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Systematic review of the impact of urinary tract infections on health-related quality of life

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Accepted for publication 19 April 2012

The aim of this review was to identify studies that have evaluated the impact of symptomatic urinary tract infection (UTI) and UTI-associated bacteraemia on quality of life, and to summarize these data in a way that is useful for a health researcher seeking to populate a cost–utility model, design a clinical study or assess the effect of UTIs on quality of life relative to other conditions. We conducted a systematic search of the literature using MEDLINE, EMBASE, the NHS Economic Evaluations database, Health Technology Assessment database, Health Economics Evaluations database, Cost-Effectiveness Analysis Registry and EuroQol website. Studies that reported utility values for symptomatic UTI or UTI-associated bacteraemia derived from a generic QoL measurement tool or expert opinion were included. Studies using disease-specific instruments were excluded. Twelve studies were identified that included a generic measure of health-related quality of life for patients with UTIs. These measures included: the short-form (SF)-36 and SF-12 questionnaires; the Health Utilities Index Mark 2; Quality of Well Being; the Index of Well Being, standard gamble; the Health and Activity Limitation Index; and expert opinion. The authors of studies using either of the SF questionnaires were contacted for additional data. One research group provided previously unpublished data from a large cohort study; these scores were mapped to EuroQol 5-Dimension (EQ-5D) values using published algorithms and probabilistic simulations. The present review provides health researchers with several sources from which to select utility values to populate cost–utility models. It also shows that very few studies have measured quality of life in patients with UTI using generic preference-based measures of health and none have evaluated the impact of this health state on quality of life in children. Future studies ought to consider the inclusion of commonly used preference-based measures of health, such as the EQ-5D, in all patient populations experiencing symptomatic UTI or UTI-related complications.

What's known on the subject? and What does the study add?

Values for equivalent health states can vary substantially depending on the measure used and method of valuation; this has a direct impact on the results of economic analyses. To date, the majority of existing economic evaluations that include UTI as a health state refer to an analysis in which the Index of Well Being was used to estimate the quality of life experienced by young women with UTIs. Currently, there are no validated methods or filters for systematically searching for the type of generic quality of life data required for decision analytic models.

This study is the only systematic review of quality of life in people with UTI in the literature. Twelve studies were identified which report quality of life using a variety of generic methods; the results of these papers were summarized in a way that is useful for a health researcher seeking to populate a decision model, design a clinical study or assess the effect of UTI on quality of life relative to other conditions. One research group provided previously unpublished data from a large cohort study; these scores were mapped to EuroQol 5-Dimension values using published algorithms and probabilistic simulations.

KEYWORDS

quality of life, urinary tract infection, kidney infection, bacteraemia, spinal cord injury, women, cost–utility analysis

INTRODUCTION

Urinary tract infection is the most common healthcare-acquired infection in the world, accounting for ~40% of all nosocomial infections [1]. Although most UTIs are mild and easily resolved with appropriate antibiotic treatment, more severe infections can be devastating, resulting in bacteraemia, sepsis and death. Because of the frequency with which they occur, UTIs also impose a substantial economic burden on healthcare systems [1]. Despite the clinical and economic impact of UTIs, there is a surprising lack of data on their effect on quality of life (QoL). This fact was brought to our attention while searching for health-related QoL data to inform a cost–utility analysis developed as part of the National Institute for Health and Clinical Excellence (NICE) guideline on Infection Prevention and Control [2].

In cost–utility analyses, measures of health benefit are valued in terms of quality-adjusted life years (QALYs). The QALY is a measure of a person's length of life

   doi:10.1111/j.1464-410X.2012.11337.x

weighted by a valuation of their QoL over that period. The weighting comprises two elements: the description of changes in QoL and an overall valuation of that description. In order to ensure comparability and consistency across appraisals and reduce bias in the selection of values, NICE requires the use of a reference case which recommends that: measurement of changes in QoL should be reported directly from patients; valuation of changes in patients' QoL should be based on public preferences elicited using a choice-based method, such as the time trade-off or standard gamble, but not rating scale, in a representative sample of the UK population; and the use of utility estimates from published literature must be supported by evidence that demonstrates that they have been identified and selected systematically [3].

To date, the majority of existing economic evaluations that include UTI as a health state [4–7] refer to an analysis by Barry *et al.* [8] in which the Index of Well Being (IWB) was used to estimate QoL for women with UTIs. The IWB was first introduced in the 1970s as one of the first attempts to develop a generic measurement of health utility. Using medical textbook case descriptions and items from community-wide health surveys, a series of 29 function levels and 42 symptom complexes were described. By randomly combining different functional levels and symptom complexes across five different age groups, a matrix of 400 case descriptions was developed to represent a wide range of health states that may exist within a population. In order to derive weights or social preferences, a group of 62 US nurses and non-medical graduate students were then asked to rank each case description according to its desirability by placing it on a 16-point scale.

The IWB was the first instrument specifically designed to measure QoL for the estimation of QALYs. For a long time, it was one of only a few available measures. However, because it has not been used to elicit health status from patients with a UTI and preference-weightings are neither representative of the general population nor elicited according to time trade-off or standard gamble techniques, it was deemed an unsuitable source for the purposes of our economic evaluation.

The aim of the present paper was to perform a systematic search of the literature for generic preference-based measures of health, derived from patients experiencing symptomatic UTIs, pylonephritis and UTI-associated bacteraemia and to summarize these data in a way that is useful for a health researcher seeking to populate a decision model.

METHODS

We conducted a systematic search of the literature using the electronic databases Medline (Ovid MEDLINE[R] In-Process & Other Non-Indexed Citations and Ovid MEDLINE[R], 1948 to the present) and Embase (Ovid, 1980 to 2011 weeks 48). A list of the search terms used in MEDLINE is provided in Appendix SA. This search strategy was adapted for use in Embase. In addition to these biomedical databases, the NHS Economic Evaluations Database (NHS EED) and Health Technology Assessment (HTA) databases (via the Centre for Reviews and Dissemination (CRD) interface) and the Health Economics Evaluations database (HEED) were searched for relevant literature. The terms used to search HEED are shown in Appendix SB. These terms were adapted for the CRD interface to search the NHS EED and HTA databases. The Cost-Effectiveness Analysis Registry (CEAR) was also searched using the same keywords. Databases were searched from their date of inception to December 2011. Search strategies are shown in Appendices SA and SB.

Studies presenting utility values derived from a generic QoL measurement tool or expert opinion were retrieved for full review, based on title and abstract sifting. In addition to generic preference-based utility measures such as the EuroQol 5-Dimension (EQ-5D), studies using the short-form (SF)-12 and SF-36 instruments were also included. Although these instruments are not preference-based, there are several established mapping functions that allow the estimation of preference-based utility scores using these descriptive systems.

Studies using disease-specific instruments were excluded. Although these questionnaires can be more responsive to changes associated with a certain condition, they are unable to compare QoL across different illnesses. Although mapping techniques could theoretically be extended to disease-specific instruments, the use of mapping functions beyond the SF questionnaires is currently limited. Also excluded were studies published in a language other than English. When the method of QoL assessment or included health states could not be determined from the abstract, full papers were retrieved for further examination. The reference lists of all retrieved studies were also searched for relevant sources.

RESULTS

SEARCH RESULTS

A total of 864 papers were identified from MEDLINE, EMBASE, HEED, NHS EED and HTA databases. The CEAR returned seven results (three of which were also identified in the MEDLINE and EMBASE search) and the EuroQol website identified eight studies (none of which were identified in the MEDLINE and EMBASE search). Four additional relevant publications were identified by supplementary citation searching (Fig. 1).

Twelve studies (reported in 16 separate papers) met our inclusion criteria. With the exception of two papers [9,10] that were identified through citation searching and the CEAR, respectively, all were retrieved through MEDLINE and EMBASE.

Given the heterogeneity between studies in terms of patient characteristics and QoL assessment methods, there was no attempt to pool results. Instead, the population, methods and results of each study are reported below. More detailed reports of studies using preference-based measures and non-preference based measures with mapped estimates are shown in Table 1 [11–23].

The search did not identify any primary studies of QoL in patients with UTI-associated bacteraemia. Several studies contained utility values for sepsis; however, the infections were not of urinary tract origin and were thought to describe a more severe health state than the one under review.

QUALITY OF LIFE IN PATIENTS WITH A UTI

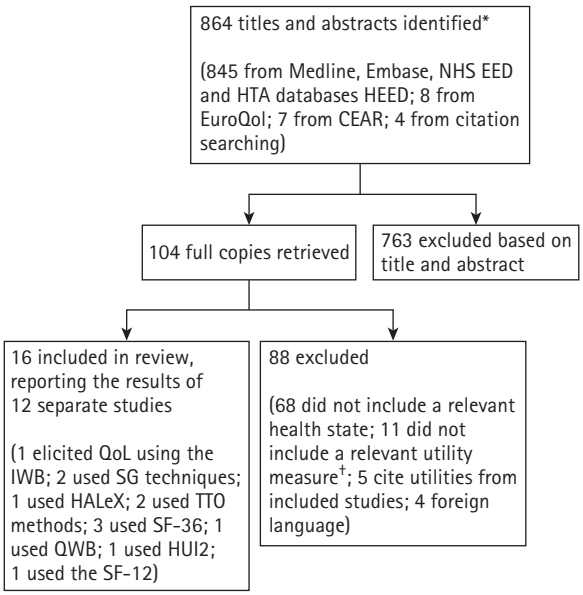
As previously discussed, Barry *et al.* [8] estimated a monthly disutility of 0.2894 for persistent dysuria and a disutility of 0.3732 for patients with pylonephritis, using the IWB. Ackerman *et al.* [24] reported utility values in 13 men with moderate to severe BPH. A series of BPH-specific health states were described according to three treatments, five short-term clinical events, and 17 possible long-term outcomes. To assign preference weights to each health state, the standard gamble was administered by a trained interviewer. Results were reported according to patients' risk attitudes. Risk-averse individuals ($n = 6$) reported a mean utility value of 97.2 (SE 1.1; range 94–99) for severe UTIs, while non-risk-averse patients ($n = 7$) reported a mean value of 89.3 (SE 4.6; range 77–99).

In 1998, Gold *et al.* [9] published a catalogue of 130 health state values developed using the Health and Activity Limitation Index (HALex), derived from the answers to two questions asked in the US National Health Interview Survey about activity limitations and self-rated health. Between 1987 and 1992, 84 443 people were included in the survey; at the time of each survey, a total of 384 people reported having a bladder infection and 387 reported having a kidney infection. Based on weights developed from a correspondence analysis and multi-attribute utility model, bladder infections were assigned a mean QoL value of 0.73 (median 0.84; interquartile range [IQR] 0.4) and kidney infection a value of 0.66 (median 0.63; IQR 0.36).

Unable to find relevant utility data for patients with acute pylonephritis, Yen *et al.* [25] asked a panel of six emergency physicians and internists to develop utility weights using the standard reference gamble technique. Pylonephritis was assigned a QALY of 0.90, 0.87 for pylonephritis with mild side effects, and 0.81 for pylonephritis with serious side effects.

Sonnenberg *et al.* [10] reported the utility associated with UTI from 'a sample of female members of the research team and advisor panel' using the time trade-off technique. They report a short-term disutility of 0.0192 for UTI. Similarly, Lawler *et al.* [26] used their judgement to arrive at an estimated utility value of 0.99 for people suffering from UTI.

*FIG. 1. Search results. *Currently, there are no validated methods or filters for searching for the type of QoL data that are required for decision analytic models [29]. The search strategy used in this study was found to be reasonably precise within MEDLINE and EMBASE, returning a manageable number of references and omitting few relevant records. The filters used for the MEDLINE & EMBASE and HEED searches, developed and used by the National Clinical Guideline Centre, are available as online appendices. †Of those that included relevant health states, 11 measured quality of life using disease-specific instruments such as the IPSS; Acute Physiology and Chronic Health Evaluation scores; Functional Assessment of Chronic Illness Therapy, and rank ordering of different conditions, among others.*



Three studies measured the impact of UTI on QoL among otherwise healthy adult women. In 2000, Ellis and Verma [11] conducted a case–control study to evaluate the effect of UTI on QoL in women using the SF-36. Although the authors mentioned that QoL was lower in patients with severe UTI, these results were not reported. The authors of this study were contacted for further information; a reply was received but additional data was not available. The algorithm published by Ara and Brazier [20] was used to map mean SF-36 scores to EQ-5D health state values (Table 1).

Ernst *et al.* [13] evaluated QoL among women with acute cystitis and the impact of treatment on QoL. Patients were randomized to receive either trimethoprim/sulfamethoxazole for 3 days or nitrofuratonin for 7 days. The Quality of Well Being (QWB) questionnaire was administered at baseline and 3, 7, 14, and 28 days after the initial visit. The QWB value at baseline (i.e. having a UTI) was 0.68 (SD 0.03) and 0.81 (SD 0.11) at the 28-day follow-up. Patients who experienced clinical cure had significantly better QoL scores at days 3 (0.77 vs 0.72), 7 (0.82 vs 0.71) and 14 (0.83 vs 0.76) compared with those who failed treatment.

Abrahamian *et al.* [12] measured QoL in women with UTIs caused by TMP/SMX-resistant isolates compared with those with susceptible isolates and evaluated the effect of treatment failure on QoL. At initial presentation, patients were treated with TMP/SMX twice daily for 3 days and phenazopyridine hydrochloride three times a day for 2 days. The SF-36 was administered 3–7 days after treatment and results were reported according to whether the patient had been infected with TMP/SMX-susceptible or -resistant strains and whether they had experienced clinical cure or failure. Results were presented alongside US national mean scores for women aged 25–34 years. For the purpose of the present analysis, mean SF-36 dimension scores were mapped to EQ-5D health state values using

TABLE 1 Reported and mapped generic preference-based utility values for patients with a symptomatic UTI

Study	Respondents	Country	Recruitment and selection	Recall	Measure	Domain	Mean	SD	Mean	SD	Mean	SD
							No UTI, *n* = 71		**UTI, *n* = 47**		**Severe UTI**	
Ellis and Verma [11]	Adult women with symptomatic UTI and healthy age-matched controls *N* = 118 Mean age = 34 Male = 0%	Canada	The SF-36 was administered to women with a diagnosed UTI, attending a family medicine clinic, student health services or urology outpatient clinic. A group of healthy undergraduate women were recruited to act as the control population.	1 day	SF-36	GH	78.90	NR	63.30	NR	Not reported	
						PF	87.60	NR	76.60	NR		
						RP	93.00	NR	53.80	NR		
						RE	88.30	NR	67.40	NR		
						VT	64.90	NR	43.00	NR		
						MH	80.20	NR	64.40	NR		
						BP	91.50	NR	58.70	NR		
						SF	90.40	NR	60.40	NR		
					Mapped EQ-5D*		0.922	–	0.724	–		
							Population norm (i.e. no UTI)		**TMP/SMX-susceptible UTI, *n* = 70**		**TMP/SMX-resistant UTI, *n* = 19**	
Abrahamian *et al.* [12]	Adult women with symptomatic UTI *N* = 139 Median age = 29 (IQR 18–40) Male = 0%	USA	Women with symptoms of acute uncomplicated cystitis were recruited from the emergency room of a hospital and neighbouring clinics. Patients were asked to return 3–7 and 4–6 weeks after treatment. During these visits patients completed the SF-36 questionnaire and submitted urine for urine analysis, culture and susceptibility.	NR	SF-36	GH	52.00	NR	52.90	NR	45.90	NR
						PF	55.10	NR	57.10	NR	57.10	NR
						RP	56.60	NR	51.90	NR	49.50	NR
						RE	55.70	NR	55.7	NR	55.70	NR
						VT	49.00	NR	52.00	NR	49.00	NR
						MH	52.40	NR	55.10	NR	49.60	NR
						BP	54.20	NR	45.10	NR	50.10	NR
						SF	56.40	NR	45.6	NR	51.00	NR
					Mapped EQ-5D*		0.584	–	0.560	–	0.565	–
							Population norm (i.e. No UTI)		**Clinical cure, *n* = 62**		**Clinical failure, *n* = 19**	
					SF-36	GH	As above		55.30	NR	52.00	NR
						PF	As above		57.00	NR	57.00	NR
						RP	As above		56.90	NR	52.00	NR
						RE	As above		55.90	NR	48.10	NR
						VT	As above		58.30	NR	45.80	NR
						MH	As above		55.60	NR	41.60	NR
						BP	As above		62.10	NR	50.30	NR
						SF	As above		51.00	NR	51.40	NR
					Mapped EQ-5D*		As above		0.611	–	0.548	–
							UTI, *n* = 146		**Patients with clinical cure, *n* = NR**		**Patients with clinical failure, *n* = NR**	
Ernst *et al.* (13)	Adult women with symptomatic UTI *N* = 146 Mean age = 34 (± 12) Male = 0%	USA	Patients with diagnosed UTI were recruited from two family medicine clinics and randomized to receive one of three different antibiotics. The QWB was administered in-person at baseline and over the telephone by a trained interviewer at 3, 7, 14 and 28 days after the initial visit.	3, 7, 14 and 28 days	QWB Scored using original weights calculated using a visual analogue rating scale in a US population		**Baseline QoL**		**QoL at 3 days**			
							0.68	0.03	0.77	NR	0.72	NR
									QoL at 7 days			
									0.82	NR	0.71	NR
									QoL at 14 days			
									0.83	NR	0.79	NR
									QoL at 28 days			
									0.82	NR	0.79	NR

TABLE 1 Continued

Study	Respondents	Country	Recruitment and selection	Recall	Measure	Domain	Mean	SD	Mean	SD	Mean	SD
							No UTI, *n* = 496		**UTI, *n* = 18**			
Maxwell *et al.* [14]	Older adults living in care homes *N* = 514 Mean age = 80.5 (±8.4) Male = 28%	USA & Canada	Adults aged 65+ living in two care homes (Calgary, Canada and Michigan, USA) who were able to communicate and provide informed consent were invited to participate. A trained interviewer administered the HUI2 and MSD-HC.	1 week	HUI2 Scored using original weights calculated using multi-attribute utility theory in a Canadian population		0.49	0.01†	0.40	0.04†		
							No UTI, *n* = 134		**UTI, *n* = 238**		**Severe UTI, *n* = 42**	
Vogel *et al.* [15], Vogel *et al.* [16] and Zebracki *et al.* 2010 [17]	Adults with SCI *N* = 415 Mean age = 30.9 (±5.3) Male = 63% Time since SCI = 16.6 years (±6.2) Aetiology of SCI: Trauma 89% Medical 9% Other 2% Tetraplegia: 54%	USA & Canada	Eligible participants were former patients enrolled in SCI programmes at Shriners Hospitals for Children and were located using the hospitals' databases, White Pages directories, and a professional search service. Subjects were administered the SF-12 by telephone. Information about medical complications was also obtained.	1 year	SF-12	MCS-12	53.73	7.58	52.56	9.40	52.12	9.79
						PCS-12	47.39	10.13	43.53	10.64	42.73	10.92
					Mapped EQ-5D‡		0.831	0.01	0.782	0.01	0.738	0.03
							No UTI, *n* = 167		**UTI, *n* = 138**			
Haran *et al.* [18] and Lee *et al.* [19]	Individuals with SCI predominantly living in the community *N* = 305 Mean age = 44 (±14) Male = 83% Time since SCI = 15.7 years (±11.6) Aetiology of SCI: NR Tetraplegia: 55%	Australia	Subjects were identified from a register comprised of a state-wide database and admissions records for two acute spinal units. They were invited to participate in a clinical trial of antiseptic agents for the prevention of UTI. Subjects completed the SF-36 at enrolment and again on development of UTI. If no UTI was experienced, the SF-36 was completed at 6-month follow-up.	6 months (no UTI) 1 week (UTI)**	SF-36	NR	NR	NR	NR	NR		
					Mapped SF-6D§		0.68	0.01†	0.58	0.01†		
					Mapped SF-6D¶		0.70	0.01†	0.60	0.01†		

**Mapped based on algorithm developed by Ara and Brazier [20]. †Calculated as SD/SQRT(n). ‡Mapped based on algorithm developed by Gray* et al. *[21]. §Derived from SF-36 responses using algorithm developed by Brazier* et al. *(2002) [22]. ¶SF-12 values were calculated from SF-36 scores and mapped to SF-6D based on an algorithm developed by Brazier and Roberts [23]. **For subjects who developed UTI, follow-up assessments were completed on development of UTI. Specific recall time not reported; we assumed the assessment occurred within one week. For subjects who did not develop UTI, follow-up assessments were completed at 6 months. GH, general health; PF, physical functioning; RP, role physical; RE, role emotional; VT, vitality; MH, mental health; BP, bodily pain; SF, social functioning; MCS, mental component summary; PCS, physical component summary; NR, not reported; NA, not applicable.*

the algorithm described by Ara and Brazier [20] (Table 1).

Maxwell *et al.* [14] measured QoL in older adults living in care homes using the Health Utilities Index Mark 2 (HUI2). Results were reported according to the presence or absence of several different clinical conditions, including UTI. The HUI2 was scored according to the published Canadian preference weights.

Two different research groups have used the SF questionnaires to evaluate the effect of UTIs on individuals with spinal cord injury (SCI). Haran *et al.* [18] and Lee *et al.* [19,27] have published a series of articles reporting the use of the SF-36 in individuals with SCI. Haran *et al.* [18] specified that individuals with a UTI have worse general health, vitality, and mental health domain scores than those who do not have a UTI, but did not report specific domain values for these groups. This paper cites a website containing SF-36 data stratified by age, sex and impairment group, but at the time of writing this link was not functional. The authors were contacted but were unable to provide additional information. In 2008, the group published mapped SF-6D values derived from both the full SF-36 and the recalculated SF-12 scores [19].

A long-term cohort study of individuals with SCI by Vogel *et al.* [15] reported a statistically significant difference in SF-12 scores for patients with a UTI or severe UTI compared with patients without a UTI; however, the SF-12 values were not reported. Upon request, the authors provided us with anonymized patient-level SF-12 responses from their most recent follow-up [16,17]. Five of the 415 cases contained missing data; they were assumed to be missing completely at random and were omitted from the analysis. Using an algorithm developed by Gray *et al.* [21] and the accompanying spreadsheet available on the Health Economics Research Centre website [28], EQ-5D values were estimated. Because the Gray algorithm contains random number generators, it was necessary to run a simulation (10 000 times) in order to obtain mean EQ-5D estimates for each health state. All calculations were performed using Microsoft Excel 2007. The results of the mapping, as well as the physical and mental component summary scores provided by the authors are shown in Table 1.

DISCUSSION

Health state utility values are key variables in economic decision models and are increasingly used as primary outcome measures in clinical trials. Values for equivalent health states can vary substantially depending on the measure and method of valuation. It is important that researchers use questionnaires that are responsive to change in clinically relevant domains and carefully consider recall periods. The 2005 paper by Ernst *et al.* [13] was the only paper to explicitly justify the choice of QWB as a QoL measure (rejecting the SF-36 on the basis that it is better suited to chronic conditions), while Maxwell *et al.* [14] specified that the HUI2 was chosen over the HUI3 because of the inclusion of the self-care domain, which is particularly important to older people living in care homes. In individuals with SCI, Lee *et al.* [19,27] reported floor effects in the physical function domain of the SF-36 and a large proportion of respondents who marked the physical activity question as not applicable or problematic. These authors have suggested that a modified version of the SF-36 in which the word 'walk' is replaced with 'wheel' as a more relevant measure of health in this population.

Two studies evaluated the impact of treatment failure on QoL [12,13], with Abrahamian *et al.* [12] also including the effect of infection with an antimicrobial resistant strain and Ernst *et al.* [13] including the effect of antimicrobial-related adverse events. Both studies were conducted in women with acute uncomplicated cystitis and found that QoL is adversely affected by treatment failure.

It should be noted that the mapped EQ-5D values presented in the present review were calculated using algorithms based on preferences derived from a UK community sample. In other countries, other algorithms may be more appropriate. Mapping is considered a pragmatic alternative for estimating preference-based utility scores when no other suitable measures exist. All mapping algorithms are associated with a degree of error. Future studies within these populations ought to consider the inclusion of commonly used preference-based measures of health.

ACKNOWLEDGEMENTS

We are very grateful to Drs Kathy Zebracki, Lawrence Vogel, Caroline Anderson, and Ms Kathleen Chlan for providing us with access to SF-12 data collected from their research cohort and their feedback on the manuscript. We are also grateful to David Wonderling for his comments on the manuscript.

FINANCIAL SUPPORT

This work was undertaken by the National Clinical Guideline Centre which received funding from NICE. The views expressed in this publication are those of the authors and not necessarily those of the institute. The authors declare that they have no competing interests.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **QoL**, quality of life; **NICE**, National Institute for Health and Clinical Excellence; **QALYs**, quality-adjusted life years; **IWB**, Index of Well Being; **NHS EED**, NHS Economic Evaluations Database; **HTA**, Health Technology Assessment; **CRD**, Centre for Reviews and Dissemination; **HEED**, Health Economics Evaluations Database; **CEAR**, cost-effectiveness Analysis Registry; **EQ-5D**, EuroQol 5-Dimension; **SF**, short-form; **HALex**, Health and Activity Limitation Index; **IQR**, interquartile range; **QWB**, Quality of Well Being; **HUI2**, Health Utilities Index Mark 2; **SCI**, spinal cord injury.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix SA Medline search strategy.
Appendix SB Heed search strategy.