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### cTable 1. Family history information in ovarian cancer cases

<table>
<thead>
<tr>
<th>Age</th>
<th>Manchester study</th>
<th>Scotland study</th>
<th>SIGNPOsT study</th>
<th>Washington study</th>
<th>Overall</th>
<th>OC cases in population</th>
<th>FH+ OC cases in population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total OC cases</td>
<td>FH+ OC cases</td>
<td>Total OC cases</td>
<td>FH+ OC cases</td>
<td>Total OC cases</td>
<td>FH+ OC cases</td>
<td>Proportion of FH+ in OC cases</td>
</tr>
<tr>
<td>&lt;30</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>30-34</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>35-39</td>
<td>18</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>40-44</td>
<td>54</td>
<td>27</td>
<td>20</td>
<td>6</td>
<td>11</td>
<td>43</td>
<td>20</td>
</tr>
<tr>
<td>45-49</td>
<td>101</td>
<td>39</td>
<td>27</td>
<td>10</td>
<td>36</td>
<td>17</td>
<td>75</td>
</tr>
<tr>
<td>50-54</td>
<td>131</td>
<td>55</td>
<td>58</td>
<td>24</td>
<td>39</td>
<td>7</td>
<td>110</td>
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<tr>
<td>55-59</td>
<td>184</td>
<td>68</td>
<td>48</td>
<td>14</td>
<td>48</td>
<td>3</td>
<td>146</td>
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<tr>
<td>60-64</td>
<td>63</td>
<td>33</td>
<td>63</td>
<td>16</td>
<td>42</td>
<td>2</td>
<td>155</td>
</tr>
<tr>
<td>65-70</td>
<td>89</td>
<td>26</td>
<td>72</td>
<td>17</td>
<td>33</td>
<td>4</td>
<td>143</td>
</tr>
<tr>
<td>70-74</td>
<td>46</td>
<td>12</td>
<td>79</td>
<td>21</td>
<td>43</td>
<td>0</td>
<td>83</td>
</tr>
<tr>
<td>75-79</td>
<td>33</td>
<td>12</td>
<td>40</td>
<td>18</td>
<td>23</td>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td>80-84</td>
<td>11</td>
<td>3</td>
<td>17</td>
<td>6</td>
<td>8</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td>85+</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>751</td>
<td>291</td>
<td>434</td>
<td>134</td>
<td>298</td>
<td>49</td>
<td>908</td>
</tr>
</tbody>
</table>

FH+ – family history positive, OC – ovarian cancer

The numbers of ovarian cancer cases by age group in the population are obtained from Cancer Research UK 2015\(^1\) and US Cancer Statistics 2015\(^2\). The probability of having a positive FH among unselected patients is 1964/7443 in the UK and 5459/20442 in the USA.
**eTable 2. Probabilities of different pathways in the model**

<table>
<thead>
<tr>
<th>Probability</th>
<th>Value</th>
<th>(95% CI) [Range]</th>
<th>Description</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>0.1614</td>
<td>(0.1469, 0.1768)</td>
<td>Germline BRCA1/BRCA2 PV prevalence in unselected OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P2</td>
<td>0.0193</td>
<td>(0.0134, 0.0274)</td>
<td>RAD51C/RAD51D/BRIP1 PV prevalence in unselected OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P3</td>
<td>0.0403</td>
<td>(0.0295, 0.0535)</td>
<td>Somatic BRCA1/BRCA2 PV prevalence in unselected OC patients</td>
<td>Manchester study, SIGNPOsT study, Washington study</td>
</tr>
<tr>
<td>P4</td>
<td>0.2957</td>
<td>(0.2775, 0.3144)</td>
<td>Probability of having a positive FH among unselected OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P5</td>
<td>0.3267</td>
<td>(0.2922, 0.3627)</td>
<td>Germline BRCA1/BRCA2 PV prevalence in FH-positive OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P6</td>
<td>0.0358</td>
<td>(0.0230, 0.0518)</td>
<td>RAD51C/RAD51D/BRIP1 PV prevalence in FH-positive OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P7</td>
<td>0.0486</td>
<td>(0.0382, 0.0608)</td>
<td>BRCA1/BRCA2 VUS prevalence in OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P8</td>
<td>0.0393</td>
<td>(0.0267, 0.0564)</td>
<td>RAD51C/RAD51D/BRIP1 VUS prevalence in OC patients</td>
<td>Manchester study, SIGNPOsT study, Scotland study, Washington study</td>
</tr>
<tr>
<td>P9</td>
<td>0.0869</td>
<td>(0.0755, 0.0999)</td>
<td>Reclassification rate of VUS</td>
<td></td>
</tr>
<tr>
<td>P10</td>
<td>0.55</td>
<td>(0.40, 0.76)</td>
<td>HR for ovarian cancer survival with PARP inhibitors</td>
<td></td>
</tr>
<tr>
<td>P11</td>
<td>0.47</td>
<td>(0.34, 0.56)</td>
<td>Uptake of RRM in unaffected PV carriers</td>
<td></td>
</tr>
<tr>
<td>P12</td>
<td>0.55</td>
<td>(0.45, 0.64)</td>
<td>Uptake of RRSO in unaffected carriers</td>
<td></td>
</tr>
<tr>
<td>P13</td>
<td>0.911</td>
<td>(0.62, 0.98)</td>
<td>Reduction in breast cancer risk from RRM without RRSO in unaffected PV carriers</td>
<td></td>
</tr>
<tr>
<td>P14</td>
<td>0.95</td>
<td>(0.78, 0.99)</td>
<td>Reduction in breast cancer risk from RRM with RRSO in unaffected PV carriers</td>
<td></td>
</tr>
<tr>
<td>P15</td>
<td>0.96</td>
<td>[0.8, 0.96]</td>
<td>Reduction in ovarian cancer risk from RRSO in BRCA1/BRCA2</td>
<td></td>
</tr>
<tr>
<td>P16</td>
<td>0.94</td>
<td>(0.83, 0.98)</td>
<td>Reduction in ovarian cancer risk from RRSO in RAD51C/RAD51D/BRIP1</td>
<td></td>
</tr>
<tr>
<td>Probability</td>
<td>Value</td>
<td>(95% CI) [Range]</td>
<td>Description</td>
<td>Source</td>
</tr>
<tr>
<td>-------------</td>
<td>-------</td>
<td>------------------</td>
<td>-------------</td>
<td>--------</td>
</tr>
<tr>
<td>P17</td>
<td>0.46</td>
<td>(0.27,0.79)</td>
<td>HR for breast cancer survival following RRSO (in women with breast cancer)</td>
<td>11</td>
</tr>
<tr>
<td>P18</td>
<td>0.8</td>
<td>(0.76,0.83)</td>
<td>Compliance of HRT</td>
<td>12</td>
</tr>
<tr>
<td>P19</td>
<td>0.71</td>
<td>(0.60,0.83)</td>
<td>HR of breast cancer risk from chemoprevention</td>
<td>13</td>
</tr>
<tr>
<td>P20</td>
<td>0.163</td>
<td>(0.136,0.19)</td>
<td>Uptake of breast cancer chemoprevention</td>
<td>14</td>
</tr>
<tr>
<td>P21</td>
<td>0.0072</td>
<td>(0.0068,0.0076)</td>
<td>Annual excess risk of developing CHD after RRSO</td>
<td>10</td>
</tr>
<tr>
<td>P22</td>
<td>0.0303</td>
<td>(0.011,0.043)</td>
<td>Cumulative mortality from CHD after RRSO without HRT</td>
<td>10</td>
</tr>
</tbody>
</table>

95%CI - 95% confidence interval, CHD - coronary heart disease, FH - family history, HR - Hazard Ratio, HRT - hormone replacement therapy, RRSO – risk-reducing salpingo-oophorectomy, RRM – risk-reducing mastectomy, VUS – variant of uncertain significance, PV- pathogenic variant, PARP-i -

**Explanations:**

P1: The probabilities of carrying a BRCA1/BRCA2 PV in unselected ovarian cancer patients are taken from 2,391 cases unselected for family history in the Manchester study (n=751), SIGNPOsT study (n=298), Scotland study (n=434), and Washington study (n=908).

P2: The probabilities of carrying a RAD51C/RAD51D/BRIP1 in unselected ovarian cancer patients are obtained from 1640 cases unselected for family history in the SIGNPOsT study (n=298), Scotland study (n=434) and Washington study (n=908).

P3: The prevalence of somatic mutations in BRCA1/BRCA2 is taken from unselected ovarian cancer patients in SIGNPOsT study and Washington study.

P4: We obtained the proportion of having a positive family history by stage among 2,391 unselected ovarian cancer cases from the Manchester study, Scotland study, SIGNPOsT study and Washington study. Then we used the number of ovarian cancer cases by age from Cancer Research UK1 or US Cancer Statistics: to calculate the overall proportion of having a positive family history among unselected ovarian cancer patients.

P5: The Germline BRCA1/BRCA2 mutation prevalence among FH positive ovarian cancer patients is
obtained from the Manchester, SIGNPOsT, Scotland, and Manchester studies. 231 patients were identified as germline BRCA1/BRCA2 mutation carriers among 707 FH-positive ovarian cancer patients.

P6: The RAD51C/RAD51D/BRIP1 mutation prevalence among FH positive ovarian cancer patients is obtained from 707 patients in the Manchester, SIGNPOsT, Scotland and Manchester studies.

P7: The BRCA1/BRCA2 VUS prevalence in OC patients is obtained among 1,483 unselected ovarian cancer cases from the Manchester study, SIGNPOsT and Scotland studies.

P8: The RAD51C/RAD51D/BRIP1 VUS prevalence in OC patients is obtained from 732 unselected ovarian cancer cases in the SIGNPOsT and Scotland studies.

P9: The reclassification rate of VUS is taken from Mersch et al 2018. 8.69% of VUS (178 of 2048) were upgraded to pathogenic or likely pathogenic variants.

P10: SOLO-1 is a double-blind phase III randomised clinical trial of olaparib compared with placebo in patients with newly diagnosed BRCA mutated advanced ovarian cancer after first-line platinum-based chemotherapy. In post-hoc analysis, median progression-free survival (PFS) was 56.0 months with olaparib versus 13.8 months with placebo (hazard ratio [HR] = 0.33, 95% confidence interval [CI] 0.25 to 0.43)15. Recently published overall survival data indicated an increase in overall survival in the PARP-I group with a HR=0.55 (0.40, 0.76).4 We also explored the uncertainty of overall survival in a sensitivity and scenario analyses, along with varying costs of PARP-I treatment.

P11: The probability that unaffected PV carriers will undergo RRM is taken from a study of UK BRCA1/2 carriers by Evans et al 2009. A composite uptake rate for BRCA1 (60% RRM rate) and BRCA2 (43% RRM rate) carriers weighted for the relative prevalence of BRCA1 and BRCA2 mutations was computed.

P12: The uptake of RRSO in unaffected BRCA1/BRCA2 carriers is taken from a study of high-risk UK women.

P13: The reduction in breast cancer risk following RRM in BRCA1/BRCA2 PV carriers not undergoing RRSO is taken from the PROSE study data in Rebbeck et al 2004.

P14: The reduction in breast cancer risk for BRCA1/BRCA2 PV carriers undergoing RRM and RRSO is taken from the PROSE study data in Rebbeck et al 2004.
P15: The reduction in ovarian cancer risk obtained from RRSO is taken from previous studies which report a 4% residual-risk of primary peritoneal cancer following RRSO.

P16: Reduction in ovarian cancer risk from RRSO in RAD51C/RAD51D/BRIP1 carriers is obtained from risk reduction observed in the general population (non-BRCA1/BRCA2 carriers) reported by Parker 2013, as no specific data for RAD51C/RAD51D/BRIP1 exist.

P17: The Hazard Ratio for breast cancer survival from RRSO in women who get breast cancer is obtained from Metcalfe 2015.

P18: HRT compliance rate is obtained from a UK cohort (Read et al, 2010).

P19: The Hazard Ratio for breast cancer risk from chemoprevention in high-risk women is obtained from the extended long-term follow-up of the IBIS-I breast cancer prevention trial (Cuzick et al 2015).

P20: The uptake of breast cancer chemoprevention is obtained from a recent meta-analysis by Smith et al 2016.

P21: Excess risk of CHD after RRSO is estimated using data from Parker 2013. The absolute excess CHD incidence is obtained by subtracting CHD incidence in women undergoing RRSO from those not.

P22: The risk of CHD mortality is obtained from the Nurses Health Study (Parker et al 2013).

Death from CHD is reported in 1 in 33 pre-menopausal women undergoing RRSO and not taking HRT.

\textit{Nb- We assume no reduction in breast cancer risk from RRSO in unaffected women undergoing RRSO.}
eTable 3. Generating Cohort of Relatives

<table>
<thead>
<tr>
<th>Country</th>
<th>UK</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-degree relatives</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average number</td>
<td>Mother</td>
<td>Father</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Age relative to index case</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>Sex, probability female</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Probability mutation</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Second-degree relatives</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average number</td>
<td>Grandparents</td>
<td>Uncle/aunts</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.82</td>
</tr>
<tr>
<td>Age relative to first-degree relatives</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Sex, probability female</td>
<td>50%</td>
<td>50.76%</td>
</tr>
<tr>
<td>Probability mutation</td>
<td>25%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Reference

Office for National Statistics\textsuperscript{16}  
National Centre for Health Statistics\textsuperscript{17}

\textsuperscript{16}This supplementary material was supplied by the author(s) and appears in its originally submitted form. JNCCN disclaims any responsibility or liability for any information provided herein.

\textsuperscript{17}Manchanda R, et al. doi:10.6004/jnccn.2023.7331 © 2024 JNCCN
The average number of first or second-degree relatives, ages relative to index cases, and the probability of being female are derived from data from the Office for National Statistics (UK)\textsuperscript{16} and the National Centre for Health Statistics (USA)\textsuperscript{17}. The number of ovarian cancer cases by age group is reported by Cancer Research UK 2015\textsuperscript{1} and US Cancer Statistics 2015\textsuperscript{2}. Based on the average number of relatives and the age relative to the index cases (see table above), we calculated the number of first-/second-degree relatives at different ages. Then we used the lifetables based on age and gender\textsuperscript{18,19} to obtain the probability of being alive for relatives at different ages and to calculate the number of relatives that need to be tested. The probability of carrying a pathogenic variant (PV) in a first-degree relative of a known PV (mutation) carrier (following predictive testing) is 50%. The probability of carrying a PV in a second-degree relative of a known PV-carrier (following predictive testing) is 25%. The number of unaffected female relative PV-carriers identified through cascade testing is calculated to be 1.41 (UK) and 1.49 (US) per index path var carrier with OC. Male first-degree relatives were tested to inform the need to test second-degree relatives but they were not followed in the model. Long-term outcomes-&-costs were only modelled for females.
### eTable 4. Summary of medical costs used in the model (2019 prices) and Explanation

<table>
<thead>
<tr>
<th>Item</th>
<th>GBP</th>
<th>USD</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of germline testing</td>
<td>150</td>
<td>200</td>
<td>20,21</td>
</tr>
<tr>
<td>Cost of somatic testing</td>
<td>360</td>
<td>480</td>
<td>SIGNPOST</td>
</tr>
<tr>
<td>Cost of counselling (per session)</td>
<td>22</td>
<td>43</td>
<td>22-25</td>
</tr>
<tr>
<td>Cost of RRSO (and HRT and osteoporosis prevention)</td>
<td>3,616</td>
<td>9,206</td>
<td>26-29</td>
</tr>
<tr>
<td>Cost of ovarian cancer diagnosis and initial treatment</td>
<td>15,497</td>
<td>31,160</td>
<td>26,28,30</td>
</tr>
<tr>
<td>Yearly cost of ovarian cancer treatment and follow-up: years 1-2</td>
<td>5,901</td>
<td>15,895</td>
<td>26,28,30,31</td>
</tr>
<tr>
<td>Yearly cost of ovarian cancer treatment and follow-up: years 3-5</td>
<td>5,528</td>
<td>15,895</td>
<td>26,28,30,31</td>
</tr>
<tr>
<td>Terminal care cost with ovarian cancer</td>
<td>17,869</td>
<td>101,015</td>
<td>28,32</td>
</tr>
<tr>
<td>Yearly costs of PARP inhibitor treatment</td>
<td>60,462</td>
<td>169,067</td>
<td>33,34</td>
</tr>
<tr>
<td>Cost of mamography</td>
<td>65</td>
<td>169</td>
<td>26,35,36</td>
</tr>
<tr>
<td>Cost of MRI</td>
<td>220</td>
<td>1,604</td>
<td>26,28,36,37</td>
</tr>
<tr>
<td>Cost of RRM (and reconstruction and complications)</td>
<td>8,060</td>
<td>24,014</td>
<td>26,28,38-41</td>
</tr>
<tr>
<td>Cost of chemoprevention</td>
<td>97</td>
<td>4,883</td>
<td>27,28</td>
</tr>
<tr>
<td>Cost of breast cancer diagnosis and initial treatment (Sporadic)</td>
<td>21,356</td>
<td>97,795</td>
<td>26,28,42,43</td>
</tr>
<tr>
<td>Cost of breast cancer diagnosis and initial treatment (BRCA1/BRCA2)</td>
<td>19,463</td>
<td>90,836</td>
<td>26,28,42,43</td>
</tr>
<tr>
<td>Yearly cost of breast cancer follow-up and adjuvant treatment: years 1-5 (Sporadic)</td>
<td>1,298</td>
<td>8,741</td>
<td>26-28,35,42-44</td>
</tr>
<tr>
<td>Yearly cost of breast cancer follow-up and adjuvant treatment: years 1-5 (BRCA1/BRCA2)</td>
<td>1,292</td>
<td>8,741</td>
<td>26-28,35,42-44</td>
</tr>
<tr>
<td>Terminal care cost with breast cancer</td>
<td>17,869</td>
<td>73,880</td>
<td>28,32</td>
</tr>
<tr>
<td>Cost of fatal CHD</td>
<td>3,679</td>
<td>25,995</td>
<td>26,32,45</td>
</tr>
<tr>
<td>Cost of excess CHD</td>
<td>3,720</td>
<td>213,398</td>
<td>10,46-50</td>
</tr>
</tbody>
</table>

**BNF** – British National Formulary, **CPM** – contralateral prophylactic mastectomy, **GCaPPS** – Genetics Cancer Prediction through Population Screening study, **HRT** – hormone replacement therapy, **NHS** – National Health Service, **NICE** – National Institute for Health and Clinical Excellence, **PSSRU** – Personal Social Services Research Unit, **RRSO** – risk-reducing salpingo-oophorectomy, **RRM** – risk-reducing mastectomy. Model costs are estimated at 2019 prices.
Explanations:

All costs are adjusted for 2019 price index. Costing data were obtained from published NHS-reference costs for the UK\textsuperscript{51,52} and from the literature for the US. Costs were converted wherever needed using the Hospital and Community Health-Service-Index.\textsuperscript{53} Costs of breast cancer (BC), ovarian cancer (OC) and excess coronary heart disease (CHD) are included. In line with NICE recommendations, future healthcare costs not associated with BC, OC, or CHD were not considered.\textsuperscript{54}

**Cost of genetic testing/counselling**

The cost of \textit{BRCA1/BRCA2/RAD51C/RAD51D/BRIP1} testing is $200 based on testing costs for these genes in an accredited laboratory within the PROMISE research programme as well as confirmatory testing costs in an accredited national genetics laboratory for those testing positive. The cost of somatic mutation testing is £360 based on clinical testing costs in an accredited laboratory in the SIGNPOST study. We estimated the US somatic testing cost based on the ratio of UK and US germline testing costs. The UK national unit cost assumed for genetic counselling is £44 per hour of client contact from PSSRU Unit costs of Health and Social Care 2010.\textsuperscript{22,23,55} The US genetic counselling cost estimates are obtained from Schwartz et al 2014\textsuperscript{24}. All costs are adjusted for the 2019 price index. We assume/cost for 20 minutes of administrator time, 20 minutes of counsellor preparation and 20 min of counselling time (total 40 minutes of counsellor time)\textsuperscript{24} for each counselling appointment. In the analysis we include costs for (a) pre-test counselling for all patients, (b) post-test counselling for path-vars and VUS, and (c) also for repeat counselling for VUS which get reclassified as pathogenic subsequently.

**RRSO costs**

The UK RRSO costs are obtained from NHS reference costs\textsuperscript{26}, and the US costs are from Grann 2011\textsuperscript{28} inflated using the medical component of the US consumer price index to 2019 US$. Costs of HRT for the UK are taken from BNF \textsuperscript{27} and for the US from William-Frame 2009.\textsuperscript{29} Costs assume HRT is given from average age of RRSO to the average age of 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.

**RRM costs**

The UK RRM cost is obtained from NHS reference costs, and the US costs are from Grann 2011 inflated using the medical component of the US consumer price index to 2019 US$. Reconstruction rates of around 91% have been reported after RRM. Costs for the UK are derived from NHS reference costs (code JA33Z). Bilateral prophylactic mastectomy costs for the USA is $20,827 (2016 price) to include reconstructive surgery. For risk reducing bilateral prophylactic mastectomy (RRM) and reconstruction we assume a 26.2% minor complication rate and 5.6% major complication rate, additional costs for which have been included for both minor and major complications.

Minor complications are costed at an additional cost of $822 (US) and £278 (UK) and major complications at $7492 (US) and £2535 (UK) (2016 prices). All costs are adjusted for 2019 price index. UK costs were converted wherever needed using the Hospital and Community Health-Service-Index.

**Costs of ovarian cancer treatment**

We assume that the costs of ovarian cancer diagnosis include a pelvic examination, ultrasound scan, CA125 test, CT scan, percutaneous biopsy, and peritoneal cytology. The costs of ovarian cancer treatment include 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 is assumed that in the first and second years treated survivors would have a further three consultant visits, a CT scan and four CA125 tests each year. In the third to fifth years post-surgery it is assumed that survivors would have two consultant visits and two CA125 tests.
Costs for ovarian cancer diagnosis and treatment in the UK are derived from national reference costs and a recent ovarian cancer guideline developed by NICE\textsuperscript{26,30}. Annual costs of ovarian cancer treatment in the US are taken from Grann et al 2011\textsuperscript{28} and inflated using the medical component of the US consumer price index to 2019 US$. We include the costs of treatment of recurrence, taken from Cancer Research UK\textsuperscript{31} and Grann 2011\textsuperscript{28}.

The costs of ovarian cancer terminal care are derived from end-of-life costs for cancer patients based on a report from the National Audit office UK \textsuperscript{32}. For the US the terminal care costs for ovarian cancer are obtained from Grann 2011 \textsuperscript{28}, inflated using the medical component of the US consumer price index to 2019 US$. In line with NICE recommendations future healthcare costs not associated with ovarian cancer are not considered \textsuperscript{54}.

**Costs of PARP inhibitors**

Olaparib (a PARP inhibitor) is recommended for use within the Cancer Drugs Fund as an option for the maintenance treatment of \textit{BRCA} mutated advanced ovarian cancer that has responded to first-line platinum-based chemotherapy\textsuperscript{56}. Among \textit{BRCA} mutated ovarian cancers, 88\% respond to first-line platinum-based chemotherapy\textsuperscript{57} and 81\% are at advanced stages\textsuperscript{58}.

Olaparib is taken orally and the dosage as tablets is 300mg (2*150mg tablets) taken twice daily (600mg per day). The list price for tablets is £2,317.5 per 14-day pack in the UK and $13,886 per 30-day pack in the US. \textsuperscript{33,34} In the randomized, double-blind, placebo-controlled, phase 3 SOLO-1 trial of maintenance Olaparib in patients with newly diagnosed advanced ovarian cancer, patients who had no evidence of disease at 2 years stopped receiving olaparib, but patients who had a partial response at 2 years were permitted to continue receiving olaparib in a blinded manner\textsuperscript{59}. Only 10\% patients in SOLO-1 continued to receive Olaparib beyond this time\textsuperscript{56}. We therefore assumed in the model that all eligible patients received Olaparib for two years and 10\% of them would receive Olaparib for another year.
Cost of breast cancer screening

For non-carriers, we assume routine triennial mammography between 50-70 years as per UK NHS breast cancer screening programme^60 (seven mammograms on average). Breast screening in the US assumes mammography every two years starting at 50 years.

For BRCA1/BRCA2 mutation carriers, we assume annual mammogram from 40-69 years and annual MRI from 30-49 years as per NICE guidelines for familial breast cancer^37. For the US, it is based on annual mammography and MRI starting at 30 years, and annual mammography only from age 50 years.^36

Cost of chemoprevention

BRCA1/BRCA2 mutation carriers are offered Tamoxifen (premenopausal) or Raloxifene (postmenopausal) for 5 years^37,^61 to reduce breast cancer risk. The drug costs are obtained from BNF (UK)^27 and Grann 2011 (US).^28 16.3% uptake is assumed for chemoprevention based on existing literature.^14

Costs of breast cancer treatment

In the general population, 10% breast cancer is non-invasive DCIS and 90% is invasive. 95% of invasive breast cancer is early and locally advanced (stage 1-3), and 5% of invasive breast cancer is advanced breast cancer (stage 4).^44 In BRCA1/2 carriers, 20% of cancers are DCIS and 80% invasive.^62,^63

Annual breast cancer treatment costs in the USA are obtained from Grann et al 2011,^28 and inflated using the medical component of the USA consumer price index to 2019 US$. In the UK, breast cancer treatment costs are estimated based on clinical guidelines and unit costs detailed as below.

70% of invasive breast cancers are ER-positive,^43,^64 among which 49% are premenopausal. 15% of early/locally advanced breast cancers and 25% of advanced breast cancers are HER2-positive. 27%
BRCA1 and 67% BRCA2 breast cancers are ER-positive; 5% BRCA1 and 14% BRCA2 breast cancers are HER2-positive. All costs are adjusted for BRCA1/BRCA2 breast cancers for differences in stage at presentation, the proportion of being non-invasive, and the proportion of being ER-positive or HER2-positive.

Diagnosis costs: Whether suspected at breast screening or through presentation to the GP, diagnosis in the breast clinic is made by triple assessment (clinical assessment, mammography, and ultrasound imaging with core biopsy and/or fine needle aspiration cytology). Clinical examination and mammography costs are from the paper by Robertson C et al. Breast ultrasound and biopsy costs are obtained from NHS reference costs in the UK. For all patients presented with suspected advanced breast cancer, MRI should be offered to assess for bone metastases.

Sentinel lymph node biopsy (SLNB) costs: SLNB is used for staging axilla for early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy (73% of early and locally advanced invasive cancers). The SLNB costs are obtained from NHS reference costs including sentinel lymph node scan and unilateral intermediate breast procedures.

Pretreatment axilla ultrasound costs: Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered. The commissioning cost of pre-treatment ultrasound evaluation of the breast and axilla is the same as that of the breast only. The costing model considers the cost of ultrasound-guided needle sampling only, obtained from NHS reference costs (UK).

Axillary lymph node dissection (ALND) costs: ALNB is undertaken for lymph node positive cancers (~31% early and locally advanced invasive cancers - NICE guideline and BCCOM project; 30% node positive for BRCA1/2 breast cancer- familial breast cancer screening studies, breast cancer case
Breast surgery costs include costs of breast conserving surgery (assumed for all non-invasive cancers, and 75% of early/locally advanced invasive cancers) and costs of mastectomy (for 25% early/locally advanced and all advanced cancers). Reconstruction rates following mastectomy are reported to be 34% in the UK and 55% in the US. The complication rate following mastectomy alone is 21.5% (19.5% minor and 2% major) and complication rate following mastectomy and reconstruction is 28.6% (24.5% minor & 4.1% major). Costs are obtained from the national NHS reference costs (UK).

Chemotherapy and radiotherapy costs: Invasive breast cancers who are not at low risk 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 for all advanced cancers. Radiotherapy costs include planning and 40Gy in 15 fractions over 3 weeks or palliative treatment, taken from national NHS reference costs. Chemotherapy costs based on polychemotherapy, include administration costs, costs of 1st and 2nd line therapy and toxicity from NICE guidelines.

Endocrine therapy costs: As per NICE guidelines, ER-positive invasive breast cancers receive Tamoxifen 20mg/day (premenopausal) or Anastrazole 1mg/day (postmenopausal). 70% of invasive breast cancers are ER-positive, among which 49% are premenopausal. We assume the length of endocrine therapy is 5 years. The drug costs are obtained from the BNF in the UK. ER testing costs are obtained from a local NHS trust and included for all invasive breast cancers.

Target therapy costs: HER2-positive breast cancer patients can be given at 3-week intervals for 1 year or until disease recurrence as per NICE guidelines. Breast cancer patients with positive HER2 are eligible for treatment with trastuzumab. 10% of the eligible patients are intolerant of trastuzumab.
Among women suitable for this treatment, 80% receive trastuzumab 44. HER2 testing costs are obtained from a local NHS trust and included for all invasive breast cancers. The trastuzumab cost per patient including administration of treatment and cardiac monitoring is £15080, obtained from NICE costing report 44.

Follow up costs: Breast cancer patients are offered mammographic surveillance and clinical follow-up, with the screening cost of £141.45 per women in 201135. We assume patients are followed up every four months in the first two years, every six months from the third to the fifth year, and every year from the sixth to the tenth year.

Bisphosphonate costs: Bisphosphonates is considered to be offered to patients newly diagnosed with bone metastases, to prevent skeletal-related events and reduce pain 64. 74% patients with advanced breast cancer will develop bone metastases and 65% patients with bone metastases are offered bisphosphonates44,78. Bisphosphonates that are currently offered include oral sodium clodronate, ibandronic acid, zoledronic acid, and pamidronate. The proportions of patients receiving the four drugs are 20%, 30%, 25%, and 25% respectively. The annual costs including administration for the four drugs are £1971, £2541.96, £3208, and £3208 respectively, obtained from NICE costing report 44. We assume the average length of bisphosphonates treatment is 2.7 years, which is the life expectancy of advanced breast cancers based on one-year survival rate (63.2%) 79.

Recurrence costs: For non-invasive breast cancers, the non-invasive and invasive relapse rates are both 12.5%. 35% of early and locally advanced invasive breast cancers progress to advanced disease 44. The recurrence rates for early and locally advanced breast cancer are 15.9% for node-positive 80 and 11% for node-negative disease 81. Weighted for 31% node positive and 69% node negative, the composite recurrence rate for early and locally advanced breast cancer is 12.5%. The recurrence rate for the advanced disease is 66% (34% relapse-free five-year survival) 82.
Terminal care costs: The costs of terminal care for breast cancer are derived from end-of-life costs for cancer patients based on a report from the National Audit office UK. For the US the terminal care costs for breast cancer are obtained from Grann 2011, inflated using the medical component of the US consumer price index to 2019 US$. In line with NICE recommendations future healthcare costs not associated with breast cancer were not considered.

**Cost of CHD**

Cost of excess CHD: British Heart Foundation statistics reports costs per capita across four Commissioning Regions in England (London, Midlands and East, North and South). The costs of CHD and stroke are averaged across the four regions. The prevalence of CHD is estimated at 12.0% in the UK and 11.7% in the USA with the onset of CHD estimated at 55 years of age.

The yearly cost of CHD in the UK is obtained by dividing the per capita cost by the population prevalence of CHD. Using the report published by the American Heart Association, the total cost of CHD, CHF and stroke were divided by the population with CHD giving the yearly cost of CHD in the USA. This yearly cost is multiplied by the number of years between onset of CHD and average life expectancy to provide the cost attributed to excess CHD.

Cost of fatal CHD: This is costed on the basis of a fatal myocardial infarction using NHS reference costs. USA costs are obtained from Afana et al 2015, inflated using the medical component of the US consumer price index to 2019 US$.

In line with NICE recommendations, future healthcare costs not associated with BC, OC, or CHD were not considered.
eMethods 1. Examination of Productivity Loss

The retirement ages for females are 65 in the UK and 62 in the USA. The female labour force participation rates are 58% in the UK and 57% in the USA, obtained from the World Bank. The weekly earnings are presented in the table below.

<table>
<thead>
<tr>
<th>Age</th>
<th>UK (£)</th>
<th>USA ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-19</td>
<td>427</td>
<td>329</td>
</tr>
<tr>
<td>20-24</td>
<td>563</td>
<td>407</td>
</tr>
<tr>
<td>25-29</td>
<td>788</td>
<td>507</td>
</tr>
<tr>
<td>30-34</td>
<td>788</td>
<td>589</td>
</tr>
<tr>
<td>35-39</td>
<td>920</td>
<td>589</td>
</tr>
<tr>
<td>40-44</td>
<td>920</td>
<td>601</td>
</tr>
<tr>
<td>45-49</td>
<td>904</td>
<td>601</td>
</tr>
<tr>
<td>50-54</td>
<td>904</td>
<td>532</td>
</tr>
<tr>
<td>55-59</td>
<td>880</td>
<td>532</td>
</tr>
<tr>
<td>60-64</td>
<td>880</td>
<td>464</td>
</tr>
<tr>
<td>65-69</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Source: 84

We categorised the productivity costs as three subcomponents: 1) temporary disability due to short-term work absences following diagnosis, 2) permanent disability due to reduced working hours following a return to work or workforce departure; and 3) premature mortality due to death before retirement, detailed below.

**eTable 5b Descriptive statistics for productivity loss in breast and ovarian cancer patients**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Breast cancer</th>
<th>Ovarian cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(1) Temporary disability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of temporary disability cases</td>
<td>94.0%</td>
<td>98%¹</td>
</tr>
<tr>
<td>Average time taken off work following diagnosis (weeks)</td>
<td>44.9</td>
<td>47.2²</td>
</tr>
<tr>
<td><strong>(2) Permanent disability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of permanent disability: reduced hours</td>
<td>26%</td>
<td>40%³</td>
</tr>
<tr>
<td>Reduced hours per week after returning to work (hours)</td>
<td>5.5</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>(3) Premature mortality (before retirement)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of permanent disability: workforce departure</td>
<td>12.9%</td>
<td>30%³</td>
</tr>
</tbody>
</table>

The descriptive statistics for productivity loss in breast cancer patients are obtained from Hanly et al. 2012. 86.

¹ We assume 98% ovarian cancer patients have cancer-related short-term work absences after diagnosis.
² We assume ovarian cancer patients experience four weeks for surgery, 24 weeks for chemotherapy, and 24 weeks for recurrence treatment with the recurrence rate of 80% 87.
³ We assume the percentages of permanent disability for ovarian cancer are 40% for reduced working hours and 30% for workforce departure.
We estimated temporary disability as time absent from work multiplied by age-specific gross earnings.

We calculated productivity costs due to permanent disability by applying age-specific gross earnings to the reduction in working hours, or the number of working hours if permanent workforce departure, until retirement age. Regarding productivity loss from premature mortality, we assumed that without cancer, the productive capacity of an individual would continue from the age of diagnosis until age of retirement. We multiplied the projected years of life lost by the age-specific gross earnings for the remainder of the working life to generate monetary estimates.
eMethods 2. Estimates for age of onset and survival for breast and ovarian cancers

Our analysis incorporates lifetime risks and long-term consequences providing a lifetime time-horizon. Female lifetables from the Office of National Statistics (UK)\textsuperscript{18} and National Centre for Health Statistics (USA)\textsuperscript{19} were used for life expectancy by 80-years for women not developing OC/BC.

We assumed that the median age for undergoing RRM and RRSO in unaffected path var carriers was 37 and 40 years respectively.\textsuperscript{5} The uptake rates of RRSO and RRM are obtained from established literature.\textsuperscript{5,6} OC/BC outcomes were modelled using five-year survival data. No statistically significant overall long-term survival differences between germline and sporadic OC/BC have been reported.\textsuperscript{58,88,89} For BC, five-year survival rates are 85.6\% (CI: 85.4, 85.9) in the UK, 90.2\% (CI: 90.1, 90.4) in the US\textsuperscript{90}. For OC the five-year survival rates are 36.2\% (CI: 35.7, 36.8) in the UK and 43.4\% (CI: 43.1, 43.8) in the US \textsuperscript{90}. After five-years, we assumed the probability of death for all patients was same as the general-population.

The excess risk of CHD following premenopausal oophorectomy is incorporated in the analysis.\textsuperscript{10,91} We incorporated the fact that contralateral BC is associated with a higher risk of dying from BC.\textsuperscript{92}
eMethods 3. Quality-adjusted life years (QALYs) and Utility Scores

QALY is a measurement of health-outcomes in economic evaluations recommended by NICE. It equals time spent in the relevant health states multiplied by an appropriate utility-score. Utility-score is an indication of individual preferences for specific health-states where 1=perfect health and 0=death. Utility-score is an adjustment for quality-of-life and QALY adjusts changes in length-of-life by potential alterations in quality-of-life. The utility-scores for early, advanced, recurrent, remittent, and end-stage BC are 0.71, 0.65, 0.45, 0.81, and 0.16 respectively. The utility-scores for early, advanced, recurrent, remittent, and end-stage OC are 0.81, 0.55, 0.50, 0.83, and 0.16 respectively. In addition, women undergoing RRM or RRSO also experience negative health-effects. We used utility-scores of 0.88 (SD=0.22) for RRM, 0.95 (SD=0.10) for RRSO, and 0.84 (SD=0.02) for CHD to account for the disutility.
Supplementary Figure S1

A

Testing option

Unselected testing

Patients

Relatives

Mutation carriers

VUS

Non carriers

Redeclassification

Yes

No

Somatic BRCA1/2 positive

ParP inhibitor

Somatic OC

Germline OC

Sporadic OC

BC and OC

Dead

Clinical cancer

FH testing

Patients

Relatives

Positive FH

Negative FH

Germline BRCA1/2 positive

RAD51C/RAD51D/BRIP1 positive

BRCA1/BRCA2/RAD51C/RAD51D/BRIP1 negative

Somatic BRCA1/2 undetected

Germline BRCA1/2 undetected

RAD51C/RAD51D/BRIP1 undetected
Supplementary Figure S1
Figure 1. Schematic diagram showing the microsimulation model structure for unselected panel germline and clinical criteria–based/FH-based genetic testing for (A) patients with OC and (B) their unaffected relatives identified through cascade testing (see below for further details).

Abbreviations: BC, breast cancer; FH, family history; OC, ovarian cancer; PARPi, PARP inhibitor; RRM, risk-reducing mastectomy; RRSO, risk-reducing salpingo-oophorectomy; PV, pathogenic variant; VUS, variant of uncertain significance.

aIncludes individuals testing negative and VUS not reclassified as pathogenic variants.

bThese individuals are identified only through the unselected testing arm. Relatives in the clinical criteria/FH testing arm only undergo BRCA1/BRCA2 testing.

cIncludes individuals testing negative, VUS not reclassified as pathogenic variants, and untested individuals in the clinical criteria/FH testing arm not found to carry BRCA1/BRCA2/RAD51C/RAD51D/BRIP1 pathogenic variants.

dUnaffected relatives can progress from no cancer to germline BC (BRCA1/BRCA2), germline OC (BRCA1/BRCA2/RAD51C/RAD51D/BRIP1), sporadic BC, or sporadic OC (or remain in that health state).

eBRCA1/BRCA2 relatives who develop germline OC can get PARPi therapy.

Progression through the model is dependent on the probabilities provided in Supplementary Table S2.

**Figure 1A**

**Patients in Unselected Testing Arm**

In the unselected testing arm, all OC patients are offered genetic testing and get classified as pathogenic variant carriers, VUS, or noncarriers. A proportion (8.7%) of patients with VUS results will subsequently get reclassified as pathogenic variant carriers.

Germline BRCA1/BRCA2 OC carriers identified are offered PARP inhibitor therapy. Depending on the probability of patients undertaking PARP inhibitor therapy, they may either stay in the state of germline OC or die of germline OC. Also, they have a probability of developing germline BC and progressing to the health state of “BC and OC.” Patients who do not progress or die would stay in the state of germline OC and undertake the next cycle.

Somatic BRCA1/BRCA2 OC carriers identified are offered PARP inhibitor therapy. Depending on the probability of patients undertaking PARP inhibitor therapy, they may either stay in the state of somatic OC or die of somatic OC. Age-dependent probabilities allow them to develop sporadic BC and progress to the health state of “BC and OC.” Patients who do not progress or die would stay in the state of somatic OC and undertake the next cycle.

RAD51C/RAD51D/BRIP1 OC carriers may stay in the state of germline OC or die of germline OC. Age-dependent probabilities allow them to develop sporadic BC and progress to the health state of “BC and OC.” Patients who do not progress or die would stay in the state of germline OC and undertake the next cycle.
BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-negative patients have sporadic OC. Age-dependent probabilities allow them to develop sporadic BC and progress to the health state of “BC and OC.” They also have a probability of dying from sporadic OC. Women who do not progress to “BC and OC” or die would stay in the health state of sporadic OC to undertake the next cycle.

Patients in Clinical Criteria/FH Testing Arm

In the clinical criteria/FH testing arm, patients with positive FH (fulfilling clinical criteria) undergo genetic testing and are classified as pathogenic variant carriers, VUS, or noncarriers. A proportion of patients with VUS results will subsequently get reclassified as pathogenic variant carriers.

Patients with negative FH do not undertake genetic testing. They can be undetected somatic BRCA1/BRCA2 carriers, undetected germline BRCA1/BRCA2 carriers, undetected RAD51C/RAD51D/BRIP1 carriers, or BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-negative.

Options of PARP inhibitor and disease progression for identified germline or somatic BRCA1/BRCA2 OC carriers and disease progression for RAD51C/RAD51D/BRIP1 OC carriers or BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-negative patients with O, is the same as those in the unselected testing arm and are described above.

Undetected germline BRCA1/BRCA2 carriers are not offered PARP inhibitor therapy. They may die of germline OC or develop germline BC and progress to the health state of “BC and OC.” Patients who do not progress or die would stay in the state of germline OC and undertake the next cycle.

Undetected somatic BRCA1/BRCA2 carriers are not offered PARP inhibitor therapy. They may die of somatic OC or develop sporadic BC and progress to the health state of “BC and OC.” Patients who do not progress or die would stay in the state of somatic OC and undertake the next cycle.

Figure 1B

Relatives in the Unselected Testing Arm

In the unselected testing arm, relatives of OC pathogenic variant carriers are offered BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-predictive genetic testing (depending on the familial variant) and classified as pathogenic variant carriers or noncarriers. Relatives of patients with OC with VUS (8.7%) who get reclassified as pathogenic variant carriers are also offered predictive BRCA1/BRCA2/RAD51C/RAD51D/BRIP1 testing.

Relatives identified with BRCA1/BRCA2 pathogenic variants are offered options of RRM and RRSO. Unaffected relatives can also opt for chemoprevention for BC. Those identified with RAD51C/RAD51D/BRIP1 pathogenic variants are offered RRSO. Depending on the probability of pathogenic variant carriers undertaking an RRM and/or RRSO (± chemoprevention), they progress to either germline BC (BRCA1/BRCA2) or germline OC (BRCA1/BRCA2/RAD51C/RAD51D/BRIP1) or stay in the health state of no cancer. They have a probability of dying from the background all-cause mortality.

BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-negative women progress to sporadic BC or sporadic OC or stay in the health state of no cancer. They have a probability of dying from the background all-cause mortality.

Relatives in the Clinical Criteria/FH Testing Arm
In the clinical criteria/FH testing arm, relatives of identified \textit{BRCA1/BRCA2} germline mutation patients undergo predictive \textit{BRCA1/BRCA2} genetic testing. They are classified as pathogenic variant carriers or noncarriers. Relatives of BC patients with VUS who get reclassified as pathogenic variant carriers also undergo predictive \textit{BRCA1/BRCA2} testing.

\textit{RAD51C/RAD51D/BRIP1} pathogenic variant carriers cannot be detected with only the FH-based \textit{BRCA1/BRCA2} genetic testing being offered. Relatives of patients with negative FH may be undetected \textit{BRCA1/BRCA2 PV} carriers, undetected \textit{RAD51C/RAD51D/BRIP1 PV} carriers, or \textit{BRCA1/BRCA2/RAD51C/RAD51D/BRIP1} negative.

The options of RRM and RRSO for identified carriers are the same as in the unselected testing arm. For identified \textit{BRCA1/BRCA2/RAD51C/RAD51D/BRIP1} pathogenic variant carriers and noncarriers (\textit{BRCA1/BRCA2/RAD51C/RAD51D/BRIP1-negative}), the disease progression is the same as relatives in the unselected testing arm.

Undetected \textit{BRCA1/BRCA2} pathogenic variant carriers are not offered RRM or RRSO, and undetected \textit{RAD51C/RAD51D/BRIP1} pathogenic variant carriers are not offered RRSO. Depending on the baseline risk, they progress to either germline BC or germline OC or stay in “no cancer” health state. Also, they have a probability of dying from the background all-cause mortality.
eFigure 2. One-way sensitivity analyses Tornado Diagrams

a. Incremental cost-effectiveness ratios – UK payer perspective

b. Incremental cost-effectiveness ratios – UK payer perspective (panel germline-testing only with no PARP-i)

c. Incremental cost-effectiveness ratios – US payer perspective

d. Incremental cost-effectiveness ratios – US societal perspective
e. Incremental cost-effectiveness ratios – US payer perspective (panel germline-testing only with no PARP-i)

f. Incremental cost-effectiveness ratios – US societal perspective (panel germline-testing only with no PARP-i)

Tornado diagrams describing the one way sensitivity analysis for the top 10 variables in the model for UK and USA analysis. A societal perspective is not highlighted for the UK, as the UK NHS and NICE only consider a payer perspective for decision making. Analysis are presented for the main comparison of parallel germline-panel and somatic-BRCA testing (including PARP-i use) compared to FH/Clinical criteria based BRCA-germline testing; as well as the scenario of unselected panel germline-testing only (with no PARP-i) compared to FH/Clinical criteria based BRCA-germline testing.
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**Randomized Controlled Trial**


Research Support, N.I.H., Extramural


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Randomized Controlled Trial


