MANC-RISK-SCREEN Parameter Update

Version 0 to Version 1

This document describes the process of updating the model parameters from those used in version 0 (the published early economic evaluation) and version 1 (the validated model).

# Utility Values

## Utility values by breast cancer stage

The utility values used in the early economic evaluation of a stratified breast cancer screening programme were taken from a study of the health related quality of life of Swedish women with different states of breast cancer [1]. This study was published in 2007 and it is likely that the experience of women with breast cancer will have changed in the preceding 15 years given changes in available treatments for different stages of breast cancer. As such, new utility values were sought for inclusion in the full version of the model.

Two recent systematic reviews have sought to identify health state utility values to represent different health states, adverse events, and treatments associated with living with breast cancer [2,3]. Pourrahmat et al. (2021) sought to identify utility values for different stages of a range of cancers including breast cancer. This systematic review identified 9 studies reporting utility values. Kaur et al. (2022) aimed to create a catalogue of health utility value associated with “different stages of breast cancer and treatment interventions”. This systematic review identified 79 relevant studies for inclusion.

To identify potentially relevant utility values for inclusion in the discrete event simulation model, the included studies of these two systematic reviews were searched. A number of criteria were used to identify a sub-set of potentially relevant utility values for the model. Studies had to have been conducted in a high income country as treatment regimens and therefore utility values would be more likely to be similar to those in the UK. Included studies must have included estimates for utility values for all stages of breast cancer or utility values that could be easily adapted to represent the different stages of breast cancer. Finally, a preference ordering was placed on the method used to derive the utility values: EQ-5D with value set derived for the country the study was conducted in; EQ-5D with value set derived from another country; time-trade off; standard gamble; visual analogue scale; other methods.

Only two potentially relevant studies were identified from the candidate set. Naik et al. (2017) estimated utility values for local or regional (0.82) and distant or metastatic (0.75) breast cancer from EQ-5D questionnaires completed by women with cancer in Canada [4]. No differentiation was provided for first year or subsequent year utility values. Rautalin et al. (2018) sought to investigate the health related quality of life of Finnish women with breast cancer using three instruments: the EQ-5D 3L, visual analogue scale, and the 15D (a HRQoL instrument developed in Finland) [5]. Values were estimated for primary treatment, recovery, remission, metastatic disease, and palliative care. These were mapped to the values required for the model such that primary treatment (0.85 EQ-5D) was used to represent the utility of stages I, II, and III in the first year while metastatic disease (0.74 EQ-5D) was used for stage IV disease. Subsequent year utilities for stage I, II, and III were taken from the recovery value (0.87 EQ-5D) while the metastatic value continued to be used for stage IV.

In order to select the most appropriate utility values for inclusion in the model, a focus group was held with 3 women who had previously been diagnosed with breast cancer. The researchers (SW and KP) first provided a brief presentation explaining the research and why the patients’ input was being sought. Two exercises were conducted wherein the participants were asked to consider their quality of life now and during the cancer treatment that had the greatest impact on their quality of life. Participants were asked to consider what number they would have rated their health out of 100 in these scenarios. Participants were then shown visual analogue scales with values representing those reported in Naik et al. (2017), Rautalin et al. (2018), and Lidgren et al. (2007) for comparison. Values were shown for the first year and then for subsequent years. Participants were not told which values came from which study. Following a group discussion of the values, a consensus was sought as to which values were most appropriate.

The final values chosen for inclusion in the model were those from Naik et al. (2017). One of the main reason these values were chosen was because they were the same in the first and subsequent years. The women in the focus group emphasised the ongoing psychological impact of breast cancer even post-recovery. For example, the women discussed their worry that the cancer might be coming back when they experienced episodes of ill health.

While the values in Naik et al. (2017) were deemed appropriate for use in the updated model, areas for further research arose in the group discussion. The women felt that they could not speak for women with metastatic cancer given that they had each recovered from stage I cancer. Furthermore, the women emphasised that people are likely to have different types of treatment and those treatments have different impacts on quality of life. In the women’s experience, chemotherapy had a very large impact on their quality of life. It was suggested by the researchers that weighted values representing the expected utility of women given the proportion of women receiving different treatment types for each stage of cancer and the utility values of those treatments may be more appropriate. It was also recommended that studies of the HRQoL of women in the UK be conducted to provide more valid utility values.

## Population Norm Health Utility Values

Studies referencing the original source of population norm utility values were searched for appropriate updated values. No new values were identified in this search.

# Costs

## The cost of the risk stratification strategy

In the early economic evaluation of a risk stratified breast cancer screening programme, the cost of the risk stratification strategy was estimated to be £10.57. This cost was estimated using a number of pragmatic assumptions by the researchers in the absence of data on resource use associated with risk stratification.

To produce a more accurate estimate of the cost of the stratification strategy, a microcosting study was undertaken. A clinical pathway for the risk stratification strategy was first created with input from medical oncologists, consultant geneticists and clinical trials assistants working on the BC-PREDICT project [6]. The resources required to provide the intervention were determined using the clinical pathway and the levels of resources required were estimated following semi-structured interviews with a medical oncologist, a consultant geneticist, a clinical geneticist, and two clinical trials assistants. Costs were attached to the resource use using a range of sources including the Personal Social Services Research Unit (PSSRU) Unit costs of Health and Social Care and NHS reference costs [7,8]. Costs were estimated for risk stratification strategies incorporating the Tyrer-Cuzick (TC) questionnaire alone, TC with Volpara breast density estimate (VBD), and TC, VBD, and a panel of 142 single nucleotide polymorphisms. Costs were estimated in the presence and absence of a number of implementation barriers which had been faced in the conduct of the BC-PREDICT study.

In the updated model, the cost estimated for the TC+VBD when the strategy was perfectly implemented in the NHS was used (£8.45).

## Treatment costs

To identify potential sources of updated treatment costs, a systematic review of papers seeking to estimate the cost of treating breast cancer was conducted.

### Search strategy

A previous systematic review of the global cost of treating breast cancer was published by Li et al. in 2018 [9]. This study identified 20 studies, all of which estimated the cost of treating breast cancer by stage. However, only one study from the UK was identified and this was published in 1991. To explore whether any studies had been published more recently, the search used by Li et al. was re-run from inception up to 2021. Furthermore, Li et al. included search terms limiting the results to studies which included a cost by cancer stage. In this study these terms broadened to include cancer costs by stage or by a number of prognostic indicators.

### Inclusion criteria

The inclusion criteria was based around the ‘PICOS’ system (see Table 1) and used to find relevant empirical (primary) studies reporting relevant treatment costs for breast cancer. The following papers were excluded: not full primary studies that have collected empirical data and not written in English. This means that papers reporting editorials, commentaries, conference abstracts and reviews were excluded from this review.

**Table 1:** Study inclusion criteria

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| --- | --- |
| **Characteristic** | **Description** |
| **Patient** | Adults (18 years and over) with breast cancer |
| **Interventiona** | Treatments including hospital visits, surgery, medicines, radiotherapy and imaging costs for monitoring disease progression |
| **Comparator** | Other types of cancer and all other health conditions or the absence of other health conditions |
| **Outcome** | Costs by prognostic indicator or stage of disease |
| **Study Design** | Primary empirical study using retrospective or prospective data collection |
| **Setting** | UK NHS |
| Language | English |
| Publication type | Primary study reporting an empirical analysis |

a Intervention relates to the primary treatment being costed

### Study Selection

The study selection process involved double screening of all the titles and abstracts identified by the electronic search. The selection process was conducted in two-stages (i) titles and abstracts screened by two reviewers (SW and KP); (ii) full-text versions of the selected studies were obtained and screened by two reviewers (SW and KP) (iii) hand searching of the reference lists of included studies and any identified review papers by one reviewer (SW). Any discrepancies concerning the inclusion or exclusion of studies will be resolved through discussion with a third reviewer.

### Results

The initial literature search identified 2,213 potentially relevant papers. After initial screening, the full texts of 50 studies were reviewed. From these studies only one potentially relevant study was identified [10]. In addition, a second potentially relevant study was added based on the researchers knowledge of the literature base [11]. This study was missed by search used in the original systematic review as the abstract references that costs were broken down by “staging” rather than “stage”.

#### Relevance of estimates from Laudicella et al. (2016)

In 2016 Laudicella et al published a retrospective cohort study of the cost of treating all patients over the age of 18 with breast, colorectal, prostate and lung cancer in the UK. The authors used data from the National Cancer Data Repository combined with Hospital Episode Statistics to determine resource use of the patients and then applied costs using the National Schedule of Reference Costs. Costs are estimated for incidence and prevalence and broken down by a number of factors including age and cancer stage.

There are a number of issues which limit the utility of the data in Laudicella et al. for updating the parameters in the model. Firstly, while the study was published in 2016, resource use was collected for patients diagnosed with cancer between 2001 and 2007. As such the data is still likely to be significantly out of data in terms of representing current treatment patterns for breast cancer. The use of only cancer registry data and hospital episode statistics means that the cost of primary care use is likely to be omitted. In addition, the costs are not compared to those experienced by patients without cancer and so do not represent the incremental costs of cancer. Finally, the cost of treating breast cancer is only broken down into stages 1 and 2 compared to stages 3 and 4.

#### Relevance of estimates from Sun et al. (2020)

In 2020, Sun et al published a study estimated the cost of treating women with early stage (I to IIIa) breast cancer in the UK NHS. This study used data from the National Audit of Breast Cancer in Older Patients project which contains information on cancer registrations linked to various datasets including Hospital Episode Statistics, Systematic Anti-Cancer Therapy (chemotherapy), and National Radio-therapy. NHS reference costs were used to assign costs to resource use. The included women were diagnosed with breast cancer between 2014 and 2015. Costs in the first year following diagnosis were estimated for each stage using a variety of generalised linear regression models with different link functions.

The estimates produced by Sun et al also have limited utility as inputs for the model in this paper. Only first year costs following diagnosis were estimated whereas the model requires lifetime costs. The paper only investigates the cost of early stage cancer and therefore does not include stage IIIb or IV cancer. Data would have to be adapted to produce estimates of the cost by NPI category rather than by stage, Furthermore, no comparator group was used and the costs therefore do not represent the incremental cost of breast cancer compared to normal health care resource use. As in Laudicella et al. there is limited data on primary care resource use potentially leading to underestimates of treatment

#### **Choice of Costs for Inclusion in the Model**

The cost estimates produced by Laudicella et al were chosen for inclusion in the model despite their limitations as they represent the most up to date costs of breast cancer in the UK. As the costs are reported by age, stage, and treatment year, the structure of the model was adapted to include the costs. The costs are read into the model in a table and the values inflated to 2021 levels. An exponential regression is then estimated in the model to predict a patient’s total cancer treatment cost given their age, stage of cancer, and the number of years they live with their cancer before dying.

When a simulated patient in the model is diagnosed with cancer, their age, stage of cancer and time until death are entered into the model and a predicted total cancer treatment cost assigned. This value is then discounted according to the current year in the model.

Cancer screening provide value by ensuring cancer is diagnosed at an earlier stage, age, or both, resulting in lower treatment costs for the patient.

## The Costs of Treating Ductal Carcinoma in-Situ

No costs for treating DCIS were provided in Laudicella et al. As such the costs included in the original early economic evaluation were inflated to 2021 values using the NHS cost inflation index [7].

## Screening and Diagnosis

The costs of biopsy, ultrasound screening and MRI screening were taken from those reported in the NHS national reference costs [8]. The cost of follow-up was inflated from the early economic evaluation using the NHS inflation index.

The cost of mammography screening is no longer reported in reference costs and existing values are significantly out of date. As such the authors used pragmatic assumptions, guided by input from consultant medical oncologists, to estimate the cost of mammography using available cost data. The cost of the mammogram itself was assumed to be equal to a plain film X-Ray (£29.50: £2021) and required 10 minutes of radiographer time (£9) and 5 minutes each for two consultant radiologists to read the film (£20.50). It was assumed that one invitation letter and one results letter would be required (£0.12 each) and both would be posted second class (£0.66 each). The total cost was estimated to be £60.56. The authors recommend that a more robust microcosting study is conducted to estimate the cost of mammography to provide more accurate cost estimates.

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