
Sheffield  
S1 4DA  
Telephone: +44 (0) 114 222 5453  
Fax: +44 (0) 114 272 4096  
Email: k.woodhead@sheffield.ac.uk  

Project title: Broadening the perspective in economic evaluation in healthcare – a case study in dementia in the UK.  
6 digit URMS number: 139738

Dear Thaison

LETTER TO CONFIRM THAT THE UNIVERSITY OF SHEFFIELD IS THE PROJECT'S RESEARCH GOVERNANCE SPONSOR

The University has reviewed the following documents:

1. A University approved URMS costing record;
2. Confirmation of independent scientific approval;
3. Confirmation of independent ethics approval.

All the above documents are in place. Therefore, the University now confirms that it is the project’s research governance sponsor and, as research governance sponsor, authorises the project to commence any non-NHS research activities. Please note that NHS R&D approval will be required before the commencement of any activities which do involve the NHS.

You are expected to deliver the research project in accordance with the University’s policies and procedures, which includes the University’s Good Research & Innovation Practices Policy: www.shef.ac.uk/ris/other/gov-ethics/grippolicy. Ethics Policy: www.sheffield.ac.uk/ris/other/gov-ethics/ethicspolicy and Data Protection Policies: www.shef.ac.uk/cjcs/records.

Your Supervisor, with your support and input, is responsible for monitoring the project on an ongoing basis. Your Head of Department is responsible for independently monitoring the project as appropriate. The project may be audited during or after its lifetime by the University. The monitoring responsibilities are listed in Annex1.

Yours sincerely

Miss Kirsty Woodhead

cc. Supervisor: Professor John Brazier  
ScHARR Research Administrator: Mari Bullock
Annex 1

To access the University’s research governance website go to:

http://www.sheffield.ac.uk/ris/other/gov-ethics/governance

Monitoring responsibilities of the Principal Investigator (‘PI’):

The primary responsibility for project monitoring lies with the PI. You agree to:

1. Establish a site file before the start of the project and ensure it remains up to date over the project’s entire lifetime:
   http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/rg-forms

2. Provide progress reports/written updates to the Head of Department at reasonable points over the project’s lifetime, for example at:
   a. three months after the project has started; and
   b. on an annual basis (only if the project lasts for over 18 months); and
   c. at the end of the project.
   See: http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/rg-forms

3. Report adverse events, should they occur, to the Head of Department:
   http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/rg-forms

4. Provide progress reports to the research funder (if externally-funded).

5. Establish appropriate arrangements for recording, reporting and reviewing significant developments as the research proceeds – i.e. developments that have a significant impact in relation to one or more of the following:
   • the safety or physical or mental integrity of the participants in the project;
   • the project’s scientific direction;
   • the conduct or management of the project.
   The Head of Department should be alerted to significant developments in advance wherever possible.

Monitoring responsibilities of the Head of Department

You agree to:

1. Review the standard monitoring progress reports, submitted by the PI, and follow up any issues or concerns that the reports raise with the PI.

2. Verify that adverse events, should they occur, have been reported properly and that actions have been taken to address the impact of the adverse event(s) and/or to limit the risk of similar adverse event(s) reoccurring.

3. Verify that a project is complying with any ethics conditions (e.g. that the information sheet and consent form approved by ethics reviewers is being used; e.g. that informed consent has been obtained from participants).

4. Introduce a form of correspondence (e.g. regular email, annual meeting) with a project’s PI, that is proportionate to the project’s potential level of risk, in order to verify that a project is complying with the approved protocol and/or with any research funder conditions. Whatever correspondence is chosen the Head of Department should, as a minimum, ensure that s/he is informed sufficiently in advance about significant developments wherever possible.
WORKSHOP AGENDA

Broadening the perspective in economic evaluation in health care – a case study in dementia

Date: 24th September 2015
Time: 9:15 AM – 11:30 AM
Venue: Room B57C, the Portobello Centre, S1 4ET

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:15</td>
<td>Arriving</td>
<td></td>
</tr>
<tr>
<td>9:20</td>
<td>Introduction</td>
<td>• Welcome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consent forms collected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Opening speech: Prof. John Brazier</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Introducing members</td>
</tr>
<tr>
<td>9:30</td>
<td>The evaluation framework and the case study (Presentation)</td>
<td>• Introduction: economic evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Workshop aim and objectives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The decision problem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The evaluation criteria</td>
</tr>
<tr>
<td>9:50</td>
<td>Workshop 1: valuing different costs</td>
<td>• Presentation (Thaison Tong)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Group discussion for ranking</td>
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<td></td>
<td>• Individual preference elicitation</td>
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<tr>
<td>10:30</td>
<td>Coffee break</td>
<td></td>
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<tr>
<td>10:40</td>
<td>Workshop 2: valuing different benefits</td>
<td>• Presentation (Thaison Tong)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Group discussion for ranking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Individual preference elicitation</td>
</tr>
<tr>
<td>11:10</td>
<td>Discussion</td>
<td>• Other important criteria</td>
</tr>
<tr>
<td>11:30</td>
<td>Conclusion and finish</td>
<td>• Summarising and concluding</td>
</tr>
</tbody>
</table>

- Refreshment and lunch are provided
BROADENING THE PERSPECTIVE IN ECONOMIC EVALUATION IN HEALTHCARE
A CASE STUDY IN DEMENTIA IN THE UK

Sheffield, 24th Sep 2015

OPENING

• Opening speech: Professor John Brazier
• Member Introduction: Name, profession, background
1. Background

2. Workshop 1: Valuing costs

3. Coffee Break: 10 minutes

4. Workshop 2: Valuing benefits

5. Discussion

6. Conclusion and finish

- NHS: CCGs, Hospitals, GPs, Memory services
- City council: Social Services, Public Health
- Patient and family: Informal care, private payment
NICE’s reference case for technology appraisal (NICE, 2013):

- **Costs**: NHS and Personal Social Service (PSS)
- **Benefits**: all direct health effects
- **Health effects expressed in Quality Adjusted Life Years (QALYs)**.
  The **EQ-5D** is the preferred measure of health-related quality of life in adults.
- **An additional QALY has the same weight** regardless of the other characteristics of the individuals receiving the health benefit

A broader perspective:

- Explicitly weighing different costs: NHS, social care, private payment, informal care.
- Explicitly weighing patient benefits and carer benefits.
- Discuss other important criteria

Aim of the workshop:

*to explore a broader framework using direct preferences from decision makers and stakeholders.*

Feel free to express your opinions
THE CASE STUDY

- Options for dementia care:
- Setting: local population in Sheffield
- How should we evaluate different options in dementia care?

THE EVALUATION CRITERIA

Comparing the new intervention with the baseline (standard care)

COSTS
- NHS
- Local authority/ City council
- Private payment for care
- Unpaid/ Informal care

BENEFITS
- Patients
- Caregivers

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What is a Quality Adjusted Life Year (QALY)?

A year is adjusted for its quality: 0 (death) – 1 (perfect health)

- Health is “a complete state of physical, mental and social well-being, and not merely the absence of disease or infirmity”. (WHO definition of health)

- E.g. Health Related Quality Of Life as described by the EQ-5D:
  - Mobility (e.g. I have no problem in walking about)
  - Self Care (e.g. I have no problem with self-care)
  - Usual Activities (e.g. work, study, housework, family or leisure activities) (e.g. I have no problem with performing my usual activities)
  - Pain/Discomfort (e.g. I have no pain or discomfort)
  - Anxiety/Depression (e.g. I am not anxious or depressed)
### VALUING COSTS

#### COSTS

- **NHS**
- Local authority/City council
- Private payment for care
- Unpaid/Informal care

#### COSTS

<table>
<thead>
<tr>
<th>COSTS</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS</td>
<td>Care funded by the NHS.</td>
<td>Treatments, GPs, hospitals, memory services</td>
</tr>
<tr>
<td>Local authority/City council</td>
<td>Care funded by the local authority/city council</td>
<td>Social care, public health</td>
</tr>
<tr>
<td>Private payment for care</td>
<td>Care funded privately</td>
<td>Payment for a care home placement</td>
</tr>
<tr>
<td>Unpaid/informal care</td>
<td>Caring time provided by relatives, friends or volunteers which is unpaid.</td>
<td>A wife is caring for her husband with dementia</td>
</tr>
</tbody>
</table>
Note: here we only consider the time costs of informal/unpaid care. For example, the caregiver could have spent that time for other activities such as work, leisure, etc.

The impacts on carer wellbeing are considered separately.

- We need to aggregate these costs by attaching a weight to each (exchange rates)
- Given the NHS cost a weight of 1
- We compare the importance of other costs to the NHS cost:
  - A zero weight: the cost is not important at all compared to the NHS cost; it is not counted
  - A 1 weight: the cost is as important as the NHS cost
  - A weight > 1: the cost is more important than the NHS cost (E.g. weight = 1.2, 2, ...)
  - A weight < 1: the cost is less important than the NHS cost (E.g. weight = 0.5, 0.2, ...)
<table>
<thead>
<tr>
<th>COSTS</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 NHS</td>
<td>1</td>
</tr>
<tr>
<td>2 Local authority/city council</td>
<td>$W_2 =$</td>
</tr>
<tr>
<td>3 Private payment for care</td>
<td>$W_3 =$</td>
</tr>
<tr>
<td>4 Unpaid/informal care</td>
<td>$W_4 =$</td>
</tr>
</tbody>
</table>

- **Impact of increasing weight of a cost**: if you give more weight to a type of cost, interventions that incur more of that cost will look less cost-effective.
- **Example**: more weight to costs to local authority; interventions that cost more to local authorities will become less cost-effective.

<table>
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<tr>
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<tr>
<td>1 NHS</td>
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<td>$W_2 =$</td>
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<tr>
<td>3 Private payment for care</td>
<td>$W_3 =$</td>
</tr>
<tr>
<td>4 Unpaid/informal care</td>
<td>$W_4 =$</td>
</tr>
</tbody>
</table>

- **What is your opinion?**
  - **Step 1**: Discuss ranking of weights in the group
  - **Step 2**: Individual preferences for weights
    (complete a questionnaire)
VALUING BENEFITS

We have discussed the concept of QALY above.

• Interventions in dementia care might impact both patients and carers. For example:
  ○ Respite care
  ○ Psychosocial interventions
• Who should have more priority?
• Given a patient QALY gained a weight of 1
• We compare the weight of a carer QALY gained to a patient QALY gained:
  o A zero weight: A carer QALY gained is not important at all compared to a patient QALY gained; it is not counted
  o A 1 weight: A carer QALY gained is as important as a patient QALY gained
  o A weight > 1: A carer QALY gained is more important than a patient QALY gained
  o A weight < 1: A carer QALY gained is less important than a patient QALY gained

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A patient QALY gained</td>
<td>1</td>
</tr>
<tr>
<td>2 A carer QALY gained</td>
<td>$W =$</td>
</tr>
</tbody>
</table>

• Impact of changing the weight of a carer QALY gained: if you give more weight to a carer QALY gained, interventions that bring more benefits to caregivers will become more cost-effective (e.g. we pay more attention to caregivers). If you give less weight to a carer QALY gained, interventions that bring more benefits to caregivers will become less cost-effective (e.g. we focus more on patients).
**Weighting**

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A patient QALY gained</td>
<td>1</td>
</tr>
<tr>
<td>2 A carer QALY gained</td>
<td>$W = $</td>
</tr>
</tbody>
</table>

• What is your opinion?
  - Step 1: Discuss ranking of weights as a group
  - Step 2: Individual preferences for weights (complete a questionnaire)

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**DISCUSSION**

**OTHER CONSIDERATIONS?**

Comparing the new intervention with the baseline (standard care)

**COSTS**

- NHS
- Local authority/City council
- Private payment for care
- Unpaid/informal care

**BENEFITS**

- Patients
  - Patient QALYs
- Caregivers
  - Care QALYs
Thank you
Please write your initials here: …

QUESTIONNAIRE 1: WEIGHTING COSTS

1. Please state your ranking for different costs:
   (Ranking 1 for the most important cost, ranking 4 for the least important cost)

<table>
<thead>
<tr>
<th>Category</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS/health care costs (C1)</td>
<td></td>
</tr>
<tr>
<td>Local authority costs (C2)</td>
<td></td>
</tr>
<tr>
<td>Private payment for care (C3)</td>
<td></td>
</tr>
<tr>
<td>Unpaid care (C4)</td>
<td></td>
</tr>
</tbody>
</table>

2. Given the healthcare cost a weight of 1. Please state your opinion for weights of other costs to reflect their relative importance to healthcare costs (fill in the yellow boxes below)
   • A zero weight: the costs are not important at all, they are not counted.
   • A 1 weight: the costs are as important as healthcare costs
   • A weight more than 1: the costs are more important than healthcare costs
   • A weight less than 1: the costs are less important than healthcare costs

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS/health care costs (C1)</td>
<td>£ 1 per patient</td>
<td>$w_1 = 1</td>
</tr>
<tr>
<td>Local authority costs (C2)</td>
<td>£ 1 per patient</td>
<td>$w_2 = ...</td>
</tr>
<tr>
<td>Private payment for care (C3)</td>
<td>£ 1 per patient</td>
<td>$w_3 = ...</td>
</tr>
<tr>
<td>Unpaid care (C4)</td>
<td>£ 1 per patient</td>
<td>$w_4 = ...</td>
</tr>
</tbody>
</table>

(If you need to recall the example of each cost, please turn to the next page).

Thank you
PIC: ...

Please write your initials here: ...

QUESTIONNAIRE 2: PATIENT QALY AND CARER QALY

1. Please state your ranking for different benefits:
   (Ranking 1 for the most important benefit, ranking 2 for the least important benefit)

<table>
<thead>
<tr>
<th>Category</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient QALY gained (Q₁)</td>
<td></td>
</tr>
<tr>
<td>Carer QALY gained (Q₂)</td>
<td></td>
</tr>
</tbody>
</table>

2. Given the patient QALY gained a weight of 1. Please state your opinion for the weight of the carer QALY gained to reflect its relative importance to the patient QALY gained: (fill in the yellow box)
   - A zero weight: the carer QALY is not important at all, it is not counted.
   - A 1 weight: the carer QALY is as important as the patient QALY
   - A weight more than 1: the carer QALY is more important than the patient QALY
   - A weight less than 1: the carer QALY is less important than the patient QALY

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient QALY gained (Q₁)</td>
<td>1 QALY for a patient</td>
<td>( w_1 = 1 )</td>
</tr>
<tr>
<td>Carer QALY gained (Q₂)</td>
<td>1 QALY for a carer</td>
<td>( w_2 = \ldots )</td>
</tr>
</tbody>
</table>

(If you need to recall the meaning of the QALY measure, please turn to the next page).

Thank you