EFFECTS OF CANCER TREATMENT ON QUALITY OF LIFE (ECTQOL): FINAL RESULTS

REPORT BY THE DECISION SUPPORT UNIT

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Anju Keetharuth[1], Simon Dixon[1], Matthew Winter[2],
Peter Clark[3], Sandra Gutcher[2] and Marie Horton[3]

[1] School of Health and Related Research, University of Sheffield

[2] Weston Park Hospital, Sheffield

[3] The Clatterbridge Cancer Centre, Wirral

Decision Support Unit, ScHARR, University of Sheffield, Regent Court, 30 Regent Street
Sheffield, S1 4DA

Tel (+44) (0)114 222 0734
E-mail dsuadmin@sheffield.ac.uk
Website www.nicedsu.org.uk
Twitter @NICE_DSU

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EXECUTIVE SUMMARY

The main aim of the ECTQoL study is to assess the feasibility of collecting data from patients to determine the effects of cancer treatments on patients' quality of life. This report contains the findings from breast cancer clinics at the two sites: Weston Park Hospital in Sheffield and The Clatterbridge Cancer Centre in the Wirral.

It took 5 months to recruit 40 patients at one site. Across the two sites, Sheffield and Clatterbridge, 79 breast cancer patients were recruited and were asked to complete the EQ-5D. Oncology consultants filled in a brief questionnaire that provided additional details about the stage of the disease, the therapy and the response. The mean EQ-5D score for the 79 patients was 0.718 (standard error = 0.027). EQ-5D scores have been calculated by disease stage, line of therapy, response and patient groups. In most cases the scores have a logical ordering with but the complexity of the disease and treatment means that numerous combinations of therapy, stage, line and response are possible. Consequently the finding is that a large sample size is needed to allow any conclusions to be drawn. In addition, the study reveals that adverse events and disease response are difficult to classify without additional testing (and funding).

However, whilst the study has identified some difficulties and the need for much larger sample sizes, it was successful in demonstrating the feasibility of collecting utility data from routine practice. The value of any future work, therefore, needs to be considered in the context of alternative sources of utility values. Whilst a scaled-up version of this study would be complex, it would provide data with considerable advantages; EQ-5D estimates in an England and Wales population of patients in routine care precisely matches NICE's needs.

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ABBREVIATIONS AND DEFINITIONS

QoL	Quality of Life
sd	Standard Deviation
WHO	World Health Organisation

1. INTRODUCTION

1.1. BACKGROUND

NICE Technology Appraisals are integral to the treatment choices made available to patients and clinicians in oncology. These appraisals are based on all available evidence relating to treatment effects, side-effects, patients' health-related quality of life, and costs. These data are then combined within a cost-effectiveness model, which becomes central to the appraisal committee's decision.

Within this process, it is recognised that the best available evidence is not always of high quality. In these circumstances, the committee will rely on estimates obtained from less valid/relevant methods. One aspect of appraisal where this problem is encountered is the measurement of patient quality of life (QoL).

Whilst for most appraisals good QoL data are available in the necessary form, it has become apparent that cancer treatments frequently do not have the necessary QoL data. The format required by NICE is to have QoL measured using EQ-5D responses from comparable patient populations which can then be applied to the cost-effectiveness model. So, for example, many cancer treatments are represented by a simple three health state model of 'pre-progression', 'progression' and 'death'. In addition to these, the impact of adverse events related to treatments also needs to be considered. In which case, we need an average QoL value from patients completing the EQ-5D who are either in the 'pre-progression' or 'progression' health state, plus decrements in QoL value associated with adverse events. However, to date, very few cancer trials use the EQ-5D, or other preference based outcome measures, and so alternative methods are used to derive the QoL values.

A common alternative source of QoL values in cancer appraisals is the valuation of hypothetical health state descriptions that aim to match the health states within the cost-effectiveness model. One such study, which is frequently used within breast cancer appraisals, for example, is by Lloyd and colleagues[1]. The latter study provides health state utilities for metastatic breast cancer. The health states used were obtained from a rapid literature review and qualitative research with expert physicians and oncology nurses. The utility values were obtained from the general population. Therefore the main limitation of the paper is the health state values were generated from vignettes and not directly obtained from

patient. This is therefore not in accordance with the NICE reference case which also suggests EQ-5D as the preferred measure[2]. In recent appraisals there has been growing disquiet among the committees about the validity of these values, but alternative values have not been identified. When faced with uncertainties of this kind, the tasks of the committees are rendered more difficult and it is less likely that new treatments will be approved.

The aim of this study is to pilot an approach to obtain more robust estimates of QoL in breast cancer that are can be used within cost-effectiveness models. Such estimates, if available, will then help produce better decisions relating to breast cancer treatment in England and Wales. The study will also serve as the first in a possible series of such studies that broaden the focus from breast cancer to other cancers.

The objectives are:

- To test patient identification and consent procedures in this patient population.
- To estimate participation rates and number of patients recruited (in total and within the three groups targeted).
- To estimate mean utility and standard deviations relating to QoL in the three patient groups targeted and by line of therapy.
- To estimate the sample sizes and patient populations required for a subsequent survey that can identify statistically significant differences between important patient sub-groups.

2. METHODS

Breast cancer patients were recruited at two sites: Weston Park (Sheffield) and the Clatterbridge Cancer Centre (Liverpool). As part of the study, each patient was required to answer the EQ-5D (3L) and the oncologist responded to five questions relating to the site, stage and status of the cancer together with simple treatment details (Appendix 1). The clinical questions were designed collaboratively with Professor Peter Clark and Dr Matthew Winter.

In addition to this, data has been collected on the numbers of patients attending clinic, numbers eligible, numbers invited to participate (as some eligible patients may not be asked to participate by the doctor) and numbers consented to enter the study.

This study was approved by NHS Research Ethics Committee Yorkshire and Humber – Sheffield with the reference number 12/YH/0001 in February 2012. Research and Development permission was obtained from both sites.

2.1. INCLUSION CRITERIA

Three separate sets of breast cancer patients were to be included in the study. Firstly, those completing the first half of the chemotherapy – cycle 3 or 4 ('treatment'). Secondly, those finishing chemotherapy, before the completion of treatment ('treatment failures'). Among the latter category, a further distinction was made as to whether the 'failure' was associated with toxicity or disease progression. Thirdly, those attending for a review at least one year following treatment completion ('treatment success').

These four groups were chosen as they fit the data requirements of the typical cancer model used in NICE Technology Appraisals.

- 'Treatment' represents an average utility experienced over the course of the 6 cycles (on the assumption that mid-treatment utility approximates average utility over the full treatment period).
- 'Treatment failure (toxicity)' and 'treatment failure (progression)' are self-explanatory.
- 'Treatment success' represents longer-term quality of life associated with progression-free survival. The annual review was chosen for convenience and to ensure that any toxicity relating to treatment would have ended.

2.2. RECRUITMENT

Patients with breast cancer coming into breast cancer clinics for treatment or routine follow-ups were invited to take part in the survey. For those patients who were coming for treatment at intervals of less than 4 weeks, an invitation letter, participant information sheet and consent form was handed out at the end of a clinic visit. For those patients who were coming for treatment more than four weeks after a previous visit, they were invited via a letter sent by

their consultant (including the information sheet and consent form). For both groups of patients, they were asked to read the information sheet and if they were willing to take part, complete the consent form when they next attended the clinic.

Patients were recruited over a five month period; mid April 2012 to mid-September 2012 in Sheffield and over a similar period of five months from November 2012 to March 2013 in Clatterbridge. Patients were recruited from the breast cancer clinics of two consultant oncologists and five main consultants in Sheffield and Clatterbridge respectively.

3. RESULTS

The descriptive results from this study are arranged under three different main headings and throw light on patient identification and procedures, participation rates and EQ-5D by current stage, lines of therapy, response and patients groups. Given that there were only 79 participants in the study, only descriptive statistics are meaningful. In addition, it is pointed out that there are very low numbers in some of the categories under consideration which limits the inference from the results provided.

3.1. PARTICIPATION RATES

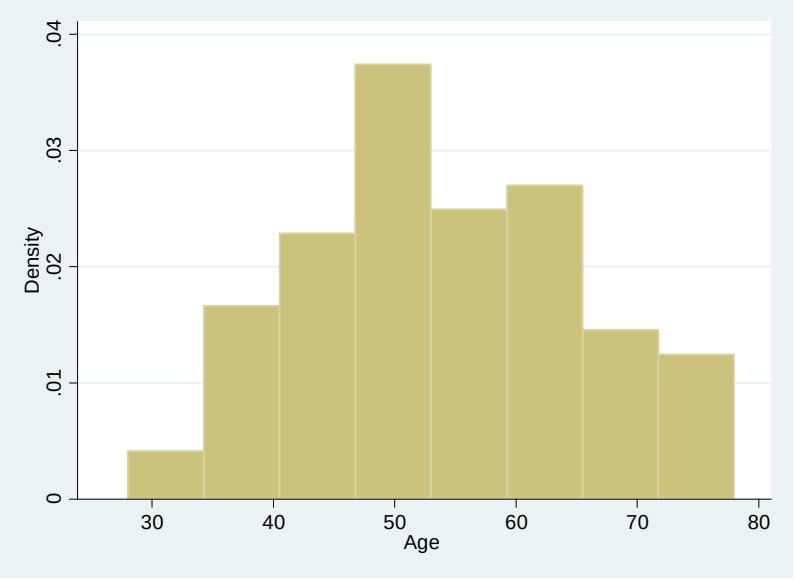
Over a period of five months in Sheffield, out of 43 patients who were eligible as per inclusion criteria for the study, three did not consent to participate, bringing the number of participants to 40 and the participation rate to 93%. There were four neo-adjuvant patients who also presented themselves at the clinic but were not invited to participate as they were not eligible for participation as this patient group is rarely the focus of a NICE Technology Appraisal, and therefore, the need for utility data is not there. One neo-adjuvant patient had been invited and consented to the study but her data has been excluded from the analysis. An explanation was provided to the patient as to the reason why her data could not be used and an apology was also presented. In Clatterbridge, 41 patients were approached for the study; one refused to participate and another person who had actually consented withdrew consent and her data has not been used. It took five months to recruit 40 patients in Clatterbridge. A total of 79 patients were recruited for the study.

The three potential cancer therapies were chemotherapy, endocrine therapy and immunotherapy. Out of 79 patients recruited, 78 patients were undergoing chemotherapy and only one was undergoing endocrine therapy.

At the design stage of the study, it was thought that it would have been possible to recruit 40 patients within a period of three months but it took 2 months longer. The average recruitment rate is eight patients per month which is exactly half that originally anticipated. It is noted that there is a lead in time of at least three weeks from when the first patient is identified to when next seen for possible consent.

The year of birth of the participant was recorded and the mean age is 54.0 years (sd 11.5) and the range is between 28 and 78. Age was missing for two participants. The age distribution is shown in Figure 1 below.

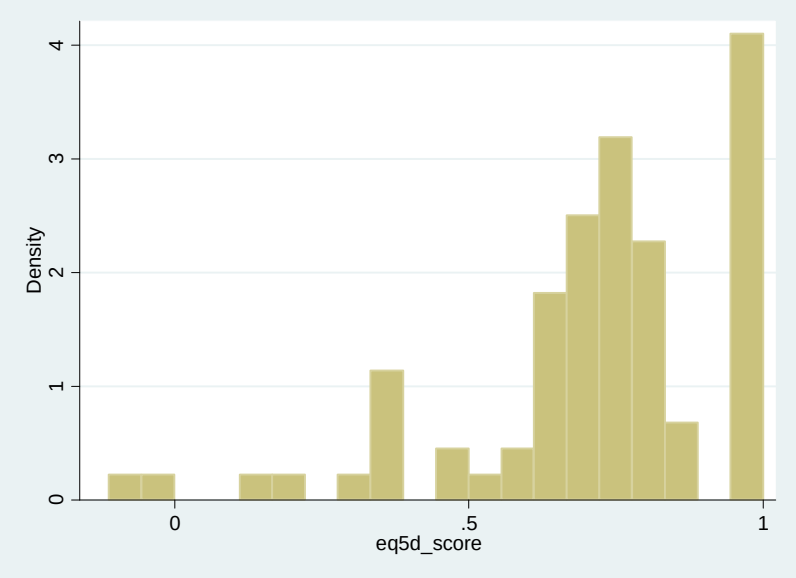
Figure 1 Age distribution



3.2. MEAN EQ-5D SCORES

EQ-5D scores have been using the Measurement and Valuation of Health UK weights[3]. The mean score for the 79 patients is 0.718 with a standard deviation of 0.239. The distribution is represented in Figure 2 below.

Figure 2 EQ-5D distribution



Only two participants have an EQ-5D score of less than 0. As is typically the case with EQ-5D distributions, there are a high proportion of patients reporting full health: 18 patients undergoing cancer treatments in our study report full health. Over 81% of participants record an EQ-5D score of 0.6 and over. The ceiling effects of the EQ-5D are well documented in other disease areas and even in breast cancer. It is pointed out that the distribution is very similar to that observed in other disease areas[4] and breast cancer.[5]

3.2.1. EQ-5D scores by stage

For the purpose of this study, the different cancer stages identified with the help of oncologists were: early breast cancer with a curative intent, locally advanced breast cancer with a curative intent and locally advanced or metastatic cancer with a palliative intent (**Error! Reference source not found.**)

Table 1 EQ-5D scores by stage

Stage	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Early breast cancer (curative intent)	59	0.761	0.202	-0.112	1
Locally advanced breast cancer (curative intent)	4	0.700	0.231	0.485	1
Locally advanced or metastatic cancer (palliative intent)	16	0.566	0.311	-0.16	1

While 59 and 16 patients were recruited in the early breast cancer stage and metastatic cancer with palliative intent respectively, only four were recruited in the locally advanced stage. As expected, those with metastatic cancer with palliative intent, the EQ-5D were significantly lower than those with early breast cancer. One patient with a negative EQ-5D score was from the metastatic stage with palliative intent and the other was at an early breast cancer stage. Even in the latter category, three participants recorded full health, a typical finding with QoL measures reflecting considerable heterogeneity of utilities among patients.

3.2.2. EQ-5D by line of therapy

There are five different lines of therapy represented by the study sample (Table 2 and 3). As shown in Table 4, 80% of patients recruited (60% in Sheffield and 100% in Clatterbridge) are receiving adjuvant cancer therapy, and in this case this refers to chemotherapy being provided post-surgery. Mean EQ-5D scores vary by line of therapy with the highest EQ-5D score observed among patients receiving adjuvant to surgery therapy. The six women undergoing 2nd line of therapy record the lowest mean EQ-5D of 0.326 but with a high standard deviation of 0.264. For the two patients undergoing 4th line therapy, their current stage is locally advanced or metastatic cancer with palliative intent and their mean EQ-5D scores is 0.810.

Table 2 EQ-5D scores by line of therapy in Sheffield

Line of therapy	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Adjuvant to surgery	24	0.866	0.139	0.556	1
1st line advanced disease	5	0.691	0.220	0.383	1
2nd line advanced disease	6	0.326	0.264	-0.016	0.639
3rd line advanced disease	3	0.673	0.357	0.293	1
4th line advanced disease	2	0.810	0.269	0.620	1

Table 3 EQ-5D scores by line of therapy in Clatterbridge

Line of therapy	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Adjuvant to surgery	39	0.690	0.207	-0.112	1

Table 4 EQ-5D scores by line of therapy at both sites

Line of therapy	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Adjuvant to surgery	63	0.757	0.202	-0.112	1
1st line advanced disease	5	0.691	0.219	0.383	1
2nd line advanced disease	6	0.326	0.264	-0.016	0.639
3rd line advanced disease	3	0.673	0.356	0.293	1
4th line advanced disease	2	0.810	0.269	0.620	1

3.2.3. EQ-5D by response

There are 4 categories of responses: stable disease, progressive disease, complete or partial response and unknown (Table 5 to 7). As shown in Table 7, the response is unknown for 83% of patients (67% in Sheffield and 100% in Clatterbridge) and their EQ-5D mean score is 0.757 (sd 0.202). Unsurprisingly, those with progressive disease (n = 7) report an EQ-5D score of 0.693 which is lower than those with an unknown response.

Table 5 EQ-5D scores by response in Sheffield

Response	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Stable disease	1	0.691	.	0.691	0.691
Progressive disease	7	0.693	0.342	0.189	1
Complete or partial response	4	0.372	0.357	-0.016	0.725
Unknown	27	0.824	0.185	0.362	1

Table 6 EQ-5D scores by response in Clatterbridge

Response	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Unknown	39	0.690	0.208	-0.112	1

Table 7 EQ-5D scores by response at both sites

Response	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Stable disease	1	0.691		0.691	0.691
Progressive disease	7	0.693	0.342	0.189	1
Complete or partial response	4	0.371	0.357	-0.016	0.725
Unknown	66	0.745	0.208	-0.112	1

3.2.4. EQ-5D by treatment outcomes

80% of participants are still undergoing treatment (60% in Sheffield and 100% in Clatterbridge) but six in total have had treatment failures, one of whom due to toxicity and the rest due to progression of the disease (Table 10). The patients who have stopped treatment due to progression have the highest EQ-5D scores of 0.873 (sd 0.176). Those patients subject to successful treatment have slightly higher EQ-5D (mean difference 0.077) than those still undergoing treatment. There was just one patient who stopped treatment due to toxicity and not surprisingly her EQ-5D is the lowest.

Table 8 EQ-5D scores by treatment outcomes in Sheffield

Treatment outcomes	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Treatment	24	0.745	0.221	0.159	1
Treatment failure (toxicity)	1	0.189	.	0.189	0.189
Treatment failure (progression)	5	0.873	0.176	0.639	1
Treatment success	9	0.788	0.334	-0.016	1

Table 9 EQ-5D scores by treatment outcomes in Clatterbridge

Treatment outcomes	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Treatment	39	0.690	0.208	-0.112	1

Table 10 EQ-5D scores by treatment outcomes at both sites

Treatment outcomes	N	Mean EQ-5D scores	Standard deviation	Min EQ-5D	Max EQ-5D
Treatment	63	0.711	0.213	-0.112	1
Treatment failure (toxicity)	1	0.189		0.189	0.189
Treatment failure (progression)	5	0.873	0.176	0.639	1
Treatment success	9	0.788	0.334	-0.16	1

Further details of the study sample are given in Appendix 2.

3.3 SAMPLE SIZE CALCULATION

On the basis of the above results, sample sizes have been calculated to provide an indication of how many patients need to be recruited to provide a reasonable chance (80% power) of detecting a difference in utility values, statistically significant at the 5% two-sided level. In the current study, the numbers in the category of progressive disease is very low. Therefore to calculate sample sizes, data from two sources have been used to complement the results obtained [1, 6].

Table 11 Utility decrements used in sample size calculation

Decrement used	Source	Required sample size	Size of population
0.272	Lloyd et al (2006) (Stable to progression)	13	143
0.11	Lloyd et al (2006) (toxicity *)	69	-
0.07	Liverpool Reviews and Implementation Group (2013) Based on progression for non-small lung cancer	183	2013
0.02	Liverpool Reviews and Implementation Group (2013) Based on toxicity for non-small lung cancer **	2242	-

* Based on one toxicity ** Decrement from observed toxicity whilst on treatment pemetrexed

The utility decrement associated with progression of cancer of 0.272 has been used for two reasons. First it is widely used and uses a reasonable methodology. Second, the paper is based on a similar patient population (breast cancer) to this pilot study. The utilities for decrement and toxicity from Evidence Report Group (ERG) evidence report on pemetrexed have also been used as it is one of the very few trials that collected EQ-5D data.

In calculating the population sample size required to obtain robust values for progression state, the proportion of patients reported in Table 5 recruited in the various stages of cancer in Sheffield has been used as all the stage patients recruited in Clatterbridge was ‘unknown’. The standard deviation obtained in the pooled data has been used in the sample size calculation. It has not been possible to calculate the number of patients required to obtain robust estimates for decrements associated with toxicity because during the study there was incomplete reporting for toxicity.

4. DISCUSSION

4.1. RECRUITMENT AND MISSING DATA

Over a period of five months at each site, 79 participants have been recruited for this study at Weston Park Hospital in Sheffield and Clatterbridge Cancer Centre in the Wirral. This has taken longer than expected and this is due to the fact that on average, there are only two eligible patients per clinic per week as opposed to four as originally anticipated. The participation rate is quite high with 94% of eligible participants having consented to take part in the study. Missing data were rare, with only three fields across all 79 patients not completed, and these could be ascertained through a search of medical records (although not in this study as ethics approval does not cover this).

4.2. EQ-5D SCORES

Mean EQ-5D scores and standard deviations have been calculated by current stage, line of therapy, response and patient group. Analyses by these sub-groups is required as the licensed indication for therapies are usually defined by stage and line of therapy (e.g. metastatic breast cancer with no previous chemotherapy) and the cost-effectiveness models structured in terms of response (e.g. stable or progressed disease).

The scores are difficult to interpret due to small patient numbers in some categories (e.g. individual lines of therapy), but where the larger sample sizes are present, the scores are generally as expected, for example, those patients with more advanced cancer having lower QoL. Mean EQ-5D scores have not been calculated for smaller subgroups than those presented as small sample sizes make any interpretation problematic. However, these problems of interpretation are understandable as the study was designed to assess feasibility of data collection, not to accurately estimate QoL.

4.3. PROBLEMS

Five problems are important to consider for any future studies attempting to capture EQ-5D data in support of NICE Appraisals through routine care.

Firstly, diagnosing adverse events and categorizing their severity is problematic as the World Health organization (WHO) criteria require additional testing that is not supported in routine NHS care[7]. Less costly and onerous classification of adverse events was investigated, for example, focusing on events which can be accurately ascertained clinically and dichotomising severity into 'requiring hospitalisation' and 'not requiring hospitalisation'. However, matching these data to trial data, where more accurate diagnosis is present, would be problematic. Consequently, this was not pursued within this study.

Secondly, response to therapy was not clinically confirmed in the majority of cases. Response is not relevant in the adjuvant setting and is therefore not measured. Again, with the additional funding present in drug trials, clinicians are able to more accurately classify response. Whilst 'unknown' is not technically missing data, it does reduce the value of the data appreciably given that many cancer models are based around response.

Thirdly, the types of patients across both sites were quite different. In Clatterbridge, all the patients recruited were undergoing adjuvant treatment and therefore there were no recruits in the other treatment outcomes categories. While Sheffield recruited seven patients who had experienced progressive disease, the treatment response for all patients in Clatterbridge was unknown. This difference may be explained by clinic effects where consultants at both sites are dealing with very different patients. Therefore the implication of this observation is that to obtain robust EQ-5D estimates, multi sites need to be involved making the study design more complex.

Fourthly, the set of values that could be produced by the data collection tool we have developed is aimed at supporting any (non neo-adjuvant) appraisal, rather than a specific indication. As a consequence, we have captured information by stage of disease, line of disease and type of therapy. This leads to the sample being spread across numerous patient populations. Therefore, any study that aims to produce EQ-5D estimates with low standard

errors, will require considerably large data collection efforts (x10 or more), especially for the rarer stage and line combinations.

Finally, an attempt has been made to calculate the number of patients that are to be recruited to a potential future study to obtain reliable estimates of utilities associated with progression and toxicity. To calculate sample, the utility differences were obtained from secondary sources and standard deviations from the pooled sample including Sheffield and Clatterbridge. To have 80% to detect a difference at the 5% level would require 13 cases and 143 recruits. This figure is only indicative and should be interpreted with caution. Similarly, if the decrement from progression is lower, as many as 2013 patients need to be recruited.

5. CONCLUSIONS

High quality data can be captured in routine practice using a simple data collection tool combining clinical and QoL data. Even for such a study, however, the logistics are quite complex to ensure that the concerns of research ethics are satisfied (e.g. patient information sheets, consent and cooling-off period). On the other hand, the recruitment rate was very high and once designed and established in clinic practice, the study was easy to conduct. This suggests that this type of study is a feasible way of collecting patient data in routine practice.

The simple, low-cost nature of the data collection contrasts with the data from drug trials, and as a consequence, the resultant data do not match in two important regards: adverse events and disease response are difficult to classify without additional testing (and funding). It is not clear how this could be overcome.

Additionally, the complexity of the disease and treatment means that numerous combinations of therapy, stage, line and response are possible. As a consequence, data are invariably sparse for some combinations. Whilst this can be overcome by undertaking larger studies, exploratory analysis suggests that these may require over a thousand patients.

It should also be noted that EQ-5D estimates are now starting to become more prevalent in cancer trials. The Pemetrexed appraisal used to identify treatment effects in Table 11, for example, has detailed data and precluded the need for utility estimates external to the trial [6].

Producing accurate estimates for all combinations would require considerably larger sample sizes.[6] We are aware of other recent oncology trials that include these data. As such, the need to generate EQ-5D estimates external to trials, as an alternative to the non-reference case estimates that are frequently used, is becoming less important assuming the trend of including EQ-5D in future trials continues.

The relative merits of alternative methods to collecting utility data need to be considered so that the most cost-effective approach can be adopted. The key methods are; use of existing published estimates, use of trial data within submissions and prospective data collection from routine care (i.e. the approach tested in this report).

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APPENDIX 1 CONSULTANT'S QUESTIONNAIRE

Date: dd / mm / yyyy **Date of birth:** dd / mm / yyyy **Gender:** male / female

Current stage

Early breast cancer (curative intent)	☐
Locally advanced cancer (curative intent)	☐
Locally advanced or metastatic cancer (palliative intent)	☐

Patient Group

Treatment	☐
Treatment failure (toxicity)	☐
Treatment failure (progression)	☐
Treatment success	☐

Current cancer therapies

Chemotherapy	☐
Endocrine therapy	☐
Immunotherapy	☐

Line of therapy

Adjuvant to surgery	☐
1st line advanced disease	☐
2nd line advanced disease	☐
3rd line advanced disease	☐
4th or more line	☐

Response

Stable disease	☐
Progressive disease	☐
Complete or partial response	☐
Unknown	☐

APPENDIX 2 DETAILED SAMPLE DESCRIPTION

Table A1 Patient groups by current stage in both sites (Sheffield and Clatterbridge)

	Current stage			
Patient groups	**Early**	**Locally advanced (curative intent)**	**Locally advanced or metastatic (palliative intent)**	**Total**
Treatment	53 (15,38)	3 (2,1)	7 (7,0)	63 (24,39)
Treatment failure (toxicity)	0	0	1 (1,0)	1 (1,0)
Treatment failure (progression)	0	0	5 (5,0)	5 (5,0)
Treatment success	6 (6,0)	1 (1,0)	2 (2,0)	9 (9,0)
Total	59 (21,38)	4 (3,1)	15 (15,0)	78

Table A2 Patient group by line of therapy in both sites (Sheffield and Clatterbridge)

	Line of therapy					
Patient groups	**Adjuvant**	**1st**	**2nd**	**3rd**	**4th or more**	**Total**
Treatment	56 (17,39)	3 (3,0)	3 (3,0)	0	1 (1,0)	63 (24,39)
Treatment failure (toxicity)	0	0	1 (1,0)	0	0	1 (1,0)
Treatment failure (progression)	0	1 (1,0)	1 (1,0)	2 (2,0)	1 (1,0)	5 (5,0)
Treatment success	7 (7,0)	1 (1,0)	1 (1,0)	0	0	9 (9,0)
Total	63	5 (5,0)	6 (6,0)	2 (2,0)	2 (2,0)	78

Table A3 Patient group by response in both sites (Sheffield and Clatterbridge)

	Response				
Patient groups	**Stable disease**	**Progressive disease**	**Complete or partial response**	**Unknown**	**Total**
Treatment	1 (1,0)	0	2 (2,0)	59 (20,39)	62 (23,39)
Treatment failure (toxicity)	0	1 (1,0)	0	0	1 (1,0)
Treatment failure (progression)	0	5 (5,0)	0	0	5 (5,0)
Treatment success	0	0	2 (2,0)	7 (7, 0)	9 (9,0)
Total	1 (1,0)	6 (6,0)	4 (4,0)	66	77 (38, 39)