

Supplementary table-1: Explanation for Costs in the decision analysis model

Explanation of Costs:

The cost of RRSO was based on national reference costs for an upper genital tract laparoscopic/endoscopic intermediate procedure.[1]
Costs of HRT[2] assumes HRT is given from age at RRSO (45 years) to menopause (51 years). These costs are calculated for the 80% assumed to be compliant with HRT.
Costs include the cost of three follow up DEXA scans for monitoring bone health and calcium and vitamin-D3 for additional osteo-protection.

Ovarian Cancer Costs

Costs for ovarian cancer diagnosis and treatment were derived from national reference costs and a recent ovarian cancer guideline developed by NICE.[1, 3] We assumed that the cost of diagnosis to include a pelvic examination, ultrasound scan, CA125 test, CT scan, percutaneous biopsy and peritoneal cytology.

The cost of treatment included the reference cost for a lower and upper genital tract very complex major procedure and administration of chemotherapy based on 6 cycles of carboplatin and paclitaxel treatment. It was assumed that in years-1 and -2 treated survivors would have a further three consultant visits, a CT scan and 4 CA125 tests each year. In years 3 to 5 post-surgery it was assumed that survivors would have 2 consultant visits and 2 CA125 tests. We were conservative in our cost-estimates and did not include costs for additional investigations, treatment of recurrence or management of complications in the analysis.

Costs for terminal care for ovarian cancer were derived from end-of-life costs for cancer patients based on a report from the National Audit Office, UK.[4]

In line with NICE recommendations future healthcare costs not associated with ovarian cancer were not considered.[5]

Breast Cancer Costs

Assumptions and costs for Breast Cancer diagnosis and treatment are derived predominantly from the 'National costing report: Implementing NICE guidance (Feb 2009)' from NICE, which provides estimates of the national cost impact arising from implementation of NICE guidelines for diagnosis and treatment of early and locally advanced breast cancer and advanced breast cancer in England, UK[6]; from UK Department of Health NHS reference costs 2012[1]; the BNF[2], and other relevant NICE guidelines on breast cancer care.[7, 8, 9]

Cost of breast cancer screening assumes routine mammography of 8 mammograms between 50 to 70 years in line with the UK NHS breast cancer screening programme.[10]

Cost of breast cancer treatment:

In the general population: 10% breast cancer is non-invasive Ductal Carcinoma Insitu (DCIS); 90% breast cancer is invasive; 95% of invasive breast cancer is early and locally advanced (41% Stage-1, 45% stage-2, 9% stage-3[6, 11, 12, 13]); 5% of invasive breast cancer is advanced breast cancer (stage 4)[6, 11, 12]; 35% of early & locally advanced breast cancer will progress to advanced breast cancer (NICE costing report, 2009).[6]

The cost of diagnosis includes the triple test of clinical examination, mammogram, ultrasound (US) & biopsy. Mean prevalence of Axillary lymph node metastasis in early invasive breast cancer is 31.4% (obtained from systematic reviews conducted within the NICE breast cancer guideline[8] and breast cancer clinical outcome measures (BCCOM) project.[14, 15]

Cost of Sentinel lymph node biopsy (SLNB): is obtained from NICE national costing report.[6] SLNB is used to stage the axilla for early invasive breast cancer and no evidence

of lymph node (LN) involvement on Ultrasound (US)/ negative US-guided biopsy (73% of invasive cancers).

Cost of axillary lymph node dissection (ALND): is assumed to be 25% of cost of breast surgery in line with the NICE guideline development group recommendation.[6] ALND is undertaken for lymph node positive cancers (31% early and locally advanced invasive cancers).[6, 8]

Breast Surgery Costs: This includes, costs of breast conserving surgery (assumed for all non-invasive cancers, and 75% of early/locally advanced (stage 1-3) invasive cancers); and costs of mastectomy with reconstruction (for 25% early/locally advanced cancers). Costs are obtained from the national NHS reference costs.[1]

Radiotherapy and Chemotherapy: Invasive breast cancers who are not low risk[14, 16, 17] receive adjuvant treatment in line with NICE guidelines. Costs include, radiotherapy costs for 60% of early invasive/locally advanced, radiotherapy and chemotherapy costs for 40% early invasive/locally advanced and chemotherapy costs for all advanced cancers.

Radiotherapy costs include planning and 40Gy in 15 fractions over 3 weeks (NICE guidelines[8]) or palliative treatment, taken from national NHS reference costs.[1]

Chemotherapy costs based on polychemotherapy,[15] include cost of administration, costs of 1st and 2nd line therapy and toxicity from NICE guidelines.[6, 7]

70% of general population invasive breast cancers are ER positive; 15% of early invasive breast cancers are HER2 positive and 25% of patients with advanced breast cancer are HER2 positive.[7, 8] ER & HER2 testing costs are obtained from a local NHS trust and included for all breast cancers.

Endocrine therapy costs: In line with NICE guidelines[6, 8], ER positive invasive breast cancers receive Tamoxifen 20mg/day (premenopausal)/ Anastrozole 1mg/day (postmenopausal) for 5 years: costed from the BNF.[2] Rates are adjusted for ER positivity and menopause status.

Biphosphonate costs: 74% of patients with advanced breast cancer will develop bone metastases and 65% of patients with bone metastases (48% advanced breast cancers) would be offered bisphosphonates.[6, 18, 19] In line with NICE guidelines, costs (from BNF[2]) are based on the assumption that 50% of these patients receive oral clodronate and oral ibandronic acid, and 50% receive intravenous zoledronic acid or pamidronate.[6]

Cost of Trastuzumab: For HER2 positive patients, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period) in line with NICE guidelines and costs obtained from NICE costing report for early and locally advanced/ advanced breast cancer.[6]

Of note 35% of early/locally advanced breast cancer progress to advanced breast cancer (NICE guidelines).[6] Recurrence rates for early/locally advanced breast cancer (from the USA National Surgical Adjuvant Breast and Bowel Project (NSABP)): 15.9% for node positive[20] and 11% for node negative[21] breast cancer giving a composite recurrence rate of 12.6% weighted for 31% node positive and 69% node negative disease. Recurrence rate for advanced or metastatic breast cancer is 66%, based on a reported 34% relapse free survival at 5yrs.[22]

Follow up Costs: Includes annual mammograms and six monthly consultations. MRI scan for all stage 4 cancers. Costs also include a progression rate of 35% from early and locally advanced to advanced disease,[6] and 66% relapse rate for advanced disease.[22]

Costs for terminal care for breast cancer were derived from end-of-life costs for cancer patients based on a report from the National Audit Office, UK.[4] In line with NICE recommendations future healthcare costs not associated with breast cancer were not considered.[5]

Cost of CHD fatal

Cost of fatal CHD was costed on the basis of a myocardial infarction using NHS reference costs.[1]

BNF- British National Formulary, CHD- Coronary heart disease, HRT- hormone replacement therapy, MRI- Magnetic resonance imaging, NHS- National Health Service, NICE- National Institute of Health and Care Excellence, RRSO- Risk reducing salpingo-oophorectomy

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