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Women's experiences of risk-stratified breast cancer screening in the MyPeBS trial: a qualitative comparative study across two European countries

Lorna McWilliams^a, Alexandra Roux^b, Rhiannon Hawkes^a , Rachel Cholerton^a, H el ene Delattre^c, Agn es Bernoux^d, Marie-Laure Forzy^e, D. Gareth Evans^f, Corinne Balleyguier^g, Debbie Keatley^h, C ecile Vissac-Sabatierⁱ, Suzette Delalogue^g, Sandrine de Montgolfier^b, David P. French^a and On behalf of the MyPeBS Consortium

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ABSTRACT

Objective: Risk-stratification should improve the benefits-to-harms ratio for breast screening, whereby higher-risk women receive additional screening and low-risk women are screened less. This study investigated the effects of healthcare context by comparing how women in England and France experienced risk-based breast screening.

Methods and measures: Fifty-two women were purposively sampled from participants who underwent risk-based screening in the MyPeBS trial. Women received objectively-derived 5-year breast cancer risk estimates (low = < 1%, average = 1–1.66%, high = ≥ 1.67 to <6%, very-high-risk = ≥ 6%). This determined future trial-related screening schedules and prevention options. Semi-structured interviews were transcribed for thematic framework analysis.

Results: Two overarching themes were produced: *the importance of supported risk communication* and *accessibility of risk management*. Overall, risk-based breast screening was viewed positively. However, trial procedures, especially in risk estimate provision, differed across sites. Women at increased risk were more reassured when appointments were with specialist healthcare professionals (HCP). When absent, this resulted in reduced satisfaction with risk communication and greater uncertainty about its personal relevance. Low-risk women's views on extended mammogram schedules seemed linked to how health services are organised differently.

Conclusions: Context is an important consideration regarding acceptability of healthcare innovations such as risk-stratified screening: it should not be assumed that findings from one country apply universally.

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Introduction

Breast cancer is the leading cause of death among women worldwide (Sung et al., 2021). To improve early detection of breast cancers, breast screening has been implemented in many countries (Marmot et al., 2013). Generally, these programmes use age and sex as primary eligibility criteria and current public health policies recommend screening using mammography. However, screening frequency varies from annually (United States of America [USA]), two-yearly (many European countries, including France) to three-yearly (United Kingdom [UK] and Malta). Similarly, the age range of the population routinely invited differs between countries, e.g. 45–74 years in Italy to 50–69 years in Belgium (Cardoso et al., 2023).

Despite studies evidencing benefits of breast screening including the reduction in deaths and early detection of the disease (Marmot et al., 2013), on-going debates include what is the optimal screening interval (Canelo-Aybar et al., 2022), whether younger women would benefit from screening (Usher-Smith et al., 2023), and potential screening harms. Such harms include overdiagnosis of tumours and subsequent overtreatment that would not otherwise have been detected during a woman's lifetime and long-term anxiety from false-positive findings (Long et al., 2019; Moutel et al., 2014). Risk-stratified screening has been suggested to increase these benefits whilst reducing harms, where individuals are assigned to a risk group based on established risk factors such as breast cancer family history and reproductive history (Evans et al., 2012, 2022; Pashayan et al., 2020). Thus, prevention and early detection interventions (e.g. additional screening, risk-reducing medication if applicable) can be offered systematically to those at increased risk (Burton et al., 2013). This could both reduce the number of high-risk women diagnosed with interval cancers in-between screening intervals and improve detection of breast tumours at an earlier stage where less intense treatment can be offered. For example, following indication that risk assessment can provide accurate risk stratification for higher stage breast cancer (Evans et al., 2019), a study called BC-Predict showed that it was possible to offer breast cancer risk assessment as part of the English NHS Breast Screening Programme (NHSBSP) and higher risk women accept risk-reducing interventions (Evans et al., 2023). Specifically, between 63 and 79% of women identified at higher risk in BC-Predict and who had an appointment to discuss their risk opted for risk-reducing and early detection interventions (additional screening and/or risk-reducing medication). It might also be possible to reduce screening frequencies for women at low-risk, to reduce screening harms outlined earlier (McWilliams et al., 2020). This could also result in the reallocation of resources for interventions for higher risk women such as more frequent screening, although the cost-effectiveness of this reallocation is uncertain (Wright et al., 2024). Ongoing trials will provide evidence on effectiveness of risk-stratified breast cancer screening compared to current screening including MyPeBS (NCT03672331) in Europe (UNICANCER, 2018) and USA-based Wisdom (NCT02620852; Esserman et al., 2021).

MyPeBS is a randomised controlled trial across six countries: Italy, France, Israel, UK (England), Belgium, and Spain. The trial assesses whether risk-stratified screening is non-inferior or improved at reducing the incidence of advanced breast cancer

(cancers diagnosed at stage two or higher), compared to routine breast screening. In the standard arm, women participate in the breast cancer screening programme in their respective country. In the risk-based arm, screening frequency depends on individual 5-year predicted breast cancer risk estimates (Tice et al., 2015; Tyrer et al., 2004) according to four groups: low (<1%), average (1–1.66%), high (≥ 1.67 to <6%) and very-high ($\geq 6\%$ at 5-years).

Despite potential benefits of undertaking risk-stratified screening, it is important to assess whether the process is acceptable to stakeholders involved (Wilson & Jungner, 1968). For example, the UK National Screening Committee (UKNSC) is responsible for making recommendations to Government ministers about whether a change to an existing screening programme or the introduction of a new programme should be implemented. Of the list of twenty, one criterion includes: 'There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public' (UK National Screening Committee [UKNSC], 2022). Without such evidence within the context of risk-stratified breast screening, it would not be recommended or implemented in the UK healthcare system. Specific challenges raised by risk stratification may need to be addressed, for example, how to optimally communicate individual risk of developing cancer (Hall et al., 2014; Rainey et al., 2018). This is particularly important to minimise increased general anxiety or worry about cancer that may be induced by risk estimate provision (French et al., 2018, 2023). Additionally, as health behaviours have a role in breast cancer risk, specific interventions may need to be developed to promote successful behaviour change (Harvie et al., 2019) rather than by only providing information about this during risk communication (French et al., 2017).

The ethical, psychological, and socio-economic impact of risk-stratified screening are being examined within MyPeBS (Roux et al., 2022). The use of qualitative methods is recommended for process evaluation (Moore et al., 2015) and can give insight into acceptability of being offered risk-stratified screening. This is especially important to gather evidence on how risk-stratified breast screening should be implemented, should these effectiveness trials demonstrate success.

Given that MyPeBS involves implementation of risk-stratified screening in countries with different screening programmes and background healthcare contexts, it provided an ideal opportunity to examine the extent to which this new form of screening is received varies by those experiencing it. For example, the UK NHSBSP invites women aged 50–70 years, 3-yearly for a mammogram (Borrelli et al., 2016) whilst the French national screening programme invites women aged 50–74 years every 2 years using mammograms, clinical breast examinations and for those with dense breasts, ultrasound imaging (Moutel et al., 2014). Previous acceptability research has focussed either on single countries where findings may not be universally applicable (McWilliams et al., 2023) or included participants considering risk-based screening hypothetically (Rainey et al., 2019). The present study therefore aimed to explore MyPeBS participants' views of risk-based screening focusing on an explicit comparison of women who underwent screening within two different healthcare contexts.

Materials and methods

Design, setting and participants

The wider MyPeBS trial randomised women to receive risk-stratified screening or whatever constituted standard screening in each country. All participants completed baseline data collection before randomisation to the risk-based or standard trial arm. Standard-arm participants completed psychosocial questionnaires and received the routine screening schedule for their country. In the risk-based arm, risk was estimated using validated methods (Breast Cancer Surveillance Consortium-derived Mammorisk™ (Tice et al., 2015) or Tyrer-Cuzick™ (Tyrer et al., 2004)) to tailor mammographic screening schedules. Breast cancer risk was estimated based on baseline self-reported risk factor information, mammographic breast density calculated from (mammogram) breast images and a polygenic risk score. Polygenic risk was calculated from a DNA saliva sample and analysed according to 313 known breast cancer single nucleotide polymorphisms (Mavaddat et al., 2019). Risk communication aimed to be provided approximately 10–12 weeks post-randomisation and women also completed psychosocial questionnaires throughout the study. Key intended risk-based trial arm procedures are outlined in Table 1.

We sampled women who underwent risk-stratified screening from two countries (England and France). Although MyPeBS recruits from multiple areas per country, women were recruited for this study from one NHSBSP centre covering Greater Manchester, England (6th most deprived Local Authority of 326; Ministry of Housing Communities and Local Government, 2019a) and from two large French screening regions (involving numerous investigating centres) in Paris and Northern France with similar socio-economically heterogeneous populations. One of the two northern French regions is however homogeneously deprived relative to the rest of France (Institut national de la statistique et des études économiques [Insee], 2018). Eligible women were aged 40–70-years when joining MyPeBS and agreed to invitations about future ethically-approved research. Participants were purposively sampled by risk group (low, average, high, and very-high-risk). We aimed to recruit approximately six women across each group per country (i.e. approximately 48 women) to gain experiences from women allocated to different groups. It was possible to identify estimated socio-economic status (SES) in England to ensure, where possible, that women living in different deprivation areas were invited. This was estimated by the MyPeBS local trial co-ordinator using the Index of Multiple Deprivation (IMD); residential postcodes were used to calculate deciles (1, most deprived to 10, least deprived; Ministry of Housing Communities and Local Government, 2019b). Where possible, women living in deciles <8 were invited.

Procedure

Recruitment and data collection in France was November 2021–January 2022 and in England, July–November 2022, see Figure 1 for flow chart.

The later data collection period in Manchester was due to the trial starting later here and the wider interval between risk communication and interview in France was

Table 1. Intended MyPeBS risk-based trial arm procedures^a between England and France.

	Participating country intended trial arm procedures ^a and <i>participant accounts of these^b</i>	
	England	France
Age invited to trial	50–70 years from organised breast screening programme or 40–49 years from recruiting centre family history clinic.	40–70 years
Recruitment strategy	Invite letter from breast screening programme directing to MyPeBS website or if 40–49 years, from recruiting site family history clinic.	Invite letter from breast screening programme directing to MyPeBS website, opportunistically e.g. introduced to study by gynaecology, radiology, general practitioner (GP) HCP or <i>via media</i> e.g. campaign.
<i>Recruitment strategy from participant perspective^b</i>	<i>Invite letter 'from' breast screening office on behalf of research team directing to [Trial Name] website.</i>	<i>Highly varied: introduced to study by HCP, Facebook/radio adverts, letter from insurance company or letter from breast screening office.</i>
Inclusion/Recruitment	Completed <i>via</i> email or telephone with trial co-ordinator; personal log-in for MyPeBS online portal created.	At an in-person visit with HCP (hospitals or small practices who are GPs, radiologists or gynaecologists); personal log-in for MyPeBS online portal created.
Baseline data collection completion	By participant using portal.	During HCP inclusion visit using portal.
Saliva sample	Sent to participant's home with return envelope.	Completed during HCP inclusion visit.
Risk feedback	Face-to-face or telephone risk communication depending on risk group or local recommendations to provide individual 5-year breast cancer risk estimates and associated screening schedule. Written 'risk sheet' and information within participants' MyPeBS portal was available. Portal information should only be available after initial risk communication.	
<i>Risk feedback communication format from participant perspective^b</i>	<i>Low/Average risk groups received risk estimate information by post. High/Very-high risk groups received risk sheet by email from local research team before phone appointment with HCP^c.</i>	<i>Highly varied, even within risk groups: face-to-face appointment with HCP^d, during appointment for something else in primary care, telephone/videocall with HCP^d, via email from HCP^d, risk sheet collected at radiology department reception or via [Trial Name] website portal only^e.</i>
Change ^f in mammogram screening schedule per risk group (during 4-year trial if aged ≥50 years)	<ul style="list-style-type: none"> Low=changed from 3-yearly to 4-years, yearly breast cancer awareness reminder Average=changed from 3 to 2-yearly High/Very-High=changed from 3-yearly to 1-yearly 	<ul style="list-style-type: none"> Low=changed from 2-yearly to 4-years, yearly breast cancer awareness reminder Average = 2-yearly interval unchanged High/Very-High=changed from 2-yearly to 1-yearly
Risk-reduction recommendations	<p>Very-High also annual MRI if <60 years</p> <p>Recommendations related to health behaviours (e.g. diet) provided in written feedback and during HCP consultations.</p> <p>Risk-reducing medication discussed with HCP based on guidelines (National Institute for Health and Care Excellence [NICE], 2017); if interested, sent standard postal information.</p>	<p>Very-High also annual MRI if <60 years</p> <p>Recommendations related to health behaviours (e.g. diet) provided in written feedback and during HCP consultations.</p> <p>Risk-reducing medication not applicable; not authorised in France for this indication.</p>

Note. GP=General Practitioner; HCP=Healthcare Professional; MRI=Magnetic Resonance Imaging. ^aDifferences based on trial documentation and information from local trial co-ordinators. ^bItalicised text is based on accounts from participants during data collection. ^cLocal [Trial Name] research team confirmed this was the same HCP with breast cancer risk communication expertise. ^dHCP communicating risk where specified by participants: gynaecologist, primary care doctor, radiologist. ^eThis should only be possible if HCP reports that risk communication has taken place. ^fTrial schedules were new for women aged 40–49, as not offered routine screening until 50-years.

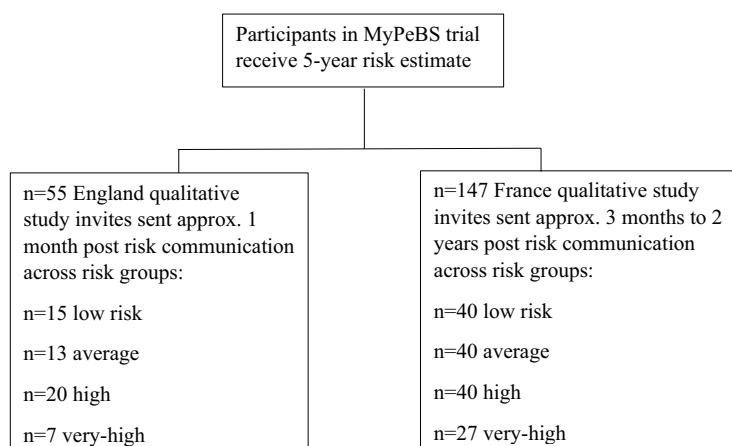


Figure 1. Participant recruitment procedures.

due to the longer duration of the trial being open there. In France, fewer invites were sent for very-high as only 27 very high-risk women were eligible to be invited for the present study during the recruitment period. In England, fewer women had received their risk during the recruitment period. Women in England were sent invitation letters and participant information sheets for the present study from the MyPeBS trial co-ordinator at the NHSBSP centre and in France, two regional screening centres. For each risk group, invitation letters were sent in batches of approximately 10–20. One follow-up letter was sent around two weeks later, where required. Those interested in participating or who had questions were asked to contact the researchers in the respective countries *via* email or telephone.

Interviews took place at a mutually convenient time with one of two members of the research team in England or France (both White ethnicity female postdoctorate-level researchers with qualitative experience and younger than breast screening age). Researchers were not known to participants. Interviews were conducted by videocall, telephone, or face-to-face (private university or hospital room). Upon ensuring any study questions were answered, participants provided informed consent prior to study procedures (written consent for in-person otherwise audio-recorded verbal consent using the written consent sheet separate to interview audio-files). Ethical approval was obtained for this study [NHS HRA London—Chelsea Research Ethics Committee 18/LO/2039, England and CPP SO-OM 4 23/09/2021, France]. The MyPeBS clinical study is conducted in accordance with the principles of ethics as stated in the last version of the Declaration of Helsinki, the relevant provisions of Good Clinical Practices defined by the International Conference on Harmonisation (ICH–E6 R2, December 2016), and according to the country specific laws and regulations.

Using a qualitative interview schedule, participants were asked about their experiences of participating in the MyPeBS risk-based arm. The schedule ([Appendix 1](#)) was informed by previous risk-stratified breast screening research (McWilliams et al., 2020, 2021) and by members of patient and public involvement (PPI) groups in UK ($n = 16$ Manchester) and patient organisations in France ($n = 15$ Paris). These comprised women of similar age to MyPeBS eligibility who informed the study design and draft interview

schedule which were subsequently revised before use. This was used flexibly during data collection.

Optional demographic information (age, education, occupation; ethnicity in England only) was collected from participants during interviews. After interviews, participants were debriefed verbally and provided with the qualitative researcher's contact information and country-specific breast health websites and helplines by paper or email. The written information also recommended they speak with their primary care provider if they have any health concerns. Data was collected until the core project team (LMcW, AR, DPF, SDM) agreed there was sufficient data across the four risk categories to answer the research aim within the time available to collect data (O'Reilly & Parker, 2013).

Data analysis

Interview audio-files were transcribed verbatim in the language the interview took place in by an accredited transcription company or researcher that conducted them. French transcriptions were translated into English (neural machine translation service DeepL Pro™). Transcriptions were checked by the respective interviewer and pseudonymised with participants allocated a pseudonym.

Thematic framework analysis was conducted to identify patterns in the data and interpret how these patterns account for participants' views on their experiences of MyPeBS risk-based screening (Spencer et al., 2014). Data were analysed using framework as it facilitates organisation of large qualitative datasets and collaboration between researchers involved in analysis (Gale et al., 2013). A comparative approach was then used to explain possible reasons underpinning differences between women's experiences of the MyPeBS risk-based arm between both countries. That is, whether contrasting patterns within the dataset identified during analysis could be accounted for by directly comparing the English and French accounts. Such approaches have previously elucidated differences in cancer symptom awareness according to educational status (Marcu et al., 2017) and between stakeholder groups about extending breast screening intervals for those at low breast cancer (Taylor et al., 2022). Data were stored and organised within NVivo Version 12 (QSR International) and exported to Excel (framework matrix charting). Employing a manifest level approach, two researchers (AR, RC) developed an initial coding frame using the French transcripts (as it was collected first). They frequently met to discuss codes and develop the framework with input from two senior investigators (DPF, SDM). This framework was then applied to the English data following initial inductive line-by-line coding of two transcripts by one researcher (LMcW) who discussed developing codes and how they mapped on to the pre-existing framework with the French researcher (AR). The coding framework was subsequently amended and French transcripts re-coded where necessary. Codes were organised into categories before creating framework matrices. Data extracts within the framework were charted by one researcher (LMcW) and used to generate overarching themes. Following this, an explicit comparison between participants in England and France was conducted with consideration taken for possible risk group variance. Analysis continued until the analysis team were satisfied that themes adequately represented the dataset.

Results

Overall, 52 women took part in an interview across the four risk groups. Of 55 women invited in England, 25 indicated initial interest; 23 took part in an interview. In France, of 147 women invited, 34 indicated initial interest and 29 took part in an interview. A higher proportion of French participants were younger, in employment and received tertiary education (Table 2). Interviews took place 1–3 months after receiving risk estimation in England (median 1-month) and 4–24 months (median 10-months) in France. Risk estimate group and time since risk estimation was self-reported in France during interviews. Interviews lasted 17–78 min (median 44-min, range 25–78 min in England, range 17–65 min in France).

Across the dataset, women were positive about the possibility of a risk-stratified breast cancer screening programme such as they received in MyPeBS. Regardless of risk group, women described it as especially beneficial rather than having a mammogram only and it could lead to better breast cancer outcomes. Despite differences in how women found out about and were recruited into MyPeBS, overall, women appreciated finding out their risk. This was largely attributed to perceiving receipt of low or average-risk estimates as a ‘positive’ result and for high or very-high-risk women, that additional screening would be available as part of MyPeBS.

Our comparative thematic analysis comparing patterns of experiences of women participating in the MyPeBS trial between the two healthcare settings produced two overarching themes: (1) The importance of supported risk communication and (2) Accessibility of risk management with two sub-themes each outlined in Table 3.

The findings are considerably influenced by MyPeBS trial procedure variance related to how participants described the risk estimate communication they received, some of which indicate divergence from intended trial procedures outlined earlier (Table 1). As such, key differences described by women are highlighted in the two italicised rows of Table 1. Quotes are presented with pseudonyms followed by ENG or FR to indicate

Table 2. Participant demographics, per country.

	Demographic	England (n = 23)	France (n = 29)
Age (years)	41–49	0	7 (24%)
	50–59	9 (39%)	9 (31%)
	≥60	14 (61%)	13 (45%)
Work status	Employed and/or self-employed	13 (57%)	19 (66%)
	Retired and self-employed	0	2 (3%)
	Retired	9 (39%)	8 (31%)
	Homemaker (working age)	1 (4%)	0
Education level	Tertiary education (≥undergraduate degree)	12 (52%)	19 (66%)
	Secondary education	11 (48%)	9 (31%)
	Primary/no education	0	1 (3%)
Risk group	Low	7	10
	Average	6	7
	High	6	8
	Very high	4	4
Ethnicity	White (British, European or other)	23	Unavailable
IMD decile	1–2 (most deprived)	1 (4%)	Unavailable
	3–4	5 (22%)	Unavailable
	5–6	8 (35%)	Unavailable
	7–8	4 (17%)	Unavailable
	9–10 (least deprived)	5 (22%)	Unavailable

Note. IMD = Index of Multiple Deprivation.

Table 3. Thematic structure.

Theme	Sub-theme
1. The importance of supported risk communication	1.1. Aiding acceptance of increased risk feedback 1.2. Lasting unanswered questions
2. Accessibility of risk management	2.1. Enabling personal control 2.2. Screening system differences

where the interview took place, respectively along with risk group and participant age at time of interview.

1. The importance of supported risk communication

All women reflected on how their risk estimate was communicated within MyPeBS and overall, reported feeling satisfied that they had found out their risk. However, women described the ways in which they received risk communication supported how they emotionally reacted to the information, whether positively or negatively. The accounts highlighted the short- and longer-term psychological reactions to receiving breast cancer risk information that appeared to subsequently impact acceptance of risk estimates and awareness of MyPeBS trial procedures such as how risk was estimated and related mammogram schedules.

1.1. Aiding acceptance of increased risk

In Manchester, all high and very-high-risk women reported having a telephone appointment with an HCP. They added that once this was arranged, they found out their risk in written format beforehand. These appointments were described as beneficial for two main reasons. First, women viewed the HCP as having specialist knowledge which facilitated their understanding of how their risk was calculated beyond the information provided in written materials or MyPeBS portal. Secondly, women said appointments provided an opportunity to receive advice about their risk commenting that the HCP showed good communication skills. This was particularly important to the women as they all recalled feeling surprised when they received higher risk estimates.

I felt more reassured after I'd spoken to him. Because obviously, I'd said to him, "oh, gosh, I'm shocked actually", that I'm in the high-risk. (Denise-ENG, High;54).

However, despite finding the HCP interaction useful, Deborah appeared undecided whether she believed her risk was as high as the provided estimate indicated, based on the conversation she had. Deborah reported having a detailed discussion about how the 'degree' of breast cancer family history affects risk in that although her relative had breast cancer, they were diagnosed at a late age and did not die from it.

...the breast cancer risk came out as high which I was very surprised about [...] he went through, sort of, family history and stuff and he said, well, actually, I don't think that's correct. So, whether that will be eventually changed or not, I don't know. (Deborah-ENG, High;66)

Separately, as risk sheets were provided in advance of HCP appointments, these same women also highlighted preferences in how risk estimates should be initially disclosed. Whilst some recalled this approach as useful to psychologically prepare for

the appointment with '*time to process the information*' (Kelly-ENG, Very-High;61), others found it difficult to manage the emotional impact of receiving high or very-high-risk estimates without simultaneous HCP support.

I think it would have been better, less of a shock, to have the two things the other way round, so to speak to a doctor and have any questions answered immediately. (Gillian-ENG, Very-High;58)

The women in French settings who received higher risk estimates at HCP appointments also generally described appreciating this risk communication format and having the opportunity to ask any questions. Unlike in England where women did not appear to know the HCP involved in MyPeBS, several higher risk French women reported having pre-existing relationships with the HCP that communicated their risk. This appeared related to how they were invited to the trial and was viewed as beneficial either based on previous positive healthcare experiences with that HCP, or due to knowing the HCP as they also work in breast screening. For example, Lucette described the faith she has in her breast screening radiologist which facilitated acceptance of her risk without need for emotional support.

So no, it's been very good, no, I have every confidence in him, he's really very very good (Lucette-FRA, High;71)

On the other hand, this variability in who recruited the women and communicated their risk in France seemed to affect the credibility of some these interactions. Despite risk being communicated verbally by a primary care doctor, they were unable to sufficiently explain why Madeleine received a very-high-risk estimate. Madeleine felt they did not have adequate breast cancer risk expertise and subsequently recalled this as an upsetting experience. Even nine months later when taking part in an interview, Madeleine questioned whether she believes the risk estimate.

It was a cold shower, almost a denial, saying "But it's not possible, they made a mistake". And I still have this idea in mind. (Madeleine-FRA, Very-High;66)

On two occasions, French women found out their high or very-high-risk estimate by letter or the MyPeBS portal without opportunity to speak with an HCP. Receiving her written risk sheet alone led Anne-Marie to misinterpret the risk estimate information as providing certainty that she '*was going to get cancer in the next five years*' (Anne-Marie-FRA, Very-High;64). She reported preferring to receive this information during an HCP appointment to facilitate understanding and without realising this is the routine MyPeBS risk communication procedure, went on to explain she had not recommended the trial to others.

1.2. Lasting unanswered questions

In England, women who received average or low-risk estimates recalled receiving this information *via* letter. Women in these categories explained that this format was appropriate as it told them 'good news' and believed they could discuss further if necessary. However, some did not recall or understand that their risk estimate related

to specific mammogram schedules during MyPeBS as separate to the national screening programme.

I can't remember now, is it normal five years between breast screening, I think it is isn't it? Or it was. But I wasn't sure if they were reducing it to four years, or in fact, everybody was going for four-year screening, or, you know? It didn't really make it clear what that meant... (Cheryl-ENG, Low;65)

Meanwhile in France, the low and average-risk women reported varied risk communication experiences. Where women received risk estimates by letter or email, they mostly echoed the positive views of English women and in one account, Armelle felt her face-to-face appointment was an unnecessary journey due to receiving an average-risk estimate.

I must admit, I was more in the spirit of "Oh dear, I came specifically for something that wasn't a big deal...". (Armelle-FRA, Average;41)

However, on three occasions low or average-risk women received their risk estimate *via* the MyPeBS web portal, at a radiology reception or in passing during an HCP professional appointment for their child. They received no other communication from their recruiting HCP. These women indicated being unsure of their mammogram schedule or having unanswered questions about their risk. Having accessed the MyPeBS portal at home without any HCP interaction, Caroline reported feeling '*forgotten*', wanted to know how her risk was calculated and how it might change.

And why... this risk, why this risk and why we say there is a risk, in fact. The cause of it. That's it. If it's genetic or if it's because I smoke... (Caroline-FRA, Low;49)

2. Accessibility of risk management

Access to HCPs during MyPeBS and the healthcare systems within England and France seemed to underpin how women discussed the ways that breast cancer risk can be managed. This influenced how they reported being able to manage their risk and how they viewed aspects of MyPeBS related to mammogram schedules.

2.1. Enabling personal control

Prevention offers that enable women to personally manage their risk were different between both countries. Women in England who received high or very-high-risk estimates reported they more readily discussed weight loss or maintaining pre-existing protective health behaviours as a method to mitigate their risk. This appeared partly underpinned by the HCP consultation, as from the women's accounts, it was more personalised for each woman beyond the standardised health behaviour risk management information within the risk sheets. For example, Lisa cites the discussion of weight as a risk factor with the HCP as a positive motivator to engage in health behaviour change.

And then you start thinking, oh, maybe I need to lose... I'll lose a bit of weight then and it makes you start thinking about lifestyle changes after you've spoken to him, which, in

your head, makes you feel even better about it. And you know the lifestyle changes to make. (Lisa-ENG, high;55)

In comparison, the higher risk French women who discussed their risk with HCPs did not recall this being a focus of risk communication appointments. For example, Emmanuelle did not remember discussing this at all with her HCP and cites non-breast cancer risk reasons for engaging in health behaviours.

I don't recall that he told me to pay attention, but I do a bit of sport. I'm careful with my diet. I'm cutting back on certain things, because as we get older, we're afraid of cholesterol, and all that with the menopause, so I'm careful. (Emmanuelle-FRA, High;52)

For both women who did not have an HCP interaction about being at higher risk, they expressed a greater level of vigilance about monitoring breast cancer symptoms. They subsequently sought information about this independently as a way to manage their perceived level of threat.

I thought about it, still! And that's when I said to myself, "I have to learn to self-palpate." And so I went to the [hospital] website and I thought, well, there's a high risk in the next 4-5 years. So yes, I want to know what's going on... (Corinne-FRA, High;57)

Women in England were potentially offered breast cancer risk-reducing medication as a form of risk management. This option appeared useful particularly for those women who described themselves as already practicing positive health behaviours. However, women described delays to feeling in control of their risk by having to wait for their primary care doctor to prescribe the medication following the initial MyPeBS HCP appointment.

I live a healthy lifestyle. Absolutely. So I'm not...that's not going to be enhanced any further, it's the DNA bit that I need to sort of get to grips with and see if we can lower the risk a bit more. And these tablets lower the risk considerably so that's great. [...] I'm just eager to...I'm just waiting for the GP [general practitioner]...to have a consultation with the GP. (Heather-ENG, Very-High;51)

2.2. Screening system differences

With differences in mammogram schedules according to risk group, women's reported acceptability of this primarily related to the existing screening programmes and women's health services they can access. Many French women cited their gynaecologists' views on the importance of frequent screening and ability to prescribe mammograms. This appeared to influence attendance at mammograms before routine invites (50-years) and in some cases, more frequently than the 2-yearly programme invitation. Given that all high and very-high-risk women viewed their annual mammogram screening schedule positively, this contrast was most apparent between low-risk women. For French low-risk women over age 50, their schedule was being extended by two years as opposed to one during the trial in England. This was generally viewed as a long period "*where things can go awry*" (Constance-FRA, Low;49). In addition, French women appeared more aware of breast density as a factor that can reduce mammogram effectiveness in detecting breast changes where some

reported receiving ultrasound imaging for this. These factors seemed to underpin Annick's lack of enthusiasm surrounding the 4-year mammogram schedule given that she has an annual gynaecology appointment which can 'override' the national breast screening programme and also previously received ultrasound examinations for dense breasts.

I prefer to have it. But then, I mean, I can ask my gynaecologist to do it every year. (Annick-FRA, Low;62)

By contrast, this greater level of active monitoring of breast health in the French healthcare system also contributed to an acceptance of the longer interval as is shown in Véronique's case highlighting that 'backdoor' access to breast screening is possible.

Yes, frankly, it suits me, yes because already anyway, I have to go for ultrasound usually for my cysts, they puncture me about every 18 months, so... I'm monitored, you know? It's not like I'm not monitored. (Véronique-FRA,Low;50)

On the other hand, low-risk women in England appeared less aware of the usual screening NHSBSP interval and more readily mentioned altruistic reasons linked to resource use as a factor in accepting the 4-year interval, perhaps due to the healthcare system being fully nationalised.

And the fact that I'm low-risk, so if they said to me, right, you're not having any more mammograms, and I know that I'm lowest risk, then I'm quite happy with that because then it frees up NHS money for somebody who's younger that, perhaps, does need it. (Tracey-ENG, Low;62)

However, Angela discussed feeling apprehensive about having a longer screening schedule given that public health messages highlight that early diagnosis of cancer is important. She explained that assuming the 3-yearly interval was based on research evidence, she therefore wants to know the MyPeBS trial outcome before deciding whether a 4-year mammogram interval for low-risk women would be safe.

I think it's got to be very...the study has to come up with some really good evidence bases behind it to change the mindset of us all 'cause at some point somebody said, it's clinically right to do it at three years. (Angela-ENG, Low;53)

Discussion

This is the first study to compare women's experiences of receiving risk-stratified breast screening within the context of population-based screening between differently organised healthcare settings using qualitative methods. Overall, women across both settings appreciated the opportunity to find out their breast cancer risk and were optimistic that risk-stratified screening may eventually replace existing breast screening programmes. The comparison findings highlight how, even within the context of a trial, differences in the way healthcare systems and risk-stratified screening are locally organised influence the psychological impact of women receiving such an approach to breast screening. The standardisation of risk communication appeared to affect the degree of emotional and cognitive impact of receiving breast cancer risk estimates.

For high and very-high-risk women, having a dedicated appointment to discuss their risk with an HCP perceived as having specialist knowledge seemed particularly important to facilitate risk estimate acceptance. However, this was not always available for the French women resulting in potential longer-term uncertainty about their risk. Additionally, differences in the way breast screening programmes are organised in each country impacted how women viewed risk-stratified screening. This especially underpinned views of those identified at low-risk and who received a mammogram schedule of 4-years. French women reported being able to readily access mammograms *via* their gynaecologist in primary care (a service which does not exist in England) and may be less likely to adhere to the longer MyPeBS screening interval.

Relation to previous research

Follow-up support from appropriately trained HCPs has previously been identified as important for women who received higher than average breast cancer risk estimates linked to organised breast screening (McWilliams et al., 2023; Woof et al., 2023). This has also been recommended in a systematic review of qualitative studies, which suggested that supported risk communication is especially important for women who may perceive their risk as lower or higher than the clinical estimates provided (Woof et al., 2022). Our findings extend this by also highlighting the variance in preferences for the initial disclosure of risk estimates for high-risk groups prior to follow-up discussions, where some do prefer to know their risk in advance. This appears at odds with the views of HCPs involved in breast screening when considering risk communication to women where concerns were raised about disclosure of risk without immediate HCP support (French et al., 2022; Hawkins et al., 2022). On the other hand, it did not appear to be an acceptability issue for the low and average-risk women who received their risk information *via* letter. This aligns with previous findings when considering how different levels of breast cancer risk should be communicated (Gorman et al., 2022).

Limited research has explored geographical and related healthcare system differences in the context of risk-stratified breast screening. Previous quantitative research has shown little differences on attitudes towards risk-based breast screening between women living in four Canadian provinces, where local organisation of breast screening may vary (Mbuya Bienge et al., 2021). However, the country employs a nationally-funded programme therefore, differences are likely to be limited and women hypothetically considered risk-stratified screening unlike those in the present study. The only similar qualitative study we are aware of conducted focus groups with women from three European countries (Rainey et al., 2019). Although findings indicated differences in how women thought about the emotional and behavioural impact of risk-stratified breast screening programmes between the countries (UK, Sweden and Netherlands), only the UK sample had received risk estimate information (Evans et al., 2016). Swedish and Dutch participants only considered this hypothetically. Therefore, it is difficult to ascertain whether any differences were healthcare context related.

Some higher risk women interviewed from the Manchester site in England reported that the HCP they had an appointment with explained their risk might not be as high as estimated in MyPeBS. It could be that this occurred because the HCP was

situated within a family history clinic which estimate breast cancer risk using 10-year risk (NICE, 2017). In this context, the threshold for high-risk (and used to offer prevention/risk-reducing options) is 8% and equivalent to a 4% 5-year risk. This is much higher than the 1.67% threshold for high-risk used within MyPeBS. These estimates, depending on the age of a woman, may mean communicating risk differently about the potential longer-term consequences. On the other hand, a general practice HCP in France was unable to adequately explain high-risk results in one instance resulting in frustration and uncertainty for the woman. Reduced confidence in supporting women in risk-stratified breast screening within primary care has previously been identified as a factor affecting the readiness of primary care's involvement should a risk-stratified breast screening programme be implemented (Bellhouse et al., 2021). Nevertheless, some higher risk women in France found it comforting that an HCP they had a pre-existing relationship with communicated their breast cancer risk.

Across both settings, higher risk women were positive about receiving additional breast screening in MyPeBS which has been previously highlighted in risk-stratified breast screening research (McWilliams et al., 2023). However, French participants who received a low-risk estimate appeared less accepting of having a mammogram in 4-years rather than the standard 2-yearly interval. The French healthcare system includes annual gynaecology appointments where mammograms may be prescribed outside of the organised screening programme and younger than the age 50 first routine invite. Indeed, women cited their gynaecologist as influencing their views about screening frequency, which was both reassuring for some low-risk women as a back-up option during a longer screening interval and in contrast, underpinned concerns having had long-term frequent access. A small German focus group study, including gynaecologists, explored views around recommending women a mammogram depending on hypothetical risk factors and highlighted concerns about communicating risk estimates and advising low-risk women to have less frequent screening (Fürst et al., 2018). However, there was no explicit discussion on reduced screening frequency for low-risk women as the two illustrative cases used to guide discussions focused on average and high-risk only. Given that low-risk women in England only had a year difference within the MyPeBS trial (compared to the NHSBSP), this may also explain some of this difference in views. Previous research with women who received low 10-year risk estimates demonstrated fairly positive views about the prospect of receiving less frequent screening to free up resources within the national healthcare system (McWilliams et al., 2021). Similarly, less frequent screening in this risk group seems broadly acceptable to multiple stakeholder groups (Taylor et al., 2022).

Strengths and weaknesses

To the authors' knowledge, this is the first study to explicitly compare experiences of risk-based breast screening with women between two different healthcare systems, who all received risk estimates and associated screening schedules. The study design and interview schedule questions were informed by substantial PPI input in both countries. Although the same topics were covered in the English and French schedules, nuances may have been lost during translation of French transcripts into English. The French researcher therefore reviewed all translations to ensure data quality.

At the time the French qualitative data was collected, MyPeBS risk-based arm participants were more likely to have experienced delays in risk communication due to COVID-19 disrupting DNA analysis and may have influenced recall. COVID-19 may have also impacted on HCP availability and formats available to deliver risk communication which might explain the discrepancies between the MyPeBS protocol and women's accounts. The French participants were interviewed up to two years following initial receipt of risk estimates and could explain why some French interviews were shorter in duration. It was not possible to collect ethnicity data within the French sample and all participants in England self-reported White ethnicity. Women with different ethnicities may have recounted experiences of MyPeBS differently. Although it was not possible to sample MyPeBS participants based on socioeconomic characteristics in France, they reported higher levels of education compared to the English participants and, the sample was younger. This could provide an alternative explanation for our findings however this did not seem to underpin differences in women's experiences during analysis. Due to screening-age eligibility differences in each country, it was not possible to explore the experiences of 40–49-year old women who received average or low-risk results within both countries in the present study. However there did not seem to be any pattern in the analysis related to age from the accounts of low and average-risk participants. The researchers did not have information on contributing risk factors for each woman's risk for example, weight. Therefore, it could be that there were differences in health behaviours between the French and English women interviewed which may have affected whether these were discussed during HCP appointments. Lastly, the women interviewed in England were recruited from one site; the other two recruiting centres may not have followed the same standardised procedures or have the same level of expertise involved in risk communication.

Implications for practice

A risk-stratified breast screening programme appears acceptable however, components of such a programme are not. For instance, access to HCPs who have breast cancer risk expertise for higher risk women is important to minimise psychological harms of communicating risk and ensure risk-management offers are available. Nevertheless, despite the same HCP discussing risk in England (Manchester site) with women who received high or very-high-risk estimates, findings highlight the need to consider individual communication preferences for the initial disclosure of estimates. It should be possible to identify women's preferences in advance and multiple formats of risk communication should be offered. It may not be necessary to communicate risk estimates for low or average-risk women at an appointment however, any subsequent mammogram schedule alterations should be made clear with mechanisms in place to ensure women are aware. It appears worthwhile to provide personalised information and associated interventions about how breast cancer risk may be managed *via* health behaviours although this should be communicated consistently. However, if women engage in health behaviours for other reasons, it should be highlighted that such behaviours have a positive influence on other aspects of women's health, including breast cancer risk. Similarly, if risk-reducing medication is offered as part of breast cancer risk management, care pathways should be aligned to minimise delays to receiving prescriptions.

Implications for research

Further comparative qualitative studies across countries should be conducted in future implementation studies of complex interventions, given that the pre-existing healthcare context is likely to influence both uptake and effectiveness. Linked to risk-stratified breast screening, countries could be selected based on diversity in how healthcare systems are organised for example, where there are no routine organised breast screening programmes or services for women who have very-high-risk of breast cancer (e.g. due to genetics where women have high penetrance genetic mutations known to substantially increase risk). This would provide evidence of differences (or lack of differences) related to risk-stratified breast screening across a range of healthcare contexts. In turn, such evidence could then be used to develop guidance on how best to implement this approach to breast screening depending on the setting. Exploring the views of gynaecologists in healthcare settings such as France, who may be involved in breast screening referrals, would provide a perspective on their acceptability of risk-stratified breast screening. This is particularly important for any de-implementation of screening for those at low-risk of breast cancer.

Conclusions

Comparing how risk-stratified breast screening has been received by women in two different countries and health organisation systems highlighted the importance of specialist HCPs in communicating high-risk estimates. Differences in how healthcare systems are organised contribute to acceptability of altered mammogram schedules. These differences influence the psychological impact of a risk-based approach to breast screening. Should a risk-stratified breast screening approach be implemented internationally, it is vital that standardised procedures and support from HCPs are in place, particularly for women at higher risk.

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Ethical approval

Ethical approval was obtained for this study [NHS HRA London—Chelsea Research Ethics Committee 18/LO/2039, England and CPP SO-OM 4 23/09/2021, France]. The MyPeBS clinical study is conducted in accordance with the principles of ethics as stated in the last version of

the Declaration of Helsinki, the relevant provisions of Good Clinical Practices defined by the International Conference on Harmonisation (ICH-E6 R2, December 2016), and according to the country specific laws and regulations.

Authors contributions

The present research was part of the MyPeBS trial, work package 5 (WP5). MyPeBS was conceived by SD and organised by Unicancer as coordinator of the project (CVS) and sponsor of the trial. Trial oversight is provided by the Clinical Trial Steering Committee (CTSC) which includes authors on this manuscript and those listed in the 'MyPeBS Consortium' within the acknowledgements. Conceptualisation: DPF, SdM with input from DK, SD, CB, DGE; Funding acquisition: SD, CVS, DPF, SdM, CB, DGE; Methodology: DPF, SdM, DK, RH, AR; Supervision: DPF, SdM; Project administration: LMcW, AR, RH, RC, HD, AB, MLF, DGE, CB, CVS, SD, DPF, SdM; Resources: DGE, AB, MLF, HD Investigation: LMcW, AR; Data Curation: LMcW, AR, RC; Validation: LMcW, AR, RC; Formal analysis: LMcW, AR, RC, with input from DPF, SdM; Visualization: LMcW, AR, RC, with input from DPF, SdM; Writing – Original Draft: LMcW based on previous documents prepared by RC, RH, DPF, SdM, AR; Writing – Review & Editing: LMcW, AR, RC, RH, DK, DPF, SdM, SD, CVS, DGE, AB, HD, CB, MLF. The corresponding author attests that all listed authors meet authorship criteria and have approved the manuscript.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, LMcW, upon reasonable request. The data are not publicly available as participants consented to other researchers contacting the study team to access anonymised data.

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Appendix 1: Interview schedule topics

1. Prior to MyPeBS, have you already had experience of breast cancer screening?

- **If yes:** how it went
- How heard about it
- Expectations
- Experiences of results
- **If no:** why (if person meets screening age criteria)

2. Can you take me through how you were invited to participate in MyPeBS?

- Opportunity to question
- Views on documents

3. Can you talk me through your visit to the clinic for the MyPeBS trial?

- Views/understanding information
- Opportunity to question
- Completing questionnaires
- Views/understanding saliva/genetic test/
- (**previous mammogram**): mammogram process, compared to previous

4. Can you talk me through how you felt after visiting the clinic?**5. How were the results communicated to you?**

- Recall of risk category/mammogram schedule
- Communication format/explanation
- Feelings about/trust towards risk
- Information needs/seeking
- Advantages/disadvantages of knowing risk

6. Were you clear what to do after you received your results?

- Post-risk estimation processes
- Follow-up consultation
- Mammogram schedule
- Behaviour change

7. Overall, how did you find the screening process offered in MyPeBS?

- Trial processes
- Comparison to previous screening
- Trial improvement/acceptability