

OBJECTIVES

- Health state valuations (utilities) are an essential component of cost-utility analyses; the quality of utility data applied in these analyses is critical to market access decisions in a growing number of countries.
- The National Institute for Health and Clinical Excellence (NICE) in the UK stipulates that utilities should be measured in patients using a generic and validated classification system for which reliable UK population preference values, elicited using a choice-based method such as the time trade-off (TTO) or standard gamble (SG) (but not rating scale), are available.¹
- The aim of this review was to systematically identify utility weights for specified health states in breast cancer and to assess their methodological compliance with the NICE reference case.

METHODS

A systematic review of studies in English language journals reporting health-state utilities for breast cancer was completed. Searches of the following sources were performed:

- Electronic databases (PubMed, EMBASE, Cochrane Library, including Database of Abstracts of Reviews of Effectiveness, National Health Service Economic Evaluation Database, and Health Technology Assessment databases) 1990 to date
- Internet resources
- Reference lists of relevant articles and reviews

Inclusion/exclusion of studies was performed by two people. Databases were searched using a combination of MeSH and free-text terms. MeSH headings included:

- "Mastectomy"
- "Quality of life"
- "Economics"

Non-MeSH terms included:

- "Breast neoplasms"
- "Standard gamble"
- "Time trade-off"
- "Cost-utility"

Studies reporting utility weights relevant to the following health states were included:

- Remission
- First locoregional recurrence, on treatment
- First locoregional recurrence, after treatment
- Second locoregional recurrence
- Third locoregional recurrence
- Distant disease
- Terminal disease

Data extracted included characteristics of the sample population, health state descriptions, method of elicitation, and utility estimates.

Literature reviews and secondary reports of data reported previously were excluded, and data reported within them were traced to original reports. Utility estimates elicited from patients or the general public using EQ-5D, TTO, SG, or other choice-based methods were included. Estimates elicited from health professionals or using rating scales or other non-choice-based methods were excluded.

RESULTS

- Fifty-nine studies were identified as potentially reporting utility weights for breast cancer health states.
- These studies were assessed for relevance to the health states defined and for methodological compliance with the NICE reference case.
- Fifty studies were excluded (Table 1).
- Details of the nine included studies are presented in Table 2.
- The individual estimates reported are presented in Figure 1.

Table 1. Study Inclusion/Exclusion

Reason for Exclusion	Number of Studies Excluded
Studies reporting utility estimates for breast cancer	59
Excluded studies	
Literature review	3
Secondary report of data reported previously	14
Health states not relevant to those specified in this study ^a	21
Sample not consistent with NICE reference case	6
Elicitation method not consistent with NICE reference case	3
Elicitation method and sample not consistent with NICE reference case	3
Included studies	9

^aOf these, 10 studies were methodologically consistent with the NICE reference case.

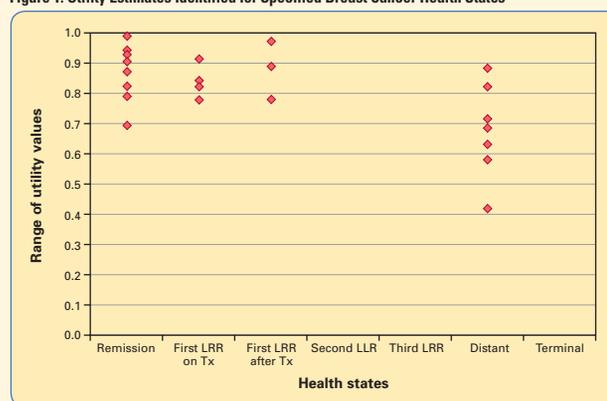
Table 2. Details of Included Studies

Study	Method of Elicitation	Sample
Jansen et al., 2001 ²	SG, TTO	94 early breast cancer patients
Jansen et al., 1998 ³	TTO	68 early breast cancer patients
Lidgren et al., 2007 ⁴	EQ-5D, TTO	345 early breast cancer patients
Mansel et al., 2007 ⁵	SG	26 early and advanced breast cancer patients
Grann et al., 1998 ⁶	TTO	54 members of the public
Lloyd et al., 2006 ⁷	SG	100 members of the public
Schleinitz et al., 2006 ⁸	SG	156 members of the public
Wolowacz et al., 2008 ⁹	EQ-5D utilities estimated from QLQ C-30 data ¹⁰	929 early breast cancer patients
Sorensen et al., 2004 ¹¹	SG	Unspecified number of early breast cancer patients

EQ-5D = EuroQol-5D; QLQ C-30 = EORTC QLQ-C30; SG = standard gamble; TTO = time trade-off.

- There was substantial variability between alternative estimates for similar health states (Figure 1).
- In some cases, the estimates within the same study were inconsistent with each other. For example, the study by Lidgren and colleagues (2007)⁴ reported EQ-5D and TTO estimates elicited from 345 early breast cancer patients. The EQ-5D estimate for "first year after primary breast cancer" (0.696 [95% CI 0.634-0.747]) was similar to that for "metastatic disease" (0.685 [CI 0.620-0.735]).
- No estimates were identified for second or third locoregional recurrences.
- Figure 1 displays the range of utility values retrieved for each of the specified health states.

Figure 1. Utility Estimates Identified for Specified Breast Cancer Health States



LRR = locoregional recurrence; Tx = therapy.

DISCUSSION

- The variability and inconsistency of reported utility estimates for breast cancer health states present a problem for researchers performing cost-utility analyses.
- In the absence of accepted methods for the formal synthesis of utility estimates, the range of available estimates should be explored. However, the degree of variability introduces substantial uncertainty into cost-utility estimates for breast cancer interventions.
- The reason for the discrepancies between studies and the inconsistencies within studies is unclear, and authors have not often commented on the variability.
- The new NICE methods guide (currently under review)¹² is likely to explicitly recommend that utility estimates be elicited from patients within trials using the EQ-5D, with an acknowledgement that this may not be appropriate in all cases. In the case of early breast cancer trials, the number of relapse events is relatively low, and most patients are in remission for the duration of the trial. Therefore, the amount of information about post-relapse health states that can be collected with the EQ-5D is limited.
- Important information about the impact of adverse events could be collected within trials. However, care should be taken in scheduling utility assessments in relation to the administration of each chemotherapy cycle. Most adverse events are transient and are resolved before the next cycle of chemotherapy is administered; if the patient is still suffering from an adverse event, the cycle is likely to be postponed until they have recovered. Collecting utility information only at the time of each chemotherapy administration will therefore underestimate the impact of adverse events on quality of life. Additional assessments should be scheduled to coincide with the period of maximum impact of adverse events.

CONCLUSIONS

- This review of utility weights for breast cancer health states revealed a high level of uncertainty about the evidence base that informs cost-utility analyses in this disease area.
- Despite the quantity of information available, there is no universally accepted set of health states covering the whole disease pathway from diagnosis of early breast cancer to death; numerous utility estimates for numerous health states have been reported.
- Rigorous research is required to address the need for high-quality and precise utility estimates for an accepted set of breast cancer health states.

REFERENCES

- NICE. Guide to the methods of technology appraisal (reference N0515). 2004. Available at: <http://www.nice.org.uk>. Accessed Mar 12, 2008.
- Jansen SJ, Kievit J, Nooij MA, Stiggelbout AM. Stability of patients' preferences for chemotherapy: the impact of experience. *Med Decis Making* 2001;21(4):295-306.
- Jansen SJ, Stiggelbout AM, Wakker PP, Vlieland TPMV, Leer JH, Nooy MA, et al. Patients' utilities for cancer treatments: A study of the chained procedure for the standard gamble and time tradeoff. *Med Decis Making* 1998;18:391-9.
- Lidgren M, Wilking N, Jonsson B, Rehnberg C. Health-related quality of life in different states of breast cancer. *Qual Life Res* 2007;16(6):1073-81.
- Mansel R, Locker G, Fallowfield L, Benedict A, Jones D. Cost-effectiveness analysis of anastrozole vs tamoxifen in adjuvant therapy for early stage breast cancer in the United Kingdom: the 5-year completed treatment analysis of the ATAC ('Arimidex', Tamoxifen alone or in combination) trial. *Br J Cancer* 2007;97(2):152-61.
- Grann VR, Panageas KS, Whang W, Antman KH, Neugut AI. Decision analysis of prophylactic mastectomy and oophorectomy in BRCA1-positive or BRCA2-positive patients. *J Clin Oncol* 1998;16:979-85.
- Lloyd A, Nafees B, Narewsky J, Dewilde S, Watkins J. Health state utilities for metastatic breast cancer. *Br J Cancer* 2006;95(6):683-90.
- Schleinitz MD, DePalo D, Blume J, Stein M. Can differences in breast cancer utilities explain disparities in breast cancer care? *J Gen Intern Med* 2006;21(12):1253-60.
- Wolowacz SE, Cameron DA, Tate HC, Bagust A. Docetaxel in combination with doxorubicin and cyclophosphamide as adjuvant treatment for early node-positive breast cancer: A cost-effectiveness and cost-utility analysis. *J Clin Oncol* 2008;26(6):925-33.
- Kind P. Measuring the value of quality of life in cancer: An index based EORTC QLQ-C30. Presented at the 41st Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.
- Sorensen S, Brown R, Benedict A, Flood E, Revicki D. Patient-rated utilities in postmenopausal early breast cancer (EBC): a cross-country comparison. Contributed Podium Presentations. *Value Health* 2004;7:637-57.
- NICE. Guide to the methods of technology appraisal. 2007. Available at: http://www.nice.org.uk/about/nice/howwe/work/devicetech/technologyappraisalprocessguides/technologyappraisalmethodsreview/technology_appraisal_methods_review.jsp. Accessed Mar 12, 2008.

CONTACT INFORMATION

Victoria Brennan, MSc
Health Economics Researcher

Williams House
Manchester Science Park
Lloyd Street North
Manchester, M15 6SE
United Kingdom

Phone: 011-441612323407
E-mail: vbrennan@rti.org

Presented at: ISPOR 13th Annual International Meeting
May 3-7, 2008
Toronto, Ontario, Canada