Accuracy of screening women at familial risk of breast cancer without a known gene mutation

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Review

Accuracy of screening women at familial risk of breast cancer without a known gene mutation: Individual patient data meta-analysis

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KEYWORDS
Magnetic resonance imaging;
Mammography;
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Genetic predisposition to disease;
Meta-analysis

Abstract
Introduction: Women with a strong family history of breast cancer (BC) and without a known gene mutation have an increased risk of developing BC. We aimed to investigate the accuracy of screening using annual mammography with or without magnetic resonance imaging (MRI) for these women outside the general population screening program.

Methods: An individual patient data (IPD) meta-analysis was conducted using IPD from six prospective screening trials that had included women at increased risk for BC: only women with a strong familial risk for BC and without a known gene mutation were included in this analysis. A generalised linear mixed model was applied to estimate and compare screening accuracy (sensitivity, specificity and predictive values) for annual mammography with or without MRI.

Results: There were 2226 women (median age: 41 years, interquartile range 35–47) with 7478 woman-years of follow-up, with a BC rate of 12 (95% confidence interval 9.3–14) in 1000 woman-years. Mammography screening had a sensitivity of 55% (standard error of mean [SE] 7.0) and a specificity of 94% (SE 1.3). Screening with MRI alone had a sensitivity of 89% (SE 4.6) and a specificity of 83% (SE 2.8). Adding MRI to mammography increased sensitivity to 98% (SE 1.8, P < 0.01 compared to mammography alone) but lowered specificity to 79% (SE 2.7, P < 0.01 compared with mammography alone).

Conclusion: In this population of women with strong familial BC risk but without a known gene mutation, in whom BC incidence was high both before and after age 50, adding MRI to mammography substantially increased screening sensitivity but also decreased its specificity. © 2017 Elsevier Ltd. All rights reserved.

1. Introduction

About 15–20% of breast cancer (BC) cases are associated with a family history of BC [1]. Women without a known mutation in a hereditary BC gene, but with a family history of breast with/without ovarian cancer, are at a higher risk of developing BC, the extent of the increased risk depends on the number of affected relatives and the age at cancer diagnosis in the relative(s) [2,3]. These women at familial risk, who have a cumulative lifetime risk of developing BC over 15–20%, are usually offered a BC screening regimen outside of the general population screening program, starting at an earlier age and including more frequent (annual) mammography [4,5].

Results of many prospective trials evaluating the accuracy of adding annual MRI to mammography for screening these women have been published [6–15]. Although these studies emphasised the significantly greater sensitivity of annual magnetic resonance imaging (MRI) and mammography in combination for screening this high-risk population, several issues remain unclear. First, inclusion criteria were heterogeneous and all the studies also included women with known gene mutations. Furthermore, the definition of familial risk for BC varied across countries and centres depending on referral criteria and risk assessment tools. Also, few studies reported results separately for women at familial risk without a known gene mutation [8,11,12] and none of the studies reported results stratified by age for this population.

In this meta-analysis, pooling individual patient data (IPD) from prospective trials, we aimed to assess the accuracy of screening women at familial risk of BC without a known gene mutation, adding MRI to mammography and stratifying outcomes by age.

2. Methods

2.1. Study design

An IPD meta-analysis was conducted, including individual data from 6 of 12 prospective trials, in which women at high risk of BC due to an inherited BRCA gene mutation or a strong family history of BC were screened with annual mammography and MRI, and the accuracy of each screening modality was reported separately [16,17]. All studies were performed in developed countries. More details about the study inclusion criteria, data acquisition and assembly and quality assessment were reported in our previous publication which focused on BRCA1/2 gene mutation carriers [17]. In the present study, we focus only on women with a strong family history of BC (defined as a cumulative lifetime BC risk of at least 15%) and without a known gene mutation. Specific inclusion criteria for the original studies contributing to this IPD meta-analysis, outlining family history criteria and whether women with a personal history of BC were included are summarised in Supplementary appendix 1.

2.2. Study population

Women aged 25 or older, who had a strong family history of BC and no known gene mutation and had
completed at least one screening round, were included in this analysis. A completed screening round was defined as a screening round in which both MRI and mammography were performed within a time interval of less than 3 months, with results of the two tests interpreted separately using blinded methods. Screens were included if there was either a pathology test or at least 1 year follow-up to confirm the presence or absence of BC. Women who were proven to be non-mutation carriers from a BRCA family were excluded, as their risk is generally considered to be comparable to that of the general population. Screen-detected or interval cancers were counted in this analysis (BCs found during preventive mastectomy were not considered).

2.3. Primary outcome and definitions

Primary outcomes were screening accuracy including sensitivity, specificity and positive/negative predictive value (PPV/NPV). To adjust for multiple screenings of the same women and differences between studies, the estimates for each modality were model-based with the following: (1) sensitivity defined as the number of BCs detected over the total number of BC diagnosed; (2) specificity defined as the number of true-negative tests over the total number of screens without BC; (3) PPV defined as the number of true-positive over the total number of positive tests; (4) NPV as the number of true-negatives over the total number of negative tests.

Imaging scores of BI-RADS 0, 3, 4 or 5 (Breast imaging-reporting and data system) were considered to be a positive screening result. Using this threshold allowed the harmonisation of the outcomes across studies. The combination of MRI and mammography was classified as a positive result if either one of these tests was positive. BI-RADS 1 or 2 was considered a negative test, and a negative outcome of the combination was based on both tests having negative results. For positive test results, the presence of BC was based on the results of histologic examination. The absence of BC was ascertained by histologic examination or 1 year follow-up with negative screening or stable imaging. Where more than one tumour was diagnosed in a woman in the same screening round, the largest BC was included. Where more than one BC was diagnosed in a woman at different screening years, the first BC was included. For analytic purposes, a BC was considered an interval cancer when it was not detected by a positive screening test (mammography or MRI) and was diagnosed between two annual rounds of screening. The above definitions were applied to all the studies when assembling the individual data to obtain consistency and comparable data from all studies, although there were slight differences between these definitions and the definitions that may have been applied in the original studies.

2.4. Statistical analysis

Characteristics of the women (follow-up time, cancer incidence, median age at entry with interquartile range [IQR]) and cancer characteristics were reported for the total study population and for each age group. Overall cancer incidence in total and stratifying by screening round, were calculated as the number of BCs per 10,000 woman-years and the 95% confidence interval (CI) was computed assuming the incidence follows a Poisson distribution.

A generalised linear mixed model (Procedure Glimmix using the QUAD option for the likelihood method of estimation the binomial distribution with logit link function, SAS version 9.4) was applied to estimate sensitivity, specificity and the predictive values of each screening modality and then compare these measures for the two screening modalities and the combination using Wald tests. One analysis is done for sensitivity and specificity simultaneously and another for predictive values. For sensitivity and specificity, repeated measurements were summarised for each woman to the total number of screens with proven BC, total number of screens without BC, the number of true-positives and the number of true-negatives. Each woman had six records: two ascertained outcomes (with or without proven BC) for each of three screening modalities (mammography, MRI and the combination). In the model, the numbers of true-positive/ negative tests followed a binomial distribution with the total number of screens with/without proven BCs and a proportion that was modelled as a function of screening modality. To address heterogeneity between studies, a bivariate random variable with an unstructured correlation matrix was added to model the study effect for each screening modality and each ascertained outcome. Analysis was performed for each age group separately. Sensitivity and specificity were modelled simultaneously to take into account their negative correlation. The same approach was used for positive and NPVs by replacing the ascertained outcomes by modality outcomes (test positive or negative) and number of screens with/without BCs by the number of screens with positive/negative test. Screening accuracy for the three modalities was compared within age groups defined by age at screening, as follows: younger than 40 years, 40–49 years and 50 years and older. In two sensitivity analyses, the year of screening was added to the model to explore its impact on the results, and screening accuracy was estimated for first and subsequent rounds to allow for prevalent cases.

3. Results

3.1. Study population and breast cancers during the study

Data on 2226 women at familial risk with at least one completed screening round were included in this
analysis, representing 7478 woman-years of follow-up (median 3 years, IQR 2–5) with ascertained outcomes (Table 1). There were 106 (4.8%) women with a personal history of BC and 193 (8.7%) women with a negative genetic test result. Amongst these 2226 women with a median age of 41 years (IQR 35–47) at study entry, 87 BCs were diagnosed at a median age of 48 (IQR 43–54) years. BC rate was estimated as 11.6 (95% CI 9.3–14) per 1000 woman-years. BC incidence increased with increasing age: 5.1 (95% CI 2.8–8.6) per 1000 woman-years in women who underwent screening before age 40, 12 (95% CI 8.3–16) per 1000 woman-years in women aged 40–49 and 22 (95% CI 15–30) per 1000 woman-years in women aged 50 and older. Of all BCs, 37 were prevalent cancers (detected at the first screening round); excluding those prevalent cancers, the rate (per 1000 woman-years) was 9.5 (95% CI 7.1–13) in all women, 5.7 (95% CI 2.7–11) in women aged <40, 8.3 (95% CI 4.9–13) in women aged 40–50 and 16.6 (95% CI 10–25) in women aged ≥50.

Amongst 87 BCs observed in the study population, three were interval cancers: all were invasive, smaller than 2 cm and diagnosed in women aged 37, 46 and 57 years. The youngest group had more invasive BCs and more large invasive BCs than the older age group (Table 1).

### 3.2. Screening accuracy in all women

In the total study population, mammography sensitivity was 55% (standard error of mean [SE] 7.0) (Table 2). The combination of MRI and mammography had the highest sensitivity but the lowest specificity. The combined sensitivity was 98% (SE 1.8) versus 89% (SE 4.6) for MRI alone (P < 0.001) and 55% (SE 7.0) for mammography alone (P < 0.001). The combination had the lowest specificity of 79% (SE 2.7) versus 83% (SE 2.8) for MRI alone (P < 0.01) and 94% (SE 1.3) for mammography alone (P < 0.01). The PPVs of the three screening modalities were generally comparable around 9%, whereas differences were observed for NPVs, as summarised in Table 2. When adjusting for year at screening (results not shown) or excluding the first screening round (Table 4), the estimates for sensitivity and specificity did not change.

### 3.3. Cancer detection: contribution of screening modalities in different age groups

Screening with the combination of MRI and mammography had higher sensitivity compared with mammography alone in all age groups (Table 2). In women younger than 40 years, the sensitivity of the combination was 95% (SE 5.6) versus 51% (SE 13) for mammography (P < 0.01) and MRI alone detected seven invasive cancers (of 14 cancers, 50%, four invasive tumours 1–2 cm), which were not detected at mammography (Table 3). In women aged 40–49, the sensitivity of the combination was 98% (SE 2) compared to mammography sensitivity 57% (SE 8.2, P < 0.01) (Table 3) and MRI detected 17 cancers (of 36 cancers, 47%) which were not detected at mammography, among which 12 were invasive cancers (six tumours were ≤1 cm), four were ductal carcinoma in situ (DCIS) and one was unspecified. In women ≥50, sensitivity of the

### Table 1

Overview of the women at familial risk and their breast cancers characteristics, stratifying by age at screening (N = 2226; BCs = 87).

<table>
<thead>
<tr>
<th></th>
<th>All ages</th>
<th>Age &lt;40</th>
<th>Age 40–49</th>
<th>Age ≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women</td>
<td>2226</td>
<td>987</td>
<td>1044a</td>
<td>527</td>
</tr>
<tr>
<td>Number of BCs</td>
<td>87</td>
<td>14</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Follow-up (1000 BCs)</td>
<td>7478</td>
<td>2733</td>
<td>2953</td>
<td>1792</td>
</tr>
<tr>
<td>Screen detected</td>
<td>84</td>
<td>13</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>DCIS</td>
<td>17</td>
<td>1</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Invasive</td>
<td>61</td>
<td>12</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Interval cancer</td>
<td>3 (invasive cancers)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tumour size of invasive cancers</td>
<td>64</td>
<td>13</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>≤10 mm</td>
<td>21 (33%)</td>
<td>1 (7.7%)</td>
<td>9 (39%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>11–20 mm</td>
<td>27 (42%)</td>
<td>7 (54%)</td>
<td>9 (39%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>&gt;20 mm</td>
<td>8 (13%)</td>
<td>2 (15%)</td>
<td>3 (13%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (13%)</td>
<td>3 (23%)</td>
<td>2 (8.7%)</td>
<td>3 (11%)</td>
</tr>
</tbody>
</table>

BC, breast cancer; DCIS, ductal carcinoma in situ; IQR, interquartile range.

a Of those 987 women included in the model for women age <40, 194 women started their screening before the age of 40 and became 40 in one of the follow-up rounds. These women were also counted in the age group 40–49.

b Of those 1044 women included in the model for women age 40–49, 138 women started their screening between age 40–49 and became 50 in one of the follow-up rounds. These women were also counted in the age group ≥50.
Table 2
Screening accuracy in women at familial risk of breast cancer (N = 2226, BCs = 87, median screening rounds: 3 [IQR 2–5]).

<table>
<thead>
<tr>
<th>Modality (BCs detected [N]; positive tests; [N])</th>
<th>Women at all ages</th>
<th>Sensitivity %; SE; (95% CI)</th>
<th>Specificity %; SE; (95% CI)</th>
<th>PPV %; SE; (95% CI)</th>
<th>NPV %; SE; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography (48; 458)</td>
<td>55(^a)</td>
<td>94(^b)</td>
<td>9.7</td>
<td>99(^a)</td>
<td></td>
</tr>
<tr>
<td>MRI (75; 997)</td>
<td>7.0 (41–69)</td>
<td>1.3 (90–96)</td>
<td>4.5 (6.3–19)</td>
<td>0.0 (99–100)</td>
<td></td>
</tr>
<tr>
<td>Combination (84; 1287)</td>
<td>4.6 (76–96)</td>
<td>2.8 (77–88)</td>
<td>3.3 (4.1–18)</td>
<td>0.0 (99.6–100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>79</td>
<td>7.9</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.8 (86–100)</td>
<td>2.7 (73–84)</td>
<td>2.5 (4.1–15)</td>
<td>0.0 (99.8–100)</td>
<td></td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value; SE, standard error of mean.

\(^a\) Compared to the combination sensitivity: P = 0.0008.
\(^b\) Compared to the combination specificity: P < 0.0001.
\(^c\) Compared to the combination specificity: P = 0.002.
\(^d\) Compared to the combination specificity: P = 0.002.
\(^e\) Compared to the combination NPV: P = 0.0002.

combination was 97% (SE 3.0) (compared to 67%, SE 7.8, P > 0.05, for mammography), and MRI alone detected 12 cancers (of 37 cancers, 32%, including two cases of DCIS and one invasive tumour ≤1 cm) that were not detected by mammography (Table 3).

The sensitivity of mammography improved to some extent with increasing age. The sensitivity of mammography was low in women <40 years (51% SE 13) (Table 3). In the women <40 years, mammography visualised 6 of 14 cancers and only for one case, the tumour (DCIS) would have been missed if mammography would not have been performed. In women aged 40–49, mammography sensitivity was 57% (SE 8.2). In this age-group, 18 of 35 cancers could be visualised with mammography, and four cancers (three DCIS and one invasive ≤1 cm) were missed by MRI (Table 3). In women aged ≥50, mammography had a sensitivity of 67% (SE 7.8) (Table 3). Mammography visualised 24 of

Table 3
Screening accuracy in women at familial risk of breast cancer, stratifying by age at screening.

<table>
<thead>
<tr>
<th>Age groups, N women, BCs, SR</th>
<th>Modality (BCs detected; positive tests)</th>
<th>Sensitivity %; SE; (95% CI)</th>
<th>Specificity %; SE; (95% CI)</th>
<th>PPV %; SE; (95% CI)</th>
<th>NPV %; SE; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;40, N = 987, BCs = 14, SR: 2 [IQR 1–4]</td>
<td>Mammography (6; 131)</td>
<td>51(^a)</td>
<td>95</td>
<td>5.1</td>
<td>100</td>
</tr>
<tr>
<td>MRI (12; 338)</td>
<td>13 (26–76)</td>
<td>3.5 (74–89)</td>
<td>1.5 (1.8–8.3)</td>
<td>0.0 (99.6–100)</td>
<td></td>
</tr>
<tr>
<td>Combination (13; 436)</td>
<td>95</td>
<td>7.9</td>
<td>3.6</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Age 40–50, N = 1044, BCs = 36, SR: 3 [IQR 2–5]</td>
<td>Mammography (18; 215)</td>
<td>57(^a)</td>
<td>91</td>
<td>8.8</td>
<td>99</td>
</tr>
<tr>
<td>MRI (31; 470)</td>
<td>8.2 (40–73)</td>
<td>1.6 (87–95)</td>
<td>2.2 (5.2–14)</td>
<td>0.3 (99–100)</td>
<td></td>
</tr>
<tr>
<td>Combination (35; 613)</td>
<td>92(^a)</td>
<td>80(^e)</td>
<td>7.1</td>
<td>100(^g)</td>
<td></td>
</tr>
<tr>
<td>Age ≥50, N = 527, BCs = 37, SR: 4 [IQR 2–5]</td>
<td>Mammography (24; 113)</td>
<td>98</td>
<td>75</td>
<td>6.3</td>
<td>100</td>
</tr>
<tr>
<td>MRI (32; 167)</td>
<td>2.0 (83–100)</td>
<td>3.2 (68–81)</td>
<td>1.1 (4.4–9.1)</td>
<td>0.0 (99.6–100)</td>
<td></td>
</tr>
<tr>
<td>Combination (36; 236)</td>
<td>7.8 (49–81)</td>
<td>0.6 (92–95)</td>
<td>9.5 (9.4–48)</td>
<td>0.3 (98–100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>86(^e)</td>
<td>90(^a)</td>
<td>20</td>
<td>100(^h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.6 (70–95)</td>
<td>2.7 (83–94)</td>
<td>6.2 (11–37)</td>
<td>0.2 (99–100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>97</td>
<td>85</td>
<td>19</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0 (75–100)</td>
<td>2.4 (80–90)</td>
<td>6.0 (9.5–34)</td>
<td>0.0 (99.9–100)</td>
<td></td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value; SR, screening round, median and IQR; IQR, interquartile range; SE, standard error of mean.

\(^a\) Compared to the combination sensitivity: P = 0.003.
\(^b\) Compared to the combination specificity: P = 0.002.
\(^c\) Compared to the combination specificity: P = 0.04.
\(^d\) Compared to the combination specificity: P = 0.003.
\(^e\) Compared to the combination specificity: P < 0.0001.
\(^f\) Compared to the combination specificity: P = 0.006.
\(^g\) Compared to the combination NPV: P = 0.02.
\(^h\) Compared to the combination sensitivity: P = 0.0003.
\(^i\) Compared to the combination specificity: P = 0.03
\(^j\) Compared to the combination NPV: P = 0.02.
37 cancers and four of those (one DCIS and three invasive) were not detected by MRI.

3.4. Predictive value of screening modalities in different age groups

The PPV of each modality increased by age, whereas the NPV remained at about 99% or higher: Details are shown in Table 3.

4. Discussion

Our IPD meta-analysis examined the accuracy of screening mammography with or without MRI in women with a strong family history of BC and without a known gene mutation: Based on data for 2226 women, the observed BC incidence rate was high (12 per 1000 woman-years) and this was evident in both younger and older women, highlighting the BC burden in this population. The sensitivity of mammography was only 55% (SE 7.0). However, mammography was the most specific modality compared to MRI alone or the combination of MRI and mammography. Combining MRI and mammography detected the great majority of cancers with a sensitivity of 98%, significantly higher than the 55% sensitivity of mammography or 89% of MRI alone (P < 0.001). The higher sensitivity of the combination of mammography and MRI was evident in all age groups. The combination, however, had the lowest specificity due to a relatively high number of false-positives from MRI.

The accuracy of screening mammography for women at elevated risk due to family history and without a proven mutation was examined in some of the original primary studies contributing data for this IPD meta-analysis, and the results were generally comparable to this IPD meta-analysis, though based on fewer cases. Of those eligible studies that did not participate in this IPD meta-analysis [6,7,9,10,18], one study reported a low mammography sensitivity (25%) in women with an estimated lifetime BC risk of 21–40% [7]. Another study reported that mammography detected two of four BCs in 142 women with >25% lifetime risk of developing BC [18]. Although outside the scope of this IPD, a prospective screening study including women (mean age 55, range 25–91) at familial risk and who had heterogeneously dense or extremely dense parenchyma reported a mammography sensitivity of 50% (95% CI 34–66) [19]. Another retrospective study showed that annual mammography did not contribute to cancer detection over annual MRI in a retrospective cohort of women younger than 40 years with a lifetime risk of more than 20%, in whom four BCs were diagnosed [20]. Similarly, our IPD meta-analysis showed that mammography sensitivity was relatively modest (51% [SE 7.0]), whereas adding MRI increased the sensitivity up to 95% (SE 1.8).

Adding MRI screening has been shown to improve screening accuracy compared to mammography alone in other populations at increased BC risk, specifically in women with BRCA1/2 mutation [16]. However, adding MRI to mammography gave a significantly higher number of false-positive results. In addition, adding MRI is costly. It should be noted that in these studies, MRI and mammography were performed and interpreted independently, and a positive result was referred to whenever either test was positive—joint interpretation may potentially help reduce the number of false-positives. Yet, there still remains a lack of evidence regarding the long-term effects of annual MRI plus mammography compared with annual mammography.

The strength of this IPD meta-analysis is that it collected individual data from six prospective screening studies, creating the first pooled analysis of women with strong family history and without a known gene mutation. Further, it allowed implementation of common definitions and thresholds as well as subgroup analyses, through the collective data sets and through the use of IPD methodology. Nonetheless, there are several limitations to this meta-analysis. First, the number of women and cancers in some subgroup analyses remained too small to obtain either a clear trend or statistical significance. Second, we might have underestimated the accuracy of screening because the data collected in these studies are based on relatively older imaging technology [17]. Although we explored this issue by adding year of screening to our model and
found that it did not substantially change the estimates for sensitivity and specificity. We acknowledge that higher accuracy may be expected for current mammography and MRI technology because of improved MRI technology [21,22], better defined MRI BI-RADS descriptors and diagnostic categories [23] and the increasing use of breast digital tomosynthesis for screening [24,25]. Third, we included IPD from six prospective screening trials, yet each original study had its own recruitment time frame, age at recruitment, inclusion criteria and risk assessment tool for women without a proven mutation (Supplementary 1); thus, there was unavoidable heterogeneity in the format for family history data and probably risk level, reflecting real-life practices. It was therefore not possible to estimate BC risk for all the study population using one common criterion or assessment model without making some assumptions. In addition, despite some small differences between countries, the overall lifetime risk to develop BC in countries where the included studies were performed is 1 in 8 [26,27], which is not expected to have any impact on the here presented results on comparative accuracy. Furthermore, there was no information about CHEK2 prevalence in these cohorts, and the effect of this gene mutation in screening accuracy was not examined. Future research focussing on the burden of family history and other gene mutations may potentially help refine and personalise screening strategies in these women. Finally, as the included studies investigated screening accuracy and did not report data on long-term outcomes such as survival, we could not include such outcomes in our analysis.

Our IPD meta-analysis highlights that adding MRI to mammography significantly improves BC detection in women with a strong family history of BC and without known gene mutations; however, this should be considered against the higher false-positive rate (lower specificity) caused by adding MRI screening. Our findings might lead to the conclusion that MRI screening alone may be appropriate for these women; however, comparative accuracy studies, such as reported in this work, need to be complemented by health-economic evaluation to determine whether such an approach could be cost-effective. Also, future research in this population of women is critically needed to examine alternate screening approaches, investigating new, faster (and less costly) MRI techniques and tomosynthesis as a replacement for 2-D mammography to develop screening strategies that optimise BC detection without significantly increasing the false-positive recall burden.

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Conflict of interest statement

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejca.2017.07.055.

References


