Women’s perceptions of personalised risk-based breast cancer screening and prevention: an international focus group study

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Dear Dr. Watson,

We would like to re-submit a revised version of our manuscript entitled ‘Women’s perceptions of personalised risk-based breast cancer screening and prevention: an international focus group study’ to ‘Psycho-oncology’.

We have addressed Reviewer 2’s comment and revised the manuscript accordingly.

We hope that you will find our revised manuscript of interest to your readers. We look forward to hearing from you in due course.

Yours sincerely,

On behalf of all authors,

Linda Rainey
**Reviewers’ comments on manuscript PON-18-0795**

**Reviewer 2**

Thanks so much for sending the author’s response where they explained that screening based solely on age is the practice in those countries. I was not aware of that and therefore found it difficult to follow. I would only recommend that they put a sentence in the Introduction to highlight this difference in national screening programs so that it is not confusing for US audiences and those who are familiar with breast cancer screening practices in the US. There are so many breast cancer guidelines in the US that I think this would just give the manuscript more credibility in the US. Otherwise, I had no other issues with the manuscript.

**Response:**

We thank Reviewer 2 for their positive appraisal of the manuscript. We have added some information to the background section of the manuscript to clarify current screening practice in the Netherlands, the United Kingdom, and Sweden.

We have made the following changes to the manuscript:

**Background, page 3**

Therefore, this study aims to evaluate the adoption of risk-based breast cancer screening and prevention by exploring perceptions of women who participated in the well-established national screening programmes of the Netherlands (NL), the United Kingdom (UK), and Sweden (SE). Screening eligibility in these countries is solely based on age, without access to additional risk information or screening modalities. Therefore, risk-based screening would be a considerable departure from current age-based screening practices in these three countries.
Women's perceptions of personalised risk-based breast cancer screening and prevention: an international focus group study

Running title. Women’s perceptions of risk-based screening and prevention

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ABSTRACT

Objective: Increased knowledge of breast cancer risk factors enables a shift from one-size-fits-all breast cancer screening to a risk-based approach, tailoring screening policy to a woman’s individual risk. New opportunities for prevention will arise. However, before this novel screening and prevention programme is introduced, its acceptability from a woman’s perspective needs to be explored.

Methods: Women eligible for breast cancer screening in the Netherlands, United Kingdom, and Sweden, were invited to take part in focus groups. A total of 143 women participated. Data were transcribed verbatim and analysed using thematic analysis.

Results: Analysis identified five themes across the three countries. The first theme ‘impact of knowledge’ describes women’s concern of not being able to unlearn their risk, perceiving it as either a motivator for change or a burden which may lead to stigma. The second theme ‘belief in science’ explains women’s need to trust the science behind the risk assessment and subsequent care pathways. Theme three ‘emotional impact’ explores, e.g. women’s perceived anxiety and (false) reassurance which may result from knowing their risk. Theme four ‘decision-making’ highlights cultural differences in shared versus individual decision-making. Theme five ‘attitude to medication’ explores the controversial topic of offering preventative medication for breast cancer risk reduction.

Conclusions: Acceptability of risk-based screening and prevention is mixed. Women’s perceptions are informed by a lack of knowledge, cultural norms and common emotional concerns, which highlights the importance of tailored educational materials and risk counselling to aid either shared or individual informed decision-making.

Key words: breast cancer, oncology, prevention, risk prediction, risk stratification, screening, attitudes, acceptability
**BACKGROUND**

Population-based breast cancer screening programmes, adhering to a one-size-fits-all approach based on age, have successfully led to early detection and subsequent breast cancer mortality reduction.\(^1\) However, screening may become more effective if tailored to women’s differing levels of breast cancer risk, potentially optimising the benefit-harm ratio of screening.\(^2\) Breast cancer risk prediction models are becoming more accurate by adding, e.g. breast density and polygenic risk score to classic risk factors.\(^3\) Risk prediction also offers new opportunities for breast cancer prevention, targeting women who would benefit most from reducing their risk through lifestyle changes or risk-reducing medication. Successful implementation of risk-based screening and prevention relies on women’s participation. However, eligible women’s perceptions of adopting this novel programme have never been explored.

A risk-based screening and prevention programme is inherently more complex than current age-based screening programmes. Women need to reflect on participation at different stages (Figure 1). Although Figure 1 is an illustration which does not necessarily follow current pathways of care, it shows that women need to decide whether they (1) want to know their risk, (2) are willing to change their screening strategy based on risk, and (3) are prepared to participate in preventative practices. Women’s interest in knowing their breast cancer risk is high.\(^4\) However, knowledge of their risk did not lead to any consistent changes in screening or preventative behaviours.\(^5\) Additionally, although women generally appear in favour of increased screening for high-risk women, lowering screening intensity for low-risk women is more contested.\(^6\)\(^7\) Women are concerned about the accuracy of breast cancer risk estimates with some believing that risk-based screening is mainly motivated by a desire to save money.\(^8\) Their perceptions of prevention also seem mixed.\(^5\) However, risk-reducing medication has mostly been discussed with high-risk women who tend to be monitored outside of national screening programmes, which potentially limits the generalizability of these results to the screening population.

Risk-based screening may bring about considerable benefits to healthcare policy by directing screening and preventative resources to women who are most in need.\(^9\) However, there is a lack of knowledge on the acceptability of an integrated risk-based breast cancer screening and prevention programme from the perspective of European women who would be eligible to participate, i.e. women at population-level risk who meet current age criteria for screening. Therefore, this study aims to evaluate the adoption of risk-based breast cancer screening and prevention by exploring perceptions of women who participated in the well-established national screening programmes of the Netherlands (NL), the United Kingdom (UK), and Sweden (SE). Screening eligibility in these countries is solely based on age, without access to additional risk information or screening modalities. Therefore, risk-based screening would be a considerable departure from current age-based screening practices in these three countries.

**METHODS**

**Design**

Focus groups (FGs) following a semi-structured interview guide were performed to explore women’s perceptions of adopting risk-based breast cancer screening and prevention in NL, UK, and SE. Ethics approval
was acquired from the regional ethics committee CMO Arnhem-Nijmegen (2015-1773) in NL, London Central NHS Research Ethics Committee (16/LO/0925) in UK, and the Regional Ethical Review Board at the Karolinska Institutet Stockholm (2017/375-31/2) in SE. Written (NL, UK) or verbal (SE) informed consent was obtained from all participants prior to the start of the FGs. The participant selection process and procedure are described in Supplement 1.

Data analysis
Data were thematically analysed per country, independently by pairs of two researchers (LR & DvdW, LR & MB, YW & AJ) using an inductive approach. Six stages were adhered to during analysis, i.e. familiarisation with the data, coding, developing themes, reviewing themes, defining and naming themes, and final analysis. Consensus was reached through discussion when discrepancies arose. Descriptive analyses were performed with IBM SPSS version 22 (Armonk, NY: IBM Corp).

RESULTS
Participants
From the 1650 women invited to take part, 143 women participated across the three countries (8.7%). Participant characteristics are outlined in Supplement 2. Nine FGs were conducted in NL (54 participants), five in SE (38 participants), and six in UK (51 participants). Group sizes ranged from 5 to 10 participants. Swedish participants were considerably older than Dutch and British participants: median ages 67.0, 57.5, and 56.0, respectively. British women had fewer years of education (median: 15.0) than Dutch (17.0) and Swedish women (21.0). More British women had a first-degree family history of breast cancer (47.1%), than Dutch (16.7%) and Swedish women (21.1%). British women showed a marked discrepancy between their perceived breast cancer risk and their actual risk as relayed by the PROCAS study team. Most British participants had a high risk of developing breast cancer (70.6%), however only 23.5% of participants perceived their risk as high. No participants had a below average breast cancer risk.

Thematic analysis
Dutch and Swedish women were generally positive about receiving breast cancer risk feedback. None of the British women expressed regret about finding out their risk. Women in all three countries emphasised, however, that participation should be optional, offering screening according to current country guidelines to women who do not want to adopt this approach. Figure 2 displays the themes representing perceptions of the adoption of risk-based screening and prevention of Dutch, Swedish, and British women. Supplement 3 provides a breakdown of the themes per country with relevant quotes. In general, there was extensive overlap in perceptions of women across the three countries. Therefore, we were able to identify five superordinate themes: (1) impact of knowledge, (2) belief in science, (3) emotional impact, (4) decision-making, and (5) attitude to medication. Although the overarching themes showed similarities, subthemes sometimes differed per country. Both will be discussed below using FG data extracts.
Theme 1. Impact of knowledge (NL, SE, UK)
The superordinate theme ‘impact of knowledge’ deals with women’s perception that once they know their breast cancer risk, they feel the need to act upon that information. A moderate-high risk result in particular elicited either a beneficial response, i.e. the subthemes perceived control, proactive attitude, motivation, and empowerment, or was perceived as a burden, i.e. avoidance, guilt, and fatalistic view. As a Swedish participant put it: “A high risk result almost feels like it’s close to a diagnosis”. British participants, who had chosen to have their breast cancer risk relayed, generally perceived knowledge of risk as an opportunity: “Perhaps being more aware, and doing something proactively about your high risk, makes you feel more in control, and so you’re less stressed”. Although women in all three countries generally welcomed preventative options to manage their risk, they also mentioned the potential for stigma and guilt, e.g. “It puts a lot of responsibility for health on women and not everyone is equally capable of maintaining a healthy lifestyle; financially or intellectually. It can’t become a woman’s own fault if she develops breast cancer” (Dutch participant).

Theme 2. Belief in science (NL, SE, UK)
The superordinate theme ‘belief in science’ illustrates women’s concerns regarding the scientific basis of the risk prediction model and the effectiveness of risk-reducing medication and lifestyle changes. Dutch women were particularly concerned about extending the screening interval for women at below average risk, wondering whether it is financially motivated rather than evidence-based. Swedish women displayed a greater trust in the scientific evidence behind any new screening policy, e.g. “Yes, personalised screening intervals are acceptable provided you know how they are developed and what the criteria are: why some women are asked to go for a screening more often than others”. Dutch women also described the role of perceived breast cancer risk in the acceptability of a personalised screening plan. They believe that if their relayed risk does not correspond to their perceived risk, they will be less likely to accept the accompanying screening and prevention advice. Both British and Dutch women were sceptical about the scientific link between lifestyle changes and breast cancer risk. The acceptability of risk-reducing medication depended on the magnitude of the effect, with women balancing the potential for side-effects and risk reduction. Moreover, women would like to monitor the effect of preventative measures to determine potential reclassification of risk: “So, I think, if you can really see, find out that you have made a difference through prevention, then you could potentially screen less frequently. Particularly if you have changed your risk” (Swedish participant).

Theme 3. Emotional impact (NL, UK)
The superordinate theme ‘Emotional impact’ describes how women think risk-based screening and prevention will affect their psychological wellbeing, with the subthemes: awareness, anxiety, (false) reassurance, and impact on quality of life. These themes were more prevalent in Dutch and British women’s perceptions, whereas Swedish women phrased their perceptions in more rational terms, with fewer references to emotional states, e.g. “But, if they determine you have a higher risk of developing breast cancer, surely, that doesn’t mean you’ll definitely get it. Because there are other contributing factors too”. The main difference between British and Dutch women’s perceptions concerned the level of reassurance. The majority of Dutch women did
not perceive the hypothetical message of below average-average risk to be particularly reassuring: “It remains a risk and it is never no risk; even if you tell me I have a 95% chance of not developing breast cancer, I might still be in the 5%; it doesn’t provide real reassurance”. However, British women who actually received their risk, indicated that receiving a letter stating that you have an average risk of developing breast cancer was very reassuring, filing the letter and forgetting all about it. Dutch women worried that they would become preoccupied: “I don’t want to know my risk, because it will make me worry about every little ache or change in my breast”. Some British women at high risk described needing professional help: “It has massive impact, because I’m still undecided with the treatments I’ve been offered, what to do. So I’m seeing a clinical psychologist”. Women from both counties worried about the impact that risk-reducing medication would have on their current quality of life due to potential side-effects.

Theme 4. Decision-making (SE, UK)
‘Decision-making’ is a superordinate theme that received specific attention during the British and Swedish FGs. Swedish women emphasised individual decision-making, considering the process a personal responsibility, balancing anecdotal knowledge of breast cancer and preventative options, and the impact that the risk assessment and subsequent recommendations may have on the quality of life of others and yourself: “I don’t think I’d consult anyone about the actual decision, because the decision is for me to make. It’s my responsibility”. British women on the other hand emphasised a shared decision-making process with family, friends and professionals, taking into account responsibility to oneself and family, and potential life-events that could influence decision-making, e.g. divorce, illness. Professional endorsement appeared particularly elementary in the adoption of risk-reducing medication, with British women who were at first adverse to the idea of medication changing their mind due to professional advice: “Well, for me it was a no-brainer because, I mean, I don’t like the idea of taking tablets constantly, I just don’t like it. But the doctor said it was a no-brainer for me personally, you know, because of the advantages”. British women were also influenced more by media coverage about breast cancer, speaking of the perceived ubiquitous nature of the disease: “Not through being told, but I think because it’s constantly in the media, breast cancer, I don’t think even if you’re average you feel safe”.

Theme 5. Attitude to medicine (NL, UK)
The superordinate theme ‘attitude to medicine’ reflects the apparent controversial nature of risk-reducing medication for breast cancer which was mostly addressed by British and Dutch women. Swedish women tended to have a more pragmatic approach to medication, stating that they preferred lifestyle changes but that they would be willing to try medication to determine the level of side-effects. Most Dutch women, however, expressed an aversion to medication, perceiving it to be a radical and unnecessary daily hassle when dealing with a risk instead of a diagnosis. Anecdotal knowledge of particularly tamoxifen as a breast cancer drug induced worry and anxiety. Some Dutch women argued that preventative medication is normalised, referring to e.g. cardiovascular medication, reasoning that medication is a convenient, easy solution to lower your risk. A considerable number of British women who participated in the FGs had been advised to take risk-reducing
medication. Although the British women’s attitudes to medicine were very similar to Dutch women’s, they generally opted to take it, with one participant stating: “Most of us think it’s worth the risk”.

**DISCUSSION**

The present study provides an overview of British, Dutch, and Swedish women’s perceptions of adopting risk-based breast cancer screening and prevention. To our knowledge, this is the first study of its kind which has been performed in a population-based European screening setting. It showed that, overall, women appear in favour of finding out their breast cancer risk, although the acceptability of subsequent screening and preventative strategies is mixed. Importantly, women emphasise that strategies should be evidence-based and participation voluntary. There is considerable overlap in the perceptions of women across the three countries.

This suggests that the variation in hypothetical (NL, SE) versus ‘actual’ (GB) risk scenarios did not hinder women’s ability to participate in the discussion. However, Swedish women experienced more difficulty than Dutch women relating to both the concepts of risk and hypothetical risk scenarios, requiring more clarification and encouragement to start a discussion.

The superordinate themes associated with women’s perceptions of risk-based screening and prevention across the three countries are rooted in behavioural theory. Women’s perceptions seem to be best reflected by the ‘health belief model’ and ‘self-determination theory’. These two theoretical frameworks assume a cost-benefit analysis of particular health behaviours, whereby a person takes into account perceived severity and susceptibility to disease, psychological factors, social context, autonomy, and personal competence. The relevance of these two frameworks to the adoption of this novel screening and prevention paradigm by women has previously been demonstrated. However, the way in which the underlying constructs of the theoretical frameworks are represented in women’s perceptions sometimes differs across the three countries, potentially pointing to culture-specific attitudes or customs.

Cross-cultural concordance was seen in the themes ‘impact of knowledge’ and ‘belief in science’. Women from all three countries deliberated that breast cancer risk information may not be without consequence, enticing activity or potential emotional turbulence. The importance of perceived competence in health behaviour decision-making is highlighted. Dutch and Swedish women reported a great need to understand the scientific basis of the risk prediction model and subsequent screening and prevention recommendations. They appear to perceive a greater sense of control when more knowledgeable. However, research shows that risk information is difficult to understand. A comprehensive information leaflet which meets all of women’s perceived information needs may therefore hinder informed decision-making. This is in accordance with the attitude of British women in this study who only received a basic level of information at every stage of the programme, but did not report a perceived lack of information or knowledge. The theme ‘belief in science’ also highlighted some women’s scepticism about the accuracy of risk estimates and the rationale behind risk-based screening, suspecting a financial motive. These concerns were previously mentioned by US women who professed a reluctance to change current screening habits, fearing missed breast cancers with a changed screening interval.
The emotional impact of risk assessment was hypothesised by Dutch women and reported by British women about a year after receiving risk feedback. Some British women who were classified as moderate-high risk reported a decrease in psychological wellbeing with some women seeking professional help. These findings are tentatively confirmed by a survey study among PROCAS participants who received breast cancer risk feedback and PROCAS participants who were awaiting their risk feedback. Women who had received their risk feedback reported lower levels of anxiety, but higher levels of cancer worry than women awaiting their risk feedback. Additionally, women with a moderate-high risk of developing breast cancer reported higher anxiety than women with a below average risk. However, overall anxiety levels were still relatively low. This is in line with previous research showing no significant long-term impact of genetic risk estimation on psychological outcomes.

A pronounced difference between Swedish and British women’s perceptions was visible in the decision-making process precipitating participation. Swedish participants favoured a more autonomous process than British participants, who emphasised a shared approach. Previous studies have found that medical decision-making is affected by gender, age, and education, with younger, highly qualified women being most likely to desire higher levels of autonomy. This partially corresponds with our findings since Swedish women were, on average, more educated than British women. However, Swedish women were also considerably older on average than British women, contradicting previous findings. Moreover, a qualitative study of Swedish people’s values regarding participation in colorectal cancer screening showed a similar need for autonomy, pointing to a potential societal attitude.

The superordinate theme ‘attitude to medicine’ shows a general reluctance of women to try risk-reducing medication. Particularly noteworthy is the reliance of British women on professional endorsement in the decision-making process. Although our British participants were generally not in favour of medication, professional endorsement changed their views almost unanimously. This is in concordance with previous research suggesting that people look to physicians for decisions on medication use, because of their perceived superior knowledge. It is unclear whether the unfavourable opinion of Dutch and Swedish women regarding risk-reducing medication is related to the hypothetical nature of the risk scenarios. However, Dutch women are known for their reluctance to take medication, which is supported by the relatively low number of women reporting current/past HRT use in this study. Breast cancer risk reduction through medication is notoriously difficult to achieve, with few women showing willingness to commit to a five-year preventative treatment regimen. The use of tamoxifen as a preventative drug elicits a strong response from women because of the association with breast cancer treatment. Additionally, the perceived side-effects often deter women, which was confirmed in the present study. Currently, studies are being undertaken, e.g. KARMA Intervention Study (KARISMA) in SE, to determine the lowest effective dose of tamoxifen to potentially increase its applicability as a preventative drug.

CONCLUSIONS

Study limitations

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The present study is the first exploration of European women’s perceptions of adopting an integrated risk-based breast cancer screening and prevention programme. The large number of women from three European countries allowed for an extensive cross-cultural exploration of the acceptability of this new paradigm from the perspective of potential future participants. However, we have to be careful in our interpretation of the results and culture-specific variations cannot be assumed. Selection bias is likely to have affected group composition in all three countries. In general, FG participants were relatively highly educated women who had previously participated in breast cancer screening and scientific research. They were more likely to have had favourable perceptions of screening, potentially limiting the generalisability of our findings to women who do not currently participate in screening. Moreover, an unequal number of British women were invited per risk category, which led to an overrepresentation of high-risk women. Below-average risk women were not at all represented, although some women reported a low perceived breast cancer risk. Moreover, perceptions of Dutch and Swedish women could have been affected by the hypothetical nature of the risk scenarios with inherently lower stakes. Additionally, FGs were moderated by different researchers due to a language barrier. Although we relied on a semi-structured interview guide to standardise discussion, variation is plausible. Future research is required to confirm the identified perceptions in a larger group of women. We are therefore currently performing a survey study aiming for equal representation of women with below average, average, and above average breast cancer risk who are eligible for screening.

Clinical implications

Acceptability of risk-based screening and prevention is mixed. More intensive screening for women with above average breast cancer risk was generally welcomed. However, screening pathways for the other risk categories and general prevention strategies were met with some scepticism. This has implications for clinical practice that need to be addressed by stakeholders and policy-makers before implementation. Women’s perceptions seem to be informed by a lack of knowledge, cultural norms and common emotional concerns, which highlights the importance of tailored educational materials and risk counselling to aid either shared or individual informed decision-making.

Acknowledgements

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Conflict of interest statement

The authors declare no conflict of interest.
REFERENCES


FIGURE LEGENDS

Figure 1. Illustration of a risk-based breast cancer screening and prevention programme
*Current screening guidelines: NL: women aged 50-75, screening interval 2 years; SE: women aged 40-75, screening interval 1.5-2 years; UK: women aged 50-70, screening interval 3 years

Figure 2. Overview of the themes associated with Dutch, English and Swedish women’s perceptions of risk-based breast cancer screening and primary prevention
*Agreement in themes is displayed in bold. Fig adapted from Fritzell et al. 2017.
Women's perceptions of personalised risk-based breast cancer screening and prevention: an international focus group study

Running title. Women's perceptions of risk-based screening and prevention

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ABSTRACT

Objective: Increased knowledge of breast cancer risk factors enables a shift from one-size-fits-all breast cancer screening to a risk-based approach, tailoring screening policy to a woman’s individual risk. New opportunities for prevention will arise. However, before this novel screening and prevention programme is introduced, its acceptability from a woman’s perspective needs to be explored.

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Results: Analysis identified five themes across the three countries. The first theme ‘impact of knowledge’ describes women’s concern of not being able to unlearn their risk, perceiving it as either a motivator for change or a burden which may lead to stigma. The second theme ‘belief in science’ explains women’s need to trust the science behind the risk assessment and subsequent care pathways. Theme three ‘emotional impact’ explores, e.g. women’s perceived anxiety and (false) reassurance which may result from knowing their risk. Theme four ‘decision-making’ highlights cultural differences in shared versus individual decision-making. Theme five ‘attitude to medication’ explores the controversial topic of offering preventative medication for breast cancer risk reduction.

Conclusions: Acceptability of risk-based screening and prevention is mixed. Women’s perceptions are informed by a lack of knowledge, cultural norms and common emotional concerns, which highlights the importance of tailored educational materials and risk counselling to aid either shared or individual informed decision-making.

Key words: breast cancer, oncology, prevention, risk prediction, risk stratification, screening, attitudes, acceptability
BACKGROUND

Population-based breast cancer screening programmes, adhering to a one-size-fits-all approach based on age, have successfully led to early detection and subsequent breast cancer mortality reduction. However, screening may become more effective if tailored to women’s differing levels of breast cancer risk, potentially optimising the benefit-harm ratio of screening. Breast cancer risk prediction models are becoming more accurate by adding, e.g. breast density and polygenic risk score to classic risk factors. Risk prediction also offers new opportunities for breast cancer prevention, targeting women who would benefit most from reducing their risk through lifestyle changes or risk-reducing medication. Successful implementation of risk-based screening and prevention relies on women’s participation. However, eligible women’s perceptions of adopting this novel programme have never been explored.

A risk-based screening and prevention programme is inherently more complex than current age-based screening programmes. Women need to reflect on participation at different stages (Figure 1). Although Figure 1 is an illustration which does not necessarily follow current pathways of care, it shows that women need to decide whether they (1) want to know their risk, (2) are willing to change their screening strategy based on risk, and (3) are prepared to participate in preventative practices. Women’s interest in knowing their breast cancer risk is high. However, knowledge of their risk did not lead to any consistent changes in screening or preventative behaviours. Additionally, although women generally appear in favour of increased screening for high-risk women, lowering screening intensity for low-risk women is more contested. Women are concerned about the accuracy of breast cancer risk estimates with some believing that risk-based screening is mainly motivated by a desire to save money. Their perceptions of prevention also seem mixed. However, risk-reducing medication has mostly been discussed with high-risk women who tend to be monitored outside of national screening programmes, which potentially limits the generalizability of these results to the screening population.

Risk-based screening may bring about considerable benefits to healthcare policy by directing screening and preventative resources to women who are most in need. However, there is a lack of knowledge on the acceptability of an integrated risk-based breast cancer screening and prevention programme from the perspective of European women who would be eligible to participate, i.e. women at population-level risk who meet current age criteria for screening. Therefore, this study aims to evaluate the adoption of risk-based breast cancer screening and prevention by exploring perceptions of women who participated in the well-established national screening programmes of the Netherlands (NL), the United Kingdom (UK), and Sweden (SE). Screening eligibility in these countries is solely based on age, without access to additional risk information or screening modalities. Therefore, risk-based screening would be a considerable departure from current age-based screening practices in these three countries.

METHODS

Design

Focus groups (FGs) following a semi-structured interview guide were performed to explore women’s perceptions of adopting risk-based breast cancer screening and prevention in NL, UK, and SE. Ethics approval
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RESULTS
Participants
From the 1650 women invited to take part, 143 women participated across the three countries (8.7%). Participant characteristics are outlined in Supplement 2. Nine FGs were conducted in NL (54 participants), five in SE (38 participants), and six in UK (51 participants). Group sizes ranged from 5 to 10 participants. Swedish participants were considerably older than Dutch and British participants: median ages 67.0, 57.5, and 56.0, respectively. British women had fewer years of education (median: 15.0) than Dutch (17.0) and Swedish women (21.0). More British women had a first-degree family history of breast cancer (47.1%), than Dutch (16.7%) and Swedish women (21.1%). British women showed a marked discrepancy between their perceived breast cancer risk and their actual risk as relayed by the PROCAS study team. Most British participants had a high risk of developing breast cancer (70.6%), however only 23.5% of participants perceived their risk as high. No participants had a below average breast cancer risk.

Thematic analysis
Dutch and Swedish women were generally positive about receiving breast cancer risk feedback. None of the British women expressed regret about finding out their risk. Women in all three countries emphasised, however, that participation should be optional, offering screening according to current country guidelines to women who do not want to adopt this approach. Figure 2 displays the themes representing perceptions of the adoption of risk-based screening and prevention of Dutch, Swedish, and British women. Supplement 3 provides a breakdown of the themes per country with relevant quotes. In general, there was extensive overlap in perceptions of women across the three countries. Therefore, we were able to identify five superordinate themes: (1) impact of knowledge, (2) belief in science, (3) emotional impact, (4) decision-making, and (5) attitude to medication. Although the overarching themes showed similarities, subthemes sometimes differed per country. Both will be discussed below using FG data extracts.
Theme 1. Impact of knowledge (NL, SE, UK)

The superordinate theme ‘impact of knowledge’ deals with women’s perception that once they know their breast cancer risk, they feel the need to act upon that information. A moderate-high risk result in particular elicited either a beneficial response, i.e. the subthemes perceived control, proactive attitude, motivation, and empowerment, or was perceived as a burden, i.e. avoidance, guilt, and fatalistic view. As a Swedish participant put it: “A high risk result almost feels like it’s close to a diagnosis”. British participants, who had chosen to have their breast cancer risk relayed, generally perceived knowledge of risk as an opportunity: “Perhaps being more aware, and doing something proactively about your high risk, makes you feel more in control, and so you’re less stressed”. Although women in all three countries generally welcomed preventative options to manage their risk, they also mentioned the potential for stigma and guilt, e.g. “It puts a lot of responsibility for health on women and not everyone is equally capable of maintaining a healthy lifestyle; financially or intellectually. It can’t become a woman’s own fault if she develops breast cancer” (Dutch participant).

Theme 2. Belief in science (NL, SE, UK)

The superordinate theme ‘belief in science’ illustrates women’s concerns regarding the scientific basis of the risk prediction model and the effectiveness of risk-reducing medication and lifestyle changes. Dutch women were particularly concerned about extending the screening interval for women at below average risk, wondering whether it is financially motivated rather than evidence-based. Swedish women displayed a greater trust in the scientific evidence behind any new screening policy, e.g. “Yes, personalised screening intervals are acceptable provided you know how they are developed and what the criteria are: why some women are asked to go for a screening more often than others”. Dutch women also described the role of perceived breast cancer risk in the acceptability of a personalised screening plan. They believe that if their relayed risk does not correspond to their perceived risk, they will be less likely to accept the accompanying screening and prevention advice. Both British and Dutch women were sceptical about the scientific link between lifestyle changes and breast cancer risk. The acceptability of risk-reducing medication depended on the magnitude of the effect, with women balancing the potential for side-effects and risk reduction. Moreover, women would like to monitor the effect of preventative measures to determine potential reclassification of risk: “So, I think, if you can really see, find out that you have made a difference through prevention, then you could potentially screen less frequently. Particularly if you have changed your risk” (Swedish participant).

Theme 3. Emotional impact (NL, UK)

The superordinate theme ‘Emotional impact’ describes how women think risk-based screening and prevention will affect their psychological wellbeing, with the subthemes: awareness, anxiety, (false) reassurance, and impact on quality of life. These themes were more prevalent in Dutch and British women’s perceptions, whereas Swedish women phrased their perceptions in more rational terms, with fewer references to emotional states, e.g. “But, if they determine you have a higher risk of developing breast cancer, surely, that doesn’t mean you’ll definitely get it. Because there are other contributing factors too”. The main difference between British and Dutch women’s perceptions concerned the level of reassurance. The majority of Dutch women did

http://mc.manuscriptcentral.com/pon
not perceive the hypothetical message of below average-average risk to be particularly reassuring: “It remains a risk and it is never no risk; even if you tell me I have a 95% chance of not developing breast cancer, I might still be in the 5%; it doesn’t provide real reassurance”. However, British women who actually received their risk, indicated that receiving a letter stating that you have an average risk of developing breast cancer was very reassuring, filing the letter and forgetting all about it. Dutch women worried that they would become preoccupied: “I don’t want to know my risk, because it will make me worry about every little ache or change in my breast”. Some British women at high risk described needing professional help: “It has massive impact, because I’m still undecided with the treatments I’ve been offered, what to do. So I’m seeing a clinical psychologist”. Women from both counties worried about the impact that risk-reducing medication would have on their current quality of life due to potential side-effects.

Theme 4. Decision-making (SE, UK)

‘Decision-making’ is a superordinate theme that received specific attention during the British and Swedish FGs. Swedish women emphasised individual decision-making, considering the process a personal responsibility, balancing anecdotal knowledge of breast cancer and preventative options, and the impact that the risk assessment and subsequent recommendations may have on the quality of life of others and yourself: “I don’t think I’d consult anyone about the actual decision, because the decision is for me to make. It’s my responsibility”. British women on the other hand emphasised a shared decision-making process with family, friends and professionals, taking into account responsibility to oneself and family, and potential life-events that could influence decision-making, e.g. divorce, illness. Professional endorsement appeared particularly elementary in the adoption of risk-reducing medication, with British women who were at first adverse to the idea of medication changing their mind due to professional advice: “Well, for me it was a no-brainer because, I mean, I don’t like the idea of taking tablets constantly, I just don’t like it. But the doctor said it was a no-brainer for me personally, you know, because of the advantages”. British women were also influenced more by media coverage about breast cancer, speaking of the perceived ubiquitous nature of the disease: “Not through being told, but I think because it’s constantly in the media, breast cancer, I don’t think even if you’re average you feel safe”.

Theme 5. Attitude to medicine (NL, UK)
The superordinate theme ‘attitude to medicine’ reflects the apparent controversial nature of risk-reducing medication for breast cancer which was mostly addressed by British and Dutch women. Swedish women tended to have a more pragmatic approach to medication, stating that they preferred lifestyle changes but that they would be willing to try medication to determine the level of side-effects. Most Dutch women, however, expressed an aversion to medication, perceiving it to be a radical and unnecessary daily hassle when dealing with a risk instead of a diagnosis. Anecdotal knowledge of particularly tamoxifen as a breast cancer drug induced worry and anxiety. Some Dutch women argued that preventative medication is normalised, referring to e.g. cardiovascular medication, reasoning that medication is a convenient, easy solution to lower your risk. A considerable number of British women who participated in the FGs had been advised to take risk-reducing
medication. Although the British women’s attitudes to medicine were very similar to Dutch women’s, they generally opted to take it, with one participant stating: “Most of us think it’s worth the risk”.

**DISCUSSION**

The present study provides an overview of British, Dutch, and Swedish women’s perceptions of adopting risk-based breast cancer screening and prevention. To our knowledge, this is the first study of its kind which has been performed in a population-based European screening setting. It showed that, overall, women appear in favour of finding out their breast cancer risk, although the acceptability of subsequent screening and preventative strategies is mixed. Importantly, women emphasise that strategies should be evidence-based and participation voluntary. There is considerable overlap in the perceptions of women across the three countries. This suggests that the variation in hypothetical (NL, SE) versus ‘actual’ (GB) risk scenarios did not hinder women’s ability to participate in the discussion. However, Swedish women experienced more difficulty than Dutch women relating to both the concepts of risk and hypothetical risk scenarios, requiring more clarification and encouragement to start a discussion.

The superordinate themes associated with women’s perceptions of risk-based screening and prevention across the three countries are rooted in behavioural theory. Women’s perceptions seem to be best reflected by the ‘health belief model’ and ‘self-determination theory’. These two theoretical frameworks assume a cost-benefit analysis of particular health behaviours, whereby a person takes into account perceived severity and susceptibility to disease, psychological factors, social context, autonomy, and personal competence. The relevance of these two frameworks to the adoption of this novel screening and prevention paradigm by women has previously been demonstrated. However, the way in which the underlying constructs of the theoretical frameworks are represented in women’s perceptions sometimes differs across the three countries, potentially pointing to culture-specific attitudes or customs.

Cross-cultural concordance was seen in the themes ‘impact of knowledge’ and ‘belief in science’. Women from all three countries deliberated that breast cancer risk information may not be without consequence, enticing activity or potential emotional turbulence. The importance of perceived competence in health behaviour decision-making is highlighted. Dutch and Swedish women reported a great need to understand the scientific basis of the risk prediction model and subsequent screening and prevention recommendations. They appear to perceive a greater sense of control when more knowledgeable. However, research shows that risk information is difficult to understand. A comprehensive information leaflet which meets all of women’s perceived information needs may therefore hinder informed decision-making. This is in accordance with the attitude of British women in this study who only received a basic level of information at every stage of the programme, but did not report a perceived lack of information or knowledge. The theme ‘belief in science’ also highlighted some women’s scepticism about the accuracy of risk estimates and the rationale behind risk-based screening, suspecting a financial motive. These concerns were previously mentioned by US women who professed a reluctance to change current screening habits, fearing missed breast cancers with a changed screening interval.
The emotional impact of risk assessment was hypothesised by Dutch women and reported by British women about a year after receiving risk feedback. Some British women who were classified as moderate-high risk reported a decrease in psychological wellbeing with some women seeking professional help. These findings are tentatively confirmed by a survey study among PROCAS participants who received breast cancer risk feedback and PROCAS participants who were awaiting their risk feedback. Women who had received their risk feedback reported lower levels of anxiety, but higher levels of cancer worry than women awaiting their risk feedback. Additionally, women with a moderate-high risk of developing breast cancer reported higher anxiety than women with a below average risk. However, overall anxiety levels were still relatively low. This is in line with previous research showing no significant long-term impact of genetic risk estimation on psychological outcomes.

A pronounced difference between Swedish and British women’s perceptions was visible in the decision-making process precipitating participation. Swedish participants favoured a more autonomous process than British participants, who emphasised a shared approach. Previous studies have found that medical decision-making is affected by gender, age, and education, with younger, highly qualified women being most likely to desire higher levels of autonomy. This partially corresponds with our findings since Swedish women were, on average, more educated than British women. However, Swedish women were also considerably older on average than British women, contradicting previous findings. Moreover, a qualitative study of Swedish people’s values regarding participation in colorectal cancer screening showed a similar need for autonomy, pointing to a potential societal attitude.

The superordinate theme ‘attitude to medicine’ shows a general reluctance of women to try risk-reducing medication. Particularly noteworthy is the reliance of British women on professional endorsement in the decision-making process. Although our British participants were generally not in favour of medication, professional endorsement changed their views almost unanimously. This is in concordance with previous research suggesting that people look to physicians for decisions on medication use, because of their perceived superior knowledge. It is unclear whether the unfavourable opinion of Dutch and Swedish women regarding risk-reducing medication is related to the hypothetical nature of the risk scenarios. However, Dutch women are known for their reluctance to take medication, which is supported by the relatively low number of women reporting current/past HRT use in this study. Breast cancer risk reduction through medication is notoriously difficult to achieve, with few women showing willingness to commit to a five-year preventative treatment regimen. The use of tamoxifen as a preventative drug elicits a strong response from women because of the association with breast cancer treatment. Additionally, the perceived side-effects often deter women, which was confirmed in the present study. Currently, studies are being undertaken, e.g. KARMA Intervention Study (KARISMA) in SE (https://karmastudy.org/ongoing-research/), to determine the lowest effective dose of tamoxifen to potentially increase its applicability as a preventative drug.

CONCLUSIONS

Study limitations
The present study is the first exploration of European women’s perceptions of adopting an integrated risk-based breast cancer screening and prevention programme. The large number of women from three European countries allowed for an extensive cross-cultural exploration of the acceptability of this new paradigm from the perspective of potential future participants. However, we have to be careful in our interpretation of the results and culture-specific variations cannot be assumed. Selection bias is likely to have affected group composition in all three countries. In general, FG participants were relatively highly educated women who had previously participated in breast cancer screening and scientific research. They were more likely to have had favourable perceptions of screening, potentially limiting the generalisability of our findings to women who do not currently participate in screening. Moreover, an unequal number of British women were invited per risk category, which led to an overrepresentation of high-risk women. Below-average risk women were not at all represented, although some women reported a low perceived breast cancer risk. Moreover, perceptions of Dutch and Swedish women could have been affected by the hypothetical nature of the risk scenarios with inherently lower stakes. Additionally, FGs were moderated by different researchers due to a language barrier. Although we relied on a semi-structured interview guide to standardise discussion, variation is plausible. Future research is required to confirm the identified perceptions in a larger group of women. We are therefore currently performing a survey study aiming for equal representation of women with below average, average, and above average breast cancer risk who are eligible for screening.

Clinical implications
Acceptability of risk-based screening and prevention is mixed. More intensive screening for women with above average breast cancer risk was generally welcomed. However, screening pathways for the other risk categories and general prevention strategies were met with some scepticism. This has implications for clinical practice that need to be addressed by stakeholders and policy-makers before implementation. Women’s perceptions seem to be informed by a lack of knowledge, cultural norms and common emotional concerns, which highlights the importance of tailored educational materials and risk counselling to aid either shared or individual informed decision-making.

Acknowledgements
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Conflict of interest statement
The authors declare no conflict of interest.
REFERENCES


FIGURE LEGENDS

Figure 1. Illustration of a risk-based breast cancer screening and prevention programme

*Current screening guidelines: NL: women aged 50-75, screening interval 2 years; SE: women aged 40-75, screening interval 1.5-2 years; UK: women aged 50-70, screening interval 3 years

Figure 2. Overview of the themes associated with Dutch, English and Swedish women’s perceptions of risk-based breast cancer screening and primary prevention

*Agreement in themes is displayed in bold. Fig adapted from Fritzell et al. 2017.
Figure 1. Illustration of a risk-based breast cancer screening and prevention programme

*Current screening guidelines: NL: women aged 50-75, screening interval 2 years; SE: women aged 40-75, screening interval 1.5-2 years; UK: women aged 50-70, screening interval 3 years

254x190mm (96 x 96 DPI)
Figure 2. Overview of the themes associated with Dutch, English and Swedish women’s perceptions of risk-based breast cancer screening and primary prevention

*Agreement in themes is displayed in bold. Fig adapted from Fritzell et al. 2017.

254x142mm (96 x 96 DPI)

Participants
Women were selected from three European countries that are currently developing breast cancer risk prediction models to guide screening and prevention delivery for women at varying levels of risk, i.e. NL (Personalised Risk-Based Mammography Screening – PRISMA), the UK (Predicting the Risk of Cancer at Screening – PROCAS
1
), and SE (Karolinska Mammography Project for Risk Prediction of Breast Cancer – KARMA
2
). All three studies recruited women through the country’s national breast cancer screening programme, therefore all participating women had attended screening at least once. Women from NL and SE were unaware of their personal breast cancer risk. The breast cancer risk of the British women had previously been assessed with the the Tyrer-Cuzick algorithm including breast density and/or single-nucleotide polymorphisms (SNPs) and relayed.3 Screening and prevention advice was provided according to the following general guidelines: below average, average, and moderate risk women were advised to maintain ‘screening as usual’, i.e. a mammogram every three years. High risk women were recommended to increase their screening frequency to once every 18 months, and along with moderate risk women were offered the option of a lifestyle programme and risk-reducing medication if appropriate (i.e. dependent on weight and breast density, respectively). Breast cancer risk was relayed between February and December 2016.

Women were sent an information leaflet about the study if they were a previous participant of the PRISMA, PROCAS, or KARMA study who consented to being approached for follow-up studies. British participants were randomly sampled within their risk category, aiming to have an equal number of participants per risk category. Women with a prior breast cancer diagnosis were excluded. We scheduled a focus group (FG) date with women who expressed interest in participating through contact with the research team. The Dutch FGs took place from September – November 2016, the British in February 2017, and the Swedish in April 2017.

Procedure
The FGs in all three countries adhered to the same semi-structured interview guide. This guide was based on a systematic review of available literature on women’s perceptions and a previous qualitative study with professionals from NL, UK, and SE.4,5 The interview guide includes general questions exploring women’s thoughts and feelings regarding having their breast cancer risk assessed, and subsequent screening and preventative options. To illustrate potential risk scenarios the guide contains three vignettes, describing hypothetical women at different levels of risk (i.e. below average, average, above average) and their recommended tailored screening and prevention pathway (based on Figure 1). For the British women, the hypothetical vignettes were not used. Instead, perceptions of their actual risk and subsequent screening and prevention advice were discussed. The questions listed in the interview guide were used a memory tool for the FG moderators. They were not asked consecutively during the FGs. Rather, a single prompt like ‘what are your thoughts about this’ was used after the introduction of, for example, a risk vignette to engage discussion. Only when a topic remained completely unaddressed, were the moderators encouraged to ask the specific question to engage the participants in a discussion about that topic. The complete interview guide is available in Supplement 4.
FGs lasted between 60 to 90 minutes and were performed in the native language of the participants under supervision of one to two moderators with extensive experience in qualitative interviewing (LR or AJ & YW). Moderators refrained from asking leading questions, instead offering only open-ended prompts to entice an open discussion about perceived harms and/or benefits of risk-based breast cancer screening and prevention. Whenever clarification was required, this was offered in a factual manner. All FGs were recorded and transcribed verbatim. The Swedish transcripts were translated into English to facilitate independent data analysis. Participants also completed a short questionnaire on demographics and risk perception. FGs were organised until data saturation was achieved, i.e. no new themes were identified.

References
### Supplement 2. General characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>The Netherlands</th>
<th>Sweden</th>
<th>United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invited total, N</td>
<td>638</td>
<td>512</td>
<td>500</td>
</tr>
<tr>
<td>Invited per risk category, n (%) (UK only)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below average</td>
<td>125 (25.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>125 (25.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>79 (15.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>171 (34.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants total, N (response rate, %)</td>
<td>55 (8.6)</td>
<td>38 (7.4)</td>
<td>51 (10.2)</td>
</tr>
<tr>
<td>Participants per risk category, n (%) (UK only)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below average</td>
<td>- ( )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>10 (19.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (9.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>36 (70.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age(a) (years), median [range]</td>
<td>57.5 [50-72]</td>
<td>67.0 [44-76]</td>
<td>56.0 [50-69]</td>
</tr>
<tr>
<td>Education (years), median [range]</td>
<td>17.0 [6-20]</td>
<td>21.0 [9-21]</td>
<td>15.0 [9-31]</td>
</tr>
<tr>
<td>Employment (% yes)</td>
<td>55.6</td>
<td>42.1</td>
<td>62.7</td>
</tr>
<tr>
<td>Religion (% yes)</td>
<td>42.6</td>
<td>39.5</td>
<td>80.4</td>
</tr>
<tr>
<td>HRT use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past (%)</td>
<td>9.3</td>
<td>26.3</td>
<td>15.7</td>
</tr>
<tr>
<td>Current (%)</td>
<td>3.7</td>
<td>7.9</td>
<td>3.9</td>
</tr>
<tr>
<td>Previous breast biopsy (% yes)</td>
<td>9.3</td>
<td>7.9</td>
<td>21.6</td>
</tr>
<tr>
<td>First degree family history breast cancer (% yes)</td>
<td>16.7</td>
<td>21.1</td>
<td>47.1</td>
</tr>
<tr>
<td>Perceived breast cancer risk (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>24.1</td>
<td>13.2</td>
<td>3.9</td>
</tr>
<tr>
<td>Below average</td>
<td>18.5</td>
<td>7.9</td>
<td>-</td>
</tr>
<tr>
<td>Average</td>
<td>51.9</td>
<td>55.3</td>
<td>17.6</td>
</tr>
<tr>
<td>Above average</td>
<td>5.6</td>
<td>15.8</td>
<td>54.9</td>
</tr>
<tr>
<td>High</td>
<td>-</td>
<td>2.6</td>
<td>23.5</td>
</tr>
<tr>
<td>Perceived 10-year risk, median [range]</td>
<td>15.0 [0-60]</td>
<td>30.0 [0-75]</td>
<td>50.0 [0-98]</td>
</tr>
</tbody>
</table>

\(a\) The eligible screening age in NL is 50-74, SE 40-74 years, and UK 50-70.
### Supplement 3. Overview of all themes with illustrative statements per country

<table>
<thead>
<tr>
<th>Theme</th>
<th>Example of statement (country)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impact of knowledge</strong></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Knowing my breast cancer risk will enable me to change my risk (NL)</td>
</tr>
<tr>
<td></td>
<td>I would only want to know my breast cancer risk if I can exert some control over it (NL)</td>
</tr>
<tr>
<td></td>
<td>But I take your point, that there are some things, and perhaps being more aware, and doing something proactively about that, makes you feel more in control, and so you’re less stressed, and maybe all that, helps to…yes (UK)</td>
</tr>
<tr>
<td></td>
<td>You want to be pre-warned (UK)</td>
</tr>
<tr>
<td>Proactive</td>
<td>Women need to take responsibility for their own health and prevent diseases actively (NL)</td>
</tr>
<tr>
<td></td>
<td>Knowing my risk can motivate me to change my lifestyle (NL)</td>
</tr>
<tr>
<td></td>
<td>Knowing helps you to be more proactive, I think, you know, just in every sphere (UK)</td>
</tr>
<tr>
<td></td>
<td>But then talking to people, they said actually, by knowing, you can do the preventative things, take the drug, have more increased mammograms, you know, checks and everything (UK)</td>
</tr>
<tr>
<td>Stigma</td>
<td>It puts a lot of responsibility for health with the woman, not everyone is equally capable of maintaining a healthy lifestyle (financial, intellectual). It can’t become a woman’s own fault if she develops breast cancer (NL)</td>
</tr>
<tr>
<td></td>
<td>Will I have to tell my insurance company that I’m high risk and will I notice the consequences (NL)</td>
</tr>
<tr>
<td></td>
<td>I think that telling people that it’s their fault if they don’t lose the ten pounds, 15 pounds, 20 pounds, it’s their fault that they’re going to get cancer. I find that really…I find it a really difficult thing (UK)</td>
</tr>
<tr>
<td></td>
<td>Because otherwise a few years down the line if I was to get breast cancer, then somebody turned round and said, well, you were given the chance [to have risk-reducing medication red.], and then you go through all that (UK)</td>
</tr>
<tr>
<td>Avoidance</td>
<td>I don’t want to face the idea of breast cancer until a tumour is actually diagnosed (NL)</td>
</tr>
<tr>
<td></td>
<td>As long as I don’t know anything, nothing is wrong (NL)</td>
</tr>
<tr>
<td>Motivation</td>
<td>The level of the risk doesn’t matter for motivation, risk is a motivator regardless (SE)</td>
</tr>
<tr>
<td></td>
<td>I wear one of those devices on my arm during exercise so, if I were told I was at risk, I’d do that little bit more, with greater dedication (SE)</td>
</tr>
<tr>
<td>Burden</td>
<td>But is risk, …is it a way to make us more involved in our own choices, life? I think it’s a different way of saying: You must do this if you want to continue to live (SE)</td>
</tr>
<tr>
<td></td>
<td>So it’s this way, how much do you need to do, how many things do you need to do, it could get so that it ends up being more distress than the disease (SE)</td>
</tr>
<tr>
<td>Fatalistic view</td>
<td>Because if you know too much you can become paranoid instead. The slightest thing becomes a catastrophe (SE)</td>
</tr>
<tr>
<td></td>
<td>High risk almost feels like it’s coming close to a diagnosis, and that’s different (SE)</td>
</tr>
<tr>
<td>Guilt</td>
<td>And also what you can do to have an influence yourself and how much put the blame on yourself or not, aha, you eat red meat, yes then you need to expect a 5 percent higher risk and then, yes, you have also been sunbathing every summer and then you have been sunbathing without sun protection (SE)</td>
</tr>
<tr>
<td></td>
<td>I’ve thought about it not so much for my own sake, but because you pass it on. You know, like ‘If I’d only known’ (SE)</td>
</tr>
<tr>
<td>Empowerment</td>
<td>I think that’s a key word, it’s about being informed. It may be really that there’s nothing you can really do, or very little you can do without it. But just being more informed give you a little bit more power I think (UK)</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td></td>
<td>Knowing your risk empowers people to make changes in their life to reduce their risk (UK)</td>
</tr>
<tr>
<td>Belief in Science</td>
<td>I view this as a decision purely based on economics, so I don’t trust it (NL)</td>
</tr>
<tr>
<td>Societal costs</td>
<td>I don’t believe that overweight women can change their lifestyle sufficiently to lose weight, therefore investing money in this would be wasted money (NL)</td>
</tr>
<tr>
<td></td>
<td>At the same time, why aren’t mammogram appointments done more often? Is it an economic issue, or is it not a good idea? (SE)</td>
</tr>
<tr>
<td></td>
<td>Exactly that, it’d be an economic saving for society if our habits changed and if we adopted a different lifestyle (SE)</td>
</tr>
<tr>
<td></td>
<td>I think, to tell somebody they’re high risk, and then say, and if you want more mammograms you’re going to have to pay, to me there’s a real issue around that (UK)</td>
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<td>Effect measurement</td>
<td>If you had…when I picked up my prescription from the pharmacy over there, she said to me, have you got breast cancer. And I said, no, this is preventative. And she said, well, if you had breast cancer, you wouldn’t pay for this (UK)</td>
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<td>Reclassifying risk</td>
<td>Your risk is an estimate surrounded by a lot of uncertainty (NL)</td>
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<td>I would continue drinking alcohol, because I don’t want to become low risk, because then I would receive less screening (NL)</td>
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<td>I think it would be nice to have a follow up, having being told I’m high risk, at some point, to see if my risk has reduced (UK)</td>
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<td>I guess it’s something they might always have to keep under review, though, ‘cause we must be changing, we’re constantly evolving aren’t we, in very small ways (UK)</td>
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<td>Trust in the model</td>
<td>Yes, say that the model is very safe. Then I would think: this is great! And then I wouldn’t worry (SE)</td>
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<tr>
<td>Risk measurement</td>
<td>Yes, that I am not at any great risk, then I want to continue to get at least as many check-ups as I’ve had up to now, I just don’t want to end up on the outside because I don’t really trust your risk system perhaps (SE)</td>
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<td>Emotional impact</td>
<td>How often should you check your percentage to know if you are right or not right (SE)</td>
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<tr>
<td>Awareness</td>
<td>It would make me more aware of breast cancer; I would carry that with me (NL)</td>
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<td></td>
<td>Knowing my risk would make me aware of my bad (eating) habits and would make me feel guilty (NL)</td>
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<td></td>
<td>Yeah, I would agree with that. I’m in my head all the time, but I am more aware because I’m taking the drug every day, and for what it’s for, so yes, it is in your head more (UK)</td>
</tr>
<tr>
<td></td>
<td>It [knowing your risk red.] makes you a bit more aware, I’m more focused on my next mammogram (UK)</td>
</tr>
</tbody>
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Anxiety
I don’t want to know my risk, because it will make me worry about every little ache or change in my breast. I will think I’ve developed breast cancer (NL)
Knowing my risk could feel like Damocles’ sword (NL)
In some respects, knowing your risk is harder, because you’re waiting for what you think is the inevitable, you know (UK)
It is the worry. I think even between an 18 month period you know how cancer can progress, that I’ve only had mine [mammogram red.] done, and I’m thinking now it might have struck (UK)
Reassurance (false)
It remains a risk and it is never no risk; even if you tell me I have a 95% chance of not developing breast cancer, I might still be in the 5%; it doesn’t provide reassurance (NL)
Knowing your low risk could make you careless/neglectful; you can think you’ll never get breast cancer (NL)
Well, thinking about it, I found out I’m high risk, I’m on a drug to help reduce it, I’m being tested regularly. I’m on this…if I do get it, because it will be found so quickly (UK)
I feel protected in a way, increased protection (UK)
Quality of life
I don’t want to know my risk, because it would negatively influence my wellbeing (NL)
Knowing your risk may enable you to make better life-choices that make you feel happier (NL)
I’ve been asked to take or I’ve been recommended to take it as a preventative measure, but I think it’s going to have a really detrimental effect on the lifestyle I actually lead (UK)
You can’t be absolutely obsessed with that [healthy lifestyle red.], that that’s all you’re concentrating on, you’ve got to live your life, have some fun as well (UK)

Decision-making
Responsibility
(personal v. shared)
I don’t think I’d consult anyone about the actual decision, because the decision is for me to make. It’s my responsibility. I was going to say it is so obvious that you wouldn’t even ask the family and would just tell them (SE)
But on the other hand, if I were to discuss it with someone who then persuades me that I should do one thing or the other, or I’m not going to take that medicine, I’m not going to do it, and then I get severe breast cancer, because he said I should… then I would blame it on him. That’s my responsibility, I think (SE)
Obviously you go on the internet and stuff, and ask around, and ask friends about what they thought as well [about risk-reducing medication red.], and the friend who’d had breast cancer, she said take it. So (UK)
I discussed it very openly with my family. Yeah, you know? My son is a doctor anyway, and my daughter-in-law, so (UK)
Quality of life
But, how can you maintain quality of life if you’re aware all the time that you’re in a high-risk zone… you’d constantly be worried (SE)
Yes, and you need to feel like crap for five years [taking risk-reducing medication red.] (SE)
Impact on others
But it’s a decision made with regard to what commitments you have to people, whether you depend on anyone, or if you have someone who is dependent, and so on, too (SE)
I would make the decision with as much regard as possible for my family so that they can have me around for a long time (SE)
Anecdotal knowledge
And I believe that, since many people who already have breast cancer and need to take this, stop taking it because the side effects are so terrible, I’m thinking: should I be taking this for preventive purposes. I don’t think so (SE)
I’ve been living in a “cancer marriage” so I have… maybe a little more of a natural attitude to what disease is and so on. It’s something that you just deal with. Working with it and living with it, getting out (SE)
Professional endorsement

Well, he said, if you were my wife he would recommend the mammograms. I thought, well, if I have a mammogram every 18 months, and he said yes, and he sort of suggested that, well (UK)

The professor said for me that Raloxifene was a no-brainer because of the positive effects that it has as well, you know, reduces osteoporosis and cholesterol. And there were various other things and so I just thought, well, you know, what can I lose (UK)

Media coverage

Do you not think it’s scaremongering in it all though, in all of this, oh, breast cancer, breast cancer, breast cancer, everywhere you look, all the magazines, everywhere, all the time (UK)

I think breast cancer’s very much in the news as well. I think we’re more aware of it now, aren’t we, and I think that makes us all want to know more and do more, really (UK)

Life events

My risk was not a motivator to change my lifestyle, and I’m a bit embarrassed because I’m a nurse and the most overweight. No, I was just going through a very difficult separation at the time, and subsequent divorce. So it was kind of just like something that happened in the middle of that (UK)

I think, in terms of changing lifestyle, I think it’s hardest when, I’ve seen two people who have led impeccable lives of health and they’re not overweight, don’t smoke, don’t drink to excess, ate healthily, and they got it and died (UK)

Attitude to medicine

Aversion

It is a poison; it is unnatural (NL)

I try not to take any medication (NL)

I got the same information, but I’ve not took anything, and I’m really quite against taking any medication whatsoever, full stop (UK)

I mean, I don’t like the idea of taking tablets constantly, I just don’t like it (UK)

Anecdotal knowledge

I’ve seen the side-effects of hormonal tables in my friends/mother and it was horrible (NL)

My mother took tamoxifen to prevent cancer recurrence and she is still alive, so I would consider taking tamoxifen preventively (NL)

I just didn’t want to go down that road, my mum had Tamoxifen and it made her really poorly (UK)

I’ve known a couple of friends that have been on it (risk reducing medication red.) and it’s been a nightmare for them (UK)

Convenient

Taking a pill to decrease your risk, that’s nice and easy (NL)

Taking a pill is too easy (NL)

Normalisation

I already take medication on a daily basis, so that would not stop me from taking tamoxifen (NL)

More and more people in my environment use medication for other conditions and this does not control their lives (NL)

Radical

At the moment, I’m not diagnosed with anything, and I know, it might not happen. It might not happen, and I’m not trying to, why should I put stuff in my body that I might not need (UK)

But all I question is the giving of drugs to people who are just deemed to be at risk and haven’t actually had it. That raises a big question in my mind (UK)

Daily hassle

But yes, it’s a bit of a chore, a bit of a pain, but there we are, it’s a little thing (UK)

Do you know what really struck me. I, up until starting that tablet, have never had to take medication other than an occasional paracetamol here or there. The worst thing for me was this business of having to take a tablet every day. And I thought, do you know, I’m going to have to do this now for the next five years (UK)
Semi-structured interview guide focus group discussions

“Women’s perceptions on personalised risk-based breast cancer screening and primary prevention”
Before we start we would like to emphasise that all information will be treated as strictly confidential and your identity will not be revealed in any reports. The recordings will be kept securely under lock and key.

Suggested topics general

1. Would you like to know your personal risk of developing breast cancer?
2. Would knowing your personal risk influence your participation in the screening programme?
3. How do you think you’d feel about receiving personal risk information?
4. What would you like about receiving personal risk information/what would be the best part?
5. What would you dislike about receiving personal risk information?
6. Who do you think should determine your personal breast cancer risk?
7. Who do you think should inform you of your personal breast cancer risk?
8. How do you feel you should be informed of your risk (letter, telephone, face-to-face)?
9. When do you think you should be informed of your personal breast cancer risk?
10. How do you feel about actively working on reducing your risk?
   a. How do you feel about taking risk-reducing medication?
   b. How do you feel about altering your lifestyle?
11. How do you think personalised risk-based screening could benefit you?
12. How do you think breast cancer prevention options could benefit you?
13. What do you think the drawbacks of personalised screening could be for you?
14. What do you think the drawbacks of primary prevention could be for you?
15. What information would you need about personalised risk-based screening to make an informed decision about screening/prevention?
16. What information would you need about prevention to make an informed decision?
   a. Risk reducing medication
   b. Lifestyle alterations
17. How would you feel if your neighbour/friend/relative has a different screening strategy to you?
18. How would you feel about providing a blood sample to determine your breast cancer risk?
19. Which new screening strategy would be acceptable to you:
   a. Screen women aged 35-50 at above average risk, and all women who were already eligible
   b. Only screen women aged 35 years and older who are at above average risk
c. Other options...

*We are now going to tell you about Delia. We would like to ask you to listen carefully and try to put yourself in Delia’s place. Imagine what you would think and feel if you were in her position.*

**Vignette 1:** Delia is a 58 year old woman. She is told that her risk of developing breast cancer is lower than average. Delia is therefore advised to decrease her screening frequency from once every 3 years to once every 5 years?

**Suggested topics** *Personalised risk-based breast cancer screening*

1. How would you feel if you were in Delia’s shoes?
2. What thoughts does the low risk result provoke?
3. What feelings does the low risk result provoke?
4. What thoughts does the advice on screening frequency provoke?
5. What feelings does the advice on screening frequency provoke?
6. What impact would receiving this risk information have on your life?
7. How do you think this screening advice could benefit you?
8. What do you think the drawbacks of this screening advice could be for you?
9. What information on personalised screening would you need to be able to make an informed choice?
10. How would you like the information on your personal breast cancer risk presented to you?
11. What support would you like to be able to make an informed choice about altering your screening strategy?
12. Would you like to involve other people in the decision making process?
13. How would you feel if your neighbour/friend/relative received mammograms more frequently compared with you?

**Suggested topics** *Primary prevention*

1. Do you feel Delia should be advised to change her lifestyle to further lower her breast cancer risk?
Next, we are going to tell you about Patricia. Again, we would like to ask you to listen carefully and put yourself in Patricia’s place. Imagine what you would think and feel if you were in her position.

**Vignette 2:** Patricia is a 50 year old woman. She is told that her risk of developing breast cancer is in the high-risk category. Patricia is advised to increase her screening frequency to once a year. In addition, she is offered the risk reducing medication called Tamoxifen. Tamoxifen is a tablet medication which Patricia would have to take daily for 5 years.

**Suggested topics  Personalised risk-based breast cancer screening**

1. How would you feel if you were in Patricia’s shoes?
2. What thoughts does the high risk result provoke?
3. What feelings does the high risk result provoke?
4. What thoughts does the advice on changing screening age and frequency provoke?
5. What feelings does the advice on changing screening age and frequency provoke?
6. What impact would receiving this risk information have on your life?
7. How do you think this screening advice could benefit you?
8. What do you think the drawbacks of this screening advice could be for you?
9. What information on personalised screening would you need to be able to make an informed choice?
10. How would you like the information on your personal breast cancer risk presented to you?
11. What support would you like to be able to make an informed choice about altering your screening strategy?
12. Would you like to involve other people in the decision making process?

**Suggested topics  Primary prevention**

1. What thoughts does the advice on Tamoxifen provoke?
2. What feelings does the advice on Tamoxifen provoke?
3. How do you think this prevention advice could benefit you?
4. What do you think the drawbacks of this prevention advice could be for you?
5. What information on Tamoxifen would you need to be able to make an informed choice?
6. How would you like the information on Tamoxifen presented to you?
7. Who do you think should inform you about Tamoxifen?
8. What support would you like to be able to make an informed choice about Tamoxifen?
9. Would you like to involve other people in the decision making process?

Finally, we would like to introduce you to Mary. Please listen carefully and imagine what you would think and feel if you were in Mary's position.

Vignette 3: Mary is 50 years old, she is told that she has an average risk for developing breast cancer. She is told that her screening strategy will remain as it is. She will start screening at 50 years and will be invited every three years. She is advised to change her lifestyle to further reduce her breast cancer risk. The following lifestyle choices are recommended:
- Obtain and maintain a healthy weight; Mary is currently somewhat overweight
- Eat a healthy Mediterranean diet
- Participate in moderate physical exercise 3-4 hours a week
- Reduce alcohol intake to 1 glass a day

Suggested topics  Personalised risk-based breast cancer screening
1. How would you feel if you were in Mary's shoes?
2. What thoughts does the average risk result provoke?
3. What feelings does the average risk result provoke?
4. What thoughts does the advice on screening provoke?
5. What feelings does the advice on screening provoke?
6. What impact would receiving this risk information have on your life?
7. How do you think this screening advice could benefit you?
8. What do you think the drawbacks of this screening advice could be for you?
9. What information on personalised screening would you need to be able to make an informed choice?
10. How would you like the information on your personal breast cancer risk presented to you?
11. What support would you like to be able to make an informed choice?
12. Would you like to involve other people in the decision making process?
13. How would you feel if your neighbour/friend/relative received mammograms less frequently compared with you?

Suggested topics  Primary prevention
1. What thoughts does the advice on lifestyle choices provoke?
2. What feelings does the advice on lifestyle choices provoke?
3. How do you think this prevention advice could benefit you?

4. What do you think the drawbacks of this prevention advice could be for you?

5. What information on lifestyle choices would you need to be able to make an informed choice?

6. How would you like the information on lifestyle choices presented to you?

7. Who do you think should inform you about lifestyle choices?

8. What support would you like to be able to make an informed choice about lifestyle changes?

9. Would you like to involve other people in the decision making process?