# Uptake rates of risk-reducing surgeries for women at increased risk of hereditary breast and ovarian cancer applied to cost-effectiveness analyses

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File S1. Search Strategy

**Search term for literature search (PUBMED):**

((costs and cost analysis[Mesh] OR decision support techniques\*[Mesh] OR cost-effectiveness[TIAB] OR cost-utility[TIAB] OR cost-benefit[TIAB])) AND ((breast neoplasms[Mesh]) OR (ovarian neoplasms[Mesh]) OR (breast-ovarian[TIAB]) OR population-based[TIAB] OR (mammary cancer[TIAB]) OR (mammalian carcinoma)) AND (early detection of cancer[Mesh] OR genetic testing[Mesh] OR mutation\*[TIAB] OR BRCA[TIAB] OR PALB2[TIAB] OR RAD51c/d[TIAB] OR TP53[TIAB] OR SNP[TIAB] OR ATM[TIAB])

**Search term for literature search in the CRD Datebase, NHS EED, HTA, DARE and CEA Registry:**

((breast cancer OR ovarian cancer OR BRCA) AND (cost effectiveness OR cost utility OR cost benefit) AND (genetic testing OR gene analysis OR multigene assay))

Table S1. Input parameters for the German model included in the value of information analysis (reproduction from Müller et al **[1]**).

| Parameter Set | Input parameters | Value (SD) | Distributions |
|---|---|---|---|
| **Uptake rates** | Uptake of RRM | 0.06 (0.02) | Beta |
| | Uptake of RRSO | 0.42 (0.04) | Beta |
| | Uptake of both RRSO | 0.45 (0.04) | Beta |
| | Uptake of intensified surveillance | 0.07 (0.02) | Beta |
| **Incidence of cancer in *BRCA* carriers** | Incidence of Breast Cancer Carriers | 35–39: 0.031 (0.002), 40–44: 0.021 (0.002), 45–49:0.023 (0.002), 50–54: 0.027 (0.002), ≥ 55: 0.033 (0.002) | Beta |
| | Incidence of Ovarian Cancer Carriers | 0.039 (0.005) | Beta |

| | | | |
|---|---|---|---|
| | Incidence of contralateral breast cancer Carriers | 0.067 (0.008) | beta |
| **Risk reduction due to preventive surgery** | Risk reduction of breast cancer after RRM | 0.08 (0.01) | Log-normal |
| | Risk reduction of breast cancer after RRM and RRSO | 0.05 (0.03) | Log-normal |
| | Risk reduction of ovarian cacner after RRSO | 0.28 (0.01) | Log-normal |
| | Risk reduction of ovarian cancer after RRM and RRSO | 0.14 (0.01) | Log-normal |
| | Risk reduction of contralateral breast cancer after RRM | 0.05 (0.01) | Log-normal |
| | Risk reduction of contralateral breast cancer after RRM and RRSO | 0.59 (0.02) | Log-normal |
| **Health related quality of life** | Health related quality of life in stage well | 0.920 (0.002) | Beta |
| | Health related quality of life in stage well with positive test result | 0.890 (0.02) | Beta |
| | Health related quality of life after RRSM | 0.850 (0.24), | Beta |
| | Health related quality of life after RRSO | 0.830 (0.24), | Beta |
| | Health related quality of life after RRM and RRSO | 0.780 (0.25) | Beta |
| | Health related quality of life in stage breast cancer | 0.679 (0.031) | Beta |
| | Health related quality of life in stage metastatics breast cancer | 0.629 (0.045) | Beta |
| | Health related quality of life in stage ovarian cancer | 0.52 (0.050) | Beta |
| | Health related quality of life in end stage ovarian cancer | 0.160 (0.250) | Beta |

Table S2. Input parameters for the German model not included in the value of information anaysis (reproduction from Müller et al [1]).

| Parameter Set | Input parameters | Value (SD) | Distributions |
|---|---|---|---|
| **Other trasnistion probabilties** | Genetic testing positive | 0.24 (0.003) | Beta |
| | Incidence of Breast Cancer non Carriers | 35–39: 0.004 (0.001), 40–44: 0.007 (0.001), 45–49: 0.008 (0.001), 50–54: 0.012 (0.002), ≥ 55: 0 (0.001) | Beta |
| | Incidence of Ovarian Cancer non Carriers | 0.002 (0.001) | Beta |
| | Incidence of contralateral breast cancer non Carriers | 0.015 (0.003) | Beta |
| | Mortality of all causes | Age and gender specific | Beta |
| | Breast cancer mortality | 35–39: 0.00 (0.000), 40–49: 0.001 (0.000), 50–59: 0.002 (0.000), 60–69: 0.004 (0.000), | Beta |

| | | | |
|---|---|---|---|
| | | 70–79: 0.007 (0.000), 80–89: 0.028 (0.001), 90–99: 0.139 (0.001), ≥ 100: 0.404 (0.002) | |
| | Ovarian cancer mortality | 0.015 (0.005) | Beta |
| | Incidence ovarian cancer in previous breast cancer patients | 0.015 (0.005) | Beta |
| | Probaility of developing metastasis in breast cancer patients | All ages: 0.0267 (0.0055) | Beta |
| **Cost parameters** | **Variable** | **Value in € (SD)** | |
| Diagnosis and monitoring | | | Gamma |
| | Ongoing high-risk screening / monitoring | 560 (224) | Gamma |
| Surgical options | | | |
| | Prophylactic mastectomy | 8317 (3327) | Gamma |
| | Prophylactic oophorectomy | 2854 (1142) | |
| | Prophylactic mastectomy + oophorectomy | 11,171 (4468) | |
| | Prophylactic oophorectomy in case of BC | 2854 (1142) | |
| | Prophylactic mastectomy in case of OC | 4783 (1913) | |
| | Therapeutic mastectomy | 6556 (2622) | Gamma |
| | Breast-conserving surgery | 4318 (1727) | Gamma |
| | Therapeutic oophorectomy | 2854 (1142) | Gamma |
| Medication BC | | | |
| | Chemotherapy BC (year 1, proportion in hormone receptor subgroups) | | Gamma |
| |     Triple – (0.60) | 6371 (2548) | |
| |     Her2neu (0.10) | 26,537 (10,615) | |
| |     HR + (0.30) | 6371 (2548) | |
| |     Chemotherapy metastatic BC | 19,488 (7795) | |
| |     Triple – (0.60) | 48,775 (19,510) | |
| |     Her2neu (0.10) | 12,201 (4880) | |
| |     HR + (0.30) | | |
| | Endocrine therapy (Her2neu/HR) BC, year 1/year 2-5 metastatic BC | 1120 (448) / 320 (128) / 1120 (448) | Gamma |
| | Neutropenic sepsis | 5782 (2313) | Gamma |
| | Neulasta (Pegfilgrastim) | 9852 (3941) | Gamma |
| | Antiemetics | 495 (198) | Gamma |
| | Bisphosphonates | 421 (168) | Gamma |
| Other treatment BC | | | |
| | Adjuvant radiotherapy | 1791 (716) | Gamma |
| | Local surgeries | 8381 (3328) | Gamma |

| | Psychological treatment in case of cancer diagnosis [EBM, Consortium] | 1231 (492) | Gamma |
|---|---|---|---|
| | Lymphatic drainage / physiotherapy (BC) | 1480 (592) | Gamma |
| Medication OC | | | |
| | Not advanced | 10,387 (4155) | Gamma |
| | Advanced | 30,080 (12,032) | |
| | Recurrence (in advanced Ca) | | Gamma |
| | Platin-resistent | 5408 (2163) | |
| | Platin-sensitive | 30,080 (12,032) | |
| Palliative care | | | |
| | End of life treatment in metastatic BC or OC | 11,145 (4458) | Gamma |

Table S3. Excluded studies

| Study/year | Main reason for exclusion |
|---|---|
| Balmana 2005 [2] | Risk reducing surgeries not considered |
| Gamble 2017 [3] | Populational testing |
| Patel 2018 [4] | Populational testing |
| Rubinstein 2009 [5] | Populational testing |
| Manchanda 2015 [6] | Risk reducing surgeries for sporadic cancer (not BRCA mutation carriers) |
| Manchanda 2016 [7] | Risk reducing surgeries for sporadic cancer (not BRCA mutation carriers) |
| Manchanda 2017 [8] | Populational testing |
| Manchanda 2018 [9] | Populational testing |
| Zhang 2019 [10] | Populational testing |
| Norum 2018 [11] | Insufficient reporting of the uptake rates of risk-reducing surgeries |
| Hoskins 2019 [12] | Choice of uptake rates was based on assumed perfect adherence |
| Tengs 2000 [13] | Choice of uptake rates was based on assumed perfect adherence |

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