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Title: COST EFFECTIVENESS OF USING COGNITIVE SCREENING TESTS FOR DETECTING DEMENTIA AND MILD COGNITIVE IMPAIRMENT IN PRIMARY CARE

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Running head: Cost Effectiveness of cognitive screening tests in primary care

Article keywords: decision model; dementia; cost-effectiveness; 6CIT; MMSE; GPCOG; early intervention; primary care

Article key points:

- A patient-level model has been built to estimate the long-term cost-effectiveness of GP-based diagnostic interventions.
- Using any of the three cognitive screening tests (MMSE, 6CIT, GPCOG) in primary care for assessing cognitive impairment could be considered a cost-effective strategy compared with GPs unassisted judgement, given the NICE threshold range between £20,000 and £30,000 per QALY (the GPCOG was considered the most cost-effective use of NHS resources at this range).

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ETHICS STATEMENT: This study is part of a PhD research project conducted at School of Health and Related Research (ScHARR), University of Sheffield. The project was granted

ethical approval by the ScHARR Research Ethics Committee and the University of Sheffield was the project's research governance sponsor.

ABSTRACT

Introduction: We estimated the cost effectiveness of different cognitive screening tests for use by General Practitioners (GPs) to detect cognitive impairment in England.

Methods: A patient-level cost-effectiveness model was developed using a simulated cohort that represents the elderly population in England (65 years and older). Each patient was followed over a life time period. Data from published sources were used to populate the model. The costs include government funded health and social care, private social care, and informal care. Patient health benefit was measured and valued in Quality Adjusted Life Years (QALYs).

Results: Base-case analyses found that adopting any of the three cognitive tests (MMSE, 6CIT, or GPCOG) delivered more QALYs for patients over their life-time and made savings across sectors including health care, social care, and informal care compared with GP unassisted judgement. The benefits were due to early access to medications. Among the three cognitive tests, adopting the GPCOG was considered the most cost-effective option with the highest Incremental Net Benefit (INB) at the threshold of £30,000 per QALY from both the NHS PSS perspective (£195,034 per 1000 patients) and the broader perspective that includes private social care and informal care (£196,251 per 1000 patients). Uncertainty was assessed in both deterministic and probabilistic sensitivity analyses.

Conclusions: Our analyses indicate that the use of any of the three cognitive tests by GPs could be considered a cost-effective strategy compared with GP unassisted judgement. The most cost-effective option in the base-case was the GPCOG.

1. INTRODUCTION

Timely diagnosis has consistently been a top priority in recent policies for dementia care in the United Kingdom (UK) (Department of Health, 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 implies 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 is 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) is low for detecting dementia, especially those in the early stages of dementia or those with pre-dementia MCI.

This study aims to investigate the cost-effectiveness of using the three most commonly used cognitive screening tests for detecting cognitive impairment in primary care in England: MMSE, GPCOG, and 6CIT. Our recent survey[1] found 29% of GPs in the UK used 6CIT; 26% used MMSE; and 21% used GPCOG to screen for patients with dementia. The baseline comparator is GP unassisted judgement.

2. 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 interviews with clinicians, commissioners, and other experts in dementia care.

[1] The survey was conducted in the GP section of an online forum for doctors in the UK (www.doctors.net.uk)

This model only examines dementia in the Alzheimer's disease (AD) form. The simulated population represented the English population 65 years and older. Each patient was tracked over a life time period. Benefits were measured in terms of QALYs gained for patients. The QALY is a measure of health benefit that captures both impacts on morbidity (health-related quality of life [HRQOL]) 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 benefit of GP-based diagnostic interventions comes from improving HRQOL over the patients' life. 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 1. All costs were reported in pounds sterling in 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.

2.1. **Model structure**

The conceptual models are illustrated in figure 1a and 1b. 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. The same cohort is analysed for four scenarios: (1) GP's unassisted judgement; and GPs administer either MMSE (2); 6CIT (3); or GPCOG (4).

---Insert figure 1 and 2 about here ----

Patients are followed up, with their characteristics updated every year until they die. Patients move between four health states as described in figure 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 a raised risk of being institutionalised.

Figure 2 describes the healthcare events (service pathway) in the model. The model annually checks the status of a patient to see whether they have already had a dementia diagnosis; whether they have already been diagnosed with MCI and is 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 sends the patient to the relevant route (see figure 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 patients receive dementia medications. Newly diagnosed MCI patients are followed up by memory services for two years. Confirmed non-cases (not dementia or MCI) just return to the population.

The model updates patient characteristics 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 their total costs and QALYs calculated.

2.2. Input Data

2.2.1. The cohort

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).

2.2.2. 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 being followed up by memory services, they can be assessed by GPs for dementia within any given year. Since a national dementia

screening programme is not implemented in England, the annual probability for a 65+ patient to receive a dementia assessment by GPs should be less than 100%.

We estimated the number of new dementia diagnoses per year and the proportion of undiagnosed dementia cases diagnosed per year using published data (Health & Social Care Information Centre, 2014). Using the average sensitivity of GPs for assessing dementia, we estimated the proportion of undiagnosed individuals with dementia, who had a GP assessment for dementia per year 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. Using their reported proportions, we estimated 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. Knowing the prevalence of dementia and MCI in the simulated cohort, we estimated the relative proportions of MCI and non-cases who were diagnosed by memory services per year. Then, using the average sensitivity of GPs for MCI and the average specificity of GPs for non-case, we estimated the proportions of MCI and non-cases who would have a GP assessment for cognitive impairment per year: 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 the 6CIT compared with the MMSE:

It was assumed that severe dementia was always detected with 100% sensitivity by GPs regardless of the screening tool. This assumption is similar to one used in a published diagnostic model for AD (Biasutti et al., 2012). Thus, the effect of GP-based interventions only comes into play in detecting mild dementia, moderate dementia, MCI and non-cases.

Table 1 shows the sensitivity and specificity of each assessment strategy.

---Insert Table 1 about here ---

Data from three studies were used to derive the relative sensitivity and specificity for each strategy. The first one is a UK pragmatic diagnostic accuracy study of the use of 6CIT in primary care settings (Abdel-Aziz and Larner, 2015). The performance of 6CIT in detecting dementia and MCI was compared to that of the simultaneously administered MMSE. The

relative sensitivity and specificity of the GPCOG was derived from an Australian study (Brodaty et al., 2002) and the relative sensitivity and specificity for the unassisted strategy (no cognitive test) was derived from a UK study (O'Connor et al., 1988).

c. Cost per assessment for different strategies:

The base cost per assessment for each strategy includes one GP consultation, one practice nurse consultation and laboratory tests (NICE, 2010).

The MMSE is associated with a small license fee of £0.96 per test (PAR, 2016), whereas the 6CIT and GPCOG are free. Furthermore, their administration time per assessment is different (Cordell et al., 2013): the MMSE requires 7-10 minutes; GPCOG requires 2-5 minutes; and 6CIT requires 4-6 minutes. This difference in administered time is converted to healthcare costs by multiplying with the cost per minute of a GP in a surgery. Sensitivity analyses explored the results when using the cost per minute of a nurse for administration time.

2.2.3. 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. performed a systematic review of estimates for MCI prevalence and incidence. They found 13 studies reporting incidence of MCI; among them, five studies reporting age-stratified rates (none of the studies were UK studies) (Ward et al., 2012). The annual probability in our base-case analysis was derived from the pooled data of five studies which reported MCI incidence rates in Italy, Germany, Sweden, and France.

The annual probability of having dementia for not-impaired patients was derived from data for dementia incidence rates in England and Wales (Matthews and Brayne, 2005). All new incident dementia was modelled as undiagnosed mild dementia in community.

MCI patients were modelled to have two types of transitions: some of them progressed to dementia; 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 revert to normal cognition, the annual rate was derived from a UK study on 3,020 individuals diagnosed with MCI (Koepsell and Monsell, 2012).

2.2.4. Parameters for dementia progression

Progression was described in terms of annual worsening rates for MMSE, NPI, ADL and IADL measures. The annual declining rate for MMSE score was derived from the Consortium to Establish A Registry for Alzheimer's Disease (CERAD) data, whereas the equations for the worsening in terms of NPI, ADL, and IADL were estimated from data collected in donepezil trials (Getsios et al., 2010).

People with dementia living in community also have an annual probability of institutionalisation based on their MMSE score. The probability was calculated based on a published equation (Nagy et al., 2011) that used data from a UK-based study (Stewart, 1997).

2.2.5. Effectiveness of dementia medications:

NICE currently recommends donepezil, rivastigmine, or galatamine for mild to moderate AD; whereas memantine is recommended for severe AD, or moderate AD who are intolerant of other dementia medications (NICE, 2015). It was assumed that all diagnosed mild to moderate dementia were given donepezil 10 mg once daily whereas diagnosed severe dementia were given memantine 10 mg once daily.

The improvement in clinical scores for donepezil and memantine was based on the meta-analysis results reported in the recent Health Technology Assessment (HTA) report (Bond et al., 2012). Being consistent with previous models, the clinical improvement was assumed to only occur in the first year (symptomatic effect), after that, patients would not gain any further improvement while remaining on the medication; they would progress at the same rate as untreated patients.

2.2.6. Mortality

The age and gender-specific annual mortality rates from the national life tables were applied for people with normal cognition and people with MCI in the simulation. For people with dementia, a relative risk of death was used to adjust their annual mortality rates (Helmer et al., 2001).

2.2.7. Costs

Data for health, social care, and informal care costs were from the largest and most recent cost study for dementia in the UK: the dementia UK report (Prince et al., 2014). This study estimated the annual figures for the UK for 2013 using the best currently available information. According to this report, healthcare 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 cost of medications (donepezil and memantine) for diagnosed dementia are from 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).

2.2.8. Health utilities

The recent UK HTA did not find any study which provides utility values for people with AD in the UK (Bond et al., 2012). They chose the study by Jonsson et al. (2006) which reports EQ-5D valuations of utility across different MMSE scores from people with AD in Sweden, Denmark, Finland, and Norway (Jonsson et al., 2006). Getsios et al. (2010) in their cost effectiveness analysis of donepezil in the UK also used the published regression equation for AD patient EQ-5D scores 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.

The evidence for the utility of the informal caregivers of people with dementia is limited (Bond et al., 2012). Being consistent with the recent HTA model (Bond et al., 2012), caregiver utility was not included in our base-case analyses.

2.3. 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.

Uncertainty in key inputs into the model was examined through sensitivity analysis. A deterministic sensitivity analysis (DSA) was undertaken where we examined the impact of specific ranges in possible values for each input variable one at a time. A more sophisticated probability sensitivity analysis (PSA) was undertaken where all key variables are varied at the same time and the values are sampled from a distribution of values given to each variable.

3. RESULTS

3.1. Base-case Analyses

Table 2 reports the base-case results. Adopting any of the cognitive tests delivered more QALYs and saved costs compared to the baseline scenario (GP unassisted judgement). The benefits were due to early access to AD medications.

--- Insert Table 2 about here ---

Among the three cognitive tests, the 6CIT resulted in the most QALYs gained (3.48 QALYs per 1000 patients). This is because the 6CIT has the highest sensitivity (patients were diagnosed earlier).

Regarding costs, overall, the GPCOG made the highest saving (£187,064 per 1000 patients) compared to the MMSE (£66,566 per 1000 patients) and the 6CIT (£7,485 per 1000 patients). This mainly came from saving in health care resources. The GPCOG has the highest specificity therefore less false positive cases were sent to memory services when it was used. Although the 6CIT made the highest savings for government social care, private social care, and informal care (thanks to earlier diagnosis and access to dementia medications), the total amount was still less than the saving in healthcare resources by the GPCOG.

The Incremental Net Benefit (INB) is the overall incremental value in a monetary unit. It is calculated by subtracting the incremental cost from the multiplication of the incremental QALYs and the cost-effectiveness (CE) threshold. A positive INB means the intervention is cost-effective compared to the baseline option. At the CE threshold of £30,000 per QALY, the INBs of the three interventions (MMSE, 6CIT, and GPCOG) are positive from both the NHS PSS perspective and the broader perspective. The GPCOG option has the highest INB among the three interventions. Thus, at the NICE referenced threshold (£30,000 per QALY), all three interventions were considered cost-effective and the GPCOG was considered the best option.

3.2. One-way Sensitivity Analyses

One-way sensitivity analyses (Table 3) show that the results for INBs are robust in most scenarios. The interventions made savings and delivered more QALYs in all sensitivity scenarios compared to unassisted GPs. The results are most sensitive to assumptions about the effectiveness of dementia medications. When the assumed duration for the symptomatic improvement with medication was increased to three years, the GPCOG was no longer the option with the highest INB; the 6CIT became the best option with the highest INB. However, this is quite unlikely given the current evidence for clinical effectiveness of AD medications (Bond et al., 2012).

--- Insert Table 3 about here ---

3.3. Probability sensitivity analyses (PSA)

Figure 3 shows the cost-effectiveness acceptability curve (CEAC) in our PSA. At the CE threshold of £30,000 per QALY, the probability of the GPCOG being the best option was 75% from the NHS PSS perspective and 71.8% from the broader perspective. The probability of the 6CIT being the best option became higher than the GPCOG's when the threshold was above £50,000 per QALY from the NHS PSS perspective and £47,000 per QALY from the broader perspective.

--- Insert Figure 3 about here ---

4. DISCUSSION AND CONCLUSIONS

The study reported in this paper is the first to evaluate the cost-effectiveness of GPs using different cognitive screening tests compared with their unassisted judgement in England. The patient-level simulation model developed for the evaluation captured the pathway from normal ageing to the development of cognitive impairment and the dementia progression.

Our analyses estimated that using any of the three cognitive screening tests was more cost-effective than the GP unassisted judgement. Among the three cognitive tests, the GPCOG was considered the most cost-effective option for the NHS given the referenced NICE threshold. The results are sensitive to assumptions about the effectiveness of dementia medications. The model results should be treated with caution because of the following limitations in our analyses.

First, the model assumed all dementia followed the pattern of the AD sub-type. However, there are also other dementia sub-types which can have some different features besides 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 negative impact on patient

quality of life but evidence is limited. Our model can be improved in the future by relaxing that assumption when more data are available.

Third, the model assumed that diagnosed dementia was only given AD medications. However, there could be a wide range of other treatment options and support for diagnosed dementia in practice. 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 are not available to accurately estimate all model parameters. The study had to combine the best available evidence from different sources to estimate the model inputs. Nevertheless, we have addressed this uncertainty in our deterministic and probabilistic sensitivity analysis.

The results in this study are specific for the situation in England. The model structure and logic can be generalised to similar healthcare systems, though the input estimates would need to be adjusted to reflect the situation in other countries. The model code (SIMUL8 and Visual Basic Application) can be made available on request to others who are interested in adapting the model to other contexts.

CONFLICTS OF INTEREST

None known.

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Figure 1: the conceptual model: *patient health states and disease progression*

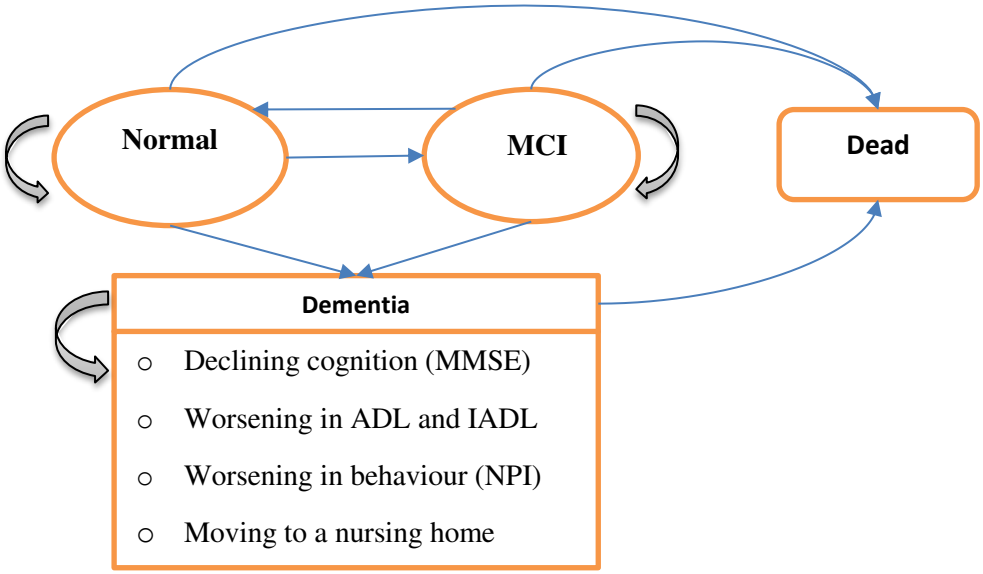


Figure 2: the conceptual model: *healthcare events*

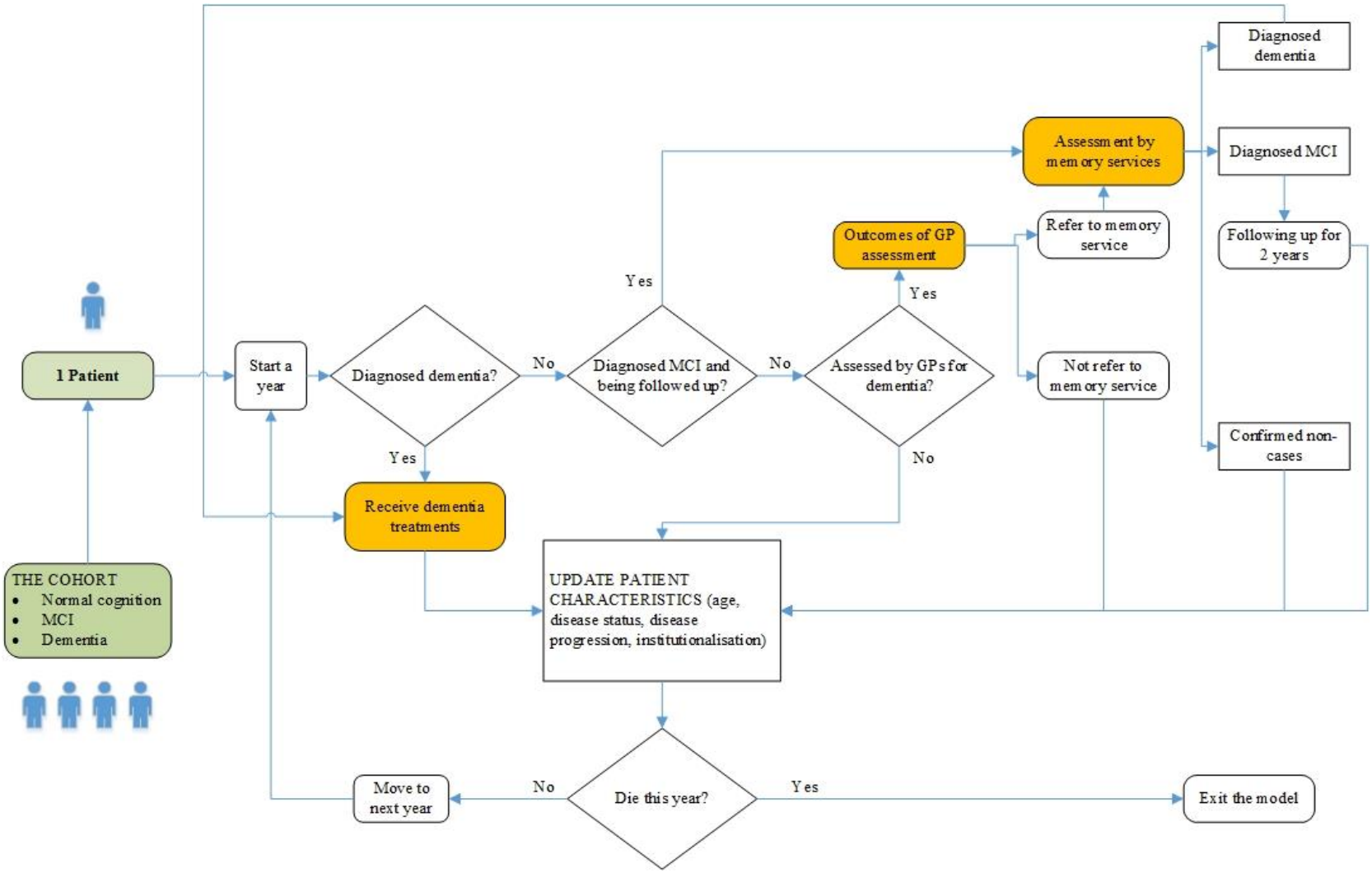
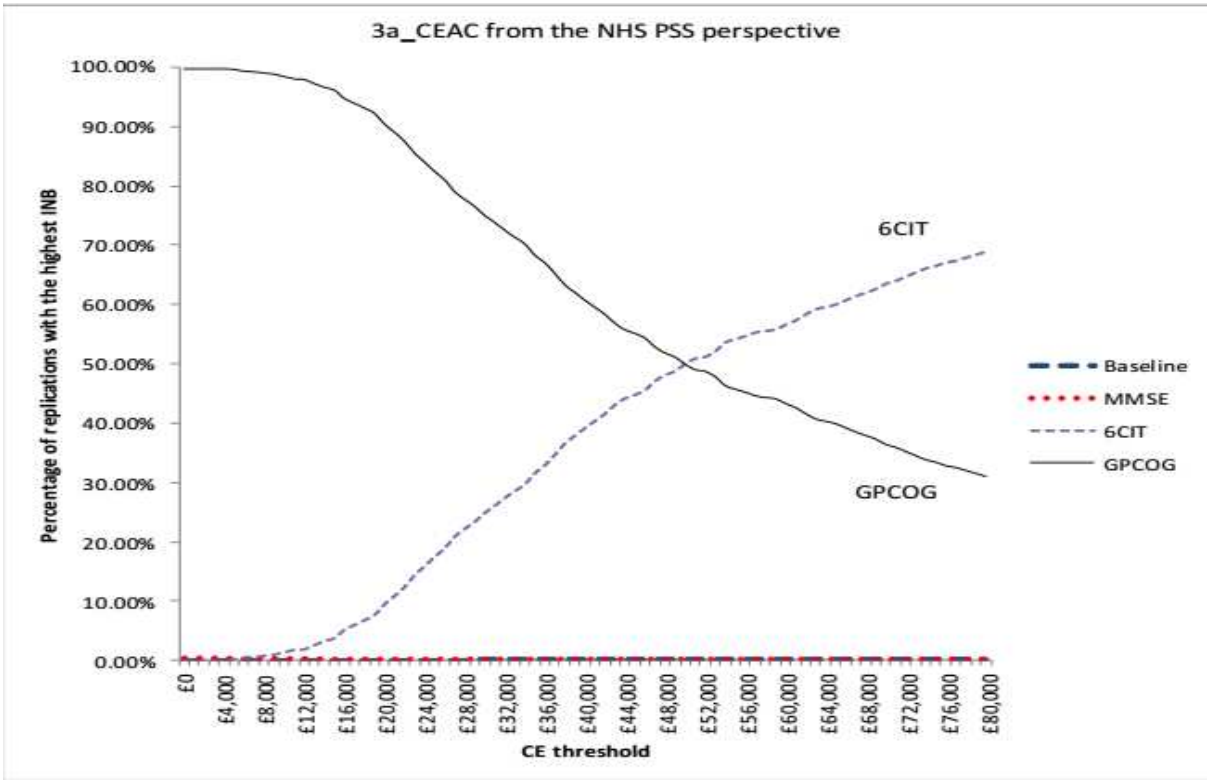


Figure 3: Cost-effectiveness acceptability curves



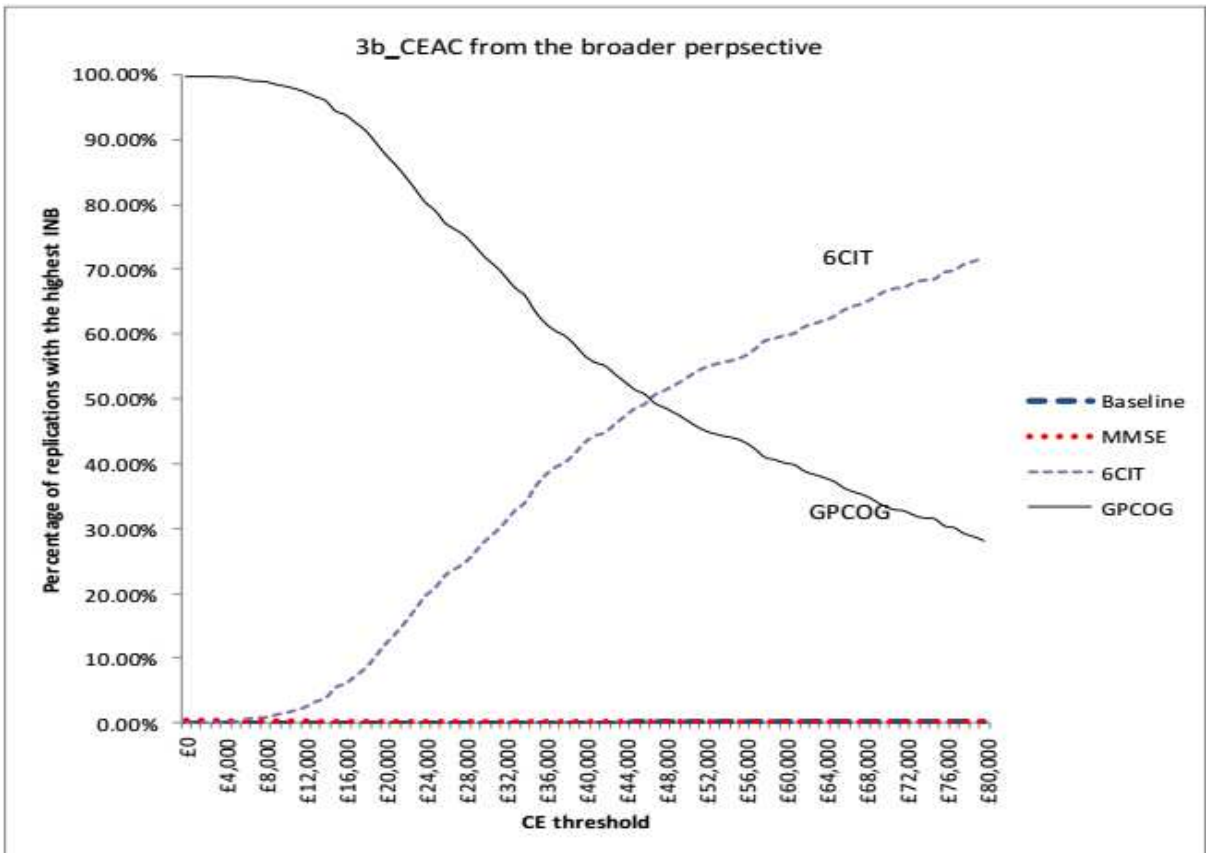


Table 1: Sensitivity and specificity of assessment strategies

	Mean and Range (95% CI)				Data source
	Sensitivity (dementia)	Sensitivity (MCI)	Specificity (no dementia)	Specificity (no MCI)	
GP unassisted judgement	0.58 (0.38 – 0.78)	0.50 (0.35 – 0.65)	0.75 (0.66 – 0.80)	0.66 (0.58 – 0.74)	Computed based on (O'Connor et al., 1988)
MMSE	0.59 (0.39 – 0.80)	0.51 (0.36 – 0.66)	0.85 (0.79 – 0.91)	0.75 (0.66 – 0.84)	(Abdel-Aziz and Larner, 2015)
6CIT	0.88 (0.78 – 0.97)	0.66 (0.54 – 0.77)	0.78 (0.72 – 0.84)	0.70 (0.62 – 0.78)	
GPCOG	0.60 (0.39 – 0.81)	0.52 (0.36 – 0.67)	0.93 (0.82 – 0.99)	0.82 (0.72 – 0.92)	computed based on (Brodaty et al., 2002)

Table 2: Base-case results (per 1000 patients)

	Incremental results (compared to baseline)		
Per 1000 patients	MMSE	6CIT	GPCOG
COSTS			
Diagnostic costs, GPs	£42,394	£23,212	£16,838
Diagnostic costs, memory services	-£107,993	-£40,793	-£203,655
Medications	£1,686	£39,174	£3,938
Other health care	-£1,708	-£18,423	-£2,657
Government social care, community	£0	-£671	-£70
Government social care, institutional	-£134	-£1,806	-£241
Total government health and social care	-£65,755	£693	-£185,846
Private social care costs, community	£0	-£447	-£47
Private social care costs, institutional	-£249	-£3,354	-£447
Informal care costs	-£562	-£4,377	-£723
Total all costs	-£66,566	-£7,485	-£187,064
QALYS			
QALYs (patient)	0.1031	3.4847	0.3063
Incremental Net Benefit at the threshold of £30,000 per QALY			
From the NHS PSS perspective	£68,848	£103,848	£195,034
From the broader perspective	£69,659	£112,027	£196,251

Table 3: One-way sensitivity analysis results (per 1000 patients)

Sensitivity Analysis Scenario		Incremental Net Benefit per 1000 patients at the threshold of £ 30,000 per QALY					
		From NHS PSS Perspective			From the broader perspective		
		MMSE	6CIT	GPCOG	MMSE	6CIT	GPCOG
Base case		£68,848	£103,848	£195,034	£69,659	£112,027	£196,251
Medication symptomatic improvement duration increased to 3 years		£72,738	£262,799	£207,230	£73,942	£285,240	£209,197
Medication effectiveness	Upper 95% CI value	£70,876	£190,404	£201,966	£71,687	£203,739	£203,404
	Lower 95% CI value	£66,869	£22,921	£188,409	£67,680	£28,770	£189,466
Annual medication costs (including monitoring costs)	▲+25%	£68,426	£94,055	£194,050	£69,237	£102,233	£195,267
	▼-25%	£69,269	£113,642	£196,019	£70,080	£121,820	£197,236
Annual probability of being assessed by GP	Upper range value	£86,720	£123,128	£247,034	£87,407	£134,005	£248,752
	Lower range value	£39,140	£106,767	£116,630	£39,541	£114,632	£117,420
No license fee for using MMSE		£70,148	£103,848	£195,034	£70,959	£112,027	£196,251
Nurses administered the test		£98,537	£121,165	£207,251	£99,348	£129,344	£208,468

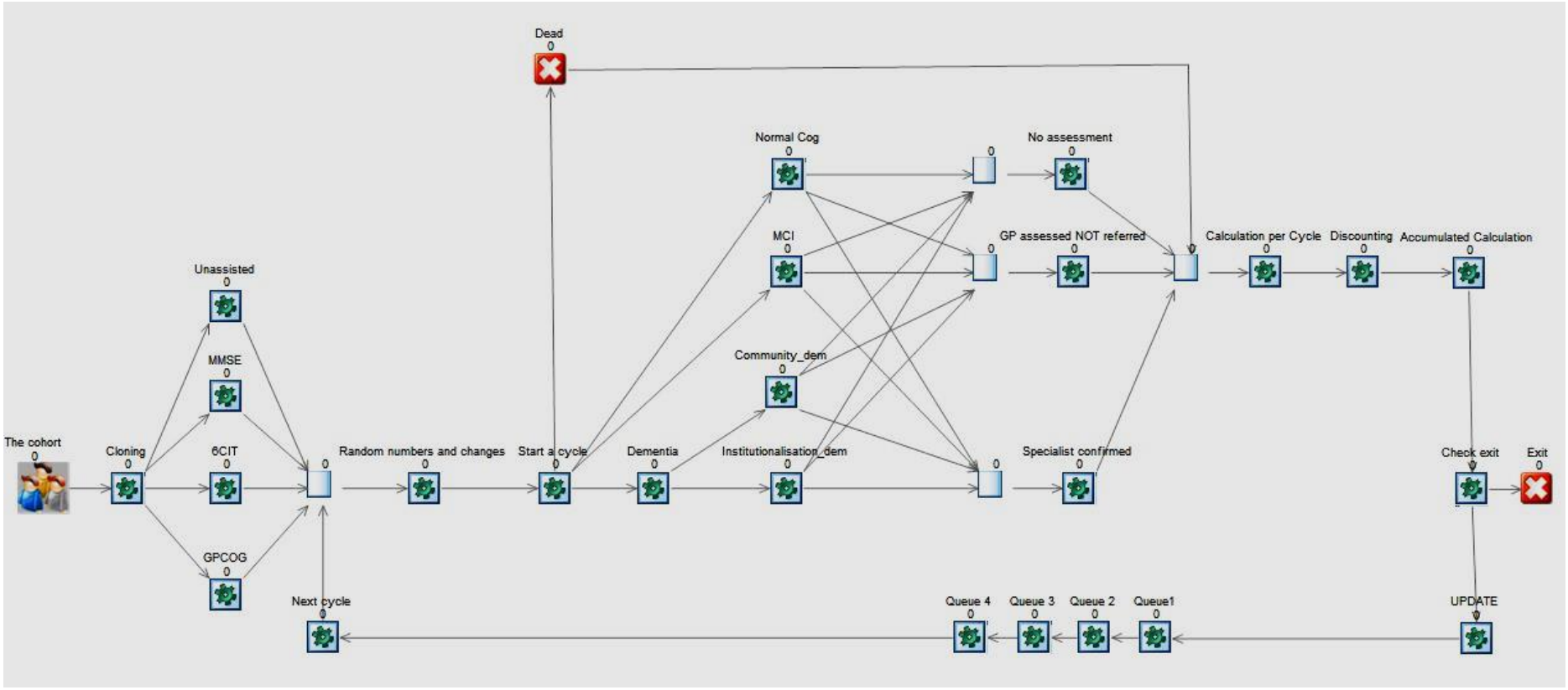
Appendix 1: Input data

Item	Data					
Costs	Severity	Quantity	Value	Value Unit	Price Year	Source
Costs of a GP consultation		12 minutes	36	£	2009	NICE, 2010
Cost of a practice nurse consultation		12 minutes	10	£	2009	
Base cost for a GP cognitive assessment		per assessment	55.0	£	2009	
Cost of a specialist assessment (memory service)		per assessment	650.0	£	2012	Prince, 2014
MMSE license fee		per assessment	0.96	£	2016	PAR,2016
Donepezil 10 mg tablet once a day	mild-mod	per person/year	446.9	£	2016	BNF, 2016
Memantine 10 mg tablet once a day	severe	per person/year	312.7	£	2016	
Post-diagnosis monitoring		per person/ year	100.0	£	2007	Getsios, 2010
Other healthcare, community	Mild	per person/ year	2751.0	£	2012	Prince, 2014
	Moderate	per person/ year	2695.0	£	2012	
	Severe	per person/ year	11258.0	£	2012	
Other healthcare, institutionalisation	Mild	per person/ year	4504.0	£	2012	
	Moderate	per person/ year	9438.0	£	2012	
	Severe	per person/ year	8689.0	£	2012	
Social care, community	Mild	per person/ year	3121.0	£	2012	
	Moderate	per person/ year	7772.0	£	2012	
	Severe	per person/ year	10321.0	£	2012	
Social care, institutionalisation	Mild	per person/ year	24737.0	£	2012	
	Moderate	per person/ year	25715.0	£	2012	
	Severe	per person/ year	25874.0	£	2012	
Informal care, community	Mild	per person/ year	19714.0	£	2012	
	Moderate	per person/ year	32237.0	£	2012	
	Severe	per person/ year	33482.0	£	2012	
Informal care, residential care	Mild	per person/ year	1067.0	£	2012	
	Moderate	per person/ year	2901.0	£	2012	
	Severe	per person/ year	2119.0	£	2012	
% community social care funded privately			0.4			
% residential social care funded privately			0.65			

Medication effectiveness		**Effect**	**95% CI**		Bond et al., 2012
On NPI					
Donepezil vs placebo		-2.683	-5.673	0.207	
Memantine vs placebo		-1.6	-4.762	1.54	
On MMSE					
Donepezil vs placebo		1.24	0.81	1.66	
Memantine vs placebo		0.7	0.02	1.38	
On ADCS-ADL					
Donepezil vs placebo		2.02	1.06	3.28	
Memantine vs placebo		1.41	0.04	2.78	
MCI incidence	Age group	**MCI incidence per 1000 person-years**			Ward et al., 2012
	65 to 69	12.30			
	70 to 74	17.75			
	75 to 79	32.73			
	80 to 84	31.67			
	85+	23.33			
Dementia incidence	Age group	**Dementia incidence per 1000 person-years**			Matthews and Brayne, 2005
		Female	Male		
	65 to 69	6.3	6.9		
	70 to 74	6.1	14.5		
	75 to 79	14.8	14.2		
	80 to 84	31.2	17		
	85+	71.7	58.4		
Progressing from MCI to dementia	Annual rate	0.049			Mitchell and Shiri-Feshki, 2009
Reverting from MCI to normal cognition	Annual rate	0.16			Koepsell and Monsell, 2012
Relative risk of death for dementia		Mean	95% CI		Helmer et al., 2001
		1.82	1.77	2.68	

MMSE progression	$\Delta MMSE_i^{annual} = 5.4663 - 0.4299 * \text{Min}(PrevMMSE, 9) - 0.0042 * \text{Max}(0, \text{Min}[PrevMMSE - 9, 9]) + 0.1415 * \text{Max}(0, \text{Min}[PrevMMSE - 18, 12]) - 0.0791 * Prev\Delta MMSE + 0.0747 * Age + \delta_i$	Getsios et al., 2010
NPI progression	$\Delta NPI_i^{annual} = \left(5.74 + 0.03 * weeks - 0.59 * NPI_{base} - 0.59 * NPI_{base} * weeks + 0.24 * NPI_{previous} - 1.74 * White - 3.82 * Black + 2.34 * PsyMed + 0.12 * MMSE_{base} - 0.22 * MMSE_{previous} + \delta_i^{NPI}\right) * 1.44$	
ADL progression	$\Delta ADL_i^{annual} = 1.35 + 0.06 * weeks - 0.79 * ADL_{base} + 0.71 * ADL_{previous} + 0.12 * MMSE_{base} + 0.09 * Age + 0.81 * PsyMed - 3.05 * Black - 0.49 * MMSE_{previous} + \delta_i^{ADL}$	
IADL progression	$\Delta IADL_i^{annual} = 1.27 + 0.17 * weeks - 0.84 * IADL_{base} + 0.002 * IADL_{base} * weeks + 0.84 * IADL_{previous} - 0.67 * Male + 0.20 * MMSE_{base} - 0.28 * MMSE_{previous} - 0.16 * ADL_{base} + 0.18 * ADL_{recent} + \delta_i^{IADL}$	
Patient Utility	$\text{Utility (EQ5D)} = 0.408 + 0.010 \text{ x MMSE} - 0.004 \text{ x NPI} - 0.159 \text{ x Institutionalised} + 0.051 \text{ x Caregiver}$	
Annual probability of institutionalisation	$\text{Probability of institutionalisation} = 0.512 - 0.016 \text{ x MMSE } [R^2 = 0.711]$	Nagy et al., 2011

Appendix 2: Simul8 Schematic for the model



Appendix 3: Results from our online survey on www.doctors.net.uk

Question for GPs: What screening test do you most often use for dementia?		
Cognitive screening test	Responses	Percentage
6-Item Cognitive Impairment Test (6CIT)	30	29 (%)
Mini-Mental State Examination (MMSE)	27	26 (%)
General Practitioner Assessment of Cognition (GPCOG)	21	21 (%)
Abbreviated Mental Test Score (AMTS)	7	7 (%)
Montreal Cognitive Assessment (MoCA)	6	6 (%)
Mini-cog	2	2 (%)
Addenbrookes Cognitive Examination-III (ACE-III)	1	1 (%)
Others	8	8 (%)
Total	102	100 (%)

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