Appendix J: Health Economics

J.1 General

The economic approach to provide evidence to support decision making around a clinical review question begins with a systematic search of the literature. The aim of this is to source any published economic evaluations of relevance to the topic of interest. At this stage it may become apparent that evidence exists in the literature which exactly meets the review question criteria and therefore there is no need for original economic analysis. If this proves not to be the case it may be decided that economic modelling can generate some useful analysis. The aim is to produce a cost–utility analysis weighing up the benefits and harms of comparable interventions. The extent to which this is possible will be driven by the availability of evidence upon which to parameterise the clinical pathway and disease natural history.

J.2 Decision problem

Patent-holders of pharmacological interventions used in dementia have incentives to conduct economic studies for their products, and this has contributed to a comparatively rich evidence base. However, there is a relative lack of evidence for non-pharmacological interventions. Therefore, the guideline committee's (GC's) highest priority for original health economic modelling were 3 review questions relating to non-pharmacological interventions in dementia (shown in Table 1).

Table 1: Research questions

What are the most effective non-pharmacological interventions for supporting cognitive functioning in people living with dementia?
What are the most effective non-pharmacological interventions for supporting functional ability in people living with dementia?
What are the most effective non-pharmacological interventions to support wellbeing in people living with dementia?

The GC advised that, although some non-pharmacological interventions have been recommended in NICE guidance since CG42, they are not very well implemented. The GC expressed the view that, if a more explicit case could be made for the value such interventions add, it would act as a powerful lever for commissioning of effective services.

These RQs could potentially encompass a wide and heterogeneous range of interventions. For this reason, GC input was used to prioritise the interventions of particular interest as worthy of detailed economic analysis.

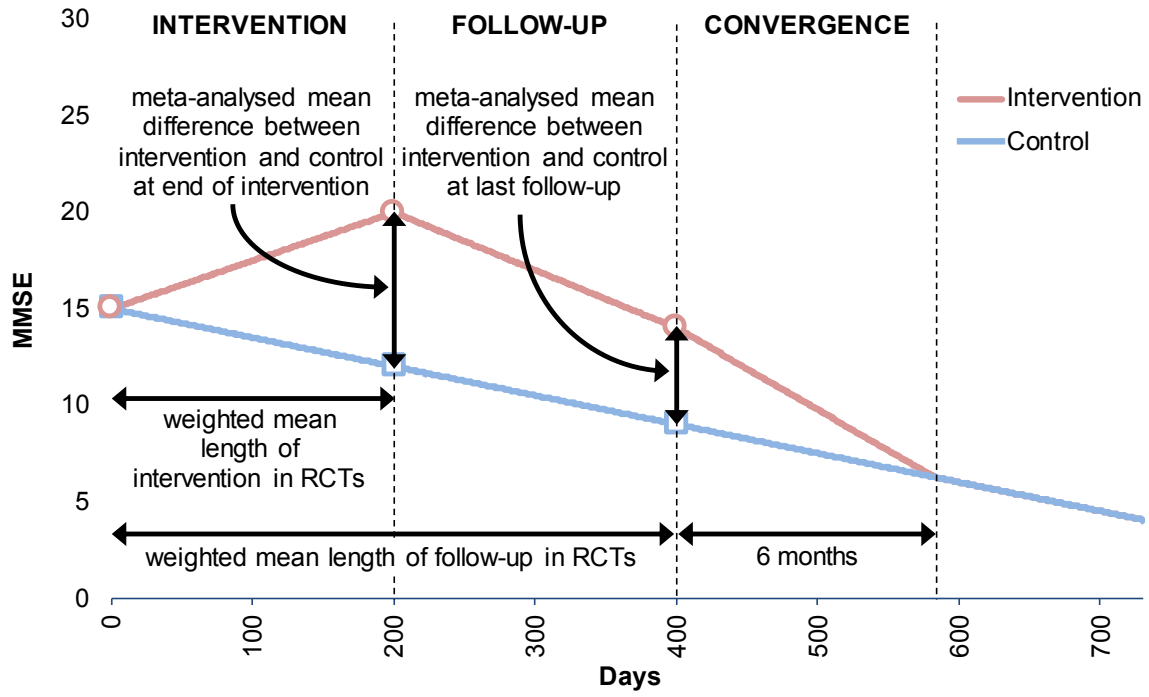
J.3 Methods

J.3.1 Structure of the model

We developed a series of cost–utility models that sought to simulate the average patient receiving each intervention of interest, compared with usual care. The models used a simple area-under-the-curve method to estimate differences, over time, between a person receiving the intervention and one receiving usual care in multiple clinical outcomes that could then be used to estimate health-related quality of life (and, consequently, quality-adjusted life-years; QALYs).

We used the systematic reviews undertaken for these questions (see full guideline, section 13.2.2) to identify non-pharmacological interventions for which sufficient data were available for modelling. The model takes single summary estimates for each continuous variable of interest from the meta-analyses, and substitutes these into published utility models, drawn from a review of available literature, to estimate the health-related quality of life that could be expected for the typical person living with dementia receiving the intervention in question. The constraints of available utility models dictated that clinical outcomes of interest were effects in cognitive, functional and behavioural domains.

Figure 1 provides a schematic depiction of the method, using the example of change in MMSE (where the multivariable utility model was used, similar analyses were performed for other relevant outcomes and the joint effect of intervention on all domains estimated).



Model shown reflects base-case assumptions; alternative scenarios (including immediate onset of treatment benefit, and longer and shorter durations of post-follow-up benefit) were explored in sensitivity analysis
NB some quantities have been exagerrated, compared with empirical data, for schematic clarity

Figure 1: Schematic depiction of model

In the base case, the effect difference between any 2 time points occurred in a linear fashion. Patients in the model revert to their expected condition without treatment 6 months after the average follow-up period in a linear fashion. In 1 or 2 cases, the average follow-up period exceeded 18 months; in these instances, patients in the control and interventions arms were assumed to converge at 24 months (730 days), the maximal time horizon for the model. A two year maximum time horizon for the base case model was chosen as this was consistent with the longest follow-up period of a study included in the meta-analysis (Amieva 2016).

Aside from the effects of discounting, this model structure could be written as a simple sum:

$$\Delta MMSE = \frac{\Delta_1 t_1 + (\Delta_1 + \Delta_2)(t_2 - t_1) + \Delta_2 \min(0.5, 2 - t_2)}{2} \quad \textbf{(1)}$$

, where Δ_1 and Δ_2 are the meta-analysed effect estimates at end of intervention and follow-up, respectively, and t_1 and t_2 are the associated timepoints (in years) for these 2 junctures. However, in order to calculate discounted values correctly, and to make it easier to depict model inputs and outputs, we implemented the model by summing effects over a series of 1-day cycles, with QALYs calculated for each.

In order to estimate treatment effects, data synthesised as standardised mean differences (SMDs) were re-expressed in units needed for the utility models (e.g. cognition→MMSE, functional→DAD, behavioural→NPI), using pooled standard deviations from the assembled evidence-base.

The analyses used a patient perspective for outcomes and an NHS+PSS perspective for costs, in line with *Developing NICE guidelines* (2014). Costs and outcomes were discounted at the rate of 3.5% per annum (assuming continuous discounting throughout). All calculations were undertaken in Microsoft Excel.

Modelled population(s) and intervention(s)

The modelled populations represent a generic cohort of people living with dementia. Because the model did not account for mortality and the relationship between clinical variables and health-related quality of life was always linear (owing to evidence used to estimate; see J.3.2.5), baseline characteristics and assumed natural history are essentially arbitrary. For example, the baseline MMSE score in Figure 1 could be 20 or 10 without altering the difference between intervention and control, so estimated incremental QALYs would be identical. The calcuation is similarly invariant to the rate at which people not receiving the intervention are assumed to progress. Nevertheless, we set these parameters at a plausible level to aid interpretation of model outputs. In one instance (group music therapy), data were available to estimate different costs and effects in cohorts of people with either mild–moderate or severe dementia, so we used these separately (see below); however, there are no differences in the way the model itself handles these inputs.

The interventions modelled were those for which sufficient data were available in the systematic review.

Key assumptions

There are several developer assumptions for these economic analyses which need to be considered when analysing the results generated. These are summarised in Table 2.

Table 2: Key assumptions of original cost–utility model

- Non-pharmacological interventions are unable to alter the disease process or mortality rates in patients with dementia.
- The maximal effects of the interventions are likely to be limited to the duration of which the patient receives it.
- The utility scores change in a steady linear fashion between points of which measurements are estimated.
- Both the control group and the intervention group start with the same baseline utility value.
- The intervention is administered immediately after baseline.
- The model estimates results for the 'average' patient in a cohort using mean values from the literature review. If, at an individual level, expectation of benefit is asymmetric around the mean,

then this may introduce some degree of bias; however, the direction and magnitude of any such bias is impossible to quantify without much more detailed data than are available.

- The model does not consider any difference of resource use (i.e. hospital inpatient stays, GP appointments, delayed entry to ful time care, etc.) or disutility as a result of interventions.

J.3.2 Parameters

J.3.2.1 General approach

Identifying sources of parameters

With the exception of treatment effects, which were derived from a series of meta-analyses drawn from the systematic review conducted for these research questions (see full guideline, section 13.2.2), parameters were identified through informal searches that aimed to satisfy the principle of 'saturation' (that is, to 'identify the breadth of information needs relevant to a model and sufficient information such that further efforts to identify more information would add nothing to the analysis' (Kaltenthaler et al., 2011). We conducted searches in a variety of general databases, including Medline (via PubMed), the Cochrane Database of Systematic Reviews and Google Scholar.

When searching for resource use and cost parameters, searches were conducted in specific databases designed for this purpose, the CEA (Cost-Effectiveness Analysis) Registry and the NHS Economic Evaluation Database (NHS EED) for example.

We asked the GC to identify papers of relevance. We reviewed the sources of parameters used in the published CUAs identified in our systematic review; during the review, we also retrieved articles that did not meet the formal inclusion criteria, but appeared to be promising sources of evidence for our model. We studied the reference lists of articles retrieved through any of these approaches to identify any further publications of interest.

In cases where there was paucity of published literature for values essential to parameterise key aspects of the model, data were obtained from unpublished sources; further details are provided below.

Selecting parameters

Our overriding selection criteria were as follows:

- The selected studies should report outcomes that correspond as closely as possible to the health states and events simulated in the model.
- The selected studies should report a population that closely matches the UK population (ideally, they should be drawn from the UK population).
- All other things being equal, more powerful studies (based on sample size and/or number of events) were preferred.
- Where there was no reason to discriminate between multiple possible sources for a given parameter, we gave consideration to quantitative synthesis (meta-analysis), to provide a single summary estimate.

J.3.2.2 Cohort parameters and natural history

Natural history

A key assumption of the model was that any intervention does not permanently alter disease progression or rates of mortality.

In this model, we were only interested in (time-limited) differences in quality of life between the control arms and intervention arms for each non-pharmacological intervention. When patients in the treatment arm revert to natural history and follow the same trajectory as patients in the control arm, the difference in quality of life would be zero.

Mortality

Due to the assumption that any treatment, including the non-pharmacological interventions being modelled here, is fundamentally unable to alter the disease process and mortality in patients with dementia, rates of mortality are assumed to be equal in both the control groups and intervention groups. Furthermore, it was assumed that expected mortlity over the modelled period would not significantly attenuate any benefits ascribable to interevetions. Mortality is therefore not required to be represented in this model to reflect the difference in quality of life between control arms and intervention arms.

J.3.2.3 Treatment effects

Meta-analysis

Meta-analyses were conducted on data extracted from the systematic review. Based on the result of the meta-analyses, sufficient data (that is, at least one RCT) were available to model the interventions shown in Table 3.

Table 3: Modelled interventions

Intervention	Mode	Severity
Cognitive rehabilitation	Individual	All
Cognitive stimulation therapy	Group	All
Cognitive training	Group	All
Reminiscence therapy	Group	All
Exercise	Individual	All
Exercise	Group	All
Exercise	Group	Severe
Music therapy (active)	Group	All
Music therapy	Individual	All
Occupational Therapy	Individual	All

All studies for each of the interventions in the systematic review contained data about change in clinical outcomes on measures in terms of mean difference in scores from baseline, standard deviation of the change of score from baseline and the number of patients for both the control group and the intervention group on at least one of the clinical measures of interest and at least one timepoint (post-intervention/ post-intervention +follow-up).

For some scales used within clinical trials, scores increased with disease severity whilst in others, scores decreased with disease severity. To ensure that the meta-analysis accounted for this effect, data points (mean difference from baseline data) were ‘flipped‘, by being multiplied by −1, so that in increase in scores would mean a positive outcome for patients.

Each clinical outcome for each trial was associated with one or more severity levels of dementia (mild, moderate or severe), modality of intervention (if it was delivered in a group setting, an individual setting, or a combination of both), subgroup of intervention type, (e.g. individualised exercise, weight resistance, etc.) and time point of measurement (at end of intervention, or long-term, post-intervention follow-up).

When multiple measures in a domain were meta-analysed, the measures were converted from mean differences (MD) in change from baseline values on their natural scale to standardised mean difference (SMD) change from baseline value. Table 5 shows the SMDs used in the model for each intervention for ADL, BPSD and cognition at the end of the intervention and at a long-term follow-up period.

SMDs were converted back into MD values on their natural scale before being substituted into univariable and multivariable models to generate utility values. To convert from SMD values to MD values on their natural scale, SMD values were multiplied by the pooled standard deviations of all interventions and control arms of all trials in the dataset, using the usual formula for pooled variance:

$$\hat{s} = \sqrt{\frac{\sum s^2(n-1)}{\sum(n-1)}} \quad \textbf{(2)}$$

All trials reporting a standard deviation for change from baseline were included in these calculations, regardless of intervention (i.e. a single, pooled number was calculated for all interventions).

The pooled SDs used are shown in Table 4.

Table 4: Standard deviations for change from baseline (pooled across all interventions in dataset) used to express SMDs in natural units

Measure	At end of intervention	Follow-up
ADL – DAD	8.664	9.737
BPSD – NPI	14.099	14.044
Cognition – MMSE	4.136	4.535

The term ADL stands for "activities of daily living," and refers to the basic tasks of everyday life, such as eating, bathing, dressing, toileting, and transferring. When people are unable to perform these activities, they need help in order to cope, either from other human beings or mechanical devices or both. The term BPSD stands for ‘behavioral and psychological symptoms of dementia’. BPSD are distressing for patients and their caregivers. Cognition measures are used to detect change in cognitive abilities, including memory and thinking skills.

The resultant MDs – which form the critical effectiveness inputs for the model – are shown in Table 6.

Table 5: Standardised mean differences (SMDs) at end of intervention and long-term follow-up

Intervention	SMD at end of intervention			SMD at long-term follow-up		
	ADL (95% CI)	BPSD (95% CI)	Cognition (95% CI)	ADL (95% CI)	BPSD (95% CI)	Cognition (95% CI)
Cognitive rehabilitation	0.437 (-0.088, 0.961)	-0.136 (-0.362, 0.090)	0.415 (-0.361, 1.191)	0.623 (-0.052, 1.298)	-0.066 (-0.809, 0.676)	-0.040 (-0.299, 0.219)
Cognitive stimulation therapy	0.114 (-0.099, 0.327)	0.187 (-0.152, 0.525)	0.422 (0.291, 0.553)	0.434 (-0.107, 0.974)	0.369 (-0.129, 0.866)	0.098 (-1.117, 1.313)
Cogitive training	0.131 (-0.077, 0.339)	-0.123 (-0.353, 0.106)	0.866 (-0.281, 2.013)	-0.034 (-0.274, 0.207)	-0.232 (-0.490, 0.026)	-0.081 (-0.322, 0.159)
Reminiscence therapy	0.017 (-0.104, 0.139)	-0.043 (-0.203, 0.118)	0.231 (0.071, 0.392)	0.000 (-0.315, 0.315)	-0.107 (-0.368, 0.153)	-0.045 (-0.282, 0.191)
Exercise (Individual)	0.639 (-0.371, 1.650)	0.188 (-0.262, 0.638)	0.940 (-0.258, 2.138)	-	-	-0.326 (-0.765, 0.113)
Exercise (Group)	0.307 (0.102, 0.512)	0.175 (0.019, 0.331)	0.581 (0.280, 0.881)	0.197 (0.002, 0.393)	0.536 (0.215, 0.858)	0.418 (-0.126, 0.963)
Exercise (Group -- Severe)	0.211 (-0.164, 0.586)	-0.011 (-0.385, 0.362)	-	-	-	-
Music therapy (Active)	0.807 (0.100, 1.513)	-0.076 (-0.721, 0.569)	0.245 (-0.024, 0.513)	-	0.135 (-0.510, 0.781)	0.229 (-0.075, 0.533)
Music therapy (Individual)	-	-	1.518 (0.692, 2.344)	-	-	-
Occupational therapy	0.237 (0.014, 0.460)	-	-	0.195 (-0.191, 0.581)	-	-
NB all meaures have been rescaled such that positive numbers indicate beneficial effects						

Table 6: Mean differences (MDs) at end of intervention and long-term follow-up

Intervention	MD at end of intervention			MD at long-term follow-up		
	ADL – DAD[a] (95% CI)	BPSD – NPI[b] (95% CI)	Cognition – MMSE[a] (95% CI)	ADL – DAD[a] (95% CI)	BPSD – NPI[b] (95% CI)	Cognition – MMSE[a] (95% CI)
Cognitive rehabilitation	3.78 (-0.76, 8.33)	-1.92 (-5.10, 1.27)	1.72 (-1.49, 4.93)	6.06 (-0.51, 12.64)	-0.93 (-11.36, 9.50)	-0.18 (-1.35, 0.99)

Intervention	MD at end of intervention			MD at long-term follow-up		
	ADL – DAD[a] (95% CI)	BPSD – NPI[b] (95% CI)	Cognition – MMSE[a] (95% CI)	ADL – DAD[a] (95% CI)	BPSD – NPI[b] (95% CI)	Cognition – MMSE[a] (95% CI)
Cognitive stimulation therapy	0.98 (-0.86, 2.83)	2.63 (-2.14, 7.40)	1.75 (1.20, 2.29)	4.22 (-1.04, 9.49)	5.18 (-1.81, 12.16)	0.44 (-5.07, 5.95)
Cogitive training	1.14 (-0.67, 2.94)	-1.74 (-4.98, 1.50)	3.58 (-1.16, 8.32)	-0.33 (-2.67, 2.01)	-3.26 (-6.89, 0.37)	-0.37 (-1.46, 0.72)
Reminiscence therapy	0.15 (-0.90, 1.20)	-0.60 (-2.87, 1.66)	0.96 (0.29, 1.62)	0.00 (-3.07, 3.06)	-1.51 (-5.17, 2.15)	-0.20 (-1.28, 0.87)
Exercise (Individual)	5.54 (-3.22, 14.29)	2.65 (-3.70, 9.00)	3.89 (-1.07, 8.84)	-	-	-1.48 (-3.47, 0.51)
Exercise (Group)	2.66 (0.89, 4.44)	2.47 (0.27, 4.66)	2.40 (1.16, 3.64)	1.92 (0.02, 3.83)	7.53 (3.01, 12.05)	1.90 (-0.57, 4.37)
Exercise (Group -- Severe)	1.83 (-1.42, 5.08)	-0.16 (-5.43, 5.11)	-	-	-	-
Music therapy (Active)	6.99 (0.86, 13.11)	-1.07 (-10.17, 8.02)	1.01 (-0.10, 2.12)	-	1.90 (-7.17, 10.96)	1.04 (-0.34, 2.42)
Music therapy (Individual)	-	-	6.28 (2.86, 9.69)	-	-	-
Occupational therapy	2.05 (0.12, 3.98)	-	-	1.90 (-1.86, 5.65)	-	-

a Positive values indicate benefit
b Negative values indicate benefit

1

In order to reflect the duration of intervention and follow-up represented in the pooled effect estimates, intervention and follow-up period were assumed to be equal to a weighted mean of the relevant durations in each contributing RCT, with weights defined by the relevant meta-analysis (that is, each study had the same weight in arriving at a pooled estimate of duration as it did in arriving at a pooled estimate of effect).

Table 7 shows the mean number of days for the duration of intervention and long-term follow-up for ADL, BPSD and cognition measures used in the model.

Table 7: Duration of intervention and long-term follow-up for interventions in the model (days)

	Duration of intervention (days)			Duration of long-term follow-up (days rom baseline)		
	ADL	BPSD	Cognition	ADL	BPSD	Cognition
Cognitive rehabilitation	75.3	86.9	75.4	482.6	517.1	720.0
Cognitive stimulation therapy	144.2	100.2	153.5	300.0	265.5	90.4
Cogitive training	109.1	90.0	159.9	642.7	720.0	642.2
Reminiscence therapy	155.8	205.5	75.5	491.1	720.0	624.7
Exercise (Individual)	155.3	87.9	104.3	-	-	360.0
Exercise (Group)	217.9	241.8	178.7	191.8	180.0	220.4
Exercise (Group -- Severe)	360.0	360.0	-	-	-	-
Music therapy (Active)	90.0	28.0	48.3	-	56.0	86.8
Music therapy (Individual)	-	-	119.0	-	-	-
Occupational therapy	93.9	-	-	364.0	-	-

J.3.2.4 Resource use and costs

Costs included in the analyses only related to the costs of delivering the interventions themselves. While it might be hypothesised that effective interventions would reduce other health and social care costs (for example, improvements in functional ability might reduce requirement for domiciliary support), there was no evidence of significant differences in costs between treatment and control in any of the within-trial analyses identified in our systematic review (see full guideline section 13.4.1). Therefore, it was assumed that, aside from the expense incurred in delivering the intervention in question, there would be no difference in total costs between people who do and do not receive the intervention. Resource use for each of the interventions was estimated, where possible, using evidence from the assembled RCTs. This included the number of sessions, length of sessions and grade of staff required to deliver the intervention. Where data were not available from clinical papers, the GC provided estimates of resource use in the English NHS setting. Where unit cost data were not available from study papers and PSSRU unit costs, the guideline committee were consulted to provide estimates of unit costs in the English NHS setting. Resource use and unit cost data were combined to produce a cost for each intervention modelled.

The Personal Social Services Research Unit (PSSRU) generates the Unit Costs for Health and Social Care report which includes costs for both community and hospital-based healthcare staff.

Across all interventions, staff travel, patient travel, venue and admin costs where applicable were standardised for each session, or for each participant per session, based on the values observed in Woods et al. (2016) and D'Amico et al. (2015).

J.3.2.4.1 Cognitive stimulation therapy – costs and resource use

Cognitive stimulation (CST) is defined as engagement in a range of activities and discussions (usually in a group) aimed at general enhancement of cognitive and social functioning.

Input parameters for Group CST are shown in Table 8. The number of sessions and participants per sessions for group cognitive stimulation therapy were based on D'Amico et al. (2015). Hourly rates for costs for staff delivering the intervention were taken from the Curtis et al. 2016, (henceforth referred to as PSSRU 2016) whilst time required for staff to deliver the intervention was taken from the GC. The GC advised that a therapist at agenda for change band 6, supported by a therapist at agenda for change band 4, would be sufficient to lead Group CST. It is assumed that the Group CST intervention takes place at an external venue, which both staff and patients must travel to. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 8: CST – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	14.00	Not varied in PSA	D'Amico 2015
Patients per session	5.00 (3.10, 6.90)	Uniform: min=3.00; max=7.00	D'Amico 2015
Staff required			
Band 4 (e.g. OT technician; clinical psychology assistant)	1.00	Not varied in PSA	GC advice
Band 6 (e.g. OT specialist; clinical psychology trainee)	1.00	Not varied in PSA	GC advice
Staff hourly rate			
Band 4 (e.g. OT technician; clinical psychology assistant)	£30.00	Not varied in PSA	PSSRU 2016
Band 6 (e.g. OT specialist; clinical psychology trainee)	£42.00	Not varied in PSA	PSSRU 2016
Staff delivery hours per session			
Band 4 (e.g. OT technician; clinical psychology assistant)	0.75 (0.51, 0.99)	Uniform: min=0.50; max=1.00	GC advice
Band 6 (e.g. OT specialist; clinical psychology trainee)	0.75 (0.51, 0.99)	Uniform: min=0.50; max=1.00	GC advice
Staff preparation/admin hours per session			
Band 4 (e.g. OT technician; clinical psychology assistant)	0.50 (0.03, 0.98)	Uniform: min=0.00; max=1.00	GC advice
Band 6 (e.g. OT specialist; clinical psychology trainee)	0.50 (0.03, 0.98)	Uniform: min=0.00; max=1.00	GC advice
Staff travel time per session			
Band 4 (e.g. OT technician; clinical psychology assistant)	0.62	Not varied in PSA	Clare et al. in press

Name	Value (95%CI)	Distribution & parameters	Source
Band 6 (e.g. OT specialist; clinical psychology trainee)	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£134.44		Sum of above
Staff training			
Cost per staff member	£100.00 (£52.50, £147.50)	Uniform: min=£50.00; max=£150.00	GC advice
Number of groups seen by the HCP, after which training will no longer be valid	10.0 (5.3, 14.8)	Uniform: min=5.00; max=15.00	GC advice
Training costs apportioned per session	£1.43		Training cost for all staff members divided by number of sessions multiplied by number of groups seen over life time
Staff travel per session	£14.00		Woods et al. 2016 (see J.3.2.4.4)
Patient travel per session	£60.70		
Venue per session	£19.89		
Admin per session	£2.74		
Cost per session	£233.19		Sum of all costs per session
Cost per course	£3,264.70		Cost per session multiplied by number of sessions
Cost per patient per course	**£652.94**		Cost of course divided by number of patients per session/ses session

J.3.2.4.2 Cognitive rehabilitation – costs and resource use

Cognitive rehabilitation (CR) is defined an individualised approach where personally relevant goals are identified and the therapist works with the person and his or her family to devise strategies to address these. The emphasis is on improving functioning in everyday life rather than performance on cognitive tests, building on the person's strengths and developing ways of compensating for impairments.

Input parameters for cognitive rehabilitation are shown in Table 9. The costing of individual cognitive rehabilitation was based on Clare et al. (in press), a study that is currently in press at the time of writing this modelling report.

Table 9: Cognitive rehabilitation – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Month 0 to month 3			Clare et al. in press
Number of visits	9.61	Not varied in PSA	
Total hours of visits	20.17	Not varied in PSA	
Mean duration per completed visit (hours)	2.10	Not varied in PSA	
Costs (£)			
a) Face-to-face visits	£523.00	Not varied in PSA	
b) Preparation	£85.00	Not varied in PSA	
c) CR training & individual supervision	£320.00	Not varied in PSA	
d) Travel (time and mileage)	£331.00	Not varied in PSA	
Mean cost per person (includes a-d)	£1,259 (£1,224, £1,295)	Gamma: α=4892; β=0.26	
Month 3 to month 9			Clare et al. in press
Number of visits	3.74	Not varied in PSA	
Total hours of visits	7.46	Not varied in PSA	
Mean duration per completed visit (hours)	2.00	Not varied in PSA	
Costs (£)			
a) Face-to-face visits	£188.00	Not varied in PSA	
b) Preparation	£33.00	Not varied in PSA	
c) CR training & individual supervision	£124.00	Not varied in PSA	
d) Travel (time and mileage)	£128.00	Not varied in PSA	
Mean cost per person (includes a-d)	£474 (£455, £494)	Gamma: α=2247; β=0.21	
Total (month 0 to month 9)			Calculated from above
Number of visits	13.35		
Total hours of visits	27.63		
Mean duration per completed visit (hours)	2.07		
Total mean cost per person over the 9 months	£1,733.00		
Total cost inflated from 2013/14 to 2016/17	**£1,826.70**		Inflated using the National tariff update and draft prices for 2016/17

J.3.2.4.3 Cognitive training – costs and resource use

Cognitive training (CT) is defined as guided practice on a set of standard tasks designed to reflect particular cognitive functions; a range of difficulty levels may be available within the standard set of tasks to suit the individual's level of ability. It may be offered in individual or group sessions, with pencil and paper or computerised exercises.

Due to lack of evidence in the literature base, the GC advised to treat the cost of group cognitive training the same as that of group cognitive stimulation therapy.

J.3.2.4.4 Reminiscence therapy – costs and resource use

Input parameters for reminiscence therapy are shown in Table 10. The costing was based on REMCARE, a trial published in Woods et al. (2016). Although the committee felt that the therapy delivered in REMCARE was more intensive than would be realistically implemented in the NHS (in terms of number of sessions. Etc.), the committee agreed that the individual items in REMCARE were well costed, and likely to reflect true costs in an English NHS setting. Therefore, this was seen as a high-quality source for other costs in the model.

Table 10: Reminiscence therapy - Group - Costs and Resource Use

Name	Value (95%CI)	Distribution & parameters	Source
Training	£299.00 (£200.25, £417.23)	Gamma: α=£29.00; β=£10.31	Woods et al. 2016
Facilitators	£4,931.00 (£4,266.58, £5,642.79)	Gamma: α=£197.09; β=£25.02	Woods et al. 2016
Support staff	£906.00 (£504.33, £1,423.38)	Gamma: α=£14.76; β=£61.39	Woods et al. 2016
Staff travel	£266.00 (£100.84, £509.86)	Gamma: α=£6.33; β=£42.05	Woods et al. 2016
Venue	£378.00 (£192.06, £625.84)	Gamma: α=£11.49; β=£32.89	Woods et al. 2016
Participant / carer travel	£2,258.00 (£1,603.04, £3,023.40)	Gamma: α=£38.66; β=£58.41	Woods et al. 2016
Materials and resources	£158.00 (£110.96, £213.23)	Gamma: α=£36.50; β=£4.33	Woods et al. 2016
Refreshments	£185.00 (£168.31, £202.47)	Gamma: α=£450.33; β=£0.41	Woods et al. 2016
Administration	£52.00 (£37.47, £68.88)	Gamma: α=£41.94; β=£1.24	Woods et al. 2016
Cost per 19-session programme	£9,433.00		Sum of above
Average no. of participant dyads per course	9.79	Not varied in PSA	Woods et al. 2016
Cost per participant per course	**£963.53**		Cost of 19-session programme divided by

Name	Value (95%CI)	Distribution & parameters	Source
			number of participants

J.3.2.4.5 Exercise (one-to-one) – costs and resource use

Input parameters for individualised exercise therapy are shown in Table 11. The number of sessions for individualised exercise therapy was based on the systematic review. Hourly rates for staff delivering the intervention were taken from the PSSRU 2016. It is assumed that the venue in which individualised exercise therapy is delivered is the patients own home, and therefore no additional venue costs are incurred. The GC agreed that a band 4 member of staff would be sufficiently skilled to be able to deliver individualised exercise therapy. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 11: Exercise -Individual - Costs and Resource Use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	34.00 (32.10, 35.90)	Uniform: min=32.00; max=36.00	Review of literature
Staff required			
Band 4	1	Not varied in PSA	
Staff hourly rate			
Band 4	£30.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 4	0.54 (0.50, 0.66)	Uniform: min=0.50; max=0.67	Systematic Review
Staff preparation/admin hours per session			
Band 4	0.21 (0.01, 0.41)	Uniform: min=0.00; max=0.42	GC assumption
Staff travel time per session			
Band 4	0.62	Not varied in PSA	Clare et al. in press
Per session costs:			
Total staff cost per session	£41.02		
Staff travel per session	£7.00		Woods et al. 2016 (see J.3.2.4.4)
Administration per session	£2.74		
Venue per session	£0.00		
Cost per session	£50.75		Sum of all costs per session
Materials and resources per participant per course	£50.00 (£2.50, £97.50)	Uniform: min=£0.00; max=£100.00	GC assumption
Cost per course	**£1,775.58**		Cost per session multiplied by

Name	Value (95%CI)	Distribution & parameters	Source
			number of sessions

J.3.2.4.6 Exercise (group) – costs and resource use

Input parameters for group exercise for people with mild/moderate dementia are shown in Table 12. The number of sessions, the average number of patients per session and staff time required to deliver group exercise therapy for people with mild/moderate dementia was based the systematic review. Hourly rates for staff were taken from the PSSRU 2016 whilst GC advice was used to derive the cost of training staff to be able to train people with mild/moderate dementia. The GC advised that in English NHS practice, group exercise usually takes place at an external venue, which would require both staff and people with dementia to travel to. With regards to staff members required, the GC advised that 2 staff members at agenda for change band 4 would be sufficient to provide group exercise training to people with dementia. Indicative assumptions were made as to the cost of training these staff members, and the duration for which the training would last for. The GC also highlighted practice where a gym venue is paid £50 to provide group exercise training for one session. This practice was incorporated into a scenario analysis. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 12: Exercise (group) – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	65.0 (9.8, 152.3)	Uniform: min=6.00; max=156.00	Review of literature
Patients per session	12.1 (4.4, 17.7)	Uniform: min=4.00; max=18.00	Review of literature
Staff required			
Band 4 (e.g. OT technician; clinical psychology assistant)	2.0	Not varied in PSA	GC advice
Staff hourly rate			
Band 4 (e.g. OT technician; clinical psychology assistant)	£30.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 4 (e.g. OT technician; clinical psychology assistant)	1.17 (0.38, 1.96)	Uniform: min=0.33; max=2.00	Review of literature
Staff preparation/admin hours per session			
Band 4 (e.g. OT technician; clinical psychology assistant)	0.50 (0.03, 0.98)	Uniform: min=0.00; max=1.00	GC assumption
Staff travel time per session			
e	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£137.17		Sum of above
Staff training			
Cost per staff member	£150.00 (£102.50, £197.50)	Uniform: min=£100.00; max=£200.00	Developer assumption

Name	Value (95%CI)	Distribution & parameters	Source
Number of groups seen by the HCP, after which training will no longer be valid	20.0 (10.5, 29.5)	Uniform: min=10.00; max=30.00	Developer assumption
Training costs apportioned per course	£15.00		Training cost for all staff members divided by Number of groups seen by the HCP, after which training will no longer be valid
Staff travel per session	£14.00		Woods et al. 2016 (see J.3.2.4.4)
Patient travel for all patients per session	£146.34		
Venue per session	£19.89		
Admin per session	£2.74		
Cost per course	£20,824.45		Sum of above
Cost per patient per course	**£1,727.37**		Cost per course divided by number of patients per session
Scenario analysis: £50 all-in sessions	£1,073.39		

J.3.2.4.7 Exercise (group – severe) – costs and resource use

Input parameters for group exercise for people with severe dementia are shown in Table 13. The number of sessions and the average number of patients per session for group exercise therapy for those with severe dementia were taken from Rolland et al. (2007). The GC advised that a single agenda for change band 5 member of staff, when supported by regular carehome staff (for whom no additional opportunity costs should be assumed), was sufficient to provide group exercise therapy to people with severe dementia. Hourly rates for staff delivering the intervention were taken from the PSSRU 2016. As the GC was unable to provide information with regards to the cost of training these staff members to deal with patients with severe dementia, or the duration for which the training would last for, a developer assumption was made. The GC however noted that they expected the training costs to be higher to train staff members to deal with people with severe dementia. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 13: Exercise (group – severe) – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	104.0	Not varied in PSA	Rolland et al. (2007)
Patients per session	5.2 (2.1, 6.9)	Uniform: min=2.00; max=7.00	Rolland et al. (2007)
Staff required			

Name	Value (95%CI)	Distribution & parameters	Source
Band 5 (Occupational Therapist)	1.00	Not varied in PSA	GC assumption
Staff hourly rate			
Band 5 (Occupational Therapist)	£32.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 5 (Occupational Therapist)	1.00 (0.53, 1.48)	Uniform: min=0.50; max=1.50	GC assumption
Staff preparation/admin hours per session			
Band 5 (Occupational Therapist)	0.43 (0.02, 0.85)	Uniform: min=0.00; max=0.87	GC assumption
Staff travel time per session			
Band 5 (Occupational Therapist)	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£65.62		Sum of above
Staff training			
Cost per staff member	£300.00 (£252.50, £347.50)	Uniform: min=£250.00; max=£350.00	Developer assumption
Number of groups seen by the HCP, after which training will no longer be valid	20.0 (10.5, 29.5)	Uniform: min=10.00; max=30.00	Developer assumption
Training costs apportioned per course	£15.00		Training cost for all staff members divided by number of groups seen by the HCP, after which training will no longer be valid
Staff travel per session	£7.00		Woods et al. 2016 (see J.3.2.4.4)
Patient travel per session	£0.00		
Venue per session	£0.00		
Admin per session	£2.74		Woods et al. 2016 (see J.3.2.4.4)

Name	Value (95%CI)	Distribution & parameters	Source
Cost per session	£75.35		Sum of above
Cost per course	£7,851.75		Cost per session multiplied by number of sessions
Cost per patient per course	£1,509.95		Cost of course divided by number of patients

J.3.2.4.8 Music therapy (participatory) – costs and resource use

Input parameters for participatory group music therapy for people with dementia are shown in Table 14. The number of sessions, the average number of patients per session and staff time required to deliver participatory group music therapy for people with dementia was based on the systematic review. The GC advised an agenda for change band 6 music therapist would be sufficient to provide participatory music therapy to people with demenia, if supported by patient's carers who would be expected to accompany the person with dementia. Hourly rates for staff were taken from the PSSRU 2016. As the staff member who would provide the music therapy is a qualified music therapist, no additional training costs are assumed to be required. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 14: Music therapy (participatory) – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	15 (8, 24)	Uniform: min=8; max=24	Review of literature
Patients per session	6.3 (4.1, 7.9)	Uniform: min=4.00; max=8.00	Review of literature
Staff required			
Band 6 music therapist	1.00	Not varied in PSA	GC advice
Staff hourly rate			
Band 6 music therapist	£42.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 6 music therapist	0.75 (0.51, 0.99)	Uniform: min=0.50; max=1.00	Review of literature
Staff preparation/admin hours per session			
Band 6 music therapist	0.52 (0.03, 1.02)	Uniform: min=0.00; max=1.04	GC assumption
Staff travel time per session			

Name	Value (95%CI)	Distribution & parameters	Source
Band 6 music therapist	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£79.30		Sum of above
Staff training			
Cost per staff member	£0.00	Not varied in PSA	
Number of groups seen by the HCP, after which training will no longer be valid	20.0 (10.5, 29.5)	Uniform: min=10.00; max=30.00	GC assumption
Training costs apportioned per course	£0.00		
Staff travel per session	£7.00		Woods et al. 2016 (see J.3.2.4.4)
Patient travel per session all patients	£75.87		
Venue per session	£19.89		
Admin per session	£2.74		
Cost per session	£184.80		Sub of above
Cost per course	£2,710.37		Cost per session multiplied by the number of sessions plus cost of materials and resources
Materials and resources	£0.00	Not varied in PSA	GC assumption
Cost per patient per course	**£433.66**		Cost per course divided by number of participants per course

J.3.2.4.9 Music therapy (one-to-one) – costs and resource use

Input parameters for individualised music therapy for people with dementia are shown in Table 15. The staff time required to deliver individualised music therapy for people with dementia was based on the systematic review. The GC advised an agenda for change band 6 music therapist would be sufficient to provide individualised music therapy to people with demenia. As the staff member who would provide the music therapy is a qualified music therapist, and training is assumed to take place in the patients own home, no additional training costs are assumed to be required, no venue costs are assumed to be requied and no patient travel costs are assumed to be requied. Time for administration was assumed to be required to contact patients about appointments and to to make notes in patient records.

Table 15: Music therapy (one-to-one) – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	13.00 (10.15, 15.85)	Uniform: min=10.00; max=16.00	Review of literature
Staff required			
Band 6 music therapist	1.00	Not varied in PSA	GC advice
Staff hourly rate			
Band 6 music therapist	£42.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 6 music therapist	0.75 (0.51, 0.99)	Uniform: min=0.50; max=1.00	Review of literature
Staff preparation/admin hours per session			
Band 6 music therapist	0.25 (0.01, 0.49)	Uniform: min=0.00; max=0.50	GC assumption
Staff travel time per session			
Band 6 music therapist	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£67.92		Sum of above
Staff training			
Cost per staff member	£0.00	Not varied in PSA	
Staff travel per session	£7.00		Woods et al. 2016 (see J.3.2.4.4)
Admin per session	£2.74		
Venue per session	£0.00		GC advice
Cost per session	£77.66		Sum of above
Cost per course	**£1,009.56**		Cost per course divided by number of participants per course

J.3.2.4.10 Occupational therapy – costs and resource use

Input parameters for individualised occupational therapy for people with dementia are shown in Table 16. Although the committee agreed that various levels of staff on the agenda for change payscale could deliver occupational therapy, it was agreed that in clinical practice in England, a band 6 member of staff with some additional training would be sufficient to provide occupational therapy to people with dementia. The number of sessions and staff time required to deliver this intervention was based on the systematic review. Hourly rates for staff were taken from the PSSRU 2016. It was assumed that occupational therapy would be delivered in patients own home, thus avoding the need for patient travel costs and venue hire costs.

Table 16: Occupational therapy – costs and resource use

Name	Value (95%CI)	Distribution & parameters	Source
Number of sessions	9.33 (8.05, 9.95)	Uniform: min=8.00; max=10.00	Systematic Review
Staff required			
Band 6 (e.g. OT specialist; clinical psychology trainee)	1.00	Not varied in PSA	GC advice
Staff hourly rate			
Band 6 (e.g. OT specialist; clinical psychology trainee)	£42.00	Not varied in PSA	PSSRU 2016
Staff hours per session			
Band 6 (e.g. OT specialist; clinical psychology trainee)	1.50 (1.03, 1.98)	Uniform: min=1.00; max=2.00	Systematic Review
Staff preparation/admin hours per session			
Band 6 (e.g. OT specialist; clinical psychology trainee)	0.50 (0.03, 0.98)	Uniform: min=0.00; max=1.00	GC assumption
Staff travel time per session			
Band 6 occupational therapist	0.62	Not varied in PSA	Clare et al. in press
Total staff time per session	£109.92		Sum of above
Staff travel per session	£7.00		Woods et al. 2016 (see J.3.2.4.4)
Patient travel per session	£0.00		
Venue per session	£0.00		
Materials and resources	£150.00		As per DESCANT trial (provided by committee member)
Cost per course	**£1,240.88**		Sum of above

J.3.2.5 Quality of life

Quality adjusted life years (QALYs) are composite indicators expressed as years of life lived but adjusted for quality of life spent during those years. This model is concerned with detecting the QALY difference between control treatments and modelled interventions. For this reason, an absolute baseline starting point in any measure was not necessary.

We conducted a literature search to locate utility values to be applied to the health states within the economic model. As utility values were not available for any of the non-pharmacological interventions in the model, another method was required to estimate quality of life from clinical outputs of the trials identified in the systematic reviews.

Models estimating quality of life in dementia were identified from the systematic reviews, and papers references. A subsequent informal literature search, including looking at how health-related quality of life had been estimated in technology appraisals and Google scholar

searches, identified an additional small number of multivariable and univariable models that could potentially be used to get from clinical effectiveness measures to utility values. All available models were examined and evaluated against inputs available from the studies identified from the systematic review. We ultimately identified 2 univariable and one multivariable models that fitted these criteria. Models were rejected if we did not have data on the continuous clinical variables to populate them.

Univariable models

A univariable model developed in 2001 by Brazier et al. was based on a statistical regression of individual's Mini-Mental State Examination (MMSE) score versus the Health Utilities Index, version 3 (HUI III Furley et al 1998) utility index as mapped in the ADENA Exelon trials. The MMSE is a 30-point questionnaire used to measure cognitive impairment with lower scores indicating a greater deal of cognitive impairment. This model allows us to estimate the utility state based on the patient's MMSE score alone (shown in Table 17). Table 18 shows results of the statistical regression of indivuals' MMSE scores versus utility.

Table 17: MMSE to utility – Brazier (2001)

Utility = 0.0982 + 0.0298 × MMSE

This model, directly predicting HRQoL from MMSE alone, has been used in previous cost–utility analyses including by Loveman et al. (2006), to assess the clinical and cost-effectiveness of donepezil, rivastigamine, galanatamine and memantine for Alzheimer's disease. Although this is a significant benefit of the model, as the MMSE is a widely reported clinical measure, a draw back of the model is that it ignores the majority of other continuous clinical outcome variables on other domains in which we are interested in.

Table 18. Result of the statistical regression of individuals' MMSE scores versus utility (taken from Brazier et al. 2001)

Variable	B	95% Confidence Interval for B		t-value	Significance
Constant	0.0982	0.0735	0.1228	7.8130	0.0000
MMSE score	0.0298	0.0286	0.0310	48.4330	0.0000

Another univariable model developed by Rive et al. (2010) examined the relationship between utility in the pre-full-time care state and activities of daily living (as measured by the Alzheimer's Disease Cooperative Study - Activities of Daily Living [ADCS-ADL] scale). The ADCS-ADL is a multi-item instrument used to assess the degree of disability or the need for assistance. Scores on the ADCS-ADL range from 0 to 78, with higher scores indicating less functional impairment. Utilities in the dataset from which the the Rive et al. model was derived from were measured using an unvalidated patient-level mapping from the 12-item health status questionnaire (HSQ-12) to the EQ-5D (Rive et al. 2010).

Rive et al.'s model, the only model identified that allowed the use of ADL as a standalone continuous clinical variable to generate utility, accounts for baseline differences (which would be inappropriate, in this instance) and time effects (which, as there are no interaction terms,

will cancel out between different cohorts, resulting in no incremental difference); therefore, it may be expressed in the simple univariable form shown in Table 19.

Table 19: Activities of daily living to utility score – Rive (2010)

Utility = 0.202 + 0.008 × ADCS-ADL

As no information on the standard error, or any other estimate of variability were available for the Rive et al. (2010) model, we assumed 20% of the mean as a standard error.

Multivariable models

One multivariable model developed in 2016 by Lacey et al. examined the associations (regression coefficients) between multiple continuous clinical variables outcomes and HUI-3 using mixed effects models for repeated measure. This model was preferred as the base-case model as it allowed us to use the maximum amount of data from the clinical trials from the meta-analyses, to measure the effects on the various domains on which the non-pharmacological interventions may have an impact. However, one noteable drawback of this model was the models' use of the uncommon DAD instrument, which is not commonly reported in trials.

The model (shown in Table 20) containsthe MMSE, Disability Assessment for Dementia (DAD) scale and Neuropsychiatric Inventory (NPI) variables.

The DAD scale is used to quantitatively measure functional abilities in the activities of daily living in individuals with cognitive impairment, with higher scores representing less impairment. The NPI scale ranges from 1 to 144, with higher scores representing worse outcomes.

In both of the univariable models and the multivariable model, we had no information on the correlation betaween the intercept and the slope, so we sampled these independently in the probabilistic sensitivity analysis.

Table 20: HUI-3 model from Lacey et al. (2015) linear equation

HUI-3 Total Score = 0.359 + 0.00745 × MMSE + 0.00394 × DAD − 0.0054 × NPI

The author of the HUI-3 multivariable model was contacted to obtain covariate parameter estimates, standard errors and t values, which were supplied (Table 21).

Table 21: Parameter estimates for the Lacey et al. (2015) model

Variable	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	0.35895	0.02410	14.90	<.0001
MMSE	0.00745	0.00055890	13.33	<.0001
DAD	0.00394	0.00013809	28.55	<.0001
NPI	-0.00540	0.00019005	-28.39	<.0001

J.3.3 Sensitivity analyses and scenario analyses

Sensitivity analyses were performed in the model to evaluate uncertainty.

J.3.3.1 Deterministic sensitivity analyses

One-way sensitivity analyses

One-way sensitivity analyses were conducted to examine the effects on the ICER of modifying individual parameters that were subject to uncertainty. Parameters were varied within ranges reflecting their plausible values – where possible, thiese were to the upper and lower limits of 95% confidence intervals in underlying data (e.g. treatment effects; see Table 5).

Extrapolation of treatment effects

Once values for each clinical variable at each follow-up period have been generated, a method of extrapolation is required to estimate future progression beyond the observed follow-up period. Under such circumstances, advice from the *Guide to the methods of technology appraisal* (2013) stipulates that a range of assumptions should be explored, ranging from no additional benefit to an indefinite preservation of gains achieved over the course of the intervention.

In the base case, patients revert to natural history in a linear fashion after the average follow-up period in the assembled evidence. On GC advice, this convergence was assumed to take 6 months in the base case.

In scenario analyses, we tested the following alternative assumptions:

Immediate convergence at the longest follow-up period. This assumes that no benefit is retained at any point after the last measurement is made (at either post-intervention or long-term follow-up), and both the control arms and intervention arms revert to the natural history.

Indefinite preservation of benefit. This assumes that any difference between the control arm and the intervention arm at the last follow up period is maintained until the maximal model horizon.

Zero-overheads

In reflection of feedback from a GC member, who advised that some interventions can be provided ‘in-house’ with little overhead (for, e.g., room hire and admin), we undertook a scenario analysis in which all such costs were set to zero – accounting only for staff time and participant travel expenses.

Onset of effect

In its base case, the model assumes that treatment effect accrues in a gradual linear fashion through duration of the intervention, peaking at the end of intervention delivery. A scenario analysis tested our model’s sensitivity to this assumption by assuming the onset of treatment effect is immediate, with maximal effect experienced as soon as the intervention is delivered.

Standard deviation for calculating SMDs

An alternative method for taking mean differences on clinical outcome measures from trials and turning them into standardised mean differences, suitable for meta-analysis, would be to

use the standard deviations of each measure pooled across all arms of all trials. This is in contrast to the typical method of meta-analysis using Hedges *g* as per Review Manager 5.3.

Additional staff costs for travel time

The GC felt that the treatment interventions prioritised for modelling contained significant uncertainty in terms of additional staff costs for travel time. The model therefore deployed a sensitivity analysis where additional staff costs for travel time were considered.

Utility model deployed

Three potential models (two univariable models and one multivariable model) were identified that could calculate utility from clinical outputs of trials. Therefore, another appropriate sensitivity analysis, where data are available, was to select between the different models to generate alternative utility values to generate a range of plausible cost-effectiveness estimates.

J.3.3.2 Probabilistic sensitivity analyses

We configured the models to perform probabilistic sensitivity analysis to quantify uncertainty in the true values of input parameters.

Probability distributions were estimated for all input variables with the exception of the number of staff required to provide interventions and hourly rates for staff on the Agenda for Change pay scales. Distribution parameters were sourced from the study in which the value was obtained, where possible, or were estimated based on the usual properties of data of that type.

The distribution for each of the parameters used within the probabilistic sensitivity analysis is driven by the variable type and the availability of reported information. A normal distribution was used for constants and coefficients in the univariable and multivariable models. Skewed distributions fit cost better so a gamma distribution was used for cost data obtained from studies which were directly used in the model (such as Woods et al, D'Amico et al. (2015) and Clare et al. (in press)).

To estimate resource use for interventions (e.g. number of sessions per course of therapy), uniform distributions encompassing the whole range of values oibserved in the underlying effectiveness data were used. This has the disadvantages that uncertainty in the mean value is overstated, and the expected value of the distribution will only be equal to the deterministic (mean) value in cases where the observed range happens to be symmetrical. However, the approach was considered appropriate as, alongside capturing parameter uncertainty, it functioned as a structural uncertainty analysis testing the assumption that the relationship between duration of intervention and effect can be assumed to be represented by the mean values of each (in other words, it would create spurious precision to assume that the average effect observed in trials would be achieved by an intervention of average intensity).

J.4 Original cost–utility model – results

J.4.1.1 Group cognitive stimulation therapy

Effectiveness inputs (Figure 4) showed that CST is associated with point-estimate benefits in cognitive, functional and behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 5), that amounts to a benefit that lasts for a little over a year and, at its greatest, exceeds 0.04 points on the utility scale.

The base-case model suggested that group CST was associated with a benefit of a little over 0.03 QALYs relative to control, at an additional cost of £650, leading to an ICER of £20,165/QALY (Table 22). One-way sensitivity analysis found that the model was extremely sensitive to almost all parameters in the model: varying any parameter within plausible range generates results lying on either side of a £20,000/QALY threshold (Figure 6).

A regression analysis was performed to investigate the presence of a correlation between treatment intensity and duration of effect, but no such relationship was found.

Table 22: Incremental costs and effects for group cognitive stimulation therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£653	1.196	£653	0.032	£20,165	£648
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£653	1.079	£653	0.010	£63,379	£206
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£653	1.052	£653	0.021	£30,547	£427

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 2) suggested that the probability that intervention is cost-effective is around 50%, if QALYs are valued at £20,000 each, or 70%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 3) shows that group CST versus control was unlikely to generate more than 0.1 QALYs or cost more than £1,000.

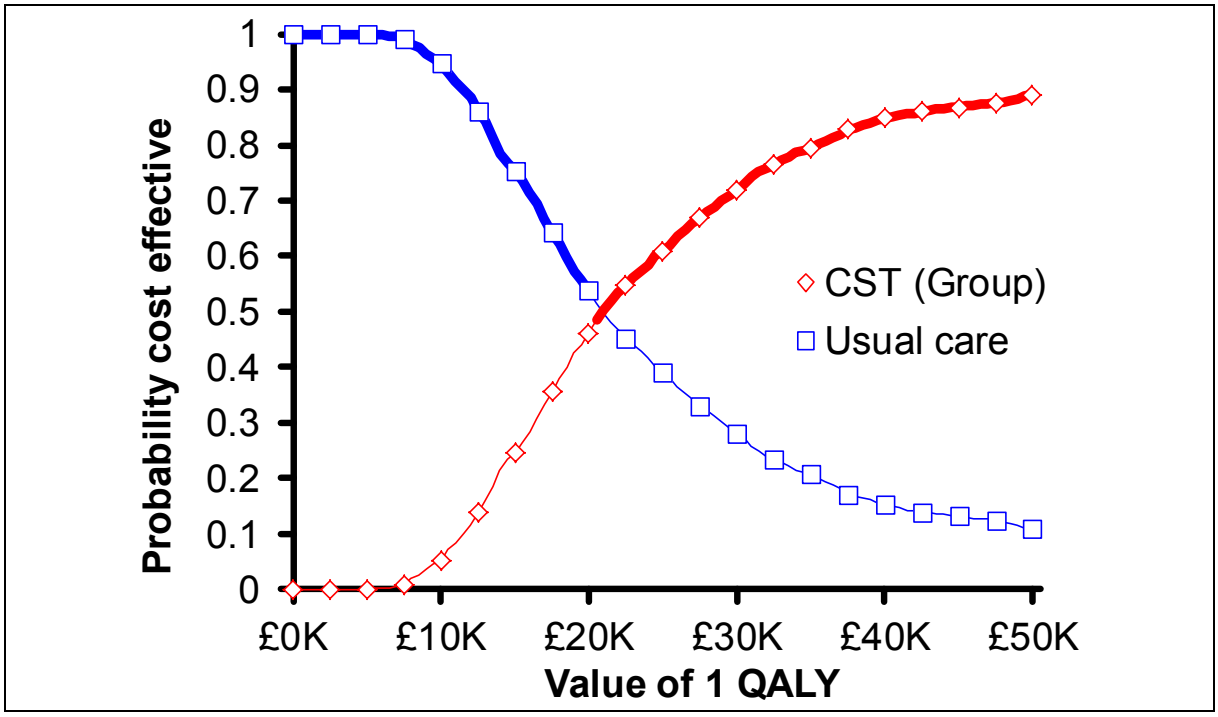


Figure 2: Cost-effectiveness acceptability curve for group cognitive stimulation versus usual care

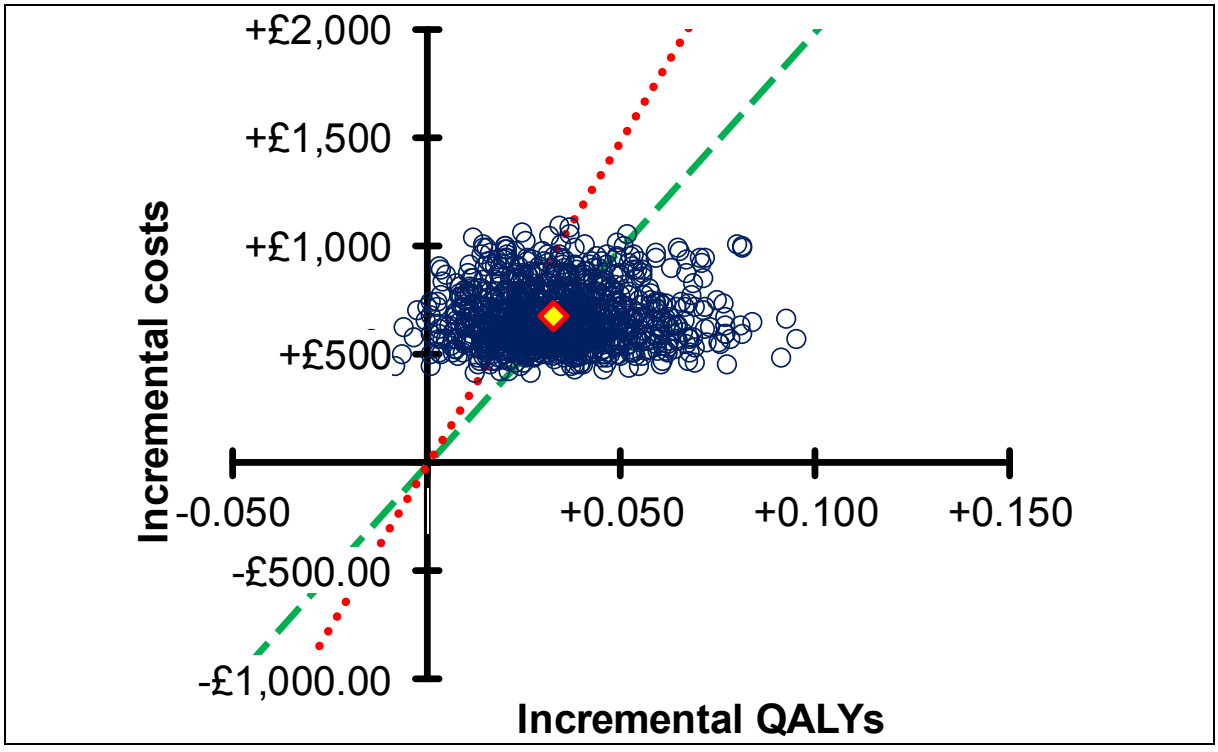


Figure 3: PSA for group cognitive stimulation versus usual care

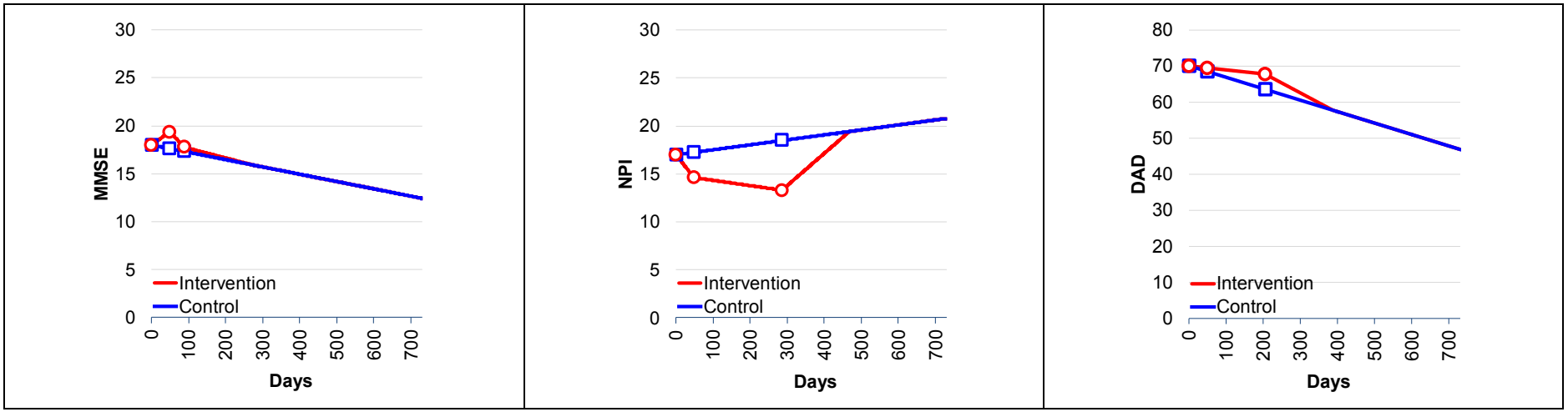


Figure 4: Change in clinical variables over time for group cognitive stimulation versus usual care

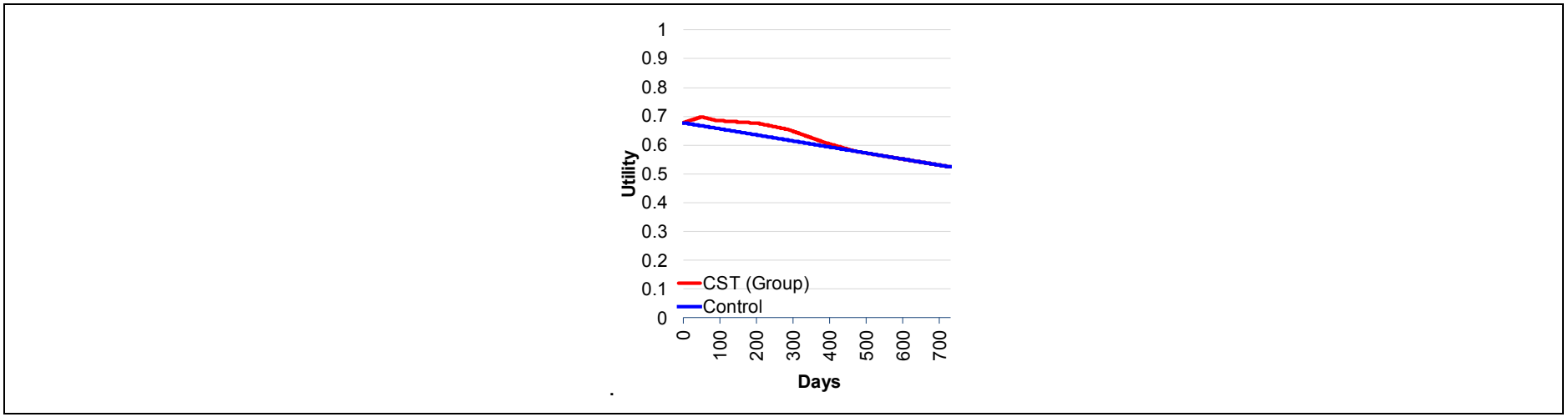


Figure 5: Estimated health-related quality of life as a function of clinical variables over time for group cognitive stimulation versus usual care

1 **Figure 6: One-way sensitivity analysis – cognitive stimulation versus usual care**

J.4.1.2 Cognitive rehabilitation

Effectiveness inputs (Figure 9) showed that cognitive rehabilitation is associated with point-estimate benefits in cognitive and functional domains, and a point-estimate harm in the behavioural domain (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 10), that amounts to a benefit that lasts for a little over a year and a half and, at its greatest, exceeds 0.02 points on the utility scale.

The base-case model suggested that cognitive rehabilitation was associated with a benefit of a little over 0.027 QALYs relative to control, at an additional cost of £1,827, leading to an ICER of £66,863/QALY (Table 23). One-way sensitivity analysis found that the model was most sensitive to the SMD value for BPSD at long term follow-up; however, no parameter variations resulted in an ICER lower than £20,000/QALY.

Table 23: Incremental costs and effects for cognitive rehabilitation versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,827	1.191	£1,827	0.027	£66,863	£546
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£1,827	1.113	£1,827	0.044	£41,900	£872
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£1,827	1.101	£1,827	0.070	£26,006	£1,405

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 7) suggested that the probability that intervention is cost-effective is around 2%, if QALYs are valued at £20,000 each, or 15%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 8) shows that all iterations of cognitive rehabilitation versus control cost between £1,500 and £2,000, whilst the number of QALYs generated ranged betwteen -0.050 and 0.150.

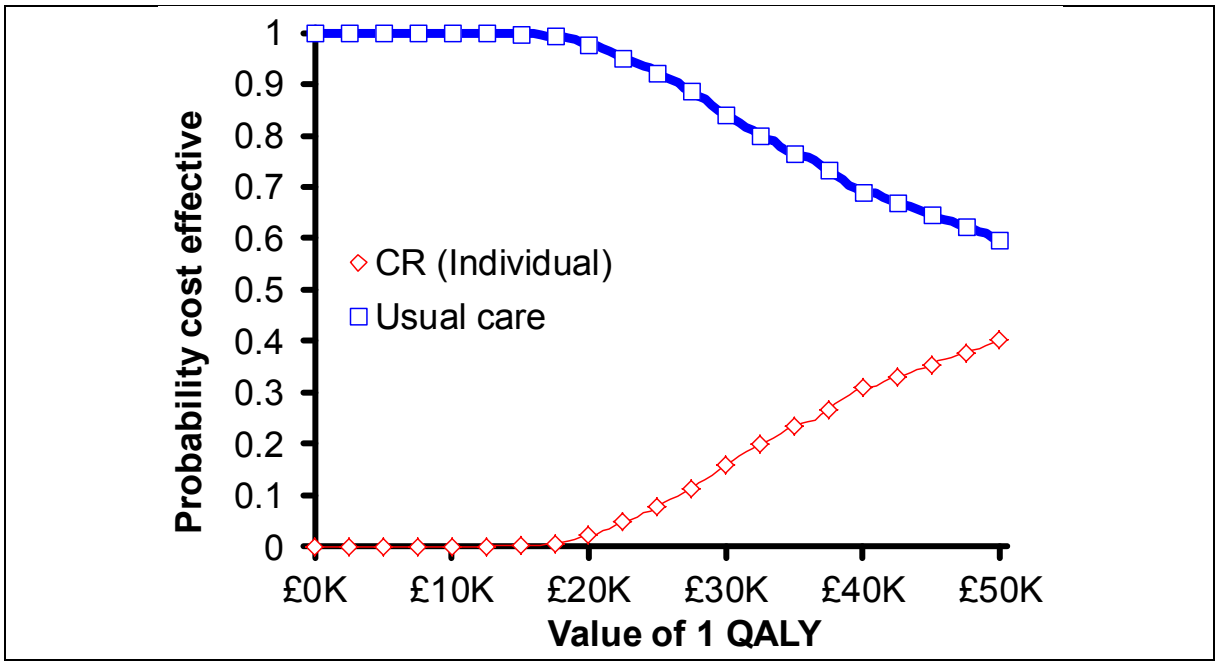


Figure 7: CEAC for cognitive rehabilitation versus control

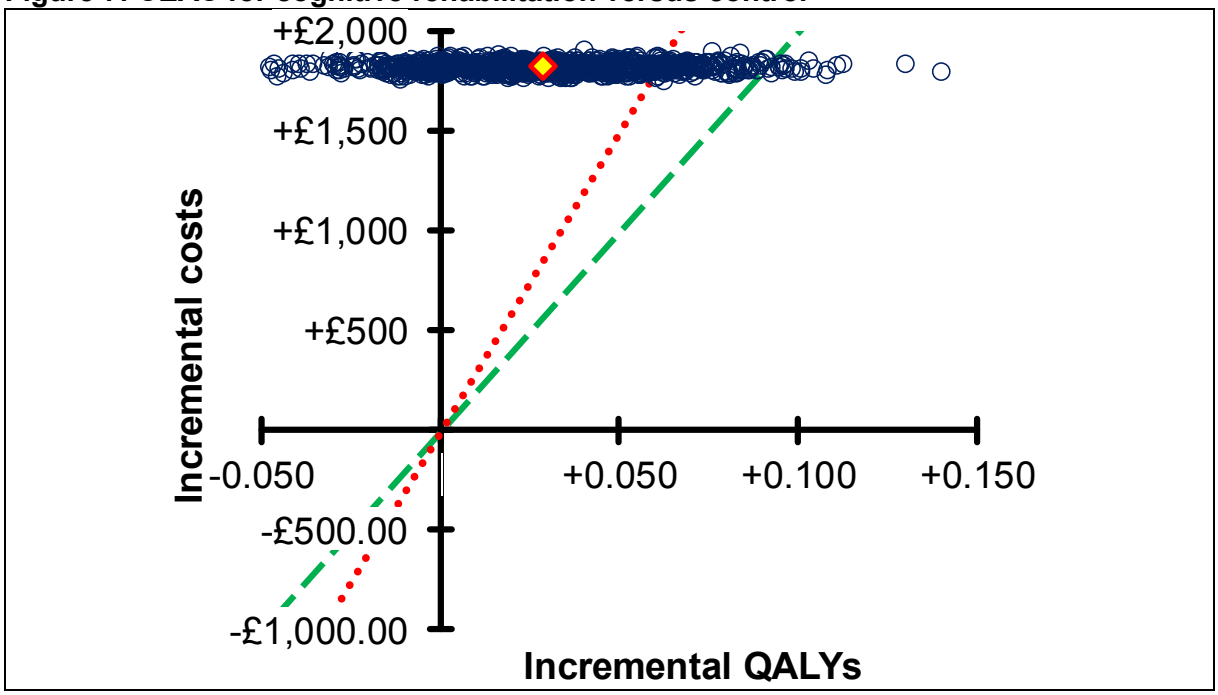


Figure 8: PSA for cognitive rehabilitation versus control

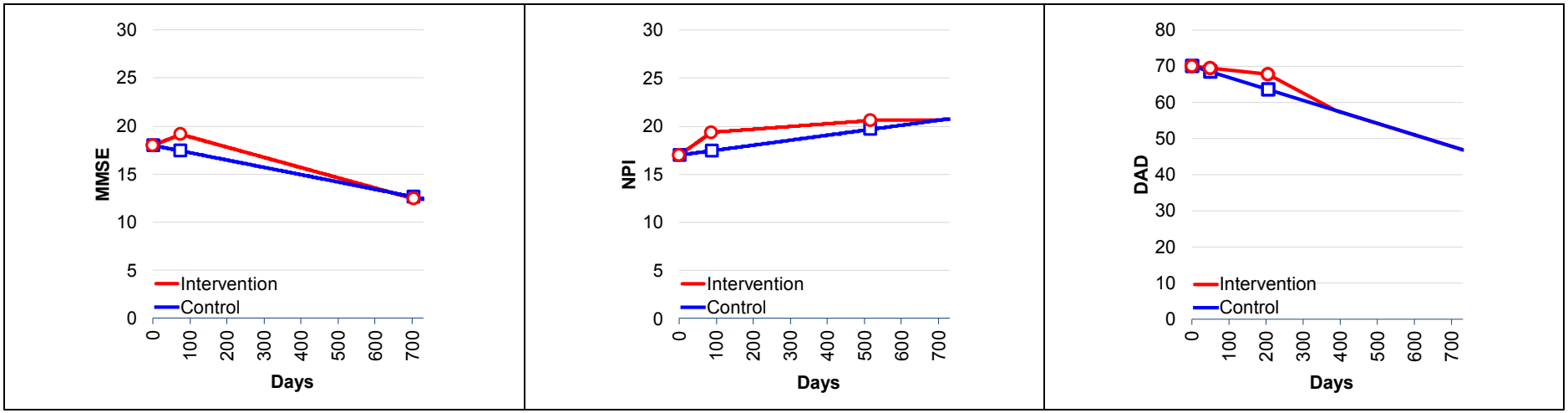


Figure 9: Change in clinical variables over time for cognitive rehabilitation versus usual care

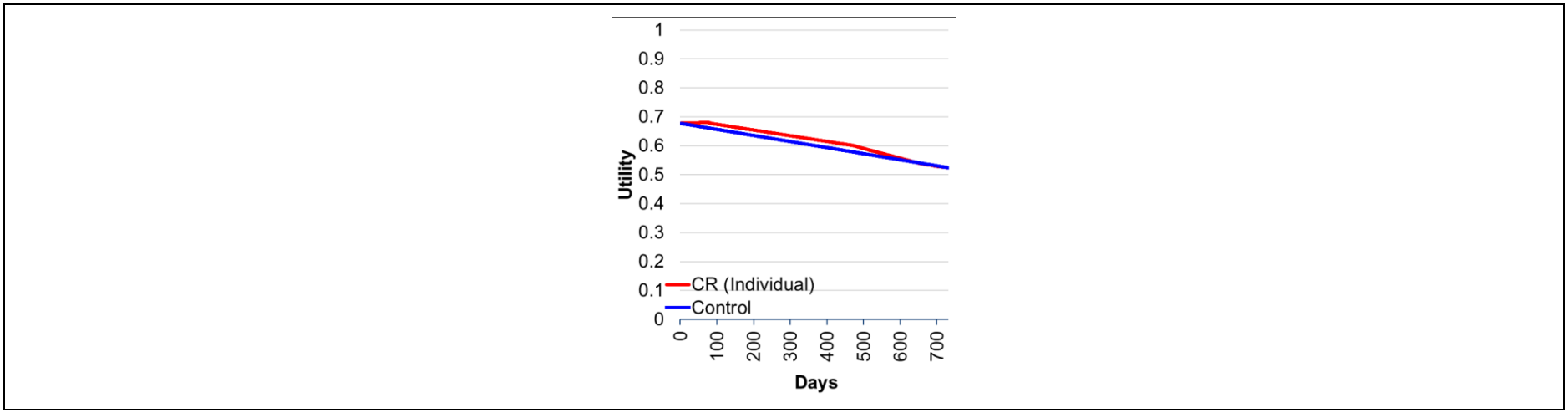
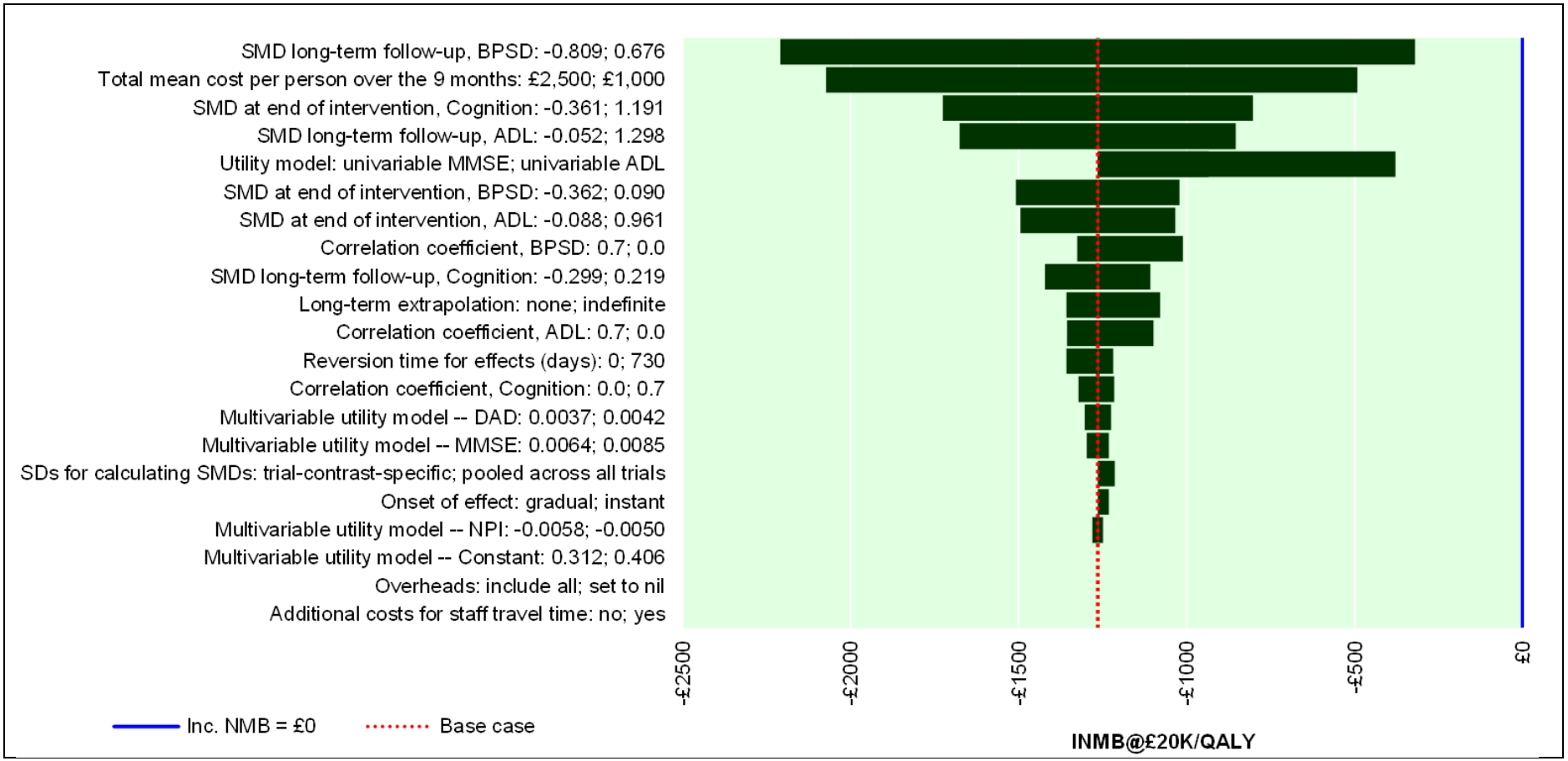


Figure 10: Estimated health-related quality of life as a function of clinical variables over time for cognitive rehabilitation versus usual care



1 **Figure 11: One-way sensitivity-analysis for individual cognitive rehabilitation versus control**

2

J.4.1.3 Group cognitive training

Effectiveness inputs (Figure 14) showed that cognitive training is associated with point-estimate benefits in cognitive and functional domains, and a point-estimate harm in the behavioural domain (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 15), that amounts to a benefit that peaks at 0.02 points on the utility scale for half a year. Beyond this, the benefit provided by cognitive training converges with control, and thereafter people receiving cognitive training have a lower utility as compared to those in the control arm.

The base-case model suggested that cognitive training was associated with a benefit of a little over 0.003 QALYs relative to control, at an additional cost of £653, leading to an ICER of £254,615/QALY. One-way sensitivity analysis found that the model was most sensitive to the use of the univariable MMSE model and the SMD for cognition at the end of the intervention. If the MMSE values in the univariable MMSE model and the SMD for cognition at the end of the intervention were increased to their highest plausible value, cognitive training may be a cost-effective treatment as the incremental net monetary benefit would be greater than zero.

Table 24: Incremental costs and effects for cognitive training versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£653	1.166	£653	0.003	£251,615	£52
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£653	1.163	£653	0.094	£6,978	£1,871
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£653	1.039	£653	0.008	£78,324	£167

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 12) suggested that the probability that intervention is cost-effective is around 11%, if QALYs are valued at £20,000 each, or 20%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 13) shows that almost all iterations of cognitive training versus control cost between £500 and £1,000, whilst the number of QALYs generated were distributed mostly betwteen -0.050 and 0.050.

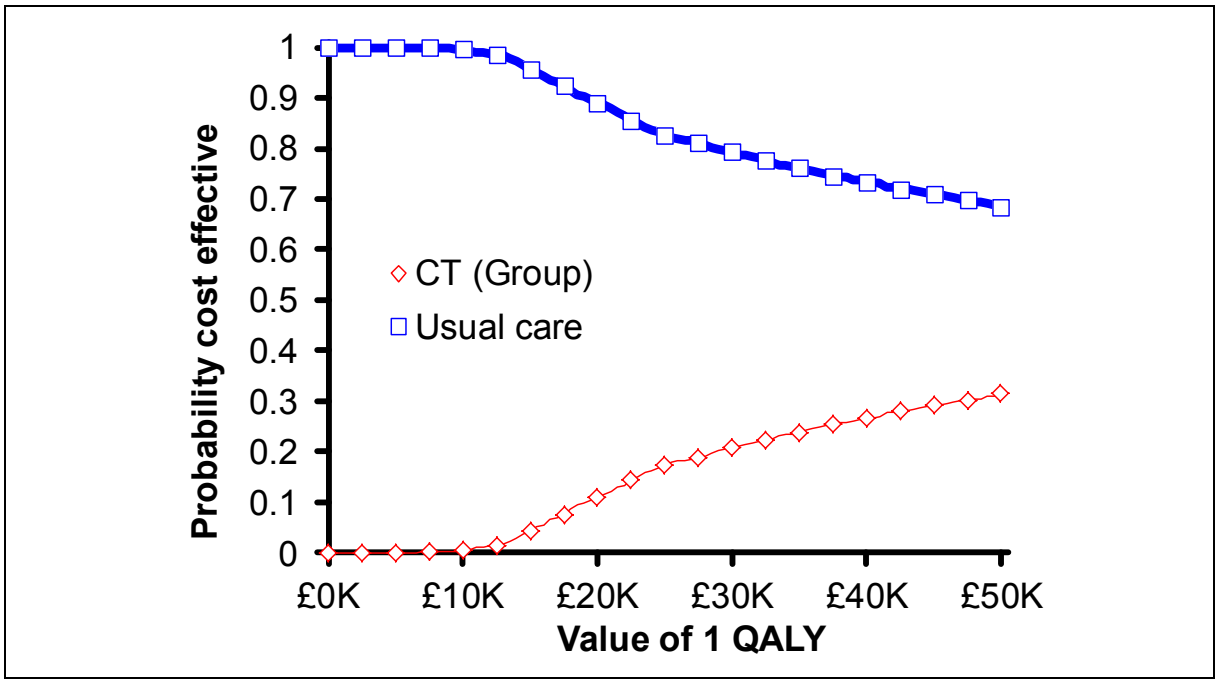


Figure 12: CEAC for group cognitive training versus control

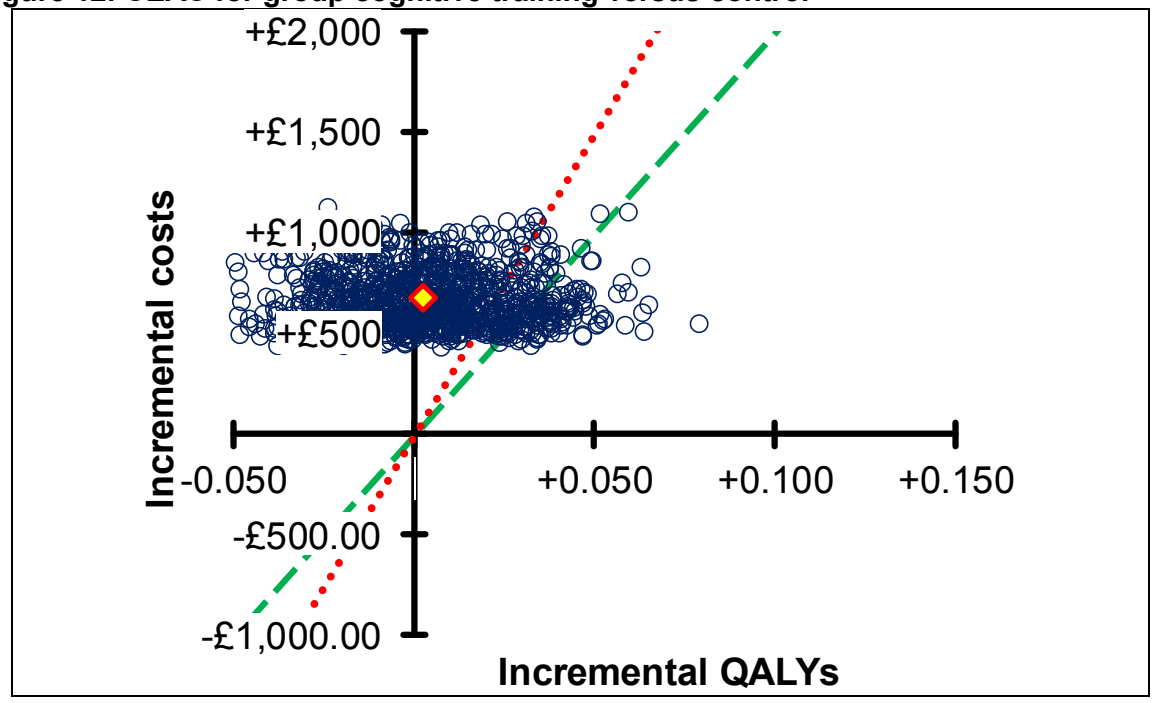


Figure 13: PSA for group cognitive training versus control

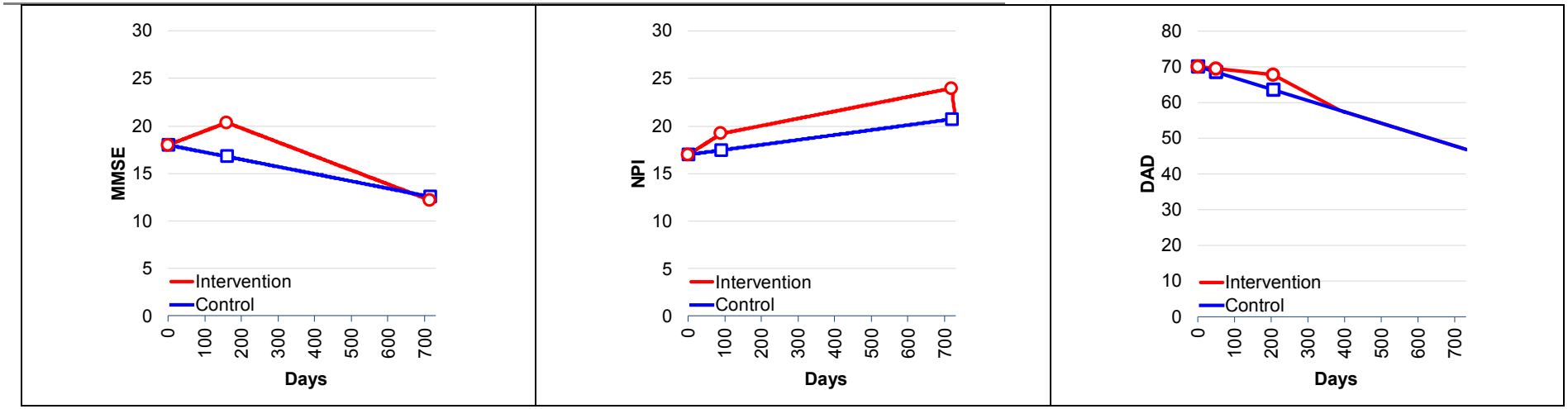


Figure 14: Change in clinical variables over time for group cognitive training versus usual care

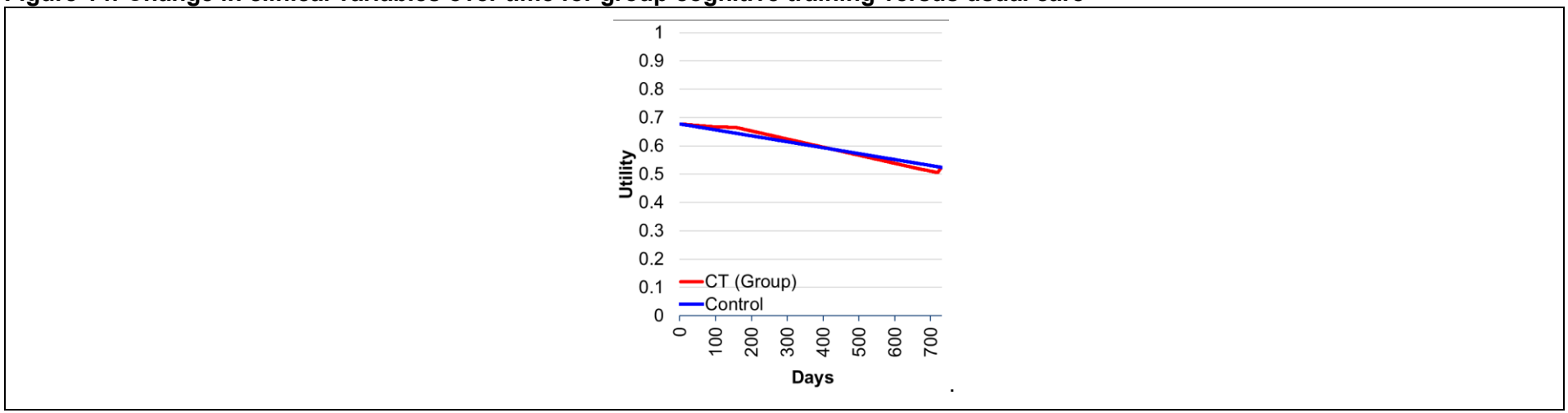


Figure 15: Estimated health-related quality of life as a function of clinical variables over time for group cognitive training versus usual care

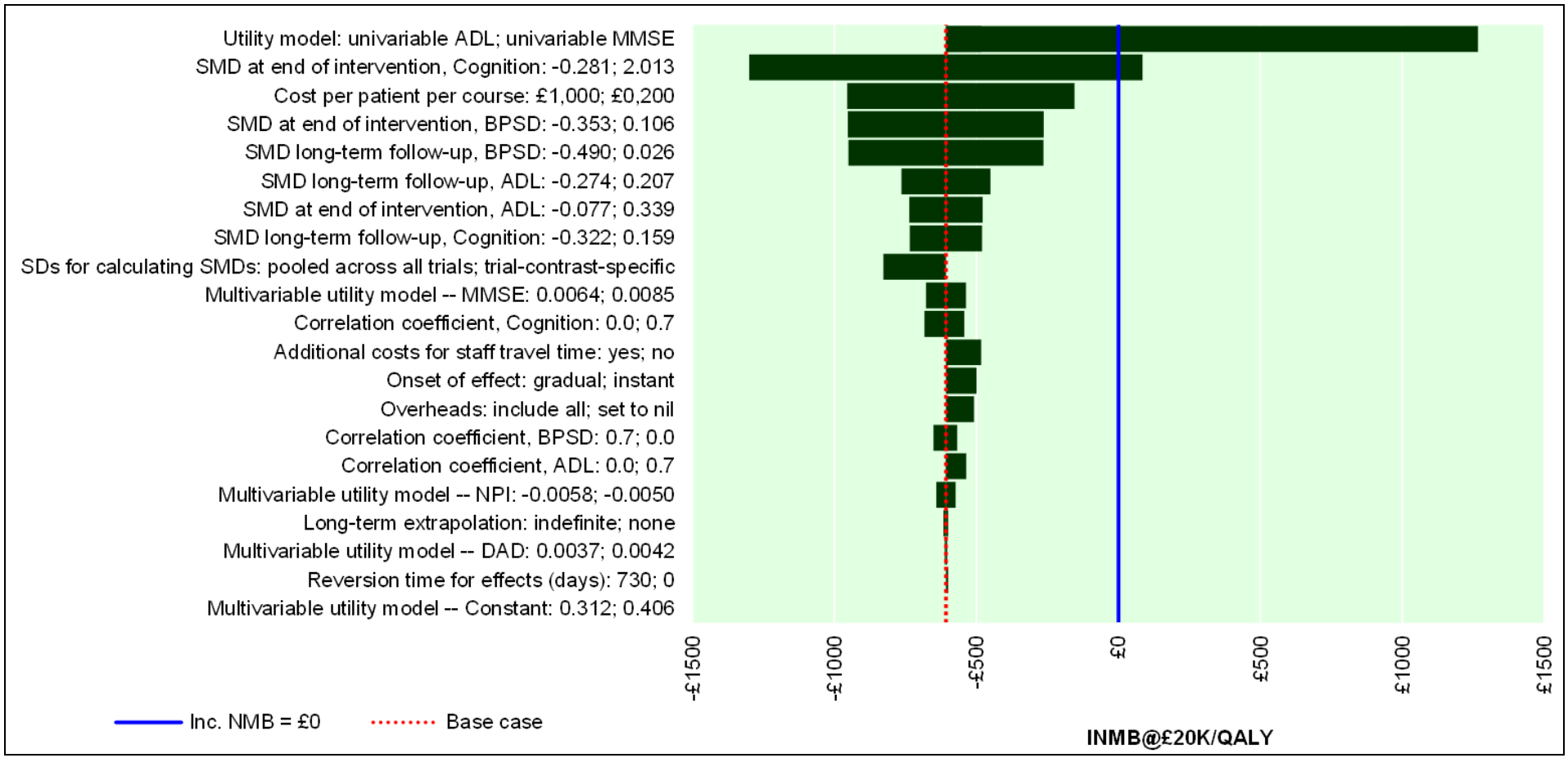


Figure 16: One-way sensitivity-analysis for group cognitive training versus control

J.4.1.4 Group reminiscence therapy

Effectiveness inputs (Figure 19) showed that reminiscence therapy is associated with a point-estimate benefit in the cognitive domain, a point-estimate harm in the behavioural domain and a point estimate of no change relative to control in the functional domain (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 20), that amounts to a benefit of almost zero points on the utility scale over the 700-day period.

Reminiscence therapy in a group setting relative to control was dominated in the base case, and had high ICERs in the univariable MMSE and ADCS-ADL models (Table 25). One-way sensitivity analysis found that the model was most sensitive to a lower cost per participant per course; however, variations to any single parameter did not result in ICERs below a £20,000/QALY threshold.

Table 25: Incremental costs and effects for group reminiscence therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£964	1.160	£964	-0.004	dominated	-£74
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£964	1.087	£964	0.018	£52,853	£365
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£964	1.032	£964	0.001	£809,456	£24

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 17) suggested that the probability that intervention is cost-effective is around 0%, if QALYs are valued at £20,000 each, or 0%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 18) shows that almost all iterations of reminiscence therapy in a group setting versus control cost between £750 and £1,250, whilst the number of QALYs generated were distributed tighly betwteen -0.050 and 0.050.

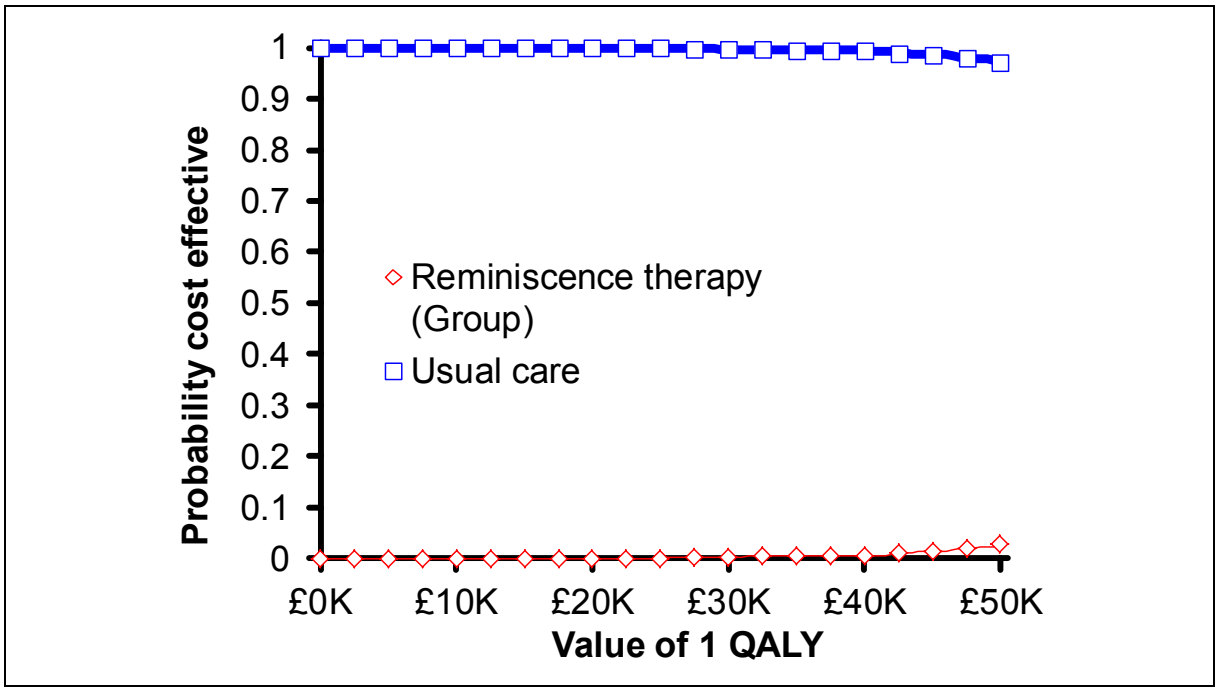


Figure 17: CEAC for group reminiscence therapy versus control

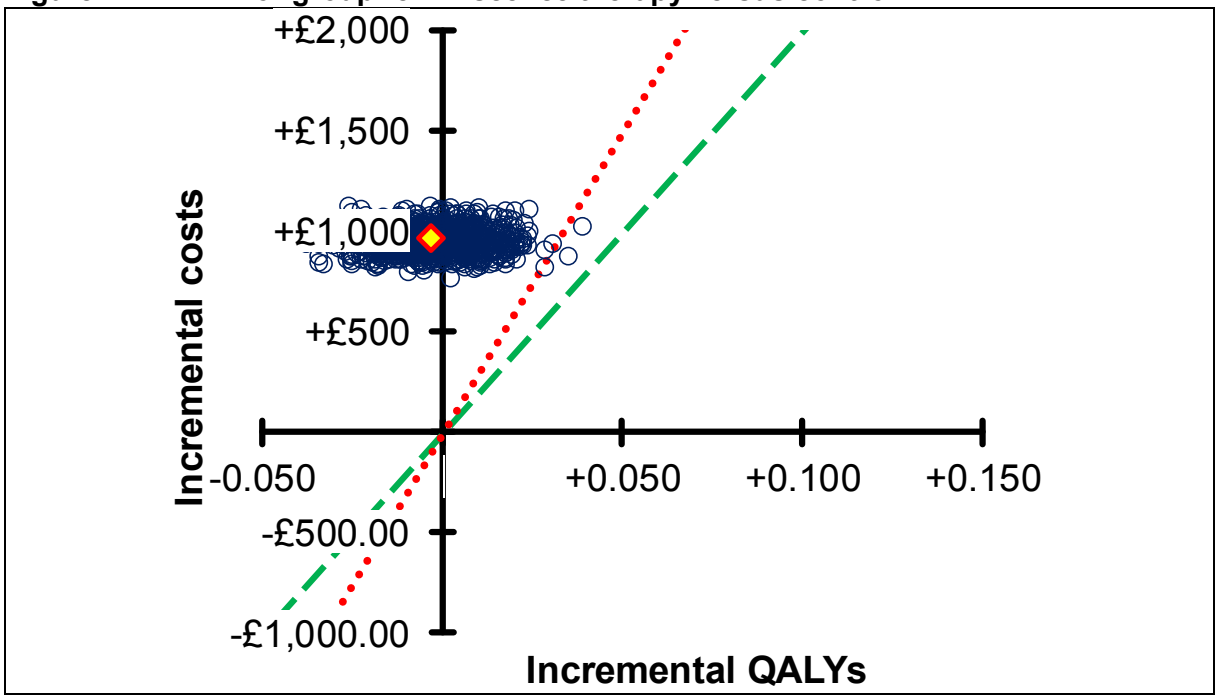


Figure 18: PSA for group reminiscence therapy versus control

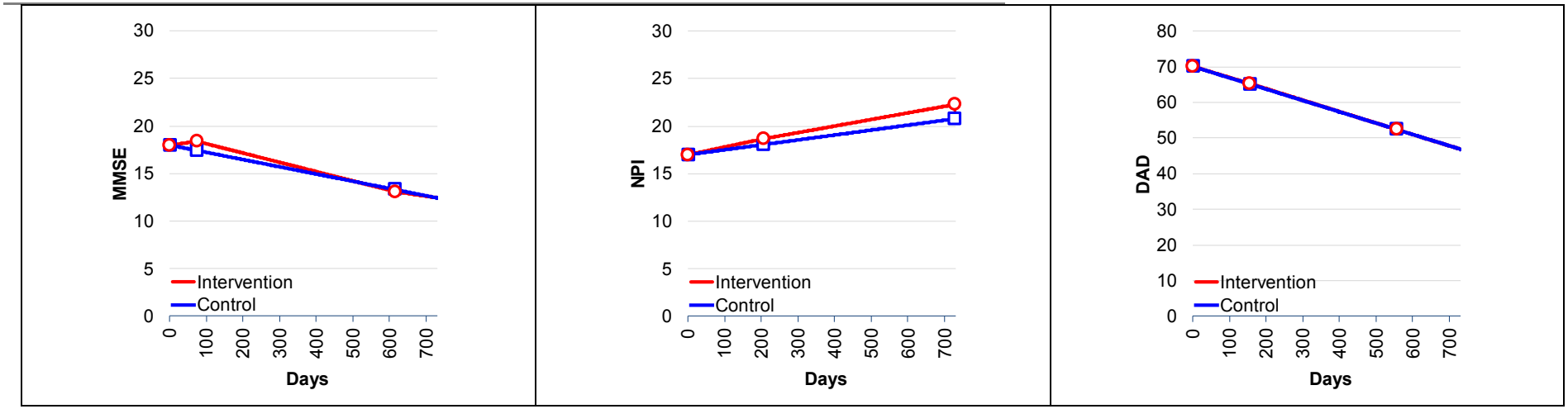


Figure 19: Change in clinical variables over time for reminiscence therapy versus usual care

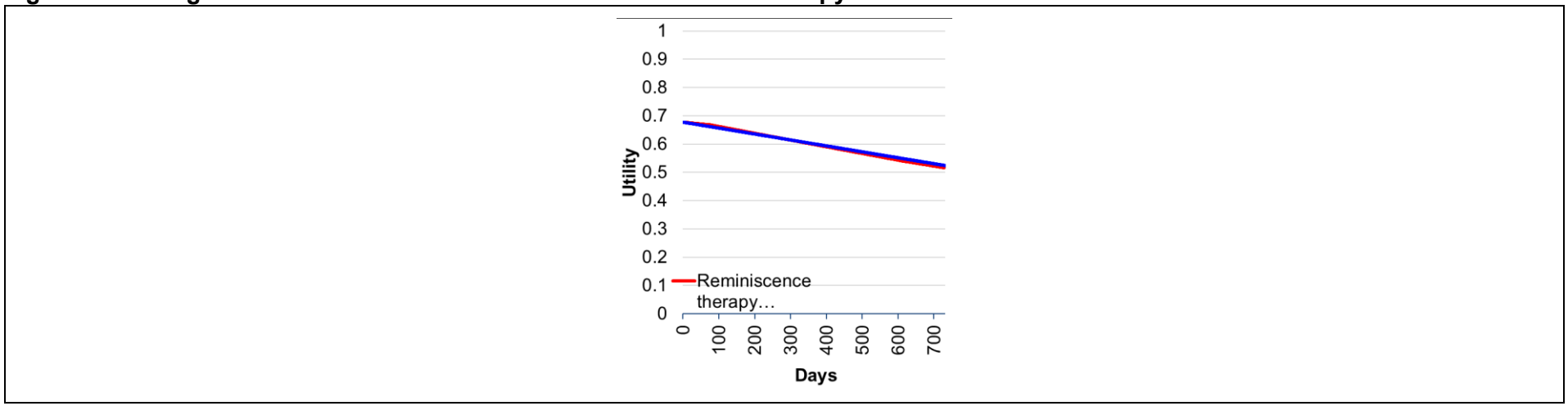


Figure 20: Estimated health-related quality of life as a function of clinical variables over time for reminiscence therapy versus usual care

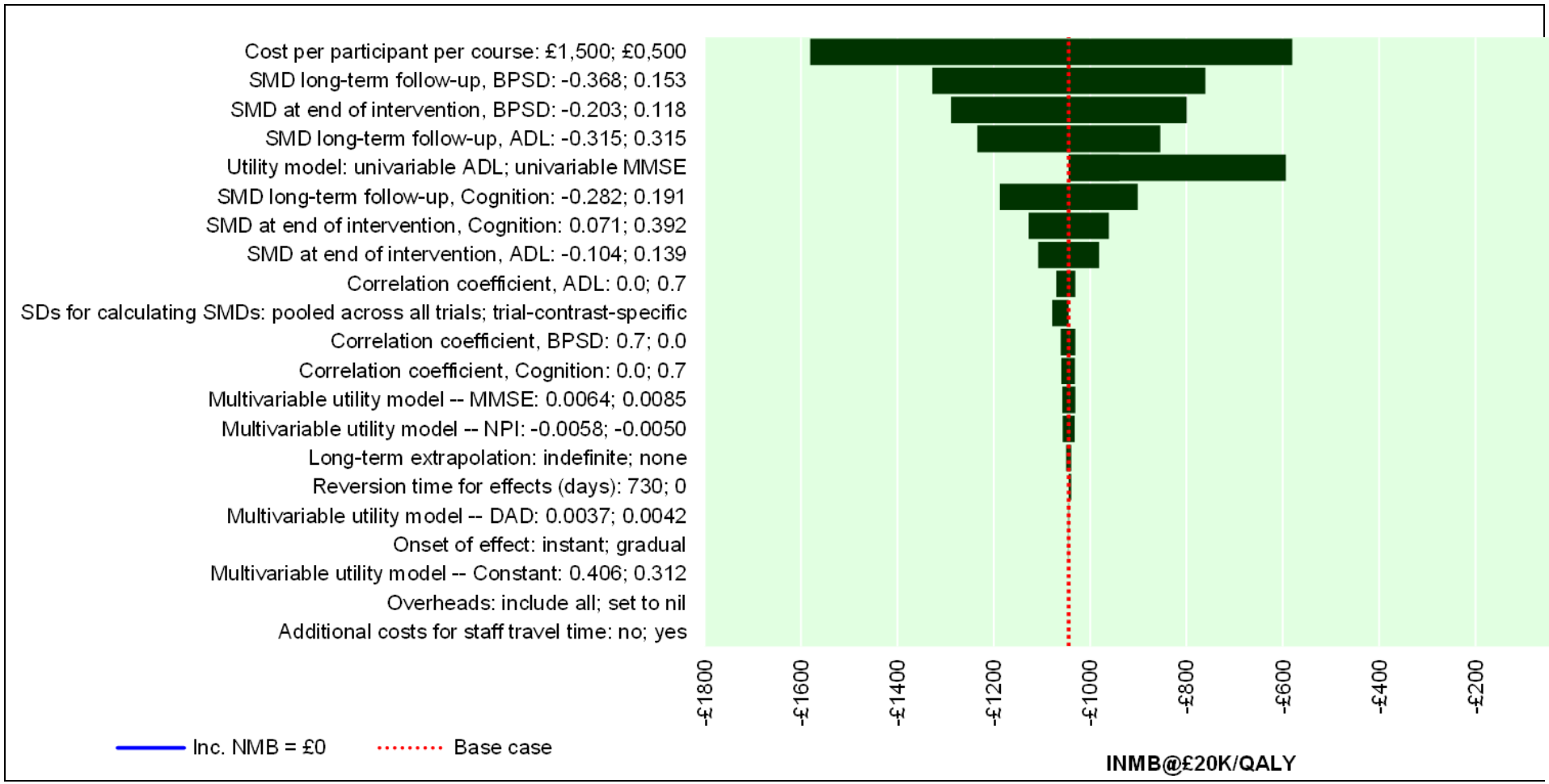


Figure 21: One-way sensitivity-analysis for group reminiscence therapy versus control

J.4.1.5 One-to-one exercise therapy

Effectiveness inputs (Figure 24) showed that one-to-one exercise therapy is associated with point-estimate benefits in cognitive, functional and behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 25), that amounts to a benefit that lasts for a little under a year and, at its greatest, exceeds 0.05 points on the utility scale, after which people in the intervention arm experience a small disutility for just over half a year.

The base-case model suggested that one-to-one exercise therapy was associated with a benefit of a little over 0.023 QALYs relative to control, at an additional cost of £1,776, leading to an ICER of £76,678/QALY (Table 26). One-way sensitivity analysis found that the model was most sensitive to a lower cost per course of individualised exercise therapy, but would still not make individualised exercise therapy a cost-effective treatment at the £20,000/QALY threshold.

Table 26: Incremental costs and effects for one-to-one exercise therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,776	1.187	£1,776	0.023	£76,678	£463
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£1,776	1.101	£1,776	0.032	£55,573	£639
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£1,776	1.058	£1,776	0.027	£65,402	£543

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 22) suggested that the probability that intervention is cost-effective is around 0%, if QALYs are valued at £20,000 each, or 2%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 23) shows that almost all iterations of one-to-one exercise therapy versus control cost between £1,250 and £2,250, whilst the number of QALYs generated were distributed mostly betwteen -0.025 and 0.075.

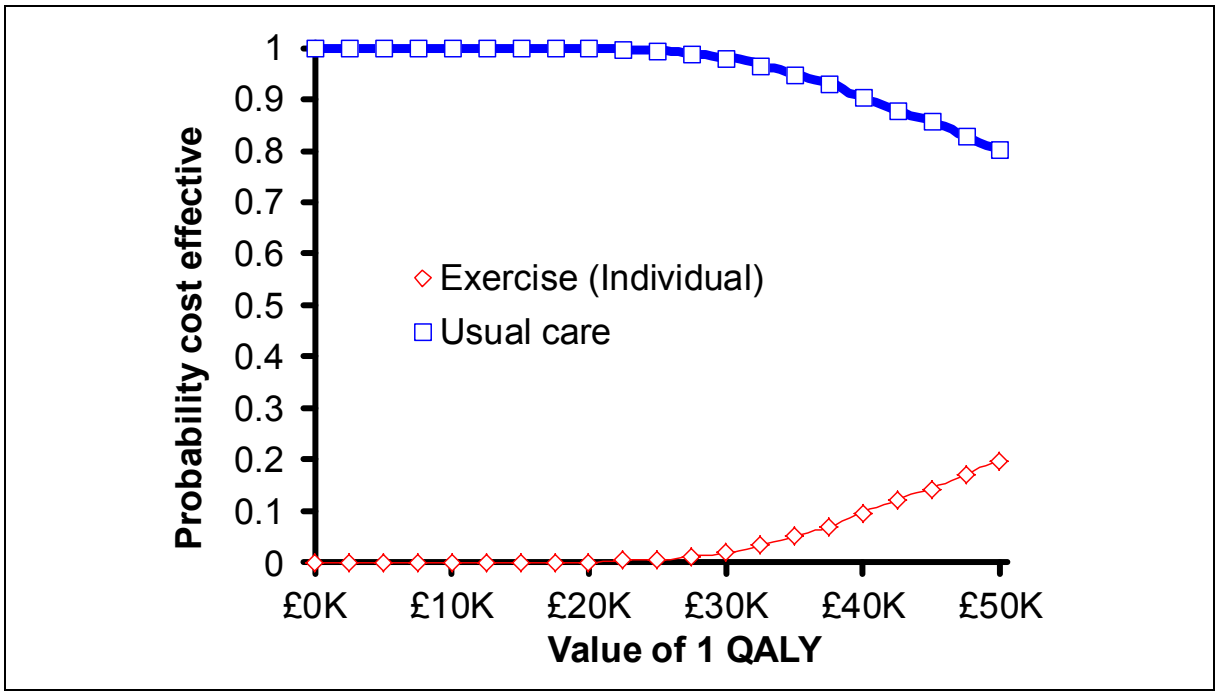


Figure 22: CEAC for one-to-one exercise therapy versus control

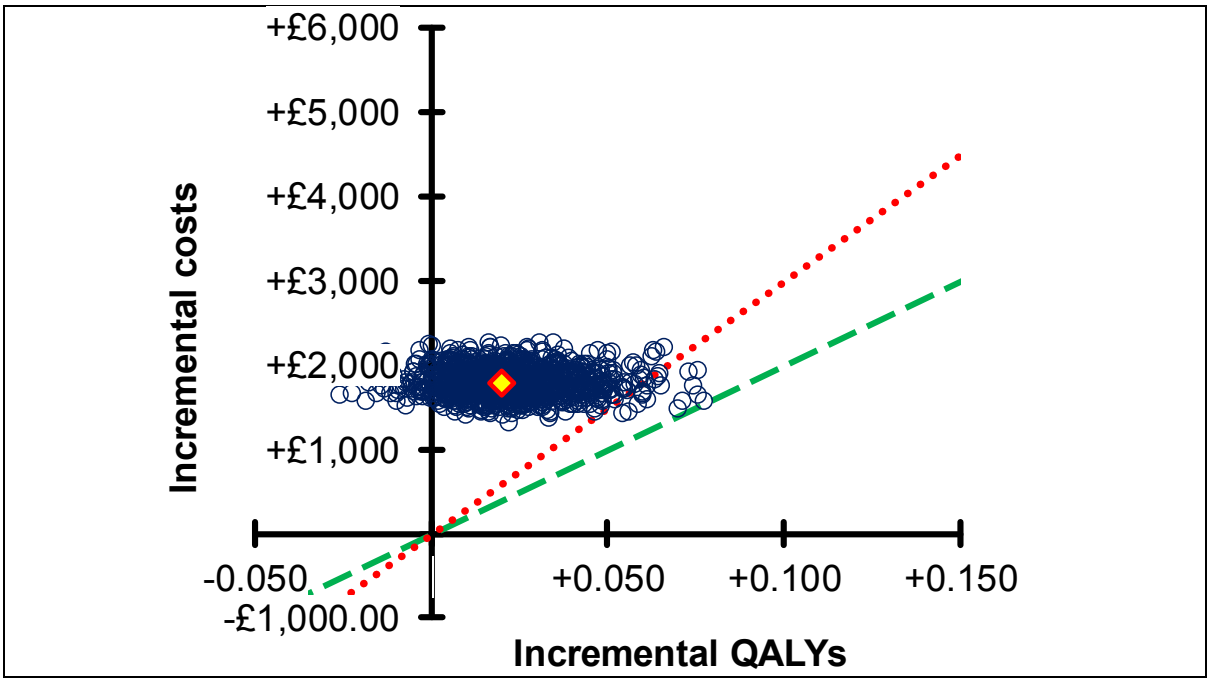


Figure 23: PSA for one-to-one exercise therapy versus control

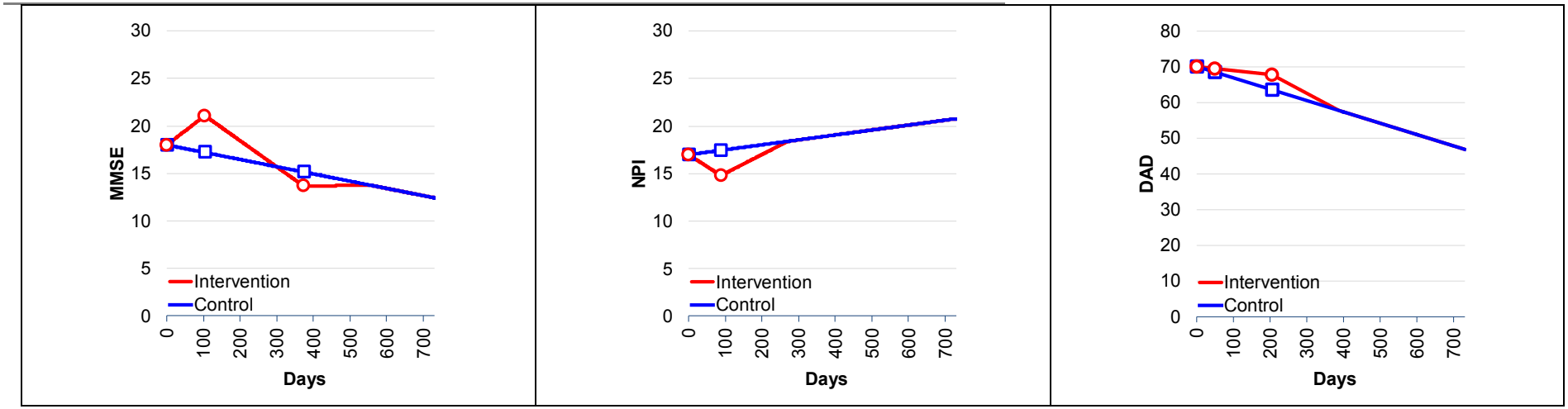


Figure 24: Change in clinical variables over time for one-to-one exercise therapy versus usual care

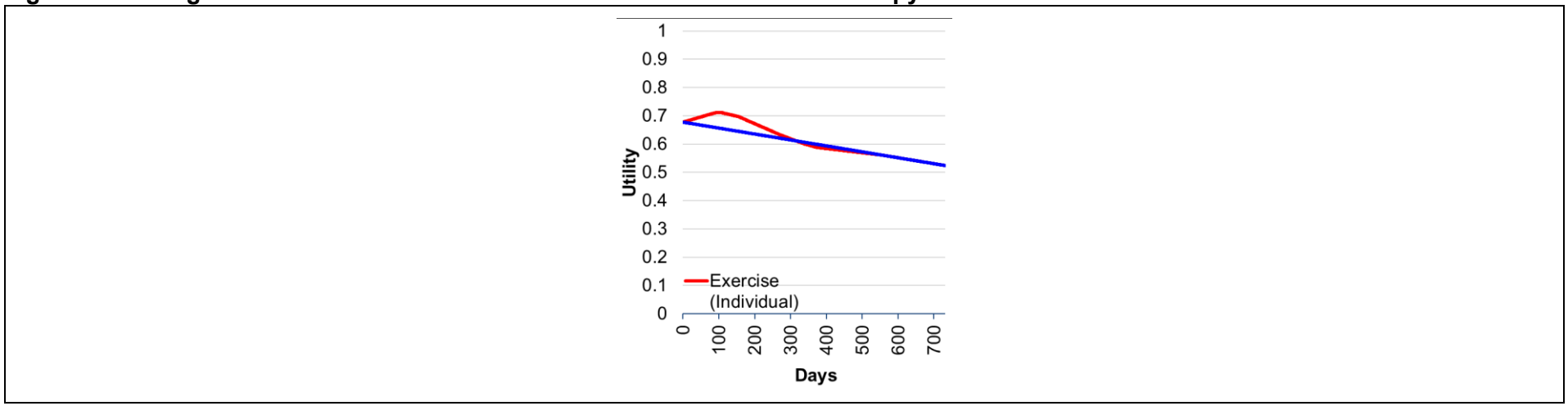


Figure 25: Estimated health-related quality of life as a function of clinical variables over time for one-to-one exercise therapy versus usual care

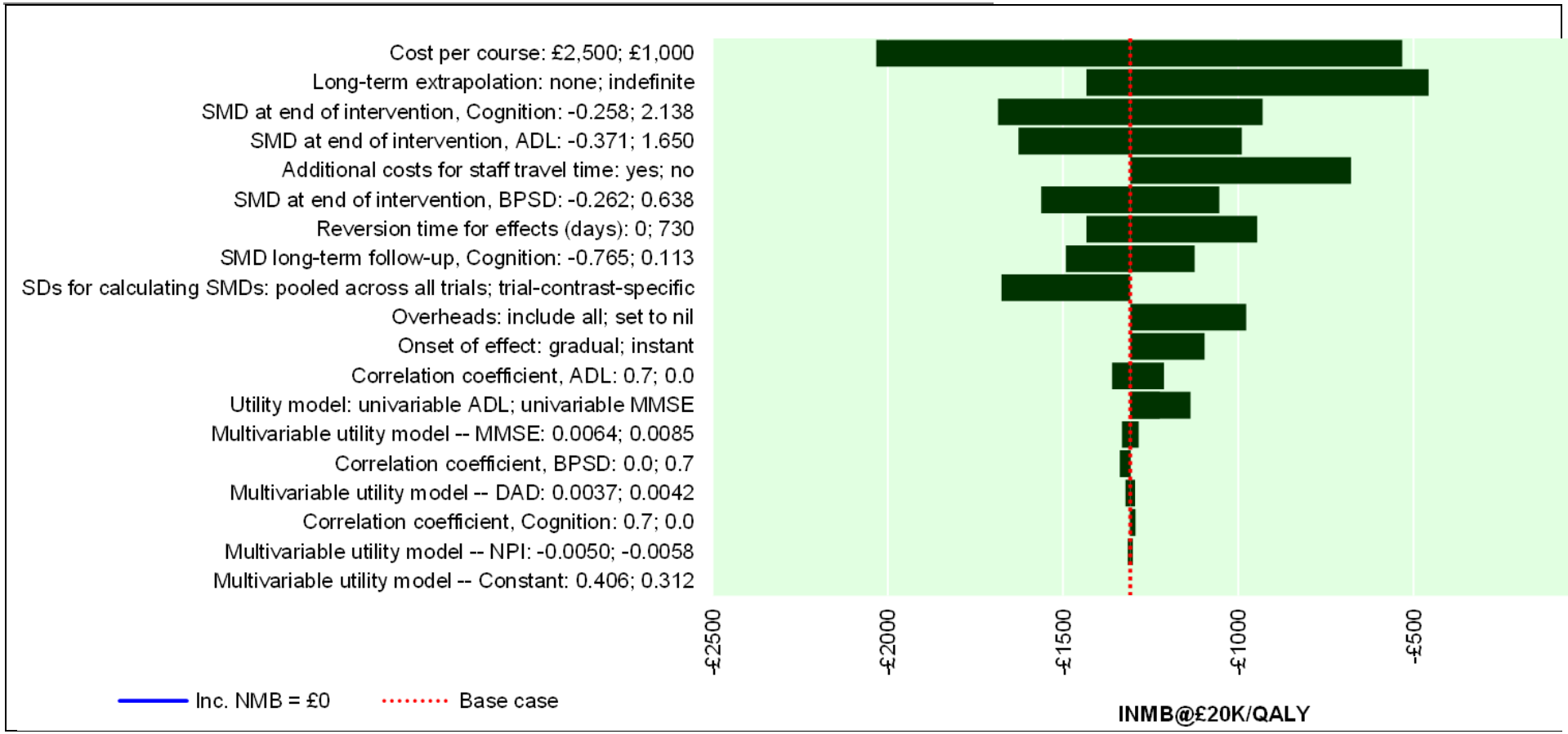


Figure 26: One-way sensitivity-analysis for one-to-one exercise therapy versus control

J.4.1.6 Group exercise therapy

Effectiveness inputs (Figure 29) showed that group exercise therapy is associated with point-estimate benefits in cognitive, functional and behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 30), that amounts to a benefit that lasts for a little over 16 months and, at its greatest, exceeds 0.06 points on the utility scale.

The base-case model suggested that group exercise therapy was associated with a benefit of a little over 0.042 QALYs relative to control, at an additional cost of £1,727, leading to an ICER of £41,359/QALY (Table 27). One-way sensitivity analysis found that the model was most sensitive to the cost per group session but only the indefinite long-term extrapolation scenario resulted in an ICER lower than £20,000/QALY.

Table 27: Incremental costs and effects for group exercise versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,727	1.206	£1,727	0.042	£41,359	£835
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£1,727	1.124	£1,727	0.054	£31,791	£1,087
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£1,727	1.049	£1,727	0.019	£92,373	£374

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 27) suggested that the probability that intervention is cost-effective is around 15%, if QALYs are valued at £20,000 each, or 22%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 28) shows iterations of group exercise therapy versus control cost had costs widely distributed between £0 and £6,000 – this was mostly because the number of sessions delivered was extremely variable (ranging from 6 to 156) in the underlying evidence. The QALYs generated were distributed mostly between 0.025 and 0.075.

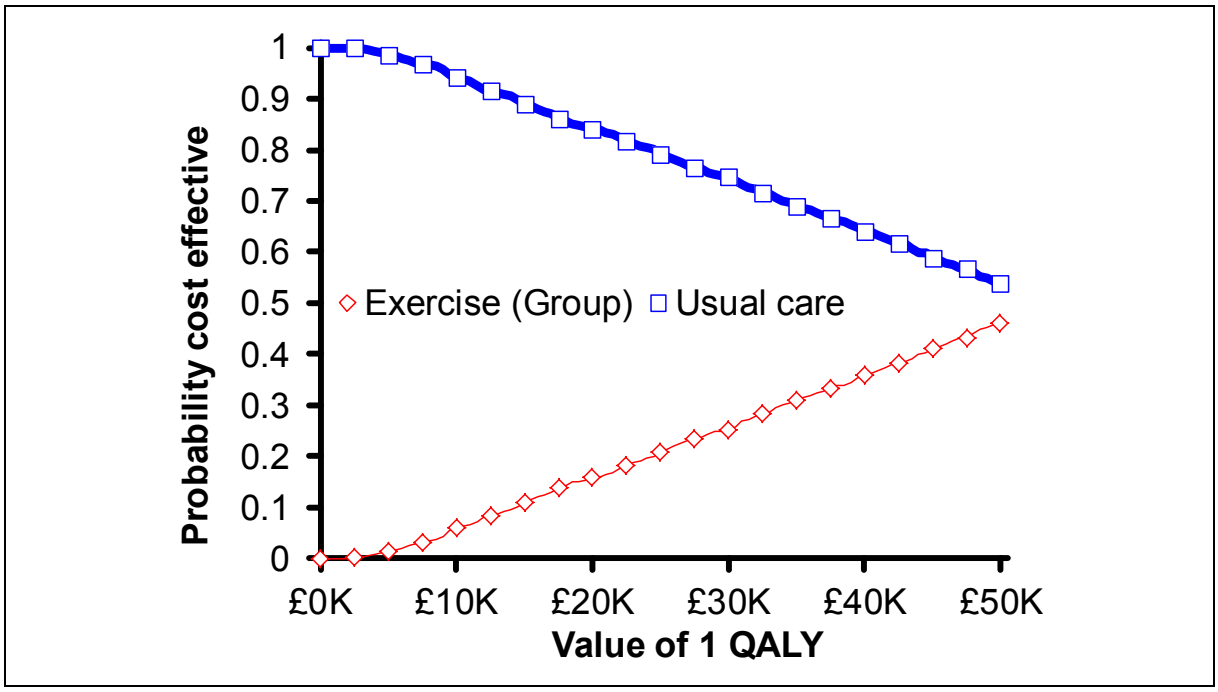


Figure 27: CEAC for group exercise versus control

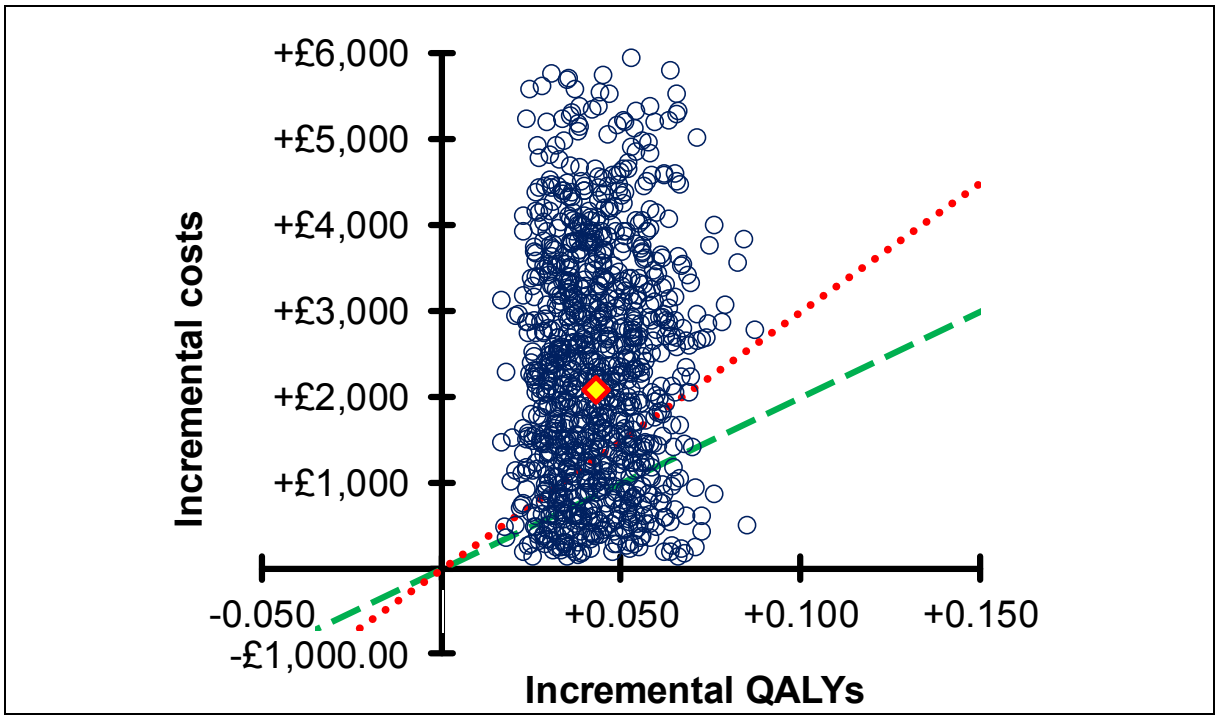


Figure 28: PSA for group exercise versus control

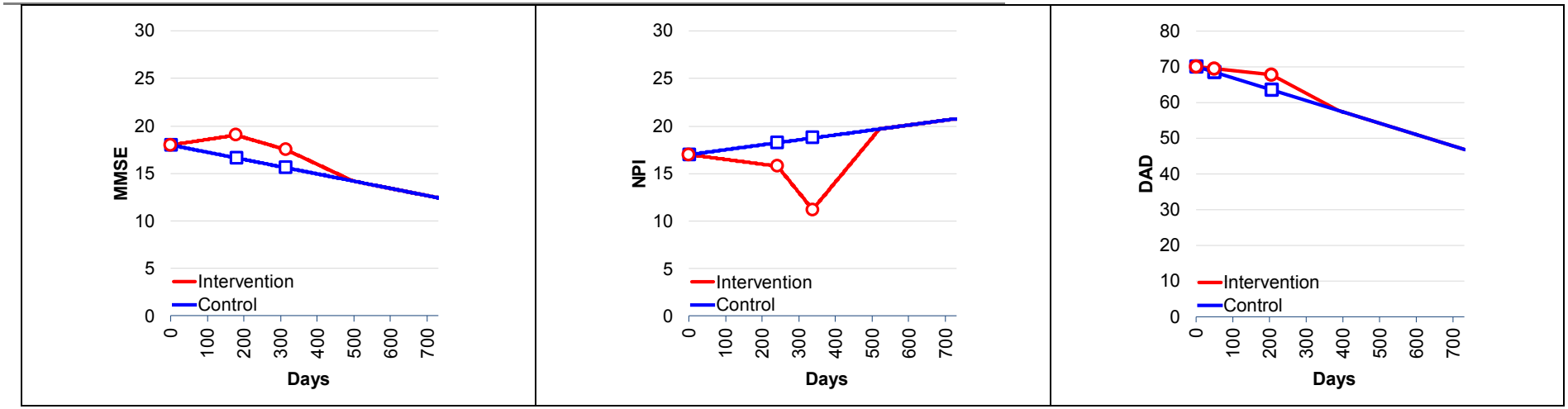


Figure 29: Change in clinical variables over time for group exercise versus usual care

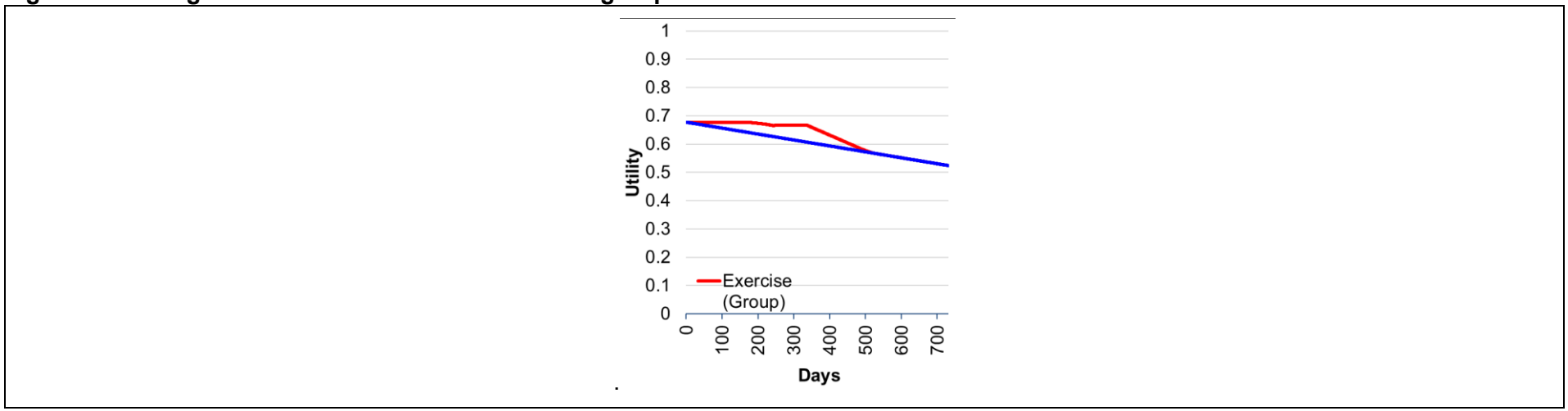


Figure 30: Estimated health-related quality of life as a function of clinical variables over time for group exercise versus usual care

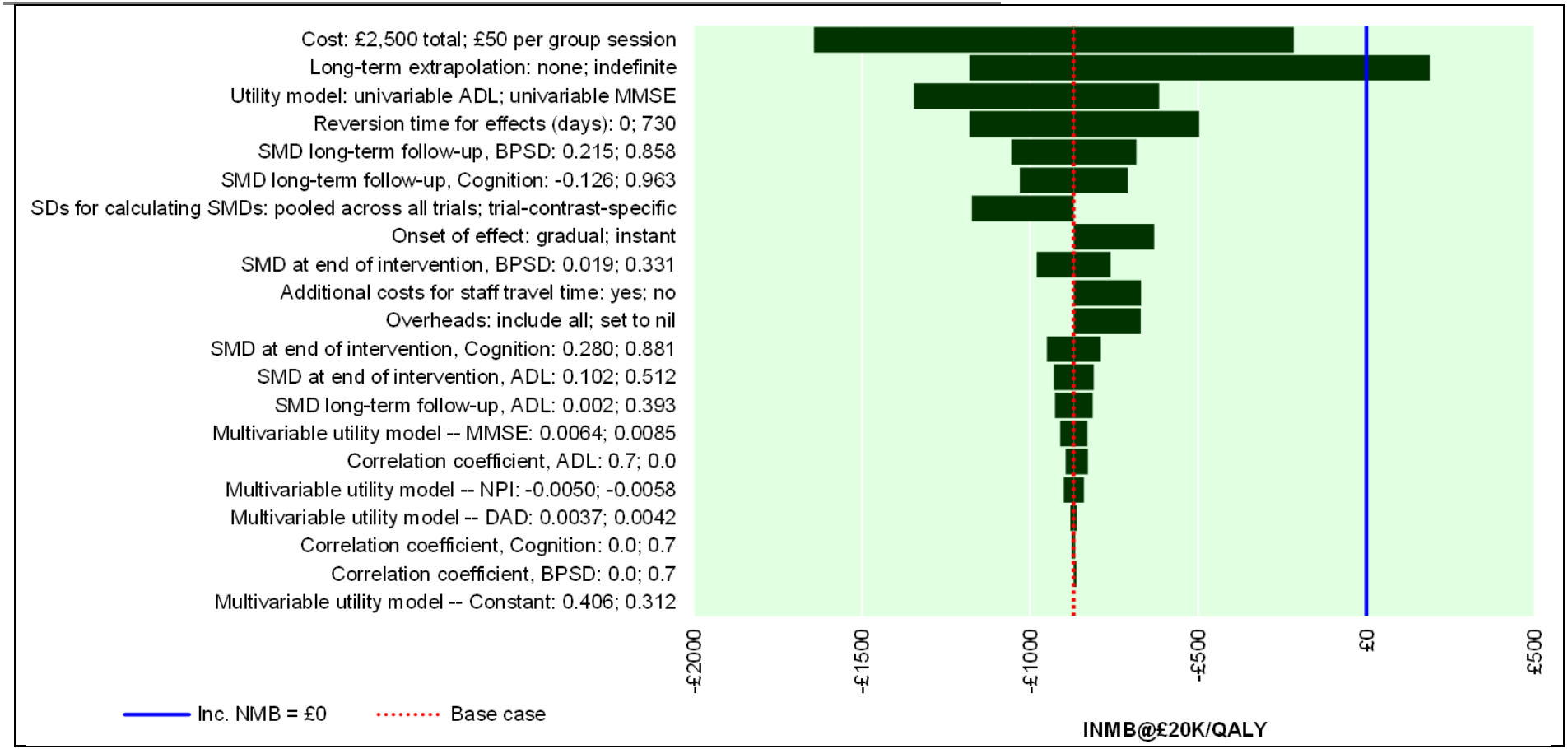


Figure 31: One-way sensitivity-analysis for group exercise versus control

J.4.1.7 Group exercise therapy for people with severe dementia

Effectiveness inputs (Figure 34) showed that group exercise therapy for people with severe dementia is associated with a point-estimate benefit on the functional domain, whilst no point-estimate change relative to control was observed for the cognitive or behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 35), that amounts to a benefit, at its greatest, of almost 0.001 points on the utility scale over the two year follow up period.

The base-case model suggested that group exercise therapy for people with severe dementia was associated with a benefit of a little over 0.05 QALYs relative to control, at an additional cost of £1,510, leading to an ICER of £329,685/QALY (Table 28). One-way sensitivity analysis found that the model was most sensitive to the cost per patient per course, but no parameter variations suggested that the intervention would cost effective at a £20,000/QALY threshold.

Table 28: Incremental costs and effects for group exercise therapy for people with severe dementia versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,510	1.168	£1,510	0.005	£329,685	£92
Univariable model (MMSE)						
Control	–	–				
Intervention	–	–	–	–	–	–
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£1,510	1.045	£1,510	0.014	£105,987	£285

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 32) suggested that the probability that intervention is cost-effective is around 0%, if QALYs are valued at £20,000 each, or 0%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 33) shows iterations of group exercise therapy for people with severe dementia versus control cost had costs distributed mostly between £750 and £5,000, whilst the number of QALYs generated were distributed mostly betwteen -0.050 and 0.050.

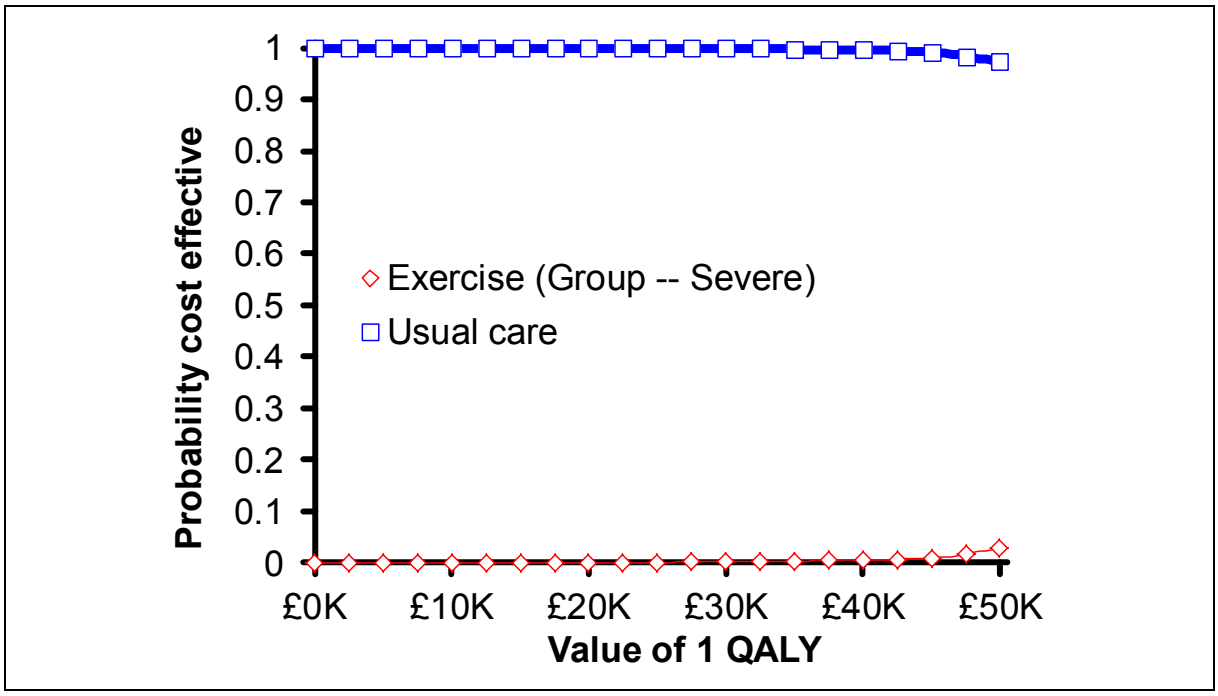


Figure 32: CEAC for group exercise therapy for people with severe dementia versus control

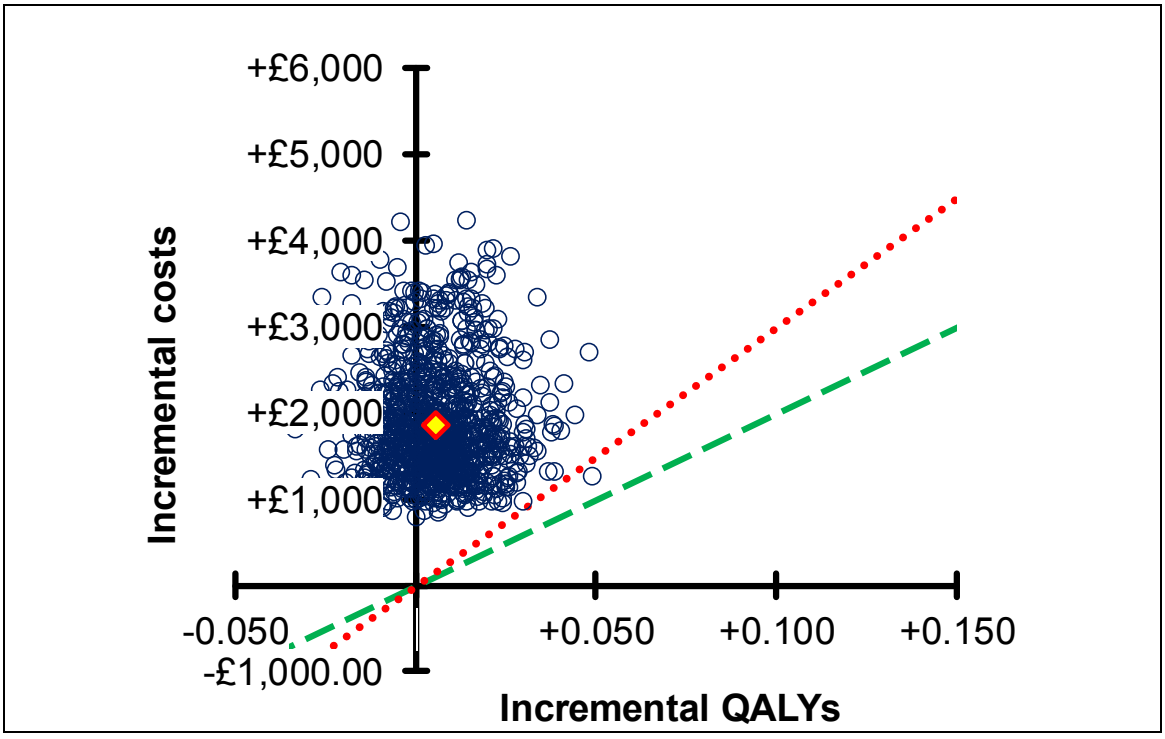


Figure 33: PSA for exercise therapy for people with severe dementia versus control

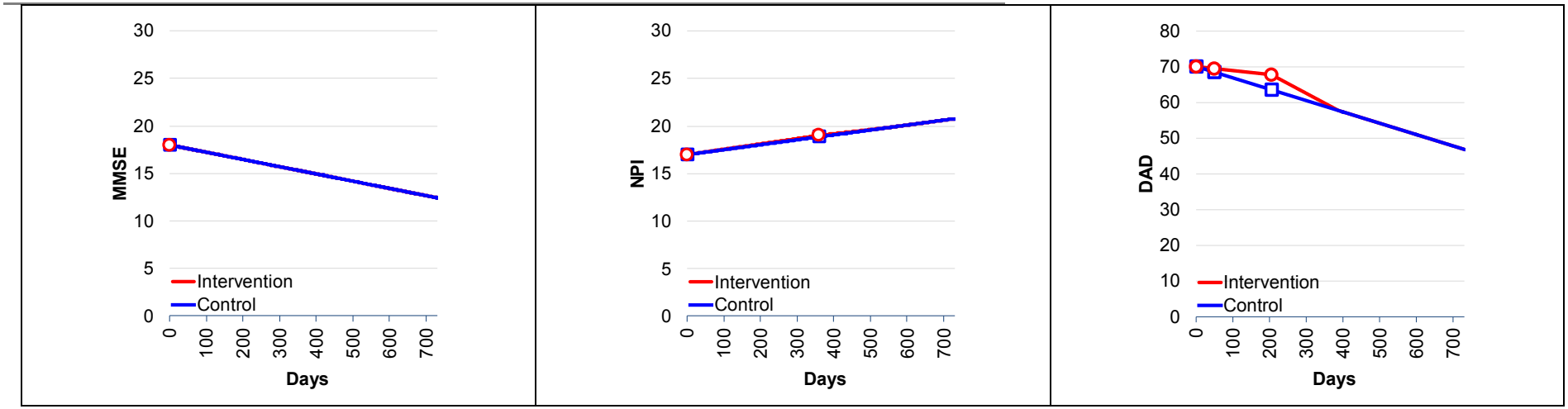


Figure 34: Change in clinical variables over time for exercise therapy for people with severe dementia versus usual care

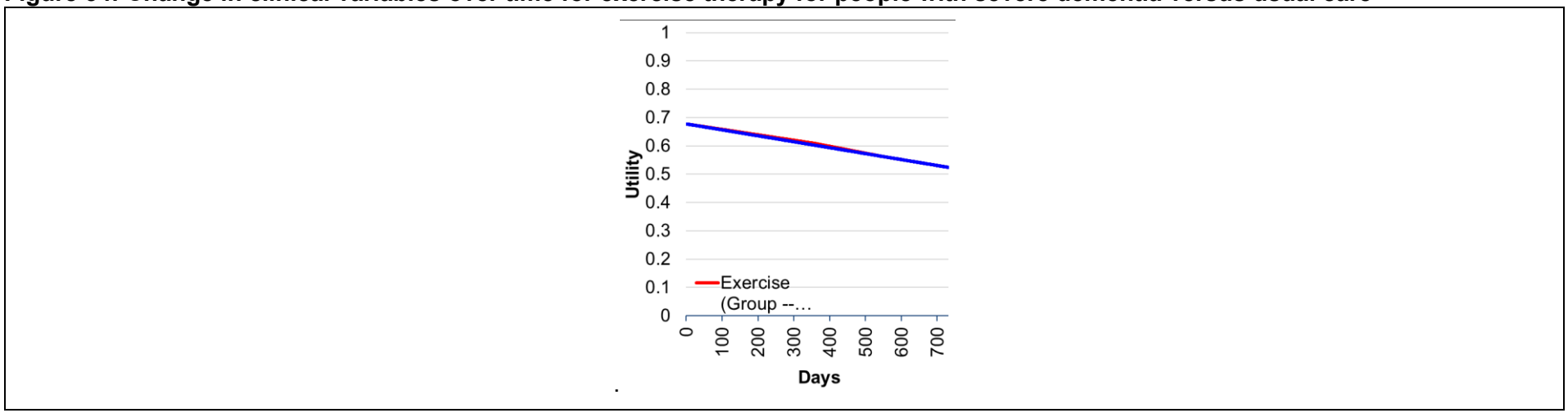


Figure 35: Estimated health-related quality of life as a function of clinical variables over time for exercise therapy for people with severe dementia versus usual care

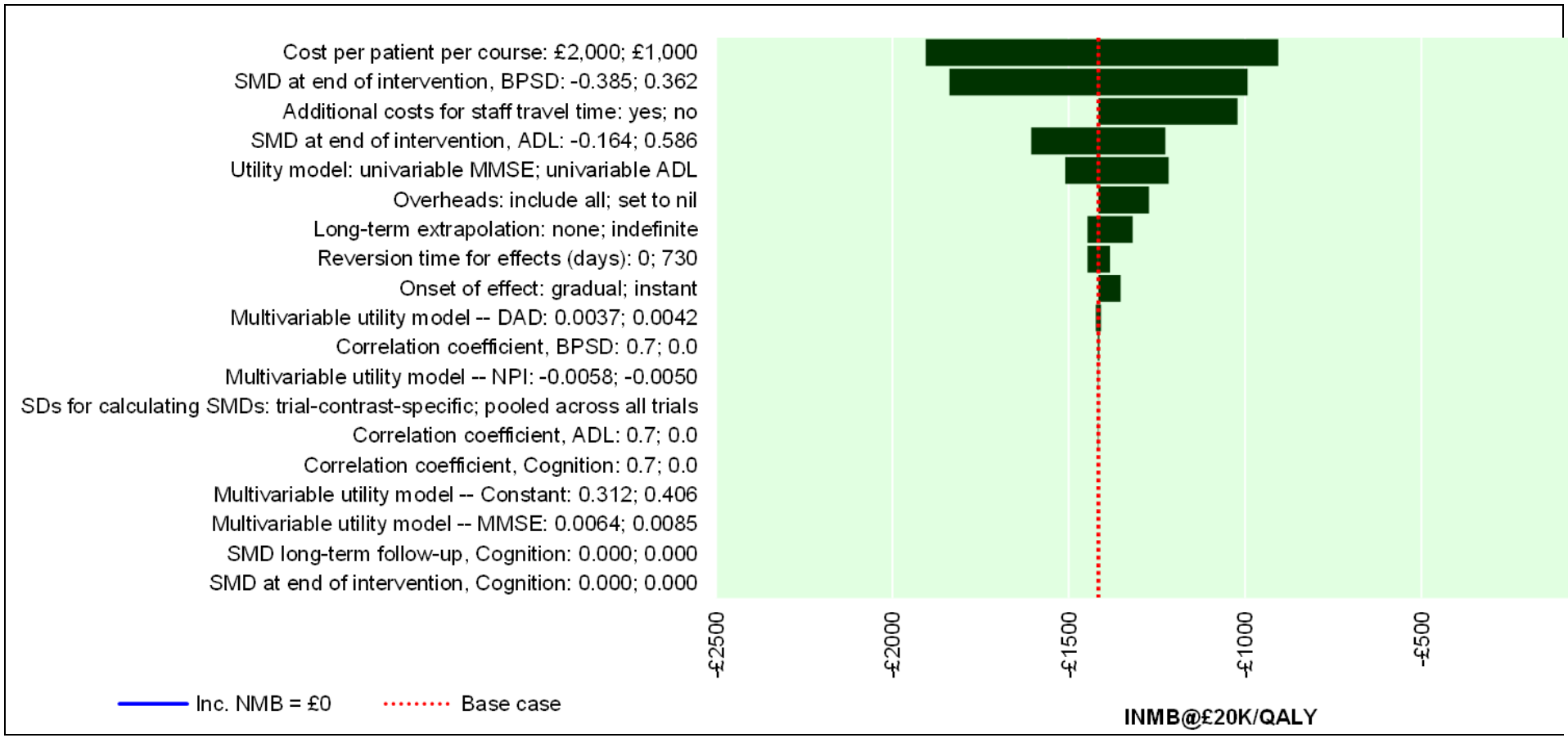


Figure 36: One-way sensitivity-analysis for exercise therapy for people with severe dementia versus control

J.4.1.8 Group music therapy (participatory)

Effectiveness inputs (Figure 39) showed that participatory group music therapy is associated with point-estimate benefits in cognitive, functional and behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 40), that amounts to a benefit that lasts for a little over 9 months and, at its greatest, exceeds 0.04 points on the utility scale.

The base-case model suggested that participatory group music therapy was associated with a benefit of a little over 0.016 QALYs relative to control, at an additional cost of £434, leading to an ICER of £26,944/QALY (Table 29). One-way sensitivity analysis found that plausible variations to 8 parameters resulted in ICERs lower than £20,000/QALY, including those relating to long-term extrapolation of treatment effects, lower costs of treatment, and treatment effects at the upper 95% confidence interval of synthesised estimates.

Table 29: Incremental costs and effects for group music therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£434	1.180	£434	0.016	£26,944	£322
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£434	1.083	£434	0.014	£31,369	£276
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£434	1.059	£434	0.028	£15,599	£556

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 37) suggested that the probability that intervention is cost-effective is around 22%, if QALYs are valued at £20,000 each, or 40%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 38) shows iterations of group music therapy versus control cost had costs distributed mostly between £250 and £1,000, whilst the number of QALYs generated were distributed mostly betwteen -0.025 and 0.075.

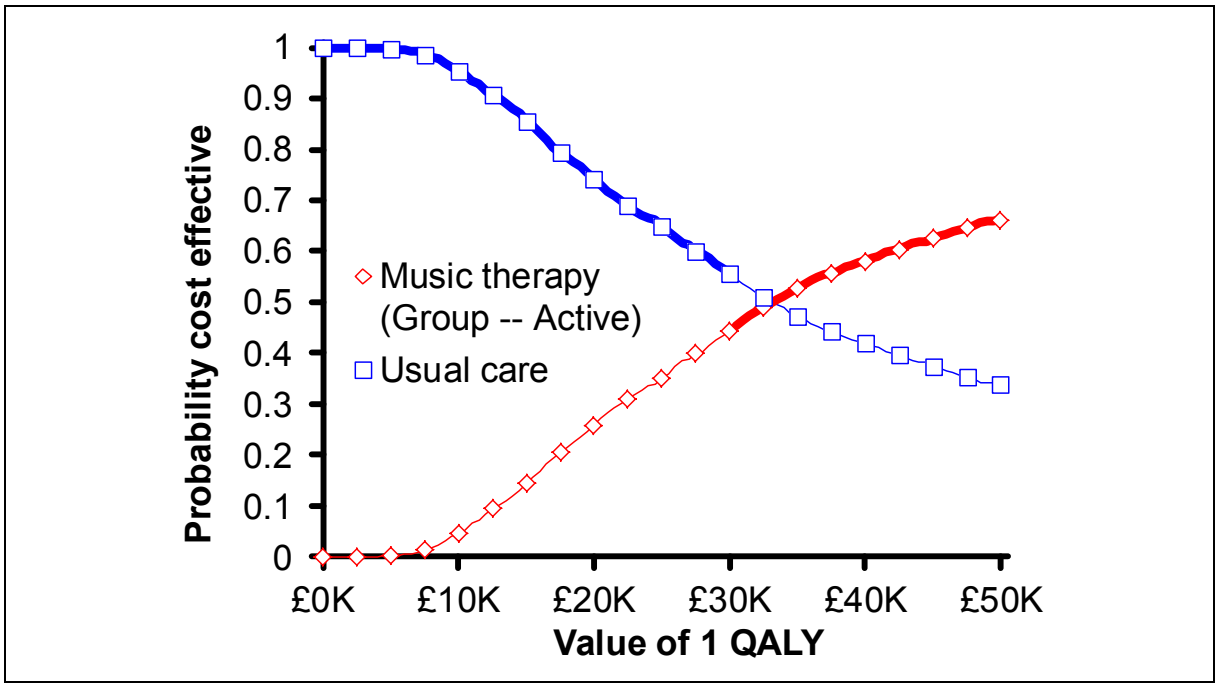


Figure 37: CEAC for group music therapy versus control

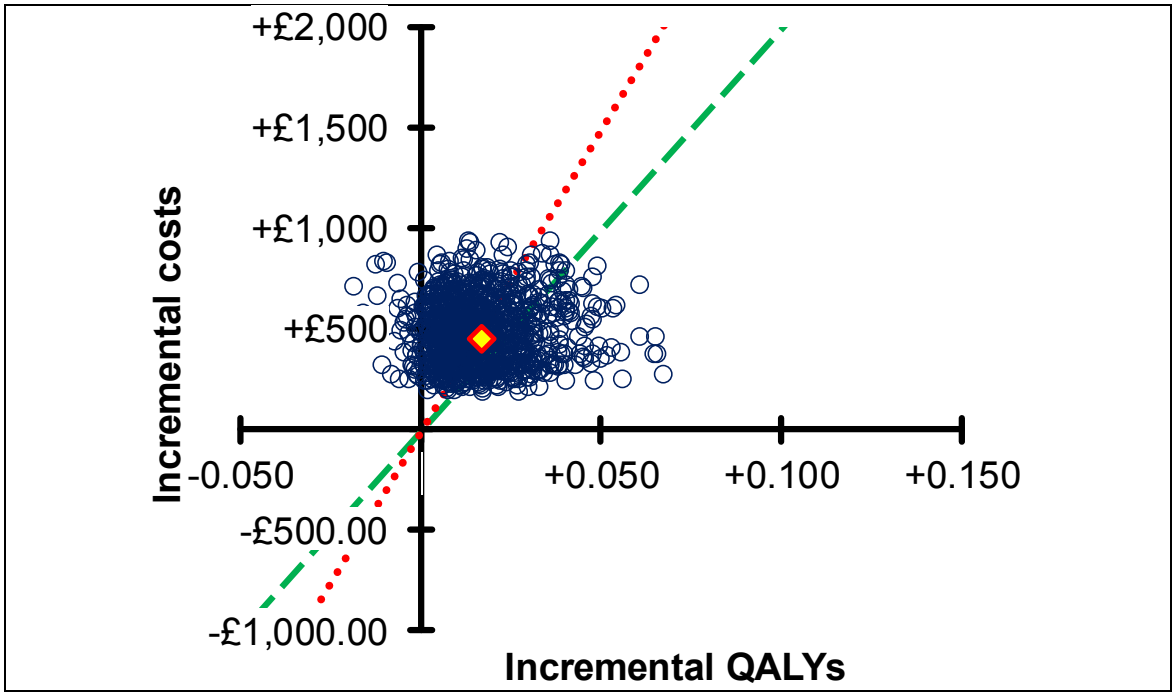


Figure 38: PSA for group music therapy versus control

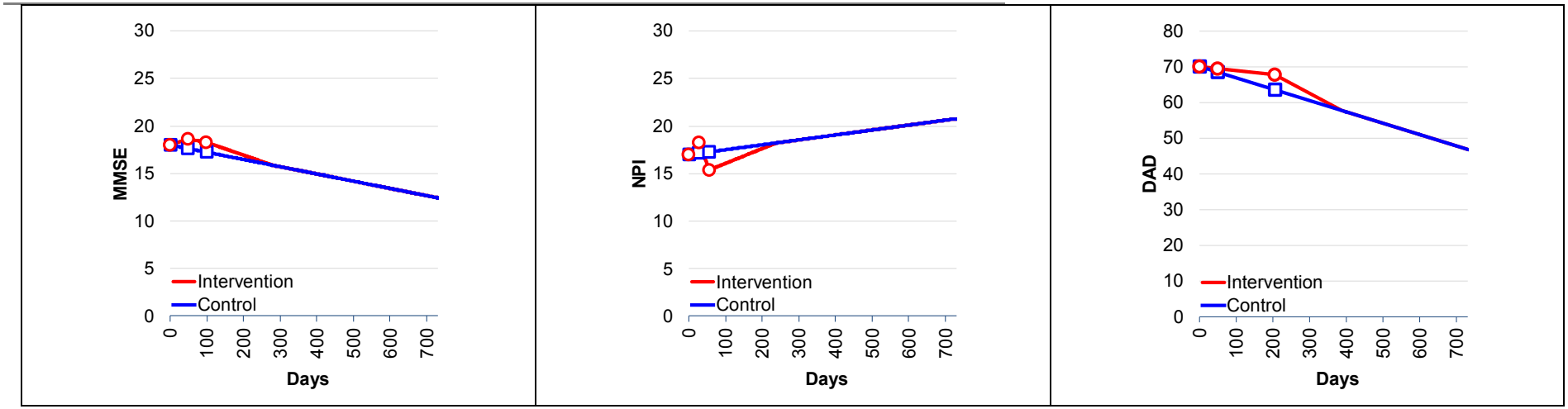


Figure 39: Change in clinical variables over time for group music therapy versus usual care

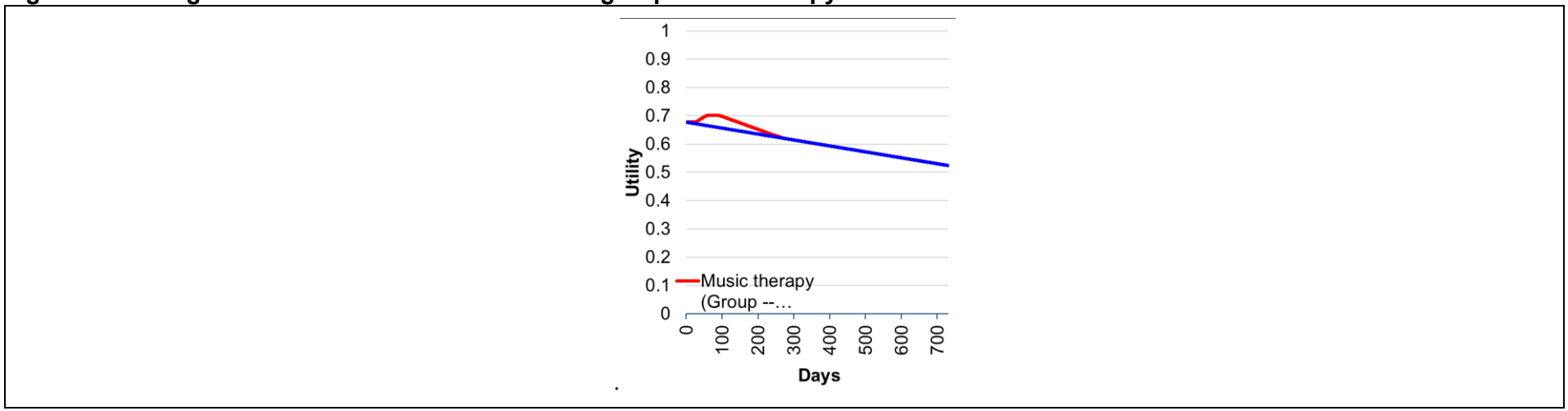


Figure 40: Estimated health-related quality of life as a function of clinical variables over time for group music therapy versus usual care

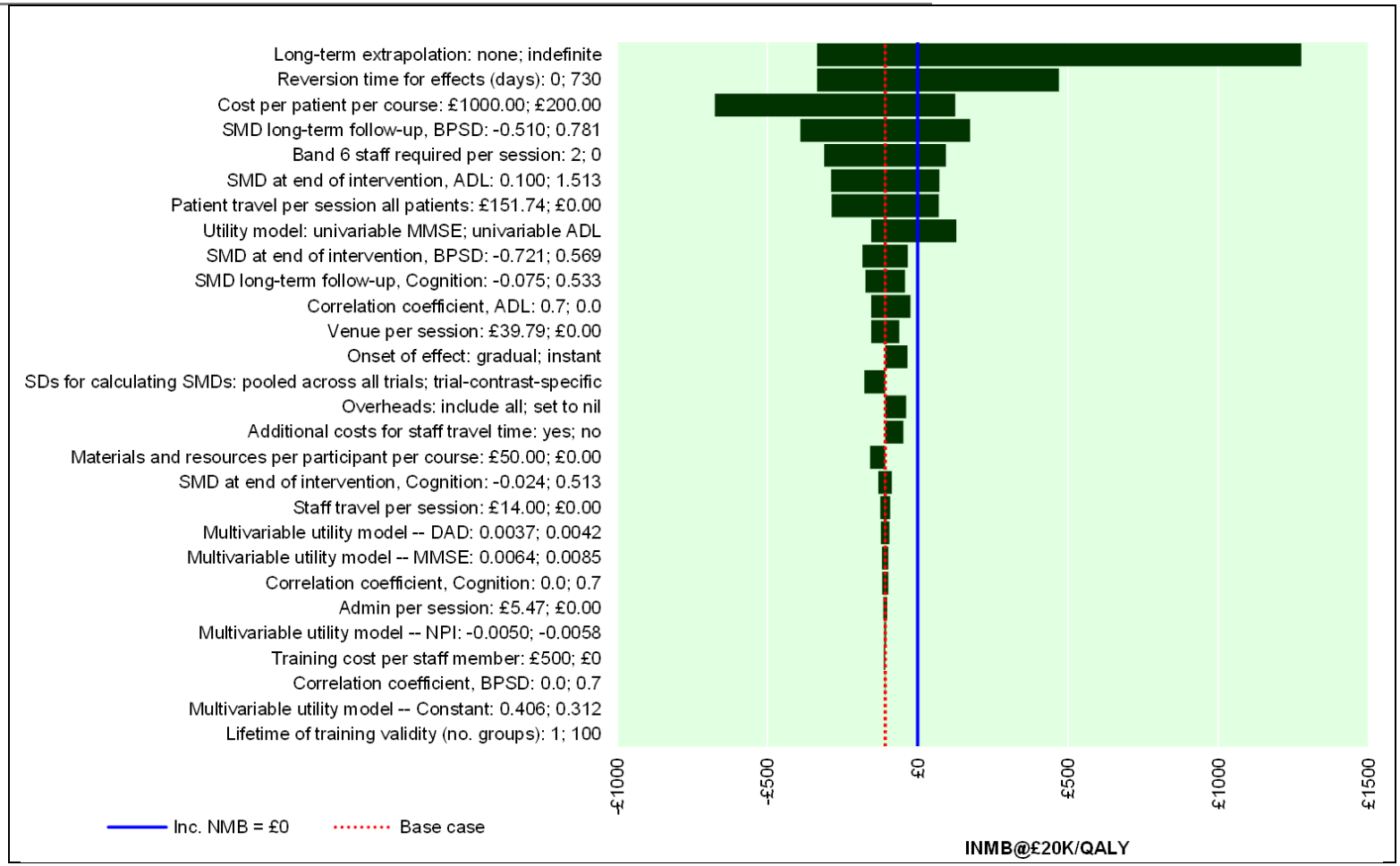


Figure 41: One-way sensitivity-analysis for group music therapy versus control

J.4.1.9 One-to-one music therapy

Effectiveness inputs (Figure 44) showed that one-to-one music therapy is associated with point-estimate benefits in cognitive and functional domains, whilst no estimate of change relative to control was available for the behavioural domain (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 45), that amounts to a benefit that lasts for a little under a year and, at its greatest, exceeds 0.05 points on the utility scale.

The base-case model suggested that one-to-one music therapy was associated with a benefit of a little over 0.019 QALYs relative to control, at an additional cost of £1,010, leading to an ICER of £52,970 (Table 30). One-way sensitivity analysis found that the model was most sensitive to the long-term extrapolation scenario, with indefinitely projected benefit producing ICERs below £20,000/QALY.

Table 30: Incremental costs and effects for one-to-one music therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,010	1.183	£1,010	0.019	£52,970	£381
Univariable model (MMSE)						
Control	£0	1.069				
Intervention	£1,010	1.145	£1,010	0.076	£13,243	£1,525
Univariable model (ADCS-ADL)						
Control	–	–				
Intervention	–	–	–	–	–	–

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 42) suggested that the probability that intervention is cost-effective is around 0%, if QALYs are valued at £20,000 each, or 10%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 43) shows iterations of one-to-one music therapy versus control cost had costs distributed mostly between £500 and £1,500, whilst the number of QALYs generated were distributed mostly betwteen 0.000 and 0.050.

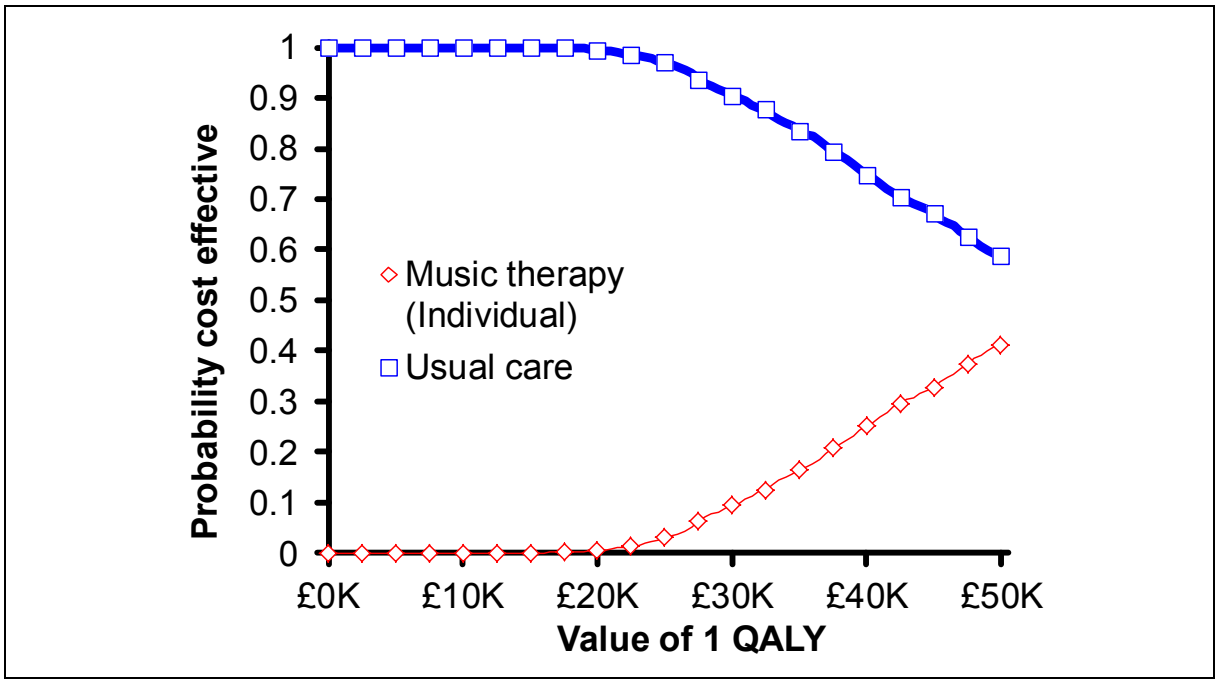


Figure 42: CEAC for one-to-one music therapy versus control

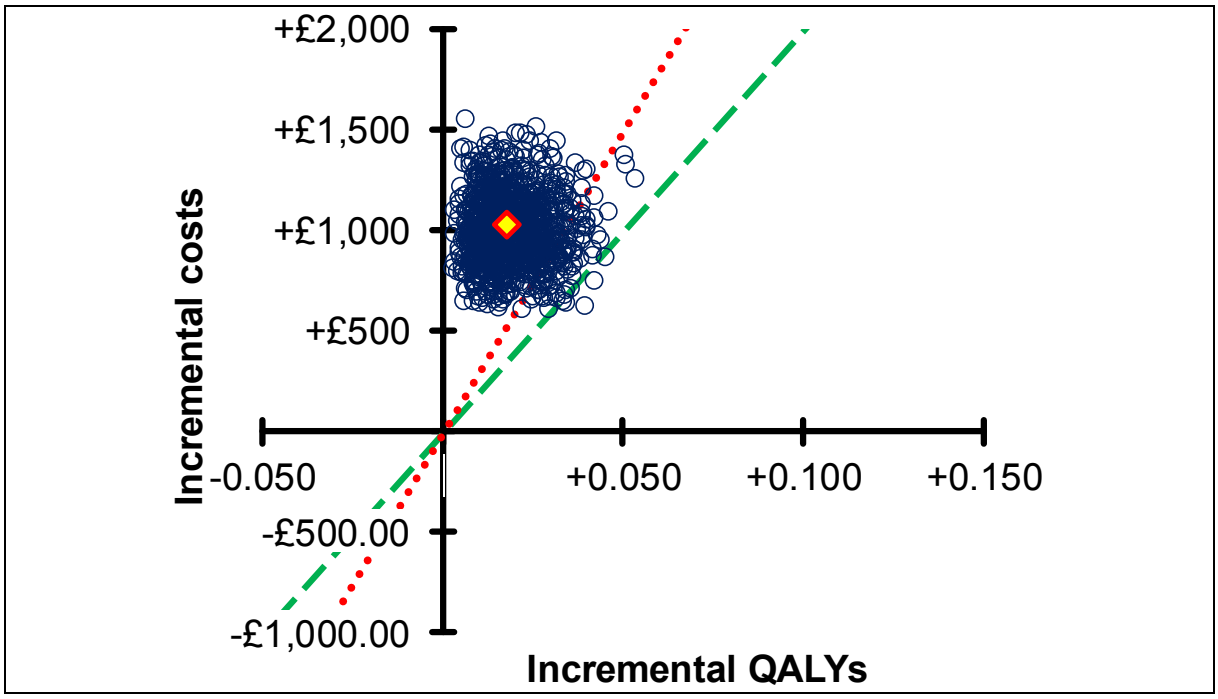


Figure 43: PSA for one-to-one music therapy versus control

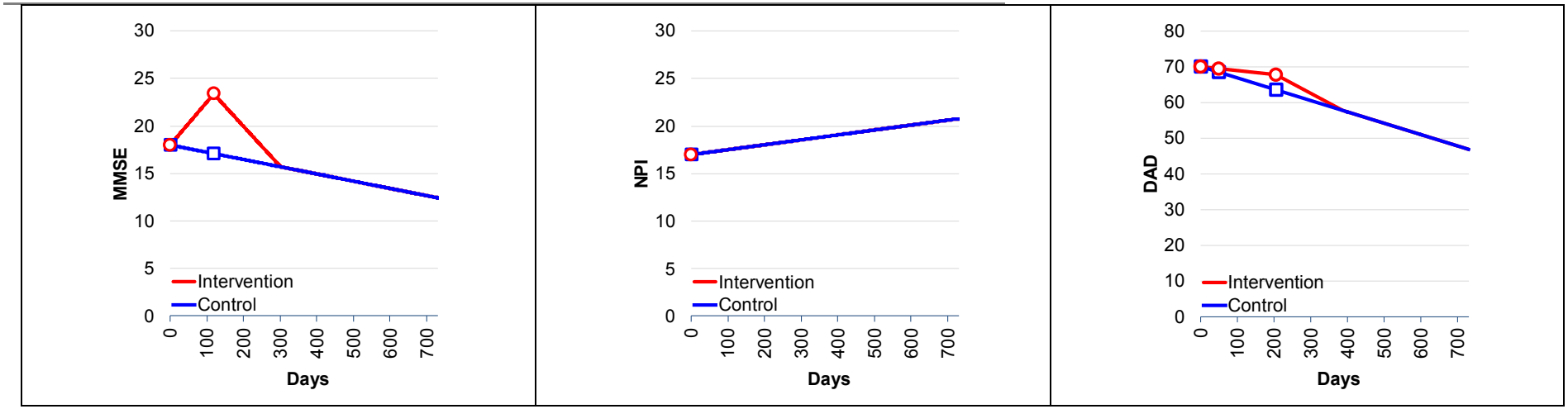


Figure 44: Change in clinical variables over time for one-to-one music therapy versus usual care

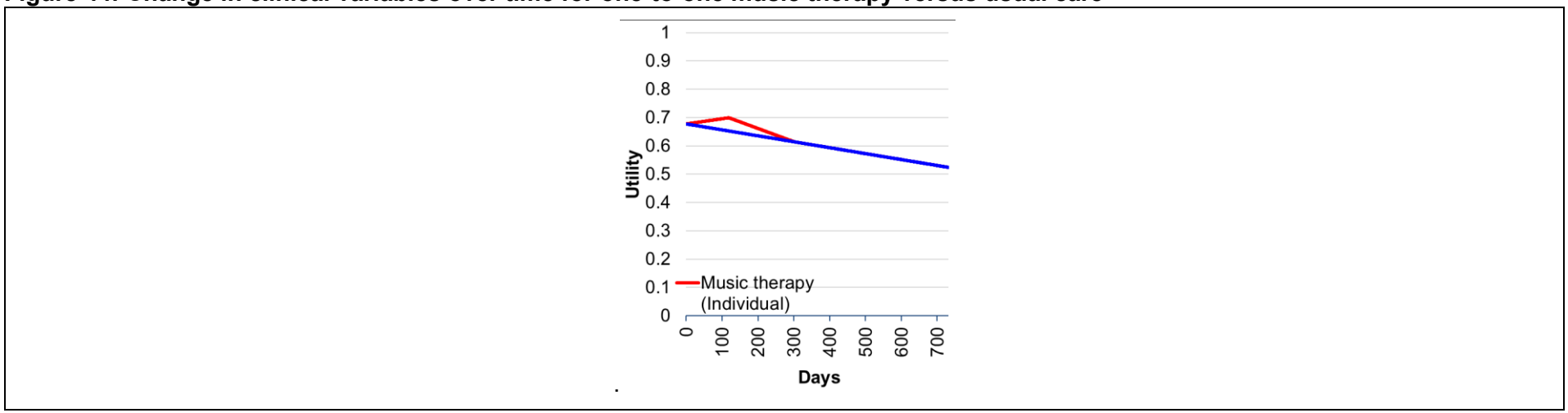


Figure 45: Estimated health-related quality of life as a function of clinical variables over time for one-to-one music therapy versus usual care

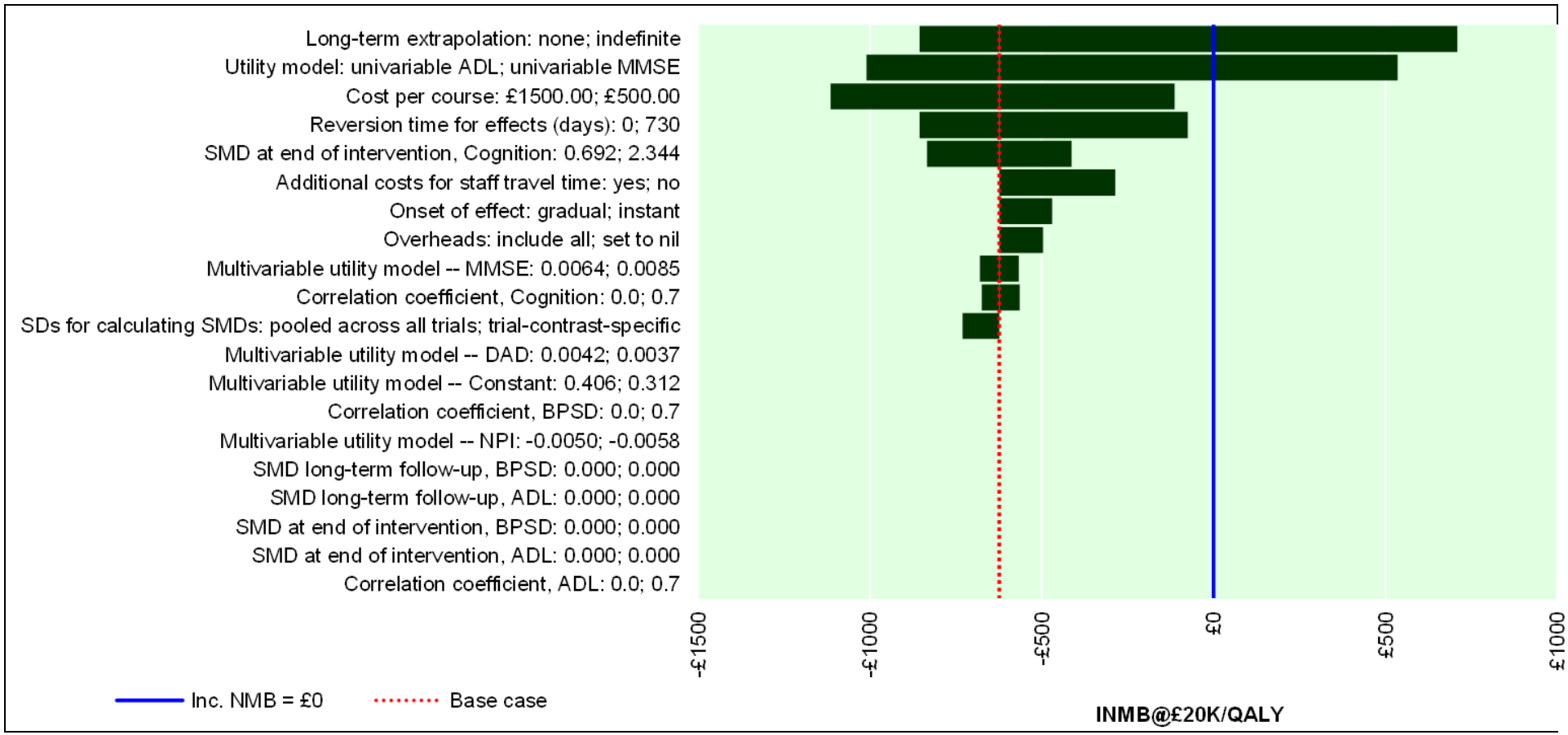


Figure 46: One-way sensitivity-analysis for one-to-one music therapy versus control

J.4.1.10 Occupational therapy

Effectiveness inputs (Figure 49) showed that occupational therapy is associated with point-estimate benefits on the functional domain, whilst no point-estimate benefit relative to control was available for the cognitive or behavioural domains (cf. Table 6, on p. 7). Once translated into estimated health-related quality of life (Figure 50), that amounts to a benefit that lasts for a little over a year and a half, and, at its greatest, exceeds 0.01 points on the utility scale.

The base-case model suggested that occupational therapy was associated with a benefit of a little over 0.010 QALYs relative to control, at an additional cost of £1,241, leading to an ICER of £130,249/QALY (Table 31). One-way sensitivity analysis found that the model was most sensitive to the MMSE and ADL variables, but no sensitivity analysis resulted in an ICER lower than £20,000/QALY.

Table 31: Incremental costs and effects for occupational therapy versus control

	Absolute		Incremental			Ceiling £ for this benefit[a]
	Costs	QALYs	Costs	QALYs	ICER	
Base case (multivariable model)						
Control	£0	1.164				
Intervention	£1,241	1.173	£1,241	0.010	£130,249	£191
Univariable model (MMSE)						
Control	–	–				
Intervention	–	–	–	–	–	–
Univariable model (ADCS-ADL)						
Control	£0	1.031				
Intervention	£1,241	1.055	£1,241	0.025	£50,509	£491

[a] *The maximum intervention cost at which benefits of the magnitude estimated here would lead to an ICER of £20,000/QALY or better*

Probabilistic sensitivity analysis (Figure 47) suggested that the probability that intervention is cost-effective is around 0%, if QALYs are valued at £20,000 each, or 0%, if a higher threshold of £30,000/QALY is used. The associated PSA (Figure 43) shows iterations of occupational therapy versus control cost had costs distributed mostly between £500 and £1,750, whilst the number of QALYs generated were distributed mostly betwteen -0.010 and 0.040.

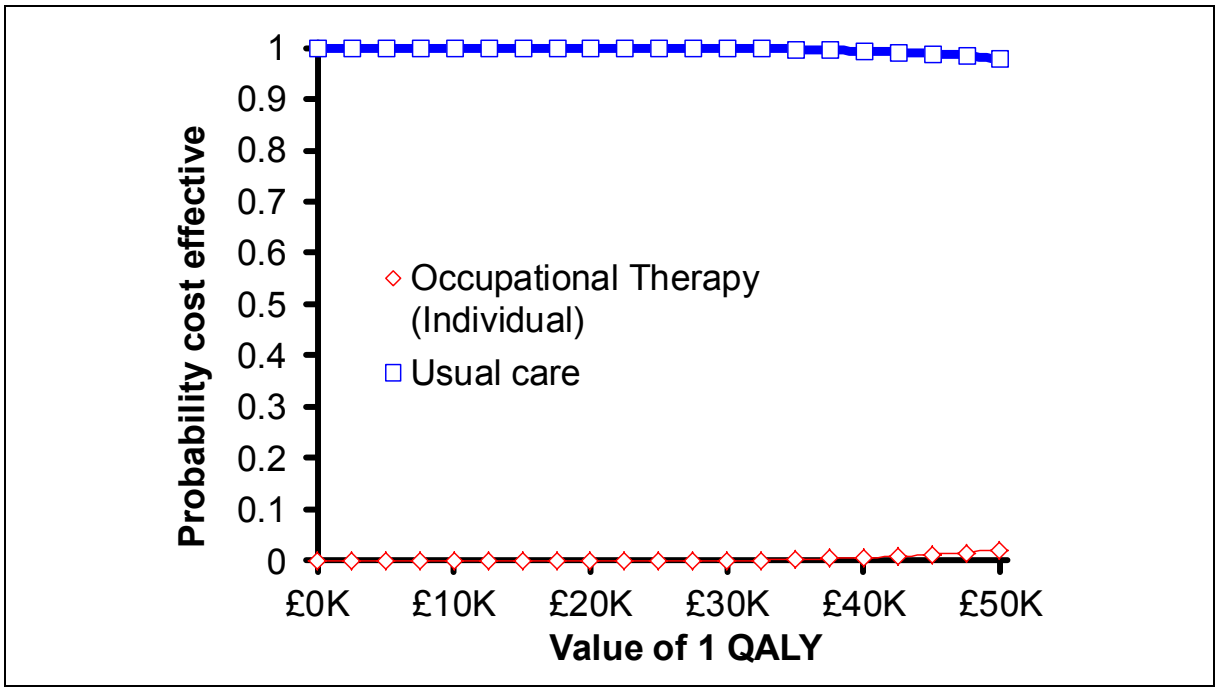


Figure 47: CEAC for occupational therapy versus control

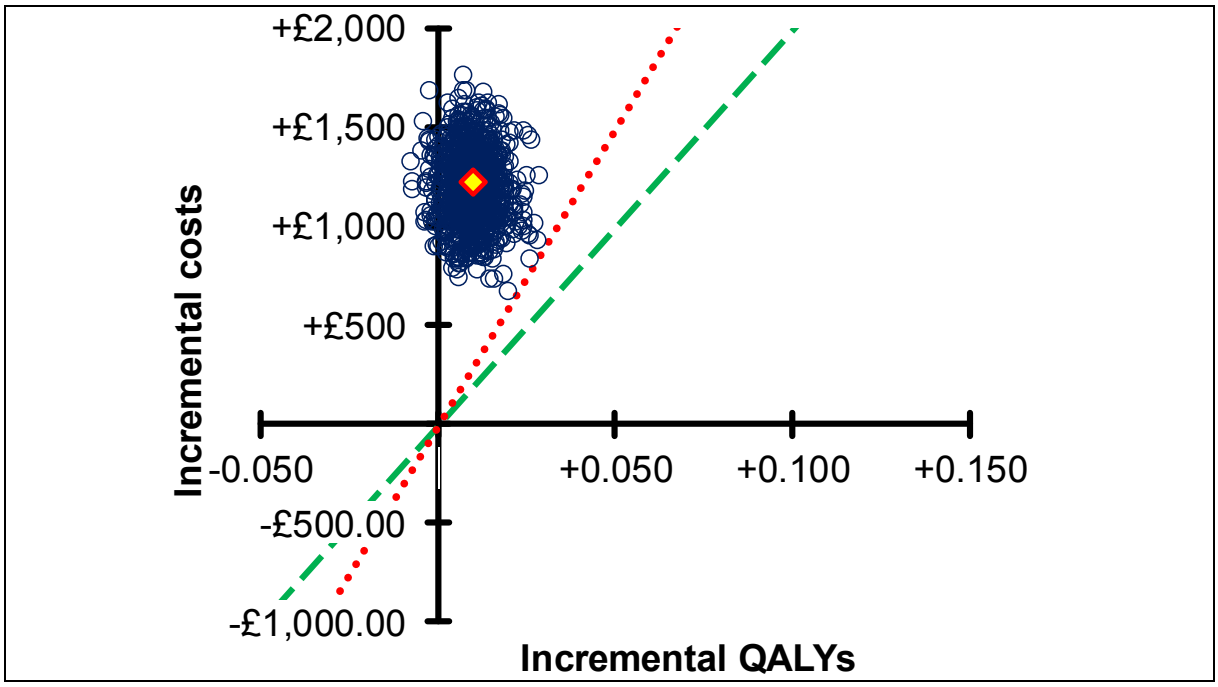


Figure 48: PSA for occupational therapy versus control

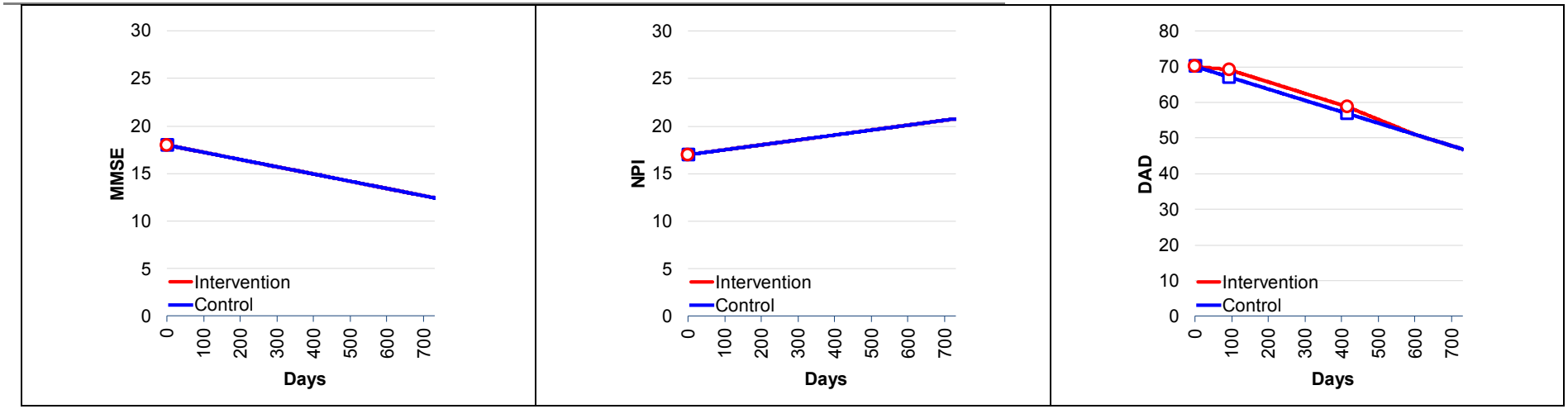


Figure 49: Change in clinical variables over time for occupational therapy versus usual care

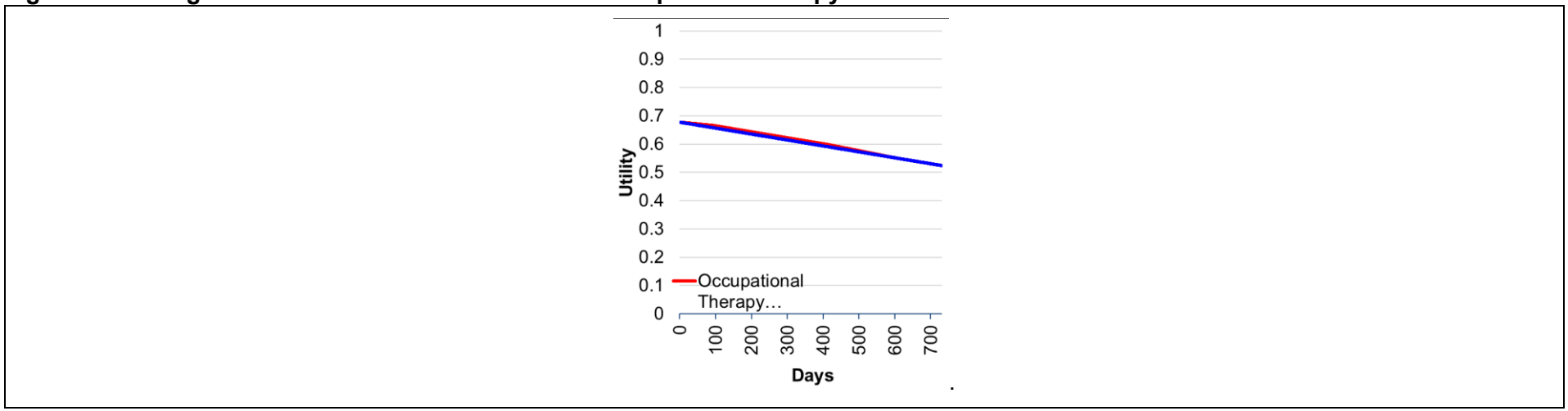


Figure 50: Estimated health-related quality of life as a function of clinical variables over time for occupational therapy versus usual care

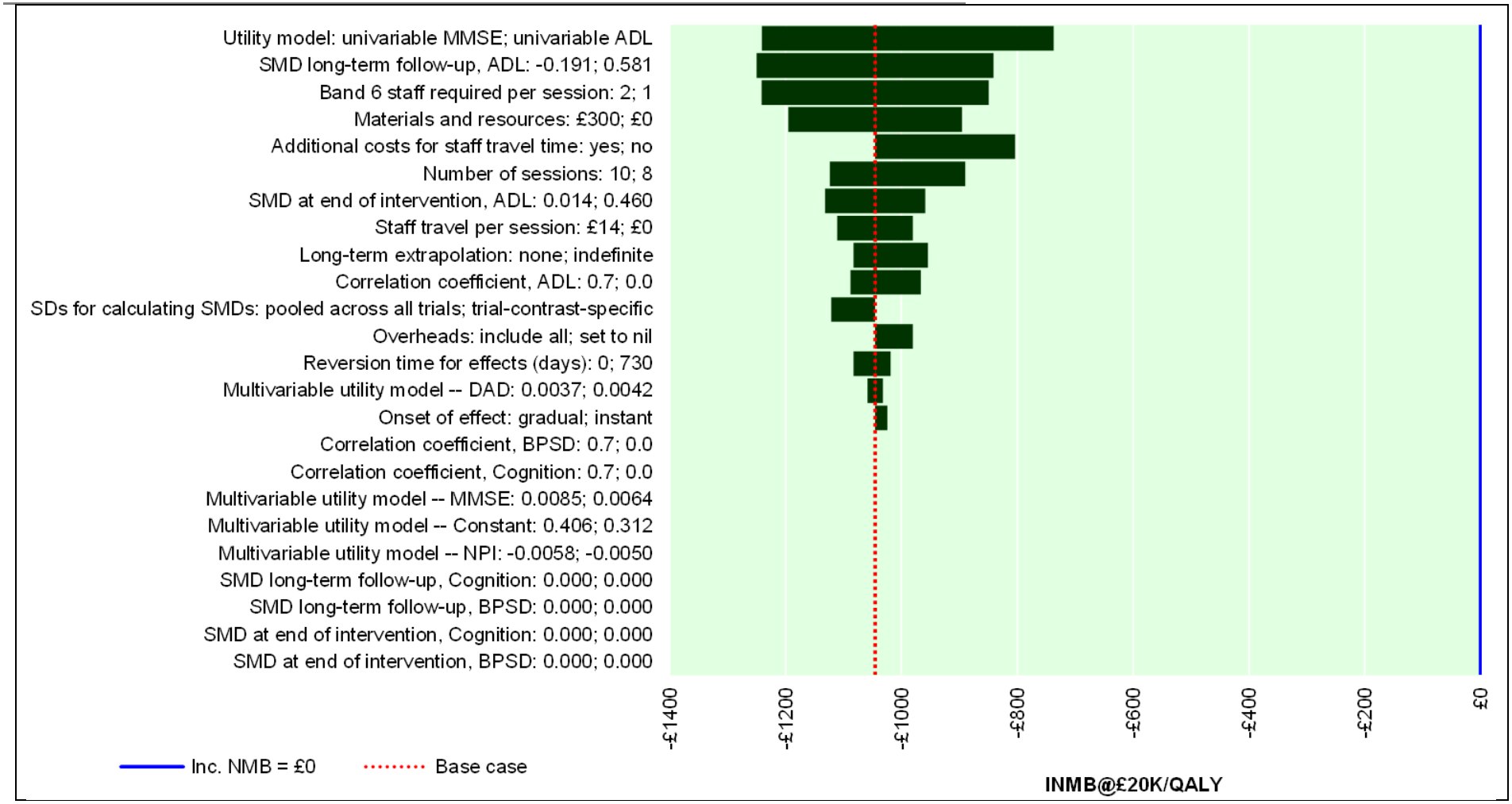


Figure 51: One-way sensitivity-analysis for occupational therapy versus control

J.5 Discussion

J.5.1.1 Principal findings

All interventions modelled were associated with small QALY gains, typically in the order of 0.01–0.03 QALYs, in the base case, which the exception of reminiscence therapy which was associated with a very small QALY loss of -0.004. Probabilistic analyses tended to show that it is extremely unlikely that any of these interventions are harmful (i.e. result in net QALY loss), but it is equally improbable that any accrues benefits of 0.1 QALYs or more. In most cases, the costs estimated to be incurred by the interventions – at least in the form taken in the trials – were higher than would normally be considered reasonable for benefits of this magnitude.

Although studies used to inform the meta-analysis were from a large range of countries and not all interventions represented were in all respects indicative of practice in the UK, a wide representation of interventions were used that were plausible representations of future practice if supported by evidence.The studies used contained a large amount of variability with significant variability in the sub-types of interventions, a wide range of the number of sessions administered for each intervention, a wide range in the number of staff used to administer the interventions, and a wide duration of the length of each session. For this reason, GC guidance was used to ensure that the sum of the synthesis of this data were suitable for use in the model. The GC largely agreed with the outcome of the synthesis of this data and provided some guidance of the use of staff time for administration, venue costs and training costs.

The processed used to select which non-pharmacological interventions identified in the systematic literature review to model was based on the identification of any intervention with some positive incremental effect on at least one of the quantitatively synthesised clinical outcomes compared to usual care. We would therefore expect any intervention modelled using the univariable and multivariable regression liner models to have some corresponding positive incremental effect on the number of QALYS relative to usual care, and this certainly has been the case across all interventions; albeit with a very small number of QALYS gained.

In the base case, where the Lacey multivariable model is used to map from continuous clinical variables synthesised by the meta-analyses, none of the interventions have an ICER less than £20,000 per QALY as compared to the control, with reminiscence therapy in a group setting being a dominated intervention (higher costs and lower QALYs than control). However, group cognitive stimulation therapy (Table 22) and occupational therapy (Table 31) have ICERS that are below the £30,000 per QALY as compared to the control.

Due to the ICER of group cognitive stimulation therapy being £20,165 in the base case, is not therefore surprising that the one-way sensitivity-analyses found that the model was extremely sensitive to almost all parameters in the model: varying any parameter within plausible range generates results lying on either side of a £20,000/QALY threshold (Figure 6).

The one-way sensitivity-analyses found many other interventions may become cost-effective at the £20,000/QALY threshold if one or more of the parameters were varied within their plausible ranges. Cognitive training for groups was found to be cost-effective if the univariable MMSE model was used instead of the multivariable model used in the base case, and if the SMD at the end of the intervention was raised to its highest plausible value. Group exercise therapy was found to be cost-effective if long-term extrapolation was made to be

indefinite. Participatory group music therapy was found to be cost-effective if long-term extrapolation was made to be indefinite, the reversion time to natural history was increased to 730 days, the cost per patient per course was reduced to £200, the SMD value at long-term follow-up for BPSD was 0.781, zero band 6 staff were used the SMD value at long-term follow-up for ADL was 1.513, costs for patient travel per session for all patients was reduced to zero, or if the univariable ADL model was used instead of the multivariable model used in the base case. One-to-one music therapy was found to be cost-effective if long-term extrapolation was made to be indefinite or if the univariable MMSE model was used instead of the multivariable model used in the base case.

J.5.1.2 Weaknesses of the analysis

The original economic modelling

- Did not consider any adverse effects that might have been associated with any of the treatments. This includes adverse events, change in the level of resource use such as GP visits and hospital inpatient stays, etc. The omission of this could easily change the cost-utility situation of any of the modelled non-pharmacological interventions in the model.
- Was not able to control for patients who were receiving any other interventions. This means that the model was unable to determine if treatment effects would be additive (i.e if patients would be able to accrue benefits from multiple treatments).
- Developer assumptions were used for various input parameters in the model.
- Did not incorporate death.
- Did not examine the change in likleihod for a patient to be transferred to full-time care for each intervention.
- The method of getting from effects from the studies (continuous clinical variables) to the QALYS is indirect and relies on the HUI-3.

J.5.1.3 Comparison with other CUAs

- The ICER for group cognitive stimulation therapy in the base-case model (£20,165/QALY) is not too dissimilar to the ICER identified for maintenance cognitive stimulation therapy by D'Amico et al (2015), where quality of life for the person with dementia was measured using the proxy rated EQ-5D (£26,835/QALY).
- The analysis for cognitive rehabilitation in the base-case model shares Clare et al.'s (2017) conclusion that a relatively high-intensity intervention such as that explored in the GREAT trial is unlikely to produce QALY gains at a cost that would be considered an effective use of NHS+PSS resources. However, our ICER of £66,863/QALY is substantially lower than the ICER from Clare et al. (2017), £1,110,000/QALY. This is because our method predicts a greater quality of life benefit from the intervention than was observed in the practice.
- In the base-case model, reminiscence therapy is a dominated strategy. This is not too dissimilar to the situation in Woods et al. (2016) where reminiscence therapy was found to have an ICER of £1,544,000/QALY. This is not too surprising as the costing for reminiscence therapy was taken from the Woods et al. (2016) study, where the QALY difference was found to be less than 0.001.
- The ICER for group exercise therapy in the in the base case model is £41,359/QALY, which is somewhat lower than the ICER reported by Sopina et al. (2017), €87,157/QALY, when patient utility was measured using the caregiver EQ-VAS. In the Sopina et al. (2017) study base care, where the participant assessed EQ-5D-5L data was used to measure utility, the ICER was €158,520/QALY.

J.6 References

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