Breast cancer (BC) is the most common cancer among women in most Western countries and may cluster in families. It has been estimated that 1/500 to 1/300 of US women have a deleterious mutation in BRCA1 or BRCA2. Around 10% of BC cases exhibit a higher familial incidence and functional mutations in BRCA1 or BRCA2. The mutations are responsible for the development of malignant tumours in approximately half of the cases. In Norway, genetic testing has been offered increasingly to patients with BC and/or ovarian cancer (OC) fulfilling traditional guidelines. This testing is here called the family history (FH) approach. Despite the use of the family history approach, several BRCA mutation-carrying patients with BC are not detected. An alternative is the testing of all patients with BC for BRCA mutation with sequencing and Multiplex Ligation Probe Amplification (MLPA).
health economic concerns. Today, new gene sequencing technologies and lowered cost of genetic testing may make it more feasible to test large populations.\textsuperscript{13} Several alternatives may detect the women at risk of BC and/or OC.\textsuperscript{5,16} Therefore, it is time for reviewing whether testing should be offered according to less strict criteria or not.

**MATERIALS AND METHODS**

In this non-randomised model-based study, we compared the results from a time of the traditional FH approach with the period of testing all patients with BC (both men and women) for \textit{BRCA} mutations.

**Treatment and comparator**

We used a model-based cost-effectiveness analysis and employed both a healthcare and a societal perspective. The decision tree model (figure 1) compared an intervention (alternative 1) with the traditional FH approach (alternative 2). The perspective was lifetime. Data were taken from the daily practice at Oslo University Hospital, Ullevål (OUH-U) during two periods, 2013 and 2014/2015, respectively (figure 1).

**Intervention arm (alternative 1)**

Between 1 January 2014 and 31 August 2015, all patients diagnosed with BC, where the treating physician concluded that genetic testing could influence treatment decisions, were offered \textit{BRCA} testing with sequencing...
and Multiplex Ligation Probe Amplification (MLPA) (first intervention). Up to 625 patients were treated for primary BC. Ninety-five patients (11.5%) refused the offer of testing due to unknown reasons. Seventy-two patients were not offered testing and 18 patients had undergone prior BRCA testing. Consequently, 535 patients were included into the model and 440 of them were tested in the intervention arm. We detected 13 (3%) BRCA mutation carriers (BRCA1: 10 patients, BRCA2: 3 patients). Family members of the detected mutation carriers were offered genetic counselling and testing (second intervention).

**Traditional approach (alternative 2)**

In 2013, all women were selected for testing and screening for BRCA mutation based on the national guidelines, here for simplicity named the ‘traditional-approach’. The national indicators of risk were:
- women with BC <50years;
- women with BC and two close relatives (first-degree relative or second-degree relative through a man with BC) mean age <55years or three close relatives with BC, at any age;
- men with BC;
- women with bilateral BC <60years;
- women with BC and close relative with OC;
- woman with BC and close relative with prostate cancer <55years;
- woman with OC, independent of age.

There were 388 patients treated for primary BC in 2013. Twenty-four were tested with complete sequencing of the BRCA genes and one mutation carrier detected. In total, 140 patients were tested for BRCA1/2 mutations (with sequencing and MLPA) and 116 using a more limited genetic test designed to detect Norwegian founder mutations. Two patients were mutation positive, one identified by sequencing, the other by the founder mutation test.

In the model-based economic analysis, the same number of patients had to be implemented into the two alternatives to make the costs and gains comparable. Due to a lower volume of patients in the output data from OUH-U in 2013 a balancing was done (FH=[(116+24)*535]/388]=193 patients, no FH=(535−193)=342 patients, detected mutation carriers=(1+1)*535/388=3 patients). As the total group contained 16 mutation carriers (figure 1, P1 and P11), consequently the undetected number in alternative 2 was 13 (figure 1, P14). When identifying a BRCA mutation carrier, family members were invited to testing. Figure 1 shows the decision tree and its pathway probabilities.

**Effectiveness**

We calculated the same outcome for healthy women with BRCA mutation detected through a systematic testing for BRCA mutations in both alternatives. Possible life-years gained (LYG) by prophylactic interventions among the patients with BC was not included as we had no solid data clarifying this variable.

**Costs (C)**

All costs were calculated in Norwegian unit costs (Norwegian krone) and converted into euros (€) at the rate of €1=9.2005 Kr as of 16 October 2015 (www.norges-bank.no). We calculated treatment costs according to the Norwegian diagnosis-related group (DRG) system and the 100% DRG value was used. The costing year was 2015.

**Healthcare costs (C1)**

The cost (DRG 930A) of a visit to a breast surgeon or a gynaecologist, the DRGs of breast conserving surgery (BCS) (DRG 260O) and mastectomy (DRG 258) (calculated according to the ‘no hospitalization tariff’) is shown in table 1. Thirty-five per cent of those undergoing mastectomy at the OUH-U did also undergo later reconstructions of their breasts. The cost of testing each patient with BC for mutations (sequencing and running MLPA) was calculated €5163 employing the refunding figure of the Norwegian Health Economics Administration (HELO). The cost of the limited BRCA test was €948.

The cost of testing family members for the known BRCA mutation, the cost of genetic counselling and the cost of PBM and PBSO are given in table 1. In case of bilateral surgery, the cost of surgery was raised by 25%.

During study period postoperative radiotherapy (RT) was recommended to the majority of women undergoing BCs and some of those undergoing mastectomy. We calculated the cost of RT using the DRG 851K (€216/fraction) and the 2014 data from the Northern Norway Regional Health Authority trust. Sixty-five per cent received two-field irradiation of the breast and 40 Gy in 15 fractions and 16% of them received another eight fractions as boost therapy. The remaining 35% got 50 Gy in 25 fractions. Furthermore, the DRG 850A (€275), planning of RT, was added. The mean savings per avoided patient undergoing RT was consequently calculated €4457. We calculated 75% of patients undergoing RT. Furthermore, we calculated half of them undergoing 5-year adjuvant hormonal therapy (AHT) and 50% zolodronic acid 4 mg intravenous twice a year for 5 years. This is according to the national recommendations. The cost of adjuvant chemotherapy (ACT) was given by DRG 856K (€1000). We calculated six cycles of chemotherapy and three-fourths of patients with BC were concluded candidates.

Family members underwent testing for the specific BRCA mutation detected. The cost of such a test was €67. Based on the OUH-U data, the mean number of family members tested per mutation carrier was four persons. Furthermore, the detected mutation carriers underwent several procedures causing healthcare costs (table 1). Hormonal replacement therapy for those undergoing PBSO consisted of sequential treatment with estradiol and norethisterone acetate (cost Trisekvens) (€87.4×9years – ages 46–55years = €787).
### Table 1: Costs (undiscounted and discounted (3%)) and savings per patient with BC screened by the BRCA mutation approach (alternative 1) or the traditional FH approach (alternative 2)

<table>
<thead>
<tr>
<th>Costs (C)</th>
<th>Unit cost</th>
<th>Alternative 1 Screening (€)</th>
<th>Alternative 1 Screening (€) 3% d r</th>
<th>Alternative 2 FH approach (€)</th>
<th>Alternative 2 FH approach (€) 3% d r</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients with BC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthcare costs (C1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit to breast surgeon</td>
<td>311</td>
<td>311</td>
<td>311</td>
<td>311</td>
<td>311</td>
</tr>
<tr>
<td>BCS (DRG 2600) (70%)</td>
<td>1758</td>
<td>1231</td>
<td>1231</td>
<td>1231</td>
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<td>Visit to a geneticist</td>
<td>70</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Mastectomy (DRG 258) (30%)</td>
<td>2312</td>
<td>694</td>
<td>694</td>
<td>694</td>
<td>694</td>
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<tr>
<td>Radiotherapy (75%)</td>
<td>4457</td>
<td>3343</td>
<td>3343</td>
<td>3343</td>
<td>3343</td>
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<td>Adjuvant hormonal therapy (50%)</td>
<td>1819</td>
<td>910</td>
<td>858</td>
<td>910</td>
<td>858</td>
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<tr>
<td>Adjuvant chemotherapy (75%)</td>
<td>6000</td>
<td>4500</td>
<td>4500</td>
<td>4500</td>
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<td>Zoledronic acid (50%)</td>
<td>138</td>
<td>690</td>
<td>617</td>
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<td>Reconstruction (12%)</td>
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<td>971</td>
<td>971</td>
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<td>Screening for mutation</td>
<td>5163</td>
<td>4246</td>
<td>4246</td>
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<td>BRCA INDEL screening</td>
<td>948</td>
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<td>0</td>
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<td>PBM (DRG 502)</td>
<td>15694</td>
<td>381</td>
<td>381</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>PBSO (DRG 3590)</td>
<td>2315</td>
<td>56</td>
<td>56</td>
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<td>13</td>
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<td>Hormonal replacement therapy</td>
<td>787</td>
<td>19</td>
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<td>4</td>
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<td>17226</td>
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<td>13235</td>
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<td><strong>Patient-related costs (C2)</strong></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Visit surgeon</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Visit geneticist</td>
<td>35</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Visit oncologist/radiotherapist</td>
<td>35</td>
<td>261</td>
<td>261</td>
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<tr>
<td>Travelling</td>
<td>29</td>
<td>536</td>
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<td>Sum C2</td>
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<td>833</td>
<td>835</td>
<td>835</td>
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<tr>
<td><strong>Cost in other sectors (C3)</strong></td>
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<td>Production loss</td>
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<td>19123</td>
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<td>19123</td>
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<tr>
<td><strong>Family members</strong></td>
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<td></td>
</tr>
<tr>
<td>Healthcare costs (C1&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
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<tr>
<td>Genetic counselling</td>
<td>70</td>
<td>7</td>
<td>7</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Genetic testing, mutation known</td>
<td>67</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Visit to surgeon (DRG 930O)</td>
<td>135</td>
<td>7</td>
<td>7</td>
<td>2</td>
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<tr>
<td>PBM (DRG 502)</td>
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<td>763</td>
<td>763</td>
<td>176</td>
<td>176</td>
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<tr>
<td>Visit to gynaecologist (DRG 913O)</td>
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<td>7</td>
<td>7</td>
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<td>2</td>
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<tr>
<td>PBSO DRG 3590</td>
<td>2315</td>
<td>113</td>
<td>100</td>
<td>26</td>
<td>23</td>
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<tr>
<td>Hormonal replacement therapy</td>
<td>787</td>
<td>38</td>
<td>34</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Sum C1&lt;sup&gt;2&lt;/sup&gt;</td>
<td>941</td>
<td>920</td>
<td>218</td>
<td>213</td>
<td></td>
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<tr>
<td>**Patient-related costs (C2&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Visit to surgeon (patient share)</td>
<td>35</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Visit to geneticist (patient share)</td>
<td>35</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Travelling</td>
<td>59</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sum C2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>3</td>
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<tr>
<td>**Cost in other sectors (C3&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Production loss</td>
<td>3187</td>
<td>77</td>
<td>77</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Continued
Patient/family-related costs (C2)

Patients and family members have to cover a minor amount of €35 when visiting the gynaecologist, breast surgeon and geneticist, respectively. In Norway, the Regional Health Authorities (NRH) (there are four RHAs in Norway: northern, central, western and southeastern) covers the costs of transportation. Internationally, studies include this item as patient/family-related costs. To make our study comparable, we included costs of travelling here. We used the one-way patient contribution cost on patient’s share and the qualified guess by clinicians at OUH-U (€15).

Costs in other sectors (C3)

Indirect costs in this setting were production losses. The mean income of Norwegians in 2014 was €57 127/year (www.ssb.no). We added employers’ costs due to pension and social costs (30%) and increased the costs by 3% from 2014 to 2015 based on the price index of Statistics Norway (€76 493). According to Statistics Norway, 76.9% of women, aged 25–74 years, were in the workforce and 64% of them were full-time workers. Based on these figures, we calculated the direct cost into a careful estimate of half of the mutation carriers being full-time workers. Based on the clinicians’ experience, the period out of workforce due to surgery, chemotherapy and RT was set to 6 months.

Savings (S)

The main economic savings was due to avoided BC and OC among index patients’ healthy family members.

Healthcare savings (S1)

Based on the OUH-U data, two healthy female BRCA mutation carriers were detected per family (of identified patients with BC with BRCA mutation (2.1%)). The following risk reductions were used. We calculated that the absolute lifetime risk of BC (BRCA mutation carriers) was reduced from 58% to 8% (the level of the Norwegian population) by the PBM+PBSO intervention. Similarly,
the reduction in the FH approach was calculated 23% (3/13) of the intervention arm figure. The savings, when avoiding BC, was implemented in the model. Most BRCA1-associated cancers were supposed to be infiltrative, high grade and oestrogen receptor negative. We therefore calculated that 75% underwent ACT. One-fourth was concluded candidates for 5 years of AHT (either tamoxifen or anastrozole). Furthermore, based on national recommendations, we calculated a 50-50 share between the two drugs and used the HELFO refund (tamoxifen €378 plus anastrozole €1441).1,2,19

The healthcare savings related to avoided OC due to PBM and PBSO was calculated as the value of reducing the absolute lifetime (at age 70) risk of OC by 52.2%, from 58% to 5.8%.2

Patient/family-related savings (S2)

These savings were due to avoided travelling for diagnosis, surgery, RT and chemotherapy. Similarly, patients saved copayment for these examinations and treatments.

Savings in other sectors (S3)

These were production gains. We considered half of the female family members being in the workforce.2 Furthermore, we calculated women reported ill and out of workforce for 6 months during ACT. Based on family members’ median age (46 years) and clinicians’ experience, we chose a conservative estimate and calculated that female workers avoiding BC and/or OC stayed in the workforce for another 5 years.

Life-years gained

LYGs are mainly due to avoided cancer deaths. In the OUH-U data, healthy female family members of BRCA mutation carriers were aged 20–83 years (median 46 years, mean 46 years). In such a setting (detected at an ‘older age”), a more conservative approach had to be taken. The risk of BC and OC among BRCA mutation carriers at the age of 70 years in Norway was 58% in both cancers and at the 5-year survival was 88% and 44.5%, respectively.2 The general lifetime risk of BC and OC in the Norwegian population was 8% and 1.2%. Due to late intervention (mean 46 years) we calculated the achievable level in OC to 5.8%.2 Furthermore, we employed the life expectancy of Norwegian women aged 46 years in 2014 as the expected survival curve of mutation-carrying female family members undergoing PBO and PBM. The time perspective was from the age of 46 to 90 years. Employing these figures, 5.9 undiscounted LYGs (3.0 LYGs, 3% discount rate (dr)) per women detected and undergoing PBO and PBM was concluded.

Statistics and ethics

In this study, only descriptive statistics was employed. The calculation of costs, savings and life-years gained or lost was calculated employing the Microsoft Excel for Mac 2011.

In the OUH-U study, genetic testing was performed diagnostically, all activities were part of daily routines and all clinical information was registered in the electronic patient record (EPR) system at OUH-U. The study was carried out as a model-based quality of care analysis and consequently no approval from the Regional Committees for Medical and Health Research Ethics (REK) or from the Norwegian Social Science Data Services (NSD) was necessary.

RESULTS

In the intervention arm the number of undiscounted LYGs was 0.29 (5.9 LY*13*2/535) per patient with BC offered BRCA mutation testing. The corresponding figure of the traditional FH approach was 0.07 LYGs (5.9 LY*3*2/535). Discounting the LYGs (3%), the LYG was 0.14 LYGs (3.0 LY*13*2/535) and 0.03 LYGs (3.0 LY*3*2/535), respectively. Consequently, the net LYGs was 0.11 LYG (0.22 undiscounted LYG) per patient with BC enrolled.

The net healthcare cost (healthcare perspective) was increased by €4508 (undiscounted, €4510) and the total costs (savings exclusive) by €1184 (undiscounted, €631) per patient with BC enrolled. The total discounted cost per LYG employing the healthcare perspective was €40503 (undiscounted, €40742). Focusing on the societal perspective, the corresponding figure was €5669 (undiscounted, €5374). Details are shown in table 2.

In Norway, the healthcare perspective is used when decisions with regard to the implementation of any new therapy/intervention in the healthcare service are made. Employing the frequently employed cut-off between €60 000 and €80 000/LY or quality-adjusted life year (QALY), this intervention was clearly cost-effective in Norway. To clarify the solidity of our findings, we performed a univariate sensitivity analysis. We employed the healthcare perspective figure and the 3% dr as the baseline for comparison (€40 503). This perspective is employed when national decisions in Norway are taken.27 Due to uncertainties concerning our estimates, we varied the factors by ±50%. Results are given in figure 2. The unit cost of the test (total sequencing) and the number of
LYGs per prevented cancer were the prominent factors affecting the result. None of the variations (maximum €60 755) in the sensitivity test made the cost-effectiveness figure passing reasonable cut-off level of cost per LYG.

**DISCUSSION**

We have documented that an intervention where all patients with BC are offered *BRCA* testing with sequencing and MLPA is costly, but cost-effective. The greatest benefit was achieved by the broad approach testing most patients with BC and no selection through the traditional FH approach. The sensitivity analysis revealed the major factors, influencing on the result, were the unit cost of the test itself and the LYGs per prevented cancer.

Looking at the test itself, it is costly (unit cost €5163). Employed as an offer to all Norwegian patients with BC and assuming our participation rate (82%), the national annual cost (budget impact) will be €14.1 million.\(^2^8\) However, during the last decade, the technology has improved and the cost of performing the test itself has dropped.\(^2^9\) We therefore estimated the hospital cost of running the test. This cost was one-third of the amount refunded by the HELFO. Based on this information, we believe the tariff will be reduced in the near future.

It is difficult to estimate the total LYGs due to the intervention.\(^3^0\) In our study, we did not focus on possible gains achieved by the patients with BC themselves. Following the diagnosis of BC, they underwent PBM and PBSO. Whereas this may obviously have saved life years due to prevented future new BC and/or OC, we experienced significant difficulties in defining this gain. In the study of Manchanda *et al.*,\(^2^9\) they concluded a population screening for *BRCA* mutations in Ashkenazi Jewish women saving 0.090 more life years and 0.101 more QALYs resulting in 33 days’ gain in life expectancy. Their baseline discounted (3.5% dr) incremental cost-effectiveness ratio was −£2079 per QALY. Translating these figures into a Norwegian *BRCA* mutation carrier setting (5-year survival of OC 44.5%, 5-year survival of BC 88%, lifetime risk of OC among *BRCA* mutation carriers increased by 52.2%, life expectancy of Norwegian women 83.5 years), the possible LYG by avoided OC among mutation-carrying patients with BC may be indicated 0.11 undiscounted LYG (0.05 discounted LYG) per woman screened [(83.5−(54.9+5) LY)*(1−0.445)*(0.525*(13−3)*0.88/535)]. Whereas there are several uncertainties related to this estimate, it is obvious that there are some improvements.

We believe the main benefit being connected to the prevented cancers among family members. Due to a delayed intervention in several family members, a maximum effect was not achieved.\(^3^\) This is underlined by the fact that we now are aware of three relatives who already had contracted a cancer (BC (ages 52 and 57 years) and OC (age 46 years)).


![Image of Figure 2](https://esmoopen.bmj.com/)

**Figure 2** A univariate sensitivity analysis varying several factors by ±50%. The figures are in euros (€).
before the intervention was initiated. We therefore believe our estimate was reasonable.

The effect of the comparator (traditional FH approach) was low. To clarify the potential of this approach, we retrospectively considered all the additional cases detected by the screening intervention. Following the Norwegian guidelines, in an optimal setting 12 out of the 13 (92%) detected mutation-carrying patients with BC could have been revealed. The LYG per patient with BC receiving the screening test would then be only 0.01 LYG and the cost per LYG would raise far above the suggested cut-off limit. However, running this estimate correctly, the cost of such a careful and optimal approach should have been identified and added. However, investigators have documented that the FH approach detects only about half of the mutation carriers. Consequently, such a suggested successful detection is not achievable in daily life in the clinics.

The cost of travelling was a minor factor. Whereas we have focused on the most populated areas of Norway, this cost will obviously increase when employing a national perspective. However, when looking at the factor’s minimal influence on the total result, we still argue that it will be insignificant when introducing the screening intervention on a national level.

This study was performed at one single institution. Despite this is the largest institution in Norway, it could be questioned whether our findings are fully representative for the general Norwegian, Scandinavian or European population with respect to prevalence of BRCA mutations. According to Statistics Norway (www.ssb.no), the south-eastern region of Norway does have a higher percentage of immigration compared with the other Norwegian health regions. Whereas immigrants/people with immigrant background constituted 16.3% of the Norwegian population, they constituted one-third of the population of the Norwegian capital’s population (Oslo). More than half of the immigrants/born by immigrants were from other European countries. The top countries in terms of immigration were Poland, Lithuania, Sweden, Somalia, Germany, Iraq and Denmark (www.ssb.no). Consequently, we believe the Norwegian population is becoming more and more similar to the population of the other Scandinavian and European countries and the increasing number of immigrants will be in favour of the systematic testing, as the FH approach will be more difficult to handle among immigrants.

Norwegian patients may claim compensation for malpractice experienced in the specialised healthcare. The Norwegian System of Patient Injury Compensation handles the requests. Recently, we have seen the very first examples of complaints of malpractice due to limitations in examining FH or act (refer to BRCA testing and consequently prophylactic intervention) on known information. In such a situation, the genetic testing of all patients with BC looks beneficial, as patient injury compensations may be avoided. There are advocates for the use of QALYs in economic analysis. In the setting of inherited risk of BC and/or OC and suggested prophylactic interventions, there is psychiatric distress that may influence the quality of life. We have no quality of life data for the general population in Norway. Consequently, proper Norwegian quality of life data could not be implemented into the model. However, there are available data for the general population from our neighbouring country, Sweden. Employing these data and focusing on the quality of life of women in the general population aged 50–90 years, the undiscounted QALYs gained may be indicated 0.17 per women screened (0.086, 3% dr) and the cost/QALY from a healthcare perspective would be €52419 and still below accepted cut-off levels. However, in such an assumption we have calculated patients undergoing PBM/PBSO having a similar quality of life as the general population. This is in accordance with a Dutch study that did not reveal any measurable impact on generic quality of life in high-risk women undergoing PBSO. Whereas this study may insufficiently describe patient preferences during the various health states potentially experienced in our model, it at least indicated a minor difference in quality of life.

We employed in 140 patients in the FH approach a limited genetic test designed to detect Norwegian founder mutations. This method has a lower sensitivity than the more costly sequencing and MLPA. To assess the sensitivity of this test, we employed the limited genetic test on the 13 BRCA mutation carriers detected by sequencing and MLPA (alternative 1). A total of 8 out of 13 cases were detected, indicating a detection rate of 62%. This test was specifically designed based on knowledge on frequently observed mutations in Norway, and therefore will not be relevant in other populations. Other countries have however developed similar founder mutation tests based on the prevalence and spectrum of such mutations within their populations. Studies have shown that a significant number of mutation carriers will be missed when testing only for known founder mutations in a population. We therefore hypothesise that our results may be generalised to other populations even though the exact frequency and spectrum of BRCA mutations may vary between populations.

In the future, we will experience a ‘dam fishing effect’. As more and more of the BRCA mutation-carrying families detectable by the FH approach are revealed, the remaining ones have to be detected by other means. In this setting, a population-based screening has been recommended by several investigators. We suggest that BRCA testing should be offered to all patients with BC. The share of participants is crucial for the success of a screening tool. We therefore recommend efforts spent on convincing patients with BC to participate in testing.

In Norway, our new strategy (testing all patients with BC) was cost-effective based on the frequently used cut-off limits. In countries with lower cut-offs, the figure could be improved by just screening patients with BC below a certain age (<60 years).
CONCLUSIONS
In this study, we have shown that an intervention where all patients with BC were offered BRCA testing with sequencing and MLPA was cost-effective. The major factor influencing on the result was the unit cost of the test itself. We believe the time has come for general diagnostic BRCA testing of all patients with BC. Today, too many life years are lost employing the FH approach. We believe this strategy is better than a population-based screening.

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