

Methods to account for follow-up time differences when calculating QALYs from randomised controlled trials

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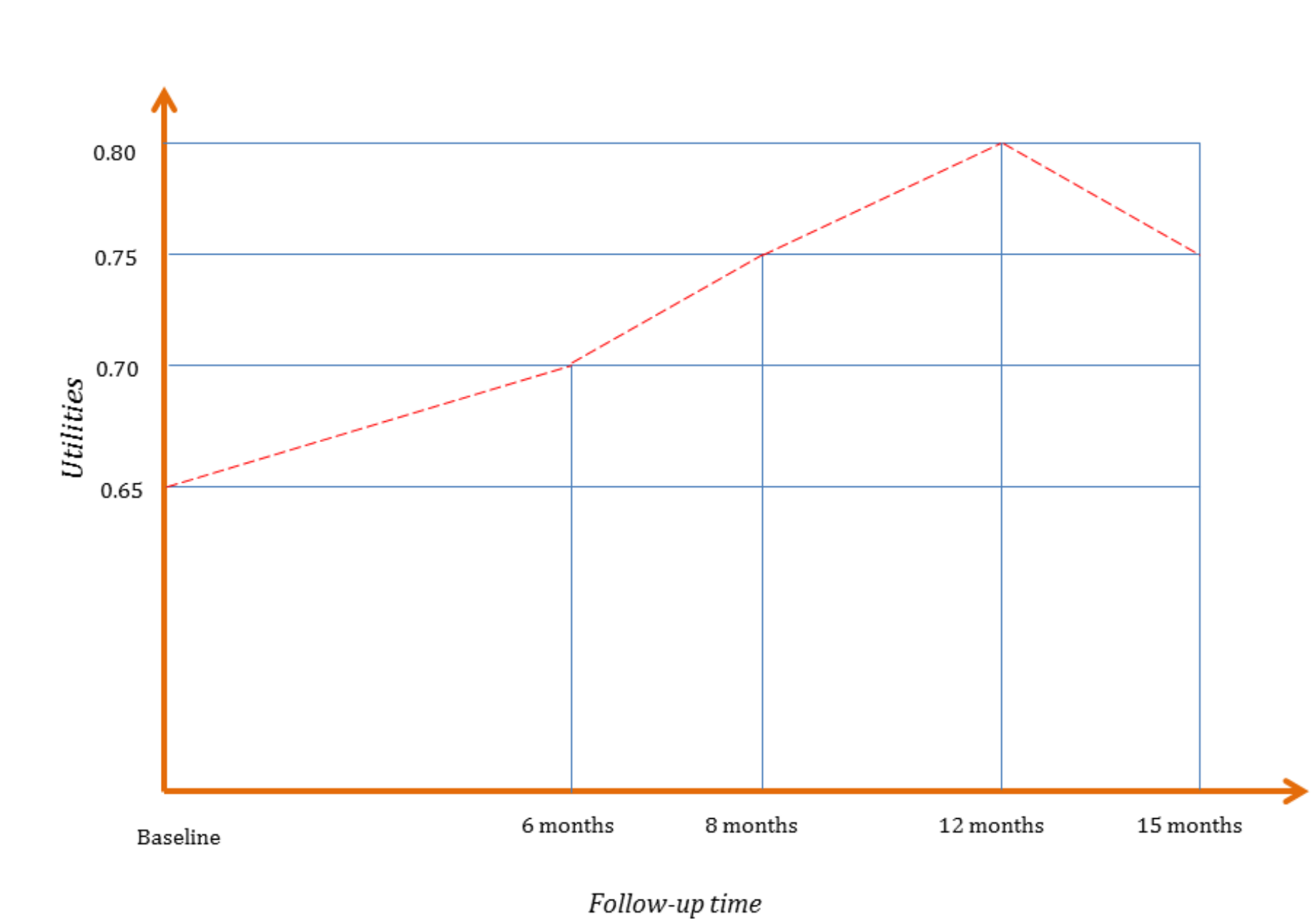
OBJECTIVES

- Methods for calculating quality-adjusted life years (QALY) are well developed and employed in economic evaluations alongside randomised controlled trials (RCTs)^{1 2 3 4 5}.
- However, patient follow-up does not always occur at the same time and the effect of these time differences in collecting EQ-5D data on QALY calculations has not been tested.
- The objective of this study was to assess different methods for estimating the differences in follow-up time when calculating QALYs from EQ-5D data collected alongside RCTs.

METHODS

- Alternative approaches were considered for estimating QALYs and five methods were identified:
 - a) assuming trial protocol follow-up;
 - b) using average follow-up timing until final time point;
 - c) using average follow-up timing until proposed time horizon;
 - d) using individual patient-level follow-up until final time point; and
 - e) using individual patient-level follow-up data until proposed time horizon.
- Methods were illustrated using a hypothetical example (figure 1).

Figure [1]: Illustrations with a hypothetical example



Calculating QALYs from the hypothetical example

- To calculate utilities at each quarterly measurement using the UAC method, the following general formula was used
$$u_{ti} = \frac{u_t + u_{t+i}}{2} \times \frac{t_{t+i} - t}{p} \quad [1]$$

where u_{ti} is the utility at time point t_i (i.e. u_3 is the utility measurement for the first quarterly follow-up at month 3), p =period, u =utilities, t =utility measurement time, $t+i$ =the subsequent measurement time.

- For this particular hypothetical patient, the utility scores using method (a) can be calculated as follows.

$$u_3 = \frac{0.65 + 0.70}{2} \times \frac{3}{12} = 0.169$$

$$u_6 = \frac{0.70 + 0.75}{2} \times \frac{3}{12} = 0.181$$

$$u_9 = \frac{0.75 + 0.80}{2} \times \frac{3}{12} = 0.194$$

$$u_{12} = \frac{0.80 + 0.75}{2} \times \frac{3}{12} = 0.194$$

$$QALY_m = \sum_{ti=1}^n u_{ti} \quad [2]$$
$$= (u_3 + u_6 + u_9 + u_{12}) = 0.738$$

- Similarly, QALY was calculated using the general equations [1] and [2] applied to each method (m = b, c, d or e) and QALY scores are presented in table 1.

Table {1}: QALY scores for the hypothetical patient

Method	QALY
a	0.738
b ₁	0.727
b ₂	0.915
c	0.719
d ₁	0.729
d ₂	0.912
e	0.574

* In methods b2 and d2, quarterly utilities were multiplied by time as proportion of protocol follow-up time rather than the actual time period

Application on RCT data

- Methods illustrated by application with empirical analyses on the ACUDep study data.
- The ACUDep in an RCT comparing acupuncture and counselling interventions to usual care for management of patient with moderate to severe depression⁶.
- A seemingly unrelated regression model was fit for estimating QALYs and costs for comparing these methods

RESULTS

- Descriptive statistics of the RCT data shows the quarterly follow up time differences as deviations from the trial protocol (table 2).

Table {2}: The RCT follow-up time periods

	n	Mean (months)	SD	Min	Max
1 st quarter period	580	4.774	0.785	3.533	8.000
2 nd quarter period	505	2.931	0.527	0.600	4.600
2 nd quarter period	489	3.072	0.500	1.467	5.867
2 nd quarter period	482	2.941	0.518	0.733	5.467
Total follow-up period	404	13.682	0.690	12.367	17.533

- Different methods have generated different estimates for QALYs; However, the magnitude of differences is relatively small ranging from -0.9% to 11.8% (n=752) when different methods were compared with the conventional method (a) - see table 3.

Table {3}: Estimated QALYs, costs and ICERs for each methods applied to the RCT data

Method	Treatment arm	n	QALY	Cost	ICER (£ per QALY)
a	Usual Care	151	0.614	£941	
	Acupuncture	301	0.679	£1,228	4,466
	Counselling	300	0.664	£1,457	Dominated
b1	Usual Care	151	0.691	£941	
	Acupuncture	301	0.761	£1,228	4,107
	Counselling	300	0.744	£1,457	Dominated
b2	Usual Care	151	0.761	£941	
	Acupuncture	301	0.744	£1,228	4,107
	Counselling	300	0.691	£1,457	Dominated
c	Usual Care	151	0.612	£941	
	Acupuncture	301	0.674	£1,228	4,626
	Counselling	300	0.657	£1,457	Dominated
d1	Usual Care	151	0.612	£941	
	Acupuncture	301	0.676	£1,228	4,497
	Counselling	300	0.659	£1,457	Dominated
d2	Usual Care	151	0.696	£941	
	Acupuncture	301	0.759	£1,228	4,538
	Counselling	300	0.739	£1,457	Dominated
e	Usual Care	151	0.608	£941	
	Acupuncture	301	0.674	£1,228	4,348
	Counselling	300	0.656	£1,457	Dominated

CONCLUSIONS

The effect of follow-up time differences in calculating QALYs using the ACUDep RCT data is relatively small. However, differences could matter when the estimated ICERs are very close to the cost-effectiveness threshold. The most appropriate method is method (e) as it uses the most data available without biasing the results due to total follow-up time differences.

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