Breast cancer risk assessment and screening for young women at high risk: Developing care pathways and assessing feasibility

A thesis submitted to The University of Manchester for the degree of Doctor of Philosophy in the Faculty of Biology, Medicine and Health

2023

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Contents

Word count: 48,203

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List of Abbreviations

ANCOVA	Analysis of covariance
BCAN-RAY	Breast CANcer Risk Assessment in Younger women
BC-PREDICT	Breast Cancer Predict
BCRAT	Breast Cancer Risk Assessment Tool
BOADICEA	Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm model
BSE	Breast self-examination
FHRPC	Family History, Risk and Prevention Clinic
GP	General practitioner
IARC	International Agency for Research on Cancer
IBIS	International Breast Cancer Intervention Study model
IMD	Index of Multiple Deprivation
MD	Mammographic density
MMAT	Mixed Methods Appraisal Tool
MRC	Medical Research Council
NHSBSP	National Health Service Breast Screening Programme
NICE	National Institute for Health and Care Excellence
OB/GYNs	Obstetrician-gynaecologists
PPIE	Patient and Public Involvement and Engagement
PROCAS	Predicting Risk of Cancer At Screening
PRS	Polygenic risk scores
pVAS	Predicted visual assessment score
RCT	Randomised controlled trial
SNPs	Single nucleotide polymorphisms
UK	United Kingdom
US	United States
USA	United States of America

Thesis Abstract

Breast cancer incidence starts to increase exponentially when women reach 30-39 years and it is the most common cause of death in women aged 35-50 years in the UK. In the majority of such cases, the women do not have a strong family history of breast cancer and have not been identified as being at increased risk of developing the disease. Identifying women aged 30–39 years at increased risk of developing breast cancer without a strong family history would allow them access to screening and preventive strategies that could facilitate earlier detection of breast cancer and reduce breast cancer mortality.

In the period up to the beginning of this PhD, much of the research investigating the provision of personalised breast cancer risk estimates has been conducted within the context of implementing a risk-based breast cancer screening programme. Consequently, little was known regarding how a similar programme could be delivered to younger women without a strong family history of breast cancer outside of an organised screening programme. Therefore, this PhD aimed to inform the development of acceptable care pathways for the provision of personalised breast cancer risk assessment and where appropriate, screening or preventive strategies, to women aged 30-39 years without a strong family history. It did this by investigating the views of primary care providers and women as the intended deliverers and recipients respectively.

A systematic review (Study One) was conducted synthesising the quantitative data on primary care providers' attitudes and routine behaviours in the context of breast cancer risk assessment and primary prevention. The findings of Study One informed the development of a qualitative study with primary care providers to explore their views on the development of a breast cancer risk assessment and primary prevention pathway for young women within primary care (Study Two). Study Three investigated women's views on, and requirements for, a breast cancer risk assessment service. This study resulted in two papers, one relating to optimising the delivery of risk assessment and one examining young women's beliefs about breast cancer risk and experiences of breast awareness. The planned methods and analyses for a study assessing the feasibility of offering breast cancer risk assessment to women aged 30-39 years without a strong family history of breast cancer is provided (Study Four) with a focus on acceptability to these women.

Breast cancer risk assessment was considered acceptable in principle to eligible women providing that a risk management plan and support from healthcare professionals is available. A 'one-stop shop' delivery model that minimised the effort required to engage with breast cancer risk assessment was desired by women. However, women may not engage with breast cancer risk assessment because of their perception of breast cancer as an older woman's disease and reported disengagement with breast awareness. Our findings suggest that general practices are likely to accept an increased role in breast cancer risk assessment, but they have concerns about managing women identified as increased risk. How risk management services for women identified at increased risk will be provided and who will be responsible for delivering them remains a key issue to be resolved. Different delivery models should be evaluated with due consideration given to the views of healthcare personnel involved in delivery to inform healthcare system capacity requirements and the views of women to ensure equity of access.

Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Acknowledgements

I would like to express my gratitude to my supervisors: Prof David French, Dr Sacha Howell, and Dr Louise Gorman. Thank you for your guidance, patience, and encouragement through what has been a challenging time to complete a PhD. A special thanks to my primary supervisor David for always making time for me whenever I needed it – it has been a privilege to learn from you. Thank you also to Dr Sarah Cotterill for being an approachable advisor.

Thank you to Manchester Cancer Research Centre for funding my PhD and all the study participants and public contributors who gave so generously of their time.

Thank you to the Girl Gang (Lorna, Vicky, Rhi, Hannah, Sam & Rachel) for helping me navigate this journey and providing emotional and practical support on tap. I am very grateful to have been surrounded by such a supportive bunch of amazing women. Special shout outs to Lorna for being the best hype woman (your encouragement kept me going through the difficult times), and Rhi for making the office a lovely place to be. To my fellow PhD students who have shared this journey with me including Vicky Woof (the best PhD sister), Hannah Long, Hannah Foote, Kate Law, and others – thanks for your friendship and pep talks when I needed them most. I would also like to thank the Manchester Centre for Health Psychology for providing a nurturing environment.

Finally, a huge thank you to my wonderful family and friends for all your support and encouragement over the years. Mum and Dad, my number one supporters in life, thank you for always being there for me, sharing in the highs and lows of this journey – I would not have made it to this point without you both. Adam, your love and positivity have sustained me throughout the past 10 years, and I can't wait for our next adventure.

The Author

Sarah Hindmarch has a first-class Bachelor of Science (Honours) degree in Psychology from the University of Nottingham. She also has a distinction Master of Science (by research) degree in Forensic & Criminological Psychology from the same institution. Sarah has worked as a research associate in the Christie Patient Centred Research team at The Christie NHS Foundation Trust and a research assistant at the University of Manchester.

Thesis structure and rationale for submitting in the Journal Format

From the outset of this PhD, the student has been writing up and submitting studies for publication in peer-reviewed journals. Chapter 2, 4 and 5 have been published in peer-reviewed journals (Cancers, Women's Health, and BMC Women's Health respectively). Chapters 3 and 6 are currently under review (BMC Cancer and BMJ Open respectively). Given the success in publishing research papers throughout this PhD, structuring and submitting the thesis in journal format was deemed most appropriate. An introductory chapter precedes the research papers, and a discussion chapter follows the research papers, to make the thesis a coherent whole. The research papers have been presented as published or submitted, with minor adjustments made to formatting to ensure the thesis maintains a consistent structure (e.g., table numbers, reference formatting).

Contributions of the candidate and co-authors

The candidate, Sarah Hindmarch, undertook the conception and design of all studies in this PhD and wrote the first draft of all papers. The majority of data collection and analysis was conducted by the candidate. The candidate's supervisory team (Prof David French, Dr Sacha Howell and Dr Louise Gorman) contributed to the conceptualisation and design of the studies, advised on data analysis, provided feedback on drafts of the papers, and approved the final versions before submission for publication. The candidate consulted Prof David French and Dr Sacha Howell during the article screening stage of the systematic review for advice on eligibility of some articles. Rhiannon Hawkes, who was a co-author on the systematic review and the two papers resulting from the qualitative study conducted with women, acted as a second-rater for article screening, data extraction and quality appraisal for the systematic review and assisted with data collection and wrote discussion summaries of the focus groups for the qualitative study. Victoria Woof, who was a co-author on the qualitative study with primary care providers, assisted with data collection and wrote discussion summaries of the focus groups. Dr Juliet Usher-Smith, who was a co-author on the qualitative study with primary care providers and the feasibility study protocol paper, contributed to the conceptualisation and design of both studies and advised on recruitment strategies and data analysis for the qualitative study. Prof D. Gareth Evans, who was a co-author on the feasibility study protocol paper, contributed to the conceptualisation and design of the study. All co-authors provided feedback on drafts of the papers they contributed to and approved the final versions before submission for publication.

List of publications and presentations related to this research

Please note that part way through completion of the PhD programme, the candidate changed her surname from Bellhouse to Hindmarch.

Papers accepted for publication

Bellhouse S, Hawkes RE, Howell SJ, Gorman L, French DP. Breast cancer risk assessment and primary prevention advice in primary care: a systematic review of provider attitudes and routine behaviours. Cancers. 2021;13(16):4150.

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk assessment for women aged 30-39 years: a qualitative study of women's views. Womens Health. 2023;19.

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. "I don't know what I'm feeling for": young women's beliefs about breast cancer risk and experiences of breast awareness. BMC Women's Health. 2023;23:312.

Papers submitted for publication

Hindmarch S, Gorman L, Usher-Smith JA, Woof VG, Howell SJ, French DP. Development of a breast cancer risk assessment and primary prevention pathway for women aged 30-39 years: views of UK primary care providers on the role of primary care. BMC Cancer. Under review.

Hindmarch S, Howell SJ, Usher-Smith JA, Gorman L, Evans DG, French DP. The feasibility and acceptability of offering breast cancer risk assessment to general population women aged 30-39 years: a mixed-methods study protocol. BMJ Open. Under review.

Published (not included in this PhD)

Usher-Smith JA, **Hindmarch S,** French DP, Tischkowitz M, Moorthie S, Walter FM., et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636-46.

Conference presentations

Bellhouse S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimates to women aged 30-39 years. European Health Psychology Society Conference, online, August 2021 (oral presentation).

Bellhouse S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimates to women aged 30-39 years: women's views. NCRI Festival: Making cancer research better together, November 2021 (poster presentation).

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. "I don't know what I'm looking for": a qualitative study examining young women's breast awareness. European Health Psychology Society Conference, Bratislava, August 2022 (oral presentation).

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. How should breast cancer risk assessment be delivered to women aged 30-39 years? A qualitative study of women's views. Greater Manchester Cancer Conference, Manchester, October 2022 (poster presentation).

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. "I don't know what I'm feeling for": young women's beliefs about breast cancer risk and experiences of breast awareness. UK Society of Behavioural Medicine 18th Annual Scientific Meeting, Birmingham, March 2023 (oral presentation).

Study days

Bellhouse S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimates to women aged 30-39 years. University of Manchester's Division of Psychology and Mental Health seminar series, Manchester, February 2021 (oral presentation).

Bellhouse S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimates to women aged 30-39 years. University of Manchester's Centre for Health Psychology seminar series, Manchester, June 2021 (oral presentation).

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimation to women aged 30-39 years: women's views. Manchester Cancer Research Centre Postgraduate Research Showcase, Manchester, May 2022 (oral presentation).

Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk estimates to women aged 30-39 years: a qualitative study of women's views. Manchester Breast Centre Symposium, Manchester, July 2022 (oral presentation).

Introduction to chapters

This thesis is presented as a series of papers, with each paper in its own chapter. Chapter 2, 4 and 5 have been published in peer-reviewed journals (Cancers, Women's Health, and BMC Women's Health respectively). Chapters 3 and 6 are currently under review (BMC Cancer and BMJ Open respectively).

Chapter 1 provides an overview of the main topics included in this thesis. Current approaches for breast cancer early detection and prevention and their limitations are discussed. A case is then made for utilising breast cancer risk prediction to inform tailored screening recommendations for screening age women and increase access to screening and preventive strategies for women below screening age. This chapter also synthesises the current state of knowledge regarding the acceptability of implementing breast cancer risk assessment and its implications for risk management from the perspective of both healthcare professionals and women. Limitations of existing research are discussed before the aim and objectives of this thesis are outlined.

Chapter 2 presents a systematic review which aimed to assess the acceptability of primary care involvement in breast cancer risk assessment and primary prevention by synthesising quantitative data on primary care providers' attitudes and routine behaviours. The findings from this systematic review informed the design of a qualitative study with primary care providers which is presented in Chapter 3. This study aimed to understand primary care providers' views on the development and implementation of a breast cancer risk assessment and primary prevention pathway within primary care for women aged 30-39 years. Data were analysed thematically and organised using a framework approach. The findings suggest that primary care

providers are willing to facilitate but not lead the delivery of a breast cancer risk assessment and primary prevention pathway. Collecting the risk factor information and calculating and communicating the risk result were considered the most acceptable stages for primary care to be involved in.

Chapter 4 is a qualitative study with women aged 30-39 years without a strong family history of breast cancer which investigated their views on, and requirements for, the introduction of breast cancer risk assessment to inform the development of an acceptable care pathway. Data were analysed thematically and organised using a framework approach. This study identified women's preferences for access to, and delivery of, breast cancer risk assessment, and their information and support needs with respect to risk assessment and risk communication. During data collection for this study, a large volume of unanticipated data was elicited regarding young women's beliefs about their own breast cancer risk and their experiences of breast self-examination and awareness. Therefore, this data was analysed separately and is reported in Chapter 5. Data were analysed using reflexive thematic analysis. This analysis highlights the need for clear guidance regarding the enactment of breast self-checking behaviours.

The findings from the qualitative study presented in Chapter 4 informed the development of the ongoing Breast CANcer Risk Assessment in Younger women (BCAN-RAY) study. The BCAN-RAY study aims to evaluate a comprehensive breast cancer risk assessment strategy amongst a diverse ethnic and socioeconomic population of women aged 30-39 years without a strong family history of breast cancer. Chapter 6 is a protocol paper describing the planned methods and analyses for the study assessing the feasibility of the breast cancer risk assessment strategy adopted within the BCAN-RAY study. A mixed-methods approach will be

undertaken to explore the impact of the invitation process on health inequalities, identify potential harms and benefits of participation in breast cancer risk assessment, and assess participants' acceptability of the risk assessment process. I have been employed to carry out the planned work following the completion of my PhD studentship.

Finally, Chapter 7 outlines the contribution of this PhD to the wider literature. A summary of the key findings is presented followed by reflections on the methodology used. The contribution of the PhD is then discussed within the context of key uncertainties about the provision of breast cancer risk assessment for young women and recommendations for future research are made.

Overview of the PhD studies

Defining the role of primary care	• Study One (Chapter 2): Systematic review of quantitative literature on the acceptability of primary care involvement in breast cancer risk assessment and primary prevention • Study Two (Chapter 3): Qualitative study recruiting primary care providers
Developing acceptable care pathways	• Study Three (Chapters 4 and 5): Qualitative study recruiting women aged 30-39 years without a strong family history of breast cancer
Assessing feasibility	• Study Four (Chapter 6): Protocol paper for assessing the feasibility of offering breast cancer risk assessment to women aged 30-39 years without a strong family history of breast cancer

Chapter 1. General Introduction

1.1 Breast cancer and screening for women over 50 years

Breast cancer is the most common cancer diagnosed worldwide in women, with over two million cases diagnosed in 2020 [1]. In the UK, the latest estimates from 2018 showed that there were approximately 55,000 new cases of invasive breast cancer per year from 2016 to 2018. Of these cases, one fifth resulted in death [2]. As such, breast cancer is the second most common cause of cancer death in women in the UK [3].

Early detection increases the chance of cure, reduces the need for invasive treatment, which could produce longer term consequences, and ultimately decreases cancer mortality [4]. Cancer screening is key to detect asymptomatic cancers at an earlier stage. The National Health Service breast screening programme (NHSBSP) was introduced in 1988 and was initially a service for women aged 50-64 years. It was extended to women aged 65-69 years between 2001 and 2004 following research demonstrating a significant decrease in breast cancer mortality for this age group [5]. Currently, all women aged 50-70 years are invited every three years to attend for a mammogram.

There has been considerable debate on whether the benefits of screening outweigh the harms [4, 6]. In 2010, the UK government commissioned the 'Independent UK Panel on Breast Cancer Screening' review. The objective was to assess the current evidence base with respect to benefits and harms associated with population-based breast screening programmes. The expert panel examined all available randomized controlled trials (RCT) which suggested an average 20% reduction in mortality in women invited for screening (relative risk of breast cancer with vs without invitation

0·80 (95% CI 0·73–0·89)) [7]. This corresponds to a best estimate of 1,300 deaths from breast cancer being prevented each year in the UK. A similar review was conducted by the EUROSCREEN working group to ascertain the benefits and harms of organised screening programmes in Europe. The calculations in this review were based on more recent observational evidence. The group estimated that breast screening reduced breast cancer mortality by between 25-31% for women invited for screening and by between 38-48% amongst women actually screened [8]. More recently, a review of evidence from both RCTs and observational studies in Europe confirmed that mammographic screening leads to reduced mortality from breast cancer; however, quantification of benefit is still lacking for Eastern Europe [9].

Potential harms associated with population-based breast screening programmes include overdiagnosis. This is when screening leads to the diagnosis of breast cancers that would never have caused any clinically apparent symptoms over the course of a person's lifetime which often, but not always, results in overtreatment [10]. Treatment of an overdiagnosed cancer subjects a patient to the harms of treatment without the benefit of life years gained [11]. Breast cancer confined to the breast ducts, known as ductal carcinoma in situ, is more likely to be associated with overdiagnosis than invasive cancer [12]. Three major studies have examined the frequency of overdiagnosis within the NHSBSP and screening programmes across Europe, with estimates ranging from 4.7-11% amongst women invited for screening, and 3.7-6.5% amongst women screened [7, 8, 13].

Another harm is women experiencing false positives. This is when a woman is recalled due to an observed abnormality on her mammogram to undergo further investigations, but subsequent tests confirm that cancer is not present. During the 2020-2021 screening period, the percentage of all women screened who returned a

false positive result was 3.1% [14]. Experiencing a false positive has been found to be associated with enduring breast cancer-specific psychological distress and some women report reluctance to re-attend subsequent screens as a result [15, 16].

Other harms include the risk of ionising radiation exposure which although small depends on how many times the patient is exposed during a lifetime. It has been estimated that screening women every three years from age 47–73 would cause 3–6 cancers per 10,000 women screened [17]. Finally, all health systems have scarce resources and are faced with opportunity costs; any investment in a screening programme will come at the cost of other health services which could improve health to a greater extent [18]. Therefore, cost effectiveness is an important consideration. The most recent evidence suggests that the NHSBSP is cost-effective in terms of cost per quality-adjusted life year but further economic analysis of the current programme is warranted as more evidence becomes available about the harms of screening [19].

Ultimately, reviews of the evidence conclude that the benefit of reduced mortality outweighs the harms and subsequently the screening programmes should continue. An International Agency for Research on Cancer (IARC) expert working group came to a similar conclusion stating that there is a net benefit from inviting women 50 to 69 years of age to receive screening [20].

Two important caveats should be considered when interpreting this conclusion regarding ratio of benefits to harms. First, it is difficult to assess the effectiveness of breast cancer screening as there have been significant developments in breast cancer treatment since the RCTs were conducted. The proportion of the observed reduction in breast cancer mortality attributable to advances in treatment rather than screening remains unclear [21]. A US study utilising simulation modelling estimated that

advances in treatment between 2002 and 2012 were associated with greater decreases in breast cancer mortality rates than advances in screening. Furthermore, there is a lack of uniformity in guidelines worldwide. Guidelines differ in terms of the screening intervals (the time period between screens) and age groups invited. This poses methodological and logistical challenges, making comparisons difficult and hindering the ability to draw definitive conclusions [22]. For example, an IARC working group concluded that data at present does not allow the most appropriate screening interval to be determined [20].

1.2. Improving the benefit to harm ratio of breast cancer screening

One proposed approach to improve the benefit to harm ratio of breast cancer screening is to offer women screening at a starting age and frequency based on their risk of developing breast cancer (risk-stratified screening) [23, 24]. Significant progress has been made with individual risk assessment for breast cancer through the development of breast cancer risk prediction models. These models aim to predict the risk of breast cancer in asymptomatic individuals based on a combination of established characteristics.

The Breast Cancer Risk Assessment Tool (BCRAT; also known as the Gail model) was the first published breast cancer risk model [25]. Since then, many other models have been developed. Four in common usage are the International Breast Cancer Intervention Study model (IBIS; also referred to as the Tyrer-Cuzick model) [26], Breast Cancer Surveillance Consortium model [27], Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm model (BOADICEA) [28], and BRCAPRO [29]. The latest version of the BOADICEA model is available in the CanRisk tool which provides healthcare professionals and researchers with a user-

friendly interface to carry out multifactorial breast and ovarian cancer risk predictions [30]. Each model differs on the classic risk factors they incorporate into their risk estimates; this includes hormonal and reproductive risk factors, previous biopsies, and hereditary risk components (family history).

Validation studies of breast cancer risk models have been conducted in screening age populations whereby model performance is assessed using calibration and discrimination metrics. Calibration, sometimes referred to as “goodness of fit”, is assessed by comparing the actual number of cases (observed; O) to predicted number of cases (expected; E) in the population under study. This is represented as the O/E ratio statistic. A well-fitting model should have a value close to 1. A value lower than 1 indicates that the model overestimates the incidence of disease whereas a value higher than 1 suggests underestimation. A systematic review found that existing breast cancer risk prediction models demonstrate O/E statistic values of between 0.87 and 1.12 indicating fair to good calibration performance [31]. Discrimination shows the model’s ability to discriminate between individuals in the population who will and will not develop the outcome of interest. It is typically measured using the concordance statistic (C-statistic) which has values between 0.5 and 1.0. A value of 0.5 means the model is no better than chance at predicting the outcome and a value of 0.7 is widely regarded as the minimum needed to conclude that a model has an acceptable level of discriminatory accuracy. If the outcome of interest is binary, then discrimination is often assessed by the area under the receiver operator curve. Breast cancer risk prediction models have poor to fair discriminatory accuracy with C-statistic values of 0.59-0.71 [31, 32].

These findings suggest that additional research is needed to better integrate existing and/or identify new risk factors that contribute to predictive ability [33]. Recently,

researchers have been assessing the added value of other known contributors of risk to improve the predictive abilities of models, namely mammographic density, and single nucleotide polymorphisms. Each of these factors will now be examined in turn.

1.2.1 The role of mammographic density in risk prediction

Mammographic density (MD) is a measure of the amount of fibroglandular tissue compared to adipose tissue (fat) in the breast. Fat absorbs fewer x-rays than fibroglandular tissue and so appears darker on mammograms whereas fibroglandular tissue appears white (see Figure 1.1). In general, women with more fibroglandular tissue have greater MD and increased breast cancer risk [34]. Consequently, MD has been identified as one of the strongest risk factors for breast cancer and previous studies have found it to be largely heritable (approximately 60%) [35-37]. Including MD in risk models has been found to increase their predictive value [38-41].

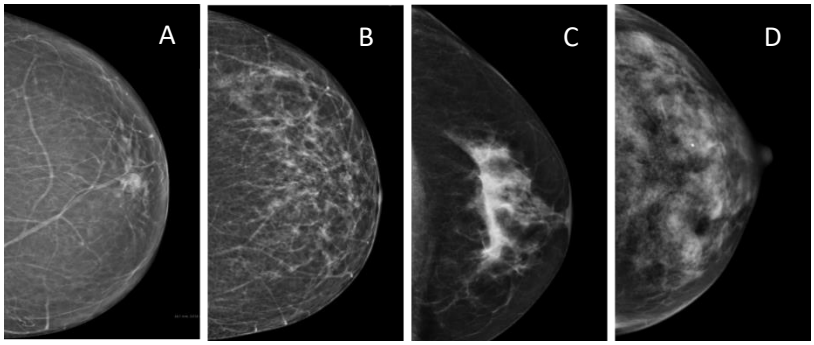


Figure 1.1 Mammograms from four different women with low to high breast density from left to right (A to D). *The white areas are the dense tissue and the darker areas are fat.*

1.2.2 The role of single nucleotide polymorphisms in risk prediction

Genetic testing of women at risk of hereditary breast cancer typically incorporates sequencing genes in which pathogenic variants result in high risk of breast cancer, such as *BRCA1* and *BRCA2*. More recently, moderate risk genes have also been identified. Approximately 3-5% of breast cancer cases are attributable to pathological variants in these genes [42]. Therefore, over recent years there has been an impetus to explore additional sources of familial breast cancer risk. To achieve this, genome wide association studies have sought to identify individual breast cancer susceptibility variants called single-nucleotide polymorphisms (SNPs). Each SNP on its own contributes minimally to risk but when variants are combined a significant increase or decrease in risk can be observed. This is because SNPs occur at higher frequencies than high risk pathological variants and there are now over 300 that have been associated with breast cancer [43, 44]. These risks can be quantified using polygenic risk scores (PRS) which combine the effect of each identified SNP [45]. Overall, improvements in discriminatory accuracy have been observed as a result of incorporating PRS into IBIS, BCRAT, BOADICEA and BRCAPRO [39, 45-49]. However, a major concern about PRS is their ability to accurately assess risk for women from ethnic minority backgrounds given that they are largely based on data from individuals of white European origin [50, 51]. A recent study demonstrated that PRS derived in white European populations overpredicted risk for women of Ashkenazi Jewish descent [52]. Therefore, there is an urgent need to develop PRS specific for other ethnicities because of differences in risk profiles between ethnicities [53].

1.2.3 Conclusion

It is important to note that each risk domain (classic risk factors, MD and SNPs) has been found to offer a unique and independent contribution to risk. Including all three domains has been found to result in better risk stratification with more women identified in the lower and higher risk groups [49, 54, 55].

1.3 The utility of risk prediction in breast cancer screening

Assessing an individual's risk of developing breast cancer at the time of mammographic screening would allow the tailoring of screening practices based on individual variation in risk (risk-stratified screening) and the opportunity for women identified as being at increased risk to be offered preventive strategies [24]. One strategy is encouraging women to engage in health protective behaviours such as not drinking alcohol, eating more healthily and being physically active through provision of weight loss or weight gain prevention interventions. It has been estimated that 15-40% of breast cancer may be preventable by engaging in health protective behaviours [56]. Another preventive strategy is the prescription of risk-reducing medication such as tamoxifen, raloxifene and anastrozole that have been shown to reduce breast cancer incidence by 30-60% [57-59].

In the UK, the Predicting Risk of Cancer At Screening (PROCAS) study was the first study to show that breast cancer risk information can be collected in the context of a population-based mammographic screening programme and communicated to a large number of women with a range of risk estimates. Reassuringly, the introduction of risk assessment did not result in a significant drop in attendance at the subsequent screen and low risk women continued to see the value in attending screening [60]. The PROCAS study team developed an intervention study called Breast Cancer Predict (BC-Predict) which assessed the feasibility of implementing risk

stratification into routine breast cancer screening [61]. This study found that a real-time offer of breast cancer risk assessment including both MD and PRS is feasible and risk feedback can be provided in a timely manner [62]. Although uptake rates to the study overall were generally low, recruitment was much higher when a research practitioner was on site to explain the study and offer a paper questionnaire. This finding suggests that additional personnel are likely to be required for successful implementation.

Recruitment is ongoing for two trials to determine the effectiveness of a risk-based approach at preventing development of later stage breast cancers via uptake of more frequent screening and preventive strategies in women identified as being at increased risk. These are the Women Informed to Screen Depending On Measures of risk (WISDOM) trial in the USA [63] and the My Personal Breast Screening (MyPeBS) trial in six European countries [64].

1.4 Breast cancer risk and screening for women aged under 50 years

Over the past decade, breast cancer incidence has been increasing in pre-menopausal women worldwide [65-70]. More than 10,000 UK women per year are diagnosed with breast cancer before the age of 50 years, with incidence starting to increase exponentially from age 30 (see Figure 1.2). Younger women are also more likely to have aggressive breast cancer subtypes, such as triple negative, which leads to poorer prognosis and outcomes despite intensive and prolonged treatment regimens [71, 72]. Consequently, breast cancer is more frequently lethal in younger women than in those diagnosed aged over 50 years (10-year survival aged <40 years at diagnosis 70% vs 87% in those >50 years [73]. As a result, 2,000 women aged 35-50 years die from their disease per year making breast cancer the leading cause of death in this

population in the UK [74]. Therefore, there is a growing urgency to implement initiatives to identify younger women at higher risk so that screening and preventive strategies can be offered [75].

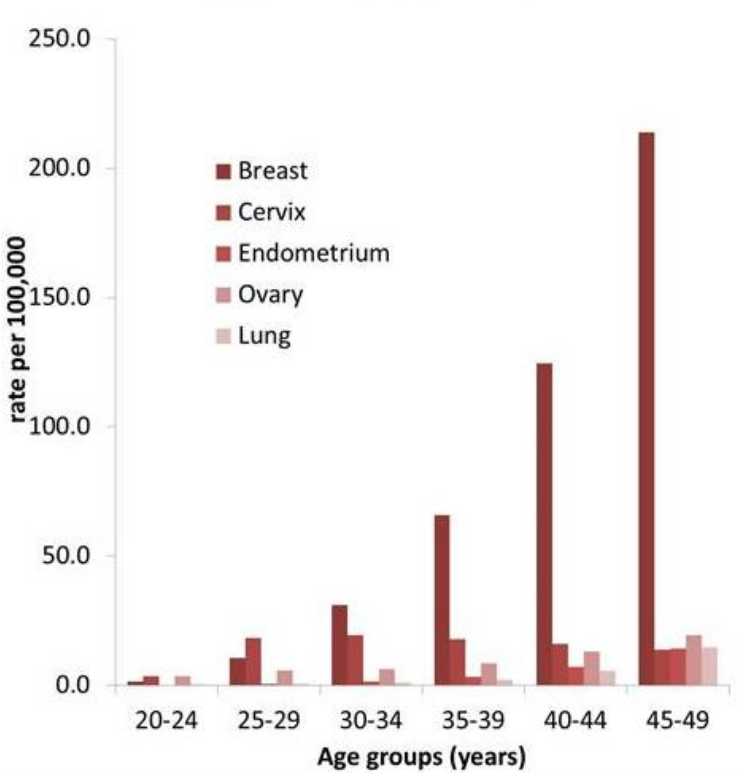


Figure 1.2. Age-specific incidence rates for female cancers in the UK, 2016-18. *Figure created from Cancer Research UK data available for each cancer type from their website [accessed 23rd August 2023].*

Younger women can only currently be identified as high risk in the UK if they present with concerns about family history in primary care or a family history is identified during investigation of a breast problem in secondary care. If certain criteria of family history are fulfilled in line with National Institute for Health and Care Excellence (NICE) guidance, a referral will be made to a specialist family history or genetics clinic for further assessment of risk using validated tools and

discussion of risk management strategies. Risk reduction and management strategies such as risk-reducing medication and earlier access to screening are recommended by NICE for those identified as being at moderate (Tyrer-Cuzick 10-year risk 3-7.9% aged 40 years) or high risk (Tyrer-Cuzick 10-year risk ≥ 8%) of breast cancer [76].

Breast screening using mammography is not recommended as a routine for all women younger than 50 years in the UK. This is due to its relatively low sensitivity, high false positive rate and concerns about the use of diagnostic doses of ionising radiation [77-79]. If mammography was performed routinely from an earlier age, women would be exposed to more doses of ionising radiation which would increase the lifetime attributable risk of breast cancer from radiation. Furthermore, a meta-analysis of RCT and observational evidence showed that population-based breast screening did not confer a significant reduction in breast cancer mortality for women aged 39 to 49 years [80]. However, annual mammographic screening appears to confer a substantial benefit for women aged 35-49 who are at high familial risk. It results in detection/diagnosis of lower stage breast cancers, with predicted improvement in mortality versus unscreened age-matched populations [81, 82]. Therefore, screening women younger than 50 years who have been identified as high risk, in this case by virtue of their family history, is supported.

However, at least 65% of women who develop breast cancer before the age of 50 years do not have a family history and are not currently identified as being at increased risk [73, 83]. Currently, there is no defined systematic mechanism to identify this group of women. Reaching these women represents a major unmet need as they could also benefit from screening and preventive strategies.

1.4.1 The utility of risk prediction for increasing access to screening and preventive strategies

For maximum patient benefit to be realised through uptake of screening and preventive strategies from the age of 40 years, the introduction of comprehensive breast cancer risk assessment from an earlier age (30-39 years) is currently being considered. To date, validation studies of breast cancer risk prediction models are largely limited to screening age populations. However, more recently, the accuracy of risk prediction has been explored using subgroup analyses including those younger than 50 years. BOADICEA and Tyrer-Cuzick models have been found to be well calibrated for women younger than 50 years regardless of BRCA status [32, 84]. In comparison, BCRAT performs poorly and as such is not recommended for the younger age group.

Women younger than 50 years without a strong family history of breast cancer may be particularly suited to risk prediction that incorporates both SNPs and MD. Studies have shown that incorporating a PRS based on either 77 or 313 SNPs improves the accuracy and therefore likely discriminatory power of risk prediction models for women younger than 50 years [48, 85]. Furthermore, SNPs explain a large proportion of risk in women who develop breast cancer in lieu of a family history [45]. Regarding MD, it is well documented that a significantly higher number of premenopausal women have dense breasts in comparison to postmenopausal women [37, 86]. Consequently, the attributable risk of MD for breast cancer has been found to be much higher in younger women (26%) than in older women (7%) [87]. This emphasises the importance of incorporating MD into risk prediction for younger women [88]. Considering these findings, a study exploring the accuracy of

breast cancer risk prediction models with SNPs and MD data incorporated for women younger than 50 years is needed.

1.4.2 Offering breast cancer risk assessment to women aged 30-39 years

A recent review determined that breast cancer risk assessment for women under 50 years currently satisfies many of the standard principles for screening [89]. However, uncertainties remain with respect to the optimal strategy for implementation. The Breast CANcer Risk Assessment in Younger women (BCAN-RAY) case-control study (NCT05305963) is evaluating a comprehensive breast cancer risk assessment strategy for women aged 30-39 years without a strong family history of breast cancer to primarily assess the impact of mammographic density on breast cancer risk in this age group [90].

In line with the Medical Research Council (MRC) Framework for Developing and Evaluating Complex Interventions [91], feasibility work is required before implementation to examine key uncertainties about the provision of breast cancer risk assessment such as its optimal delivery and acceptability. Failure to do so may result in poor uptake of the approach during the implementation phase. The assessment of acceptability is increasingly being recognised as an important component of the development of complex interventions [91, 92]. Over the past decade, a considerable literature base has developed exploring the acceptability of implementing a risk-based screening and prevention programme. Successful implementation of a healthcare intervention depends on the acceptability of the intervention to both intervention deliverers and recipients [93]. Given this, I will now evaluate this evidence base in order to summarise the current state of

knowledge with regards to acceptability from the perspective of both healthcare professionals and women.

1.5 The acceptability of a risk-based screening and prevention programme

1.5.1 Healthcare professionals' views

Many studies have captured the views of primary and secondary care professionals towards involvement in and implementation of a risk-based screening and prevention programme. In this section I will review the evidence base according to the stages of a pathway required to implement such a programme, namely conducting a risk assessment, tailoring of screening practices based on individual variation in risk (risk-stratified screening), and providing primary prevention advice.

1.5.1.1 Attitudes towards involvement in breast cancer risk assessment

Inter-country comparisons have revealed differences in attitudes towards conducting breast cancer risk assessment and management. An on-going debate is evident in the literature regarding who should be responsible for these tasks. For example, a qualitative study found that primary care professionals in Australia perceived breast cancer risk assessment and management to be within the domain of the specialist and as such it was not perceived as a routine primary care duty [94]. In contrast, 96% of 107 primary care professionals surveyed in the USA agreed that breast cancer risk assessment was a primary care provider's responsibility [95].

It is important to interpret these contrasting results within the context of each country's primary care structure and healthcare funding. For example, in the USA, obstetrician-gynaecologists (OB/GYNs) are often considered a primary care speciality as they provide additional primary care services beyond their core remit of

management of women's health [96]. An understanding of the diagnosis and clinical management of hereditary breast and ovarian cancer syndrome is essential for OB/GYNs [97]. Therefore, breast cancer is a more salient topic professionally as supported by the finding that women who see OB/GYNs are more likely to undergo screening for breast cancer compared to those who see other primary care professionals [98]. Furthermore, conversations about breast cancer have been found to occur more often with OB/GYNs than with other types of primary care professionals [99].

Implementation of a risk-based screening and prevention programme warrants the assessment of breast cancer risk for large groups of women. As the first point of healthcare contact for the general population, primary care has been repeatedly identified as the most opportune setting for breast cancer risk assessment and provision of primary prevention advice [100, 101]. Numerous barriers and facilitators to engagement in breast cancer risk assessment have been reported by primary care professionals. Firstly, a perceived lack of knowledge and confidence about cancer risk and its assessment has been described extensively in previous systematic reviews, particularly regarding genetic components of risk [102-104]. The need for additional training in assessing, interpreting, and communicating risk, and more consultation time, have been identified as key facilitators of primary care involvement in a breast cancer risk-based screening and prevention programme [101]. The strength of individual barriers and facilitators have yet to be quantified so it is unclear what components of a risk stratification pathway primary care professionals would consider acceptable to be involved in.

Qualitative studies reveal concerns about conducting a breast cancer risk assessment due to the potential negative impact on rapport; namely it would reduce eye contact

and time available to address anxieties [105]. Some primary care professionals have also questioned the appropriateness of discussing breast cancer risk in a consultation if the woman does not raise it herself as she might not be prepared to receive the information which could cause significant distress [94, 106]. The depth and intrusive nature of some of the questions required for breast cancer risk assessment have been flagged as potentially distressing, with the pregnancy and baby loss questions identified as a particular source of concern [105]. In comparison, secondary care professionals have reported feeling more confident assessing breast cancer risk, identifying a wide range of risk factors relevant to include in breast cancer risk assessment [106, 107].

Several studies in the US have explored the feasibility of conducting breast cancer risk assessment in primary care settings [108-111]. All studies concluded that completing the risk assessment in the waiting room prior to the primary care appointment was a feasible approach as it did not adversely affect clinic flow and resulted in very little additional burden for participants and staff. The only UK study conducted to date showed it was feasible to proactively engage women in familial cancer risk assessment within primary care [112]. Although these findings are promising, it is important to note that the risk assessments did not include assessment of PRS or MD so the feasibility of conducting comprehensive risk assessment in primary care remains unknown.

1.5.1.2 Attitudes towards risk-stratified screening

Both primary and secondary care professionals recognise the value of introducing risk stratification and perceive it as the logical next step for improving the benefit to harm ratio of existing breast cancer screening programmes. The purported benefits

include reducing breast cancer mortality, engaging women in shared decision making about risk-reducing options and reducing anxiety [113-115]. However, healthcare professionals have described potential barriers to successful implementation of risk stratification. Firstly, there is a concern that women may not believe their personal risk estimates. This could lead to requests for inappropriate investigations which would be challenging to manage [106, 115, 116].

Concerns have also been expressed about the accuracy of risk prediction models, notably the impact incomplete information could have on the accuracy of the risk estimate [105, 111, 117]. Apprehension is also evident regarding incorrect adoption of a screening interval if the categorisation of risk level is based on inaccurate information [117].

Healthcare professionals have reported feeling unconvinced by present evidence that adopting a risk-based approach is beneficial for all women. Notably, apprehension regarding the safety and acceptability of a less frequent screening interval for low-risk women has been reported [117-119]. Therefore, there is a need for greater evidence supporting risk stratification, particularly regarding extending screening intervals for low-risk women [120].

Additionally, healthcare professionals have expressed concerns that the introduction of risk stratification could exacerbate existing health inequalities or create new ones [50, 61]. For example, reliance on access to the programme through primary care has the potential to create health inequalities as it could leave women without a family doctor less informed and at risk [106, 115]. Furthermore, current guidelines for management of women at high-risk are vague and inconsistent between geographical

areas which could result in inequitable access to screening and preventive strategies [61].

Secondary care professionals' main concerns adopting a risk-based approach are related to its organisation. Firstly, they are concerned that many moderate risk women could be underserved or missed as specialists are at full capacity managing high risk women and primary care professionals are perceived to lack the skills and knowledge to manage them [107]. Secondly, concerns about the impact of additional workload when implementing risk stratification into cancer screening programmes has been identified as a major determinant of acceptability to secondary care professionals [61, 120]. Evidence from a qualitative study with secondary care professionals [113] demonstrates that the practice of delivering risk-stratified screening was less burdensome in terms of workload than healthcare professionals anticipated prior to delivery [61]. However, a notable limitation of these studies is the lack of representation from primary care professionals who secondary care professionals perceive as integral to the successful implementation of a risk-based screening and prevention programme [113].

1.5.1.3 Attitudes towards providing breast cancer primary prevention advice

Identification of increased risk can also act as a primary prevention opportunity whereby risk-reducing strategies can be discussed and offered. One such strategy is promoting engagement with health protective behaviours. The views of medical specialists and genetic counsellors towards providing information about health protective behaviours during genetic consultation for breast cancer have been sought [121]. Both groups reported not routinely or proactively discussing health protective behaviours during consultations as it was felt that doing so would detract from more pertinent topics such as earlier screening. Ultimately, participants did not feel

comfortable providing general health advice or promoting health protective behaviours as part of their role and believed that primary care professionals were better placed to do this. NICE guidance acknowledges the need to discuss health-related risk factors such as alcohol consumption and weight in relation to breast cancer risk [76]. However, it does not specify at what point in the risk assessment process this should be discussed nor which care setting is appropriate for the discussion to take place.

Another preventive strategy is the prescription of risk-reducing medication. Several studies have demonstrated a global reticence by primary care professionals to discuss and prescribe risk-reducing medication for women at high risk of breast cancer [106, 122-124]. Findings from two surveys suggest that relatively few GPs have ever prescribed risk-reducing medication for this purpose with estimates of 13% and 27% reported [125, 126]. Lack of familiarity with and knowledge of preventive therapy has been identified as an implementation barrier by GPs [61, 123]. This has been supported further in the PROCAS study whereby women encountered difficulties obtaining risk-reducing medication from GPs due to a perceived lack of knowledge of its preventative usage [127].

Another study reported that a quarter of GPs surveyed were not aware of the NICE guideline for prescribing tamoxifen which suggests poor dissemination of the guideline throughout primary care and may explain the lack of familiarity found in other studies [122]. This lack of awareness may also be attributable to the fact that tamoxifen was only licensed by the Medicines and Healthcare products Regulatory Agency for the primary prevention of breast cancer in 2018.

1.5.2 Women's views

Numerous studies have explored how women think and feel about the implementation of a risk-based screening and prevention programme. There are two types of evidence. Most studies have presented risk-based screening and prevention as a hypothetical prospect meaning the findings reflect women's anticipated cognitive and emotional reactions. A smaller evidence base has examined the views of women who have experienced breast cancer risk assessment at the time of mammographic screening and received a personalised breast cancer risk estimate. I will now examine each of these types of evidence in turn. It is important to note that the research findings discussed in this section predominantly reflect the views of women older than 40 years who fulfil the breast screening eligibility criteria of the country they reside in.

1.5.2.1 Risk-based screening and prevention as a hypothetical offer

Generally, most women who have participated in survey studies have reported being in favour of receiving their breast cancer risk [128-132]. A survey study conducted in the UK explored reasons for unwillingness to take up an offer of breast cancer risk assessment [129]. The most common reasons for being unwilling were concern about the worry risk assessment may cause, not wanting to know risk and having already undergone risk assessment.

Findings from qualitative studies suggest that there are concerns about the risk calculation and risk assessment process. For example, some women expressed doubts about the scientific accuracy of the risk prediction model and were concerned about the ability of healthcare professionals to explain the risk result sufficiently [133, 134]. In particular, primary care professionals were perceived as showing a disinterest in breast cancer compared to other diseases and being poorly informed

about breast cancer risk assessment [107]. Differences in willingness to provide certain types of information for the purpose of risk assessment have been found. In a qualitative study, willingness to provide information about family, reproductive history and health behaviours was higher compared with tests assessing polygenic risk and mammographic density [135]. One survey study found that two thirds of women would be comfortable providing genetic information for the purposes of breast cancer risk assessment [130]. Reasons for discomfort sharing genetic information identified by previous studies include this information being passed onto third parties such as employers and medical insurance companies and fear of potential discrimination based on the test results [136, 137]. Women have also expressed concerns about the potential psychological impact of anticipating and receiving personalised breast cancer risk estimates, in the form of increased anxiety or worry about breast cancer [138, 139].

Hypothetical preferences for delivery of risk feedback have been explored. The acceptability of receiving risk feedback in letter format has been found to differ according to the level of risk being communicated. Verbal communication methods (telephone and in person) were preferred for high-risk results as this would provide the opportunity to discuss any concerns and mitigate distress [129, 132, 140]. In contrast, letters were perceived as an acceptable delivery method for low-risk feedback. Some women felt it was important for the feedback to explicitly encourage all women, irrespective of risk level, to contact a healthcare professional should they have any queries about their feedback [140].

Overall, previous studies have found that risk-stratified breast screening is perceived favourably by women if it is supported by safety evidence and aligned with scientific and technological advances [135, 141]. However, several studies have demonstrated

scepticism towards the reason for adopting risk-stratified screening. Some women believed it was motivated by a desire to save money rather than reduce screening harms [133, 134].

The majority of women (85-90%) participating in surveys on this topic would be willing to attend breast screening more frequently if they were identified as high risk [129-132, 142]. However, fewer women report willingness to have less frequent breast screening if identified as at low-risk (Tyrer-Cuzick 10-year risk of ≤ 1.5%) with estimates of acceptance ranging from 20-59%. Results from qualitative research support these findings. Women have reported apprehension about being screened less often as it could result in a dangerous diagnosis being missed [133]. Years of familiarity with the current programme (an 'acquired right') has been identified as a possible reason for women's reluctance to give up mammography screening [136]. Furthermore, some women expressed concern around labelling women 'low risk' as they may disengage from breast cancer screening and preventive strategies [107, 137].

It is important to acknowledge that the aforementioned research is likely to be impacted by self-selection bias. Women have volunteered to participate in research and as such might have more positive views of breast cancer risk assessment and screening which may lead to overestimations of acceptability. This is supported by one survey study which explored reasons for declining participation. A third of non-respondents reported declining because the subject of cancer risk induced discomfort [130].

In comparison to risk-stratified screening, fewer studies have examined attitudes towards preventive and risk-reducing strategies for breast cancer. Few women report

having heard of breast cancer risk-reducing medication, even in samples of women at known increased risk of breast cancer [107, 143]. Additionally, women have reported limited awareness of modifiable risk factors such as alcohol consumption and obesity in relation to reducing breast cancer risk [144, 145]. Furthermore, women have expressed scepticism about the proposed link between health-related behaviours such as alcohol consumption and cancer due to inconsistent and confusing messages in the mainstream media [107, 134]. A review of Australian print media found that articles tended to report controversial study findings, contributing to an inaccurate and contradictory representation of the alcohol-breast cancer link [146].

One survey study has explored Dutch women's preferences for risk-based breast cancer prevention using hypothetical risk scenarios [132]. They found that women were generally in favour of changing health-related behaviours to actively attempt to reduce their risk, with change of diet being more popular than modifying alcohol intake or exercise habits, respectively. Increased willingness to change dietary habits was observed amongst those with higher assigned breast cancer risk. More than half of the women who completed the moderate or high-risk scenario were willing to consider taking risk-reducing medication. Half of the women who were not in favour of risk-reducing medication indicated that they would only like to take medication once diagnosed with breast cancer.

1.5.2.2 Risk-based screening and prevention as a genuine offer

The psychological impact and acceptability of participating in breast cancer risk assessment at the time of mammographic screening has been investigated in the PROCAS and BC-Predict studies using quantitative and qualitative methods. There

is now considerable quantitative evidence from these studies that providing breast cancer risk estimates to women aged 47-73 years recruited via the NHSBSP does not cause any significant adverse effects on anxiety or cancer worry [147, 148]. Notably, the strongest predictor of general anxiety and cancer worry at 3 and 6 months follow-up was the baseline levels of these variables and appeared largely independent of risk estimates [147].

Qualitative studies have explored the experiences of women having their risk assessed as part of routine breast screening and receiving breast cancer risk estimates [149, 150]. Overall, women found it acceptable and valuable to be offered breast cancer risk assessment as part of screening. Consistent with findings of quantitative studies, there was no evidence of long-lasting effects on anxiety or cancer worry following receipt of risk information. Providing statistical information and access to a healthcare professional was found to minimise long-term distress in higher risk groups [149]. Women who received a low-risk estimate found it acceptable and worthwhile to receive a low-risk result [150]. In line with the findings from hypothetical scenarios, women considered less frequent screening for those identified as at low risk to be acceptable if it is supported by safety evidence and not only due to saving money. These findings highlight the importance of effectively communicating the rationale and supporting evidence of a risk-stratified approach to screening if adopted, particularly for changes to breast screening that could be considered de-implementation of a service such as extending the screening interval for low-risk women [150].

Regarding risk feedback, substantially fewer women in the PROCAS study received their risk feedback than originally intended [60]. This was largely attributed to the inconvenience of not being able to receive feedback via a letter. However, some

women in the BC-Predict study who received their risk result by letter alone reported finding it difficult to process their anxiety and digest the information provided to be able to think about how they may mitigate their risk [149]. This suggests that additional support such as pre-made appointments to discuss risk feedback further or follow-up phone calls to arrange appointments may be beneficial for those who are informed of their risk by letter.

The PROCAS and BC-PREDICT studies also investigated uptake of screening and preventive strategies following receipt of breast cancer risk. Weight loss programmes were offered to overweight or obese women in the PROCAS study, irrespective of risk estimate. Women who were informed to be at increased risk of breast cancer were more likely to join and remain in these programmes and consequently lost more weight compared to women not at increased risk [151]. Amongst increased risk groups in the BC-PREDICT study, there was high uptake of opting for additional mammography and risk-reducing medication [62]. Risk consultation attendance was highest for those at high risk and 77.5% of these women opted for risk-reducing medication. This finding is consistent with a systematic review which found that uptake of breast cancer risk-reducing medication is higher in trial settings [152]. This review concluded that further work is needed to increase uptake of breast cancer risk-reducing medication within routine clinical practice.

1.5.3 Summary of acceptability evidence base and limitations of existing research

As the literature review presented here attests, there is a considerable literature base exploring the acceptability of a breast cancer risk-based screening and prevention programme from the perspective of healthcare professionals and women. I will now

summarise the current state of knowledge and highlight the limitations of existing research.

1.5.3.1 Summary of healthcare professionals' views

Barriers to assessing risk and implementing management recommendations are apparent for healthcare professionals, more so primary care professionals. Namely, doubts about the perceived effectiveness and accuracy of breast cancer risk prediction, burden in terms of time pressures and capacity to manage additional workload, and a lack of self-efficacy and knowledge regarding risk assessment and its implications for management. Although aware of the potential benefits of introducing risk stratification, healthcare professionals have expressed a need for robust evidence regarding its safety and acceptability amongst the public, particularly with respect to extending screening intervals for low-risk women. Key feasibility issues for implementing risk-stratified screening into routine breast cancer screening have now been identified, largely from the perspectives of screening professionals based in secondary care. Regarding prevention, primary care professionals have expressed reluctance to discuss and prescribe risk-reducing medication. It is unclear whose responsibility it is to promote engagement with health protective behaviours within the context of reducing breast cancer risk. Secondary care professionals have indicated that primary care professionals are better placed to do this, but no studies have examined the views of primary care professionals.

1.5.3.2 Summary of women's views

Results from hypothetical studies indicate that women perceive the prospect of finding out their personalised breast cancer risk estimate favourably but concerns are

evident regarding data security particularly in relation to genetic information, accuracy of risk prediction, and the psychological impact of anticipating and receiving risk estimates. Overall, women are in favour of risk-stratified screening if supported by safety evidence, with most women indicating willingness to attend breast screening more frequently if they were identified as at high risk. However, women are less accepting of reducing screening provision for low-risk women with acceptance of this dependent on robust evidence demonstrating its safety. Very few studies have examined attitudes towards preventive and risk-reducing strategies for breast cancer. Awareness of modifiable risk factors such as alcohol consumption and obesity and risk-reducing medication appears to be low but findings from one study suggest that women would be receptive to changing health-related behaviours and considering medication in an attempt to reduce breast cancer risk.

Fewer studies have examined the views of women who have experienced breast cancer risk assessment at the time of mammographic screening and received a personalised breast cancer risk estimate. Findings from these studies suggest that concerns about causing adverse psychological impact are unfounded and risk assessment is perceived as an acceptable and valuable addition to the screening offer, irrespective of the risk estimate received. High levels of uptake of additional mammography and risk reducing medication have been observed amongst women identified as being at increased risk.

1.5.3.3 Limitations of existing research

Two important limitations of the existing evidence base should be acknowledged. Much of the research investigating the provision of personalised breast cancer risk estimates has been conducted within the context of implementing a risk-based breast

cancer screening programme. However, this approach will miss younger women eligible for screening and preventive strategies. If a new care pathway were to be introduced offering breast cancer risk assessment to young women, it has been presumed that primary care will assume responsibility for conducting breast cancer risk assessment and providing primary prevention advice. This is due to their access to this population, involvement in risk assessment and prevention for other diseases, and knowledge of a woman's medical history. Although barriers and facilitators to primary care involvement have been identified, a robust and in-depth examination of acceptability has yet to be conducted. Consequently, it is not clear which components of a risk stratification pathway primary care professionals would consider acceptable to be involved in. Furthermore, views of primary care professionals have rarely been captured in qualitative research conducted to date meaning the role of primary care in supporting future risk stratification pathways remains to be determined. Therefore, there is a need to determine the likely role of primary care in a care pathway offering breast cancer risk assessment to younger women outside of an organised breast screening programme.

Moreover, conclusions about the acceptability of implementing breast cancer risk assessment and its implications for risk management for women are almost entirely limited to those who are eligible to attend national breast cancer screening programmes. Therefore, the literature represents the views and needs of women over the age of 40 years which are likely to differ to younger women who have not yet had the opportunity to engage with existing breast screening care pathways. Despite evidence of no significant adverse effects on anxiety or cancer worry following receipt of breast cancer risk estimates in women aged 47-73 years, there is a need to show an absence of adverse effects when setting up a new programme with younger

women for several reasons. Firstly, given their lack of family history of breast cancer, women identified as at increased risk may experience more acute distress due to the result being unexpected. Secondly, being identified as at increased risk between the ages of 30 and 39 years could influence women's reproductive decision-making which may induce feelings of regret over participation in breast cancer risk assessment.

In line with the MRC Framework for Developing and Evaluating Complex Interventions [91], qualitative research is needed to investigate the acceptability and feasibility of offering breast cancer risk assessment from the perspective of primary care professionals and women aged 30-39 years as the intended deliverers and recipients respectively. Such research will address uncertainties about the provision of breast cancer risk assessment such as its optimal delivery and acceptability, allowing care pathways to be developed with a greater likelihood of success during implementation.

1.6 Thesis aims and objectives

This PhD aimed to inform the development of acceptable care pathways for the provision of personalised breast cancer risk assessment and where appropriate, screening or preventive strategies, to women aged 30-39 years without a strong family history of breast cancer. Specific objectives were to: (1) understand how to optimise engagement with the process of breast cancer risk assessment and associated materials, (2) examine and define the likely role of primary care in the care pathway, and (3) assess the feasibility of a strategy to offer breast cancer risk assessment to women aged 30-39 years without a strong family history of breast cancer in a diverse ethnic and socioeconomic geographical region.

1.7 References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49.
2. Cancer Research UK. Breast cancer statistics. [Online]. 2018a [Accessed 24th May 2023]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer.
3. Cancer Research UK. Breast cancer mortality. [Online]. 2018b [Accessed 24th May 2023]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Two.
4. Autier P, Boniol M. Mammography screening: a major issue in medicine. Eur J Cancer. 2018;90:34-62.
5. Department of Health. The NHS Cancer Plan. 2000.
6. Mandrik O, Zielonke N, Meheus F, Severens JLH, Guha N, Herrero Acosta R, et al. Systematic reviews as a 'lens of evidence': determinants of benefits and harms of breast cancer screening. Int J Cancer. 2019;145(4):994-1006.
7. Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M, et al. The benefits and harms of breast cancer screening: an independent review. Br J Cancer. 2013;108(11):2205-40.
8. Paci E. Summary of the evidence of breast cancer service screening outcomes in Europe and first estimate of the benefit and harm balance sheet. J Med Screen. 2012;19(1_suppl):5-13.

9. Zielonke N, Gini A, Jansen EEL, Anttila A, Segnan N, Ponti A, et al. Evidence for reducing cancer-specific mortality due to screening for breast cancer in Europe: a systematic review. Eur J Cancer. 2020;127:191-206.

10. Brodersen J, Schwartz LM, Heneghan C, O'Sullivan JW, Aronson JK, Woloshin S. Overdiagnosis: what it is and what it isn't. BMJ Evid Based Med. 2018;23(1):1-3.

11. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. JAMA. 2014;311(13):1327-35.

12. Morris E, Feig SA, Drexler M, Lehman C. Implications of overdiagnosis: impact on screening mammography practices. Popul Health Manag. 2015;18 (Suppl 1):S3-11.

13. Blyuss O, Dibden A, Massat NJ, Parmar D, Cuzick J, Duffy SW, et al. A case–control study to evaluate the impact of the breast screening programme on breast cancer incidence in England. Cancer Med. 2023;12(2):1878-87.

14. NHS Digital. NHS Breast Screening Programme: England, 2020-2021. [Online]. 2022 [Accessed 24th May 2023]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/breast-screening-programme/england---2020-21/qualitystatement3.

15. Bond M, Pavey T, Welch K, Cooper C, Garside R, Dean S, et al. Psychological consequences of false-positive screening mammograms in the UK. Evid Based Med. 2013;18(2):54-61.

16. Long H, Brooks JM, Harvie M, Maxwell A, French DP. How do women experience a false-positive test result from breast screening? A systematic review and thematic synthesis of qualitative studies. Br J Cancer. 2019;121(4):351-8.

17. Berrington de González A. Estimates of the potential risk of radiation-related cancer from screening in the UK. J Med Screen. 2011;18(4):163-4.

18. Drummond M, Weatherly H, Ferguson B. Economic evaluation of health interventions. BMJ. 2008;337:a1204.

19. Morton R, Sayma M, Sura MS. Economic analysis of the breast cancer screening program used by the UK NHS: should the program be maintained? Breast Cancer: Targets Ther. 2017;9:217-25.

20. Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, et al. Breast-cancer screening — viewpoint of the IARC working group. N Engl J Med. 2015;372(24):2353-8.

21. Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2013(6):CD001877.

22. Begg CB. The mammography controversy. Oncologist. 2002;7(3):174-6.

23. Broeders M, Paci E. The balance sheet of benefits and harms of breast cancer population-based screening in Europe: outcome research, practice and future challenges. Womens Health. 2015;11(6):883-90.

24. Pashayan N, Antoniou AC, Ivanus U, Esserman LJ, Easton DF, French D, et al. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. Nat Rev Clin Oncol. 2020;17(11):687-705.

25. Gail M, Brinton L, Byar D, Corle D, Green S, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989;81(24):1879-86.

26. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med. 2004;23(7):1111-30.

27. Tice JA, Cummings SR, Smith-Bindman R, Ichikawa L, Barlow WE, Kerlikowske K. Using clinical factors and mammographic breast density to estimate breast cancer risk: development and validation of a new predictive model. Ann Intern Med. 2008;148(5):337-47.

28. Antoniou AC, Cunningham AP, Peto J, Evans DG, Lalloo F, Narod SA, et al. The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. Br J Cancer. 2008;98(8):1457-66.

29. Parmigiani G, Berry DA, Aguilar O. Determining carrier probabilities for breast cancer–susceptibility genes BRCA1 and BRCA2. Am J Hum Genet. 1998;62(1):145-58.

30. Carver T, Hartley S, Lee A, Cunningham AP, Archer S, Babb de Villiers C, et al. CanRisk tool—A web interface for the prediction of breast and ovarian cancer risk and the likelihood of carrying genetic pathogenic variants. Cancer Epidemiol Biomarkers Prev. 2021;30(3):469-73.

31. Anothaisintawee T, Teerawattananon Y, Wiratkapun C, Kasamesup V, Thakkinstian A. Risk prediction models of breast cancer: a systematic review of model performances. Breast Cancer Res Treat. 2012;133(1):1-10.

32. Terry MB, Liao Y, Whittemore AS, Leoce N, Buchsbaum R, Zeinomar N, et al. 10-year performance of four models of breast cancer risk: a validation study. Lancet Oncol. 2019;20(4):504-17.

33. Meads C, Ahmed I, Riley RD. A systematic review of breast cancer incidence risk prediction models with meta-analysis of their performance. Breast Cancer Res Treat. 2012;132(2):365-77.

34. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev. 2006;15(6):1159-69.

35. Boyd NF, Dite GS, Stone J, Gunasekara A, English DR, McCredie MRE, et al. Heritability of mammographic density, a risk factor for breast cancer. N Engl J Med. 2002;347(12):886-94.

36. Holowko N, Eriksson M, Kuja-Halkola R, Azam S, He W, Hall P, et al. Heritability of mammographic breast density, density change, microcalcifications, and masses. Cancer Res. 2020;80(7):1590-600.

37. Vachon CM, Sellers TA, Carlson EE, Cunningham JM, Hilker CA, Smalley RL, et al. Strong evidence of a genetic determinant for mammographic density, a major risk factor for breast cancer. Cancer Res. 2007;67(17):8412-8.

38. Brentnall AR, Cohn WF, Knaus WA, Yaffe MJ, Cuzick J, Harvey JA. A case-control study to add volumetric or clinical mammographic density into the Tyrer-Cuzick breast cancer risk model. J Breast Imaging. 2019;1(2):99-106.

39. Vachon CM, Pankratz VS, Scott CG, Haeberle L, Ziv E, Jensen MR, et al. The contributions of breast density and common genetic variation to breast cancer risk. J Natl Cancer Inst. 2015;107(5):dju397.

40. Warwick J, Birke H, Stone J, Warren RML, Pinney E, Brentnall AR, et al. Mammographic breast density refines Tyrer-Cuzick estimates of breast cancer risk in high-risk women: findings from the placebo arm of the International Breast Cancer Intervention Study I. Breast Cancer Res. 2014;16(5):451.

41. Vilmun BM, Vejborg I, Lynge E, Lillholm M, Nielsen M, Nielsen MB, et al. Impact of adding breast density to breast cancer risk models: a systematic review. Eur J Radiol. 2020;127:109019.

42. Bane A, O'Malley FP. Familial breast cancer. In: O'Malley FP, Pinder SE, editors. Breast pathology: a volume in foundations in diagnostic pathology series. London, UK: Churchill Livingstone; 2006. p. 241-8.

43. Mavaddat N, Michailidou K, Dennis J, Lush M, Fachal L, Lee A, et al. Polygenic risk scores for prediction of breast cancer and breast cancer subtypes. Am J Hum Genet. 2019;104(1):21-34.

44. Zheng W, Zhang B, Cai Q, Sung H, Michailidou K, Shi J, et al. Common genetic determinants of breast-cancer risk in East Asian women: a collaborative study of 23 637 breast cancer cases and 25 579 controls. Hum Mol Genet. 2013;22(12):2539-50.

45. Evans D, Harkness EF, Brentnall AR, van Veen EM, Astley SM, Byers H, et al. Breast cancer pathology and stage are better predicted by risk stratification models that include mammographic density and common genetic variants. Breast Cancer Res Treat. 2019;176(1):141-8.

46. Fung SM, Wong XY, Lee SX, Miao H, Hartman M, Wee H-L. Performance of single-nucleotide polymorphisms in breast cancer risk prediction models: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev. 2019;28(3):506-21.

47. Gail MH. Discriminatory accuracy from single-nucleotide polymorphisms in models to predict breast cancer risk. J Natl Cancer Inst. 2008;100(14):1037-41.

48. Hurson AN, Pal Choudhury P, Gao C, Hüsing A, Eriksson M, Shi M, et al. Prospective evaluation of a breast-cancer risk model integrating classical risk factors and polygenic risk in 15 cohorts from six countries. Int J Epidemiol. 2021;50(6):1897-911.

49. van Veen EM, Brentnall AR, Byers H, Harkness EF, Astley SM, Sampson S, et al. Use of single-nucleotide polymorphisms and mammographic density plus classic risk factors for breast cancer risk prediction. JAMA Oncol. 2018;4(4):476-82.

50. McWilliams L, Evans DG, Payne K, Harrison F, Howell A, Howell SJ, et al. Implementing risk-stratified breast screening in England: an agenda setting meeting. Cancers. 2022;14(19):4636.

51. Roberts E, Howell S, Evans DG. Polygenic risk scores and breast cancer risk prediction. The Breast. 2023;67:71-7.

52. Roberts E, van Veen EM, Byers H, Barnett-Griness O, Gronich N, Lejbkowicz F, et al. Breast cancer polygenic risk scores derived in White European populations are not calibrated for women of Ashkenazi Jewish descent. Genet Med. 2023;25(9):100846.

53. Evans DG, van Veen EM, Byers H, Roberts E, Howell A, Howell SJ, et al. The importance of ethnicity: are breast cancer polygenic risk scores ready for women who are not of White European origin? Int J Cancer. 2022;150(1):73-9.

54. Brentnall AR, Harkness EF, Astley SM, Donnelly LS, Stavrinos P, Sampson S, et al. Mammographic density adds accuracy to both the Tyrer-Cuzick and Gail breast cancer risk models in a prospective UK screening cohort. Breast Cancer Res. 2015;17(1):147.

55. Brentnall AR, van Veen EM, Harkness EF, Rafiq S, Byers H, Astley SM, et al. A case-control evaluation of 143 single nucleotide polymorphisms for breast cancer risk stratification with classical factors and mammographic density. Int J Cancer. 2020;146(8):2122-9.

56. Parkin DM, Boyd L, Walker L. 16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. Br J Cancer. 2011;105(2):S77-81.

57. Cuzick J, Sestak I, Bonanni B, Costantino JP, Cummings S, DeCensi A, et al. Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. Lancet. 2013;381(9880):1827-34.

58. Cuzick J, Sestak I, Cawthorn S, Hamed H, Holli K, Howell A, et al. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. Lancet Oncol. 2015;16(1):67-75.

59. Cuzick J, Sestak I, Forbes JF, Dowsett M, Cawthorn S, Mansel RE, et al. Use of anastrozole for breast cancer prevention (IBIS-II): long-term results of a randomised controlled trial. Lancet. 2020;395(10218):117-22.

60. Evans D, Donnelly LS, Harkness EF, Astley SM, Stavrinos P, Dawe S, et al. Breast cancer risk feedback to women in the UK NHS breast screening population. Br J Cancer. 2016;114:1045-52.

61. French DP, Woof VG, Ruane H, Evans DG, Ulph F, Donnelly LS. The feasibility of implementing risk stratification into a national breast cancer screening programme: a focus group study investigating the perspectives of healthcare personnel responsible for delivery. BMC Womens Health. 2022;22(1):142.

62. Evans DGR, McWilliams L, Astley S, Brentnall AR, Cuzick J, Dobrashian R, et al. Quantifying the effects of risk-stratified breast cancer screening when delivered in real time as routine practice versus usual screening: the BC-Predict non-randomised controlled study (NCT04359420). Br J Cancer. 2023;128:2063–71.

63. Esserman LJ, Anton-Culver H, Borowsky A, Brain S, Cink T, Crawford B, et al. The WISDOM Study: breaking the deadlock in the breast cancer screening debate. NPJ Breast Cancer. 2017;3(1):34.

64. UNICANCER. My Personalized Breast Screening (MyPeBS). ClinicalTrials.gov identifier: NCT03672331. [Online]. 2018 [Accessed 26th May 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT03672331.

65. Baeyens-Fernández JA, Molina-Portillo E, Pollán M, Rodríguez-Barranco M, Del Moral R, Arribas-Mir L, et al. Trends in incidence, mortality and survival in women with breast cancer from 1985 to 2012 in Granada, Spain: a population-based study. BMC Cancer. 2018;18(1):781.

66. Dimitrova N, Znaor A, Agius D, Eser S, Sekerija M, Ryzhov A, et al. Breast cancer in South-Eastern European countries since 2000: rising incidence and decreasing mortality at young and middle ages. Eur J Cancer. 2017;83:43-55.

67. Ibrahim AS, Khaled HM, Mikhail NNH, Baraka H, Kamel H. Cancer incidence in Egypt: results of the national population-based cancer registry program. J Cancer Epidemiol. 2014;2014:437971.

68. Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. JAMA. 2013;309(8):800-5.

69. Keramatinia A, Mousavi-Jarrahi S-H, Hiteh M, Mosavi-Jarrahi A. Trends in incidence of breast cancer among women under 40 in Asia. Asian Pac J Cancer Prev. 2014;15(3):1387-90.

70. Leclère B, Molinié F, Trétarre B, Stracci F, Daubisse-Marliac L, Colonna M. Trends in incidence of breast cancer among women under 40 in seven European countries: A GRELL cooperative study. Cancer Epidemiol. 2013;37(5):544-9.

71. Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2− advanced breast cancer: focus on special considerations and latest advances. Clin Cancer Res. 2018;24(21):5206-18.

72. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep. 2017;7(1):11625.

73. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. Lancet Oncol. 2018;19(2):169-80.

74. Office for National Statistics. Deaths registered in England and Wales: 2021 [Online]. 2022 [Accessed 26th May 2023]. Available from: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregistrationsummarytables/2021.

75. Kudela E, Samec M, Kubatka P, Nachajova M, Laucekova Z, Liskova A, et al. Breast cancer in young women: status quo and advanced disease management by a predictive, preventive, and personalized approach. Cancers. 2019;11(11):1791.

76. National Institute for Health and Care Excellence (NICE). Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [updated 2019 Nov] (Clinical Guideline [CG164]). [Online]. 2013 [Accessed 26th May 2023]. Available from: https://www.nice.org.uk/guidance/cg164/chapter/Recommendations.

77. Buist DSM, Porter PL, Lehman C, Taplin SH, White E. Factors contributing to mammography failure in women aged 40–49 years. J Natl Cancer Inst. 2004;96(19):1432-40.

78. Rijnsburger AJ, Obdeijn I-M, Kaas R, Tilanus-Linthorst MMA, Boetes C, Loo CE, et al. BRCA1-associated breast cancers present differently from BRCA2-associated and familial cases: long-term follow-up of the Dutch MRISC screening study. J Clin Oncol. 2010;28(36):5265-73.

79. Shah TA, Guraya SS. Breast cancer screening programs: review of merits, demerits, and recent recommendations practiced across the world. J Microsc Ultrastruct. 2017;5(2):59-69.

80. Nelson HD, Fu R, Cantor A, Pappas M, Daeges M, Humphrey L. Effectiveness of breast cancer screening: systematic review and meta-analysis to update the 2009 US Preventive Services Task Force recommendation. Ann Intern Med. 2016;164(4):244-55.

81. Evans D, Thomas S, Caunt J, Roberts L, Howell A, Wilson M, et al. Mammographic surveillance in women aged 35–39 at enhanced familial risk of breast cancer (FH02). Fam Cancer. 2014;13(1):13-21.

82. FH01 Collaborative Teams. Mammographic surveillance in women younger than 50 years who have a family history of breast cancer: tumour

characteristics and projected effect on mortality in the prospective, single-arm, FH01 study. Lancet Oncol. 2010;11(12):1127-34.

83. Eccles BK, Copson ER, Cutress RI, Maishman T, Altman DG, Simmonds P, et al. Family history and outcome of young patients with breast cancer in the UK (POSH study). Br J Surg. 2015;102(8):924-35.

84. Phillips K-A, Liao Y, Milne RL, MacInnis RJ, Collins IM, Buchsbaum R, et al. Accuracy of risk estimates from the iPrevent breast cancer risk assessment and management tool. JNCI Cancer Spectr. 2019;3(4):pkz066.

85. Dite GS, MacInnis RJ, Bickerstaffe A, Dowty JG, Allman R, Apicella C, et al. Breast cancer risk prediction using clinical models and 77 independent risk-associated SNPs for women aged under 50 years: Australian breast cancer family registry. Cancer Epidemiol Biomarkers Prev. 2016;25(2):359-65.

86. Yankaskas BC, Haneuse S, Kapp JM, Kerlikowske K, Geller B, Buist DSM, et al. Performance of first mammography examination in women younger than 40 years. J Natl Cancer Inst. 2010;102(10):692-701.

87. Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med. 2007;356(3):227-36.

88. Nelson HD, Zakher B, Cantor A, Fu R, Griffin J, O'Meara ES, et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med. 2012;156(9):635-48.

89. Usher-Smith JA, Hindmarch S, French DP, Tischkowitz M, Moorthie S, Walter FM, et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636–46.

90. Manchester University NHS Foundation Trust. Breast CANcer Risk Assessment in Younger women: BCAN-RAY (BCAN-RAY). ClinicalTrials.gov identifier: NCT04336904. [Online]. 2022 [Accessed 19th April 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05305963.

91. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061.

92. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015;350:h1258.

93. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Serv Res. 2017;17(1):88.

94. Phillips K-A, Steel EJ, Collins I, Emery J, Pirotta M, Mann GB, et al. Transitioning to routine breast cancer risk assessment and management in primary care: what can we learn from cardiovascular disease? Aust J Prim Health. 2016;22(3):255-61.

95. Sabatino SA, McCarthy EP, Phillips RS, Burns RB. Breast cancer risk assessment and management in primary care: provider attitudes, practices, and barriers. Cancer Detect Prev. 2007;31(5):375-83.

96. Guerra CE, Sherman M, Armstrong K. Diffusion of breast cancer risk assessment in primary care. J Am Board Fam Med. 2009;22(3):272-9.

97. Meaney-Delman D, Bellcross CA. Hereditary breast/ovarian cancer syndrome: a primer for obstetricians/gynecologists. Obstet Gynecol Clin North Am. 2013;40(3):475-512.

98. Stormo AR, Saraiya M, Hing E, Henderson JT, Sawaya GF. Women's clinical preventive services in the United States: who is doing what? JAMA Intern Med. 2014;174(9):1512-4.

99. Lunsford NB, Sapsis KF, Smither B, Reynolds J, Wilburn B, Fairley T. Young women's perceptions regarding communication with healthcare providers about breast cancer, risk, and prevention. J Womens Health. 2017;27(2):162-70.

100. Dent T, Jbilou J, Rafi I, Segnan N, Törnberg S, Chowdhury S, et al. Stratified cancer screening: the practicalities of implementation. Public Health Genom. 2013;16(3):94-9.

101. Rainey L, van der Waal D, Jervaeus A, Wengström Y, Evans DG, Donnelly LS, et al. Are we ready for the challenge of implementing risk-based breast cancer screening and primary prevention? The Breast. 2018;39:24-32.

102. Hamilton JG, Abdiwahab E, Edwards HM, Fang M-L, Jdayani A, Breslau ES. Primary care providers' cancer genetic testing-related knowledge, attitudes, and communication behaviors: a systematic review and research agenda. J Gen Intern Med. 2017;32(3):315-24.

103. Laforest F, Kirkegaard P, Mann B, Edwards A. Genetic cancer risk assessment in general practice: systematic review of tools available, clinician attitudes, and patient outcomes. Br J Gen Pract. 2019;69(679):e97-105.

104. Mikat-Stevens NA, Larson IA, Tarini BA. Primary-care providers' perceived barriers to integration of genetics services: a systematic review of the literature. Genet Med. 2015;17(3):169-76.

105. Archer S, Babb de Villiers C, Scheibl F, Carver T, Hartley S, Lee A, et al. Evaluating clinician acceptability of the prototype CanRisk tool for predicting risk of breast and ovarian cancer: A multi-methods study. PLoS One. 2020;15(3):e0229999.

106. Collins IM, Steel E, Mann GB, Emery JD, Bickerstaffe A, Trainer A, et al. Assessing and managing breast cancer risk: clinicians' current practice and future needs. The Breast. 2014;23(5):644-50.

107. Keogh LA, Steel E, Weideman P, Butow P, Collins IM, Emery JD, et al. Consumer and clinician perspectives on personalising breast cancer prevention information. The Breast. 2019;43:39-47.

108. Anderson EE, Tejeda S, Childers K, Stolley MR, Warnecke RB, Hoskins KF. Breast cancer risk assessment among low-income women of color in primary care: a pilot study. J Oncol Pract. 2015;11(4):e460-7.

109. Hoskins KF, Tejeda S, Vijayasiri G, Chukwudozie IB, Remo MH, Shah HA, et al. A feasibility study of breast cancer genetic risk assessment in a federally qualified health center. Cancer. 2018;124(18):3733-41.

110. Kaplan CP, Karliner L, Lee A, Livaudais-Toman J, Tice JA, Ozanne E. Acceptability of an mHealth breast cancer risk-reduction intervention promoting risk assessment, education, and discussion of risk in the primary care setting. MHealth. 2021;7:54.

111. Owens WL, Gallagher TJ, Kincheloe MJ, Ruetten VL. Implementation in a large health system of a program to identify women at high risk for breast cancer. J Oncol Pract. 2011;7(2):85-8.

112. Qureshi N, Dutton B, Weng S, Sheehan C, Chorley W, Robertson JFR, et al. Improving primary care identification of familial breast cancer risk using proactive invitation and decision support. Fam Cancer. 2021;20(1):13-21.

113. Hawkins R, McWilliams L, Ulph F, Evans DG, French DP. Healthcare professionals' views following implementation of risk stratification into a national breast cancer screening programme. BMC Cancer. 2022;22(1):1058.

114. Laza-Vásquez C, Hernández-Leal MJ, Carles-Lavila M, Pérez-Lacasta MJ, Cruz-Esteve I, Rué M, et al. Barriers and facilitators to the implementation of a personalized breast cancer screening program: views of Spanish health professionals. Int J Environ Res Public Health. 2022;19(3):1406.

115. Puzhko S, Gagnon J, Simard J, Knoppers BM, Siedlikowski S, Bartlett G. Health professionals' perspectives on breast cancer risk stratification: understanding evaluation of risk versus screening for disease. Public Health Rev. 2019;40(1):2.

116. Rainey L, van der Waal D, Donnelly LS, Evans DG, Wengström Y, Broeders M. Women's decision-making regarding risk-stratified breast cancer screening and prevention from the perspective of international healthcare professionals. PLoS One. 2018;13(6):e0197772.

117. Woof VG, McWilliams L, Donnelly LS, Howell A, Evans DG, Maxwell AJ, et al. Introducing a low-risk breast screening pathway into the NHS Breast Screening Programme: views from healthcare professionals who are

delivering risk-stratified screening. Womens Health. 2021;17:17455065211009746.

118. Ayoub A, Lapointe J, Nabi H, Pashayan N. Risk-stratified breast cancer screening incorporating a polygenic risk score: A survey of UK general practitioners' knowledge and attitudes. Genes. 2023;14(3):732.

119. Laza-Vásquez C, Codern-Bové N, Cardona-Cardona À, Hernández-Leal MJ, Pérez-Lacasta MJ, Carles-Lavila M, et al. Views of health professionals on risk-based breast cancer screening and its implementation in the Spanish National Health System: a qualitative discussion group study. PLoS One. 2022;17(2):e0263788.

120. Taylor LC, Law K, Hutchinson A, Dennison RA, Usher-Smith JA. Acceptability of risk stratification within population-based cancer screening from the perspective of healthcare professionals: a mixed methods systematic review and recommendations to support implementation. PLoS One. 2023;18(2):e0279201.

121. Rees G, Young M-A, Gaff C, Martin PR. A qualitative study of health professionals' views regarding provision of information about health-protective behaviors during genetic consultation for breast cancer. J Genet Couns. 2006;15(2):95-104.

122. Smith SG, Foy R, McGowan JA, Kobayashi LC, DeCensi A, Brown K, et al. Prescribing tamoxifen in primary care for the prevention of breast cancer: a national online survey of GPs' attitudes. Br J Gen Pract. 2017;67(659):e414-27.

123. Smith SG, Side L, Meisel SF, Horne R, Cuzick J, Wardle J. Clinician-reported barriers to implementing breast cancer chemoprevention in the UK: a qualitative investigation. Public Health Genom. 2016;19(4):239-49.

124. Sutherland S, Meiser B, Kaur R, Mitchell G, Kirk J, Peate M, et al. Assessing the medical workforces perceived barriers to the prescription of risk-reducing medication for women at high-risk of breast cancer. Breast J. 2019;25(1):34-40.

125. Armstrong K, Quistberg DA, Micco E, Domchek S, Guerra C. Prescription of tamoxifen for breast cancer prevention by primary care physicians. JAMA Intern Med. 2006;166(20):2260-5.

126. Corbelli J, Borrero S, Bonnema R, McNamara M, Kraemer K, Rubio D, et al. Use of the Gail model and breast cancer preventive therapy among three primary care specialties. J Womens Health. 2014;23(9):746-52.

127. Rainey L, van der Waal D, Jervaeus A, Donnelly LS, Evans DG, Hammarström M, et al. European women's perceptions of the implementation and organisation of risk-based breast cancer screening and prevention: a qualitative study. BMC Cancer. 2020;20(1):247.

128. Fisher BA, Wilkinson L, Valencia A. Women's interest in a personal breast cancer risk assessment and lifestyle advice at NHS mammography screening. J Public Health. 2016;39(1):113-21.

129. Ghanouni A, Sanderson SC, Pashayan N, Renzi C, von Wagner C, Waller J. Attitudes towards risk-stratified breast cancer screening among women in England: a cross-sectional survey. J Med Screen. 2019;27(3):138-45.

130. Koitsalu M, Sprangers MAG, Eklund M, Czene K, Hall P, Grönberg H, et al. Public interest in and acceptability of the prospect of risk-stratified screening for breast and prostate cancer. Acta Oncol. 2016;55(1):45-51.

131. Mbuya Bienge C, Pashayan N, Brooks JD, Dorval M, Chiquette J, Eloy L, et al. Women's views on multifactorial breast cancer risk assessment and risk-stratified screening: a population-based survey from four provinces in Canada. J Pers Med. 2021;11(2):95.

132. Rainey L, van der Waal D, Broeders MJM. Dutch women's intended participation in a risk-based breast cancer screening and prevention programme: a survey study identifying preferences, facilitators and barriers. BMC Cancer. 2020;20(1):965.

133. He X, Schifferdecker KE, Ozanne EM, Tosteson ANA, Woloshin S, Schwartz LM. How do women view risk-based mammography screening? A qualitative study. J Gen Intern Med. 2018;33(11):1905-12.

134. Rainey L, Jervaeus A, Donnelly LS, Evans DG, Hammarström M, Hall P, et al. Women's perceptions of personalized risk-based breast cancer screening and prevention: an international focus group study. Psychooncology. 2019;28(5):1056-62.

135. Kelley-Jones C, Scott S, Waller J. UK women's views of the concepts of personalised breast cancer risk assessment and risk-stratified breast screening: a qualitative interview study. Cancers. 2021;13(22):5813.

136. Henneman L, Timmermans DR, Bouwman CM, Cornel MC, Meijers-Heijboer H. 'A low risk is still a risk': exploring women's attitudes towards genetic testing for breast cancer susceptibility in order to target disease prevention. Public Health Genom. 2011;14(4-5):238-47.

137. Lippey J, Keogh LA, Mann GB, Campbell IG, Forrest LE. “A natural progression”: Australian women's attitudes about an individualized breast screening model. Cancer Prev Res. 2019;12(6):383-90.

138. Liow JJ, Lim ZL, Sim TM, Ho PJ, Goh S-A, Choy SD, et al. "It will lead you to make better decisions about your health" - a focus group and survey study on women's attitudes towards risk-based breast cancer screening and personalised risk assessments. Curr Oncol. 2022;29(12):9181-98.

139. Sierra MA, Wheeler JCW, Devereux L, Trainer AH, Keogh L. Exploring implementation of personal breast cancer risk assessments. J Pers Med. 2021;11(10):992.

140. Woof VG, Ruane H, French DP, Ulph F, Qureshi N, Khan N, et al. The introduction of risk stratified screening into the NHS Breast Screening Programme: views from British-Pakistani women. BMC Cancer. 2020;20(1):452.

141. Taylor LC, Hutchinson A, Law K, Shah V, Usher-Smith JA, Dennison RA. Acceptability of risk stratification within population-based cancer screening from the perspective of the general public: a mixed-methods systematic review. Health Expect. 2023;26(3):989-1008.

142. Meisel SF, Pashayan N, Rahman B, Side L, Fraser L, Gessler S, et al. Adjusting the frequency of mammography screening on the basis of genetic risk: attitudes among women in the UK. The Breast. 2015;24(3):237-41.

143. Macdonald C, Saunders CM, Keogh LA, Hunter M, Mazza D, McLachlan SA, et al. Breast cancer chemoprevention: use and views of Australian women and their clinicians. Cancer Prev Res. 2021;14(1):131-44.

144. Meyer SB, Foley K, Olver I, Ward PR, McNaughton D, Mwanri L, et al. Alcohol and breast cancer risk: middle-aged women's logic and recommendations for reducing consumption in Australia. PLoS One. 2019;14(2):e0211293.

145. Nickel B, Armiger J, Saunders C, Vincent W, Dodd RH, Temple A, et al. "I haven't had that information, even though I think I'm really well-informed about most things": a qualitative focus group study on Australian women's understanding and views of potentially modifiable risk factors for breast cancer. BMC Womens Health. 2023;23(1):211.

146. Rudge A, Foley K, Lunnay B, Miller ER, Batchelor S, Ward PR. How are the links between alcohol consumption and breast cancer portrayed in Australian newspapers?: a paired thematic and framing media analysis. Int J Environ Res Public Health. 2021;18(14):7657.

147. French DP, McWilliams L, Bowers S, Woof VG, Harrison F, Ruane H, et al. Psychological impact of risk-stratified screening as part of the NHS Breast Screening Programme: multi-site non-randomised comparison of BC-Predict versus usual screening (NCT04359420). Br J Cancer. 2023;128:1548-58.

148. French DP, Southworth J, Howell A, Harvie M, Stavrinos P, Watterson D, et al. Psychological impact of providing women with personalised 10-year breast cancer risk estimates. Br J Cancer. 2018;118(12):1648-57.

149. McWilliams L, Ruane H, Ulph F, Woof VG, Harrison F, Evans DG, et al. What do women think about having received their breast cancer risk as part of a risk-stratified NHS Breast Screening Programme? A qualitative study. Br J Cancer. 2023;129:356–65

150. McWilliams L, Woof VG, Donnelly LS, Howell A, Evans DG, French DP. Extending screening intervals for women at low risk of breast cancer: do they find it acceptable? BMC Cancer. 2021;21(1):637.

151. Harvie M, Pegington M, French D, Cooper G, McDiarmid S, Howell A, et al. Breast cancer risk status influences uptake, retention and efficacy of a weight loss programme amongst breast cancer screening attendees: two randomised controlled feasibility trials. BMC Cancer. 2019;19(1):1089.

152. Smith SG, Sestak I, Forster A, Partridge A, Side L, Wolf MS, et al. Factors affecting uptake and adherence to breast cancer chemoprevention: a systematic review and meta-analysis. Ann Oncol. 2016;27(4):575-90.

Chapter 2. Breast cancer risk assessment and primary prevention advice in primary care: a systematic review of provider attitudes and routine behaviours

Journal:	Cancers
Submission status:	Published
Journal article reference:	Bellhouse S, Hawkes RE, Howell SJ, Gorman L, French DP (2021). Breast cancer risk assessment and primary prevention advice in primary care: a systematic review of provider attitudes and routine behaviours. Cancers, 13(16), 4150.

2.1 Simple summary

There is growing international interest in adopting a risk-based approach to breast cancer screening, where an individual's risk would inform screening practices. It has been suggested that primary care will contribute to the delivery of this service by conducting risk assessment and providing primary prevention advice. The aim of our review was to understand what primary care providers think and feel about performing these tasks by examining their attitudes and typical activity in clinical practice (routine behaviours). The results suggest that primary care providers mainly assess breast cancer risk by collecting family history information but feel less comfortable advising on risk-reducing medications. Primary care will need to proactively assess breast cancer risk for women to get the most benefit from risk-based screening and prevention. To promote risk assessment and prevention activities, improved education/training and changes to resources (integrated risk assessment tools, better patient materials etc.) will be necessary.

2.2 Abstract

Implementing risk-stratified breast cancer screening is being considered internationally. It has been suggested that primary care will need to take a role in delivering this service, including risk assessment and provision of primary prevention advice. This systematic review aimed to assess the acceptability of these tasks to primary care providers. Five databases were searched up to July-August 2020, yielding 29 eligible studies, of which twenty-seven were narratively synthesised. The review was pre-registered (PROSPERO: CRD42020197676). Primary care providers report frequently collecting breast cancer family history information, but rarely using quantitative tools integrating additional risk factors.

Primary care providers reported high levels of discomfort and low confidence with respect to risk-reducing medications although very few reported doubts about the evidence base underpinning their use. Insufficient education/training and perceived discomfort conducting both tasks were notable barriers. Primary care providers are more likely to accept an increased role in breast cancer risk assessment than advising on risk-reducing medications. To realise the benefits of risk-based screening and prevention at a population level, primary care will need to proactively assess breast cancer risk and advise on risk-reducing medications. To facilitate this, adaptations to infrastructure such as integrated tools are necessary in addition to provision of education.

2.3 Introduction

Population based screening programmes aim to detect asymptomatic cancers at an earlier stage to reduce mortality rates and the need for aggressive treatments associated with long term morbidities [1]. A substantial reduction in breast cancer related mortality has been observed since the introduction of mammographic screening programmes [2,3]. However, harms of breast cancer screening include overdiagnosis and false positive test results. Overdiagnosis refers to the diagnosis of breast cancers via screening that would never have caused any clinically apparent symptoms over the course of a person's lifetime [4]. A false positive result is an abnormality on a screening test that necessitates further investigations, ultimately ruling out the presence of cancer. Whether the benefits of screening outweigh the known harms has been much debated [2,5].

Adopting an alternative risk-based approach to breast cancer screening has the potential to improve the benefit to harm ratio [6]. The development of risk algorithms, such as the Gail and Tyrer-Cuzick models, has made estimation of an individual's breast cancer risk possible [7,8]. The provision of personalised breast cancer risk estimates would allow screening and prevention services to be offered that are commensurate with degree of risk, thus improving the benefit to harm ratios [9,10]. In the UK, the Predicting Risk of Cancer At Screening (PROCAS) study demonstrated that breast cancer risk information can be collected and communicated to women participating in a population-based mammographic screening programme [11]. International trials are currently ongoing to establish the effectiveness of a risk-based screening regimen in comparison to standard screening practices [12,13].

A key benefit of risk estimation is the ability to identify women at increased risk, affording them the opportunity to benefit from preventative strategies. There are two strategies that have proven benefit in reducing breast cancer risk. The use of selective oestrogen-receptor modulators and aromatase inhibitors, commonly referred to as chemoprevention or risk-reducing medication, have been shown to reduce breast cancer incidence [14,15]. Furthermore, evidence suggests 15–40% of breast cancers may be preventable by engaging in health-related behaviours such as increased physical activity and reduced alcohol intake [16]. Clinical guidance acknowledges the need to discuss lifestyle related risk factors in relation to breast cancer risk but the care setting where this discussion should take place is not specified [17].

As the first point of healthcare contact for the general population, primary care has been repeatedly identified as the most opportune setting to conduct breast cancer risk assessment [18,19]. Secondly, primary care providers have a critical role in delivering preventive health care services to the general population as evidenced by their current role in assessment and management of cardiovascular and diabetes risk [20,21].

As the likely roles of primary care in delivering risk-based screening and prevention will be risk assessment and provision of primary prevention advice including prescription of risk-reducing medication, it is important to assess acceptability of these activities. Acceptability is increasingly being recognised as an important component of the feasibility of complex interventions in guidance documents such as the Medical Research Council (MRC) framework [22].

A previous review identified a considerable evidence base related to the acceptability of primary care involvement in risk-based screening and prevention [19]. This review identified numerous barriers reported by primary care providers in relation to their proposed roles which suggests concerns about the acceptability of this approach. However, the scope of the review was limited as it did not examine key participant-reported evaluations of acceptability, such as confidence, as recommended by an evidence-based framework of acceptability [23]. Furthermore, the review did not quantify the strength of individual barriers and facilitators nor examine potential sources of variation such as country and healthcare specialty. The latter is important to investigate as countries vary substantially in how primary healthcare is delivered, including differences in training requirements and what types of provider are considered part of the primary care workforce [18]. Consequently, implementation of risk-based screening and prevention will likely differ across countries [19].

The present systematic review aimed to provide a robust and in-depth examination of acceptability beyond identification of barriers and facilitators. It achieves this by employing the Theoretical Framework of Acceptability which recognises the value of participant-reported evaluations of acceptability in addition to behavioural assessments [23]. However, as primary care providers' significant knowledge deficits in this area have been described extensively in previous systematic reviews [19,24-26], the present review did not assess the extent to which primary care providers understand breast cancer risk assessment and management.

Specific objectives were to summarise the evidence base on:

a. ratings of acceptability (including, attitudes, opinions, beliefs, feelings, barriers or facilitators) by primary care providers with respect to (1) breast cancer risk assessment; and (2) primary prevention advice
b. the performance of routine behaviours by primary care providers with regard to (1) breast cancer risk assessment; and (2) primary prevention advice
c. sources of variation in acceptability and behaviours

2.4 Methods

The protocol of this systematic review was pre-registered in PROSPERO (CRD42020197676) and follows the reporting guidelines detailed in the PRISMA statement [27]. The protocol covered both quantitative and qualitative literature but for reasons of space only the quantitative findings are reported here.

2.4.1 Search strategy

The following electronic databases were searched: MEDLINE, EMBASE, CINAHL Plus, PsycINFO (each up to 10th July 2020) and ProQuest Dissertations & Theses Global (up to 26th August 2020). Databases were searched from 1989 as the first breast cancer risk model incorporating multiple breast cancer risk factors was published in this year [7]. Search terms were produced using medical subject headings (MeSH), other index terms, keywords and appropriate synonyms (Appendix A.1), and refined with the input of a librarian with expertise in systematic review searching. The strategy was tailored in accordance with the technical language of each database. The searches were limited to articles for which the full text was available in English. Forward and backward citation searches and a lead author search were performed for all included papers. Relevant reviews were hand-

searched and researchers with expertise in the area were contacted to identify any additional articles not retrieved by the searches.

2.4.2 Eligibility criteria

Studies were included in the review if they met the following criteria:

1. Healthcare professionals who provided primary care services. To account for variation in professional roles between healthcare structures in different countries, samples reported as being primary care providers were regarded as such. In ambiguous cases, authors were contacted to clarify whether their samples provided primary care services in line with the World Health Organisation's definition [28].

Studies conducted with both primary and secondary care providers were only included if it was possible to separately identify those findings relevant to primary care providers.

2. Data had to be reported about risk assessment and/or providing primary prevention advice in the context of breast cancer. Studies focusing on cancer risk or primary prevention whereby data specific to breast cancer could not be extracted were excluded.

3. Either or both of the following:

(a) Acceptability defined as anticipated or experiential cognitive and emotional responses. Studies had to report one or more of the following outcomes using quantitative methodologies: attitudes, opinions (e.g. perceptions of responsibility), beliefs, feelings (e.g. confidence), barriers or facilitators.

(b) Routine behaviours defined as typical or regular activity in clinical practice. Frequency of behaviours reported in a specific timeframe were not eligible for

inclusion. Hypothetical clinical scenarios/vignettes or reflections on previous clinical cases were ineligible as these methods ascertain the action taken in a specific situation which may not be indicative of routine behaviours.

4. Studies: Full empirical article of any quantitative design published in the English language. Grey literature including PhD theses, dissertations and unpublished research were eligible for inclusion. Additionally, baseline surveys of intervention studies designed to improve breast cancer risk assessment behaviours or provision of primary prevention advice were included.

2.4.3 Selection and coding of studies

The search results were downloaded into Endnote and duplicates were removed. The library was then uploaded to Rayyan [29] to complete screening. The first author screened all titles and abstracts and a second reviewer (RH) independently screened 30% (k = 945) of these (97% agreement). Full text articles were obtained for all records that appeared to be eligible or could not be confidently excluded (k = 124). The first author read all full text articles and assessed these against the eligibility criteria. A second reviewer (RH) read 50% of the full text articles (k = 62) and disagreements regarding the eligibility of an article were resolved by discussion. In ambiguous cases, additional reviewers were consulted (DF, SH) and consensus was reached.

2.4.4 Data extraction

Following full text review, detailed information on study characteristics (authors, country, study design and outcome measures), sample characteristics (sample size, age and sex) and outcome data relevant to the objectives was extracted by the first

author for all eligible articles. A second reviewer (RH) verified the data extraction by independently extracting primary outcome data for 50% (15/29) of eligible articles.

2.4.5 Quality assessment

The Mixed Methods Appraisal Tool (MMAT) was deemed most suitable for quality assessment due to its demonstrated reliability and inclusion of quality criteria specifically designed to appraise quantitative descriptive study designs such as surveys [30]. Criteria were categorised as 'yes', 'somewhat', 'no' or 'can't tell'. The response option of 'somewhat' was added to reflect when a criterion had been partially fulfilled but lacked some key indicators of quality. This enabled a more nuanced approach to quality appraisal. The authors of the tool discourage the use of a scoring metric therefore a narrative description of quality is provided.

In line with MMAT recommendation, two authors (SB & DF) discussed which quality indicators were most important to consider for each criterion listed and following this a coding scheme was devised and agreed upon. All studies were appraised using the criteria for quantitative descriptive designs to assess the quality of the survey design and outcome measures which were of most interest to the review. A 50% rate of response was a priori regarded as satisfactory for avoidance of nonresponse bias, in line with response rates observed in previously published provider surveys [31]. Two authors (SB & RH) independently appraised the quality of the remaining studies. Reviewers met on three separate occasions to check the reliability of decisions and any disagreements were discussed and resolved. During these meetings, the coding scheme was also reviewed and refined in line with discussions to ensure consistency and fairness in coding.

2.4.6 Synthesis of the evidence

A meta-analysis was deemed inappropriate as studies varied widely in outcomes, measurement scales and study populations. Instead, a narrative synthesis was conducted with findings tabulated [32]. The outcomes from each study were organised into categories initially based on what the authors of each individual study stated the data was measuring (i.e., barrier, facilitator, confidence etc.). Additional outcomes that had not been explicitly measured as barriers or facilitators (e.g., beliefs, feelings, etc.) were reviewed and categorised as such depending on whether they could reasonably be considered to promote or impede performance of the behaviour. For example, a negative affective attitude such as discomfort was categorised as a barrier. Consensus was reached on these decisions through discussion with additional reviewers (DF, SH). Appendix A.2 provides full details of the outcomes included per study, the raw data extracted from each study, and how each outcome was categorised.

To aid interpretation and allow meaningful patterns to be identified, outcomes were categorised into broader themes depending on content (Appendix A.2). Initial themes were identified by the first author. These themes were then refined and agreed upon following several rounds of consultation with additional reviewers (DF, SH). The findings were synthesised across the included studies.

2.5 Results

2.5.1 Study characteristics

The searches identified 6,750 articles, of which 3,164 remained after duplicates were removed (Figure 2.1). A total of 29 studies were eligible for inclusion (see Appendix A.3 for list of excluded studies and reasons). Years of publication ranged from 1997 to 2020. Twenty-seven studies were included in the synthesis; two were excluded

due to using measurement scales that could not be meaningfully compared to other studies [33,34]. More than half of the included studies were conducted in the USA (k = 14) (Table 2.1). Sample sizes ranged from 28 [35] to 1,311 [36] individuals. The most commonly studied population were physicians. The majority (24/27, 89%) of studies assessed at least one outcome relevant to breast cancer risk assessment. In comparison, fewer studies assessed outcomes pertinent to primary prevention (9/27, 33%). No studies investigating health-related behaviours within the context of breast cancer risk were identified so primary prevention findings are limited to risk-reducing medications only.

Table 2.1. Characteristics of studies included in the synthesis (*n* = 27)

Characteristic	Number of studies
Year of publication	
1997-2004	7
2005-2012	9
2013-2020	11
Study country	
USA	14
UK	5
Switzerland	2
Multiple countries*	2
France	1
Canada	1
Belgium	1
Australia	1
Sample size (*n*)	
1-250	12
251-500	8
501-750	3
751-1000	2
>1000	2
Study population	
Physicians only	16
Mixed[1]	5
Physicians and nursing staff	4
Nursing staff only	2
Study outcomes	
Risk assessment	24
Primary prevention	9
% women in provider cohort	
0-25	1
26-50	11
51-75	10
76-100	0
Not reported	5

Notes.
*Nippert et al. (2014) – France, the Netherlands, UK and Germany; Mainous et al. (2013) –

USA & Canada
[1]These studies recruited other professional groups in addition to physicians and nursing staff, namely physician assistants, midwives and residents

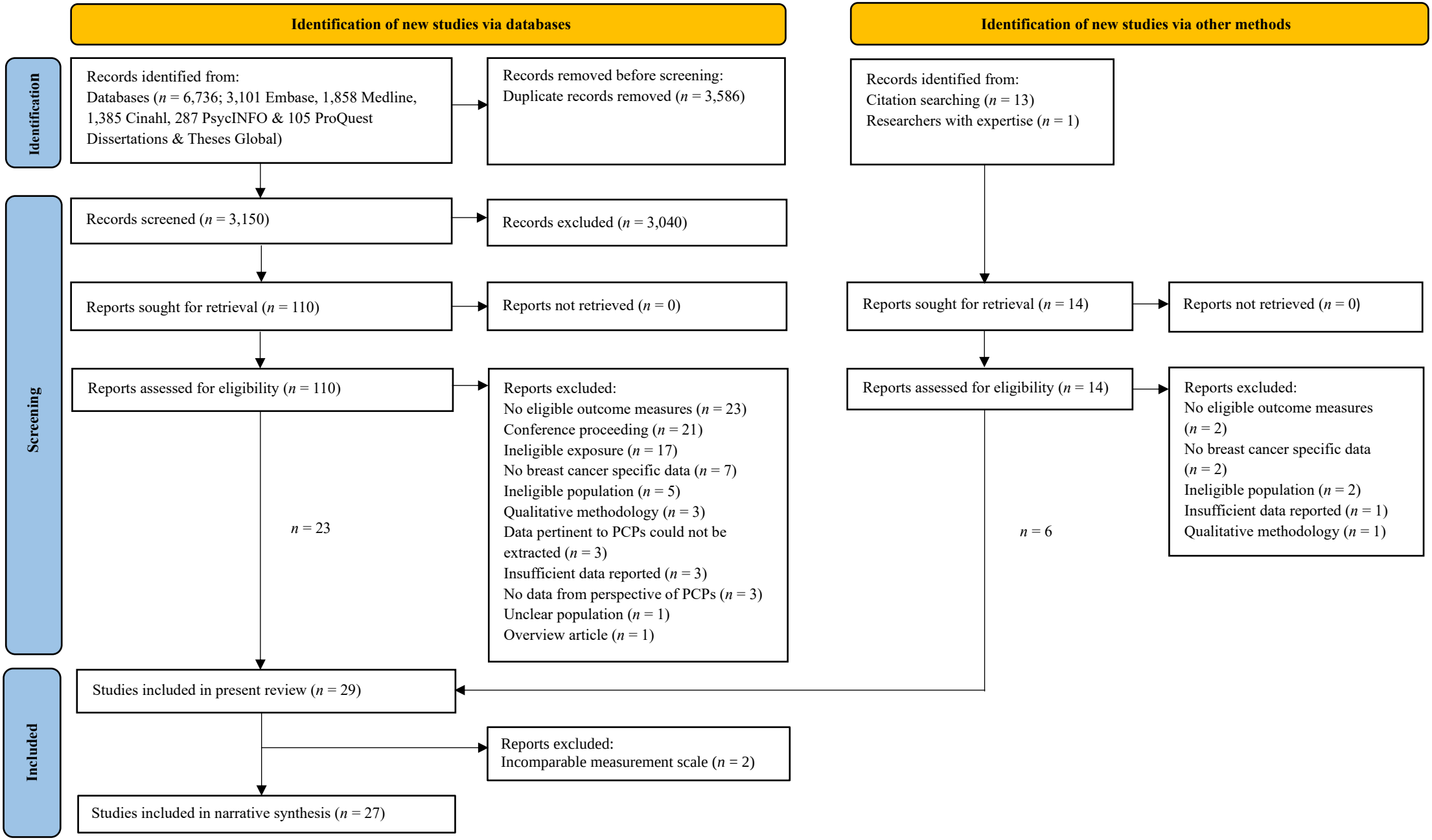


Figure 2.1. PRISMA flow diagram of study selection

2.5.2 Perceived practice responsibilities with respect to both risk assessment and primary prevention

Primary care providers' perceptions of responsibility with respect to tasks implicated in breast cancer risk assessment and primary prevention were examined in several studies. Taking a family history was overwhelmingly perceived as a primary care responsibility (88.8-98.1%; Table 2.2). Additionally, primary care providers readily identified counselling about risk and providing follow up support post genetic testing as practice responsibilities. In comparison, discussion of genetic testing and disclosure of results were less likely to be perceived as primary care responsibilities. Inter-country differences were apparent in a study that recruited participants from four European countries [37]. GPs from France ascribed most practice responsibilities to themselves whereas GPs from the UK considered genetic risk and genetic testing to be the responsibility of genetic specialists. The most commonly assumed responsibilities for primary prevention were writing ongoing prescriptions for risk-reducing medications and initiating discussions about preventative measures.

Table 2.2. Primary care providers' perceived responsibilities in breast cancer risk assessment and primary prevention

Tasks	Percentage reporting primary care responsibility [mean and range reported if multiple values]	Associations with perceived roles
Breast cancer risk assessment		
Taking or documenting a family history [31,38,39]	92.7 [89.0-98.0]	
Providing counselling regarding familial risk [38,39]	83.0 [81.0-85.0]	
Providing follow up support after genetic testing [37,38]	79.7 [66.8-92.5]	Country: One study recruited participants from four European countries (UK, France, Germany and the Netherlands). The majority of GPs from all four countries agreed that providing support after breast cancer testing was a primary care responsibility. However, the proportions varied significantly; the highest proportion was reported by the GPs from France (86.1%) and the lowest by the GPs from the UK (57.2%) [37]
Obtaining informed consent before genetic testing [38,39]	77.3 [67.0-87.5]	
Identifying families at risk [38,39]	72.0 [58.0-86.0]	
Calculating breast cancer risk [31]	62.0	
Informing about breast cancer genetic testing [37,39]	61.5 [47.0-76.0]	Country: GPs from France were significantly more likely to assume responsibility for informing patients about breast cancer genetic testing in comparison to GPs from Germany, the Netherlands and the UK (56.2% vs. 46.6%, 41.7% and 41.6%) [37]
Counseling women about breast density [40]	43.0	

Explaining the inheritance pattern of familial breast cancer [37]	42.7	Country: GPs from France were significantly more likely to assume responsibility for explaining the inheritance pattern of familial breast cancer in comparison to GPs from Germany, the Netherlands and the UK (63.6% vs. 30%, 49.7% and 33.8%) [37]
Disclosing breast cancer genetic test results [37,39]	37.2 [27.4-47.0]	Country: GPs from Germany were significantly more likely to assume responsibility for disclosing breast cancer genetic test results in comparison to GPs from France, the Netherlands and the UK (43.7% vs. 23.5%, 11.6% and 16.9%) [37]
	Primary prevention	
Writing ongoing prescriptions for risk-reducing medications [41]	97.9	
Providing options for prevention and early detection of breast cancer [38]	86.0	
Initiating discussion of risk-reducing medications [41]	75.0	
Writing first prescription for risk-reducing medications [41]	31.3	
Breast cancer risk reduction with chemopreventive agents [31]	18.0	Sex: Males more likely to agree that breast cancer risk reduction with chemopreventive agents was a primary care provider's responsibility than females (28% compared to 10%) [31]

2.5.3 Risk assessment

2.5.3.1 Barriers and facilitators

For conducting breast cancer risk assessment, the most commonly endorsed barriers were insufficient education/training followed by discomfort discussing breast density and performing the assessment (Table 2.3). The least frequently endorsed barriers included lack of primary care responsibility and concern about the implications of risk assessment for women with respect to causing unnecessary anxiety or impacting screening behaviour. None of the included studies investigated factors that could help facilitate breast cancer risk assessment behaviour.

2.5.3.2 Perceived confidence

Primary care providers reported highest levels of confidence in taking a family history (60.7-65.5%) and reassuring low-risk patients (46.0-67.7%) (Table 2.4). Very low levels of confidence were observed for using the Gail model to calculate breast cancer risk (8.6%).

2.5.3.3 Routine behaviours

The discussion and collection of breast cancer family history was reported to be a common task (Table 2.5). Rates were particularly high when the situational context increased the saliency of the topic matter; for example during a discussion about a woman's health history or a woman presents with concerns about breast cancer risk (90.4-92.6%). In comparison, routine collection of family history during a new patient appointment was found to be lower (48.4-69.3%) in two studies conducted in the UK [42,43]. Reported use of multi-factorial risk assessment tools was low with estimates ranging from 3% to 50.9%.

Professional specialty and training level were found to be associated with reported behaviours. A higher proportion of providers specialising in obstetrics and gynaecology reported using risk assessment tools in comparison to family and internal medicine providers [44,45]. Additionally, qualified physicians were significantly more likely to report routinely assessing family history and using the Gail model compared to residents in training [31,44].

Table 2.3. Primary care providers' perceptions of barriers associated with conducting breast cancer risk assessment

Themes	Percentage endorsing barrier [mean and range reported if multiple values]	Associations with barriers
Insufficient education/training [31,41,44,46]	45.2 [20.0-82.1]	
Discomfort discussing breast density [35,47,48]	36.9 [11.7-81.5]	Training level: Internal medicine providers more likely to agree that they were comfortable counselling women about breast density compared to primary care residents (38% compared to 0%) [35]
Discomfort conducting breast cancer risk assessment [46,49,50]	30.9 [29.3-33.5]	Specialty: Women's health providers more likely to respond that they were 'very comfortable/comfortable' with using a breast cancer risk assessment tool compared to other primary care providers (38% compared to 14%) [46]
More immediate issues to discuss during consultation [31]	25.0	
Insufficient provisions to conduct breast cancer risk assessment effectively (e.g. tools, patient information etc.) [31,41,44,46,51]	20.6 [11.0-40.0]	
Perceived lack of impact on patient management [44,46]	16.8 [7.9-25.6]	
Low perceived utility and acceptability of genetic testing for determining breast cancer risk [36,52]	14.0 [5.1-22.9]	
Concern that risk prediction models are not accurate enough [51]	13.0	

Do not see patients for whom risk assessment is indicated [44,46]	12.5 [7.9-17]
Concern about creating unnecessary anxiety/worry for many women [51]	7.9 [2.0-13.7]
Assessment of breast cancer risk is not part of routine practice [41]	7.0
Perceived lack of primary care responsibility [46]	5.9
Reluctance to assess risk because a woman at low risk of breast cancer might decide not to undergo mammography screening [51]	6.0

Table 2.4. Primary care providers' perceived confidence in performing breast cancer risk assessment behaviours

Tasks	Percentage reporting confidence [mean and range reported if multiple values]	Associations with confidence
Taking a family history [42,53,54]	63.5 [60.7-65.5]	Training: Nurses who had attended training about genetic issues in the 12 months were more likely to report being 'confident or very confident' compared with those who did not attend (72% compared to 59%) [42]
Reassuring low-risk patients [42,53,54]	58.8 [46.0-67.7]	Training: Confidence providing reassurance for those at low risk of breast cancer was significantly associated with attending training about genetic issues [42]
Making a basic risk assessment [42,53]	57.4 [53.9-60.8]	
Ability to provide information to patients about BRCA cancer risks and inheritance [55]	55.8 [50.0-61.6]	
Ability to provide information to patients about BRCA test methods and interpretation [55]	39.6 [37.2-41.9]	
Ability to answer patients' questions during a consultation about risk [54]	23.2	
Ability to use Gail scores to identify women at increased risk for breast cancer [31]	8.6	

Table 2.5. Primary care providers' reported behaviours with respect to breast cancer risk assessment

Behaviours	Percentage reporting behaviour [mean and range reported if multiple values]	Associations with behaviour
Discussing family history as part of a woman's health history [56]	92.6	
Considering a discussion of family history with a woman consulting with concerns about breast cancer risk [57]	90.4	
Collecting family history during routine clinical practice [31,46,58]	86.3 [71.0-95.0]	Training level: Staff more likely to report 'usually or always' assessing family history during routine visits compared to residents (79% compared to 58%) [31]
Discussing family history to assess breast cancer risk [45,49]	67.0 [37.1-96.9]	
Collecting family history during new patient appointment [42,43]	58.9 [48.4-69.3]	
Using multi-factorial breast cancer risk assessment tools [45,47,50]	33.1 [22.4-50.9]	Specialty: Obstetric-gynaecologists more likely to report using breast cancer risk assessment tools compared to family medicine physicians and internists to (67.2% vs. 44.0% and 41.7%) [45]
Assessing risk using the Gail model [31,44,49]	16.8 [3.0–40.9]	Training level: Attending physicians more likely to report use of the Gail model compared to resident physicians [44] Specialty: Gynaecology more likely to report use of the Gail model compared to family medicine and internal medicine physicians (60% vs. 33.3% and 36.9%) [44]

2.5.4 Primary prevention advice

2.5.4.1 Barriers and facilitators

Overall, there was higher endorsement of barriers for primary prevention than risk assessment. The most prevalent barriers for providing primary prevention advice were concern and discomfort prescribing risk-reducing medication and insufficient education/training, in line with barriers to risk assessment (Table 2.6). Furthermore, a greater proportion of primary care providers were more likely to report they see fewer patients for whom risk-reducing medications are indicated in comparison to patients suitable for risk assessment (39.6% vs. 12.5%). The majority of primary care providers did not report beliefs indicating scepticism about the evidence base underpinning risk-reducing medications. More specifically, few indicated that they believed the risks of prescribing risk-reducing medications outweighed the benefits (6.5-20.5%) or expressed doubts about effectiveness of risk-reducing medications (1.0-31.5%). Lack of scepticism was a consistent finding reported across all five studies that assessed this outcome.

Primary care providers endorsed all facilitators to a relatively high degree (32.0-61.6%; Table 2.7). Availability of provisions to discuss risk-reducing options more effectively was endorsed as the strongest facilitator for providing primary prevention advice.

Providers specialising in women's health reported feeling more comfortable using a breast cancer risk assessment tool and prescribing risk-reducing medication [46]. These providers were also less likely to agree that the risks of prescribing risk-reducing medications outweighed the benefits in comparison to other primary care providers [45].

2.5.4.2 Perceived confidence and routine behaviours

Primary care providers reported low levels of confidence in providing advice/information to patients about risk-reducing medications (24%) [41]. Only one study reported a behavioural outcome relevant to primary prevention whereby 13.5% reported discussing chemoprevention ‘usually’ or ‘always’ [31].

Table 2.6. Primary care providers' perceptions of barriers associated with providing primary prevention advice

Themes	Percentage endorsing barrier [mean and range reported if multiple values]	Associations with barriers
Discomfort prescribing risk-reducing medication [44,46]	75.0 [70.1-79.8]	Specialty: Women's health providers more likely to respond that they were 'very comfortable/comfortable' with prescribing risk-reducing medication compared to other primary care providers (9% compared to 2%) [46]
Concern about prescribing off-label (unlicensed) medication [50]	58.1	
Never seen a patient for whom risk-reducing medications are indicated [44,46]	39.6 [18.4-60.7]	
Insufficient education/training [41,46,50,59]	34.6 [13.9-72.0]	
Insufficient provisions to discuss risk-reducing measures effectively (e.g. time, patient information, resources etc.) [41,44,46,50,59,60]	22.7 [6.1-50]	Specialty: Family and internal medicine physicians more likely to report time constraints as a barrier than obstetrician-gynaecologists (45.8% and 46.5% vs. 31.3%, respectively) [59]
More immediate issues to discuss during consultation [41]	18.0	
Doubts about effectiveness of risk-reducing medications (e.g. belief in ability to reduce risk and mortality, perceiving the evidence base as controversial) [41,44,45,50,60]	15.4 [1.0-31.5]	
Forgetting to discuss risk-reducing medications [41]	14.0	

Believing that the risks of prescribing risk-reducing medications outweigh the benefits [45,50,60]	13.5 [6.5-20.5]	Specialty: Obstetrician-gynaecologists less likely to agree that the evidence of preventive agents reducing breast cancer risk is controversial compared to family medicine physicians and internists (22.8% vs. 37.6% and 34.0% respectively) [45] Obstetrician-gynaecologists less likely to agree that the risk of endometrial cancer is too great to prescribe tamoxifen for breast cancer reduction compared to family medicine physicians and internists (14.8% vs. 18.4% and 18.8%) [45] Obstetrician-gynaecologists less likely to agree that the risk of thromboembolic disease is too great to prescribe preventive agents for breast cancer reduction compared to family medicine physicians and internists (10.8% vs. 26.0% and 24.8%) [45]
Women's perceived lack of interest and knowledge about risk reduction [41,59]	12.0 [1.0-27.0]	
Perceived lack of primary care responsibility [41,46,59]	11.6 [4.0-23.9]	
Lack of incentives for discussing risk reducing measures [41,59]	8.3 [3.0-13.6]	
Discomfort prescribing a 'cancer drug' to healthy women [41]	4.0	
Concern about increasing patient's worry about breast cancer [41]	2.0	
Perceived lack of impact on patient management [46]	1.2	

Table 2.7. Primary care providers' perceptions of facilitators associated with providing primary prevention advice

Themes	Percentage endorsing facilitator [mean and range reported if multiple values]
Availability of provisions to discuss risk-reducing options more effectively (e.g. tools and guidelines to identify suitable patients, better patient education materials etc.) [41,59]	61.6 [33.0-88.0]
Knowing some risk-reducing medications are available at a Government-subsidised price [41]	54.0
Endorsement as part of role by a professional body [41]	53.0
More education/training [59]	52.0 [34.5-69.4]
Patient has indications of increased breast cancer risk [41]	46.3 [36.0-54.0]
Understanding the benefits of primary prevention [41,59]	44.0 [14.0-59.1]
Peer support [41]	41.7 [27.0-64.0]
Believing that the benefits of preventive agents in breast cancer outweigh the risks [45,50]	37.6 [12.4-62.8]
Easier to discuss risk-reducing medications than bilateral mastectomy [41]	32.0

2.5.5 Quality assessment

Overall, study quality was poor (Table 2.8). A detailed breakdown of quality assessment by question for each study is available in Appendix A.4. For the majority of studies, external validity was likely to be low due to reliance on recruitment through single institutions and sampling via medical association membership lists with limited coverage of the target population. For example, membership of the American Medical Association has been declining with the most recent estimate suggesting only 15% of practising US doctors are members [61]. Inadequate reporting of how outcome measures were developed was common across studies. Furthermore, none of the outcomes of interest were assessed using standardised measures with demonstrated reliability and validity; response rates lower than 50% were reported in k = 14 (48%) studies [34-37,39,41,45,47,48,50,51,55,58,60].

Table 2.8. Quality assessment results for studies included in the review (*n* = 29)

	Yes		**Somewhat**		**No**		**Cannot tell**	
	n	%	*n*	%	*n*	%	*n*	%
Is the sampling strategy relevant to address the research question?	6	21	17	59	3	10	3	10
Is the sample representative of the target population?	9	31	5	17	7	24	8	28
Are the measurements appropriate?	0	0	18	62	0	0	11	38
Is the risk of nonresponse bias low?	3	10	11	38	12	41	3	10
Is the statistical analysis appropriate to answer the research question?	23	79	2	7	0	0	4	14

2.6 Discussion

2.6.1 Summary of main findings

The results from this systematic review indicate that primary care providers typically take a reactive role in breast cancer risk assessment that is predominantly focused on collection of family history and provision of support following identification of increased risk. Reported use of multi-factorial risk assessment tools was low. Primary care providers reported higher discomfort and lower confidence with respect to prescribing risk-reducing medications when compared to risk assessment. However, few providers reported beliefs suggestive of doubts about the evidence base underpinning risk-reducing medications. Insufficient education/training and perceived discomfort were amongst the most commonly endorsed barriers reported for both activities. The strongest facilitators for offering risk-reducing medication related to availability of provisions such as clear guidelines and tools to facilitate identification of suitable patients. Professional background, training and country were identified as sources of variation in acceptability and behaviours. The methodological quality of included studies was generally poor and common limitations were high nonresponse rates and use of non-standardised outcome measures.

2.6.2 Relevance to existing literature

Previous systematic reviews have consistently identified primary care providers' lack of knowledge about breast cancer risk assessment and management as a significant barrier to engagement [19,24,25,62]. In line with this, the present review found that insufficient education/training was a prevalent barrier reported for both risk assessment and primary prevention.

Prior to this review, widespread reticence by primary care providers to discuss and prescribe risk-reducing medications has been recognised [60,63-65]. In line with previous findings, this review found that primary care providers report high levels of discomfort and low levels of confidence associated with risk-reducing medications. However, the present review also offers novel insight: few primary care providers reported scepticism about the evidence base underpinning risk-reducing medication. This suggests that the perceived discomfort towards risk-reducing medication is not solely attributable to a lack of knowledge. The present findings on facilitators instead highlight that there is a need for more structural approaches, such as the use of guidelines or prompts, to facilitate primary care involvement in breast cancer risk assessment and management practices.

This review has been the first to investigate sources of variation in acceptability and behaviours. Examination of routine behaviours illustrated that primary care providers infrequently report using multi-factorial risk assessments such as the Gail or Tyrer-Cuzick models [7,8]. Nonetheless, family history collection was reported as a common behaviour and perceived as a core task for the majority of primary care providers. Lower levels of routine family history taking were reported by two UK studies [42, 43]. However, given the age of these studies (1997 and 2001), these findings may not be reflective of current clinical practice. Nevertheless, present guidelines in the UK and Europe discourage primary care providers from proactively identifying women with a family history of breast cancer [17,37]. A survey of GPs and breast surgeons from four different European countries revealed strong disapproval of the current purely reactive approach to family history assessment [66]. Therefore, the present guidelines are likely to hinder optimal promotion of risk

assessment and primary prevention activities in UK and European primary care settings.

Professional background was also associated with outcomes. Providers specialising in women's health issues reported feeling more comfortable with respect to both risk assessment and primary prevention as evidenced by greater reported use of quantitative risk assessments and fewer negative views about the risks of risk-reducing medications. These perceptions are likely to be the result of specialised knowledge acquired through additional training. For instance, an understanding of the diagnosis and clinical management of hereditary breast and ovarian cancer syndrome is considered essential for obstetrician/gynaecologists [67]. Therefore, in countries such as the USA, primary care providers specialising in women's health may be more prepared to assume greater responsibility for assessment and management of breast cancer risk because of their knowledge and experience acquired through training and routine practice.

2.6.3 Limitations

The present review has identified methodological biases present in the primary studies. Firstly, high rates of nonresponse were observed in a significant proportion of the studies. Primary care providers who respond to surveys might have more positive views of breast cancer risk assessment and primary prevention than non-responders which may lead to overestimations of acceptability. Furthermore, there was a reliance on convenience sampling procedures in many studies. Outcomes were not assessed using standardised measures with demonstrated reliability and validity. In addition, older studies included in the review may be a poor reflection of current clinical practice given the significant advances made in breast cancer risk assessment

and management in recent years. Primary prevention outcomes tended to be assessed in more recent studies which is in line with risk-reducing medications being a relatively new option in comparison to risk assessment. Nonetheless, findings were largely consistent across studies suggesting that methodological limitations with sampling and publication date did not unduly affect the overall conclusions.

Substantial heterogeneity across included studies was evident and therefore a meta-analysis was not possible. To allow meaningful patterns to be identified via narrative synthesis, the research team decided how outcomes were categorised and to some extent this process was subjective. Nevertheless, analytical processes were reviewed in reflective team meetings to achieve consensus and ensure a rigorous and robust synthesis.

Additionally, a wide range of values were observed for some outcomes indicating uncertainty about the average values presented. This is likely to be the result of heterogeneous outcome measurements, as well as differences in samples included. Consequently, caution is warranted when drawing conclusions about the precision of estimating strength of outcomes.

Finally, and perhaps surprisingly, the review did not identify any studies investigating primary care providers' perceptions of discussing health-related behaviours within the context of breast cancer risk reduction. There is, however, an evidence base focusing on cancer risk more generally. Inclusion of this literature may have provided a more comprehensive understanding of primary care's perceived role in primary prevention than was possible in this review.

2.6.4 Implications and future research directions

The present review suggests that provision of education/training will be necessary but not sufficient to facilitate primary care involvement in breast cancer risk assessment and primary prevention. The findings on facilitators and routine behaviour indicate that adapting infrastructure and providing prompts to utilise available resources are essential to increase the likelihood of primary care providers routinely conducting both activities. For instance, the integration of risk assessment and management tools into practice software or access to web-based applications would facilitate the desired behaviours, as has been demonstrated for cardiovascular risk assessment and management [20]. Several prototype tools for breast cancer risk assessment have been subject to usability and acceptability testing [68,69]. Primary care providers have expressed concerns about the amount of time needed to complete such tools and highlighted the lack of guidance on clinical management as a significant barrier to use. Therefore, future tool development should focus on streamlining the process and incorporating risk reduction recommendations to increase uptake in routine practice. Additionally, future research should focus on developing and evaluating the impact of educational interventions on knowledge assimilation. This will identify what implementation support primary care will require to fulfil their proposed roles in risk assessment and primary prevention. However, it is worth noting evidence which suggests not all women may be in favour of primary care performing these roles [70]. Therefore, further research assessing the acceptability of this approach to women is needed.

Nursing staff were underrepresented in the included studies. Decision makers have suggested that nurses could assume increased duties in risk assessment and management to support implementation of risk-based screening and prevention [71].

In relation to primary prevention, general practitioners have been found to perceive intervening on obesity as an inappropriate use of their time in comparison to nurses who report feeling responsible for raising the topic [72]. Given the important role of health-related behaviours in reducing breast cancer risk, it would be timely to compare and contrast the views of primary care nurses and physicians to determine their respective roles in implementing prevention recommendations for breast cancer.

Additionally, there is a clear need for more research using populations outside the US to understand the feasibility of primary care assessing and managing breast cancer risk in different healthcare contexts. Future primary studies would benefit from assessing similar outcomes across studies using measures with demonstrated reliability and validity. Wider and more representative sampling frames should be used to obtain better coverage of the target population. Furthermore, recruitment strategies that build personal connections with potential participants such as using physician recruiters ought to be considered to reduce nonresponse rates [73].

2.6.5 Conclusions

Within the context of implementing risk-based breast cancer screening and prevention, the findings of this review suggest that primary care providers are more likely to accept an increased role in breast cancer risk assessment compared to advising on risk-reducing medications. Adaptations to infrastructure will be necessary to promote enactment of breast cancer risk assessment and management behaviours in addition to provision of education. To fully realise the benefits of risk-based breast cancer screening and prevention, guidelines will need to be reviewed to ensure promotion of a proactive approach to breast cancer risk assessment in primary care.

Declarations

Author Contributions: Conceptualization, S.B., D.P.F., S.J.H. and L.G.; methodology, S.B., D.P.F., S.J.H. and L.G.; formal analysis, S.B., D.P.F. and S.J.H.; investigation, S.B. and R.E.H.; data curation, S.B.; writing—original draft preparation, S.B.; writing—review and editing, D.P.F., S.J.H., R.E.H. and L.G.; visualization, S.B.; supervision, D.P.F., S.J.H. and L.G.; project administration, S.B.; funding acquisition, D.P.F. and S.J.H. All authors have read and agreed to the published version of the manuscript.

Funding: S.B. is funded by a Manchester Cancer Research Centre PhD studentship. D.P.F and S.J.H were supported by the NIHR Manchester Biomedical Research Centre (IS-BRC-1215-20007). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Institutional Review Board Statement: This systematic review synthesises previously published data and does not include new data that require ethical approval and consent.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this review are available in Appendix A.

Conflicts of Interest: The authors declare no conflict of interest.

2.7 References

1. Autier P, Boniol M. Mammography screening: a major issue in medicine. Eur J Cancer. 2018;90:34-62.
2. Marmot MG, Altman D, Cameron D, Dewar J, Thompson S, Wilcox M. The benefits and harms of breast cancer screening: an independent review. Br J Cancer. 2013;108:2205-40.
3. Nelson HD, Fu R, Cantor A, Pappas M, Daeges M, Humphrey L. Effectiveness of breast cancer screening: systematic review and meta-analysis to update the 2009 US Preventive Services Task Force recommendation. Ann Intern Med. 2016;164:244-55.
4. Brodersen J, Schwartz LM, Heneghan C, O'Sullivan JW, Aronson JK, Woloshin S. Overdiagnosis: what it is and what it isn't. BMJ Evid Based Med. 2018;23:1-3.
5. Mandrik O, Zielonke N, Meheus F, Severens J, Guha N, Herrero Acosta R, et al. Systematic reviews as a 'lens of evidence': determinants of benefits and harms of breast cancer screening. Int J Cancer. 2019;145:994-1006.
6. Pashayan N, Morris S, Gilbert FJ, Pharoah PD. Cost-effectiveness and benefit-to-harm ratio of risk-stratified screening for breast cancer: a life-table model. JAMA Oncol. 2018;4:1504-10.
7. Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, et al.. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989;81:1879-86.
8. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med. 2004;23:1111-30.

9. Evans DG, Astley S, Stavrinos P, Harkness E, Donnelly LS, Dawe S, et al. Improvement in risk prediction, early detection and prevention of breast cancer in the NHS Breast Screening Programme and family history clinics: a dual cohort study. Programme Grants for Appl Res. 2016;4:1-210.

10. Pashayan N, Antoniou AC, Ivanus U, Esserman LJ, Easton DF, French D, et al. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. Nat Rev Clin Oncol. 2020;17:687-705.

11. Evans DGR, Donnelly LS, Harkness EF, Astley SM, Stavrinos P, Dawe S et al. Breast cancer risk feedback to women in the UK NHS breast screening population. Br J Cancer. 2016;114:1045-52.

12. Delaloge S, Gorgio-Rossi P, Balleyguier C, Guindy M, Burrion JB, Gilbert F. My Personal Breast Screening (MyPeBS). [Online]. n.d. [Accessed 12th April 2021]. Available from: https://www.mypebs.eu/.

13. Esserman LJ. The WISDOM Study: breaking the deadlock in the breast cancer screening debate. NPJ Breast Cancer. 2017;3(1):34.

14. Cuzick J, Sestak I, Bonanni B, Costantino JP, Cummings S, DeCensi A, et al. Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. Lancet. 2013;381:1827-34.

15. Cuzick J, Sestak I, Cawthorn S, Hamed H, Holli K, Howell A, et al. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. Lancet Oncol. 2015;16:67-75.

16. Parkin DM, Boyd L, Walker L. 16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. Br J Cancer. 2011; 105:S77-81.

17. National Institute for Health and Care Excellence (NICE). Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [updated 2019 Nov] (Clinical Guideline [CG164]). [Online]. 2013 [Accessed 12th October 2020]. Available from: https://www.nice.org.uk/guidance/cg164.

18. Dent T, Jbilou J, Rafi I, Segnam N, Törnberg S, Chowdhury S, et al. Stratified cancer screening: the practicalities of implementation. Public Health Genom. 2013;16:94-9.

19. Rainey L, van der Waal D, Jervaeus A, Wengström Y, Evans DGR, Donnelly LS, et al. Are we ready for the challenge of implementing risk-based breast cancer screening and primary prevention? The Breast. 2018;39:24-32.

20. Phillips KA, Steel EJ, Collins I, Emery J, Pirotta M, Mann GB, et al. Transitioning to routine breast cancer risk assessment and management in primary care: what can we learn from cardiovascular disease? Aust J Prim Health. 2016;22:255-61.

21. Public Health England. NHS Health Check programme best practice guidance [updated 2020 Mar]. [Online]. 2019 [Accessed 20th October 2020]. Available from: https://www.healthcheck.nhs.uk/commissioners-and-providers/national-guidance/.

22. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby J, et al. Framework for the development and evaluation of complex interventions: gap analysis, workshop and consultation-informed update. Health Technol Assess. 2021;25:1-132.

23. Sekhon M, Cartwright M, Francis JJ. Acceptability of health care interventions: A theoretical framework and proposed research agenda. Br J Health Psychol. 2018;23:519-31.

24. Hamilton JG, Abdiwahab E, Edwards HM, Fang M-L, Jdayani A, Breslau ES. Primary care providers' cancer genetic testing-related knowledge, attitudes, and communication behaviors: A systematic review and research agenda. J Gen Intern Med. 2017;32:315-24.

25. Mikat-Stevens NA, Larson IA, Tarini BA. Primary-care providers' perceived barriers to integration of genetics services: a systematic review of the literature. Genet Med. 2015;17:169-76.

26. Scheuner MT, Sieverding P, Shekelle PG. Delivery of genomic medicine for common chronic adult diseases: a systematic review. JAMA. 2008;299:1320-34.

27. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. J Clin Epidemiol. 2021;134:103-12.

28. World Health Organisation. Main terminology. [Online]. n.d. [Accessed 20th October 2020]. Available from: https://www.euro.who.int/en/health-topics/Health-systems/primary-health-care/main-terminology.

29. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev. 2016;5:210.

30. Hong QN, Fàbregues S, Bartlett G, Boardman F, Cargo M, Dagenais P, et al. The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. Educ Inf. 2018;34:285-91.

31. Sabatino SA, McCarthy EP, Phillips RS, Burns RB. Breast cancer risk assessment and management in primary care: provider attitudes, practices, and barriers. Cancer Detect Prev. 2007;31:375-83.

32. Petticrew M, Roberts H. Systematic reviews in the social sciences: a practical guide. Oxford: Blackwell; 2006.

33. Saunders-Goldson SA. Web-based education intervention on breast cancer risk assessment of indigent women in primary care. ABNF J. 2018;29:106-11.

34. Carroll JC, Wilson BJ, Allanson J, Grimshaw J, Blaine SM, Meschino WS, et al. GenetiKit: a randomized controlled trial to enhance delivery of genetics services by family physicians. Fam Pract. 2011;28:615-23.

35. Casas RS, Ramachandran A, Gunn CM, Weinberg JM, Shaffer K. Explaining breast density recommendations: an introductory workshop for breast health providers. MedEdPORTAL. 2017;13:10654.

36. Mainous III AG, Johnson SP, Chirina S, Baker R. Academic family physicians' perception of genetic testing and integration into practice: a CERA study. Fam Med. 2013;45: 257-62.

37. Nippert I, Julian-Reynier C, Harris H, Evans G, van Asperen CJ, Tibben A, et al. Cancer risk communication, predictive testing and management in France, Germany, the Netherlands and the UK: general practitioners' and breast surgeons' current practice and preferred practice responsibilities. J Community Genet. 2014;5:69-79.

38. Escher M, Sappino AP. Primary care physicians' knowledge and attitudes towards genetic testing for breast-ovarian cancer predisposition. Ann Oncol. 2000;11:1131-6.

39. Pichert G, Dietrich D, Moosmann P, Zwahlen M, Stahel RA, Sappino AP. Swiss primary care physicians' knowledge, attitudes and perception towards genetic testing for hereditary breast cancer. Fam Cancer. 2003;2:153-8.

40. Gunn CM, Kressin NR, Cooper K, Marturano C, Freund KM, Battaglia TA. Primary care provider experience with breast density legislation in Massachusetts. J Womens Health. 2018;27: 615-22.

41. Macdonald C, Saunders CM, Keogh LA, Hunter M, Mazza D, McLachlan SA, et al. Breast cancer chemoprevention: use and views of Australian women and their clinicians. Cancer Prev Res. 2021;14:131-44.

42. Bankhead C, Emery J, Qureshi N, Campbell H, Austoker J, Watson E. New developments in genetics-knowledge, attitudes and information needs of practice nurses. Fam Pract. 2001;18:475-86.

43. Summerton N, Garrood PV. The family history in family practice: a questionnaire study. Fam Pract. 1997;14:285-8.

44. Corbelli J, Borrero S, Bonnema R, McNamara M, Kraemer K, Rubio D, et al. Use of the Gail model and breast cancer preventive therapy among three primary care specialties. J Womens Health. 2014;23:746-52.

45. Samimi G, Heckman-Stoddard BM, Holmberg C, Tennant B, Sheppard BB, Coa KI, et al. Assessment of and interventions for women at high risk for breast or ovarian cancer: a survey of primary care physicians. Cancer Prev Res. 2021;14:205-14.

46. Bidassie B, Kovach A, Vallette MA, Merriman J, Park YA, Aggarwal A, et al. Breast cancer risk assessment and chemoprevention use among veterans affairs primary care providers: a national online survey. Mil Med. 2020;185: 512-8.

47. Khong KA, Hargreaves J, Aminololama-Shakeri S, Lindfors KK. Impact of the California breast density law on primary care physicians. J Am Coll Radiol. 2015;12:256-60.

48. Maimone S, McDonough MD, Hines SL. Breast density reporting laws and supplemental screening—a survey of referring providers' experiences and understanding. Curr Probl Diagn Radiol. 2017;46:105-9.

49. Edwards QT, Maradiegue A, Seibert D, Saunders-Goldson S, Humphreys, S. Breast cancer risk elements and nurse practitioners' knowledge, use, and perceived comfort level of breast cancer risk assessment. J Am Assoc Nurse Pract. 2009;21:270-7.

50. Tighe M-K. An examination of Canadian family physicians' knowledge and practice patterns regarding breast cancer prevention. Master's Thesis, Queen's University, Kingston, ON, Canada, August 2009.

51. Guerra, CE, Sherman M, Armstrong K. Diffusion of breast cancer risk assessment in primary care. J Am Board Fam Med. 2009;22:272-9.

52. Welkenhuysen M, Evers-Kiebooms G. General practitioners and predictive genetic testing for late-onset diseases in Flanders: what are their opinions and do they want to be involved? Community Genet. 2002;5:128-137.

53. Bethea J, Qureshi N, Drury N, Guilbert P. The impact of genetic outreach education and support to primary care on practitioner's confidence and competence in dealing with familial cancers. Community Genet. 2008;11: 289-94.

54. Wilson BJ, Torrance N, Mollison J, Watson MS, Douglas A, Miedzybrodzka Z, et al. Cluster randomized trial of a multifaceted primary care decision-

support intervention for inherited breast cancer risk. Fam Pract. 2006;23: 537-44.

55. Dekanek EW, Thull DL, Massart M, Grubs RE, Rajkovic A, Mai PL. Knowledge and opinions regarding BRCA1 and BRCA2 genetic testing among primary care physicians. J Genet Couns. 2020;29:122-30.

56. Hall PH. Documentation of breast cancer family history in primary care. Master's Thesis, University of Minnesota, Minneapolis, MN, USA, January 2001.

57. Walter FM, Kinmonth AL, Hyland F, Murrell P, Marteau TM, Todd C. Experiences and expectations of the new genetics in relation to familial risk of breast cancer: a comparison of the views of GPs and practice nurses. Fam Pract. 2001;18:491-4.

58. Ganry O, Boche T. Prevention practices and cancer screening among general practitioners in Picardy, France. Public Health. 2005;119:1023-30.

59. Kaplan CP, Haas JS, Pérez-Stable EJ, Des Jarlais G, Gregorich SE. Factors affecting breast cancer risk reduction practices among California physicians. Prev Med. 2005;41:7-15.

60. Armstrong K, Quistberg DA, Micco E, Domchek S, Guerra C. Prescription of tamoxifen for breast cancer prevention by primary care physicians. Arch Intern Med. 2006;166:2260-5.

61. Collier R. American Medical Association membership woes continue. Can Med Assoc J. 2011;183:e713-4.

62. Jbilou J, Halilem N, Blouin-Bougie J, Amara N, Landry R, Simard, J. Medical genetic counseling for breast cancer in primary care: a synthesis of

major determinants of physicians' practices in primary care settings. Public Health Genom. 2014;17:190-208.

63. Smith SG, Side L, Meisel SF, Horne R, Cuzick J, Wardle J. Clinician-reported barriers to implementing breast cancer chemoprevention in the UK: a qualitative investigation. Public Health Genom. 2016;19:239-49.

64. Smith SG, Foy R, McGowan JA, Kobayashi LC, DeCensi A, Brown K, et al. Prescribing tamoxifen in primary care for the prevention of breast cancer: a national online survey of GPs' attitudes. Br J Gen Pract. 2017;67:e414-27.

65. Collins IM, Steel E, Mann GB, Emery JD, Bickerstaffe A, Trainer A et al. Assessing and managing breast cancer risk: clinicians' current practice and future needs. The Breast. 2014;23:644-50.

66. Harris H, Nippert I, Julian-Reynier C, Schmidtke J, van Asperen C, Gadzicki D, et al. Familial breast cancer: is it time to move from a reactive to a proactive role? Fam Cancer. 2011;10:501-3.

67. Meaney-Delman D, Bellcross CA. Hereditary breast/ovarian cancer syndrome: a primer for obstetricians/gynecologists. Obstet Gynecol Clin North Am. 2013;40:475-512.

68. Archer S, Babb de Villiers C, Scheibl F, Carver T, Hartley S, Lee A, et al. Evaluating clinician acceptability of the prototype CanRisk tool for predicting risk of breast and ovarian cancer: a multi-methods study. PLoS One. 2020;15:e0229999.

69. Lo LL, Collins IM, Bressel M, Butow P, Emery J, Keogh L, et al. The iPrevent online breast cancer risk assessment and risk management tool: usability and acceptability testing. JMIR Form Res. 2018;2:e24.

70. Rainey L, van der Waal D, Jervaeus A, Donnelly LS, Evans DGR, Hammarström M, et al. European women's perceptions of the implementation and organisation of risk-based breast cancer screening and prevention: a qualitative study. BMC Cancer. 2020;20:247.

71. Esquivel-Sada D, Lévesque E, Hagan J, Knoppers BM, Simard J. Envisioning implementation of a personalized approach in breast cancer screening programs: stakeholder perspectives. Healthc Policy. 2019;15:39-54.

72. Warr W, Aveyard P, Albury C, Nicholson B, Tudor K, Hobbs R, et al. A systematic review and thematic synthesis of qualitative studies exploring GPs' and nurses' perspectives on discussing weight with patients with overweight and obesity in primary care. Obes Rev. 2021;22:e13151.

73. Johnston S, Liddy C, Hogg W, Donskov M, Russell G, Gyorfi-Dyke E. Barriers and facilitators to recruitment of physicians and practices for primary care health services research at one centre. BMC Medical Res Methodol. 2010;10:109.

Chapter 3. Development of a breast cancer risk assessment and primary prevention pathway for women aged 30-39 years: views of UK primary care providers on the role of primary care

Journal:	BMC Cancer
Submission status:	Under review
Journal article reference:	Hindmarch S, Gorman L, Usher-Smith JA, Woof VG, Howell SJ, French DP. Development of a breast cancer risk assessment and primary prevention pathway for women aged 30-39 years: views of UK primary care providers on the role of primary care. BMC Cancer. Under review.

3.1 Abstract

Background: Identifying women aged 30–39 years at increased risk of developing breast cancer would allow them to receive screening and prevention offers. For this to be feasible, the practicalities of organising risk assessment and primary prevention must be acceptable to the healthcare professionals who would be responsible for delivery. It has been proposed that primary care providers are best placed to deliver a breast cancer risk assessment and primary prevention pathway. The present study aimed to investigate a range of primary care provider's views on the development and implementation of a breast cancer risk assessment and primary prevention pathway within primary care for women aged 30-39 years.

Methods: Twenty-five primary care providers working at general practices in either Greater Manchester or Cambridgeshire and Peterborough participated in five focus groups (n=18) and seven individual interviews. Data were analysed thematically and organised using a framework approach.

Results: Three themes were developed. *Challenges with delivering a breast cancer risk assessment and primary prevention pathway within primary care* highlights that primary care are willing to facilitate but not lead delivery of such a pathway given the challenges with existing workload pressures and concerns about ensuring effective clinical governance. *Primary care's preferred level of involvement* describes the aspects of the pathway participants thought primary care could be involved in, namely co-ordinating data collection for risk assessment and calculating and communicating risk. *Requirements for primary care involvement* captures the need to provide a training and education package to address deficits in knowledge prior to involvement. Additionally, the reservations primary care have about being involved

in the management of women identified as being at increased risk are discussed and suggestions are provided for facilitating primary care to take on this role.

Conclusions: Despite optimism that primary care might lead a breast cancer risk assessment and primary prevention pathway, participants had a range of concerns that should be considered when developing such a pathway.

3.2 Introduction

Pre-menopausal breast cancer incidence is increasing worldwide [1]. Younger women are more likely to develop aggressive breast cancer subtypes, which are associated with higher mortality despite intensive treatment regimens [2, 3]. As a result, breast cancer is the leading cause of death in women aged 35-50 years in the UK with 2,000 deaths reported per year [4]. There is, therefore, a need to identify younger women at increased risk of developing breast cancer who could benefit from earlier screening and preventive strategies [5].

In the UK, a strong family history of breast cancer or known high risk genetic variant in a close relative are the only criteria by which women aged under 50 years can access breast cancer screening and preventive strategies [6]. This approach relies on women either presenting with concerns about family history in primary care or having a family history identified during investigation of a breast problem in secondary care. However, at least 65% of women who develop breast cancer before the age of 50 years do not have a strong family history and are not currently identified as being at increased risk [7, 8]. The development of risk prediction models has made it possible to estimate an individual woman's risk of developing breast cancer with reasonable levels of accuracy. These models allow the tailoring of screening practices based on individual variation in risk (risk-stratified screening) and the opportunity for women to be offered preventive strategies such as weight loss or weight gain prevention interventions and risk-reducing medication.

It has been proposed by a number of researchers that primary care involvement in the delivery of a population wide risk-based screening and prevention programme is critical to its success, with their suggested role being to conduct the risk assessment

and provide primary prevention advice in the form of discussing health behaviour change and risk-reducing medication [9-11]. A recent systematic review showed that primary care providers typically take a reactive role in breast cancer risk assessment that is predominantly focused on the collection of family history [12]. However, since June 2022, the proactive identification of women at increased risk of breast cancer within primary care has been facilitated by a change to National Institute for Health and Care Excellence (NICE) guidance [13]. Further, a recent review determined that proactive breast cancer risk assessment for women under 50 years within primary care currently satisfies many of the standard principles for screening but identified implementation into clinical practice as a key area of uncertainty [14].

The roles of individuals within a risk-based programme should be clearly defined and developed in conjunction with healthcare professionals themselves to ensure acceptability [15, 16]. Qualitative studies conducted in the UK have identified barriers and facilitators with respect to primary care involvement. However, these studies have focused on specific stages of the pathway required to provide breast cancer risk assessment and primary prevention advice, for example, the implementation of risk assessment [17-19], or risk-reducing medication [20]. Furthermore, only the views of general practitioners (GPs) and nurses have been captured in qualitative research to date. The primary care workforce in the UK has grown and diversified in recent years and now includes a wider range of allied healthcare professionals and healthcare associate professionals such as pharmacists and physician associates who contribute to risk assessment and primary prevention activities. Therefore, it is important to examine the views of a range of primary care professions to understand how the wider workforce could support implementation considering declining GP numbers [21].

The present study aimed to explore primary care providers' views on the development and implementation of a breast cancer risk assessment and primary prevention pathway within primary care for women aged 30-39 years. Offering breast cancer risk assessment to this age group is necessary to ensure that maximum patient benefit can be realised through uptake of screening and preventive strategies from the age of 40 years. Specific objectives were to:

a. Understand primary care providers' views on involvement in breast cancer risk assessment and primary prevention activities
b. Identify perceived barriers and facilitators to implementation of a breast cancer risk assessment and primary prevention pathway within primary care
c. Identify the aspects of a prototype pathway that primary care providers consider more or less acceptable to be involved in

3.3 Methods

3.3.1 Design

A cross-sectional qualitative design primarily using focus groups was employed. Focus groups were considered the most appropriate method of data collection because they encourage lively debate and exploration of contradictions among members resulting in rich data [22]. They enable perspectives to evolve and become co-created, allowing insight into the degree of group consensus on the topic which was important given the objective of identifying which aspects of the prototype pathway are more or less acceptable [23]. One-to-one interviews were conducted when participants were unable to attend scheduled focus groups.

3.3.2 Participants and setting

Participants were eligible if they were: (1) employed at a general practice within Greater Manchester or Cambridgeshire and Peterborough Integrated Care Systems, (2) a primary care provider in one of the following professions: nurse, doctor, pharmacist, physician associate, nursing associate, or healthcare assistant, (3) able to provide informed consent, and (4) able to speak and understand English. We deliberately sought heterogeneity in profession amongst focus group participants to reflect current multidisciplinary professional practice. Group diversity encourages people to explain their reasoning revealing how the groupings construct their positions on the topic being examined [24]. This provides the opportunity to identify where the disputes and boundaries lie between different professions.

The locations were chosen so that pre-existing links the research team had with primary care contacts could be utilised given personal connections have been found to be a particularly effective way of recruiting primary care providers [25]. The patient populations in both geographical areas are different, with Greater Manchester having higher levels of deprivation and ethnic diversity than Cambridgeshire and Peterborough [26, 27].

3.3.3 Procedure

A variety of recruitment methods were used to target the eligible professions. Emails promoting the study were sent by the lead author to key individuals including clinical academic GPs known to the research team, a programme assistant at the North West GP training school, and primary care contacts at the Greater Manchester and Cambridgeshire and Peterborough Integrated Care Boards. Those contacted were asked to cascade a letter of invitation and participant information sheet across their primary care networks. Study advertisements were also circulated in primary care

newsletters and shared on Twitter. Finally, snowball sampling was employed whereby participants shared the study information within their own professional networks to assist in identifying future participants. For all strategies, prospective participants were asked to contact the research team to express their interest in taking part and following confirmation of eligibility they were sent a participant information sheet if they had not already received one.

An initial draft of the topic guide was developed by the lead author, with questions guided by the aims of the study. Feedback on this draft was obtained from members of the research team (JAU-S, DPF and SJH) who have a wealth of clinical and research expertise in breast cancer and screening services, primary care and health services research, health psychology, and qualitative methods. The topic guide was pilot tested with a clinical academic GP who was not part of the research team, who provided feedback on wording and relevance of questions, prompts and flow. Questions focused on eliciting views about primary care involvement in breast cancer risk assessment and primary prevention, including perceived confidence in performing tasks, consideration of which primary care professions could be involved and perceived barriers and facilitators to involvement at each stage of the pathway (Appendix B.1). As the material to be discussed was likely to be unfamiliar to participants, background text was circulated as pre-reading material prior to each focus group and interview (Appendix B.2). During the focus groups and interviews, a prototype breast cancer risk assessment and primary prevention pathway was presented to participants to stimulate discussion about the potential role of primary care. Three components of breast cancer risk assessment were proposed in line with an approach currently being offered to women aged 30-39 years in a Cancer Research UK funded feasibility study [28]: (1) a questionnaire for self-reported

assessment of breast cancer risk factors, (2) a saliva sample for assessment of polygenic risk and mutations in high-risk genes, and (3) a low-dose mammogram for assessment of breast density. The topic guide was followed flexibly, allowing participants to raise issues important to their professional experience.

Online focus groups and interviews were conducted between July 2022 and March 2023, using Zoom video conferencing. Audio-recorded verbal consent was obtained prior to any study procedures. Following consent, participants gave demographic information (gender, age, ethnicity, employment details (job title and years in current role) and practice postcode).

Data were audio-recorded and transcribed verbatim by an external transcription company. Data collection was primarily conducted by the lead author (SH) with another member of the research team taking notes and providing a verbal summary of the discussion prior to each focus group ending (VGW). Both facilitators were female doctoral students with a psychology disciplinary background, and at least five years postgraduate training and experience conducting qualitative research with healthcare professionals. Interviews were conducted by the lead author (SH). Data collection continued until the research team deemed that sufficient data had been collected to answer the research question [29]. A £50 cash payment and additional Internet expenses (£5 an hour) was offered to participants in recognition of their time given to the study.

3.3.4 Data analysis

Data were analysed thematically and organised using a framework approach within NVivo 12 [30]. A critical realist approach was taken meaning we treated the data as indicating the participants' perception of their reality, which is shaped by and

embedded within their cultural context, language and experiences [31, 32]. Primary data analysis was conducted by the lead author with input from LG, JAU-S, and DPF. Initial coding was deductive to ensure the study objectives were addressed. Additional codes were also developed inductively during data analysis to capture nuances in the data. The lead author constructed a working thematic framework of codes contained within categories which was reviewed and refined as coding progressed by way of regular meetings with LG and JAU-S before being applied to all remaining transcripts. The 'framework' feature in NVivo12 was used to plot each category onto a separate thematic matrix with codes presented in separate columns, and participants (cases) on separate rows. Data in each cell were summarized to synthesise the data set and illustrative extracts were noted. The resulting data in the framework matrices were compared across and within cases to highlight similarities and differences and develop the final themes. Regular meetings were held between members of the research team (SH, LG, JAU-S, and DPF) throughout analysis and interpretation to discuss explanations for findings and determine the overall thematic structure.

3.4 Results

A total of 25 primary care providers were recruited, with 18 taking part in focus groups (n = 2-5 per group) and seven taking part in interviews. Focus group duration ranged from 62 to 85 minutes (median 65 minutes) and interviews lasted between 48 and 65 minutes (median 54 minutes). Demographic and professional characteristics of the sample are presented in Table 3.1. The majority of participants were female (84%) and medically qualified (76%). Based on practice postcode, most participants worked in practices located in areas of high deprivation.

Table 3.1. Demographic and professional characteristics of participants (*n* = 25)

Characteristic	N (%)
Gender	
Female	21 (84)
Male	4 (16)
Age (years)	
18-30	5 (20)
31-40	12 (48)
41-50	6 (24)
51-60	2 (8)
Ethnicity[a]	
White British	15 (60)
White (Other)	2 (8)
White Irish	1 (4)
Indian	1 (4)
Pakistani	1 (4)
Chinese	1 (4)
Black (Other)	1 (4)
Mixed (White & Asian)	1 (4)
Other	1 (4)
Prefer not to say	1 (4)
Profession	
GP trainee	10 (40)
GP	9 (36)
Trainee nursing associate	2 (8)
Healthcare assistant	1 (4)
Physician associate	1 (4)
Advanced nurse practitioner	1 (4)
Advanced clinical pharmacist	1 (4)
Years in current role	
0-4	18 (72)
5-9	3 (12)
10-14	2 (8)
15-19	1 (4)
≥20	1 (4)
Practice location	
Greater Manchester	23 (92)
Cambridgeshire or Peterborough	2 (8)
Deprivation decile of practice location[b]	
1-2 (most deprived)	13 (52)
3-4	6 (24)
5-6	3 (12)
7-8	3 (12)
9-10 (least deprived)	0

[a]Detailed ethnicity classifications reported in line with the current ethnicity harmonised standard [33]

[b]Derived from practice postcode using the Index of Multiple Deprivation 2019, a measure of relative deprivation for small areas in England [26]

Data are presented as three themes with six sub-themes (see Table 3.2). Quotes are identified by participant profession type and number followed by interview (I) or focus group (FG) number.

Table 3.2. Thematic structure

Theme	Sub-theme
1. Challenges with delivering a breast cancer risk assessment and primary prevention pathway within primary care	1.1 Resolving existing workload and workforce capacity limitations
	1.2 Ensuring effective clinical governance
2. Primary care's preferred level of involvement	2.1 Co-ordinating data collection for risk assessment
	2.2 Calculating and communicating risk
3. Requirements for primary care involvement	3.1 Upskilling primary care providers
	3.2 Overcoming reservations towards managing women at increased risk

3.4.1 Theme 1: Challenges with delivering a breast cancer risk assessment and primary prevention pathway within primary care

3.4.1.1 Resolving existing workload and workforce capacity limitations

Participants considered involvement in breast cancer risk assessment and primary prevention to be within the scope of primary care responsibilities. This was largely because involvement in risk assessment and primary prevention activities for other conditions, such as cardiovascular risk, was part of their routine practice. Despite this, given the challenges with existing workload pressures in the aftermath of the COVID-19 pandemic, all participants thought that primary care could facilitate but not lead the delivery of a breast cancer risk assessment and primary prevention pathway.

> it's what are you going to give up, you know, so that you know, that's the decision. Yeah, of course we can do it, but are we not going to do flu vaccines or childhood immunisations, or cervical screening to make time for this as we can't do everything. (GP, 18, FG5)

Participants were particularly concerned about the proportion of women who would be identified as at increased risk as management of these women would be more time consuming. To cope with this additional workload, some participants discussed the possibility of nominating a member of the practice team as a champion who would have protected time to manage women at increased risk should the workload implications warrant it.

By contrast, other participants discussed the option of delegating the additional workload across different professions within the primary care networks including practice-based roles such as physician associates and pharmacists. For example, pharmacists could be responsible for risk-reducing medication. Many participants viewed this positively and believed it would facilitate primary care involvement. However, one participant was concerned about variation in practitioner composition of the workforce across different general practices as this could lead to a lack of standardisation in delivery exacerbating existing health inequalities:

> whilst it is very good to have this flexibility and we can devolve it to a lot of people working in the practice, for those small practices that don't have that luxury, I think - I mean, potentially, are they going to be in the more deprived areas anyway with less resources, and then there's isolated women in an isolated practice. (GP trainee, 5, FG2)

Ultimately, participants did not think delivery of a breast cancer risk assessment and primary prevention pathway in primary care was viable unless resourced appropriately in line with the expected increase in workload. The provision of financial incentives to calculate breast cancer risk such as inclusion in the quality and outcomes framework was perceived as necessary for increasing the likelihood of primary care performing the behaviour proactively.

> You'd need to offer incentives, I would have thought, especially when you think about the time it will take from the workforce (Trainee nursing associate, 11, FG3)

3.4.1.2 Ensuring effective clinical governance

Participants expressed concerns about safely co-ordinating the delivery of a breast cancer risk assessment and primary prevention pathway within primary care. Their key concern focused on ensuring effective clinical governance arrangements with many participants preferring a centralised service delivery model akin to cancer screening programmes for this reason. Benefits of this delivery model were perceived to be robust quality assurance standards, a dedicated team to provide support to women and a systematic approach of following up on missing data to ensure accurate risk estimates. The latter was considered particularly important given the multifactorial nature of the risk assessment.

> I think I echo what other people have said, that it's [co-ordinating breast cancer risk assessment] a big risk to hold within primary care, where there's specialist services available (Physician associate, 9, FG3)

> if there was like three different chunks to it, um, you know, what happens if they don't bring back the saliva or what happens if they don't come in for

> their history bit, because then who would do that chasing? […] how would that work in terms of getting all of it complete together so that you can get a meaningful result. (GP, 24, I6)

Furthermore, the multifactorial nature of the risk assessment was perceived as a logistical challenge to primary care co-ordinating the process of risk assessment. Participants questioned how results from the mammography component completed in secondary care could be accessed in primary care to allow risk to be calculated. On the contrary, one participant thought that not co-ordinating the process of risk assessment in primary care would be a missed opportunity as the multifactorial nature of the risk assessment could be leveraged to identify additional information to breast cancer risk which would be useful for informing the patient's care:

> I think the difficulty we'd have with not doing it in primary care is, even if we didn't deal with the women who were high risk of breast cancer, obviously, the measurements that you're taking can flag up a number of other issues. So, for instance, if they came back with a low risk of breast cancer but they had a really high cholesterol, or they turned out to be diabetic, then that will inevitably get bounced back to us anyway. (GP, 13, FG4)

A decentralised service delivery model co-ordinated through primary and secondary care was also discussed but largely dismissed. Participants were concerned that splitting the pathway across primary and secondary care could result in care fragmentation compromising the quality of care women receive.

3.4.2 Theme 2: Primary care's preferred level of involvement

Despite concerns about leading the delivery of a breast cancer risk assessment and primary prevention pathway, participants highlighted which aspects of the pathway

they felt primary care could most appropriately be involved in and provided suggestions for facilitating implementation.

3.4.2.1 Co-ordinating data collection for risk assessment

Much of the risk factor information required for a breast cancer risk assessment would already be captured in electronic medical records and participants felt the remaining information such as age at menarche could be collected easily by sending a questionnaire to patients' mobile phones. Participants described how this mode of communication has become commonplace following the COVID-19 pandemic. This was viewed by most participants as a better use of resources in comparison to taking up consultation time.

> There is, and this is partly thanks to COVID, there is now much better ways of communicating with patients, like doing questions that you can just send them on their phones […] They're getting cannier about responding to things online, we've been sending them links that we perhaps - you know, in the old days we might have given them a printout about something (GP, 19, I1)

However, one participant was cautious of relying on a digital approach only to collect this information given her experience of speaking to many young women who did not own a mobile phone. Therefore, an alternative method of providing risk factor information would need to be considered such as an appointment with a healthcare assistant to ensure women from socioeconomically deprived areas have equitable access to risk assessment.

When considering potential opportunities for integrating components of the risk assessment into existing routine appointments, participants acknowledged the difficulty of doing so for the target population given limited points of contact; it's

actually a bit of an awkward demographic, isn't it, because they're too young for all of the chronic disease stuff, but they're too old for things like university checks (GP trainee, 15, FG5). Participants did not think it was appropriate to add a breast cancer risk assessment to cervical screening appointments due to this already being an anxiety provoking appointment for many women.

3.4.2.2 Calculating and communicating risk

Participants were similarly happy to calculate breast cancer risk providing a risk assessment tool similar to QRISK (cardiovascular disease risk assessment tool) was available and integrated into their IT system. To make the process of calculating risk more efficient, it was considered particularly useful if the tool could automatically extract the relevant information coded in patient's medical records. Overall, participants would be willing to communicate the result of a breast cancer risk assessment if education for providers was available to help them interpret the risk result. Risk was recognised as an abstract and often difficult to understand concept for patients. Therefore, participants desired visual representations of risk such as icon arrays and a feature to demonstrate the impact of reducing risk on patient outcomes on the risk assessment tool to aid communication of the result.

> in terms of relaying the information to the patient, it's very easy to translate QRISK into case plots and use that visual, you know, representation of risk reduction, for maybe people who struggle with numbers. (GP trainee, 4, FG2)

3.4.3 Theme 3: Requirements for primary care involvement

3.4.3.1 Upskilling primary care providers

Whichever pathway was used to introduce breast cancer risk assessment, there was an expectation from participants that primary care providers would need to be

upskilled to be involved in this new area of patient care. Participants were unfamiliar with the evidence base underpinning and supporting the introduction of breast cancer risk assessment for young women. Possibly due to this unfamiliarity, some participants expressed reservations about the robustness of the risk algorithm to accurately identify those at increased risk, particularly regarding accuracy of self-reported information and the stability of risk over time. Moreover, participants reported that availability of evidence demonstrating tangible differences in outcomes for young women participating in breast cancer risk assessment, such as numbers of lives saved, would make primary care more accepting of greater involvement:

> One of the things as well is I think that a lot of it relies on is how effective the whole thing is, so if you told me this will save of a population of women in my practice, this will save this many lives or you know, you know, you could convince me to get a lot more involved in it. (GP trainee, 17, FG5)

Participants did not feel they possessed sufficient knowledge about topics required to deliver a breast cancer risk assessment and primary prevention pathway; notably genetics, interpretation of risk results, and counselling about risk-reducing medication. Therefore, provision of a training and education package to address deficits in knowledge was perceived as essential prior to involvement.

> I can just think of the spectrum of questions that women are going to be asking about their risk, about different contraceptive choices, IVF, you know. […] I can just imagine, a lot of the questions, we just might not have the answers to. (GP trainee, 6, FG2)

3.4.3.2 Overcoming reservations towards managing women at increased risk

Most participants were comfortable with having health behaviour change conversations, with many describing it as primary care's "bread and butter". However, participants in one focus group acknowledged the complexity of changing people's health behaviours and felt it would be more effective to signpost directly or via social prescribers to community health interventions for continued and more in-depth support than a primary care provider has the time or expertise to provide.

> because it is complex, you can't just give a one-off intervention to somebody and expect them to change so, you know, I would have thought that you probably need community services for those who are interested in changing to help coach them through it. (GP, 18, FG5)

The majority of participants who were prescribers expressed discomfort in discussing and prescribing Tamoxifen as a preventive medication; I wouldn't touch it [Tamoxifen] with a bargepole now (GP trainee, 17, FG5). When prompted to consider the similarity with prescribing a statin to reduce cardiovascular risk, participants appreciated how the situations were analogous but expressed a reluctance to discuss and prescribe Tamoxifen. Reasons given for this reluctance included Tamoxifen prescribing not being part of routine practice in primary care and a lack of knowledge about its side effects and monitoring requirements to counsel women and manage Tamoxifen appropriately. Additionally, one participant believed that statins were underpinned by a more robust evidence base than Tamoxifen.

> I'm not familiar with things like side effects, monitoring […] How do I know when to stop it, like which of the patients in the high-risk group would just be the lifestyle modification, which ones would be for Tamoxifen, those sorts of

> things like I don't know about. So, how can I prescribe safely if I don't know about it? (GP trainee, 15, FG4)

A major area of concern for many participants was the perceived appropriateness of prescribing Tamoxifen to the target population of women aged 30-39 years given it was believed to increase the risk of thrombosis and endometrial cancer. As family planning is likely to be a consideration for many women in this age group, some participants questioned the likelihood of women agreeing to take Tamoxifen (as an anti-oestrogen) due to its interference with childbearing.

> You are giving a drug to reduce the risk of something […] but what is the actual absolute risk of increasing the endometrial cancer? Is it just a pointless exercise in some regards? (GP trainee, 4, FG2)

Despite their concerns, participants acknowledged that a change in practice was possible and made suggestions about how primary care could be made to feel more comfortable assuming responsibility for managing Tamoxifen. For example, if a specialist in secondary care wrote the first prescription or a NICE guideline was developed focused on the initiation and ongoing management of Tamoxifen for breast cancer risk reduction in the target population.

> I guess there are things that maybe ten, fifteen years ago that we would never have foreseen - that we wouldn't have felt comfortable doing in primary care, that we now do. So, you know, things do change, and a lot of sometimes our beliefs are held because of what we're traditionally used to doing. […] If you look at the management of diabetes, you know, that's transformed in the last ten years and we've got used to doing it. (GP, 13, FG4)

3.5 Discussion

3.5.1 Summary of main findings

The primary care providers taking part in this study viewed their involvement in a breast cancer risk assessment and primary prevention pathway for women aged 30-39 years as logical given it complemented their existing responsibilities with respect to risk assessment and prevention for other diseases. However, they did not think it was feasible, at present, for the pathway to be led by primary care given workload pressures and concerns about ensuring effective clinical governance within primary care. Collecting the risk factor information and calculating and communicating the risk result were considered the most acceptable stages for primary care to be involved in and management of women at increased risk the least. Provision of a training and education package was considered essential to facilitate primary care involvement in this new area of patient care.

3.5.2 Relevance to existing literature

Previous literature has consistently identified primary care as the most opportune setting to conduct breast cancer risk assessment and provide prevention advice as part of the implementation of a risk-based screening and prevention programme [9-11]. However, the present findings suggest that primary care providers are concerned about leading such a pathway and are particularly cautious about assuming responsibility for the management of women identified as at increased risk. In line with previous research [12, 20], this study found that primary care providers are particularly uncomfortable with the prospect of discussing and prescribing Tamoxifen as a breast cancer risk-reduction strategy. However, the present study also offers novel insight into perceived concerns about offering Tamoxifen to young women. Participants were concerned that Tamoxifen would increase the risks of thrombosis and endometrial cancer. Although the risk of thrombosis is increased, the

absolute risk remains low in young women being comparable to treatment with the combined oral contraceptive. The increase in endometrial cancer risk is only observed when Tamoxifen is used by post-menopausal women [34]. Therefore, concerns about Tamoxifen use in this population could be alleviated through provision of education.

Although such education could be provided to facilitate primary care involvement in risk management, it may be challenging to justify the considerable resources needed to upskill primary care providers to take on risk management if few women would be eligible for this per practice. If this were the case, it may be more appropriate for primary care to identify women at increased risk and refer them to a Family History, Risk and Prevention Clinic for discussion of risk management strategies. This approach would also be in line with participants' preferred level of involvement.

A key consideration underpinning participants' views about involvement in breast cancer risk assessment and primary prevention was the expected impact on workload given existing workload pressures within primary care. The diversity of the primary care workforce was perceived as a facilitator to their involvement as additional workload could be delegated across different professions. However, regional differences in the composition of the primary care workforce in England have been found, with integration of allied healthcare and healthcare associate professionals lacking [35]. Therefore, a service delivery model reliant on contributions from these professionals has the potential to introduce or exacerbate existing health inequalities. Nonetheless, practice-based pharmacists contribute towards detailed tasks related to medicine prescription, reducing the burden of these activities for existing staff and improving prescribing practices [36, 37]. This suggests that pharmacists could play

an important role in facilitating primary care involvement in risk-reducing medication.

In the present study, the multifactorial nature of the risk assessment was also perceived as a barrier to primary care co-ordinating the process of risk assessment. Participants were concerned about ensuring effective clinical governance arrangements for breast cancer risk assessment because of the risk of missing data and implications of this for the accuracy of risk estimates. Additionally, how the results from the mammography component would be accessible by primary care to enable risk calculation was unclear to participants. Mammographic density is a well-established risk factor for breast cancer in older women but its contribution to risk in women aged 30-39 years remains unknown. A study is currently ongoing to determine the magnitude of breast cancer risk associated with mammographic density in women aged 30-39 years [28]. Depending on the results of this study, assessment of mammographic density may well be necessary so how this could be co-ordinated within primary care would be important to consider.

3.5.3 Strengths and limitations

This study elicited primary care providers' views across a breast cancer risk assessment and primary prevention pathway. This is considered a strength of the study as a more comprehensive understanding of involvement was achieved compared to previous research which has been limited in scope to specific stages of the pathway. Furthermore, we recruited a range of professionals including allied healthcare and healthcare associate professionals, with varying levels of clinical experience. This facilitated a more holistic understanding of the issues affecting primary care involvement in breast cancer risk assessment and primary prevention as

staff were able to offer their views from the perspective of their differing roles. However, we acknowledge that the views of the nursing profession were underrepresented, and many participants were relatively new to their posts.

Recruitment to focus groups proved challenging given the time commitment required to participate. An alternative approach could have been to recruit multiple members of staff from the same practice so that a team meeting could be utilised for the focus group. This approach may have resulted in more solution focused dialogue as they would be able to reflect on their own experiences as a working group to inform how the pathway could work within their own practice. Nevertheless, those who did partake in focus groups brought a range of perspectives and disagreements were voiced which may not have been the case if participants had known each other.

3.5.4 Implications and future research directions

The present study has identified that primary care providers are willing in principle to be involved in the delivery of a breast cancer risk assessment and primary prevention pathway for young women, but a range of concerns were identified. Future research should focus on developing and evaluating strategies for implementing multifactorial risk assessment within primary care, taking into account the views of primary care, and paying particular attention to clinical governance requirements and how delivery can minimise exacerbation of health inequalities. Better modelling and communication of the numbers of women involved per general practice is needed to inform the scope of primary care's involvement.

3.5.5 Conclusion

Despite optimism that primary care might lead a breast cancer risk assessment and primary prevention pathway, participants had a range of concerns that should be considered when developing such a pathway.

Declarations

Ethics approval and consent to participate: Ethical approval was received from the University Research Ethics Committee, University of Manchester (Ref: 2019-7900-12761) and HRA and the study was carried out following the Good Clinical Practice principles and relevant regulations. All participants provided informed consent to take part in the study.

Consent for publication: Not applicable.

Availability of data and materials: The data that support the findings of this study are openly available in Figshare at http://doi.org/10.48420/24058629.

Competing interests: The authors declare that they have no competing interests.

Funding: SH is funded by a Manchester Cancer Research Centre PhD studentship. VGW is funded by a Medical Research Council PhD studentship (MR/N013751/1). DPF and SJH are supported by the NIHR Manchester Biomedical Research Centre (IS-BRC-1215-20007 and NIHR203308). JAU-S is funded by an Advanced Fellowship from the National Institute for Health and Social Care Research (NIHR300861). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Authors' contributions: SH, DPF, SJH and LG conceived and designed the study. SH, DPF, JAU-S and SJH developed the study materials. SH and VGW recruited all participants and collected the data. SH led the analysis, with input from LG, JAU-S and DPF. SH drafted the manuscript and all authors provided feedback on versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgements: We would like to thank all the participants who kindly gave their time to take part in this study. We would also like to thank Brian McMillan for reviewing the topic guide and advising on recruitment strategies.

3.6 References

1. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. Lancet Glob Health. 2020;8(8):e1027-37.
2. Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2− advanced breast cancer: focus on special considerations and latest advances. Clin Cancer Res. 2018;24(21):5206-18.
3. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep. 2017;7(1):11625.
4. Office for National Statistics. Deaths registered in England and Wales: 2021 [Online]. 2022 [Accessed 26th May 2023]. Available from: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregistrationsummarytables/2021.
5. Kudela E, Samec M, Kubatka P, Nachajova M, Laucekova Z, Liskova A, et al. Breast cancer in young women: status quo and advanced disease management by a predictive, preventive, and personalized approach. Cancers. 2019;11(11):1791.
6. National Institute for Health and Care Excellence (NICE). Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [updated 2019 Nov] (Clinical Guideline [CG164]). [Online]. 2013 [Accessed 27th July 2023]. Available from: https://www.nice.org.uk/guidance/cg164/chapter/Recommendations.
7. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, et al. Germline BRCA mutation and outcome in young-onset

breast cancer (POSH): a prospective cohort study. Lancet Oncol. 2018;19(2):169-80.

8. Eccles BK, Copson ER, Cutress RI, Maishman T, Altman DG, Simmonds P, et al. Family history and outcome of young patients with breast cancer in the UK (POSH study). Br J Surg. 2015;102(8):924-35.

9. Dent T, Jbilou J, Rafi I, Segnan N, Törnberg S, Chowdhury S, et al. Stratified cancer screening: the practicalities of implementation. Public Health Genom. 2013;16(3):94-9.

10. Rainey L, van der Waal D, Jervaeus A, Wengström Y, Evans DG, Donnelly LS, et al. Are we ready for the challenge of implementing risk-based breast cancer screening and primary prevention? The Breast. 2018;39:24-32.

11. Selby K, Bartlett-Esquilant G, Cornuz J. Personalized cancer screening: helping primary care rise to the challenge. Public Health Rev. 2018;39(1):4.

12. Bellhouse S, Hawkes RE, Howell SJ, Gorman L, French DP. Breast cancer risk assessment and primary prevention advice in primary care: a systematic review of provider attitudes and routine behaviours. Cancers. 2021;13(16):4150.

13. National Institute for Health and Care Excellence (NICE). 2022 exceptional surveillance of familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (NICE guideline CG164). [Online]. 2022 [Accessed 12th September 2023]. Available from: https://www.nice.org.uk/guidance/cg164/resources/2022-exceptional-surveillance-of-familial-breast-cancer-classification-care-and-managing-

breast-cancer-and-related-risks-in-people-with-a-family-history-of-breast-cancer-nice-guideline-cg164-pdf-14358610516165.

14. Usher-Smith JA, Hindmarch S, French DP, Tischkowitz M, Moorthie S, Walter FM, et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636–46.

15. Blouin-Bougie J, Amara N, Simard J. Toward a population-based breast cancer risk stratification approach? The needs and concerns of healthcare providers. J Pers Med [Internet]. 2021; 11(6).

16. Taylor LC, Law K, Hutchinson A, Dennison RA, Usher-Smith JA. Acceptability of risk stratification within population-based cancer screening from the perspective of healthcare professionals: a mixed methods systematic review and recommendations to support implementation. PLoS One. 2023;18(2):e0279201.

17. Archer S, Stutzin Donoso F, Carver T, Adelaide Y, Cunningham A, Ficorella L, et al. Exploring the barriers and facilitators of implementing CanRisk in primary care: a qualitative thematic framework analysis. Br J Gen Pract. 2023;73(733):e586-96.

18. Archer S, Babb de Villiers C, Scheibl F, Carver T, Hartley S, Lee A, et al. Evaluating clinician acceptability of the prototype CanRisk tool for predicting risk of breast and ovarian cancer: A multi-methods study. PLoS One. 2020;15(3):e0229999.

19. Usher-Smith JA, Silarova B, Ward A, Youell J, Muir KR, Campbell J, et al. Incorporating cancer risk information into general practice: a qualitative study using focus groups with health professionals. Br J Gen Pract. 2017;67(656):e218.

20. Smith SG, Side L, Meisel SF, Horne R, Cuzick J, Wardle J. Clinician-reported barriers to implementing breast cancer chemoprevention in the UK: a qualitative investigation. Public Health Genom. 2016;19(4):239-49.

21. British Medical Association. Pressures in general practice data analysis. [Online]. 2023 [Accessed 27th July 2023]. Available from: https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/pressures-in-general-practice-data-analysis.

22. Kitzinger J. Qualitative research: introducing focus groups. BMJ. 1995;311(7000):299-302.

23. Ivanoff SD, Hultberg J. Understanding the multiple realities of everyday life: basic assumptions in focus-group methodology. Scand J Occup Ther. 2006;13(2):125-32.

24. Clavering EK, McLaughlin J. Crossing multidisciplinary divides: exploring professional hierarchies and boundaries in focus groups. Qual Health Res. 2007;17(3):400-10.

25. Johnston S, Liddy C, Hogg W, Donskov M, Russell G, Gyorfi-Dyke E. Barriers and facilitators to recruitment of physicians and practices for primary care health services research at one centre. BMC Medical Res Methodol. 2010;10:109-.

26. Ministry of Housing, Communities, Local Government. English indices of deprivation 2019. [Online]. 2019 [Accessed 14th August 2023]. Available from: https://imd-by-postcode.opendatacommunities.org/imd/2019.

27. Office for National Statistics. Ethnic group, England and Wales: Census 2021. [Online]. 2022 [Accessed 14th August 2023]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/eth

nicity/bulletins/ethnicgroupenglandandwales/census2021#how-ethnic-composition-varied-across-england-and-wales.

28. Manchester University NHS Foundation Trust. Breast CANcer Risk Assessment in Younger women: BCAN-RAY (BCAN-RAY). ClinicalTrials.gov identifier: NCT04336904. [Online]. 2022 [Accessed 14th August 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05305963.

29. O'Reilly M, Parker N. 'Unsatisfactory saturation': a critical exploration of the notion of saturated sample sizes in qualitative research. Qual Res. 2013;13(2):190-7.

30. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol. 2013;13(1):117.

31. Collier A. Critical realism: an introduction to Roy Bhaskar's philosophy. London: Verso Books; 1994.

32. Taylor SP. A realist philosophical approach for housing research: critical realism. Int J Hous Hum Settl Plan. 2020;6(2):1-20.

33. Government Statistical Service. Ethnicity harmonised standard. [Online]. 2011 [Accessed 14th August 2023]. Available from: https://analysisfunction.civilservice.gov.uk/policy-store/ethnicity-harmonised-standard/.

34. Nelson HD, Smith MEB, Griffin JC, Fu R. Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. preventive services task force. Ann Intern Med. 2013;158(8):604-14.

35. Sharon S, Jon G, Kath C, Anne M, Damian EH, Mark H, et al. Regional variation in practitioner employment in general practices in England: a comparative analysis. Br J Gen Pract. 2020;70(692):e164-71.

36. Francetic I, Gibson J, Spooner S, Checkland K, Sutton M. Skill-mix change and outcomes in primary care: longitudinal analysis of general practices in England 2015–2019. Soc Sci Med. 2022;308:115224.

37. Jon G, Igor F, Sharon S, Kath C, Matt S. Primary care workforce composition and population, professional, and system outcomes: a retrospective cross-sectional analysis. Br J Gen Pract. 2022;72(718):e307-15.

Chapter 4. Optimising the delivery of breast cancer risk assessment to women aged 30-39 years: a qualitative study of women's views

Journal:	Women's Health
Submission status:	Published
Journal article reference:	Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk assessment for women aged 30-39 years: a qualitative study of women's views. Women's Health. 2023;19.

4.1 Abstract

Background: Identifying women aged 30-39 years at increased risk of developing breast cancer could allow them to consider screening and preventive strategies. Research is underway to determine the feasibility of offering breast cancer risk assessment to this age group. However, it is unclear how best to deliver and communicate risk estimates to these women, in order to avoid potential harms such as undue anxiety and increase benefits such as informed decision-making.

Objectives: This study aimed to investigate women's views on, and requirements for, this proposed novel approach to risk assessment.

Design: A cross-sectional qualitative design was used.

Methods: Thirty-seven women aged 30-39 years with no family history or personal history of breast cancer participated in seven focus groups (n=29) and eight individual interviews. Data were analysed thematically using a framework approach.

Results: Four themes were developed. *Acceptability of risk assessment service* concerns the positive views women have toward the prospect of participating in breast cancer risk assessment. *Promoting engagement with the service* describes the difficulties women in this age group experience in relation to healthcare access, including mental load and a lack of cultural awareness, and the implications of this for service design and delivery. *Impact of receiving risk results* focuses on the anticipated impacts of receiving different risk outcomes, namely complacency towards breast awareness behaviours following low-risk results, an absence of reassurance following average-risk results, and anxiety for high-risk results. *Women's information requirements* highlights women's desire to be fully informed at invite

including understanding why the service is needed. Additionally, women wanted risk feedback to focus on plans for management.

Conclusion: The idea of breast cancer risk assessment was received favourably amongst this age group providing that a risk management plan and support from healthcare professionals is available. Determinants of acceptability of a new service included minimising effort required to engage with service, co-development of invitation and risk feedback materials and the importance of educational campaigning about the potential benefits of participation in risk assessment.

4.2 Introduction

Epidemiological studies from the past decade illustrate that breast cancer incidence is increasing in pre-menopausal women worldwide [1-3]. Younger women are more likely to have aggressive breast cancer subtypes, which lead to poorer prognosis and decreased survival despite intensive and prolonged treatment regimens [4, 5]. Breast cancer is more frequently lethal in younger women than in those diagnosed aged over 50 years (10-year survival aged <40 years at diagnosis 70% vs 87% in those >50 years) [6]. Consequently, there is a growing urgency to implement initiatives to identify younger women at higher risk so that screening and preventive strategies can be offered [7].

In the UK, a strong family history of breast cancer is the only basis for comprehensive breast cancer risk assessment that currently allows women aged under 50 years to access screening and preventive strategies [8]. However, at least 65% of women who develop breast cancer before the age of 50 years do not have a family history and are not currently identified as being at increased risk [6, 9].

One proposed approach to identify women at increased risk of breast cancer involves the use of personalised breast cancer risk estimates [10]. The development of risk algorithms, such as the Gail, Tyrer–Cuzick and BOADICEA models, has made it possible to estimate an individual's risk of breast cancer [11-14]. These models typically include a combination of 'classic' risk factors including family history, hormonal and reproductive history and lifestyle. In recent years, risk prediction models have incorporated polygenic risk scores and mammographic breast density, which have improved their discriminatory accuracy [15-18]. The merits of personalised risk assessment for breast cancer has predominantly been explored

within the context of implementing risk stratification into breast cancer screening programmes i.e. tailoring of screening practices based on individual variation in risk [19]. This approach has the potential to improve the benefit to harm ratio of screening [20]. Recruitment is ongoing for several international trials to determine the potential effectiveness of a risk-based screening regimen in comparison to standard screening practice [21, 22].

Given the increasing burden of breast cancer in pre-menopausal women, the feasibility of offering breast cancer risk assessment to women aged 30-39 years is currently being investigated (NCT05305963). In line with the Medical Research Council (MRC) Framework for Developing and Evaluating Complex Interventions [23], it is important to consider acceptability to potential recipients of a new service as a major determinant of feasibility. To date, the views and attitudes of women who are too young to attend breast screening and who are not at known increased risk of breast cancer have rarely been investigated. Previous research with screening age women has demonstrated that concerns about inducing unnecessary worry and perceived ability to cope emotionally with risk feedback influence decisions to participate in breast cancer risk assessment [24, 25]. Additionally, a recent multicriteria decision analysis identified service access as the most valued criteria influencing decisions to participate [26]. However, it remains unclear how best to implement breast cancer risk assessment and communicate risk information outside of an organised screening programme to younger women.

The present study aimed to investigate prospective service users' attitudes towards a proposed new breast cancer risk assessment service to inform the delivery model adopted in the feasibility study.

Specific objectives were to:

a) Understand women's views on, feelings about and attitudes towards introducing breast cancer risk assessment
b) Understand women's preferences for access to and delivery of a breast cancer risk assessment service
c) Identify women's information and support needs with respect to breast cancer risk assessment and risk communication

4.3 Methods

4.3.1 Design

A cross-sectional qualitative design was used. Given the novel and hypothetical nature of the discussion topic, focus groups were chosen as the primary method of data collection. Participants were unlikely to have considered breast cancer risk assessment previously and therefore the debate within the group would encourage participants to reflect on and clarify their own perspectives, resulting in a depth of dialogue not often found in interviews [27]. Focus groups also allow participants to consider their views in relation to others, which might result in opinions shifting during the course of discussion [28]. Therefore, this interaction between participants allows insight into the degree of group consensus on the topic [29]. One-to-one interviews were carried out when participants were unable to attend scheduled focus groups.

4.3.2 Participants

Participants were recruited through responding to study advertisements outlining the inclusion criteria and topic. Inclusion criteria were chosen to ensure that the resulting sample matched the intended recipients of the planned study assessing feasibility of

offering breast cancer risk assessment to women aged 30-39 years (NCT05305963). Participants met study inclusion criteria if they were (1) born female, (2) aged 30-39 years, (3) residing in Greater Manchester, (4) able to provide informed consent, and (5) able to understand and communicate in the English language. Women could not take part if they had received a breast cancer diagnosis or had a first-degree female relative (mother or sister) affected by breast cancer.

4.3.3 Procedure

Poster advertisements were shared on social media platforms (Facebook and Twitter) and displayed on noticeboards in public buildings (e.g., libraries and community centres). The co-founder of a community organisation made direct contact with the research team after seeing an advertisement on Twitter and facilitated the recruitment of four members of the community group who were from ethnic minority backgrounds. Prospective participants were screened against inclusion criteria via email/telephone and sent information sheets.

Topic guide development was informed by the aims of the study and a review of the literature. An initial draft was developed by the lead author, a doctoral student in health psychology with qualitative health services research experience. Feedback on this draft was obtained from public contributors and the rest of the research team who have extensive clinical and research expertise in breast cancer and screening services, medical oncology, health services research, health psychology, and qualitative methods. Modifications to the content and structure of the topic guide were made in response to the feedback received. Questions focused on the acceptability of breast cancer risk assessment in relation to the process being used in the planned feasibility study. There were three proposed components of the study

process and each of these were discussed in turn: (1) a questionnaire for self-reported assessment of breast cancer risk factors, (2) a saliva sample for assessment of polygenic risk and mutations in high-risk genes, and (3) a low dose mammogram for assessment of breast density. Additionally, views on methods of access, information and support needs, risk communication and anticipated barriers to engagement were captured (Appendix C.1).

Focus groups and interviews were conducted between February and November 2020, either in person at a University building or in participant's homes (interviews only) or later via telephone and Zoom conferencing due to COVID-19 restrictions. Following consent, participants gave demographic information. Participants were compensated for their time with a £20 cash payment. Focus groups and all interviews were audio-recorded and transcribed verbatim. A recording malfunction occurred during one online focus group meaning that only the first half of discussion was recorded. Field notes were taken to capture insights from the remaining discussion. Personally identifiable information was anonymised, and participants were assigned pseudonyms. Data collection was primarily conducted by the lead author (SH) with another member of the research team co-facilitating the focus groups (RH). Both facilitators are female researchers and have postgraduate qualitative health services research experience. Interviews were conducted by the lead author (SH). No one was present during the focus groups and interviews besides the participants and researchers. Data collection continued until the research team were satisfied that sufficient data had been collected to answer the research question [30].

4.3.4 Patient and public involvement

Community and patient stakeholders were involved in the design of this study. A research advisory group, consisting of Black, Asian and minority ethnic community leaders, was consulted regarding the research idea and intended recruitment procedures. Wording and terminology used in the recruitment poster and participant information sheet was revised following feedback from nine Black African women aged 30-39 years with no personal history of breast cancer. The topic guide was piloted with four White women aged 30-39 years with no personal history of breast cancer and they advised on wording and relevance of questions, prompts and flow.

4.3.5 Data analysis

Data were analysed in NVivo12 using thematic analysis with a framework approach to data management from a critical realist perspective [31-33]. Primary data analysis was conducted by the lead author with input from LG and DPF. The analysis involved five main stages. (1) The lead author read transcripts, noting initial thoughts and impressions of the data. (2) The lead author conducted line-by-line coding on a selection of transcripts. Initial coding was deductive based on the structured questions in the topic guide to inform the design of the planned feasibility study in terms of the delivery model adopted, the information and support provided and communication of risk feedback. Inductive methods were then used to capture additional codes and context to ensure important aspects of the data were not missed. Codes were then grouped according to similarities and differences, producing categories. This resulted in a working thematic framework of codes contained within categories, which was refined in collaboration with LG as more transcripts were coded. (3) This thematic framework was then systematically applied to all remaining transcripts. (4) Each category was plotted onto a separate thematic matrix using the 'framework' feature in NVivo12, with codes presented in separate columns, and

participants (cases) on separate rows. To reduce the data set into a more manageable form, data in each cell were summarized and illustrative quotations were noted (Appendix C.2). (5) The resulting data in the framework matrices were compared across and within cases to highlight similarities and differences. This facilitated the development of the final themes. Regular meetings were held between members of the research team (SH, LG and DPF) throughout analysis and interpretation to discuss explanations for findings, deviant cases and agreement on themes. The final thematic structure was agreed by the entire research team as representing participants' views.

4.4 Results

Sixty-one women contacted the research team expressing an interest in the study. Prospective participants were asked to confirm that they met the inclusion criteria. Twenty-four women did not respond to the research team following three contact attempts. This drop off is likely to be attributable to the primary recruitment period coinciding with the beginning of the COVID-19 pandemic (February-March 2020). Thirty-seven women participated; seven focus groups (participant range n = 3-5) and eight interviews were conducted. Focus groups lasted between 71 and 90 minutes (median 85 minutes) and interviews ranged from 40 to 81 minutes (median 55 minutes). The majority of participants were White British (see Table 4.1). Based on participant residential postcodes, a wide range of deprivation was represented. Participants fell between Index of Multiple Deprivation deciles 1 and 10 (1 is the most deprived and 10 the least), with a median decile of 4 [34].

Table 4.1. Sample demographics (*n* = 37)

Characteristic	N (%)
Age range (years)	
30-33	18 (49)
34-36	7 (19)
37-39	12 (32)
Ethnicity	
White British	29 (78)
Black African	4 (10)
Indian	1 (3)
White (Other)	1 (3)
Mixed (White/Arab)	1 (3)
Mixed (English Caribbean)	1 (3)
Deprivation decile[a]	
High (1-3)	15 (41)
Medium (4-7)	18 (49)
Low (8-10)	4 (10)

[a]Assessed by participant residential postcode using the Index of Multiple Deprivation 2019, a measure of relative deprivation for small areas in England [34]

Data are presented as four overarching themes with seven sub-themes (Table 2).

Quotes are presented with a pseudonym followed by interview (I) or focus group (FG) number.

Table 4.2. Thematic structure

Theme	Subtheme
Acceptability of risk assessment service	-
Promoting engagement with the service	Fitting with high mental load
	"it's community effort"
Impact of receiving risk results	Avoiding complacency towards breast awareness following a low-risk result
	Questioning the impact of an average risk result
	Mitigating anxiety following a high-risk result
Women's information requirements	Enabling informed decision-making at invite
	Recommendations for risk communication

4.4.1 Theme 1: Acceptability of risk assessment service

The majority of women stated they would welcome the opportunity to find out their breast cancer risk. However, some women expressed reservations, citing concerns about the potential for acute emotional distress whilst awaiting results and significant impacts on mental health thereafter.

> my first thought is, do you know what, I don't think I want to know because then that would just give me anxiety… I think the anxiety would probably kill me before the cancer does (Rebecca, FG6)

Participants contextualised the risk assessment process by reflecting on previous encounters with healthcare, for example cervical screening, pregnancy and childbirth. Consequently, participants were accepting of the questionnaire, saliva sample and mammogram as they were not regarded as invasive procedures. The content of the risk factors questionnaire was considered reasonable due to the factual, medical nature of questions. However, reliance on self-report was flagged as a potential concern in relation to how incorrect recall of information may affect accuracy. Providing a saliva sample for genetic testing was considered commonplace and therefore acceptable due to availability of direct-to-consumer genetic testing from companies such as 23andMe. The most frequently reported concern about the risk assessment process was anticipated discomfort during the mammogram. This was influenced by older relatives' anecdotal experiences of mammograms being uncomfortable and painful.

The main benefit of participating in breast cancer risk assessment was perceived to be the ability to plan and prepare for the future in terms of accessing breast cancer risk management strategies to maintain good health:

> if you know what you're facing you can deal with it, can't you? You can say, "Oh well, that's fine, we'll do this, this and this, and we can have a plan of action". (Grace, I4)

Participants were generally aware of the importance of early detection of cancer for increased chances of survival and as such, viewed the service favourably as an opportunity to detect breast cancer earlier and thus reduce breast cancer mortality. Willingness to undergo risk assessment was contingent on there being options to reduce or manage the risk, preferably with the support of healthcare professionals. There was limited awareness of preventive measures amongst participants. However, when prompted, many women were uncomfortable with the prospect of taking medication for reduction of risk in the absence of disease.

> the most common thing you take medication for is if there's something wrong with you right now. So it would almost make you feel like there was I guess. (Florence, FG5)

In contrast, one woman stated she would find medication a reassuring and preferable option to lifestyle advice, owing to the strong motivation required to change health-related behaviours.

4.4.2 Theme 2: Promoting engagement with the service

This theme describes the difficulties women experience accessing existing healthcare services and the implications of this for service design and delivery.

4.4.2.1 Subtheme 2a: Fitting with high mental load

Women perceived the proposed timing of invitation to the breast cancer risk assessment service to coincide with a defining decade in terms of managing the often

competing demands of professional and family life.

> it's not unusual for people at my age to have one, two or three children of a certain age. So you're time's already spread a bit thin, it would be spread even thinner especially if you've got multiple children, a job, a house, things like that. (Ashleigh, I3)

As a result, women reported being time-poor and experiencing difficulties accessing healthcare services at a time that suited them. In addition to physical access requirements, women described a high mental load in the form of invisible labour involved in managing a household and family, which often results in putting the needs of others before their own:

> As a group of women in their 30s, often it can be other people's health, other things going on and we're often at the bottom of the pile. (Gemma, FG4)

Therefore, women desired a 'one-stop shop' delivery model whereby all three components of breast cancer risk assessment would be completed at one appointment.

> Get it all done in one go, yeah, and then you don't have to use brain space for it twice (Laura, I1)

Participants stated they would be more likely to engage with the service if it was available in their local area. Poor public transport routes to hospitals and the resources needed to travel were identified as potential barriers to engagement. To overcome these issues, some women expressed a preference for a mobile service in community settings such as workplace and supermarket car parks.

Availability of appointments outside of normal working hours was considered an

essential requirement of the service. Furthermore, the ability to book a convenient appointment online or via phone was desired to reduce the cognitive burden of re-arranging a pre-specified appointment.

> if they can book it themselves online or over phone or whatever option is available to them something that they can select the date and the time [...] that would be really helpful if they were able to do it themselves rather than getting told you need to be here on this date and this time. (Danielle, I8*)*

4.4.2.2 Subtheme 2b: "it's community effort"

Involvement of community leaders in service delivery was considered vital. Participants described how community leaders often share the culture and language of the community they support and this shared background helps to build rapport. Additionally, community leaders were perceived to possess cultural awareness of beliefs and perceptions women may have when considering engagement with healthcare services. For example, one participant described how young women in her community worry about attending cervical cancer screening for fear of bringing dishonour to their families because of the intimate nature of the test. Participants explained how services could work with community leaders to tailor health messaging in a more meaningful and sensitive way, which women felt would increase the likelihood of engagement, particularly for women from ethnic minority backgrounds:

> if you've got community groups or community leaders involved they know how to talk, how to communicate the information to the people of their community […] they know there's this misconception or there's fear […] and they are able to address those sensitivities that the healthcare industry might

not actually be aware of (Tara, FG6)

4.4.3 Theme 3: Impact of risk results

This theme captures participants' perceptions of anticipated impacts following receipt of low, average and high-risk results. The labelling of risk results reflects the terminology the women used when asked for their thoughts about the use of risk categories.

4.4.3.1 Subtheme 3a: Avoiding complacency towards breast awareness following a low-risk result

Participants expressed reservations about provision of a low-risk result. It was thought that women labelled as low-risk may no longer perceive breast cancer as a pertinent concern, which could result in complacency towards breast awareness behaviours. One woman perceived complacency as an inevitable consequence of labelling a woman as low-risk and as such felt the word 'low' should not be used:

> scrap the language so you don't use the word low risk because that would lead to complacency in behaviours (Gemma, FG4)

Examples of possible complacency reported by women included losing vigilance around breast awareness and reluctance to seek help for breast symptoms. To avoid these potential negative impacts, women thought it would be necessary to make sure those labelled as low-risk understood that the result did not guarantee they would never develop breast cancer.

> people need to be made aware that just because it's low doesn't mean it's not impossible (Natasha, FG4)

4.4.3.2 Subtheme 3b: Questioning the impact of an average-risk result

Participants discussed the possibility of a risk category between low and high indicating average-risk for the population. Some women questioned the value of receiving such a result with one woman describing it as the 'worst category to fall into' (Tiffany, I6). For these women, it was unclear what management strategies would result from this level of risk:

> So if you are gonna tell somebody they're of average risk is there still options to prevent it […] or is average not good enough to prevent (Brittany, FG7)

Furthermore, women felt they would not have gained any new knowledge from participating in the risk assessment service if they received an average-risk result:

> I feel like I'd be in the same boat now, you, kind of, don't know either way do you? You don't know, there's a chance you could but there's a chance you might not whereas that would be our position now (Debbie, FG5)

Consequently, an average-risk result was considered to hold no meaning and in turn, women were not reassured by this result. One woman suggested it might make her feel panicked:

> if the average risk if it was just like oh well there's not much you can do just keep checking your breasts I might be a bit I don't know. I don't know if I'd get panicked about that or not. (Brittany, FG7)

4.4.3.3 Subtheme 3c: Mitigating anxiety following a high-risk result

In anticipation of significant anxiety following a high-risk result, participants welcomed the prospect of attending a clinic appointment to discuss their risk result further. However, feelings of vulnerability and apprehension were expected in anticipation of attending this appointment. Women thought attending a hospital,

particularly one specialising in oncology, would imply current illness, which would lie in tension with the intended purpose of the appointment being to reduce the risk of developing breast cancer in the future. Furthermore, women felt the name of the clinic needed careful consideration as inclusion of the word ‘risk’ implied threat. These aspects of the appointment are important to consider, as they may increase women’s perceived threat to a level that results in disengagement with risk management.

> can you imagine being invited back to a breast centre... you'd be thinking "right I'm a cancer patient" (Debbie, FG5)

During the clinic appointment, women wanted to discuss the implications of their risk result for their children’s lives, particularly daughters. One woman thought a high-risk result could be ‘life-changing information’ as it could potentially influence reproductive decision-making:

> if you found out you were super high-risk and you were a very logical person, you might just go, okay, well, I’m not going to do that [have children] because if there’s a chance that within the next ten years my life’s going to be on the line, I don’t want to bring kids into the world only to then leave them. (Kathryn, I7)

In addition to a clinic appointment, a few women desired a peer support group. For these women, an interaction with a healthcare professional was considered inadequate in fulfilling emotional support needs. Peer support was valued as an opportunity for women with shared experience to connect and learn from each other.

4.4.4 Theme 4: Women’s information requirements

This theme describes the information participants expected to be included in invitation and risk feedback material.

4.4.4.1 Subtheme 4a: Enabling informed decision-making at invite

Women expected to be informed about evidence supporting the introduction of the service and the benefits of participation. This need was rooted in women's beliefs and assumptions of breast cancer and screening. Participants assumed that screening is offered to women when breast cancer poses the greatest risk. Consequently, women perceived breast cancer as a disease predominantly affecting women older than 50 years:

> I think the fact that they don't even offer mammograms to anyone under 50, kind of, it automatically makes you think that therefore it's not a risk to you, you know, it's like oh the authorities have decided that that's the age that you're likely to get it therefore if you're younger than that like don't worry about it almost. (Brooke, FG3)

The 'helping you decide' leaflet accompanying cervical cancer screening invitations was considered a good exemplar of information giving. Some women desired a simple diagrammatic representation of the different pathways possible from engaging with the service.

Participants with professional experience of designing and producing healthcare information thought that information should be made available in different languages and formats such as easy read and braille to increase accessibility and equity of access. One woman from an ethnic minority background felt that more ethnically diverse images should be used in information materials to convey the importance of engaging with the service irrespective of cultural or racial background:

> maybe putting more information with people that look like the communities that you're trying to reach […] it becomes more personal to them like "oh wow, if someone who looks like me has been affected by it, maybe I need to take this seriously". (Rebecca, FG6)

Participants wanted access to a video resource showing a woman having the mammogram procedure. Perceived benefits of this approach included women feeling more reassured and prepared for what to expect and making the procedure easier to imagine:

> usually if it's to do with the actual procedure I prefer looking at it and sort of seeing it visually happen so I can imagine myself going through that. Whereas if you're just telling me over the phone, "Oh, well, you just go into a room, then you get your bra off and stand at a machine," I can visualise it but I don't know how I would react in that situation (Ashleigh, I3)

Women expected to be informed about timescales of activity within the service. For example, the duration between completing the risk assessment process and receiving results. A few women said they would feel more comfortable attending the clinic appointment if it was made clear in the invitation material that the radiographer performing the mammogram was a woman.

> women that come from maybe religiously conservative backgrounds, they might want to be absolutely reassured that they're going to be seen like in a women only environment (Tiffany, I6)

Women wanted to be informed about the intended scope of genetic testing. This included information on how DNA would be stored and shared as a means of reassurance that personal information was safe.

Participants were familiar with the use of mammograms in breast cancer screening to detect breast cancers. Therefore, participants presumed the risk assessment mammogram would have diagnostic capability and found it difficult to understand why the presence or absence of a breast cancer could not be confirmed at the same time as assessment of breast density. For this reason, explicit communication of the purpose of the mammogram in the invitation materials was considered essential to avoid any misunderstandings:

> I think you would assume that a mammogram would pick up on cancer if it was there […] I guess that's a really important message to get out there if you do this isn't it, this isn't a replacement for a cancer screening (Laura, I1)

4.4.4.2 Subtheme 4b: Recommendations for risk communication

Women described not wanting to be caught off guard when receiving their risk result. For example, receiving advanced notice of a phone call. This can be seen to function as a means of retaining some control in an uncontrollable situation.

> Do I want to be ambushed on the phone with someone telling me that I should go and discuss my breast cancer risk? (Roisin, FG1)

For high-risk results, women preferred a telephone call or face-to-face consultation with a healthcare professional as this would allow the opportunity to ask questions immediately, mitigating the anticipated emotional distress to receiving a high-risk result. It was acknowledged by some women that being in this heightened emotional state may interfere with cognitive processing of information and as such, written information to refer back to was desired. In contrast, receiving a low risk result via letter or text message was considered acceptable.

Irrespective of risk result, all participants expected to be given the option of accessing a healthcare professional with appropriate expertise. General practitioners were perceived as lacking the required expertise needed.

Overall, there was a lack of consensus regarding the optimal method of displaying risk information. Women thought multiple formats of risk presentation should be offered to accommodate different learning styles and low levels of literacy and numeracy.

Women assumed that each risk category would span a broad range of percentages. Consequently, women perceived knowing where they were in the category as a more informative result. In contrast, one woman felt that provision of the risk category was sufficient and easier to process from an emotional point of view. Providing comparative risk information in the form of the national average was considered beneficial to contextualise the severity of the risk result:

> It [national average] kind of creates a bit of understanding doesn't it in your mind […] what that actually means in terms of your increased risk. (Gemma, FG4)

Participants expressed reservations about using colour to differentiate between risk levels. In particular, strong emotional reactions were observed in response to the suggestion of using red to denote high risk:

> Jasmine: If I was a high risk and I saw red, I'd be like, "Oh, I'm going to die now." [Laughter] And it would probably be a bit off-putting.
>
> Carrie: Yeah, "High alert. Death round the corner." [Laughs].
>
> Nancy: Yeah, "Your boobs are going to fall off." (FG2)

In terms of risk feedback, information about the factors contributing to risk was perceived as interesting but generally unhelpful due to the perception of many breast cancer risk factors as non-modifiable. Instead, information about what would happen next in terms of proactive risk management was of utmost importance to all participants:

> I would want it to be focussed on what I do next and not on what the result is. Because if the result's scary, then I just want to know and then I want to move on and know what to do next. (Tiffany, I6)

Participants expected risk feedback to contain information on lifestyle recommendations because receiving risk was considered an opportune time for women to review and modify unhealthy lifestyle behaviours such as smoking and excessive alcohol consumption. Furthermore, guidance on how to perform breast checks and recommended frequency of doing so was desired.

4.5 Discussion

To our knowledge, this is the first study to investigate views of young women, not known to be at increased risk of breast cancer, regarding a proposed novel approach to risk assessment outside of an organised breast screening programme. Overall, women responded positively to the prospect of a breast cancer risk assessment service. However, the findings illustrate certain conditions of acceptability that will be key considerations in implementation. Participants desired a 'one-stop shop' delivery model whereby all components of a breast cancer risk assessment would be completed at a single appointment. Various concerns were apparent when anticipating receiving all risk results, not just results indicating high-risk. Women expressed low perceived susceptibility to developing breast cancer and reported

limited awareness of breast cancer as a potentially preventable disease. Consequently, women wanted to be fully informed ahead of engaging with breast cancer risk assessment. Verbal communication methods (telephone and in person) were preferred for high-risk results to mitigate any induced emotional distress. In comparison, a letter or text message was deemed acceptable for low risk. In terms of risk presentation, women advocated the use of multiple formats that combine quantitative and qualitative features. Overall, presentation of risk was considered less important than implications of the result for risk management. Irrespective of risk result, women expected to be given the option of support from a healthcare professional with appropriate expertise.

4.5.1 Strengths and limitations

The sample matched the intended recipients of the feasibility study. Adopting this approach allowed the needs of the communities who are eligible to participate to be identified, increasing the likelihood of successful implementation in the feasibility study and subsequent wider implementation. Additionally, we were interested in including the voices of Black British women as they are at greater risk of developing breast cancers with less favourable characteristics, at younger ages, resulting in reduced survival [35, 36]. The inclusion of Black women is considered a strength of the present study as their voices are typically underrepresented in cancer prevention and early detection research [37]. However, we recommend that future research focuses on examining Black women's views in greater detail.

Limitations include that many participants were motivated to participate in the study having witnessed the negative impacts of a peer or second-degree relative's breast cancer diagnosis. These experiences might have resulted in more positive views of

breast cancer risk assessment, leading to overestimations of acceptability. However, participants were given the opportunity to express positive and negative views and particular attention was given to dissenting voices during data analysis.

Secondly, women were responding to the idea of a hypothetical breast cancer risk assessment service meaning their responses reflect anticipated thoughts and feelings. Nevertheless, although women may respond differently if the service is implemented in clinical practice, the approach taken is the most appropriate given that the present research is designed to inform a new service that does not currently exist.

Lastly, we did not assess educational attainment or health literacy of the participants, which is likely to have influenced the findings particularly in relation to information requirements. Women with low health literacy may have different views and preferences with respect to the information required and this should be taken into account when developing invitation and risk feedback materials.

4.5.2 Relevance to existing literature

The ease of accessing a breast cancer risk assessment service was identified as a critical determinant of engagement, leading to women desiring a 'one-stop shop' delivery model. Women reported being unable to attend healthcare appointments due to a lack of time and service availability constraints. This finding is in line with previous research exploring non-attendance at other healthcare services such as cervical cancer screening [38, 39]. Women also described a high mental load, defined as the cognitive and emotional labour involved in managing a household and family life [40]. In addition, women recommended involving community leaders in service delivery to increase engagement of women from ethnic backgrounds which has been found to be an effective approach amongst ethnic minority groups for improving uptake to cancer screening programmes [41].

Consistent with previous research [42, 43], women expressed concern about provision of a low-risk result for fear it could result in complacency towards breast awareness behaviours such as performing breast checks. One study found that receipt of risk information did not significantly change low-risk women's intentions to attend subsequent mammograms [44]. However, it remains unknown how receipt of a low-risk result at a younger age may affect breast awareness behaviours and subsequent engagement with breast screening.

The present study offers novel insight into anticipated appraisal of average-risk feedback, which has received little attention in previous research. The findings suggest women would not feel reassured by an average-risk result. The purported benefits of receiving low and high-risk results have been reported by women in previous studies [45, 46]. However, women in the present study were unable to identify a tangible benefit of receiving an average-risk result.

4.5.3 Implications and future research directions

Given the high mental load women report experiencing which negatively affects healthcare access, a 'one-stop shop' delivery model that minimises the physical and cognitive energy required to engage with breast cancer risk assessment would be an attractive approach to implementation.

The findings suggest that women may not understand the value in engaging with breast cancer risk assessment because of their beliefs and assumptions of breast cancer and screening. Therefore, it is imperative that information is provided in the invitation materials to assure women of the need for the service. Furthermore, a mass media education campaign should be delivered prior to and during implementation to help women understand why it is important for them to consider engaging with the

service. Invitation and risk feedback materials need to be co-developed and piloted with women to ensure information requirements identified in the present study are addressed and informed choices can be made about participation. Future qualitative research should examine the views and needs of diverse communities in terms of protected characteristics, socioeconomic variability, health literacy and other geographical areas to inform localised approaches to implementation. This research would benefit from adopting an intersectional approach to reduce health disparities among marginalised populations in subsequent implementation research [47].

The present study also highlighted the possibility of harmful effects from communicating low-risk estimates. Implementation studies should consider assessing the long-term impact of communicating risk estimates on breast awareness behaviours such as performing breast checks. Additionally, appraisals of average-risk feedback warrant further attention to determine the purpose and utility of providing such information if not perceived as reassuring.

4.5.4 Conclusions

This research has demonstrated that a breast cancer risk assessment service is acceptable for women aged 30-39 years providing that a risk management plan and support from healthcare professionals with appropriate expertise is available. Minimising the effort required to engage with the service has been identified as a key determinant of acceptability. There is a need for co-development of invitation and risk feedback materials and educational campaigning about the potential benefits of risk assessment to facilitate informed decision-making about participation.

Declarations

Ethics approval and consent to participate: Ethical approval was received from the University Research Ethics Committee, University of Manchester (Ref: 2019-7900-12761) and HRA and the study was performed in accordance with the Declaration of Helsinki, Good Clinical Practice principles and relevant regulations. All participants provided informed written or verbal consent prior to taking part in the study. Verbal consent was obtained for participants of online focus groups and telephone interviews using a consent script owing to logistical difficulties obtaining written consent during the COVID-19 pandemic. Verbal consent was audio-recorded separately to the focus group or interview.

Consent for publication: All participants provided consent for publication and gave approval for quotations from their transcripts to be published.

Author contributions: Sarah Hindmarch: Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Project administration; Visualisation; Writing – original draft; Writing – review & editing. **Louise Gorman:** Conceptualisation; Formal analysis; Methodology; Supervision; Writing – review & editing. **Rhiannon E Hawkes:** Investigation; Writing – review & editing. **Sacha J Howell:** Conceptualisation; Funding acquisition; Methodology; Supervision; Writing – review & editing. **David P French:** Conceptualisation; Formal analysis; Funding acquisition; Methodology; Supervision; Writing – review & editing.

Acknowledgements: We are grateful to all the women who took part in this study. We would like to thank Farai Nhakaniso, co-founder of Everything Human Rights community group, for his support in participant recruitment. We gratefully

acknowledge the contributions of all our community and patient stakeholders.

Funding: SH is funded by a Manchester Cancer Research Centre PhD studentship. DPF and SJH are supported by the NIHR Manchester Biomedical Research Centre (IS-BRC-1215-20007). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Competing interests: The authors declare that there is no conflict of interest.

Availability of data and materials: The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

4.6 References

1. Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. JAMA. 2013;309(8):800-5.
2. Keramatinia A, Mousavi-Jarrahi S-H, Hiteh M, Mosavi-Jarrahi A. Trends in incidence of breast cancer among women under 40 in Asia. Asian Pac J Cancer Prev. 2014;15(3):1387-90.
3. Leclère B, Molinié F, Trétarre B, Stracci F, Daubisse-Marliac L, Colonna M. Trends in incidence of breast cancer among women under 40 in seven European countries: A GRELL cooperative study. Cancer Epidemiol. 2013;37(5):544-9.
4. Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2− advanced breast cancer: focus on special considerations and latest advances. Clin Cancer Res. 2018;24(21):5206-18.
5. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep. 2017;7(1):11625.
6. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. Lancet Oncol. 2018;19(2):169-80.
7. Kudela E, Samec M, Kubatka P, Nachajova M, Laucekova Z, Liskova A, et al. Breast cancer in young women: status quo and advanced disease management by a predictive, preventive, and personalized approach. Cancers. 2019;11(11):1791.

8. National Institute for Health and Care Excellence (NICE). Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [updated 2019 Nov] (Clinical Guideline [CG164]). [Online]. 2013 [Accessed 4th March 2022]. Available from: https://www.nice.org.uk/guidance/cg164/chapter/Recommendations.
9. Eccles BK, Copson ER, Cutress RI, Maishman T, Altman DG, Simmonds P, et al. Family history and outcome of young patients with breast cancer in the UK (POSH study). Br J Surg. 2015;102(8):924-35.
10. Broeders M, Paci E. The balance sheet of benefits and harms of breast cancer population-based screening in Europe: outcome research, practice and future challenges. Womens Health. 2015;11(6):883-90.
11. Gail M, Brinton L, Byar D, Corle D, Green S, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989;81(24):1879-86.
12. Lee A, Mavaddat N, Cunningham A, Carver T, Ficorella L, Archer S, et al. Enhancing the BOADICEA cancer risk prediction model to incorporate new data on RAD51C, RAD51D, BARD1 updates to tumour pathology and cancer incidence. J Med Genet. 2022;59(12):1206-18.
13. Lee A, Mavaddat N, Wilcox AN, Cunningham AP, Carver T, Hartley S, et al. BOADICEA: a comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors. Genet Med. 2019;21(8):1708-18.
14. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med. 2004;23(7):1111-30.

15. Dite GS, MacInnis RJ, Bickerstaffe A, Dowty JG, Allman R, Apicella C, et al. Breast cancer risk prediction using clinical models and 77 independent risk-associated SNPs for women aged under 50 years: Australian breast cancer family registry. Cancer Epidemiol Biomarkers Prev. 2016;25(2):359-65.

16. Evans D, Harkness EF, Brentnall AR, van Veen EM, Astley SM, Byers H, et al. Breast cancer pathology and stage are better predicted by risk stratification models that include mammographic density and common genetic variants. Breast Cancer Res Treat. 2019;176(1):141-8.

17. Hurson AN, Pal Choudhury P, Gao C, Hüsing A, Eriksson M, Shi M, et al. Prospective evaluation of a breast-cancer risk model integrating classical risk factors and polygenic risk in 15 cohorts from six countries. Int J Epidemiol. 2021;50(6):1897-911.

18. Vilmun BM, Vejborg I, Lynge E, Lillholm M, Nielsen M, Nielsen MB, et al. Impact of adding breast density to breast cancer risk models: a systematic review. Eur J Radiol. 2020;127:109019.

19. Pashayan N, Antoniou AC, Ivanus U, Esserman LJ, Easton DF, French D, et al. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. Nat Rev Clin Oncol. 2020;17(11):687-705.

20. Pashayan N, Morris S, Gilbert FJ, Pharoah PDP. Cost-effectiveness and benefit-to-harm ratio of risk-stratified screening for breast cancer: a life-table model. JAMA Oncol. 2018;4(11):1504-10.

21. Delaloge S, Gorgio-Rossi P, Balleyguier C, Guindy M, Burrion JB, Gilbert F. My Personal Breast Screening (MyPeBS). [Online]. n.d. [Accessed 4th March 2022]. Available from: https://www.mypebs.eu/.

22. Esserman LJ, Anton-Culver H, Borowsky A, Brain S, Cink T, Crawford B, et al. The WISDOM Study: breaking the deadlock in the breast cancer screening debate. NPJ Breast Cancer. 2017;3(1):34.

23. Skivington K, Matthews L, Simpson S, Craig P, Baird J, JM B, et al. Framework for the development and evaluation of complex interventions: gap analysis, workshop and consultation-informed update. Health Technol Assess. 2021;25(57):1-132.

24. Ghanouni A, Sanderson SC, Pashayan N, Renzi C, von Wagner C, Waller J. Attitudes towards risk-stratified breast cancer screening among women in England: a cross-sectional survey. J Med Screen. 2019;27(3):138-45.

25. Yanes T, Meiser B, Kaur R, Scheepers-Joynt M, McInerny S, Taylor S, et al. Uptake of polygenic risk information among women at increased risk of breast cancer. Clin Genet. 2020;97(3):492-501.

26. Wheeler JCW, Keogh L, Sierra MA, Devereux L, Jones K, Ijzerman MJ, et al. Heterogeneity in how women value risk-stratified breast screening. Genet Med. 2022;24(1):146-56.

27. Kitzinger J. Qualitative research: introducing focus groups. BMJ. 1995;311(7000):299-302.

28. Ivanoff SD, Hultberg J. Understanding the multiple realities of everyday life: basic assumptions in focus-group methodology. Scand J Occup Ther. 2006;13(2):125-32.

29. Morgan DL, Krueger RA. When to use focus groups and why. In: Morgan DL, editor. Successful focus groups: Advancing the state of the art. California: SAGE Publications, Inc; 1993. p. 3-19.

30. O'Reilly M, Parker N. 'Unsatisfactory saturation': a critical exploration of the notion of saturated sample sizes in qualitative research. Qual Res. 2013;13(2):190-7.

31. Collier A. Critical realism: an introduction to Roy Bhaskar's philosophy. London: Verso Books; 1994.

32. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol. 2013;13(1):117.

33. Taylor SP. A realist philosophical approach for housing research: critical realism. Int J Hous Hum Settl Plan. 2020;6(2):1-20.

34. Ministry of Housing, Communities, Local Government. English indices of deprivation 2019. [Online]. 2019 [Accessed 30th November 2020]. Available from: https://imd-by-postcode.opendatacommunities.org/imd/2019.

35. Copson E, Maishman T, Gerty S, Eccles B, Stanton L, Cutress RI, et al. Ethnicity and outcome of young breast cancer patients in the United Kingdom: the POSH study. Br J Cancer. 2014;110(1):230-41.

36. Gathani T, Reeves G, Broggio J, Barnes I. Ethnicity and the tumour characteristics of invasive breast cancer in over 116,500 women in England. Br J Cancer. 2021;125(4):611-7.

37. Rivera-Colón V, Ramos R, Davis JL, Escobar M, Inda NR, Paige L, et al. Empowering underserved populations through cancer prevention and early detection. J Community Health. 2013;38(6):1067-73.

38. Oscarsson MG, Wijma BE, Benzein EG. 'I do not need to… I do not want to… I do not give it priority…'– why women choose not to attend cervical cancer screening. Health Expect. 2008;11(1):26-34.

39. Waller J, Bartoszek M, Marlow L, Wardle J. Barriers to cervical cancer screening attendance in England: a population-based survey. J Med Screen. 2009;16(4):199-204.

40. Dean L, Churchill B, Ruppanner L. The mental load: building a deeper theoretical understanding of how cognitive and emotional labor overload women and mothers. Community Work Fam. 2022;25(1):13-29.

41. Bellhouse S, McWilliams L, Firth J, Yorke J, French DP. Are community-based health worker interventions an effective approach for early diagnosis of cancer? A systematic review and meta-analysis. Psychooncology. 2018;27(4):1089-99.

42. Henneman L, Timmermans DR, Bouwman CM, Cornel MC, Meijers-Heijboer H. 'A low risk is still a risk': exploring women's attitudes towards genetic testing for breast cancer susceptibility in order to target disease prevention. Public Health Genom. 2011;14(4-5):238-47.

43. Lippey J, Keogh LA, Mann GB, Campbell IG, Forrest LE. "A natural progression": Australian women's attitudes about an individualized breast screening model. Cancer Prev Res. 2019;12(6):383-90.

44. Evans D, Donnelly LS, Harkness EF, Astley SM, Stavrinos P, Dawe S, et al. Breast cancer risk feedback to women in the UK NHS breast screening population. Br J Cancer. 2016;114:1045-52.

45. Keogh LA, Steel E, Weideman P, Butow P, Collins IM, Emery JD, et al. Consumer and clinician perspectives on personalising breast cancer prevention information. The Breast. 2019;43:39-47.

46. Rainey L, van der Waal D, Jervaeus A, Donnelly LS, Evans DG, Hammarström M, et al. European women's perceptions of the implementation

and organisation of risk-based breast cancer screening and prevention: a qualitative study. BMC Cancer. 2020;20(1):247.

47. Abrams JA, Tabaac A, Jung S, Else-Quest NM. Considerations for employing intersectionality in qualitative health research. Soc Sci Med. 2020;258:113138.

Chapter 5. “I don’t know what I’m feeling for”: young women’s beliefs about breast cancer risk and experiences of breast awareness

Journal:	BMC Women’s Health
Submission status:	Published
Journal article reference:	Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. “I don’t know what I’m feeling for”: Young women’s beliefs about breast cancer risk and experiences of breast awareness. BMC Women’s Health. 2023;23:312.

5.1 Abstract

Background: Younger women are often diagnosed with advanced breast cancer. Beliefs about risk are instrumental in motivating many health protective behaviours, but there may be confusion around which behaviour is appropriate to detect breast cancer earlier. Breast awareness, defined as an understanding of how the breasts look and feel so changes can be identified early, is widely recommended. In contrast, breast self-examination involves palpation using a specified method. We aimed to investigate young women's beliefs about their risk and experiences of breast awareness.

Methods: Thirty-seven women aged 30-39 years residing in a North West region of England with no family or personal history of breast cancer participated in seven focus groups (n=29) and eight individual interviews. Data were analysed using reflexive thematic analysis.

Results: Three themes were generated. *"Future me's problem"* describes why women perceive breast cancer as an older woman's disease. *Uncertainty regarding checking behaviours* highlights how confusion about self-checking behaviour advice has resulted in women infrequently performing breast checks. *Campaigns as a missed opportunity* highlights the potential negative effects of current breast cancer fundraising campaigns and the perceived absence of educational campaigning about breast cancer for this demographic.

Conclusions: Young women expressed low perceived susceptibility to developing breast cancer in the near future. Women did not know what breast self-checking behaviours they should be performing and expressed a lack of confidence in how to perform a breast check appropriately due to limited knowledge about what to look

and feel for. Consequently, women reported disengagement with breast awareness. Defining and clearly communicating the best strategy for breast awareness and establishing whether it is beneficial or not are essential next steps.

5.2 Background

Epidemiological studies from the past decade have illustrated the growing burden of breast cancer in pre-menopausal women worldwide [1-4]. Compared to post-menopausal women, younger women are more likely to develop unfavourable breast cancer subtypes, which are associated with higher recurrence and mortality despite aggressive treatment regimens [5, 6]. Additionally, young women often present at an advanced stage or have a delayed diagnosis because of a low index of suspicion by the patient and primary doctor [1, 7]. Consequently, enhancing recognition of symptomatic presentation amongst this group is likely to result in earlier help-seeking behaviour and thus earlier stage diagnosis [8].

Recommendations for what behaviours women should be performing to facilitate early detection of breast cancer has changed over time. From 1950, teaching breast self-examination (BSE) to women by healthcare professionals was recommended. BSE is the palpation of a woman's breasts for self-detection of breast cancer at a specific time each month according to a rigorous set method [9]. However, in 2003, a Cochrane review demonstrated that regular BSE does not result in a reduction in breast cancer mortality [10]. The same review also showed that potential harms including unnecessary biopsies and health anxiety were increased in comparison with control groups [10]. This led to the abandonment of routinely teaching women BSE as a recommended practice for healthcare professionals in the UK and USA [11, 12], and the removal of BSE from clinical recommendations [13]. However, most breast cancers in younger women are detected after the development of symptoms. In one US study, 71% of cases of breast cancer in women younger than 45 years were detected by the women themselves [14]. In recent years, 'breast awareness' has replaced BSE and has been strongly promoted by breast cancer charities and health

authorities. Breast awareness involves individuals knowing what is normal for them and the signs and symptoms of breast cancer so that any concerning changes can be acted upon [15]. Breast awareness should not include recommendations for regular implementation of a set method for breast checking.

Healthcare professionals have expressed concerns that the distinction between breast awareness and BSE is unclear, with references to both terms in the same guideline documents potentially causing confusion for both healthcare professionals and women [16]. There is evidence supporting this confusion amongst healthcare professionals; 50% of US obstetrician-gynaecologists surveyed in one study did not know there were recommendations against routine BSE in national guidelines [17]. However, whether confusion is present amongst young women regarding which breast self-checking behaviours they should be performing remains unknown. There is a dearth of qualitative studies, conducted since the recommendations changed, examining pre-menopausal women's views and experiences of breast awareness [18].

Breast awareness recommendations indicate women should be engaged in self-checking behaviour [15]. To understand whether women engage in these behaviours, it is useful to consider women's perceptions of risk. The presence of family history has been found to dominate women's breast cancer risk perceptions, with other indicators of risk such as breast density typically ignored [19, 20]. Previous research has demonstrated that risk perceptions are a key predictor of many health protective behaviours including breast screening attendance [21, 22]. Given that breast awareness is a health protective behaviour and previous research has been limited to screening age and high-risk populations, it is important to explore younger women's beliefs about breast cancer risk.

The present analysis reports on data collected from a study which had the primary aim of investigating women's views on, and requirements for, the delivery of breast cancer risk assessment [23]. However, during the course of data collection for this study, a large volume of unanticipated data was elicited regarding young women's beliefs about their own breast cancer risk and their experiences of breast awareness. The aim of the present analysis is therefore to examine young women's beliefs about breast cancer risk and experiences of breast awareness.

Specific objectives were to:

a. Explore women's understanding of breast cancer risk
b. Identify the factors contributing to women's beliefs about their own breast cancer risk
c. Explore women's understanding and experiences of breast awareness

5.3 Methods

5.3.1 Design

A cross-sectional qualitative design was used. As the topic of risk assessment and screening was theoretical to participants, focus groups were deemed the most appropriate method of facilitating discussion. Focus groups allow for reflection and clarification of perspectives, adding depth to the data [24]. They also allow for perspectives to evolve and become co-created during the discussion, allowing insight into the degree of group consensus on the topic [25]. Where participants were unable to attend scheduled focus groups, individual interviews were carried out instead.

5.3.2 Participants and setting

Participants were recruited through responding to study advertisements outlining the topic and inclusion criteria. Participants were eligible if they were: (1) born female, (2) aged 30-39 years, (3) residing in Greater Manchester in England, (4) able to provide informed consent, and (5) able to understand and communicate in English. Women who had received a breast cancer diagnosis or had a first-degree female relative (mother or sister) affected by breast cancer were not eligible to participate.

5.3.3 Procedure

Advertising posters were shared on Facebook and Twitter and were also displayed on noticeboards in three local libraries and community centres. After seeing an advertisement on Twitter, the co-founder of a local ethnic minority organisation made direct contact with the research team and facilitated the recruitment of four members of their community. Prospective participants were screened against inclusion criteria via email/telephone and sent participant information sheets.

The topic guide was developed to address the primary aim of the study, which was to investigate young women's views on, and requirements for, the delivery of breast cancer risk assessment, and informed by a review of the literature (Appendix D.1). The lead author developed an initial draft and this was reviewed by public contributors and the rest of the research team who have expertise in health psychology, medical oncology, breast cancer and screening services, health services research, and qualitative methods. The content and structure of the topic guide was revised in line with the feedback received. Data were collected between February and November 2020, at first in person then later via telephone and Zoom conferencing due to COVID-19 restrictions. Participants gave demographic information (age, ethnicity and home address postcode) prior to data collection. The

full residential postcode of participants was used to extract the Index of Multiple Deprivation decile, a measure of relative deprivation for small areas in England, with 1 representing the most deprived 10% of small areas in England and 10 the least [26]. Data were audio-recorded and transcribed verbatim. A recording malfunction occurred during one online focus group meaning that only the first half of discussion was recorded. Field notes were taken to capture insights from the remaining discussion. Identifiable information was anonymised, and participants were assigned pseudonyms. Focus groups were facilitated by two female researchers (SH and REH) with postgraduate qualitative research training and experience. Interviews were conducted by the lead author (SH). Data collection continued until the research team were satisfied that sufficient data had been collected to answer the research question [27]. Participants were compensated for their time with a £20 cash payment.

5.3.4 Patient and public involvement

Public contributors were involved in the design of this study. A research advisory group, consisting of five minority ethnic community leaders advised on the research idea and intended recruitment procedures. Wording and terminology used in the recruitment poster and participant information sheet was revised following feedback from nine Black African women aged 30-39 years. During topic guide development, four White women aged 30-39 years advised on wording of questions, prompts and flow.

5.3.5 Researcher positioning

The lead author (SH) was a White British female doctoral researcher with a background in Psychology. She has worked in cancer prevention and early detection research for six years, both reflecting and shaping her positive views of early cancer

detection initiatives. SH is 31 years old meaning she was cognisant of the participant's life stage and had life experiences in common with some of her participants, for example cervical screening. Other members of the research team were a breast cancer clinician working in cancer prevention and early detection and experienced academics who have reservations about the extent to which prevention and early cancer detection initiatives allow for informed choices about participation. The data resonated with feminist views of the team meaning that data analysis and interpretation were informed by a desire to legitimise and honour women's absent or silenced experiences.

5.3.6 Data analysis

The present analysis included responses to questions focused on comprehension of breast awareness, confidence in being breast aware, and awareness and thoughts about the current breast cancer incidence and mortality rates in younger women (Appendix D.1). This data was coded during the initial coding of the complete dataset but it did not form part of the framework for answering the primary aim of the study which was to understand women's views on, and requirements for, the delivery of breast cancer risk assessment [23]. The inductive analysis reported in this paper focuses on the new data generated by the focus groups and interviews as pertinent to understanding how and why women hold particular opinions on breast cancer risk and breast awareness.

Data were analysed using reflexive thematic analysis as this allows the flexibility to combine multiple sources of data and is suited to research examining views about particular phenomena [28, 29]. A critical realist approach was taken meaning we treated the data as indicating the participants' perception of their reality, which is

shaped by and embedded within their cultural context and language [30]. Primary data analysis was conducted by the lead author with input from LG and DPF. The lead author familiarised themselves with the focus group and interview data by listening to the audio-recordings and reading the transcripts multiple times. An inductive approach was taken to analysis, working with the data from the bottom-up, to align with our interest in the experiences and perspectives of the participants. Line-by-line coding was conducted by the lead author using NVivo12. The majority of coding was semantic, capturing explicitly expressed meaning and staying close to the language of participants. However, there was a shift towards more latent coding as the analysis progressed. Related codes were then grouped together to form broader patterns of meaning and a set of initial themes were developed using thematic mapping. The initial themes were evaluated by reviewing the coded data extracts and the entire dataset to ensure the analysis was grounded in the data. The final analysis was the result of multiple rounds of theme refinement through writing (by the lead author) and discussion between members of the research team (SH, LG and DPF).

Important techniques for ensuring quality reflexive thematic analysis are the researcher's depth of engagement with the data and reflexive practice, rather than measures of accuracy or reliability [31]. The lead author kept a research journal throughout the research process to allow ongoing reflection about how her prior knowledge and assumptions were influencing data collection and analysis and guiding decision-making. Meetings with LG and DPF during the data analysis phase of the research provided opportunities for the lead author to explain and clarify thinking and further reflect on how the assumptions she brought to data analysis might be delimiting her data engagement and interpretation.

5.4 Results

Thirty-seven women took part; seven focus groups (participant range n = 3-5) and eight interviews were conducted. Focus groups ranged from 71 to 90 minutes (median 85 minutes) with five conducted via Zoom conferencing and two face-to-face. Interviews lasted between 40 and 81 minutes (median 55 minutes) with five conducted by telephone and three face-to-face. Most participants were White British (see Table 5.1). Deprivation deciles ranged from 1 to 10, with a median decile of 4 indicating that a substantial proportion of the sample were recruited from more deprived areas.

Table 5.1. Sample demographics (*n* = 37)

Characteristic	N (%)
Age range (years)	
30-33	18 (49)
34-36	7 (19)
37-39	12 (32)
Ethnicity	
White British	29 (78)
Black African	4 (10)
White (Other)	1 (3)
Indian	1 (3)
Mixed (White/Arab)	1 (3)
Mixed (English Caribbean)	1 (3)
Level of deprivation[a]	
Low (8-10)	4 (10)
Medium (4-7)	18 (49)
High (1-3)	15 (41)

[a]Ranked in deciles according to the Index of Multiple Deprivation 2019, a measure of relative deprivation for small areas in England [26]

Three themes were generated from the data: (1) "Future me's problem", (2) Uncertainty regarding checking behaviours, and (3) Campaigns as a missed opportunity. Quotes are presented with a pseudonym followed by interview (I) or focus group (FG) number.

5.4.1 Theme 1: "Future me's problem"

Participants conceptualised breast cancer as an ‘older woman’s disease’. Many participants said they did not perceive breast cancer as an immediate health concern, for example one participant stated it was future me’s problem (Florence, FG5). Women attributed this perception to the organisation of the NHS breast screening programme which invites women aged 50-70+ years. Participants reported that given finite NHS resources, they assumed that breast screening is offered when the likelihood of developing breast cancer is greatest. The absence of a breast screening programme for younger women and lack of communication from healthcare professionals regarding breast awareness was perceived to indicate lesser risk for this age group, as women expected to be told by health authorities if they were at risk of developing a disease. Consequently, women expressed low perceived susceptibility to developing breast cancer.

> I thought the risk went up after 50 and that’s the whole reason that we have the screening after 50 (Debbie, FG5)

> I think we believe innately that if we’re at medical risk, we’ll just be told about it. Yeah, or we would expect to hear from the doctors about it or, you know, it would be more present in our minds, yeah. (Laura, I1)

Some women considered healthcare interactions like cervical screening and antenatal appointments as missed opportunities to discuss breast awareness and whether breast cancer was a relevant health concern for their age group. In line with this, women reported accessing limited, if any, information about breast health.

Breast cancer as an ‘older woman’s disease’ has been reinforced further when women reported consulting healthcare professionals with breast health concerns or concerns about risk. Some women reported feeling embarrassed about seeking help

because they feared wasting NHS time. Women described feeling like a burden throughout the care pathway, in both primary and secondary care interactions. Participants who spoke about their experiences of seeking help reported an absence of reassurance following clinical interactions. They reported feeling as though their concerns had been dismissed in Primary Care because of their age.

> I went to a doctor once, I was about twenty-two, and said, "Oh, I've got weird lumps in my breasts" And she went, "No, that's just water retention" and was really dismissive […] I just think that it would be better for doctors not to turn around and tell you you're far too young when you have a genuine concern. (Nancy, FG2)

> I've got breast cancer on my dad's side. And I asked the GP what – whether that meant anything. And he was really like, "Whatever. You know, don't waste my time," kind of thing. (Carrie, FG2)

Women who had experienced being referred to secondary care reported feeling reassured after undergoing further investigations and receiving the all clear but conversely this was also seen to confirm their fears of having wasted NHS time and resources. One woman told us that a secondary care healthcare professional's demeanour during their clinical interaction left her feeling as though she had been referred unnecessarily for a biopsy, "the guy who did the biopsy was like, almost seemed annoyed that I'd been sent there" (Polly, FG1). Women reported that these types of experiences might have a negative impact on future help-seeking behaviour:

> the thought of if I did find something again, went again, again there was nothing there, that feeling of again I've, sort of, wasted a bit of NHS time,

> not that anyone ever made me feel like that but I suppose I used to think, you know, how many times can you do this. (Jodie, FG5)

When considering cultural differences in breast cancer prevalence and screening, some Black African participants expressed the view that breast cancer was more prevalent in the UK in comparison to their home countries in Africa. This was attributed to differences in diet and environment. Furthermore, these participants described very few instances of and conversations about breast cancer in their communities, which may adversely affect performance of breast self-checking behaviours.

> when I was back home anyway growing up there, cancer was not a prevalent disease […] it wasn't something that was common as it is over here so when people move over here […] you feel like cancer's not a thing that affects people of your kind. (Rebecca, FG6)

5.4.2 Theme 2: Uncertainty regarding checking behaviours

When asked for their understanding of being breast aware, women believed they should be regularly checking their breasts to know how they normally look and feel so any changes that are not normal for the woman can be detected and reported to a GP. For one participant, being breast aware did not hold any meaning, I'd say that term doesn't really mean much to me (Zoe, FG3). Some women believed breast checks should be performed monthly and that a specific technique should be used, resulting in the perception there was a 'correct' method of checking. Contrary to these beliefs, participants reported infrequently performing breast checks and being unaware of the recommended frequency for enacting this behaviour. Women tended to engage in this behaviour only when prompted by a trigger such as hearing about a

relative or peer's breast cancer diagnosis or media coverage about breast cancer. Different reasons were reported for infrequent engagement with breast checking behaviour. For some women, the anxiety and fear of potentially detecting breast cancer was a barrier to performing the behaviour:

> you still have that anxiety don't you of "oh gosh, could it be?" and I sort of notice within myself that I feel reluctance to check because of that which I know is silly. (Jodie, FG5)

Most participants reported not routinely engaging in breast checking due to a lack of confidence in how to perform the behaviour and limited knowledge about what to look and feel for. More specifically, participants expressed difficulty in distinguishing between a concerning and normal change, given natural variation during a menstrual cycle and the impact of breastfeeding. In addition, women mentioned the individuality of breasts, in terms of differences in size and consistency, rendering video demonstrations somewhat ineffective.

> you already know that you should do it you just don't know what to do. (Joyce, FG1)

> I'm breastfeeding at the moment so my boobs change on a daily basis […] at the moment, I'd have no idea if something was to do with that or if it was to do with something more, kind of, nasty I suppose. (Brooke, FG3)

> I don't know what I'm feeling for, I've watched a YouTube video, I've watched it and thought, okay, my boobs don't look like her boobs, but she's doing all this […]. It didn't help me. (Miranda, FG1)

Taken together, these comments highlight that women are finding it difficult to identify their own baseline normal, the reference point needed to make decisions

about which changes require action. As a result, training on how to check and education about normal changes, was desired in order to increase confidence.

5.4.3 Theme 3: Campaigns as a missed opportunity

Breast cancer was perceived to have a high profile in the media. Women were familiar with fundraising campaigns such as Race for Life [32] and Wear It Pink [33]. These campaigns were perceived to have served a purpose in raising awareness of breast cancer and destigmatising the disease. However, women felt these campaigns had contributed to the depiction of breast cancer as 'pink and pretty' (Natasha, FG4) in comparison with other cancers. Some believed this portrayal had the inadvertent consequence of lessening the seriousness of breast cancer:

> I think it's interesting around how breast cancer is portrayed as well, it's given a bit of a different thing like then say lung cancer or bowel cancer. It does seem a bit pink and fluffier and therefore a bit less scary in a way so therefore people don't take it as seriously (Gemma, FG4)

> It [breast cancer] feels like it's the less serious of the cancers if that makes any sense [laughs]. It's like you've got your cervical cancer and your bowel cancer and your prostate cancer, and breast cancer is somewhere down the list. (Hannah, I5)

In contrast to fundraising campaigns, women reported limited exposure to educational campaigns aimed at their age group for raising awareness of breast cancer symptoms, risk-reducing measures and preventive strategies. This was evidenced further by a lack of knowledge about preventive measures. Many women were familiar with CoppaFeel! [34], a breast health education charity, but it was viewed as targeting a younger demographic. Given the recent focus of public health

campaigning for this age group on attending cervical screening [35], some women perceived cervical cancer as their most serious health risk.

> you get like breast cancer awareness month but besides people wearing ribbons I don't know really what that's saying to the world, it's just oh breast cancer exists which we all know but we don't know how to avoid that or what we can do about that, so there's nothing, as far as I'm aware, there's nothing preventative that's being put out there (Zoe, FG3)

When asked what an effective campaign would look like, women expressed a desire for campaigns focused on effecting behaviour changes relevant to breast health such as advice to reduce risk and checking breasts to increase help-seeking behaviour. Women recommended that campaigns should be delivered in line with their target audience's preferred means of interaction. For this reason, social media was regarded as the platform of choice for delivery for women in this age group. Several women recalled having seen the 'Cervical Screening Saves Lives' national campaign from 2019 which included significant amounts of social media advertising. In addition, women thought it would be important to have a 'face' for any campaign in the form of a relevant celebrity or influencer who their age group could identify with and relate to in order to increase the likelihood of paying attention. Instagram was considered a particularly favourable platform because it would lend itself to more engaging visual content such as videos. Some women thought breast awareness should be taught in schools alongside sex education to form a habit of being breast aware from a younger age. The perceived benefit of this was to help normalise and encourage discussions about breast health with peers so it would become part of mainstream conversation.

you have sex education why aren't you having some sort of like body education like here is how you check yourself (Zoe, FG3)

5.5 Discussion

5.5.1 Summary of main findings

Participants perceived breast cancer as a distant future health concern and expressed low perceived susceptibility to developing the disease because of the focus of breast screening at 50 years and above. This perception has been reinforced further by women's experiences of help-seeking whereby they felt their breast health concerns have been dismissed because of their age. Uncertainty about what women should be doing with respect to breast health was apparent resulting in infrequent reports of performing breast checks and hesitancy towards seeking help for breast health concerns. Women described the potential negative effects of current breast cancer fundraising campaigns in terms of lessening perceptions of the seriousness and severity of breast cancer and perceived absence of educational campaigning about breast cancer targeted at their age group.

5.5.2 Relevance to existing literature

In the present study, women expressed low perceived susceptibility to developing breast cancer in the near future. Although women aged 30-39 years are at a lower absolute risk of developing breast cancer than older age groups, breast cancer is more frequently fatal in younger women than in those diagnosed aged over 50 years [36]. As a result, breast cancer is the leading cause of death in women aged 35-49 years in the UK with 2,000 deaths reported per year [37]. Identifying young women at increased risk of developing breast cancer would allow them to receive the benefits of earlier screening and preventive strategies. A recent review determined

that breast cancer risk assessment for women under 50 years currently satisfies many of the standard principles for screening [38]. The feasibility of offering breast cancer risk assessment to women aged 30–39 years is currently being investigated [39].

Risk perception has been found to influence the symptom interpretation process of help-seeking behaviour with those expressing low perceived susceptibility to breast cancer delaying help-seeking [40]. Furthermore, previous research has demonstrated that dismissive interactions with general practitioners induce a worry of unnecessary help-seeking [41]. The findings of the present study suggest that these interactions could also reduce future help-seeking behaviour. This is concerning as women who delay seeking help for symptoms of breast cancer have a reduced chance of survival [42].

Women reported more exposure to fundraising campaigns compared to educational campaigns. This is consistent with breast cancer awareness messaging in recent years, which has shifted from a focus on diagnosis and prevention to fundraising efforts [43]. For this age group, the preferred mode of delivery for campaigns was social media and women recommended partnering with relatable celebrities or influencers as spokespersons. Previous research has demonstrated that celebrities increase the reach of messages on social media platforms such as Twitter in comparison with individuals and organisations [44]. Women desired campaigns that convey actionable breast health messages such as how to perform a breast check. Examination of social media campaigns during breast cancer awareness month reveal that messaging primarily focuses on awareness and support rather than actionable health messages, suggesting that minimal behaviour change will occur as a result [44-47]. The findings discussed here suggest that current breast cancer

campaigning is ineffective and does not meet the needs of women aged 30 to 39 years.

Women reported infrequently performing breast checks despite believing they should be enacting the behaviour. In this study, lack of confidence in how to perform a breast check, distinguishing between normal and concerning changes, limited knowledge about what to look and feel for and fear of potentially detecting breast cancer were identified as contributing factors to women's disengagement with breast checking behaviours. Additionally, aspects of BSE were evident in women's understanding of breast awareness such as believing there was a recommended frequency to perform breast checks and a 'correct' method of checking. Inaccurate understandings of current recommendations for self-checking behaviour have also been found amongst women older than 50 years, whereby women explicitly cited engaging in BSE and only alluded to engaging in breast awareness [48]. These findings are in line with concerns previously raised by healthcare professionals that the distinction between breast awareness and BSE lacks clarity [9, 16]. Currently, breast cancer charities are promoting a variety of breast awareness recommendations to women in the UK, which make it difficult to separate the two concepts. For example, CoppaFeel! offers monthly text message reminders to prompt women to check their breasts (in line with breast self-examination) whilst also providing a self-checkout tool which states there are no rules for checking (in line with breast awareness) [34]. It has been argued that breast awareness is a euphemism for BSE and places an "undue burden" on women to maintain the responsibility to detect their own breast cancer, despite evidence of harms outweighing the benefits [16, 49]. Therefore, it is apparent that clarity is needed about what behaviours are

recommended and how this should be communicated to address the confusion women are experiencing.

5.5.3 Strengths and limitations

The data analysed were responses to the broad introductory questions about breast awareness that were asked to ease participants into conversation before exploring the topic of primary interest which was the delivery of breast cancer risk assessment. Therefore, we did not ask any direct questions regarding beliefs about breast cancer risk. Nevertheless, women spontaneously chose to discuss this indicating it was an important topic to them and further probing of initial responses was conducted to obtain more in-depth information.

Ethnic minority groups and those from a low socio-economic background are underrepresented in cancer prevention and early detection research despite being disproportionately affected by cancer [50]. Therefore, the sample diversity in terms of ethnic minority representation and socio-economic status is regarded as a strength of the present study. However, we acknowledge that the views of other minority groups were underrepresented.

5.5.4 Implications and future research directions

This research has demonstrated that women aged 30-39 years report uncertainty about what they should be doing with respect to breast health and a lack of confidence in how to perform a breast check appropriately due to limited knowledge about what to look and feel for. Consequently, women reported disengagement with breast awareness. To what extent this disengagement is concerning remains unknown as breast awareness continues to be promoted without any evidence of benefit. In the absence of clear evidence of benefit, future research should attempt to define the best

strategy, in terms of recommended behaviours, for breast awareness. This could facilitate consistent messaging so women know what they should be doing.

In the meantime, breast cancer charities should consider delivering and evaluating an educational campaign targeted at this demographic which clearly specifies which breast changes to be concerned about if identified. This is particularly important given current interest in offering breast cancer risk assessment to young women which will be highlighting the importance of remaining breast aware and performing breast checks in risk feedback. Further research with minority and marginalised groups including transgender individuals should be conducted to inform the design of future campaigns, as they are likely to have different needs and therefore recommendations for breast awareness communication [51]. The role of technology in assisting women to perform breast self-checks should be considered given the current development of Dotplot, an at-home breast health monitoring tool offering guided self-checks on a monthly basis to enable early detection of changes in breast tissue composition that could be cancer [52].

The present study also highlighted that young women do not perceive breast cancer as a relevant and immediate health concern. This perception has been reinforced by clinical interactions with healthcare professionals who were dismissive about breast health concerns. Therefore, future qualitative research should examine primary healthcare professionals' understanding of breast cancer risk and referral decision-making for young women to inform the development and evaluation of educational interventions aimed at improving consultations about breast health concerns amongst this age group.

5.5.5 Conclusions

Women aged 30-39 years perceived breast cancer as a future health concern. They reported not knowing what breast self-checking behaviours they should be performing and expressed a lack of confidence in how to perform a breast check appropriately due to limited knowledge about what to look and feel for. Consequently, women reported disengagement with breast awareness. Defining and clearly communicating the best strategy for breast awareness and establishing whether it is beneficial or not are essential next steps.

Declarations

Ethics approval and consent to participate: Ethical approval was received from the University Research Ethics Committee, University of Manchester (Ref: 2019-7900-12761) and HRA and the study was carried out following the Good Clinical Practice principles and relevant regulations. All participants provided informed written or verbal consent prior to taking part in the study. Verbal consent was obtained for participants of online focus groups and telephone interviews using a consent script owing to logistical difficulties obtaining written consent during the COVID-19 pandemic. Verbal consent was audio-recorded separately to the focus group or interview.

Consent for publication: Not applicable.

Availability of data and materials: The data that support the findings of this study are available from the corresponding author, SH, upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding information: SH is funded by a Manchester Cancer Research Centre PhD studentship. DPF and SJH are supported by the NIHR Manchester Biomedical Research Centre (IS-BRC-1215-20007). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Authors' contributions: SH, DPF, SJH and LG conceived and designed the study. SH, DPF and LG developed the study materials. SH and REH recruited all participants and collected the data. SH conducted the primary data analysis, continually reviewed by LG and DPF. SH wrote the manuscript. DPF, SJH, LG and

REH provided feedback on versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgements: We would like to thank all the participants who kindly gave their time to take part in this study. We would also like to thank Farai Nhakaniso, co-founder of Everything Human Rights community group, for his support in participant recruitment. We gratefully acknowledge the invaluable feedback received from our public contributors.

5.6 References

1. Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. JAMA. 2013;309(8):800-5.
2. Keramatinia A, Mousavi-Jarrahi S-H, Hiteh M, Mosavi-Jarrahi A. Trends in incidence of breast cancer among women under 40 in Asia. Asian Pac J Cancer Prev. 2014;15(3):1387-90.
3. Leclère B, Molinié F, Trétarre B, Stracci F, Daubisse-Marliac L, Colonna M. Trends in incidence of breast cancer among women under 40 in seven European countries: A GRELL cooperative study. Cancer Epidemiol. 2013;37(5):544-9.
4. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. Lancet Glob Health. 2020;8(8):e1027-37.
5. Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2− advanced breast cancer: focus on special considerations and latest advances. Clin Cancer Res. 2018;24(21):5206-18.
6. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep. 2017;7(1):11625.
7. Assi HA, Khoury KE, Dbouk H, Khalil LE, Mouhieddine TH, El Saghir NS. Epidemiology and prognosis of breast cancer in young women. J Thorac Dis. 2013;5(Suppl 1):S2-8.

8. Partridge AH, Hughes ME, Ottesen RA, Wong Y-N, Edge SB, Theriault RL, et al. The effect of age on delay in diagnosis and stage of breast cancer. Oncologist. 2012;17(6):775-82.
9. Thornton H, Pillarisetti RR. 'Breast awareness' and 'breast self-examination'are not the same. What do these terms mean? Why are they confused? What can we do? Eur J Cancer. 2008;44(15):2118-21.
10. Kösters JP, Gøtzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. Cochrane Database Syst Rev. 2003(2):CD003373.
11. Austoker J. Breast self examination. BMJ. 2003;326(7379):1-2.
12. Harris R, Kinsinger LS. Routinely teaching breast self-examination is dead. What does this mean? J Natl Cancer Inst. 2002;94(19):1420-1.
13. Lee CS, Monticciolo DL, Moy L. Screening guidelines update for average-risk and high-risk women. AJR Am J Roentgenol. 2019;214(2):316-23.
14. Coates RJ, Uhler RJ, Brogan DJ, Gammon MD, Malone KE, Swanson CA, et al. Patterns and predictors of the breast cancer detection methods in women under 45 years of age (United States). Cancer Causes Control. 2001;12(5):431-42.
15. O'Mahony M, Comber H, Fitzgerald T, Corrigan MA, Fitzgerald E, Grunfeld EA, et al. Interventions for raising breast cancer awareness in women. Cochrane Database Syst Rev. 2017(2):CD011396.
16. Mark K, Temkin SM, Terplan M. Breast self-awareness: the evidence behind the euphemism. Obstet Gynecol. 2014;123(4):734-6.
17. Anderson BL, Pearlman M, Griffin J, Schulkin J. Conflicting and changing breast cancer screening recommendations: survey study of a national sample

of ob-gyns after the release of the 2009 USPSTF guidelines. J Healthc Qual. 2013;35(4):25-35.

18. McCready T, Littlewood D, Jenkinson J. Breast self-examination and breast awareness: a literature review. J Clin Nurs. 2005;14(5):570-8.

19. Beidler LB, Kressin NR, Wormwood JB, Battaglia TA, Slanetz PJ, Gunn CM. Perceptions of breast cancer risks among women receiving mammograph screening. JAMA Netw Open. 2023;6(1):e2252209-e.

20. Woof VG, Howell A, McWilliams L, Gareth Evans D, French DP. How do women who are informed that they are at increased risk of breast cancer appraise their risk? A systematic review of qualitative research. Br J Cancer. 2022;127(11):1916-24.

21. Grimley CE, Kato PM, Grunfeld EA. Health and health belief factors associated with screening and help-seeking behaviours for breast cancer: a systematic review and meta-analysis of the European evidence. Br J Health Psychol. 2020;25(1):107-28.

22. Sheeran P, Harris PR, Epton T. Does heightening risk appraisals change people's intentions and behavior? A meta-analysis of experimental studies. Psychol Bull. 2014;140(2):511-43.

23. Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk assessment for women aged 30–39 years: A qualitative study of women’s views. Womens Health. 2023;19.

24. Kitzinger J. Qualitative research: introducing focus groups. BMJ. 1995;311(7000):299-302.

25. Ivanoff SD, Hultberg J. Understanding the multiple realities of everyday life: basic assumptions in focus-group methodology. Scand J Occup Ther. 2006;13(2):125-32.

26. Ministry of Housing, Communities, Local Government. English indices of deprivation 2019. [Online]. 2019 [Accessed 30th November 2020]. Available from: https://imd-by-postcode.opendatacommunities.org/imd/2019.

27. O'Reilly M, Parker N. 'Unsatisfactory saturation': a critical exploration of the notion of saturated sample sizes in qualitative research. Qual Res. 2013;13(2):190-7.

28. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77-101.

29. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qual Res Sport Exerc Health. 2019;11(4):589-97.

30. Pilgrim D. Some implications of critical realism for mental health research. Social Theory & Health. 2014;12(1):1-21.

31. Braun V, Clarke V. Getting your own house in order: understanding what makes good reflexive thematic analysis to ensure quality. In: Braun V, editor. Thematic analysis: A practical guide. California, USA: SAGE Publications Inc; 2021. p. 259-80.

32. Cancer Research UK. Race for Life. [Online]. n.d. [Accessed September 12th 2022]. Available from: https://raceforlife.cancerresearchuk.org/.

33. Breast Cancer Now. Wear It Pink. [Online]. n.d. [Accessed September 12th 2022]. Available from: https://www.wearitpink.org/.

34. CoppaFeel! CoppaFeel. [Online]. n.d. [Accessed September 12th 2022]. Available from: https://coppafeel.org/.

35. PHE launches 'Cervical Screening Saves Lives' campaign [press release]. Public Health England, 9th March 2019.

36. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. Lancet Oncol. 2018;19(2):169-80.

37. Office for National Statistics. Deaths registered in England and Wales: 2021 [Online]. 2022 [Accessed 11th April 2023]. Available from: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregistrationsummarytables/2021.

38. Usher-Smith JA, Hindmarch S, French DP, Tischkowitz M, Moorthie S, Walter FM, et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636–46.

39. Manchester University NHS Foundation Trust. Breast CANcer Risk Assessment in Younger women: BCAN-RAY (BCAN-RAY). ClinicalTrials.gov identifier: NCT04336904. [Online]. 2022 [Accessed 11th April 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05305963.

40. Unger-Saldaña K, Infante-Castañeda CB. Breast cancer delay: a grounded model of help-seeking behaviour. Soc Sci Med. 2011;72(7):1096-104.

41. Cromme SK, Whitaker KL, Winstanley K, Renzi C, Smith CF, Wardle J. Worrying about wasting GP time as a barrier to help-seeking: a community-based, qualitative study. Br J Gen Pract. 2016;66(648):e474.

42. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. Lancet. 1999;353(9159):1119-26.

43. Jacobsen GD, Jacobsen KH. Health awareness campaigns and diagnosis rates: evidence from national breast cancer awareness month. J Health Econ. 2011;30(1):55-61.

44. Thackeray R, Burton SH, Giraud-Carrier C, Rollins S, Draper CR. Using Twitter for breast cancer prevention: an analysis of breast cancer awareness month. BMC Cancer. 2013;13(1):508.

45. Chung JE. Retweeting in health promotion: analysis of tweets about Breast Cancer Awareness Month. Comput Human Behav. 2017;74:112-9.

46. Plackett R, Kaushal A, Kassianos AP, Cross A, Lewins D, Sheringham J, et al. Use of social media to promote cancer screening and early diagnosis: scoping review. J Med Internet Res. 2020;22(11):e21582.

47. Vraga EK, Stefanidis A, Lamprianidis G, Croitoru A, Crooks AT, Delamater PL, et al. Cancer and social media: a comparison of traffic about breast cancer, prostate cancer, and other reproductive cancers on Twitter and Instagram. J Health Commun. 2018;23(2):181-9.

48. Seaman K, Dzidic P, Breen L, Saunders C. Exploring breast health practices of post-menopausal women: implications to informed consent. J Health Psychol. 2016;23(14):1820-31.

49. Pearlman MD. Separating the baby from the bath water: breast self-awareness and breast self-examination. Obstet Gynecol. 2014;123(4):731-3.

50. Rivera-Colón V, Ramos R, Davis JL, Escobar M, Inda NR, Paige L, et al. Empowering underserved populations through cancer prevention and early detection. J Community Health. 2013;38(6):1067-73.

51. Combs R, Wendel M, Gonzales T. Considering transgender and gender nonconforming people in health communication campaigns. Palgrave Commun. 2018;4(1):98.

52. McCallum S. Tool to spot breast cancer at home wins UK Dyson award. [Online]. 2022 [Accessed 31st March 2023]. Available from: https://www.bbc.co.uk/news/technology-62807367.

Chapter 6. The feasibility and acceptability of offering breast cancer risk assessment to general population women aged 30-39 years: a mixed-methods study protocol

Journal:	BMJ Open
Submission status:	Under review
Journal article reference:	Hindmarch S, Howell SJ, Usher-Smith JA, Gorman L, Evans DG, French DP. The feasibility and acceptability of offering breast cancer risk assessment to general population women aged 30-39 years: A mixed-methods study protocol. BMJ Open. Under review.

6.1 Abstract

Introduction: Breast cancer incidence starts to increase exponentially when women reach 30-39 years, hence before they are eligible for breast cancer screening. The introduction of breast cancer risk assessment for this age group could lead to those at higher risk receiving benefits of earlier screening and preventive strategies. Currently, risk assessment is limited to women with family history of breast cancer only. The BCAN-RAY study is evaluating a comprehensive breast cancer risk assessment strategy for women aged 30-39 years incorporating a questionnaire of breast cancer risk factors, low-dose mammography to assess breast density, and polygenic risk. The present study will assess the feasibility and acceptability of the BCAN-RAY risk assessment strategy.

Methods and analysis: The present study involves women undergoing risk assessment as part of the BCAN-RAY case-control study (n = 750). They will be aged 30-39 years without a strong family history of breast cancer and invited to participate via general practice. A comparison of uptake rates by socioeconomic status and ethnicity between women who participate in the BCAN-RAY study and women who decline participation will be conducted. All participants will be asked to complete self-report questionnaires to assess key potential harms including increased state anxiety (STAI), cancer worry (Lerman Cancer Worry Scale), and satisfaction with decision to participate (Decision Regret Scale), alongside potential benefits such as feeling more informed about breast cancer risk. A sub-sample of approximately 24 women (12 at average risk and 12 at increased risk) will additionally participate in semi-structured interviews to understand the acceptability of the risk assessment strategy and identify any changes needed to it to increase uptake.

Ethics and dissemination: Ethical approval was granted by North West - Greater Manchester West Research Ethics Committee (reference: 22/NW/0268). Study results will be disseminated through peer-reviewed journals, conference presentations and charitable organisations.

Trial registration: NCT05305963.

Keywords: risk assessment, breast cancer, psychological impact, health inequalities, acceptability

6.2 Article Summary

Strengths and limitations of this study

- This is the first study to examine the feasibility and acceptability of comprehensive breast cancer risk assessment for general population women aged 30-39 years.
- This study uses a mixed methods design; the combination of qualitative and quantitative data will result in a more comprehensive understanding of the processes affecting implementation.
- The findings of this study will identify modifications needed to the breast cancer risk assessment strategy to increase the likelihood of future implementation studies being successful.
- Outcome measures assessing potential harms and benefits of participating in breast cancer risk assessment will be collected at three timepoints, allowing for assessment of short and long term effects.
- The quality and completeness of ethnicity data across general practices may be suboptimal for the planned analyses.

6.3 Introduction

Breast cancer is the most common cancer diagnosed worldwide for women, with increasing incidence rates observed in pre-menopausal women in recent years [1, 2]. This is concerning as breast cancer is more frequently lethal in younger women than in those diagnosed aged over 50 years (10-year survival aged <40 years at diagnosis 70% vs 87% in those >50 years) [3]. This is due to a combination of factors, notably later stage at presentation and a greater proportion of women developing more aggressive breast cancer subtypes [4-6]. Breast cancer is the leading cause of death in women aged 35-50 years in the UK [7]. Therefore, there is a pressing need to identify younger women at increased risk of developing breast cancer so they can be offered screening and preventive strategies [8].

Assessment of an individual's breast cancer risk is one proposed approach for identifying young women eligible for screening and preventive strategies [9]. In the UK, a strong family history of breast cancer or known high risk genetic variant in a close relative is the only criteria by which women aged under 50 years can access screening and preventive strategies prior to a diagnosis of breast cancer [10]. However, at least 65% of women who develop breast cancer before the age of 50 years do not have such a family history and are not currently identified as being at increased risk [3, 11].

The reliance on family history belies the progress over recent decades in the identification of additional breast cancer risk factors including those related to reproductive and hormonal history, alcohol consumption, polygenic risk scores and mammographic density. These additional factors have been incorporated into risk prediction models, resulting in improved discrimination across all age groups [12-

15]. In the UK, the PROCAS study confirmed it was possible to accurately estimate a woman's individual risk of developing breast cancer at the time of mammographic screening using a self-reported questionnaire of breast cancer risk factors and assessment of mammographic density and polygenic risk [16]. Using this comprehensive approach to risk assessment identified 18% of women as being at least moderate risk of developing breast cancer in comparison to only 3.7% using family history alone [17]. Therefore, a greater number of women were identified who would be eligible for consideration of screening and preventive strategies [10]. Trials are underway internationally to establish the potential effectiveness of risk-based screening strategies for women attending breast cancer screening programmes over the age of 40 years [18, 19]. However, inclusion of breast cancer risk assessment at the time of national mammographic screening programmes will miss younger women eligible for screening and preventive strategies. Therefore, the introduction of comprehensive breast cancer risk assessment from an earlier age is currently being considered.

A recent review determined that breast cancer risk assessment for women under 50 years currently satisfies many of the key principles for screening [20]. However, uncertainties remain with respect to the optimal strategy for implementation and potential impact of the invitation process on health inequalities. The Breast CANcer Risk Assessment in Younger women (BCAN-RAY) case-control study (NCT05305963) aims to evaluate a comprehensive breast cancer risk assessment strategy amongst a diverse ethnic and socioeconomic population of women aged 30-39 years without a strong family history of breast cancer [21]. The BCAN-RAY study aims to primarily assess the impact of mammographic density on breast cancer risk in this age group. To address this, we have developed a low-dose mammogram

technique which uses a tenth or less of the radiation dose of a full dose screening mammogram making it safer. Furthermore, an automated method of analysis not requiring radiologist review will be utilised, removing the risk of unnecessary recall for additional imaging. This approach has been shown to be accurate in younger women [22].

The risk assessment strategy thereby consists of a questionnaire of breast cancer risk factors, low-dose mammography to measure mammographic density, and a saliva sample to assess polygenic risk and the presence of pathogenic variants in high and moderate-risk genes. The breast cancer risk assessment strategy adopted in the BCAN-RAY study is herein referred to as the BCAN-RAY approach. Women with a strong family history of breast cancer are ineligible to participate because they can access screening and preventive strategies through referral to Family History, Risk and Prevention Clinics (FHRPCs). Women identified as being at increased risk will be offered an appointment at a FHRPC to discuss their risk result further and potential management options. Options in the UK include access to breast screening from the age of 40 years (if 10-year risk reaches 3% by 40) and preventive strategies such as weight loss or weight gain prevention interventions and risk-reducing medication. Uptake of these screening and preventive strategies by younger women has the potential to facilitate earlier detection of breast cancer and reduce breast cancer mortality [9].

In line with the MRC Framework for Developing and Evaluating Complex Interventions [23], it is imperative to assess the feasibility of the BCAN-RAY approach in order to inform future decisions about implementation. One key consideration is a need to assess whether the invitation process exacerbates health inequalities through lower recruitment of ethnic minority populations and women

from low socioeconomic backgrounds. Previous efforts to implement risk assessment at the time of mammographic screening have demonstrated these problems [24]. This is important to consider as addressing ethnic disparities in breast cancer mortality has been recognised as a key research priority [25].

Secondly, potential harms and benefits need to be identified. There is now considerable evidence on the effects of providing breast cancer risk estimates to women aged 47-73 years recruited via the NHS Breast Screening Programme. These data indicate that women subsequently had more accurate perceptions of risk with no evidence of significant adverse effects on anxiety or cancer worry [26, 27]. Nevertheless, there is a need to show an absence of adverse effects when setting up a new programme with younger women for several reasons. First, one might expect more acute distress amongst younger women at increased risk as the result may be more unexpected because of a lack of family history of the disease, suggesting anxiety and cancer worry are important outcomes to assess. Second, due to the potential implications of being identified as at increased risk for younger women in terms of reproductive decision-making, a possible harm could be that participants experience remorse or distress over their decision to take part in breast cancer risk assessment. In terms of benefits, it is anticipated that women will feel more informed about breast cancer risk as a result of participation which will enable them to make informed choices about subsequent risk management options.

Finally, it is important to consider acceptability of the BCAN-RAY approach to women aged 30-39 years to optimise the likelihood of future implementation being successful. If the processes of identification, risk assessment and feedback are unacceptable, then the potential benefits will not be realised. We have previously conducted a qualitative study with women aged 30-39 years which suggested that

undergoing breast cancer risk assessment was acceptable in principle [28]. However, risk assessment was presented as a hypothetical prospect in that study so how women may respond once they have experienced it and any changes required to increase engagement and uptake remain unknown.

The present study aims to examine the feasibility and acceptability of a strategy to offer breast cancer risk assessment to women aged 30-39 years in a diverse ethnic and socioeconomic geographical region. A mixed-methods approach will be adopted in order to capitalise on the strengths of both quantitative and qualitative methods, resulting in a more comprehensive understanding of the processes affecting implementation [29]. Specific objectives of this study are to:

a) Examine uptake rates according to socioeconomic status and ethnicity to determine impact of the invitation process on health inequalities
b) Identify potential harms and benefits of participation in breast cancer risk assessment
c) Understand the acceptability of the BCAN-RAY approach

6.4 Methods

6.4.1 Design

BCAN-RAY is a case-control study [21]. Approximately one thousand women will be recruited between May 2023 and May 2025, 250 women diagnosed with breast cancer when they were aged 30-39 years (cases) and 750 controls currently aged 30-39 years without a strong family history of breast cancer. The present feasibility study involves the control participants only and uses three different designs to address the three objectives.

6.4.1.1 Health inequalities assessment

A between-subjects comparison will be made between women who participate in the BCAN-RAY study and women who decline participation according to socioeconomic status and ethnicity.

6.4.1.2 Identification of potential harms and benefits

Quantitative questionnaires will be administered to each woman at three timepoints; baseline, 6 weeks post risk feedback and 6 months post risk feedback. A between-subjects comparison will be made between average and increased risk women for outcomes assessed at multiple timepoints.

6.4.1.3 Understanding acceptability

A cross-sectional qualitative design will be adopted employing one-to-one semi-structured interviews.

6.4.2 Setting and participants

All general practices across Greater Manchester have been approached for participation in BCAN-RAY as participant identification centres. An electronic database search will be conducted by each practice to identify women aged 30-39 years predicted to meet eligibility criteria. All potentially eligible women will be invited. We expect to recruit a diverse sample in terms of ethnicity and socioeconomic status given that Greater Manchester has one of the most ethnically diverse populations in the UK in addition to some of the most deprived areas [30, 31]. Furthermore, general practices in areas of higher ethnic and socioeconomic diversity will be prioritised during setup. Participants meet BCAN-RAY study inclusion criteria if they are (1) born biologically female, (2) aged 30-39 years, and (3) able to provide informed consent. Participants cannot take part if they meet any of the exclusion criteria outlined in Table 6.1.

Table 6.1. Study exclusion criteria

1) Strong family history of breast cancer, defined as a first degree relative diagnosed with breast cancer under the age of 50 or two or more second-degree relatives diagnosed with breast cancer at any age
2) Already under follow up in a breast cancer family history clinic or have a known mutation in a moderate or high-risk breast cancer gene
3) Any prior malignancy (excluding non-melanoma skin cancer)
4) Had a double mastectomy (both breasts removed)
5) Breast implants or breast augmentation surgery
6) Currently pregnant
7) Currently breast-feeding or stopped breast-feeding less than six months ago
8) Any condition that would make breast cancer risk assessment inappropriate such as a severe psychiatric or physical illness (assessed by the individual responsible for identifying and inviting women)
9) Unable to understand written English

6.4.3 Procedure

6.4.3.1 BCAN-RAY study

Participating general practices will send postal invitations to eligible women. The BCAN-RAY invitation letter will contain a QR code and web-link to access the participant information sheet and instructions directing prospective participants to the risk assessment web-based application. Once participants have consented to the study online, they will be directed to the BCAN-RAY risk factors questionnaire based on the Tyrer-Cuzick algorithm [32]. Participants will be able to answer part of the questionnaire, save and return to it at a later date. If a participant does not have access to the internet or is having difficulty completing the questionnaire, they can provide their answers via telephone to the study team who will manually input the participants' responses into the web-based application. Participants will be contacted by telephone to arrange the risk assessment appointment which will take place at the Nightingale Centre, part of the Manchester University NHS Foundation Trust. Before the appointment, participants will be sent a saliva sample collection tube in

the post and asked to bring the saliva sample along to the appointment, which will be analysed for polygenic risk score (SNP313) and the presence of pathogenic variants in high and moderate-risk genes. At the appointment, participants will undergo low-dose mammography (two views of one breast only). Breast density will be calculated using a new technique called predicted visual assessment score (pVAS). pVAS is an automated method of assessing mammograms using artificial intelligence techniques [22, 33]. A risk feedback letter will be generated based on the answers participants give in their questionnaire, the results of genetic testing and mammographic density. The risk feedback letter will inform women that they are at "average" risk (< 3% 10-year risk) or "increased" risk (≥ 3% 10-year risk). Each letter will explain the implications of the risk result (Appendix E.1). Participants identified as at increased risk will be offered an appointment at a FHRPC to discuss their risk result further with a breast clinician with expertise in risk assessment, screening and prevention. At this appointment, potential management options including earlier access to breast screening and risk-reducing medication will be discussed. All participants will receive their risk feedback letter within 16 weeks of the risk assessment appointment, along with leaflets providing additional detail on ways of reducing breast cancer risk, signs and symptoms of breast cancer and breast awareness. An updated risk feedback letter will be sent at the end of the study once the magnitude of risk associated with density is determined more accurately in this age group using all case control subjects. The timeline from the participant perspective is shown in Figure 6.1.

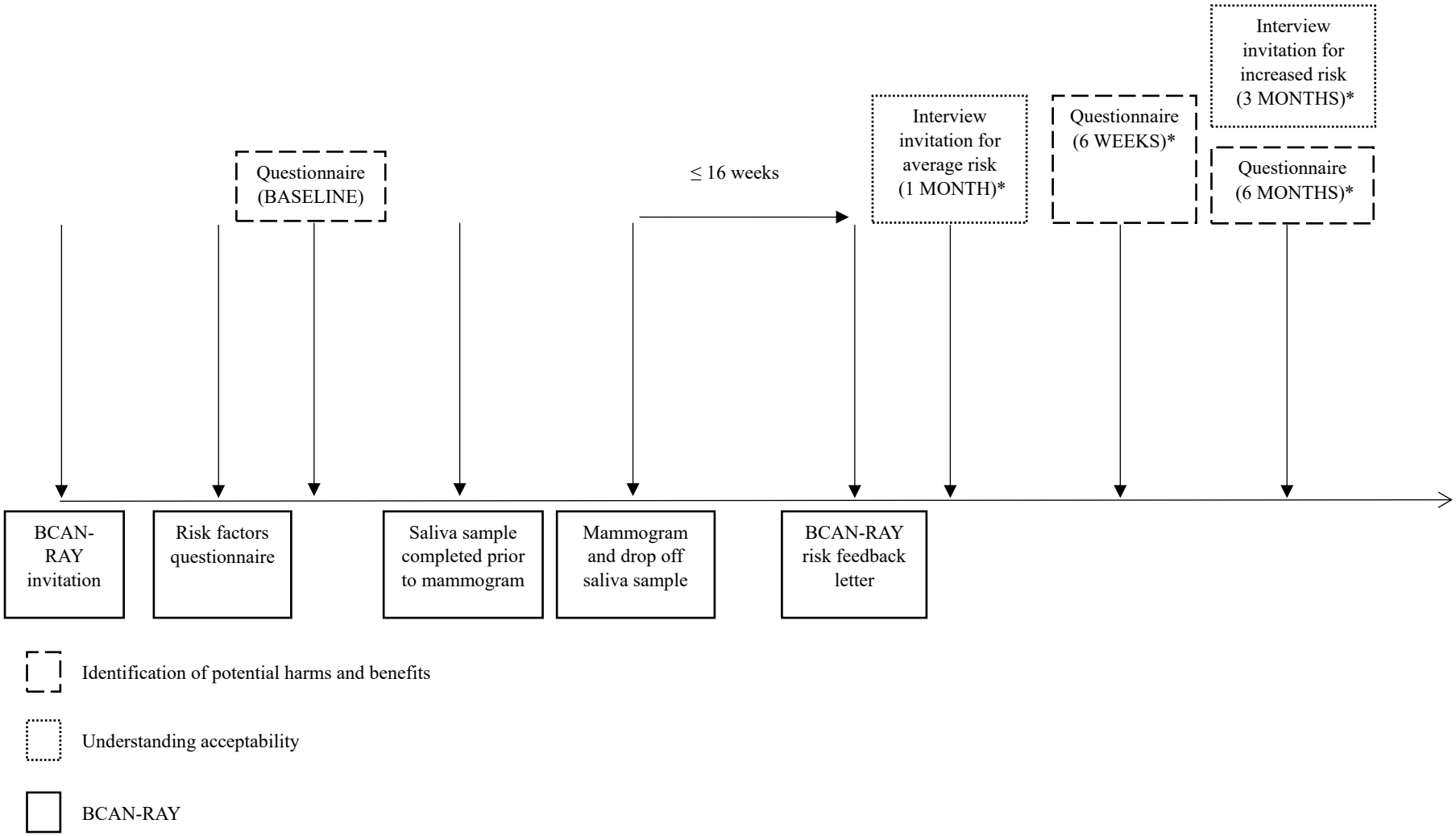


Figure 6.1. Timeline of feasibility study integrated with BCAN-RAY

6.4.3.2 Health inequalities assessment

GPs from participating general practices will extract self-reported ethnicity (where available) and deprivation information based on residential postcode for all women invited to take part in the BCAN-RAY study. They will provide this aggregated, non-identifiable data to the research team. No personally identifiable data will be shared with the research team as we predict the majority of women invited will not consent to the study. A member of the research team will then extract the same information from the BCAN-RAY study database for all participants.

6.4.3.3 Identification of potential harms and benefits

Once participants have submitted the risk factors questionnaire on the web-based application, they will be directed to complete the baseline harms and benefits questionnaire on Qualtrics (https://www.qualtrics.com/uk/). If the baseline questionnaire has not been completed by the time a member of the study team rings the participant to arrange their risk assessment appointment, a reminder to do so will be enclosed with their appointment confirmation letter. Any remaining non-completers will be asked to complete the questionnaire online or via paper in the waiting room before their risk assessment appointment.

The same women will be asked to complete follow up questionnaires 6 weeks and 6 months after they have received their risk feedback. Women will be asked to input their unique BCAN-RAY study ID and their date of birth at the beginning of each questionnaire to ensure responses can be linked. Participants are able to request paper copies of the follow up questionnaires to be sent to them via post if preferred. The data recorded on paper copies of all questionnaires will be manually inputted into the Qualtrics platform by a member of the study team. If the follow up

questionnaires have not been completed by two weeks after the initial invitations, a reminder to complete the questionnaire will be sent via email or letter.

6.4.3.4 Understanding acceptability

A purposive sample of average and increased risk women who complete the baseline questionnaire and have agreed to be contacted will be sent an invitation to participate in a semi-structured interview. Demographic characteristics and responses to questionnaires will guide sampling to allow variation in ethnicity, socioeconomic status, and anxiety levels of participants. Average risk women will be invited for interview 1 month after receiving their risk feedback letter. Increased risk women will be invited for interview 3 months after receiving their risk feedback letter. This gives women at increased risk the chance to explore extra screening options or medications prior to the interview and minimises any influence participating in the interview may have on decision-making. We will aim to recruit up to 24 women to these interviews (up to 12 women in each risk category). If no response is received following the initial invitation, a second invitation will be sent approximately 3-4 weeks later.

Interviews will last approximately 40-60 minutes and will be conducted face-to-face or over the telephone according to each participant's preference. For face-to-face interviews, written consent will be obtained. For telephone interviews, verbal consent will be obtained over the telephone before the interview begins and recorded in a separate audio file. Interviews will be audio recorded and transcribed verbatim using an accredited transcription company. Participants will be compensated for their time with a £20 shopping voucher.

6.4.4 Measures

6.4.4.1 Health inequalities assessment

Residential postcode, a proxy measure of socioeconomic status, will be converted into deprivation deciles using the Index of Multiple Deprivation (IMD), a measure of relative deprivation for small areas in England [34]. Where available, ethnicity data will be mapped onto the five high-level ethnic categories used in the 2021 Census for England (White, Asian/Asian British, Black/African/Caribbean/Black British, Mixed/Multiple, and Other ethnic group), in line with the current ethnicity harmonised standard [35]. Missing data will be captured under two additional categories of refusal to provide information about ethnic group and no data available.

6.4.4.2 Identification of potential harms and benefits

The self-reported measures of potential harms and benefits of participation in breast cancer risk assessment to be completed by participants are shown in Table 6.2. A detailed description of each of these measures is provided in Appendix E.2. Appendix E.3 contains a copy of each questionnaire.

Table 6.2. Self-reported measures to be assessed, at each of the three timepoints

Baseline	6 weeks post risk feedback	6 months post risk feedback
State anxiety [36] Cancer worry [37] Risk perception [38] Attitudes towards risk assessment [39]	State anxiety [36] Cancer worry [37] Risk perception [38]	State anxiety [36] Cancer worry [37] Risk perception [38] Attitudes towards risk assessment [39]
	Knowledge[a] Satisfaction with risk feedback information [40]	
		Satisfaction with decision to participate in breast cancer risk assessment [41]

[a]Assessed by a measure the research team has created as no validated measure available (see Appendix E.2 for more information about development of this measure)

6.4.4.3 Understanding acceptability

Topic guide development was informed by the aims of the study and a review of the literature. An initial draft was developed by the lead author, a doctoral student in health psychology with qualitative health services research experience. Feedback on this draft was obtained from public contributors and members of the research team (DPF and JAU-S) who have research expertise in breast cancer and screening services, primary care and health services research, health psychology, and qualitative methods. The content and structure of the topic guide was revised in line with the feedback received. Participants will be asked about their experience of the risk assessment process including how acceptable they found it, their views on the materials developed for BCAN-RAY, and how the risk assessment process could be improved in terms of delivery/access and provision of information and support (Appendix E.4). Furthermore, women will be asked to discuss any actions they have considered and/or made as a result of participating in BCAN-RAY (e.g. lifestyle modifications, additional screening and risk-reducing medication).

6.4.5 Data analysis

6.4.5.1 Health inequalities assessment

The Chi-squared test will be used to compare uptake rates by ethnicity and socioeconomic status (assessed by IMD deciles) between women who participate in the BCAN-RAY study and women who decline participation. To ensure sufficient instances in each group, IMD deciles will be collapsed into quintiles and ethnicity will be collapsed into 6 subgroups (White, Asian, Black, Mixed or Multiple, Other and Missing).

6.4.5.2 Identification of potential harms and benefits

The main analyses will focus on comparing the responses of the two groups of women provided with different risk estimates (average and increased) for outcomes assessed at multiple timepoints (i.e. anxiety, cancer worry, risk perceptions and attitudes towards breast cancer risk assessment). ANCOVA will be used, with baseline responses to the same variables, age and IMD deciles as covariates. Analyses will be conducted on all questionnaire measures at 6 weeks and 6 months, with the 6-month state anxiety measure being the primary outcome.

Measures administered at only one timepoint (knowledge, satisfaction with information received and satisfaction with decision to participate in breast cancer risk assessment) will be compared between the two groups of women provided with different risk estimates (average or increased). ANCOVA will be used, with age and IMD deciles as covariates.

All statistical tests will be two-sided and use a significance level of 5%. A "completer only" analysis strategy will be employed. If dropout levels are high, the a priori primary outcome (comparison of 6-month outcome scores between average and increased risk groups) will be repeated using a last occasion carried forward approach to missing data as a sensitivity analysis. Statistical analyses will be performed using SPSS.

6.4.5.3 Understanding acceptability

NVivo software will be used to organise the data. Data will be analysed using a manifest level approach to reflexive thematic analysis [42, 43]. Thematic analysis involves examining qualitative data to produce themes that summarise and interpret patterns of results. Initial coding will be deductive based on the structured questions in the topic guide to address the objective of whether the BCAN-RAY approach is

acceptable. Inductive methods will then be used to capture additional codes and context to ensure important aspects of the data are not missed. A critical realist approach will be adopted, with the researchers accepting that participants' accounts represent their perception of their reality, which is shaped by and embedded within their cultural context and language [44]. An experiential orientation to data interpretation will be adopted that seeks to stay close to participants' meanings and capture these in ways that might be recognisable to them. The analysis will be conducted by the lead researcher with input from other members of the research team and public contributors.

6.4.6 Sample size estimation

6.4.6.1 Health inequalities assessment

The BCAN-RAY feasibility study aims to recruit approximately 750 women. Based on the results of the latest NHS GP Patient Survey in which 13-19% of those invited by post aged 25-44 responded [45], we conservatively expect a response rate of 10%. Therefore, approximately 7,500 invitations will be sent. If the response rate is lower than expected, more invitations will be sent until at least 750 women have been recruited. This approach will also yield 6,750 women who decline participation. Given the geographical spread of the general practices who have provisionally agreed to be involved in the study across different boroughs of Greater Manchester, we expect to recruit a socioeconomically diverse sample (see Table 6.3).

Table 6.3. Percentage of Lower Super Output Areas (LSOAs) in each deprivation decile across the boroughs of Greater Manchester involved in the BCAN-RAY study[a]

	Location					
Deprivation decile[b]	Trafford	Manchester	Salford	Tameside	Rochdale	Stockport
1-2 (most deprived)	8.7%	59.3%	48.7%	42.6%	44.1%	16.3%
3-4	15.9%	25.8%	21.4%	22.7%	26.1%	20%
5-6	15.2%	10.7%	15.3%	20.6%	10.4%	15.3%
7-8	25.3%	3.9%	7.3%	12.1%	15%	21.6%
9-10 (least deprived)	34.8%	0.4%	7.3%	2.1%	4.5%	26.9%

[a]Data sourced from an interactive map created by Greater Manchester Poverty Action [30]
[b]Assessed by the Index of Multiple Deprivation 2019 [34]

6.4.6.2 Identification of potential harms and benefits

The sample size for the BCAN-RAY study was based on providing sufficient power to be able to detect an effect of breast density, after adjustment for age and BMI. Therefore, a post hoc analysis was conducted to estimate achieved power with respect to the primary outcome of anxiety at 6 months. Assuming a two-tailed independent samples t-test and follow up questionnaire responses from 400 average risk women and 100 increased risk women, it is estimated that there will be approximately 76% power to detect a small, standardised difference of d = 0.3.

6.4.6.3 Understanding acceptability

The sample size for the BCAN-RAY study will provide more than sufficient numbers from which to recruit participants for the acceptability assessment. Whilst we anticipate including up to 24 participants in this component of the study (12 at average risk and 12 at increased risk), the decision to stop recruitment will be guided

by the concept of ‘information power’. The research team will reflect on the information richness of their dataset throughout data collection to determine when sufficient data has been collected to answer the research question [46].

6.4.7 Public involvement

A public involvement group of 11 women aged 30-39 years was established in September 2021 to inform the development of research aimed at identifying young women at increased risk of breast cancer including the BCAN-RAY study. Five women reviewed the study documentation (participant information sheet, consent form, study invite letter, risk feedback letters, baseline and follow up questionnaires, and interview topic guide). The content and structure of documentation was revised in line with the feedback received. Changes included the removal of one question from the knowledge measure as it overlapped considerably with the content of one of the other questions and the addition of breast cancer charity contact information to risk feedback letters. We will continue to involve members of the public involvement group in subsequent stages of the research cycle including analysis of interview data and dissemination.

6.4.8 Ethics and dissemination

This study was approved by the North West - Greater Manchester West Research Ethics Committee (reference: 22/NW/0268). The study will be performed in accordance with the Declaration of Helsinki, Good Clinical Practice principles and relevant regulations. All participants in BCAN-RAY complete written consent online. All participants will provide informed consent (written if face-to-face, verbal if over telephone) prior to taking part in an interview. Quantitative study data will be

tracked via participant study IDs. Identifying information will be removed from the interview transcripts and participants will be assigned pseudonyms.

We will disseminate our findings through peer-reviewed journals, conference presentations and charitable organisations. At the time of consent for both the BCAN-RAY study and an interview, participants will be asked to indicate whether they wish to receive a summary of findings. A written lay summary will be produced and sent to those who opt to receive this.

6.5 Discussion

The present research aims to provide evidence on the feasibility of a strategy to offer breast cancer risk assessment based on family history, phenotypic risk factors, polygenic risk and mammographic density to women aged 30-39 years. It will provide information about uptake rates, potential harms and benefits of participation, and the acceptability of the risk assessment strategy including novel insight into the experience of low-dose mammography amongst a population of women not known to be at increased risk of breast cancer.

One key issue that the present research does not cover relates to whether breast cancer risk assessment in younger women is acceptable to healthcare professionals involved in its delivery, which is recognised as an important component of feasibility [23]. We have interviewed and conducted focus groups with primary care professionals to understand their views on involvement in breast cancer risk assessment and management and analysis is ongoing. However, as the optimal strategy for implementation remains unclear, it is not yet known who would be responsible for the delivery of risk assessment. Future research investigating alternative strategies for implementation ought to consider the views of healthcare

personnel involved in delivery to establish likely effects on the healthcare system when implementing risk assessment.

The study will provide valuable information about whether a primary care co-ordinated invitation process is successful at engaging women from diverse socioeconomic and ethnic backgrounds thereby informing the need to consider and evaluate alternative invitation methods prior to further implementation. Furthermore, findings will provide information about the likely harms and benefits of participation in breast cancer risk assessment and identify modifications needed to the risk assessment strategy to increase engagement and uptake in future implementation studies.

Key feasibility issues for implementing risk-stratified screening into routine breast cancer screening have now been identified. The present study provides an important first step in assessing the feasibility of introducing comprehensive breast cancer risk assessment for younger women to enable those identified as being at increased risk access to screening and preventive strategies in the absence of a family history of breast cancer.

Declarations

Author contributions

The BCAN-RAY study was conceived and designed and is being led by SJH and DGE. Funding for BCAN-RAY was led by SJH and DGE, with input from JAU-S and DPF. The feasibility study and participant documentation were designed by SH, SJH, JAU-S and DPF. SH co-ordinated the involvement of public contributors. The present article was drafted by SH. DPF, SJH, LG, JAU-S and DGE provided feedback on versions of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Funding

This study is sponsored by Manchester University NHS Foundation Trust and funded by grants from Cancer Research UK Alliance for Cancer Early Detection (ref: EDDAMC-2021\100003) and The Christie Charity. The web-based application was developed through charitable donations from the Shine Bright Foundation and Tony Thornley. The low-dose mammogram was developed with a grant from the Medical Research Council's Confidence in Concept funding scheme (2018/19). SH is funded by a Manchester Cancer Research Centre PhD studentship. DPF, DGE and SJH are supported by the NIHR Manchester Biomedical Research Centre (IS-BRC-1215-20007 and NIHR203308). JAU-S is funded by an Advanced Fellowship from the National Institute for Health and Social Care Research (NIHR300861). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. These funding sources had no role in the

design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Acknowledgements

We would like to thank Stephanie Archer who helped with the developmental work. We also gratefully acknowledge the contributions of our public involvement group.

6.6 References

1. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. Lancet Glob Health. 2020;8(8):e1027-37.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
3. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. Lancet Oncol. 2018;19(2):169-80.
4. Assi HA, Khoury KE, Dbouk H, Khalil LE, Mouhieddine TH, El Saghir NS. Epidemiology and prognosis of breast cancer in young women. J Thorac Dis. 2013;5(Suppl 1):S2-8.
5. Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2− advanced breast cancer: focus on special considerations and latest advances. Clin Cancer Res. 2018;24(21):5206-18.
6. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep. 2017;7(1):11625.
7. Office for National Statistics. Deaths registered in England and Wales: 2021 [Online]. 2022 [Accessed 19th April 2023]. Available from: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregistrationsummarytables/2021.

8. Kudela E, Samec M, Kubatka P, Nachajova M, Laucekova Z, Liskova A, et al. Breast cancer in young women: status quo and advanced disease management by a predictive, preventive, and personalized approach. Cancers. 2019;11(11):1791.

9. Evans D, Brentnall AR, Harvie M, Dawe S, Sergeant JC, Stavrinos P, et al. Breast cancer risk in young women in the National Breast Screening Programme: implications for applying NICE guidelines for additional screening and chemoprevention. Cancer Prev Res. 2014;7(10):993-1001.

10. National Institute for Health and Care Excellence (NICE). Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [updated 2019 Nov] (Clinical Guideline [CG164]). [Online]. 2013 [Accessed 19th April 2023]. Available from: https://www.nice.org.uk/guidance/cg164/chapter/Recommendations.

11. Eccles BK, Copson ER, Cutress RI, Maishman T, Altman DG, Simmonds P, et al. Family history and outcome of young patients with breast cancer in the UK (POSH study). Br J Surg. 2015;102(8):924-35.

12. Dite GS, MacInnis RJ, Bickerstaffe A, Dowty JG, Allman R, Apicella C, et al. Breast cancer risk prediction using clinical models and 77 independent risk-associated SNPs for women aged under 50 years: Australian breast cancer family registry. Cancer Epidemiol Biomarkers Prev. 2016;25(2):359-65.

13. Evans D, Harkness EF, Brentnall AR, van Veen EM, Astley SM, Byers H, et al. Breast cancer pathology and stage are better predicted by risk stratification models that include mammographic density and common genetic variants. Breast Cancer Res Treat. 2019;176(1):141-8.

14. Hurson AN, Pal Choudhury P, Gao C, Hüsing A, Eriksson M, Shi M, et al. Prospective evaluation of a breast-cancer risk model integrating classical risk factors and polygenic risk in 15 cohorts from six countries. Int J Epidemiol. 2021;50(6):1897-911.

15. Vilmun BM, Vejborg I, Lynge E, Lillholm M, Nielsen M, Nielsen MB, et al. Impact of adding breast density to breast cancer risk models: a systematic review. Eur J Radiol. 2020;127:109019.

16. Evans DGR, Donnelly LS, Harkness EF, Astley SM, Stavrinos P, Dawe S, et al. Breast cancer risk feedback to women in the UK NHS breast screening population. Br J Cancer. 2016;114(9):1045-52.

17. van Veen EM, Brentnall AR, Byers H, Harkness EF, Astley SM, Sampson S, et al. Use of single-nucleotide polymorphisms and mammographic density plus classic risk factors for breast cancer risk prediction. JAMA Oncol. 2018;4(4):476-82.

18. Esserman LJ, Anton-Culver H, Borowsky A, Brain S, Cink T, Crawford B, et al. The WISDOM Study: breaking the deadlock in the breast cancer screening debate. NPJ Breast Cancer. 2017;3(1):34.

19. UNICANCER. My Personalized Breast Screening (MyPeBS). ClinicalTrials.gov identifier: NCT03672331. [Online]. 2018 [Accessed 19th April 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT03672331.

20. Usher-Smith JA, Hindmarch S, French DP, Tischkowitz M, Moorthie S, Walter FM, et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636–46.

21. Manchester University NHS Foundation Trust. Breast CANcer Risk Assessment in Younger women: BCAN-RAY (BCAN-RAY). ClinicalTrials.gov identifier: NCT04336904. [Online]. 2022 [Accessed 19th April 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05305963.

22. Squires S, Ionescu G, Harkness E, Mackenzie A, Evans D, Maxwell A, et al., editors. Automatic density prediction in low dose mammography. Proc SPIE 11513, 15th International Workshop on Breast Imaging; 2020 May 25-27; Leuven, Belgium. Washington: SPIE Press; 2020.

23. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061.

24. Evans DGR, McWilliams L, Astley S, Brentnall AR, Cuzick J, Dobrashian R, et al. Quantifying the effects of risk-stratified breast cancer screening when delivered in real time as routine practice versus usual screening: the BC-Predict non-randomised controlled study (NCT04359420). Br J Cancer. 2023;128:2063–71.

25. U.S. Preventive Services Task Force (USPSTF). Breast Cancer: Screening (Draft Recommendation Statement). 2023 [Accessed 22nd May 2023]. Available from: https://www.uspreventiveservicestaskforce.org/uspstf/draft-recommendation/breast-cancer-screening-adults#fullrecommendationstart.

26. French DP, McWilliams L, Bowers S, Woof VG, Harrison F, Ruane H, et al. Psychological impact of risk-stratified screening as part of the NHS Breast Screening Programme: multi-site non-randomised comparison of BC-Predict versus usual screening (NCT04359420). Br J Cancer. 2023;128:1548-58.

27. French DP, Southworth J, Howell A, Harvie M, Stavrinos P, Watterson D, et al. Psychological impact of providing women with personalised 10-year breast cancer risk estimates. Br J Cancer. 2018;118(12):1648-57.

28. Hindmarch S, Gorman L, Hawkes RE, Howell SJ, French DP. Optimising the delivery of breast cancer risk assessment for women aged 30–39 years: A qualitative study of women's views. Womens Health. 2023;19.

29. Green CA, Duan N, Gibbons RD, Hoagwood KE, Palinkas LA, Wisdom JP. Approaches to mixed methods dissemination and implementation research: methods, strengths, caveats, and opportunities. Adm Policy Ment. 2015;42(5):508-23.

30. Greater Manchester Poverty Action. Deprivation at a neighbourhood level [Online]. 2023 [Accessed 22nd May 2023]. Available from: https://www.gmpovertyaction.org/pm2022-imd/.

31. Office for National Statistics. Ethnic group, England and Wales: Census 2021. [Online]. 2022 [Accessed 22nd May 2023]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity/bulletins/ethnicgroupenglandandwales/census2021#how-ethnic-composition-varied-across-england-and-wales.

32. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med. 2004;23(7):1111-30.

33. Astley SM, Harkness EF, Sergeant JC, Warwick J, Stavrinos P, Warren R, et al. A comparison of five methods of measuring mammographic density: a case-control study. Breast Cancer Res. 2018;20(1):10.

34. Ministry of Housing, Communities, Local Government. English indices of deprivation 2019. [Online]. 2019 [Accessed 22 May 2023]. Available from: https://imd-by-postcode.opendatacommunities.org/imd/2019.

35. Government Statistical Service. Ethnicity harmonised standard. [Online]. 2011 [Accessed 22nd May 2023]. Available from: https://analysisfunction.civilservice.gov.uk/policy-store/ethnicity-harmonised-standard/.

36. Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State—Trait Anxiety Inventory (STAI). Br J Clin Psychol. 1992;31(3):301-6.

37. Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. Psychological side effects of breast cancer screening. Health Psychol. 1991;10(4):259-67.

38. Weinstein ND. What does it mean to understand a risk? Evaluating risk comprehension. J Natl Cancer Inst Monographs. 1999;1999(25):15-20.

39. Ajzen I. Understanding attitudes and predicting social behavior. Englewood Cliffs, New Jersey: Prentice Hall; 1980.

40. French DP, Maissi E, Marteau TM. The psychological costs of inadequate cervical smear test results: three-month follow-up. Psychooncology. 2006;15(6):498-508.

41. Brehaut JC, O'Connor AM, Wood TJ, Hack TF, Siminoff L, Gordon E, et al. Validation of a decision regret scale. Med Decis Making. 2003;23(4):281-92.

42. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77-101.

43. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qual Res Sport Exerc Health. 2019;11(4):589-97.

44. Pilgrim D. Some implications of critical realism for mental health research. Social Theory & Health. 2014;12(1):1-21.

45. NHS England. GP Patient Survey 2022: Technical Annex. [Online]. 2022 [Accessed 22nd May 2023]. Available from: https://www.gp-patient.co.uk/surveysandreports.

46. Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. Qual Health Res. 2016;26(13):1753-60.

Chapter 7. General Discussion

7.1 Summary of key research questions and findings

In the period up to the beginning of this PhD, much of the research investigating the provision of personalised breast cancer risk estimates has been conducted within the context of implementing a risk-based screening and prevention programme at the time of routine breast cancer screening (between ages 50-70 years). Consequently, little was known regarding how a similar programme could be delivered to women aged 30-39 years without a strong family history of breast cancer outside of an organised screening programme. This PhD, therefore, aimed to inform the development of acceptable care pathways for the provision of personalised breast cancer risk assessment and where appropriate, screening or preventive strategies, to women aged 30-39 years without a strong family history of breast cancer. This was to be achieved by investigating the views of primary care providers and women aged 30-39 years as the intended deliverers and recipients respectively.

A systematic review (Study One) was conducted synthesising the quantitative data on primary care providers' attitudes and routine behaviours in the context of breast cancer risk assessment and primary prevention. The review identified several important gaps in the literature. More than half of the studies were conducted in the US which may have resulted in an overestimation of the involvement of primary care providers in breast cancer risk assessment and primary prevention given that OB/GYNs are a primary care speciality in the US. Nursing and other allied health professionals, who contribute to risk assessment and primary prevention activities for other diseases, were underrepresented in the included studies. In addition, no studies had investigated health protective behaviours within the context of breast

cancer risk reduction so primary prevention findings were limited to risk-reducing medications only. I identified a need to conduct qualitative research, therefore, to ascertain a more comprehensive understanding of primary care provider's views across professions as to how best to support implementation of a risk-based screening and prevention programme for younger women in the UK (Study Two). Findings from Studies One and Two suggest that general practices are more likely to accept an increased role in breast cancer risk assessment compared to managing women identified as increased risk.

Study Three investigated women's views on, and requirements for, a breast cancer risk assessment service. This study resulted in two papers, one relating to optimising the delivery of risk assessment and one examining young women's beliefs about breast cancer risk and experiences of breast awareness. Breast cancer risk assessment was considered acceptable in principle to eligible women providing that a risk management plan and support from healthcare professionals is available. A 'one-stop shop' delivery model that minimised the effort required to engage with breast cancer risk assessment was desired by women. However, women may not engage with breast cancer risk assessment because of their perception of breast cancer as an older woman's disease and reported disengagement with breast awareness.

Finally, the planned methods and analyses for a study assessing the feasibility of offering breast cancer risk assessment to women aged 30-39 years without a strong family history of breast cancer is provided (Study Four).

7.2 Methodological reflections

7.2.1 Risk-based screening and prevention as a hypothetical prospect

The research described in this thesis was designed to inform the development of a risk-based screening and prevention programme for younger women that does not yet exist, allowing for the opportunity to think through potential issues before implementation and understand the how and why of decision-making processes. However, questions about hypothetical situations can be challenging to interpret, particularly if respondents have varying levels of understanding of the topic. This was evident in the early stages of data collection for the qualitative study with women, as participants would often ask clarifying questions. This experience informed my decision to send pre-reading material to the primary care providers which helped to familiarise participants with the topic, resulting in greater understanding and fewer clarifying questions being asked. Additionally, responses to hypothetical questions reflect anticipated thoughts, feelings and behaviours which may differ should a programme be implemented into clinical practice. Nevertheless, the approach taken was most appropriate given the aim of the research.

7.2.2 Scope of systematic review

I originally planned to include qualitative and quantitative literature in the systematic review but decided to only include quantitative studies. On performing the searches, I identified three qualitative studies reported in four papers, one of which was unpublished and included only two primary care providers. I conducted a quality assessment of each of these studies which indicated low quality. Data analysis issues were evident, with insufficient methodological detail reported particularly with respect to the analytic process and issues of rigour. I discussed the quality appraisal results with my supervisory team, and we decided it would not be worthwhile to synthesise the findings from these studies because of the limited data available and concerns around trustworthiness of the data. However, it is important to note that the

area of breast cancer risk stratification is fast moving, with more qualitative studies published during the course of my PhD which investigated the views of primary care providers specifically [1, 2]. Therefore, it may be worthwhile to synthesise this literature in the future.

7.2.3 Patient and Public Involvement and Engagement

Patient and Public Involvement and Engagement (PPIE) is recognised as strengthening health research by having a positive influence on quality, relevance and impact of research [3]. In the first six months of my PhD programme, I focused on building relationships with community organisations to identify public contributors for my research. This involved in-person engagement activities such as providing education about breast cancer screening and presenting at tea and confidence workshops about academic careers. Building trust and relationships with public contributors is recognised as key to continued involvement throughout the life of a research project [3]. However, my efforts were undermined when in-person contact ceased due to restrictions and social distancing measures, implemented as a result of the COVID-19 pandemic. In response, researchers have had to be more flexible and adapt their approaches to allow PPIE to take place remotely [4]. My attempts to continue engaging with community organisations remotely were unsuccessful. On reflection, I think this was because I had not yet had the time to develop the trust and authenticity needed to mitigate anxieties associated with remote involvement [5]. Nevertheless, I was able to set up a PPIE group consisting of some of the women who had participated in my first qualitative study who contributed to my remaining studies remotely.

7.2.4 Approach to qualitative inquiry

A large proportion of the work undertaken in this PhD thesis was qualitative in nature. All qualitative analyses were conducted from a critical realist perspective and the same approach is planned for the qualitative component of the feasibility study (Study Four). The critical realist approach combines a realist ontology with a relativist epistemology. It therefore retains a concept of truth and reality but understanding of this reality is limited by an individual's position in it [6]. Therefore, we treated the data as indicating the participant's perception of their reality, which is shaped by and embedded within their cultural context and language [7]. Adopting a critical realist perspective enables interpretations to be developed that are as credible as possible with some degree of generalisability [6].

Focus groups were chosen as the primary method of data collection for Studies Two and Three. The debate in focus groups encourages participants to reflect on and clarify their own perspectives, resulting in a depth of dialogue not often found in interviews [8]. Furthermore, focus groups allow participants to consider their views in relation to others, which might result in opinions shifting during the course of discussion [9]. This interaction between participants, therefore, allows insight into the degree of group consensus on the topic which was important given the focus of Studies Two and Three on informing the development of acceptable care pathways. For these reasons, focus groups were considered a more appropriate method of data collection than interviews. However, I did end up including interviews as an additional data collection method due to logistical issues arranging focus groups, particularly with primary care providers. On reflection, I could have approached primary care practices to run team-based focus groups. This approach may have resulted in more solution focused dialogue as participants would be able to reflect on their own experiences as a working group to inform how the pathway could work

within their own practice. However, participants may have been less likely to express dissenting views in a group of people they knew and worked with.

There are many different methods of analysis available to the qualitative researcher. It is important to ensure alignment of the chosen analysis method with the aim of the research. Thematic analysis involves examining qualitative data to produce themes that summarise and interpret patterns of meaning. It is a versatile method meaning it offers the possibility for both inductive and deductive analyses, and the ability to capture semantic and latent meanings [10]. Additionally, it allows the flexibility to combine multiple sources of data and is suited to research examining views about particular phenomena. For these reasons, thematic analysis was considered the most appropriate method of analysis for the qualitative components of this thesis. Another method commonly used in psychological qualitative research is Interpretive Phenomenological Analysis (IPA) which aims to understand what a given experience was like and how someone made sense of it [11]. It would not have been appropriate to use this method as participants would not have had any lived experience of the phenomenon (breast cancer risk assessment) under investigation.

Two of the thematic analyses in this thesis were organised using a framework approach [12]. Framework analysis was developed in an applied policy research context so it is particularly useful for health services research which has a clear research objective to be achieved [13]. Therefore, this approach aligned well with the objectives of the two qualitative studies. Furthermore, the matrix output serves to systematically reduce the data making large qualitative datasets easier to manage whilst enabling comparisons across and within cases to highlight similarities and differences, resulting in a greater depth of analysis. However, this highly systematic method of categorising and organising qualitative data has been criticised for its

potential to delimit analytic and interpretative processes [14]. To limit the impact of this, I used inductive methods to capture additional codes and context to ensure important aspects of the data were not missed.

In comparison, reflexive thematic analysis was chosen as the method of analysis for the second paper resulting from Study Three and the qualitative component of the feasibility study (Study Four). This method is particularly suitable when the research aim is to explore participants' experiences and sense-making which aligned well with the analysis focusing on understanding women's experiences of breast awareness and sense-making about breast cancer risk, and Study Four which will explore women's experiences of undergoing risk assessment and receiving a breast cancer risk estimate [10, 15].

7.2.5 Researcher reflexivity

Critical realism acknowledges that researcher reflexivity is an important and inescapable part of the research process. Participants' situated reality is interpreted by the researcher through the lens of their own cultural memberships [16]. I kept a research journal throughout the research process to allow ongoing reflection about how my prior knowledge and assumptions were influencing data collection and analysis and guiding decision-making. I offer the following personal reflections:

I have worked in cancer prevention and early detection research for six years, reflecting and shaping my positives views of early cancer detection initiatives. This was implicated during data collection for my first qualitative study. I could sense the hesitance of some participants to express negative or dissenting views, with those that did often apologising as they did so. I think this was because they were aware of my student status so thought that positive views would help me with my studies.

Although I did reassure participants that there were no right or wrong answers, it was difficult to probe these responses as participants were reluctant to elaborate on their dissenting viewpoints and on reflection, I too felt some discomfort doing so given our differences in opinion.

I am also aware of how my age may have influenced my research, particularly in terms of recruitment and data collection. I am 31 years old meaning I was cognisant of my participant's life stage and had life experiences in common with some of my participants. I feel my position as an insider helped develop rapport with participants and this was evidenced through the disclosure of intimate healthcare experiences which were not the focus of the data collection but nevertheless of importance to women. I recognised that to be entrusted with this information was a privilege and I felt compelled to act on it which resulted in the analysis reported on in Chapter 5.

7.2.6 Benefits and challenges of remote data collection

The majority of data collection for both qualitative studies was conducted remotely using the telephone and video conferencing platform Zoom because of COVID-19 restrictions on in-person contact. Benefits of this approach include greater flexibility in time and location of data collection and opportunities for interactivity such as multimedia [17, 18]. Known shortcomings of online methods include technical issues and difficulties establishing rapport with participants [19]. In my experience, I observed few difficulties establishing rapport with and amongst participants during online focus groups. Collecting consent in a breakout room provided the opportunity to get to know the participants whilst the remaining participants could talk to each other whilst waiting to be consented. I also noticed that participants were less likely to direct their answers to me and more likely to engage in discussion with the other

participants, for example asking others to expand on their viewpoints, during the online focus groups compared to in-person focus groups. Hierarchical relations of power between researchers and participants are an important consideration in the conduct of qualitative research [20]. Qualitative inquiry proposes to reduce power differences and encourage disclosure between researchers and participants [20]. I think online video conferencing facilitated a reduction in the power imbalance between myself as the researcher and the participants as it was not possible to direct responses to a certain individual. Additionally, the absence of a room layout may have contributed to a perception of everyone as equal, helping participants to feel more comfortable engaging with each other.

More recently, researchers using online methods to recruit and collect qualitative data have noted a significant increase in people or 'bots' faking their eligibility to participate, so called 'imposter' or 'scammer' participants, who pose a threat to data integrity [21, 22]. We experienced this phenomenon during data collection for Study Two whereby people posed as primary care providers. On one occasion, two prospective participants joined an online focus group; they refused to turn on their cameras or provide consent, so they were not recruited. Over time, I noticed red flags of suspect requests such as email addresses having similar configurations, blank subject lines and receiving multiple emails in quick succession from the same email address. To discern who was genuine I took additional steps to verify the identities of potential participants by asking them to confirm the name of the general practice surgery they worked at and asking to communicate via their NHS email. This experience highlights the importance of developing a plan to mitigate against fraudulent participation in qualitative research when recruiting participants online

and conducting virtual interviews or focus groups, particularly if financial incentives are being offered.

7.3 Relationship and contribution of the thesis to the wider literature

This thesis is located in the general area of investigating the feasibility of offering risk assessment to young women, specifically examining key uncertainties about the provision of risk assessment such as its acceptability and optimal delivery. For it to be feasible, a number of issues will need to be considered, some of which have already been highlighted in a recent review which summarised the literature surrounding proactive breast cancer risk assessment within primary care against the principles of the consolidated framework for screening [23]. I contributed to this review by writing the section on screening programme acceptability and ethics from the perspective of primary care providers, based on the findings of my PhD. I will now discuss the issues that require further consideration, highlighting the contributions of this PhD thesis and suggesting future research directions.

7.3.1 Acceptability of breast cancer risk assessment amongst women aged 30-39 years

7.3.1.1 The role of candidacy

The success of risk stratification strategies is dependent upon acceptance and uptake within their target population. Findings from Study Three suggest that women aged 30-39 years consider breast cancer risk assessment to be acceptable in principle providing that a risk management plan and support from healthcare professionals is available. However, the findings also indicated that women aged 30-39 years may not understand the value in engaging with breast cancer risk assessment because of their beliefs and assumptions of breast cancer, risk and screening. Women did not

perceive breast cancer as an immediate health concern and reported disengagement with breast awareness. The notion of 'candidacy' posits that individuals' lay understandings of disease are critical in shaping their own perceptions of disease risk and response to it [24]. It has been suggested that breast cancer campaigns may be shifting women's views so that women are better able to appraise risk factors and successfully identify their own candidacy, with participation in prevention strategies potentially contingent on this [25]. Findings from Study Three suggest differently; young women reported limited exposure to educational campaigns focused on raising awareness of modifiable risk factors and preventive strategies, contributing to a lack of knowledge. Therefore, young women's perceptions of breast cancer as a disease primarily affecting older women and breast cancer risk as largely unmodifiable may mean that women either do not take up the offer of breast cancer risk assessment or do not engage with screening and preventive strategies. Further research could usefully explore young women's personal risk appraisals following notification of an increased risk estimate to understand how this information is assimilated. This would inform requirements for more effective risk communication. Additionally, an educational public health campaign should also be considered alongside future implementation studies to raise awareness about the benefits and rationale underpinning the introduction of breast cancer risk assessment for young women. This could help modify women's perceptions of breast cancer and risk.

7.3.1.2 Ease of access as a key determinant of acceptability

Previous research has identified service access as the most valued criterion influencing decisions to participate in breast cancer risk assessment amongst screening age women [26]. In Study Three, I observed that access was a key determinant of acceptability with women expressing a preference for a 'one-stop

shop' delivery model whereby all components of a breast cancer risk assessment would be completed at a single appointment. The timing of invitation to participate in breast cancer risk assessment was implicated as women aged 30-39 years are often managing competing demands of professional and family life. Flexibility in healthcare service organisation and delivery is therefore essential to overcome the difficulties young women experience in accessing healthcare.

7.3.1.3 Acceptability of risk management strategies

The potential benefits of breast cancer risk assessment are contingent upon uptake of available risk management strategies. Previous research with screening age women has demonstrated high uptake of risk-reducing medication amongst screening age women following receipt of an increased risk estimate [27]. The results of Study Three suggest women are unfamiliar with risk management strategies and when prompted many women were uncomfortable with the prospect of taking risk-reducing medication. Primary care providers in Study Two also questioned the likelihood of young women agreeing to take risk-reducing medication due to its side effects and interference with childbearing. It will be important to assess acceptability and uptake of risk-reducing medication within this population in future research.

Another risk management strategy is to include behaviour change interventions focused on promoting health protective behaviours. To prevent breast cancer, it is particularly important for young women to avoid drinking alcohol and to maintain a healthy weight by eating more healthily and being physically active. In the PROCAS study, screening age women who were informed to be at increased risk of breast cancer were more likely to join and remain in weight loss programmes and lose more weight compared to women not at increased risk [28]. Weight gain during adult life,

particularly between the ages of 18 and 35, increases the risk of postmenopausal breast cancer in women who are already at increased risk of the disease [29]. Therefore, supporting these women to avoid weight gain through the provision of weight gain prevention interventions is currently being investigated. Evidence suggests that weight gain prevention interventions are acceptable in principle [30], and a study is ongoing to establish the acceptability and usability of an app promoting health protective behaviours amongst young women aged 18-35 years who are at increased risk of breast cancer [31]. Therefore, weight gain prevention interventions could be included as an alternative risk management option for young women should acceptability and effectiveness be demonstrated.

7.3.1.4 Communicating the heritability implications of breast cancer risk

In Study Three, women reflected on the timing of invitation to participate in breast cancer risk assessment, acknowledging that for many women this coincides with the height of reproductive decision-making, involving decisions about parenthood and contraceptive use, which impact breast cancer risk. Consequently, women were concerned about what their risk result meant for their children's lives and future decisions about parenthood. Concern about reproductive decision-making has previously been identified in populations carrying *BRCA1* or *BRCA2* pathological variants which have autosomal dominant inheritance meaning a 50% chance of being passed on to each child [32, 33]. In contrast, SNPs do not carry the same predictable inherited risk and the implications for family members are less certain. Therefore, care is required that PRS information is not incorrectly conflated with monogenic results, highlighting the importance of clear communication about the implications for heredity to avoid misunderstandings [34]. Recent survey studies have revealed low levels of familiarity with the concept of PRS amongst primary and secondary

care providers [35, 36], indicating that provision of education is required for healthcare professionals to be able to communicate results effectively.

7.3.1.5 Conclusion

The findings of Study Three provide preliminary evidence that young women consider breast cancer risk assessment to be acceptable in principle and identifies factors that might impact acceptability such as the delivery model adopted, perceived value in participating, and available risk management strategies. However, future quantitative research is needed to ascertain the representativeness of these views. It will be important for this research to investigate acceptability including barriers to uptake of breast cancer risk assessment amongst those of lower socio-economic status and those from ethnic minority backgrounds given that previous efforts to implement risk assessment at the time of mammographic screening have experienced difficulties recruiting these underserved groups [27].

7.3.2 Organisation and delivery of a risk-based screening and prevention programme for women aged 30-39 years

7.3.2.1 Consideration of healthcare system capacity

It has often been proposed that primary care will assume responsibility for conducting breast cancer risk assessment and providing primary prevention advice [37-39]. The findings of Studies One and Two indicate that although primary care are likely to accept an increased role in breast cancer risk assessment, they have concerns about managing women identified as increased risk. Therefore, a delivery model involving primary care identifying women at increased risk and referring them to a FHRPC is worth exploring further. This would be in line with a change made to NICE guidance during this PhD enabling the proactive identification of

women at increased risk of breast cancer within primary care [40]. It would also overcome women's reservations towards receiving primary prevention advice from GPs given their insufficient knowledge of this specialty which was observed in Study Three.

Healthcare system capacity to manage the significant increase in demand for risk consultations resulting from identifying young women at increased risk would need to be considered. It has been proposed that 8.8% of women would meet criteria to be offered or considered for risk-reducing medication if the 3% 10-year risk at age 40 years is used in the Tyrer–Cuzick algorithm [41]. Currently, FHRPCs, of which there are around 90 in the UK, are responsible for risk consultations. Pre-existing capacity and resource constraints have been found to drive concerns about providing breast cancer risk at screening amongst FHRPC staff [42, 43]. Similar concerns were also expressed by the primary care providers in Study Two. Furthermore, the availability of FHRPCs across the UK is varied and guidelines for management of women at increased risk are inconsistent which could result in inequitable access to screening and preventive strategies [42]. New services may need to be commissioned to ensure there is capacity within the wider healthcare system to provide additional screening and risk consultations [23]. Therefore, how risk management services for women identified at increased risk will be provided and who will be responsible for delivering them remains a key issue to be resolved. Future research evaluating different implementation strategies ought to consider the views of healthcare personnel involved in delivery to establish likely effects on the healthcare system when implementing risk assessment.

7.3.2.2 Consideration of health inequalities

How to best engage women in breast cancer risk assessment without exacerbating health inequalities has been identified as a key research gap [23]. Uptake of breast cancer risk assessment questionnaires has been found to be lower amongst groups who tend to be underrepresented in existing cancer screening programmes, including those residing in areas of high deprivation and those belonging to an ethnic minority community [27, 44]. GP-endorsed letters have been found to be an effective means to engage these groups in cancer screening programmes [45]. However, reliance on access to the programme through primary care has the potential to create health inequalities as not every woman is registered with a GP surgery [46, 47]. Therefore, a range of methods are likely to be needed that are tailored to the needs of underserved populations. One method suggested by the women who took part in my qualitative study was the involvement of community leaders to tailor health messaging in a more meaningful and sensitive way to the communities they are part of. This has been found to be an effective approach among ethnic minority groups for improving uptake to cancer screening programmes [48]. Recently, studies have investigated how to optimise recruitment to lung cancer screening trials, particularly amongst underserved groups [49, 50]. Feasibility work should evaluate different invitation strategies for breast cancer risk assessment to identify optimal methods for increasing accessibility, particularly for underserved populations, in future implementation studies.

Another important factor to consider is health literacy, defined as an individual's ability to access, understand, appraise, and apply health related information [51]. Poor health literacy has been found to be associated with lower uptake of cancer screening and preventive strategies [52]. A potential misunderstanding identified in Study Three was confusion about the purpose of the mammogram component of

breast cancer risk assessment. Women were familiar with the use of mammograms in breast cancer screening to detect breast cancer so presumed the mammogram would have diagnostic capability. Similarly, healthcare professionals have been found to lack understanding of the distinction between the two steps of a risk stratification approach: evaluating the level of risk and screening for disease [47]. It will be important to effectively communicate the purpose of the mammogram because women could incorrectly presume the presence of breast cancer had been ruled out and subsequently ignore symptoms. Invitation materials need to be co-developed and piloted with women with different health literacy levels to ensure women can make informed decisions about participation in breast cancer risk assessment.

7.4 Research agenda for future research prior to implementation

A number of issues would need to be resolved before implementation of a risk-based screening and prevention programme for young women could proceed. Firstly, there needs to be further consideration of what delivery models are potentially implementable, taking into account the views of key stakeholders from primary and secondary care. Different delivery models should be evaluated, assessing the uptake of screening and preventive strategies, and modelling the potential impact on services including genetics and radiography to inform the likely effect on breast cancer outcomes and cost implications.

Reducing inequalities in access to breast cancer risk assessment is a key priority given that previous efforts to implement risk assessment at the time of mammographic screening have experienced difficulties recruiting underserved groups such as those from lower socio-economic and ethnic minority backgrounds [27]. One potential approach to delivery worth considering to increase accessibility

is a community-based programme similar to lung cancer screening which has demonstrated high uptake in areas of high socioeconomic deprivation [53]. Further research with underserved groups is needed to understand how accessibility can be maximised.

A recent recommendation by the American College of Radiologists proposes that all women should be offered a breast cancer risk assessment before the age of 25 to maximise the benefit of tailored screening and preventive strategies [54]. The inclusion of modifiable risk factors in a risk assessment such as family history and body mass index means that changes in these risk factors could potentially result in reclassification of a woman's risk category at a later time. It is still unclear how frequently breast cancer risk assessment should be repeated. Additionally, how any changes in risk would be handled and communicated to women needs to be considered.

Another key consideration is how risk assessment for younger women relates to the ongoing work focused on implementing risk assessment at the time of mammographic screening. If risk assessment of younger women is carried out, then this would be likely to facilitate risk-based screening at a later point as SNPs would not change nor would information such as age at menarche. Thus, not only could risk assessment of younger women be beneficial as a standalone service but it could add value to services offered to women when they reach the current eligible age of screening and help these services be more cost-effective [55].

Similarly, it is also important to acknowledge that there is growing interest in risk prediction, particularly PRS, for other cancers including colorectal, prostate, and ovarian [56]. Cost is a barrier to deployment of PRS at scale [34]. However, cost

effectiveness could be improved if the genotyping is only performed once with the results contributing to multiple disease predictions.

7.5 Conclusions

This thesis has provided evidence regarding the development of acceptable care pathways for the provision of a breast cancer risk-based screening and prevention programme for women aged 30-39 years without a strong family history of breast cancer. We have provided preliminary evidence that the programme is acceptable amongst the target population, with ease of access identified as key to increasing engagement. Furthermore, the PhD has contributed to advancing the research agenda of incorporating proactive breast cancer risk assessment within primary care for women younger than screening age by investigating their likely role in greater depth than previous research has. Our findings suggest general practices are likely to accept an increased role in breast cancer risk assessment, but they have concerns about managing women identified as increased risk. How risk management services for women identified at increased risk will be provided and who will be responsible for delivering them remains a key issue to be resolved. Different delivery models should be evaluated with due consideration given to the views of healthcare personnel involved in delivery to inform healthcare system capacity requirements and the views of women to ensure equity of access.

7.6 References

1. Archer S, Stutzin Donoso F, Carver T, Adelaide Y, Cunningham A, Ficorella L, et al. Exploring the barriers and facilitators of implementing CanRisk in primary care: a qualitative thematic framework analysis. Br J Gen Pract. 2023;73(733):e586-96.
2. Dunlop K, L. A., Smit A, K., Keogh L, Newson A, J., Rankin N, M., Cust A. Acceptability of risk-tailored cancer screening among Australian general practitioners: a qualitative study. Br J Gen Pract. 2023:in press.
3. Dawson S, Ruddock A, Parmar V, Morris R, Cheraghi-Sohi S, Giles S, et al. Patient and public involvement in doctoral research: reflections and experiences of the PPI contributors and researcher. Res Involv Engagem. 2020;6(1):23.
4. Clark M, van Vliet E, Collins M. Reflections from the COVID-19 pandemic on inequalities and patient and public involvement and engagement (PPIE) in social care, health and public health research. Health Expect. 2021;24(5):1547-50.
5. Adeyemi I, Sanders C, Ong BN, Howells K, Quinlivan L, Gorman L, et al. Challenges and adaptations to public involvement with marginalised groups during the COVID-19 pandemic: commentary with illustrative case studies in the context of patient safety research. Res Involv Engagem. 2022;8(1):13.
6. Brooks J, King N. Approaches to qualitative psychology. In: Brooks J, King N, editors. Applied qualitative research in psychology. London, UK: Bloomsbury Publishing; 2017. p. 14-32.
7. Willig C. Introducing qualitative research in psychology. 3rd ed. Maidenhead, UK: Open University Press; 2013.

8. Kitzinger J. Qualitative research: introducing focus groups. BMJ. 1995;311(7000):299-302.
9. Ivanoff SD, Hultberg J. Understanding the multiple realities of everyday life: basic assumptions in focus-group methodology. Scand J Occup Ther. 2006;13(2):125-32.
10. Braun V, Clarke V. Thematic analysis: a practical guide. California, USA: SAGE Publications Inc; 2021.
11. Smith JA, Flowers, P., & Larkin, M. Interpretive phenomenological analysis: Theory, method and research. 2nd ed. California, USA: SAGE Publications Ltd; 2022.
12. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol. 2013;13(1):117.
13. Spencer L, Ritchie J, O'Connor W, Morrell G, Ormston R. Analysis in practice. In: Ritchie J, Lewis J, McNaughton-Nicholls C, Ormston R, editors. Qualitative research practice: a guide for social science students and researchers. 2nd ed. California, USA: SAGE Publications Inc; 2013. p. 295-343.
14. Braun V, Clarke V. One big happy family? Understanding similarities and differences between reflexive thematic analysis and its methodological siblings and cousins. In: Braun V, editor. Thematic analysis: A practical guide. California, USA: SAGE Publications Inc; 2021. p. 223-57.
15. Braun V, Clarke V. Conceptual and design thinking for thematic analysis. Qual Psychol. 2022;9(1):3-26.

16. Braun V, Clarke V. A not-so-scary theory chapter: conceptually locating reflexive thematic analysis. In: Braun V, editor. Thematic analysis: A practical guide. California, USA: SAGE Publications Inc; 2021. p. 155-93.
17. Lo Iacono V, Symonds P, Brown DHK. Skype as a tool for qualitative research interviews. Sociol Res Online. 2016;21(2):103-17.
18. Matthews KL, Baird M, Duchesne G. Using online meeting software to facilitate geographically dispersed focus groups for health workforce research. Qual Health Res. 2018;28(10):1621-8.
19. Archibald MM, Ambagtsheer RC, Casey MG, Lawless M. Using Zoom videoconferencing for qualitative data collection: perceptions and experiences of researchers and participants. Int J Qual Methods. 2019;18.
20. Karnieli-Miller O, Strier R, Pessach L. Power relations in qualitative research. Qual Health Res. 2008;19(2):279-89.
21. Pellicano E, Adams D, Crane L, Hollingue C, Allen C, Almendinger K, et al. Letter to the Editor: a possible threat to data integrity for online qualitative autism research. Autism. 2023:in press.
22. Ridge D, Bullock L, Causer H, Fisher T, Hider S, Kingstone T, et al. 'Imposter participants' in online qualitative research, a new and increasing threat to data integrity? Health Expect. 2023;26(3):941-4.
23. Usher-Smith JA, Hindmarch S, French DP, Tischkowitz M, Moorthie S, Walter FM, et al. Proactive breast cancer risk assessment in primary care: a review based on the principles of screening. Br J Cancer. 2023;128:1636–46.
24. Davison C, Smith GD, Frankel S. Lay epidemiology and the prevention paradox: the implications of coronary candidacy for health education. Sociol Health Illn. 1991;13(1):1-19.

25. Batchelor S, Miller ER, Lunnay B, Macdonald S, Ward PR. Revisiting candidacy: what might it offer cancer prevention? Int J Environ Res Public Health. 2021;18(19):10157.

26. Wheeler JCW, Keogh L, Sierra MA, Devereux L, Jones K, Ijzerman MJ, et al. Heterogeneity in how women value risk-stratified breast screening. Genet Med. 2022;24(1):146-56.

27. Evans DGR, McWilliams L, Astley S, Brentnall AR, Cuzick J, Dobrashian R, et al. Quantifying the effects of risk-stratified breast cancer screening when delivered in real time as routine practice versus usual screening: the BC-Predict non-randomised controlled study (NCT04359420). Br J Cancer. 2023;128:2063–71.

28. Harvie M, Pegington M, French D, Cooper G, McDiarmid S, Howell A, et al. Breast cancer risk status influences uptake, retention and efficacy of a weight loss programme amongst breast cancer screening attendees: two randomised controlled feasibility trials. BMC Cancer. 2019;19(1):1089.

29. Pegington M, Harkness EF, Howell A, Evans DG, Harvie M. Magnitude and attributed reasons for adult weight gain amongst women at increased risk of breast cancer. BMC Womens Health. 2022;22(1):447.

30. Hewitt RM, Pegington M, Harvie M, French DP. How acceptable is a weight maintenance programme for healthy weight young women who are at increased risk of breast cancer? Psychol Health. 2020;35(7):854-71.

31. Pegington M, Davies A, Mueller J, Cholerton R, Howell A, Evans DG, et al. Evaluating the acceptance and usability of an app promoting weight gain prevention and healthy behaviors among young women with a family history

of breast cancer: protocol for an observational study. JMIR Res Protoc. 2022;11(12):e41246.

32. Chan JL, Johnson LNC, Sammel MD, DiGiovanni L, Voong C, Domchek SM, et al. Reproductive decision-making in women with BRCA1/2 mutations. J Genet Couns. 2017;26(3):594-603.

33. Donnelly LS, Watson M, Moynihan C, Bancroft E, Evans DGR, Eeles R, et al. Reproductive decision-making in young female carriers of a BRCA mutation. Hum Reprod. 2013;28(4):1006-12.

34. Adeyemo A, Balaconis MK, Darnes DR, Fatumo S, Granados Moreno P, Hodonsky CJ, et al. Responsible use of polygenic risk scores in the clinic: potential benefits, risks and gaps. Nat Med. 2021;27(11):1876-84.

35. Ayoub A, Lapointe J, Nabi H, Pashayan N. Risk-stratified breast cancer screening incorporating a polygenic risk score: A survey of UK general practitioners' knowledge and attitudes. Genes. 2023;14(3):732.

36. Lapointe J, Buron A-C, Mbuya-Bienge C, Dorval M, Pashayan N, Brooks JD, et al. Polygenic risk scores and risk-stratified breast cancer screening: familiarity and perspectives of health care professionals. Genet Med. 2022;24(11):2380-8.

37. Dent T, Jbilou J, Rafi I, Segnan N, Törnberg S, Chowdhury S, et al. Stratified cancer screening: the practicalities of implementation. Public Health Genom. 2013;16(3):94-9.

38. Rainey L, van der Waal D, Jervaeus A, Wengström Y, Evans DG, Donnelly LS, et al. Are we ready for the challenge of implementing risk-based breast cancer screening and primary prevention? The Breast. 2018;39:24-32.

39. Selby K, Bartlett-Esquilant G, Cornuz J. Personalized cancer screening: helping primary care rise to the challenge. Public Health Rev. 2018;39(1):4.

40. National Institute for Health and Care Excellence (NICE). 2022 exceptional surveillance of familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (NICE guideline CG164). [Online]. 2022 [Accessed 12th September 2023]. Available from: https://www.nice.org.uk/guidance/cg164/resources/2022-exceptional-surveillance-of-familial-breast-cancer-classification-care-and-managing-breast-cancer-and-related-risks-in-people-with-a-family-history-of-breast-cancer-nice-guideline-cg164-pdf-14358610516165.

41. Evans D, Brentnall AR, Harvie M, Dawe S, Sergeant JC, Stavrinos P, et al. Breast cancer risk in young women in the National Breast Screening Programme: implications for applying NICE guidelines for additional screening and chemoprevention. Cancer Prev Res. 2014;7(10):993-1001.

42. French DP, Woof VG, Ruane H, Evans DG, Ulph F, Donnelly LS. The feasibility of implementing risk stratification into a national breast cancer screening programme: a focus group study investigating the perspectives of healthcare personnel responsible for delivery. BMC Womens Health. 2022;22(1):142.

43. Hawkins R, McWilliams L, Ulph F, Evans DG, French DP. Healthcare professionals' views following implementation of risk stratification into a national breast cancer screening programme. BMC Cancer. 2022;22(1):1058.

44. Qureshi N, Dutton B, Weng S, Sheehan C, Chorley W, Robertson JFR, et al. Improving primary care identification of familial breast cancer risk using proactive invitation and decision support. Fam Cancer. 2021;20(1):13-21.

45. Duffy SW, Myles JP, Maroni R, Mohammad A. Rapid review of evaluation of interventions to improve participation in cancer screening services. J Med Screen. 2016;24(3):127-45.

46. Collins IM, Steel E, Mann GB, Emery JD, Bickerstaffe A, Trainer A, et al. Assessing and managing breast cancer risk: clinicians' current practice and future needs. The Breast. 2014;23(5):644-50.

47. Puzhko S, Gagnon J, Simard J, Knoppers BM, Siedlikowski S, Bartlett G. Health professionals' perspectives on breast cancer risk stratification: understanding evaluation of risk versus screening for disease. Public Health Rev. 2019;40(1):2.

48. Bellhouse S, McWilliams L, Firth J, Yorke J, French DP. Are community-based health worker interventions an effective approach for early diagnosis of cancer? A systematic review and meta-analysis. Psychooncology. 2018;27(4):1089-99.

49. Goodley P, Balata H, Alonso A, Brockelsby C, Conroy M, Cooper-Moss N, et al. Invitation strategies and participation in a community-based lung cancer screening programme located in areas of high socioeconomic deprivation. Thorax. 2023:in press.

50. Scobie H, Robb KA, Macdonald S, Harrow S, Sullivan F. Optimising recruitment to a lung cancer screening trial: a comparison of general practitioner and community-based recruitment. J Med Screen. 2023:in press.

51. Sørensen K, Van den Broucke S, Fullam J, Doyle G, Pelikan J, Slonska Z, et al. Health literacy and public health: a systematic review and integration of definitions and models. BMC Public Health. 2012;12(1):80.

52. Samoil D, Kim J, Fox C, Papadakos JK. The importance of health literacy on clinical cancer outcomes: a scoping review. Ann Cancer Epidemiol. 2021;5:30.

53. Crosbie P, Balata H, Evison M, Atack M, Bayliss-Brideaux V, Colligan D, et al. Implementing lung cancer screening: baseline results from a community-based 'Lung Health Check' pilot in deprived areas of Manchester. Thorax. 2019;74(4):405-9.

54. Monticciolo DL, Newell MS, Moy L, Lee CS, Destounis SV. Breast cancer screening for women at higher-than-average risk: updated recommendations from the ACR. J Am Coll Radiol. 2023:in press.

55. McWilliams L, Evans DG, Payne K, Harrison F, Howell A, Howell SJ, et al. Implementing risk-stratified breast screening in England: an agenda setting meeting. Cancers. 2022;14(19):4636.

56. Jia G, Lu Y, Wen W, Long J, Liu Y, Tao R, et al. Evaluating the utility of polygenic risk scores in identifying high-risk individuals for eight common cancers. JNCI Cancer Spectr. 2020;4(3):pkaa021.

Appendices

Appendix A: Chapter 2 supplementary materials

Appendix A.1: Search strategies for systematic review

MEDLINE

#1

acceptab* OR perception* OR perceiv* OR perspective* OR opinion* OR attitude* OR

view* OR interest* OR belie* OR knowledge OR practice* OR experience* OR behavio*

#2

((general or family) ADJ3 (practitioner* or physician* or doctor* or clinician*)) OR ((nurs*) ADJ3 (practitioner* OR specialist* OR staff OR personnel OR clinician*) OR "primary care" OR "general practice" OR exp Primary Health Care/ [MESH]

#3

breast AND (cancer OR neoplasm OR carcinoma OR tumor* OR tumour*)) OR exp Breast Neoplasms/ [MESH]

#4

risk assess* OR (assess* ADJ2 risk)) OR exp Risk Assessment/ [MESH]

#5

(prevent* OR chemoprevent* OR tamoxifen OR raloxifene OR anastrazole) OR exp Primary Prevention/ [MESH]

#6

(lifestyle OR diet* OR smok* OR tobacco OR nicotine OR alcohol OR weight OR activ* OR behavio*) OR (health* ADJ1 behavio*)

#1 AND #2 AND #3 AND #4 + #1 AND #2 AND #3 AND #5 + #1 AND #2 AND #3 AND #6

Limits applied to each combination: 1) publication date from 01.01.1989-10.07.2020 & 2) English language

Embase

#1

acceptab* OR perception* OR perceiv* OR perspective* OR opinion* OR attitude* OR

view* OR interest* OR belie* OR knowledge OR practice* OR experience* OR behavio*

#2

((general or family) ADJ3 (practitioner* or physician* or doctor* or clinician*)) OR ((nurs*) ADJ3 (practitioner* OR specialist* OR staff OR personnel OR clinician*) OR “primary care” OR “general practice” OR exp Primary Health Care/ [MESH]

#3

breast AND (cancer OR neoplasm OR carcinoma OR tumor* OR tumour*)) OR exp Breast Tumor/ [MESH]

#4

risk assess* OR (assess* ADJ2 risk)) OR exp Risk Assessment/ [MESH]

#5

(prevent* OR chemoprevent* OR tamoxifen OR raloxifene OR anastrazole) OR exp Primary Prevention/ [MESH] OR exp Preventive Medicine/ [MESH]

#6

(lifestyle OR diet* OR smok* OR tobacco OR nicotine OR alcohol OR weight OR activ* OR behavio*) OR (health* ADJ1 behavio*)

#1 AND #2 AND #3 AND #4 + #1 AND #2 AND #3 AND #5 + #1 AND #2 AND #3 AND #6

Limits applied to each combination: 1) publication date from 01.01.1989-10.07.2020 & 2) English language

CINAHL Plus

#1

acceptab* OR perception* OR perceiv* OR perspective* OR opinion* OR attitude* OR

view* OR interest* OR belie* OR knowledge OR practice* OR experience* OR behavio*

#2

((general or family) N3 (practitioner* or physician* or doctor* or clinician*)) OR ((nurs*) N3 (practitioner* OR specialist* OR staff OR personnel OR clinician*) OR “primary care” OR “general practice” OR MM “Primary Health Care”

#3

breast AND (cancer OR neoplasm OR carcinoma OR tumor* OR tumour*)) OR “Breast Neoplasms+” [MESH]

#4

(risk assess* OR (assess* N2 risk)) OR MM “Risk Assessment”

#5

(prevent* OR chemoprevent* OR tamoxifen OR raloxifene OR anastrazole) OR "Preventive Health Care+" [MESH]

#6

(lifestyle OR diet* OR smok* OR tobacco OR nicotine OR alcohol OR weight OR activ* OR behavio*) OR (health* N1 behavio*)

#1 AND #2 AND #3 AND #4 + #1 AND #2 AND #3 AND #5 + #1 AND #2 AND #3 AND #6

Limits applied to each combination: 1) publication date from 01.01.1989-10.07.2020 & 2) English language

PsycINFO

#1

acceptab* OR perception* OR perceiv* OR perspective* OR opinion* OR attitude* OR

view* OR interest* OR belie* OR knowledge OR practice* OR experience* OR behavio*

#2

((general or family) ADJ3 (practitioner* or physician* or doctor* or clinician*)) OR ((nurs*) ADJ3 (practitioner* OR specialist* OR staff OR personnel OR clinician*) OR "primary care" OR "general practice" OR exp Primary Health Care/ [MESH]

#3

breast AND (cancer OR neoplasm OR carcinoma OR tumor* OR tumour*)) OR exp Breast Neoplasms/ [MESH]

#4

risk assess* OR (assess* ADJ2 risk)) OR exp Risk Assessment/ [MESH]

#5

(prevent* OR chemoprevent* OR tamoxifen OR raloxifene OR anastrazole) OR exp preventive medicine/ [MESH]

#6

(lifestyle OR diet* OR smok* OR tobacco OR nicotine OR alcohol OR weight OR activ* OR behavio*) OR (health* ADJ1 behavio*)

#1 AND #2 AND #3 AND #4 + #1 AND #2 AND #3 AND #5 + #1 AND #2 AND #3 AND #6

Limits applied to each combination: 1) publication date from 01.01.1989-10.07.2020 & 2) English language

ProQuest Dissertations & Theses Global

#1

accept* OR perception* OR perceiv* OR perspective* OR opinion* OR attitude* OR view* OR interest* OR belie* OR practice* OR knowledge OR experience* OR behavio*

#2

((general OR family) NEAR/3 (practitioner* OR physician* OR doctor* OR clinician*)) OR nurs* NEAR/3 (practitioner* OR specialist* OR staff OR personnel OR clinician*) OR "primary care" OR "general practice"

#3

breast AND (cancer OR neoplasm OR carcinoma OR tumor* OR tumour*)

#4

(risk assess*) OR (assess* NEAR/2 risk)

#5

(prevent* OR chemoprevent* OR tamoxifen OR raloxifene OR anastrazole)

#6

(lifestyle OR diet* OR smok* OR tobacco OR nicotine OR alcohol OR weight OR activ* OR behavio*) OR (health* NEAR/1 behavio*)

#1 AND #2 AND #3 AND #4 + #1 AND #2 AND #3 AND #5 + #1 AND #2 AND #3 AND #6

Limits applied to each combination: 1) publication date from 01.01.1989-26.08.2020 & 2) English language

Appendix A.2: Data extracted from all primary studies, showing how each eligible outcome mapped onto broader themes reported in the main analyses

Primary care providers' perceived responsibilities in breast cancer risk assessment and primary prevention: data extracted from primary studies for Table 2.2, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Escher & Sappino (2000)	Document a family history of cancer	Taking or documenting a family history	Family physician	89.0
	Recognise families for which genetic testing is indicated	Identifying families at risk	Family physician	86.0
	Provide counselling regarding familial risk	Providing counselling regarding familial risk	Family physician	81.0
	Obtain informed consent before testing	Obtaining informed consent before genetic testing	Family physician	87.5
	Provide follow up support	Providing follow up support after genetic testing	Family physician	92.5
	Provide options for prevention and early detection of breast cancer	Providing options for prevention and early detection of breast cancer	Family physician	86.0

Gunn et al. (2018)	Counselling women about breast density is primarily my responsibility as a primary care physician versus the responsibility of other clinicians or imaging providers	Counselling women about breast density	Strongly agree or agree	43.0
Macdonald et al. (2020)	Initiate discussion of risk-reducing medications	Initiating discussion of risk-reducing medications	GP	75.0
	Write first prescription	Writing first prescription for risk-reducing medications	GP	31.3
	Write ongoing prescriptions	Writing ongoing prescriptions for risk-reducing medications	GP	97.9
Nippert et al. (2014)	Explain the inheritance pattern of familial breast cancer	Explaining the inheritance pattern of familial breast cancer	Myself (GP)	42.7*****
	Inform about breast cancer genetic testing	Informing about breast cancer genetic testing	Myself (GP)	47.0*****
	Disclose the breast cancer genetic test results to the patient	Disclosing breast cancer genetic test results	Myself (GP)	27.4*****
	Provide support after breast cancer testing	Providing follow up support after genetic testing	Myself (GP)	66.8*****
Pichert et al. (2003)	Do you think it is your duty to inform an individual at high risk for breast cancer that genetic counselling and testing is available?	Informing about breast cancer genetic testing	Yes	76.0
	Document family history	Taking or documenting a family history	Yes	91.0
	Identify families at risk	Identifying families at risk	Yes	58.0

	Perform genetic counselling	Providing counselling regarding familial risk	Yes	85.0
	Obtain informed consent	Obtaining informed consent before genetic testing	Yes	67.0
	Who should disclose genetic test results?	Disclosing breast cancer genetic test results	Primary care physician	47.0
Sabatino et al. (2007)	Taking a family history	Taking or documenting a family history	Definitely or mostly agree	98.0
	Calculating breast cancer risk	Calculating breast cancer risk	Definitely or mostly agree	62.0
	Breast cancer risk reduction with chemopreventive agents	Breast cancer risk reduction with chemopreventive agents	Definitely or mostly agree	18.0

Notes.

*Percentage manually calculated for whole sample (countries combined)

Primary care providers' perceptions of barriers associated with conducting breast cancer risk assessment: data extracted from primary studies for Table 2.3, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Bidassie et al. (2020)	Not enough time	Insufficient provisions to conduct breast cancer risk assessment effectively	N/A – reported by participant as free text	15.8
	Not familiar enough with it	Insufficient education/training	N/A – reported by participant as free text	50.5
	Never seen a patient for whom it was indicated	Do not see patients for whom risk assessment is indicated	N/A – reported by participant as free text	5.9
	Don't think it will impact patient management	Perceived lack of impact on patient management	N/A – reported by participant as free text	7.9
	Not a primary care responsibility	Perceived lack of primary care responsibility	N/A – reported by participant as free text	5.9
	How comfortable are you using the Gail (or other) risk model to assess a woman's risk of breast cancer?	Discomfort conducting breast cancer risk assessment	Very uncomfortable or uncomfortable	33.5
Casas et al. (2017)	I am comfortable counselling women about breast density	Discomfort discussing breast density	Strongly disagree or disagree or neutral	81.5*
Corbelli et al. (2014)	I do not see patients in whom calculation of the Gail score is indicated	Do not see patients for whom risk assessment is indicated	Strongly agree or somewhat agree	17.0

	I do not have enough time with my patients to use the Gail score	Insufficient provisions to conduct breast cancer risk assessment effectively	Strongly agree or somewhat agree	40.0
	I do not think that the results of the Gail score would change my management	Perceived lack of impact on patient management	Strongly agree or somewhat agree	25.6
	I am not sufficiently familiar with the Gail score	Insufficient education/training	Strongly agree or somewhat agree	82.1
Edwards et al. (2009)	Perceived comfort level of breast cancer risk assessment	Discomfort conducting breast cancer risk assessment	Not comfortable	29.3[1]
Guerra et al. (2009)	Information about risk creates unnecessary anxiety for many women	Concern about creating unnecessary anxiety for many women	Strongly agree or agree	13.7
	Available methods of predicting risk are not accurate enough	Concern that risk prediction models are not accurate enough	Strongly agree or agree	13.1
	Too time consuming to evaluate and discuss risk	Insufficient provisions to conduct breast cancer risk assessment effectively	Strongly agree or agree	10.5
	Reluctant to use breast cancer risk assessment because a woman at low risk of breast cancer might decide not to undergo mammography screening	Reluctance to assess risk because a woman at low risk of breast cancer might decide not to undergo mammography screening	Strongly agree or agree	6.3

Khong et al. (2015)	How comfortable do you feel answering questions about breast density?	Discomfort discussing breast density	Not comfortable	11.7
Macdonald et al. (2020)	I have inadequate training and confidence in BC risk assessment	Insufficient education/training	Strong barrier	28.0
	I find it hard to access resources to help me estimate patients' risk	Insufficient provisions to conduct breast cancer risk assessment effectively	Strong barrier	20.0
	I don't routinely assess BC risk with my patients	Assessment of breast cancer risk is not part of routine practice	Strong barrier	7.0
Maimone et al. (2017)	How comfortable are you (or would you be) in answering questions regarding breast density and offering appropriate management recommendations?	Discomfort discussing breast density	Not comfortable	17.1
Mainous et al. (2013)	Respondents asked to estimate the utility of current genetic testing capabilities in determining a patient's risk for breast cancer	Low perceived utility and acceptability of genetic testing for determining breast cancer risk	Not useful	5.1
Sabatino et al. (2007)	Too many things to do during visits	Insufficient provisions to conduct breast cancer risk assessment effectively	Most important	19.0
	Lack of confidence in one's knowledge of risk and risk assessment	Insufficient education/training	Most important	20.0
	More immediate issues	More immediate issues to discuss during consultation	Most important	25.0

Tighe (2009)	Are you comfortable estimating a woman's individual risk for breast cancer?	Discomfort conducting breast cancer risk assessment	No	30.0
Welkenhuysen & Evers-Kiebooms et al. (2002)	The acceptability (how sensible, meaningful or relevant) of performing a predictive test for an asymptomatic adult with a family history of breast cancer	Low perceived utility and acceptability of genetic testing for determining breast cancer risk	Not at all acceptable or not acceptable or somewhat not acceptable	22.9[2]

Notes.

*Manually calculated for whole sample (residents & providers combined)

[1]Manually calculated using frequencies reported in Figure 2

[2]Manually calculated from percentages provided by the senior author as incorrect n reported in paper

Primary care providers' perceived confidence in performing breast cancer risk assessment behaviours: data extracted from primary studies for Table 2.4, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Bankhead et al. (2001)	Knowing the relevant family history to take	Taking a family history	Very confident or confident	60.7
	Making a basic risk assessment	Making a basic risk assessment	Very confident or confident	60.8
	Reassuring women at low risk	Reassuring low-risk patients	Very confident or confident	62.6
Bethea et al. (2008)	Knowing the relevant family history to take	Taking a family history	Very confident or confident	65.5
	Making a basic assessment of level of risk	Making a basic risk assessment	Very confident or confident	53.9
	Reassuring women at low risk	Reassuring low-risk patients	Very confident or confident	67.7
Dekanek et al. (2020)	BRCA cancer risks	Ability to provide information to patients about BRCA cancer risks and inheritance	Completely or somewhat confident	61.6
	BRCA inheritance	Ability to provide information to patients about BRCA cancer risks and inheritance	Completely or somewhat confident	50.0

	BRCA testing methods	Ability to provide information to patients about BRCA test methods and interpretation	Completely or somewhat confident	37.2
	BRCA test interpretation	Ability to provide information to patients about BRCA test methods and interpretation	Completely or somewhat confident	41.9
Sabatino et al. (2007)	Confidence in ability to use Gail scores to identify women at increased risk for breast cancer	Ability to use Gail scores to identify women at increased risk for breast cancer	Very confident or confident	8.6
Wilson et al. (2006)	Taking appropriate family history	Taking a family history	Very or moderately confident	64.3*
	Reassuring low-risk patients	Reassuring low-risk patients	Very or moderately confident	46.0*
	Being able to answer questions	Ability to answer patients' questions during a consultation about risk	Very or moderately confident	23.2*

Notes.

*Manually calculated for whole sample (baseline intervention and control groups combined)

Primary care providers' reported behaviours with respect to breast cancer risk assessment: data extracted from primary studies for Table 2.5, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Bankhead et al. (2001)	Routine collection of family history for breast cancer at new patient appointments	Collecting family history during new patient appointment	Yes	69.3
Bidassie et al. (2020)	Do you routinely gather a woman's family history of breast cancer?	Collecting family history during routine clinical practice	Yes	92.8
Corbelli et al. (2014)	Do you calculate the Gail score as part of your clinical practice?	Assessing risk using the Gail model	Yes (even if rarely)	40.9
Edwards et al. (2009)	Using family history as a tool for assessing patient's risk for breast cancer	Discussing family history to assess breast cancer risk	Yes	37.1
	Using the Gail model as a tool for assessing patient's risk for breast cancer	Assessing risk using the Gail model	Yes	6.5
Ganry & Boche (2005)	Systematically looked for a family history of breast cancer	Collecting family history during routine clinical practice	Yes	95.0
Hall (2001)	As part of a woman's health history, do you inquire about her breast cancer family history?	Discussing family history as part of a woman's health history	Always	92.6
Khong et al. (2015)	Do you perform quantitative breast cancer risk assessments (i.e. assessments using Gail, Claus, BRCAPRO, or other standard risk factors) in your office?	Using multi-factorial breast cancer risk assessment tools	Yes	26.0

Sabatino et al. (2007)	The frequency with which providers assess family history during routine visits	Collecting family history during routine clinical practice	Always or usually	71.0
	The frequency with which providers assess risk by Gail score during routine visits	Assessing risk using the Gail model	Always or usually	3.0
Samimi et al. (2020)	How often do you discuss cancer family history in an asymptomatic patient to determine risk for breast and/or ovarian cancer?	Discussing family history to assess breast cancer risk	Used	96.9
	How often do you use a breast cancer risk assessment tool in an asymptomatic patient to determine risk for breast and/or ovarian cancer?	Using multi-factorial breast cancer risk assessment tools	Used	50.9
Summerton & Garrood (1997)	Routine family history enquiries: whether the history of breast cancer in siblings or parents was specifically enquired about on first registration	Collecting family history during new patient appointment	Yes	48.4
Tighe (2009)	If you were concerned that a woman might be at high risk for breast cancer, what would you do? Estimate her risk using available risk assessment models	Using multi-factorial breast cancer risk assessment tools	Yes	22.4
Walter et al. (2001)	Considering discussing family history with a woman consulting with concerns about her risk of breast cancer	Considering a discussion of family history with a woman consulting with concerns about breast cancer risk	Yes	90.4*

Notes.

*Manually calculated for whole sample (general practitioners & nurses combined)

Primary care providers' perceptions of barriers associated with providing primary prevention advice: data extracted from primary studies for Table 2.6, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Armstrong et al. (2006)	The risk of endometrial cancer is too great to prescribe tamoxifen for breast cancer risk reduction	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	Strongly agree or agree	15.0
	The evidence that tamoxifen significantly reduces breast cancer risk is controversial	Doubts about effectiveness of risk-reducing medications	Strongly agree or agree	27.7
	It is too time consuming to discuss taking tamoxifen with women in my practice	Insufficient provisions to discuss risk-reducing measures effectively	Strongly agree or agree	19.3
	The risk of thromboembolic disease is too great to prescribe tamoxifen for breast cancer risk reduction	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	Strongly agree or agree	12.3
Bidassie et al. (2020)	Not familiar enough with it	Insufficient education/training	N/A – reported by participant as free text	54.0
	Not a primary care responsibility	Perceived lack of primary care responsibility	N/A – reported by participant as free text	23.9
	Never seen a patient for whom it was indicated	Never seen a patient for whom risk-reducing medications are indicated	N/A – reported by participant as free text	18.4

	Not enough time	Insufficient provisions to discuss risk-reducing measures effectively	N/A – reported by participant as free text	6.1
	Don't think it will impact patient management	Perceived lack of impact on patient management	N/A – reported by participant as free text	1.2
	How comfortable are you at prescribing medication for primary prevention of breast cancer (ie, tamoxifen, raloxifene, exemestane)?	Discomfort prescribing risk-reducing medication	Very uncomfortable or uncomfortable	70.1
Corbelli et al. (2014)	I do not believe that chemoprevention benefits most women who are eligible to receive it	Doubts about effectiveness of risk-reducing medications	Strongly agree or somewhat agree	10.7
	I am not comfortable prescribing chemoprevention	Discomfort prescribing risk-reducing medication	Strongly agree or somewhat agree	79.8
	I do not have time to discuss chemoprevention with my patients	Lack of provisions to discuss risk-reducing measures effectively	Strongly agree or somewhat agree	32.1
	I have not identified a patient in whom chemoprevention was indicated	Never seen a patient for whom risk-reducing medications are indicated	Strongly agree or somewhat agree	60.7
Kaplan et al. (2005)	Not sufficiently informed about risk reduction options	Insufficient education/training	Very often or fairly often	19.1
	Not sufficiently trained in counselling	Insufficient education/training	Very often or fairly often	13.9
	Not my role/should be done by someone else	Perceived lack of primary care responsibility	Very often or fairly often	6.8

	Lack of patient interest	Women's perceived lack of interest and knowledge about risk reduction	Very often or fairly often	12.6
	Patient would not understand	Women's perceived lack of interest and knowledge about risk reduction	Very often or fairly often	7.2
	Not enough time	Insufficient provisions to discuss risk-reducing measures effectively	Very often or fairly often	40.3
	Reimbursement not sufficient	Lack of incentives for discussing risk reducing measures	Very often or fairly often	13.6
Macdonald et al. (2020)	I have insufficient knowledge of risk-reducing medications	Insufficient education/training	Strong barrier	49.0
	I am not confident in providing advice to patients about risk-reducing medications	Insufficient education/training	Strong barrier	32.0
	I have difficulty identifying patients suitable for risk-reducing medications	Insufficient provisions to discuss risk-reducing measures effectively	Strong barrier	29.0
	There are no procedures that encourage me to discuss risk-reducing medications	Insufficient provisions to discuss risk-reducing measures effectively	Strong barrier	24.0
	I have difficulty explaining the pros and cons of risk-reducing medications	Insufficient education/training	Strong barrier	23.0
	I find it hard to access good information for my patients	Insufficient provisions to discuss risk-reducing measures effectively	Strong barrier	21.0
	Medication side effects	Concern about medication side effects	Strong barrier	14.0
	I forget to discuss risk-reducing medications with my patients	Forgetting to discuss risk-reducing medications	Strong barrier	14.0

	Lack of time during consultation	Insufficient provisions to discuss risk-reducing measures effectively	Strong barrier	10.0
	It is difficult to measure whether the medication is working	Insufficient provisions to discuss risk-reducing measures effectively	Strong barrier	7.0
	It is not my role to discuss risk-reducing medications	Perceived lack of primary care responsibility	Strong barrier	4.0
	I feel uncomfortable prescribing a 'cancer drug' to healthy women	Discomfort prescribing a ‘cancer drug’ to healthy women	Strong barrier	4.0
	There is no evidence that they reduce mortality	Doubts about effectiveness of risk-reducing medications	Strong barrier	4.0
	There are no incentives for discussing risk-reducing medications with patients	Lack of incentives for discussing risk reducing measures	Strong barrier	3.0
	I'm concerned I might increase the patient's worry about breast cancer	Concern about increasing patient's worry about breast cancer	Strong barrier	2.0
	I don't think patients want to discuss risk-reducing medications for cancer prevention	Women’s perceived lack of interest and knowledge about risk reduction	Strong barrier	1.0
	I don't believe they decrease the risk of breast cancer	Doubts about effectiveness of risk-reducing medications	Strong barrier	1.0
	There are other things I wish to achieve in most consultations	More immediate issues to discuss during consultation	Strong barrier	18.0
Samimi et al. (2020)	The benefits of preventive agents in breast cancer outweigh the risks	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	Disagree	9.1

	The evidence that preventive agents significantly reduces breast cancer risk is controversial	Doubts about effectiveness of risk-reducing medications	Agree	31.5
	The risk of endometrial cancer is too great to prescribe tamoxifen for breast cancer reduction	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	Agree	17.3
	The risk of thromboembolic disease is too great to prescribe preventive agents for breast cancer reduction	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	Agree	20.5
	It is easy for me to determine who is eligible to take preventive agents for breast cancer reduction	Difficulty identifying patients who are eligible for risk-reducing medications	Disagree	50.0
Tighe et al. (2009)	Not familiar with chemoprevention strategies	Insufficient education/training	N/A – selected outcome from pre-specified list	72.0
	Not enough resources available	Insufficient provisions to discuss risk-reducing measures effectively	N/A – selected outcome from pre-specified list	16.0
	Do you find it too time consuming to assess breast cancer risk and discuss breast cancer prevention strategies with women in your practice?	Insufficient provisions to discuss risk-reducing measures effectively	Yes	17.9
	Do you have concerns about prescribing chemopreventive agents for off label reasons	Concern about prescribing off-label (unlicensed) medication	Yes	58.1

such as primary prevention of breast cancer?			
Do you think the evidence showing that chemoprevention significantly reduces breast cancer is controversial?	Doubts about effectiveness of risk-reducing medications	Yes	17.3
Do you believe that the benefits of chemoprevention for breast cancer outweigh the risks?	Believing that the risks of prescribing risk-reducing medications outweigh the benefits	No	6.5
How difficult is it to determine who is eligible to take chemopreventive agents for breast cancer risk reduction?	Difficulty identifying patients who are eligible for risk-reducing medications	Difficult	22.2

Primary care providers' perceptions of facilitators associated with providing primary prevention advice: data extracted from primary studies for Table 2.7, mapping onto responses reported in main analyses

Reference (author & year)	Eligible outcomes	Theme	Eligible response scale option(s)	Raw data extracted (%)
Kaplan et al. (2005)	Better patient education materials on options	Availability of provisions to discuss risk-reducing options more effectively	N/A – selected outcome from pre-specified list	69.8
	More information on risk reduction options	More education and training	N/A – selected outcome from pre-specified list	69.4
	More evidence to show efficacy of options	Understanding the benefits of primary prevention	N/A – selected outcome from pre-specified list	59.1
	More time with each patient	Availability of provisions to discuss risk-reducing options more effectively	N/A – selected outcome from pre-specified list	49.3
	More formal training in counselling techniques	More education and training	N/A – selected outcome from pre-specified list	34.6
Macdonald et al. (2020)	Clear guidelines/recommendations	Availability of provisions to discuss risk-reducing options more effectively	Strong facilitator	88.0
	If I had better tools to help me identify patients who were suitable	Availability of provisions to discuss risk-reducing options more effectively	Strong facilitator	68.0
	Support from specialists	Peer support	Strong facilitator	64.0

	I expect positive outcomes for women who take risk-reducing medications	Understanding the benefits of primary prevention	Strong facilitator	59.0
	If a patient has a strong family history of breast cancer	Patient has indications of increased breast cancer risk	Strong facilitator	54.0
	Knowing some risk-reducing medications are PBS (Pharmaceutical Benefits Scheme) funded	Knowing some risk-reducing medications are available at a Government-subsidised price	Strong facilitator	54.0
	If it were endorsed as part of my role by the relevant college/peak body	Endorsement as part of role by a professional body	Strong facilitator	53.0
	If the patient has LCIS that increases their risk of breast cancer	Patient has indications of increased breast cancer risk	Strong facilitator	49.0
	If the patient has atypical hyperplasia that increases their risk of breast cancer	Patient has indications of increased breast cancer risk	Strong facilitator	36.0
	Support from my peers	Peer support	Strong facilitator	34.0
	If my medical software prompted me to discuss risk-reducing medications	Availability of provisions to discuss risk-reducing options more effectively	Strong facilitator	33.0
	Sometimes it is easier to discuss risk-reducing medications than bilateral mastectomy	Easier to discuss risk-reducing medications than bilateral mastectomy	Strong facilitator	32.0
	If I knew my colleagues discuss it with their patients	Peer support	Strong facilitator	27.0
	The beneficial effects of risk-reducing medications	Understanding the benefits of primary prevention	Strong facilitator	14.0
Samimi et al. (2020)	The benefits of preventive agents in breast cancer outweigh the risks	Believing that the benefits of preventive agents in breast cancer outweigh the risks	Agree	62.8

Tighe (2009)	Do you believe that the benefits of chemoprevention for breast cancer outweigh the risks?	Believing that the benefits of preventive agents in breast cancer outweigh the risks	Yes	12.4

Appendix A.3: A list of 95 excluded studies and reasons for exclusion

Reference	Reason for exclusion
Abda, N., et al. (2017). Knowledge, Attitudes, and Preventive Practice Towards Breast Cancer among General Practitioner Health Professionals in Morocco. Asian Pacific Journal of Cancer Prevention **18**(4): 963-968.	No eligible outcome measures *Knowledge only*
Bellcross, C. A., et al. (2011). Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians. American Journal of Preventive Medicine **40**(1): 61-66.	No eligible outcome measures *Behaviour outcomes not eligible as not routine behaviour (specifies a timeframe (in the past year))*
Chamberlain, R. M., et al. (1995). Improving residents' knowledge of cancer prevention: Are physicians prepared for prevention?. Journal of Cancer Education **10**(1): 9-13.	No eligible outcome measures *Knowledge only*
Cockburn, J., et al. (1989). Encouraging attendance at screening mammography: knowledge, attitudes and intentions of general practitioners. The Medical Journal of Australia **151**(7): 391-396.	No eligible outcome measures *Knowledge only*
Cohn, J., et al. (2015). Physician risk assessment knowledge regarding BRCA genetics testing. Journal of Cancer Education **30**(3): 573-579.	No eligible outcome measures *Knowledge only*
Edwards, Q. T., & Seibert, D. (2010). Pre-and post-test evaluation of a breast cancer risk assessment program for nurse practitioners. Journal of the American Academy of Nurse Practitioners **22**(7): 376-381.	No eligible outcome measures *Knowledge only*

Haas, J. S., et al. (2004). Do physicians tailor their recommendations for breast cancer risk reduction based on patient's risk?. Journal of General Internal Medicine **19**(4): 302-309.	No eligible outcome measures *Behaviour outcome ineligible as clinical scenario*
Hapgood, R., et al. (2002). Breast cancer genetics in primary care which GPs most accurately categorise patients at low risk?. The European Journal of General Practice **8**(4): 146-150.	No eligible outcome measures *Behaviour outcome ineligible as clinical scenario*
Johnson, K. M., et al. (1998). Inner city primary care providers' breast cancer screening knowledge: implications for intervention. Journal of Community Health **23**(1): 1-14.	No eligible outcome measures *Knowledge only*
Julian-Reynier, C., et al. (2015). General Practitioners and Breast Surgeons in France, Germany, Netherlands and the UK show variable breast cancer risk communication profiles. BMC Cancer **15**(1): 1-9.	No eligible outcome measures *Ineligible as risk communication practices (what was discussed about risk and how this was presented i.e. absolute, relative risks etc.)*
Kirby, S., & Hegarty, J. (2010). Breast awareness within an intellectual disability setting. European Journal of Oncology Nursing **14**(4): 328-336.	No eligible outcome measures *Knowledge only*
Klitzman, R., et al. (2013). Attitudes and practices among internists concerning genetic testing. Journal of Genetic Counseling **22**(1), 90-100.	No eligible outcome measures *Behaviour outcomes not eligible as not routine behaviour (specifies a timeframe (in the last 6 months))*
Koil, C. E., et al. (2003). Differences in physician referral practices and attitudes regarding hereditary breast cancer by clinical practice location. Genetics in Medicine **5**(5): 364-369.	No eligible outcome measures *Behaviour outcomes not eligible as not routine behaviour (% who have ever referred)*

Nair, N., et al. (2017). Georgia primary care providers' knowledge of hereditary breast and ovarian cancer syndrome. Journal of Cancer Education **32**(1): 119-124.	No eligible outcome measures *Knowledge only*
Obeidat, N. A., et al. (2017). Are Jordanian primary healthcare practitioners fulfilling their potential in cancer prevention and community health? Findings from a cross-sectional survey. BMJ Open **7**(4): e015269.	No eligible outcome measures *Knowledge only*
Pirdehghan, A., et al. (2019). Assessing breast cancer knowledge among Iranian physicians. International Journal of Cancer Management **12**(4): e85822.	No eligible outcome measures *Knowledge only*
Rose, P. W., et al. (2001). Referral of patients with a family history of breast/ovarian cancer—GPs' knowledge and expectations. Family Practice **18**(5): 487-490.	*No eligible outcome measures* *Behaviour outcome ineligible as clinical scenario*
Samimi, G., et al. (2020). Cancer Prevention in Primary Care: Perception of Importance, Recognition of Risk Factors and Prescribing Behaviors. The American Journal of Medicine **133**(6): 723-732.	No eligible outcome measures *Behaviour outcomes not eligible as not routine behaviour (specifies a timeframe (in the last 12 months))*
Smith, S. G., et al. (2017). Prescribing tamoxifen in primary care for the prevention of breast cancer: a national online survey of GPs' attitudes. British Journal of General Practice **67**(659): e414-e427.	No eligible outcome measures *Behaviour outcome ineligible as hypothetical case study*
Soyer, M. T., et al. (2007). Breast cancer awareness and practice of breast self-examination among primary health care nurses: influencing factors and effects of an in-service education. Journal of Clinical Nursing **16**(4): 707-715.	No eligible outcome measures *Knowledge only*

Venkatesh, G. M., & Sundar, M. (2020). Breast Cancer Screening: Are 'At Risk Population' Known by Public Health Nurse Practitioners?. Indian Journal of Public Health Research & Development **11**(1): 369-373.	No eligible outcome measures *Knowledge only*
Watson, E., et al. (2001). A study of GP referrals to a family cancer clinic for breast/ovarian cancer. Family Practice **18**(2): 131-134.	No eligible outcome measures *Behaviour outcome ineligible as reflection on previous clinical case*
Weston, C., et al. (2018). The impact of interprofessional education on family nurse practitioner students' and family medicine residents' knowledge and confidence in screening for breast and cervical cancer. Journal of the American Association of Nurse Practitioners **30**(9): 511-518.	No eligible outcome measures *Confidence outcome ineligible as about secondary prevention (breast screening)*
Yong, M. C., et al. (2003). The importance of paternal family history in hereditary breast cancer is underappreciated by health care professionals. Oncology **64**(3): 220-226.	No eligible outcome measures *Knowledge only*
Yousuf, S. A., et al. (2012). Do Saudi nurses in primary health care centres have breast cancer knowledge to promote breast cancer awareness?. Asian Pacific Journal of Cancer Prevention **13**(9): 4459-4464.	No eligible outcome measures *Knowledge only*
Abittan, B., et al. (2018). Provider-Patient Communication of Personal Breast Cancer Risk (BCR): Providers' Beliefs. Obstetrics & Gynecology **131** 145S. 66th Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists, USA.	Conference proceeding

Blouin-Bougie J., et al. (2014). Breast cancer risk prediction and risk communication practices: Evidence from a Canadian survey. Current Oncology **21**(2): e385. 5th International Symposium on Hereditary Breast and Ovarian Cancer, Montreal, Canada.	Conference proceeding
Bryan T., et al. (2013). Education in delivering patient-centered care: Provider comfort level in counseling women ages 40-49 regarding breast cancer screening options. Journal of Investigative Medicine **61**(2): 524. American Federation for Medical Research Southern Regional Meeting, New Orleans, USA.	Conference proceeding
Collins I.M., et al. (2013). Development of a tailored, computerized, breast cancer risk assessment and decision support tool: What do clinicians want?. Journal of Clinical Oncology **31**(15 SUPPL. 1). 2013 Annual Meeting of the American Society of Clinical Oncology, Chicago, USA.	Conference proceeding
Corbelli J., & McNeil, M. (2013). Missed opportunities for breast cancer prevention among primary care providers. Journal of General Internal Medicine **28**(SUPPL. 1): S122. 36th Annual Meeting of the Society of General Internal Medicine, Denver, USA.	Conference proceeding
Dyer H.G., et al. (2014). Improving early detection and diagnosis of breast cancer in the Commonwealth of Dominica. Asia-Pacific Journal of Clinical Oncology **10**(SUPPL. 9): 122. 2014 World Cancer Congress. Melbourne, Australia.	Conference proceeding
Edwards Q.T., & Seibert, D. (2009). B.C.R.P - Bringing choices in reach for patients: A breast cancer risk assessment program for nurse practitioners. American Journal of Clinical Oncology **32**(5): 552. 19th	Conference proceeding

Annual National Interdisciplinary Breast Center Conference of the National Consortium of Breast Centers, Las Vegas, USA.	
Gunn C.M., et al. (2016) Primary care provider experience with breast density legislation in Massachusetts. Journal of General Internal Medicine **31**(2 SUPPL. 1): S363-S364). 39th Annual Meeting of the Society of General Internal Medicine, Florida, USA.	Conference proceeding
Larson S.L., et al. (2016). Reducing breast cancer risk: Why aren't providers screening and prescribing?. Pharmacoepidemiology and Drug Safety **25(**SUPPL. 3): 343-344. 32nd International Conference on Pharmacoepidemiology and Therapeutic Risk Management, Ireland.	Conference proceeding
Lauro C.F., et al. (2014). Breast cancer risk assessment and chemoprevention: Results of a survey. International Journal of Radiation Oncology Biology Physics **90**(1 SUPPL. 1): S592-S593). 56th Annual Meeting of the American Society for Radiation Oncology, San Francisco, USA.	Conference proceeding
Lindner D.S. (2015). Managing breast and ovarian cancer risk: A novel approach to teaching residents comprehensive risk reduction and management strategies. Cancer Research **75(**9 SUPPL. 1). 37th Annual CTRC-AACR San Antonio Breast Cancer Symposium, San Antonio, USA.	Conference proceeding
Merriman J., et al. (2017) Breast cancer risk assessment and chemoprevention use among VA primary care. Journal of Clinical Oncology **35(**15 SUPPL. 1). 2017 Annual Meeting of the American Society of Clinical Oncology, USA.	Conference proceeding

Ozanne E., et al. (2011). Automated breast cancer risk assessment: Identifying high risk women in the primary care setting. Cancer Research **71**(24 SUPPL. 3). 34th Annual CTRC-AACR San Antonio Breast Cancer Symposium, San Antonio, USA.	Conference proceeding
Phillips K.-A., et al. (2013). Assessing breast cancer risk in primary care: What can we learn from cardiovascular disease?. Journal of Clinical Oncology **31**(15 SUPPL. 1). 2013 Annual Meeting of the American Society of Clinical Oncology, Chicago, USA.	Conference proceeding
Phillips K.-A., et al. (2018). Acceptability and usability of iPrevent, a web-based decision support tool for assessment and management of breast cancer risk. Cancer Research **78**(4 SUPPL. 1). San Antonio Breast Cancer Symposium, USA.	Conference proceeding
Schellenberg A., et al. (2018). Practitioner opinion on contralateral prophylactic mastectomy: How do we steer a patient driven discussion?. Annals of Surgical Oncology **25**(2 SUPPL. 1): 94-95. 19th Annual Meeting of the American Society of Breast Surgeons, USA.	Conference proceeding
Smith S., et al. (2016). General practitioner attitudes towards prescribing tamoxifen for the primary prevention of breast cancer: Results of a vignette study. European Journal of Surgical Oncology **42**(11) (pp S233-S234). Joint BASO-ACS Annual Scientific Conference and NCRI Cancer Conference 2016, UK.	Conference proceeding
Stringhetta A. (2018). Recognizing histories: The knowledge of health professionals about hereditary cancer - a preliminary. International	Conference proceeding

Journal of Gynecology and Obstetrics **143**(SUPPL. 3): 925-926. 22nd FIGO World Congress of Gynecology and Obstetrics, Brazil.	
Vandezande L., et al. (2018). Genetic testing for breast cancer: Optimizing care for patients and their healthcare workers Development of a theoretical framework. European Journal of Cancer **92**(SUPPL. 3): S34. 11th European Breast Cancer Conference, Spain.	Conference proceeding
Wang H., et al. (2016). Breast cancer chemoprevention in primary care: Assessing readiness for change. Journal of Clinical Oncology **34**(SUPPL. 15). 2016 Annual Meeting of the American Society of Clinical Oncology, USA.	Conference proceeding
Zhang J.J., et al. (2018). Survey of physician decision-making and attitudes on preventive care priorities. Journal of General Internal Medicine **33**(2 SUPPL. 1): 351). 41st Annual Meeting of the Society of General Internal Medicine, USA.	Conference proceeding
Archer, S., et al. (2020). Evaluating clinician acceptability of the prototype CanRisk tool for predicting risk of breast and ovarian cancer: A multi-methods study. PLoS ONE, **15**(3): e0229999.	Ineligible exposure *Clinicians' appraisals of a breast cancer risk assessment tool*
Battaglia, T. A., et al. (2006). Cancer prevention trials and primary care physicians: Factors associated with recommending trial enrollment. Cancer Detection and Prevention **30**(1): 34-37.	Ineligible exposure *Assessed physician knowledge and attitudes regarding chemoprevention trials*
Brédart, A., et al. (2018). Use of the BOADICEA web application in clinical practice: appraisals by clinicians from various countries. Familial Cancer **17**(1): 31-41.	Ineligible exposure *Clinicians' appraisals of a breast cancer risk assessment tool*

Bryan, T. J., et al. (2015). Impact of an educational intervention on provider knowledge, attitudes, and comfort level regarding counseling women ages 40–49 about breast cancer screening. Journal of Multidisciplinary Healthcare, **8**: 209-216.	Ineligible exposure *Focuses on secondary prevention (breast screening)*
Colombet, I., et al. (2003). Combining risks estimations and clinical practice guidelines in a computer decision aid: a pilot study of the EsPeR system. Studies in Health Technology and Informatics **95**: 525-530.	Ineligible exposure *Clinicians' appraisals of a multi-disease risk assessment tool*
Colombet, I., et al. (2003). A computer decision aid for medical prevention: a pilot qualitative study of the Personalized Estimate of Risks (EsPeR) system. BMC Medical Informatics and Decision Making **3**(1): 1-11.	Ineligible exposure *Clinicians' appraisals of a multi-disease risk assessment tool*
de Bock, G. H., et al. (2001). How women with a family history of breast cancer and their general practitioners act on genetic advice in general practice: prospective longitudinal study. BMJ **322**(7277): 26-27.	Ineligible exposure *Women's compliance with advice provided by their* *general practitioner and comparison of GP and clinical geneticists' advice*
De Bock, G. H., et al. (1999). GPs' management of women seeking help for familial breast cancer. Family Practice **16**(5): 463-467.	Ineligible exposure *Management strategies for previous clinical cases*
Eden, K. B., et al. (2020). Use of an online breast cancer risk assessment and patient decision aid in primary care practices. Journal of Women's Health **29**(6): 763-769.	Ineligible exposure *Clinicians' appraisals of a breast cancer risk assessment tool*
Emery, J., et al. (1999). Computer support for recording and interpreting family histories of breast and ovarian cancer in primary	Ineligible exposure *Clinicians' appraisals of a breast cancer risk assessment tool*

care (RAGs): qualitative evaluation with simulated patients. BMJ **319**(7201): 32-36.	
Finkelstein, J., et al. (2017). Introducing a comprehensive informatics framework to promote breast Cancer risk assessment and chemoprevention in the primary care setting. AMIA Summits on Translational Science Proceedings: 58-67	Ineligible exposure *Focuses on development of informatics framework to increase breast cancer risk assessment and chemoprevention*
Glasspool, D. W., et al. (2001). Risk assessment in genetics: A semiquantitative approach. Studies in Health Technology and Informatics **84**(Pt 1): 459-463	Ineligible exposure *Focuses on development of genetic risk decision support tool*
Hidalgo, K. D., et al. (2016). Health promoting practices and personal lifestyle behaviors of Brazilian health professionals. BMC Public Health **16**(1): 1114.	Ineligible exposure *Health promotion practices for breast cancer patients*
Ka'ono'I, M. E., et al. (2004). Primary care physicians' knowledge, attitudes and practices related to cancer screening and cancer prevention clinical trials. Pacific Health Dialog **11**(2): 160-165.	Ineligible exposure *Focuses on secondary prevention (breast cancer screening) and cancer prevention in general*
Lane, D. S., et al. (2001). An educational approach to improving physician breast cancer screening practices and counseling skills. Patient Education and Counseling **43**(3): 289-301.	Ineligible exposure *Focuses on secondary prevention (breast screening)*
Lo, L. L., et al. (2018). The iPrevent online breast cancer risk assessment and risk management tool: usability and acceptability testing. JMIR Formative Research **2**(2): e24.	Ineligible exposure *Clinicians' appraisals of a breast cancer risk assessment tool*

Nguyen, M. N., et al. (2009). Quebec breast cancer screening program: A study of the perceptions of physicians in Laval, Que. Canadian Family Physician **55**(6): 614-620.	Ineligible exposure *Focuses on secondary prevention only (breast screening and clinical breast examination)*
Brownson, R. C., et al. (1993). Cancer control knowledge and priorities among primary care physicians. *Journal of Cancer Education* **8**(1): 35-41.	No breast cancer specific data *Focuses on cancer risk and primary prevention whereby data specific to breast cancer cannot be extracted*
Carroll, J. C., et al. (2016). Primary care providers' experiences with and perceptions of personalized genomic medicine. Canadian Family Physician **62**(10): e626-e635.	No breast cancer specific data *Focuses on experiences with, perceptions of, and desired role in personalized medicine, with a focus on cancer. Data specific to breast cancer cannot be extracted*
Flynn, B. S., et al. (2010). Primary care physicians' use of family history for cancer risk assessment. BMC Family Practice **11**(1): 45.	No breast cancer specific data *Reports a confidence outcome but data specific to breast cancer cannot be extracted*
Kurashi, N. Y. (2007). Public health care physicians' knowledge, attitudes and management about breast cancer. Public Health Medicine **6**(2): 61-67.	No breast cancer specific data *Knowledge, attitudes and practice outcomes but none about breast cancer risk assessment or primary prevention*
Mouchawar, J., et al. (2001). Colorado family physicians' knowledge of hereditary breast cancer and related practice. Journal of Cancer Education **16**(1): 33-37.	No breast cancer specific data *Behaviour outcome is not breast cancer specific (do you collect family history information as part of your routine practice?)*

Tessaro, I. A., et al. (1996). Cancer prevention knowledge, attitudes, and clinical practice of nurse practitioners in local public health departments in North Carolina. Cancer Nursing **19**(4): 269-274.	No breast cancer specific data *Attitudes & clinical practice outcomes but not specific to breast cancer*
Wilkes, M. S., Day, F. C., Fancher, T. L., McDermott, H., Lehman, E., Bell, R. A., & Green, M. J. (2017). Increasing confidence and changing behaviors in primary care providers engaged in genetic counselling. BMC Medical Education **17**: 163.	No breast cancer specific data *Self-efficacy and attitudes outcomes but not specific to breast cancer*
Douma, K. F., et al. (2016). Non-genetic health professionals' attitude towards, knowledge of and skills in discussing and ordering genetic testing for hereditary cancer. Familial Cancer **15**(2): 341-350.	No breast cancer specific data *Attitudes outcomes but not specific to breast cancer*
Teng, I., & Spigelman, A. (2014). Attitudes and knowledge of medical practitioners to hereditary cancer clinics and cancer genetic testing. Familial Cancer **13**(2): 311-324.	No breast cancer specific data *Attitudes & clinical practice outcomes but not specific to breast cancer*
Ahmad, S., et al. (2011). Knowledge, attitude and practice for breast cancer risk factors and screening modalities in staff nurses of Ayub Teaching Hospital Abbottabad. Journal of Ayub Medical College Abbottabad **23**(3), 127-129	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Alkhasawneh, I. M. (2007). Knowledge and practice of breast cancer screening among Jordanian nurses. Oncology Nursing Forum **34**(6): 1211-1217.	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Javed, M., et al. (2013). Knowledge, attitude and preventive practices for breast cancer among health professionals at Shalamar medical and	Ineligible population *Participants worked at a tertiary care private teaching hospital*

Dental College/Hospital Lahore. Pakistan Journal of Medical & Health Sciences **7**(56): 582-587.	
Karayurt, Ö., et al. (2010). Evaluation of the breast cancer train the trainer program for nurses in Turkey. Journal of Cancer Education **25**(3): 324-328.	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Panic, N., et al. (2014). Survey on knowledge, attitudes, and training needs of Italian residents on genetic tests for hereditary breast and colorectal cancer. BioMed Research International **2014**.	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Prolla, C. M. D., et al. (2015). Knowledge about breast cancer and hereditary breast cancer among nurses in a public hospital. Revista Latino-Americana de Enfermagem **23**(1): 90-97.	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Welkenhuysen, M., & Evers-Kiebooms, G. (2003). Predictive genetic testing for breast cancer and Huntington's disease: the opinions of midwives and nurses in Flanders. Public Health Genomics **6**(2): 104-113.	Ineligible population *Author confirmed that participants did not provide primary care services in line with the World Health Organisation's definition*
Collins et al. (2014). Assessing and managing breast cancer risk: Clinicians' current practice and future needs. The Breast **23**(5):644-650	Qualitative methodology *For reasons of space, the review was limited to quantitative findings only*
Donnelly et al. (2020). Implementing risk stratification into the national breast cancer screening programme: perspectives of NHS personnel responsible on feasibility and impact. Unpublished	Qualitative methodology *For reasons of space, the review was limited to quantitative findings only*

Phillips, K.-A. et al. (2016). Transitioning to routine breast cancer risk assessment and management in primary care: what can we learn from cardiovascular disease? Australian Journal of Primary Health **22**(3): 255-261.	Qualitative methodology *For reasons of space, the review was limited to quantitative findings only*
Smith et al. (2016). Clinician-Reported Barriers to Implementing Breast Cancer Chemoprevention in the UK: A Qualitative Investigation. Public Health Genomics, **19**(4): 239-249.	Qualitative methodology *For reasons of space, the review was limited to quantitative findings only*
Brown, J., et al. (2019). Physician knowledge, attitudes, and practices regarding breast density. Journal of Women's Health **28**(9): 1193-1199.	Data pertinent to PCPs could not be extracted *Author contacted to clarify sample size of PCPs who confirmed that PCPs & geriatricians were grouped for analysis therefore it is not possible to extract the findings relevant to the PCPs*
Entrekin, N. M., & McMillan, S. C. (1993). Nurses' knowledge, beliefs, and practices related to cancer prevention and detection. Cancer Nursing **16**(6): 431-439.	Data pertinent to PCPs could not be extracted *Staff nurses recruited from multiple settings so findings relevant to those working in primary care cannot be extracted*
Gabram, S. G., et al. (2009). Assessing breast cancer risk and providing treatment recommendations: immediate impact of an educational session. The Breast Journal **15**(s1): S39-S45.	Data pertinent to PCPs could not be extracted *PCPs and surgeons recruited; it is not possible to extract the findings relevant to the PCPs*
Igid, H., et al. (2019). Breast Cancer Risk Assessment and Evaluation of Risk-Based Screening Practices by Primary Care Providers: A Single Institution Experience. Clinics in Oncology **4**: 1625.	No data from perspective of PCPs *Retrospective chart review*

Owens, W. L., et al. (2011). Implementation in a large health system of a program to identify women at high risk for breast cancer. Journal of Oncology Practice, **7**(2): 85-88.	No data from perspective of PCPs *Implementation only*
Ozanne, E. M., et al. (2009). Identification and management of women at high risk for hereditary breast/ovarian cancer syndrome. The Breast Journal **15**(2): 155-162.	No data from perspective of PCPs *Implementation only*
Baker, S. K. (2016). Rural Arizona nurse practitioners' knowledge of hereditary breast and ovarian cancer risk assessment (Publication No. 10245174) [Doctoral dissertation, The University of Arizona]. ProQuest Dissertations Publishing.	Insufficient data reported *Eligible data but not sufficiently reported to include in review. No correspondence email address as it is a doctoral dissertation. Search performed on Scopus but no email address identified for the author*
Yadav, S., et al. (2019). Utilization of a breast cancer risk assessment tool by internal medicine residents in a primary care clinic: impact of an educational program. BMC Cancer **19**: 228.	Insufficient data reported *Eligible data but not sufficiently reported to include in review. Author contacted three times for additional data but no response received*
Hunter, A., et al. (1998). Physician knowledge and attitudes towards molecular genetic (DNA) testing of their patients. Clinical Genetics **53**(6): 447-455.	Insufficient data reported *Eligible data but not sufficiently reported to include in review. Corresponding author unable to provide data so forwarded query to co-author but no response was received*
Harris, H., et al. (2011). Familial breast cancer: is it time to move from a reactive to a proactive role?. Familial Cancer **10**: 501-503.	Insufficient data reported *Eligible data but not sufficiently reported to include in review. Author contacted and relevant data sent. Unable to stratify responses by country so data provided did not resolve percentage error in paper*

Yaren, A., et al. (2008). Awareness of breast and cervical cancer risk factors and screening behaviours among nurses in rural region of Turkey. European Journal of Cancer Care **17**(3): 278-284.	Unclear population *Author contacted three times for clarity on population but no response received*
Korde, L. A., & Gadalla, S. M. (2009). Cancer risk assessment for the primary care physician. Primary Care: Clinics in Office Practice **36**(3): 471-488.	Overview article *Not primary research*

Appendix A.4: Summary and detailed results of the quality appraisal using the Mixed Methods Appraisal Tool

Authors (year)	MMAT question				
	1. Is the sampling strategy relevant to address the research question?	2. Is the sample representative of the target population?	3. Are the measurements appropriate?	4. Is the risk of nonresponse bias low?	5. Is the statistical analysis appropriate to answer the research question?
Armstrong et al. (2006)	Somewhat	Yes	Can't tell	Somewhat	Yes
Bankhead et al. (2001)	Yes	Can't tell	Somewhat	Somewhat	Somewhat
Bethea et al. (2008)	Yes	Somewhat	Somewhat	Somewhat	Yes
Bidassie et al. (2020)	Somewhat	Can't tell	Somewhat	Can't tell	Yes
Carroll et al. (2011)	Yes	Somewhat	Somewhat	No	Yes
Casas et al. (2017)	No	No	Can't tell	Somewhat	Yes
Corbelli et al. (2014)	Can't tell	No	Can't tell	Somewhat	Yes
Dekanek et al. (2020)	Somewhat	No	Somewhat	No	Yes
Edwards et al. (2009)	Somewhat	Can't tell	Somewhat	Can't tell	Somewhat

Escher & Sappino (2000)	Somewhat	Can't tell	Can't tell	Yes	Yes
Ganry & Boche (2005)	Yes	Yes	Can't tell	No	Yes
Guerra et al. (2009)	Somewhat	Yes	Can't tell	Somewhat	Yes
Gunn et al. (2018)	Somewhat	No	Can't tell	Somewhat	Yes
Hall et al. (2001)	Somewhat	Can't tell	Somewhat	Somewhat	Yes
Kaplan et al. (2011)	Somewhat	Yes	Somewhat	No	Yes
Khong et al. (2015)	Can't tell	No	Can't tell	No	Yes
Macdonald et al. (2020)	Somewhat	Can't tell	Somewhat	No	Yes
Maimone et al. (2017)	Somewhat	Yes	Can't tell	No	Can't tell
Mainous et al. (2013)	Somewhat	Yes	Can't tell	No	Yes
Nippert et al. (2014)	Somewhat	Yes	Somewhat	No	Yes
Pichert et al. (2003)	Somewhat	Can't tell	Can't tell	No	Can't tell
Sabatino et al. (2007)	No	No	Somewhat	Yes	Yes
Samimi et al. (2020)	Somewhat	Yes	Somewhat	No	Yes

Saunders-Goldson et al. (2018)	No	No	Somewhat	Can’t tell	Yes
Summerton & Garrood (1997)	Yes	Somewhat	Somewhat	Somewhat	Can’t tell
Tighe et al. (2009)	Somewhat	Somewhat	Somewhat	No	Yes
Walter et al. (2001)	Can’t tell	Can’t tell	Somewhat	Somewhat	Can’t tell
Welkenhuysen & Evers-Kiebooms (2002)	Somewhat	Yes	Somewhat	Yes	Yes
Wilson et al. (2006)	Yes	Somewhat	Somewhat	Somewhat	Yes

Study: Armstrong et al. (2006)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Strengths for this criterion include the source of the sample being relevant to the target population and the use of random stratified sampling. However, the sample frame is biased as only registered members of the American Medical Association could participate.
2. Is the sample representative of the target population?
Decision: Yes The target population was primary care physicians in the USA. A national survey using random stratified sampling resulted in a sample with representation from all relevant specialties of the target population (internal medicine, obstetrics and gynaecology and family practice). Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Can't tell The measurements map onto the respective research questions and are therefore appropriate for answering the research question. They are also clearly defined in terms of wording and response scales and there is an acceptable degree of face validity. Items assessing the attitudinal and practice factors were developed based on interviews with primary care physicians and literature about clinical decision making about tamoxifen. However, there is no evidence that the measurements were subject to a comprehensive assessment of reliability and validity nor is there any evidence of the survey being pre-tested prior to data collection. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 47.2%. Respondents did not significantly differ from non-respondents on variables of interest (sex, region of the country, specialty or type of degree). Responders had graduated from medical school more recently than non-responders but this is unlikely to have biased the results.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research question. Alternative categorizations for dichotomization of outcomes were tested and did not change the main result.

Study: Bankhead et al. (2001)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population; lists of practice nurses were obtained directly from the Nurse Directors in each health authority where possible and by contacting all GP practices if the data were not available from the health authority. All practice nurses in the four regions were invited to participate. Therefore, the sampling procedure was adequate and unlikely to have introduced bias.
2. Is the sample representative of the target population?
Decision: Can't tell The target population was UK practice nurses. The sample was drawn from four regions in the UK (three regions of England and one region in Scotland). As no information is reported about the practice landscape in the four regions or socio-demographic characteristics of the sample, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. There is an acceptable degree of face validity. The questionnaire was developed in collaboration with practice nurses and it was piloted. The full response scale for confidence items is not reported. However, there is no evidence that the survey was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 66%. However, no information is reported about those who did not take part and no analysis of whether respondents were significantly different to non-respondents was conducted.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Somewhat The analysis appears to be appropriate for answering the research questions but very minimal information is reported beyond the program used (Stata) and the descriptive nature of analysis.

Study: Bethea et al. (2008)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population. The four geographical areas were chosen to represent areas that were rural and urban. All practices were sent a letter offering the opportunity to participate in the study. From the 17 practices who expressed an interest in participating, 10 were randomly selected for inclusion. Therefore, the sampling procedure was adequate and unlikely to have introduced bias.
2. Is the sample representative of the target population?
Decision: Somewhat The target population was UK GPs and practice nurses. Although the four geographical areas were chosen to represent areas that were rural and urban, they were all served by 1 hospital based genetics unit and therefore the results are likely to be limited in generalisability to the target population.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. There is an acceptable degree of face validity. The questionnaire had previously been validated in the setting it was being used in and it was developed through a series of primary care-based focus groups. Although the questionnaire had previously been validated in the setting and attempts have been made to improve the content validity, there is no evidence that the survey was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 59.4%. However, no information is reported about those who did not take part and no analysis of whether respondents were significantly different to non-respondents was conducted.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research question.

Study: Bidassie et al. (2020)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population but the non-probability sampling procedure is likely to have introduced bias; primary care chiefs at all VA nationwide were contacted and asked to complete the survey and then to forward it to eligible primary care providers at their local VA (snowball sampling).
2. Is the sample representative of the target population?
Decision: Can't tell The target population was primary care providers within the Department of Veterans Affairs. The sampling strategy relied on primary care chiefs forwarding the survey on to all eligible primary care providers. The size of the target population is not reported and therefore it is impossible to know how many primary care providers received the invite and in turn make a judgement of how representative the sample is. Nevertheless, generalisability is likely to be limited given the snowball sampling strategy.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. The survey has an acceptable degree of face validity. The VA Breast Health Research Group in consultation with survey methodology experts developed the survey. The survey was field tested among primary care providers at one VA to ensure feasibility and validity. However, there is no evidence that the survey was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Can't tell The total number of people who received the survey invitation is unknown so a response rate could not be calculated. Therefore risk of non-response bias cannot be determined.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Carroll et al. (2011)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population; lists of practicing family physicians grouped by practice from the chiefs of Family Medicine at local hospitals. Furthermore, random stratified sampling was used and attempts were made to recruit family physicians from rural and urban areas.
2. Is the sample representative of the target population?
Decision: Somewhat The target population was Canadian family physicians. The study population consisted of family physicians practising in four locations in Ontario. Although representation from different practice locations was achieved, the majority of physicians practised in large cities (69%) so the sample is likely to have limited generalisability to the target population.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. The survey has an acceptable degree of face validity. The clinical scenarios were informed by previous work, the referral guidelines and clinical experience. They were pilot tested with family physicians not involved in the study for comprehension and face validity. The list of competencies for the confidence outcome was derived from the National Coalition for Health Professional Education in Genetics and previous work. However, the authors acknowledge that the outcome measures require psychometric testing of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Poor response rate of 13%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Casas et al. (2017)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: No The source of the sample was relevant to the target population but the sampling procedure was weak. It is not clear why family medicine and obstetrics and gynaecology clinicians were not included as they are mentioned as a target group for the workshop. Arguably obstetrics and gynaecology clinicians are most likely to counsel women about breast health so their omission is a significant limitation of the sampling strategy.
2. Is the sample representative of the target population?
Decision: No The target population was practicing clinicians who counsel women about breast health. Participants were recruited from a single hospital affiliated with an academic institution (Boston University Medical Center). Coupled with the omission of relevant clinicians and small sample size, the sample has poor generalisation to the population and selection bias is likely to be present.
3. Are the measurements appropriate?
Decision: Can't tell The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. The survey has an acceptable degree of face validity. The attitude questions were derived from a review of the literature and in accord with the learning objectives. No evidence of pre-testing the survey prior to data collection is reported. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Poor response rate of 9.3%. Twenty-one clinicians who did not attend the educational session participated in the baseline survey (referent group). There was no significant difference between the intervention group and the referent group by gender, years in practice or percentage of female patients in their clinic panels.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Corbelli et al. (2014)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Can't tell Purposive sampling has been used meaning participants have been chosen based on the study's purpose. It is unclear what sample frame was used and how the web-based survey was circulated. Therefore, it is not possible to assess the appropriateness of the sampling strategy with certainty.
2. Is the sample representative of the target population?
Decision: No The target population was US internists, family physicians and gynaecologist and the resulting sample matched the target population. However, participants were recruited from a single hospital affiliated with an academic institution (University of Pittsburgh Medical Center). The authors acknowledge that their results may have limited generalisability to other regions of the country or to providers who practice in community or rural settings.
3. Are the measurements appropriate?
Decision: Can't tell The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. There is an acceptable degree of face validity. The survey was adapted from the Breast and Cervical Cancer Screening Questionnaire, part of the National Survey of Primary Care Physicians' Cancer Screening Recommendations and Practices originally conducted by the National Cancer Institute. No evidence of pre-testing the survey prior to data collection is reported. There is no evidence that the adapted survey was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 55%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Dekanek et al. (2020)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population; the questionnaire was distributed by email by the Chair of the Department of Obstetrics and Gynaecology and the Director of the Family Medicine Residency Program. This sampling strategy could have introduced bias as participants may have felt compelled to participate and respond in a certain way as the invite was sent by someone in authority.
2. Is the sample representative of the target population?
Decision: No The target population was US primary care physicians. Participants were recruited from a single hospital affiliated with an academic institution (University of Pittsburgh Medical Center). Coupled with half of the respondents having more than 15 years of experience and the hospital having a subspecialty cancer genetics clinic, the sample has poor generalisation to the population and selection bias is likely to be present.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. There is an acceptable degree of face validity. The knowledge questions were based on a previous questionnaire developed in 1999. The opinion questions were designed to reflect the research questions but how these were chosen is not described. The questionnaire was piloted with a focus group of clinicians before data collection. There is no evidence that the measurements were subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Poor response rate of 25%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Edwards et al. (2009)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample is relevant to the target population but the non-probability sampling procedure is likely to have introduced bias; due to cost and travel constraints, the authors distributed surveys via convenience sampling to nurse practitioners attending a national nurse practitioner conference.
2. Is the sample representative of the target population?
Decision: Can't tell Participants were recruited from one national nurse practitioner conference held in a Midwest US city. The national nature of the conference could have allowed for participation of nurse practitioners across the USA but whether this was the case is not known. Therefore, it is difficult to determine representativeness of the sample but it likely to be limited given the convenience sampling strategy.
3. Are the measurements appropriate?
Decision: Somewhat The survey was developed in-house by the research team and was reviewed by a group of clinicians including experts in breast cancer risk assessment and prevention and nurse practitioners. The survey was modified and revised based on reviewers' comments and recommendations. The final version was determined to have content validity. The measurements were not subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Can't tell As surveys were handed out and completed in person at the conference, all 175 were returned. It is not possible to calculate a response rate as the authors do not report how many people were approached to complete the survey. Therefore, a judgement of non-response bias cannot be made with certainty.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Somewhat Minimal information is reported with respect to analysis particularly regarding what statistical calculations were performed. Furthermore, the correlation reported in the results was not specified apriori and is unrelated to a research question.

Study: Escher & Sappino (2000)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population but the sample frame was biased as only registered members of Geneva Medical Association could participate.
2. Is the sample representative of the target population?
Decision: Can't tell Participants were recruited from one county in Switzerland. The resulting sample appears to match the target population but there is no evidence that a comparison of socio-demographic characteristics between the sample and the target population was performed. Furthermore, it is unclear whether representation from different geographic practice settings was achieved. Therefore, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Can't tell The questionnaire was developed in-house by the research team with some items adapted from a questionnaire used in a previous study for a different disease. No attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Yes Satisfactory response rate of 65%. Respondents were compared to non-respondents on two variables; specialty and sex. Response rates were similar between the specialities.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Ganry & Boche (2005)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population; all GPs working in Picardy were invited to participate with the assistance of the Regional Private Doctors Union. Therefore, the sampling procedure was adequate and unlikely to have introduced bias.
2. Is the sample representative of the target population?
Decision: Yes The target population was GPs in the Picardy region of France. The distribution of the response rate for the three departments within Picardy was comparable and representation was achieved from different geographic practice settings (urban/peri urban and rural zones) indicating that the sample is likely to generalise to the target population.
3. Are the measurements appropriate?
Decision: Can't tell Very little detail is reported about the development of the questionnaire; it appears to have been developed in-house by the research team and no rationale has been provided for selection of questions. The questionnaire has an acceptable degree of face validity. No attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: No Poor response rate of 33%. The authors do state that they found no difference in the characteristics of the responders in the discussion but no examination of whether respondents were significantly different to non-respondents is explicitly reported in the results section. Additionally, no reasons for non-responses are reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Guerra et al. (2009)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Strengths for this criterion include the source of the sample being relevant to the target population and the use of random stratified sampling. However, the sample frame was biased as only registered members of the American Medical Association could participate.
2. Is the sample representative of the target population?
Decision: Yes The target population was primary care physicians in the USA. The use of a national survey coupled with sample stratification resulted in a sample with representation from all relevant specialties of the target population (internal medicine, obstetrics and gynaecology and family practice). Therefore, the sample was representative of the target population.
3. Are the measurements appropriate?
Decision: Can't tell The PRECEDE model of health behaviour was used to guide survey development. The survey has an acceptable degree of face validity. Items adapted from other physician surveys were used to assess socio-demographic and practice characteristics. The other three content areas appear to have been developed in-house by the research team and no rationale has been provided for selection of questions. No attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was not subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Response rate of 48.3%. Respondents did not differ significantly from non-responders on variables of interest (sex, region of the country, specialty or type of degree). Responders had graduated from medical school more recently than non-responders but this is unlikely to have biased the results. Additionally, no reasons for non-responses are reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Gunn et al. (2018)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population but the non-probability sampling procedure could have introduced bias; clinical leaders within the divisions of two urban academic, safety net hospitals in Boston sent the survey link to all practising primary care physicians in general internal medicine. Participants may have felt compelled to participate and respond in a certain way as the invite was sent by someone in authority.
2. Is the sample representative of the target population?
Decision: No The target population was primary care providers practising in Massachusetts. Participants were practicing at two urban academic, safety net hospitals. The authors acknowledge that the academic centre context may have made these providers more likely to be aware of medical evidence. The safety-net status of these practices implies that the providers may have fewer resources and see higher acuity patients with complex social and medical needs. Both of these factors limit the generalisability of the results to the target population.
3. Are the measurements appropriate?
Decision: Can't tell No information is reported regarding development of the questionnaire. Although the questionnaire has an acceptable degree of face validity, no attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 55% but no reasons for non-responses are reported. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Hall et al. (2001)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population and justification for the sampling frame is provided. However, the sample frame was biased as only healthcare professionals belonging to a single management group could participate. The locations of the 16 clinical sites were dispersed geographically providing a population of great demographic variability which is a strength of the sampling strategy.
2. Is the sample representative of the target population?
Decision: Can't tell The target population was US primary healthcare professionals. Participants all worked in the Twin Cities (Minnesota) area. The resulting sample appears to match the target population but there is no evidence that a comparison of socio-demographic characteristics between the sample and the target population was performed. Furthermore, it is unclear whether the demographic and geographic variability inherent in the sampling frame was achieved. Therefore, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Somewhat The survey was developed in-house by the primary investigator. The majority of questions were designed for analysis of the variables identified in each specific aim and for comparison within HCP roles and within areas of practice. The questionnaire has an acceptable degree of face validity. A panel of experts participated in the development process of the survey tool. The survey was then piloted on four health professionals to test for reliability and suggested changes were made to the survey. The author acknowledges that replication of the study is required to demonstrate the reliability and validity of the tool.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 61.1% but no reasons for non-responses are reported. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Kaplan et al. (2011)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population and non-probability stratified sampling has been used. Although the sample frame is justified, it is biased as only registered members of the American Medical Association could participate.
2. Is the sample representative of the target population?
Decision: Yes The target population was primary care physicians in California. A large state-wide sample stratified by primary care speciality was collected and representation from different practice settings was achieved. Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Somewhat The survey was a questionnaire adapted from the physician survey literature, pretested among practising physicians and revised accordingly. The survey has an acceptable degree of face validity. There is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Satisfactory response rate of 50%. An examination of whether respondents differed significantly from non-respondents revealed that significantly more women and obstetrician/gynaecologists responded. The authors acknowledge that their findings regarding risk-reduction practices may be overestimated as a result.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Khong et al. (2015)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Can't tell Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population but the exact sampling frame used is unclear. Therefore, it is not possible to assess the appropriateness of the sampling strategy with certainty.
2. Is the sample representative of the target population?
Decision: No The target population was primary care physicians in California. Participants were recruited from a single institution affiliated with an academic medical centre and therefore results are unlikely to generalise to the population.
3. Are the measurements appropriate?
Decision: Can't tell Very minimal information is provided about the survey beyond question format and response options. No rationale is provided for selection of questions. Although the questionnaire has an acceptable degree of face validity, no attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: No Response rate of 45% and no examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Macdonald et al. (2020)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population; eligible clinicians were family physicians or breast surgeons involved in the care of women recruited to the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer cohort (kConFab). The resulting sample is therefore biased towards healthcare professionals who are likely to be more familiar with the management of women at high risk of developing breast cancer which may have affected the results.
2. Is the sample representative of the target population?
Decision: Can't tell The target population was Australian family physicians and breast surgeons. Although the sample recruited appears to match the target population, no information about socio-demographic characteristics or practice setting is reported. Therefore, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Somewhat A literature review and focus group interviews were undertaken with family physicians and breast surgeons to inform survey development. The survey has an acceptable degree of face validity and was developed using the Theoretical Domains Framework. However, there is no evidence that the survey was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Response rate of 42% and no examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses were descriptive in nature (numbers and percentages) which was an appropriate approach given the research questions.

Study: Maimone et al. (2017)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population and the survey was distributed via email but the exact sampling frame used is unclear. Attempts were made to recruit primary care professionals from rural and urban areas which is a strength of the sampling strategy.
2. Is the sample representative of the target population?
Decision: Yes The target population was Mayo Clinic primary care physicians. Participation from Mayo Clinic sites involved referring providers from three primary campuses in Minnesota, Florida and Arizona, as well as smaller satellite locations. Representation was achieved from different geographic practice settings. Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Can't tell Very minimal information is provided about the development of the survey beyond it being created by breast imaging radiologists. No rationale is provided for selection of questions. Although the questionnaire has an acceptable degree of face validity, no attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: No Response rate of 44%. No examination of whether respondents differed significantly from non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Can't tell Descriptive statistics only which appear appropriate for answering the research questions. However, a judgement of appropriateness cannot be made with certainty as there is no analysis section included in the paper.

Study: Mainous et al. (2013)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population. However, the sample frame was biased as only registered members of the four major US academic family medicine organisations could participate.
2. Is the sample representative of the target population?
Decision: Yes The target population was academic family physicians. A large sample was drawn from the four major US academic family medicine organisations and the resulting sample matched the target population. Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Can't tell The survey questions were developed following a review of the literature to identify key concepts and issues suggesting the need for additional knowledge. Although the questionnaire has an acceptable degree of face validity, no attempts at ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: No Response rate of 45.1%. The authors state that it was not possible to conduct meaningful analyses regarding differences between respondents and non-respondents due to the large amount of missing data on demographic variables in the membership database.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Nippert et al. (2014)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The sampling methods are reported in their sister paper (Den Heijer et al., 2013). Strengths for this criterion include the sources of the samples being relevant to the target population and random samples have been drawn. For some participant groups, the best available lists were used as the sample frame. However, the authors do not report how the sample of UK GPs was obtained and the Dutch GPs were drawn from the membership list of the Dutch Society of GPs, a paid association resulting in a biased sample.
2. Is the sample representative of the target population?
Decision: Yes The target population was GPs and breast surgeons in four countries. Across all four countries, representation from different geographic practice settings was achieved (inner city, middle sized or small town and town in rural area). Furthermore, participants were recruited using national surveys and the resulting sample matched the target population. Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Somewhat Information about the development of the questionnaire is reported in their sister paper (Den Heijer et al., 2013). The measurements map onto the research question and are therefore appropriate for answering it. There is an acceptable degree of face validity. The questionnaire was developed following discussions with members of the working group. It was piloted in 10 GPs and 10 specialists in each participating country and feedback was used to refine the questionnaire further. There is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Poor response rate of 33%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Pichert et al. (2003)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat The source of the sample was relevant to the target population. All relevant primary care specialties are included in the sample frame but no justification is provided for limiting the sample to physicians working in private practice. The sample frame was a pharmaceutical company mailing list obtained from a market research institute meaning that only physicians signed up to this mailing list could participate biasing the sample.
2. Is the sample representative of the target population?
Decision: Can't tell The target population was primary care physicians in the German speaking part of Switzerland. The resulting sample appears to match the target population but there is no evidence that a comparison of socio-demographic characteristics between the sample and the target population was performed. It is also unclear whether representation from different practice locations was achieved. Therefore, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Can't tell No information is reported regarding the development of the measures. The measures appear appropriate for answering the research questions and have an acceptable degree of face validity. However, no evidence of ensuring usability have been described. Furthermore, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity. Therefore, a judgement of appropriateness cannot be made with certainty.
4. Is the risk of nonresponse bias low?
Decision: No Response rate of 45%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Can't tell Descriptive statistics only which appear appropriate for answering the research questions. However, a judgement of appropriateness cannot be made with certainty as there is no analysis section included in the paper.

Study: Sabatino et al. (2007)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: No Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The sample frame was providers in the general medicine outpatient practice or 1 of 15 affiliated community practices. Relevant clinicians such as family practitioners and gynaecologists have been omitted from the sample frame and no justification is provided for why this decision was made. In the absence of justification, omission of primary care specialties most likely to counsel women about breast health is a significant limitation of the sampling strategy.
2. Is the sample representative of the target population?
Decision: No The target population was US primary care providers. Participants were recruited from a single urban hospital affiliated with an academic institution (Beth Israel Deaconess Medical Center in Boston). The authors acknowledge that generalisability to other specialties, regions and clinical or non-urban settings may be limited. Coupled with the omission of relevant clinicians the sample has poor generalisation to the population and selection bias is likely to be present.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research question. They are also clearly defined in terms of wording and response scales and there is an acceptable degree of face validity. The questionnaire was reviewed by two groups of physicians and pre-tested among seven practicing physicians. However, there is no evidence that the survey was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Yes Satisfactory response rate of 53%. Respondents did not differ significantly from non-responders on variables of interest (sex, training level or practice setting).
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions. They assessed the potential confounding of nurse practitioners.

Study: Samimi et al. (2020)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Purposive sampling has been used meaning participants have been chosen based on the study's purpose. The source of the sample was relevant to the target population but the sample frame was biased as participants were recruited from an existing opt-in health care provider panel developed and maintained by a health care market research firm. To become a panel member, healthcare providers also needed to be a member of the American Medical Association.
2. Is the sample representative of the target population?
Decision: Yes The target population was US primary care physicians. All relevant primary care specialties were recruited. Information about geographic practice setting is reported in Supplementary File 2 and this indicates that representation was achieved from all geographic practice settings (urban, suburban, rural and geographically isolated/remote). The sample is therefore representative of the target populations and results generalisable.
3. Are the measurements appropriate?
Decision: Somewhat Information about survey development is reported in their sister paper (Samimi et al., 2019). The survey was developed based on previous studies by the authors and a literature review. The survey was initially tested using semi structured Web-assisted cognitive interviews with 9 US-based primary care physicians to evaluate whether they understood the survey questions and could respond as intended. The final questionnaire was developed based on this feedback. The survey has an acceptable degree of face validity. However, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: No Poor response rate of 12% and no examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Saunders-Goldson et al. (2018)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: No The source of the sample was relevant to the target population but the sampling procedure was weak. Very little information is reported about the sampling strategy beyond convenience sampling being used. The accessible population of first through fourth year resident physicians in internal medicine and family practice differs from the target population as obstetrics and gynaecology residents have been omitted and no justification is provided for why this decision was made. In the absence of justification, omission of the primary care speciality most likely to counsel women about breast health is a significant limitation of the sampling strategy.
2. Is the sample representative of the target population?
Decision: No The target population was health care providers working in primary care settings. Participants were recruited from a medical school associated with an Ambulatory Indigent Care Center located in an urban city in the Northeastern United States. Coupled with the omission of relevant clinicians and small sample size, the sample has poor generalisation to the population and selection bias is likely to be present.
3. Are the measurements appropriate?
Decision: Somewhat Knowledge was measured using a survey instrument (the Breast Cancer Risk Assessment Knowledge Tool) developed by experts in the field of hereditary breast cancer and genetics. The tool has an established content validity and reliability with a Cronbach's alpha of 0.89. The attitudes measure was developed by a team of genetic counsellors specialising in hereditary cancers and primary care physicians and piloted by clinicians in the areas of genetic counselling, oncology, surgery, and family practice (information reported in sister paper – Koil et al., 2003). Both measures have an acceptable degree of face validity. However, there is no evidence that the attitudes measure was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Can't tell It is reported that fifty surveys were distributed to physician residents of which 22 met the inclusionary criteria. It is not possible to compare respondents and non-respondents due to the convenience sampling procedure. Therefore, a judgement of non-response bias cannot be made with certainty.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes

Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Summerton & Garrood (1997)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population; complete list of GPs practising within the Calderdale and Kirklees Health Authority area. Therefore, the sampling procedure was adequate and unlikely to have introduced bias.
2. Is the sample representative of the target population?
Decision: Somewhat The target population was UK GPs. The sample was recruited from one health authority in the UK (Calderdale and Kirklees Health Authority). The authors report that 37% of participants worked in urban practices. Whether there was sufficient representation across different geographic practice settings is not reported so generalisability to the UK may be limited. However, sample representativeness was assessed by comparing the GPs who responded to the survey with known demographic variables among British GPs. The results indicated the generally representative nature of the study.
3. Are the measurements appropriate?
Decision: Somewhat The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. Minimal information is reported about the development of the questionnaire. It was piloted among a group of GPs with the results suggesting that the questionnaire exhibited face validity and expert opinions were also supportive of the content. However, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 66.3%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Can’t tell Descriptive statistics only which appear appropriate for answering the research questions. However, a judgement of appropriateness cannot be made with certainty as there is no analysis section included in the paper.

Study: Tighe et al. (2009)

Screening question 1: Are there clear research questions?

Decision: Yes

Screening question 2: Do the collected data allow to address the research questions?

Decision: Yes

1. Is the sampling strategy relevant to address the research question?

Decision: Somewhat

Strengths for this criterion include the source of the sample being relevant to the target population and the use of random stratified sampling. The sample frame was drawn from the Canadian Medical Directory which is the largest and best available list capturing the majority of doctors practising family medicine in Canada. However, the authors state that coverage may be as low as 69%. Another strength of the sampling strategy was the attempt to achieve proportionate representation from each province by taking into account the percent of the total Canadian population in that province.

2. Is the sample representative of the target population?

Decision: Somewhat

The target population was Canadian family physicians. The resulting sample matched the target population and proportionate representation across all geographic areas in Canada was achieved. However, statistically significant differences were seen in response by gender, province/territory and medical experience which the authors acknowledge may affect the generalisability of the results.

3. Are the measurements appropriate?

Decision: Somewhat

The measurements map onto the respective research questions and are therefore appropriate for answering the research questions. Minimal information is reported about the development of the questionnaire. A focus group session was held with four family physicians in order to pilot the survey and revisions were made. The questionnaire has an acceptable degree of face validity. However, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.

4. Is the risk of nonresponse bias low?

Decision: No

Poor response rate of 38.2%. Responders and non-responders did not differ by language or graduation country. However, they did vary significantly by province and number of years practicing. Responders were also more likely to be female. The authors acknowledge that female physicians tend to be more active about prevention so it is likely that rates of prevention knowledge and practices are overestimated.

5. Is the statistical analysis appropriate to answer the research question?

Decision: Yes

Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Walter et al. (2001)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Can't tell The source of the sample was relevant to the target population; all GPs and practice nurses in the 66 practices of the Cambridge and Huntingdon Health Authority were invited to participate. However, the authors do not explicitly state the sample frame used to ensure that all eligible GPs and practice nurses were invited. Therefore, it is not possible to assess the appropriateness of the sampling strategy with certainty.
2. Is the sample representative of the target population?
Decision: Can't tell The target population was UK GPs and practice nurses. The sample was recruited from one health authority in the UK. Although the sample had similar demographic characteristics to the Cambridge and Huntingdon Health Authority, it differed from the national picture where there are more male doctors. The composition of the county is not reported so it is unclear whether representation from different geographic practice settings UK was achieved. Therefore, a judgement of representativeness cannot be made with certainty.
3. Are the measurements appropriate?
Decision: Somewhat Questionnaire development was informed by a review of published work. It was piloted among 11 practice teams in South Bedfordshire with the indicated modifications made. The questionnaire has an acceptable degree of face validity. However, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate of 69%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Can't tell The analysis appears to be appropriate for answering the research questions but very minimal information is reported in the form of a generic, vague sentence stating that parametric and non-parametric statistics were used as appropriate. Therefore, a judgement of appropriateness cannot be made with certainty.

Study: Welkenhuysen & Evers-Kiebooms (2002)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Somewhat Strengths for this criterion include the source of the sample being relevant to the target population and the use of random sampling. However, the sample frame was biased as it only contained registered members of the Scientific Association of Flemish General Practitioners, an association which only half of the GPs in Flanders are members of.
2. Is the sample representative of the target population?
Decision: Yes The target population was GPs in Flanders. A comparison of respondents with the target population of Flemish GPs was conducted which demonstrated that there was no differences in gender or year of graduation so the resulting sample matched the target population. Furthermore, representation from different geographic practice locations was achieved (town and village). Therefore, the sample is representative of the target population and results generalisable.
3. Are the measurements appropriate?
Decision: Somewhat Members of the Academic Centre for General Practice Medicine of the University of Leuven were involved in the development of the questionnaires. Questionnaires were thoroughly pilot tested in a group of 33 GPs and have an acceptable degree of face validity. However, there is no evidence the questionnaires were subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Yes Response rate of 51.8%. The group of responders did not differ from the group of non-responders with regard to gender or year of graduation.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Study: Wilson et al. (2006)
Screening question 1: Are there clear research questions?
Decision: Yes
Screening question 2: Do the collected data allow to address the research questions?
Decision: Yes
1. Is the sampling strategy relevant to address the research question?
Decision: Yes The source of the sample was relevant to the target population. All practices within the study setting were eligible for inclusion. Furthermore, there were attempts to achieve representation from different geographic practice settings which is a strength of the sampling procedure.
2. Is the sample representative of the target population?
Decision: Somewhat The target population was UK GPs. The accessible population was GPs working in the Grampian region of Scotland. The attempts to achieve representation from different geographic practice settings (urban and rural) were successful which improves the generalisability of the sample. Overall, the resulting sample matched the target population but the representativeness could have been improved if the sampling strategy wasn't limited to one specific region or the authors could have conducted a comparison of socio-demographic characteristic between the sample and the target population to assess generalisability beyond the region.
3. Are the measurements appropriate?
Decision: Somewhat No information is reported regarding the development of the measures. The measures appear appropriate for answering the research questions and have an acceptable degree of face validity. The questionnaire was developed and piloted in two practices. However, there is no evidence that the questionnaire was subject to a comprehensive assessment of reliability and validity.
4. Is the risk of nonresponse bias low?
Decision: Somewhat Satisfactory response rate to baseline survey of 78.6%. No examination of whether respondents were significantly different to non-respondents is reported.
5. Is the statistical analysis appropriate to answer the research question?
Decision: Yes Analyses are clearly stated, justified and were appropriate to answer the research questions.

Appendix B: Chapter 3 supplementary materials

Appendix B.1: Focus group and interview topic guide

1. As a researcher who does not work in primary care, I am not familiar with what happens in practice. It would help my understanding if you could you give me an example of when you've had a woman in this age group of 30-39 years present with a concern about their breast cancer risk or about breast health and talk through what happened and what you did.
   Probes: what are/were your reasons for doing that? How did you feel about the interaction? How concerned do you think colleagues are about potential litigation?
   Prompts: (if not answered) is this something you would deal with in your role, does this fit in your role, what would you do

Breast cancer becomes more common in women in their 30s and is the most common cause of death in women aged 35-50. Before the age of 50 years, at least 65% of women who develop breast cancer do not have a family history and are not currently identified as being at increased risk.

Currently, there is no defined systematic mechanism to identify this group of women. The introduction of breast cancer risk assessment for women aged 30-39 years would allow women to find out their risk of developing breast cancer in the future. Women identified as being at increased risk could then be offered earlier breast screening as well as methods to reduce breast cancer risk. One potential approach is for breast cancer risk assessment and some aspects of risk management to be conducted in primary care.

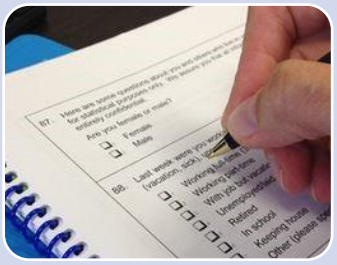
2. What are your immediate thoughts and reactions to offering women the opportunity to find out their breast cancer risk estimate from the age of 30 years?
   Probe: what are your reasons for feeling that way?

3. What are your immediate thoughts and reactions to primary care identifying and inviting women to a breast cancer risk assessment?
   Prompts: should it be primary care's responsibility, how would this be organised – remit of breast screening programme or centrally organised, specialised service

4. What are your immediate thoughts and reactions to primary care involvement in breast cancer risk assessment and management?
   Prompts: how acceptable do you think it would be, what would acceptability depend upon

Probe: what are your reasons for feeling that way?

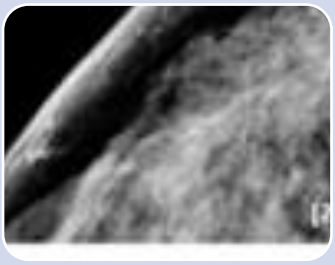
Risk of developing breast cancer is best calculated with a combination of three measures:



Self-reports:

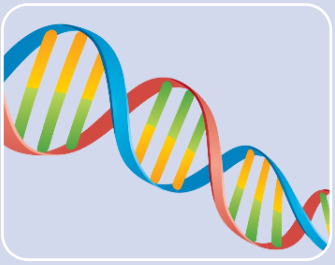
- Height and weight
- Family history of breast & ovarian cancer
- Age at first period
- Age of first pregnancy
- Oral contraceptive history
- Alcohol consumption

Assessment: self-reported questionnaire



Breast density: measure of the amount of non-fatty tissue compared to fatty tissue in the breast

Assessment: mammogram



DNA analysis: polygenic risk scores (combination of multiple common genetic changes into a single score) and mutations in high risk genes (e.g *BRCA1* and *BRCA2*)

Assessment: saliva sample

The following information known to impact breast cancer risk would need to be collected:

- **Height and weight**
- **Family history of breast and ovarian cancer**
- **Age at first period**
- **Age of first pregnancy**
- **Oral contraceptive history**
- **Alcohol consumption**

5. What do you think about primary care collecting information from women about the list of breast cancer risk factors?
   Prompts: family history (how many affected first or second-degree relatives and age of onset), hormonal factors, alcohol consumption
   a. How would you feel about primary care performing this task?
   b. Who would you envisage performing this task at your practice?

Prompts: would any additional staffing be required – primary care or risk prediction specialist, would it be appropriate to ask women to enter their own data

Probe: what are your reasons for feeling that way?

c. What are the key issues/difficulties/barriers to performing this task?
d. What would be required to perform this task successfully?
Prompts: any training/support needs, adaptations to infrastructure, guidelines

One model of how breast cancer risk assessment could work in primary care is the development of a risk assessment tool similar to QRisk. For example, scores for mammographic density and genetic risk could be fed into the tool and a risk score generated once someone in primary care has entered family history, hormonal and lifestyle factors. Primary care would then be responsible for communicating the risk score and making a management plan.

6. What do you think about primary care co-ordinating the process of breast cancer risk assessment in this way?
    a. How would you feel about taking on this role?
    Prompt: would it be appropriate/make sense to be involved in saliva sample collection too
    b. Who would you envisage taking on this role at your practice?
    Prompt: would any additional staffing be required – primary care or risk prediction specialist, who would input the information if women filled in form themselves
    Probe: what are your reasons for feeling that way?
    c. What are the key issues/difficulties/barriers to taking on this role?
    Prompts: would another model work better
    d. What would be required to take on this role successfully?
    Prompts: any training/support needs, design considerations for risk assessment tool (e.g. integration with GP records), guidelines

The output of the tool would also include recommendations for management of increased risk. Two strategies that have proven benefit in reducing breast cancer risk are:

1. **Maintaining a healthy weight through diet and exercise and limiting alcohol intake**
2. **Taking risk-reducing medication such as tamoxifen**

7. What do you think about primary care providing lifestyle advice about reducing breast cancer risk?
    a. How confident do you feel about your practice providing lifestyle advice?
       Prompts: signposting to services – appropriate for breast cancer risk, thoughts on specific (for breast cancer risk) vs generic services (e.g. weight management)
       Probe: what are your reasons for feeling that way?
    b. Do you think there's anything different about providing lifestyle advice with respect to breast cancer risk in comparison with other diseases?
    c. Who would you envisage taking on this role at your practice?
       Prompt: would any additional staffing be required – primary care or risk prediction specialist
       Probe: what are your reasons for feeling that way?
    d. What are the key issues/difficulties/barriers to taking on this role?
    e. What would be required to take on this role successfully?
       Prompts: any training/support needs, adaptations to infrastructure, guidelines

8. What do you think about primary care discussing and prescribing risk-reducing medication such as tamoxifen?
    a. How confident do you feel about your practice discussing and prescribing risk-reducing medication?
       Probe: what are your reasons for feeling that way?
    b. Who would you envisage taking on this role at your practice?
       Prompt: would any additional staffing be required – primary care or risk prediction specialist
       Probe: what are your reasons for feeling that way?
    c. What are the key issues/difficulties/barriers to taking on this role?
    d. What would be required to take on this role successfully?
       Prompts: any training/support needs, adaptations to infrastructure, guidelines

9. Do you think setting up a pathway for breast cancer risk assessment and management activities in primary care is a worthwhile idea? (if not, why not?)
   Prompts: should it be primary care's responsibility, would incentives like QOF points help, could/should it be integrated into existing health checks (e.g. cervical screening)

10. What other issues would be important to consider when setting up a pathway for breast cancer risk assessment and management activities in primary care?

Finishing comments

Thanks for your time today. We do really appreciate it.

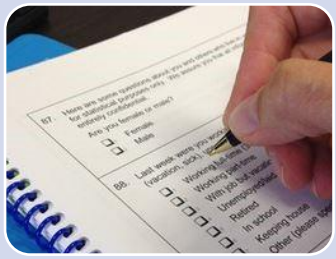
- Is there anything else you want to add?
- Is there anything you thought you would talk about today which you haven't had a chance to say and want to mention?
- What do you think is the most important message coming from this group today?

Appendix B.2: Pre-reading material

Breast cancer becomes more common in women in their 30s and is the most common cause of death in women aged 35-50. Before the age of 50 years, at least 65% of women who develop breast cancer do not have a family history and are not currently identified as being at increased risk.

Currently, there is no defined systematic mechanism to identify this group of women. The introduction of breast cancer risk assessment for women aged 30-39 years would allow women to find out their risk of developing breast cancer in the future. Women identified as being at increased risk could then be offered earlier breast screening as well as methods to reduce breast cancer risk. One potential approach is for breast cancer risk assessment and some aspects of risk management to be conducted in primary care.

Risk of developing breast cancer is best calculated with a combination of three measures:



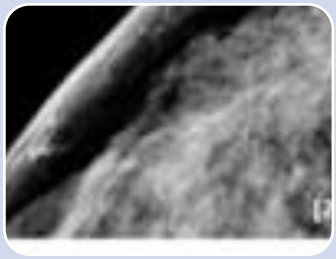
Self-reports:

- Height and weight

Family history of breast & ovarian cancer

- Age at first period
- Age of first pregnancy
- Oral contraceptive history
- Alcohol consumption

Assessment: self-reported questionnaire



Breast density: measure of the amount of non-fatty tissue compared to fatty tissue in the breast

Assessment: mammogram

DNA analysis: polygenic risk scores (combination of multiple common genetic changes into a single score) and mutations in high risk genes (e.g *BRCA1* and *BRCA2*)

Assessment: saliva sample

The following information known to impact breast cancer risk would need to be collected:

- Height and weight
- Family history of breast and ovarian cancer
- Age at first period
- Age of first pregnancy
- Oral contraceptive history
- Alcohol consumption

One model of how breast cancer risk assessment could work in primary care is the development of a risk assessment tool similar to QRisk. For example, scores for mammographic density and genetic risk could be fed into the tool and a risk score generated once someone in primary care has entered family history, hormonal and lifestyle factors. Primary care would then be responsible for communicating the risk score and making a management plan.

The output of the tool would also include recommendations for management of increased risk. Two strategies that have proven benefit in reducing breast cancer risk are:

1. Maintaining a healthy weight through diet and exercise and limiting alcohol intake
2. Taking risk-reducing medication such as tamoxifen

These risk management options would need to be discussed and offered to women identified at increased risk.

Appendix C: Chapter 4 supplementary materials

Appendix C.1: Focus group and interview topic guide

Breast awareness/behaviours

1. What is your understanding of being breast aware?
   - Probe: Can you tell me more about that?

2. How aware and well informed do you think women in your age group are about being breast aware?
   - Prompt: How aware do you think women in your age group are of the current statistics of breast cancer? Remind of stats if needed
   - Probe: Can you tell me more about that?

3. How confident are you in being breast aware?
   - Prompt: What information sources, if any, do you look at for breast health?
   - Prompt: Awareness of what to look for, confidence in carrying out self-examination (behaviours)
   - Probe: What are your reasons for feeling that way?

Acceptability of risk and process of risk assessment

As stated earlier, future breast cancer risk can be measured by completing a risk assessment which combines results from three pieces of information. These three things are a questionnaire, a spit sample and a mammogram (breast x-ray).

4. What's your initial reaction to offering women the opportunity to find out their future breast cancer risk?
   - Prompts: Benefits, concerns, questions
   - Probe: Can you tell me more about that?

5. How would finding out this information make you feel?
   - Probe: What are your reasons for feeling that way?

6. To find out risk, women would need to answer questions about family history of breast & ovarian cancer, hormonal factors such as age at first period and personal information such as weight and number of pregnancies.
   - How would you feel about answering these sorts of questions?
     Probe: What are your reasons for feeling that way?
     Prompt: Mention the different categories of questions if not addressed
   - What could stop women completing the questions?

Prompt: How could these barriers be minimised?
- What could be done to help women complete the questions?
  Prompt: What would be your preferred route (online, telephone etc) for accessing help?

7. To find out risk, women would need to provide a spit sample so that their DNA could be analysed.
   - How would you feel about providing a spit sample?
     Probe: What are your reasons for feeling that way?
   - What could stop women providing a spit sample?
     Probe: How could these barriers be minimised?
   - What could be done to help women provide a spit sample?
     Prompt: What would be your preferred route (online, telephone etc) for accessing help?

8. To find out risk, women would need to have a mammogram (breast x-ray). This will allow assessment of the different types of tissue in the breast which is known to be related to breast cancer risk.
   - How would you feel about having a breast x-ray?
     Probe: What are your reasons for feeling that way?
   - What could stop women attending a breast x-ray?
     Probe: How could these barriers be minimised?
   - What could be done to help women attend a breast x-ray?
     Prompt: What would be your preferred route (online, telephone etc.) for accessing help? How could non-attenders be encouraged to attend?

9. Depending on answers to the questionnaire, completing a breast cancer risk assessment will not be the right option for every woman. In these cases, women will be directed to another healthcare pathway.
   - How would you feel if you were invited but later found out you could not complete a risk assessment?
     Probe: What are your reasons for feeling that way?
   - What could be done to help women in this situation?

Communication of risk

10. Results from the questionnaire, spit sample and breast x-ray will be combined to give a risk score and category.
    - How would you like to receive your risk assessment results?
    - How do you think risk information should be presented?
      Prompts: numerically, graphically, labelling of categories
    - What information would you like in the risk feedback?

Prompt: would the information you like differ according to level of risk received e.g. low vs high?

- If you had any queries about your results, how and with whom would you like to discuss this with?
- What information about your breast cancer risk do you think would be important for your GP to know?

11. Women identified at increased risk of developing breast cancer would be invited to attend an appointment at a risk and prevention clinic. During this appointment, care pathways to reduce breast cancer risk such as earlier access to breast screening and medication to prevent cancer from developing will be discussed.
    - How would you feel about this?
      Probe: What are your reasons for feeling that way?
    - How would you feel about using breast cancer risk to determine access to healthcare pathways?
      Probe: What are your reasons for feeling that way?
      What are your thoughts about risk management strategies such as chemoprevention or lifestyle changes?
      Probe: What are your reasons for feeling that way? Do you believe in prevention?
    - What could stop women attending an appointment at the risk and prevention clinic?
      Prompt: How could these barriers be minimised?
    - What could be done to help women attend the appointment?
      Prompt: What would be your preferred route (online, telephone etc.) for accessing help?

12. Can you think of any additional issues which are relevant for women as they turn 30 which we should consider when designing this breast cancer risk assessment pathway/that might impact engagement with a breast cancer risk assessment programme?

Finishing comments

Thanks for your time today. We really do appreciate it.

- Is there anything else you want to add?
- Is there anything you thought you would talk about today that you haven't had a chance to say and want to mention?
- Do you have any questions for me?

Appendix C.2: Framework matrices

These are available in Figshare at http://doi.org/10.48420/24138876.

Appendix D: Chapter 5 supplementary materials

Appendix D.1: Focus group and interview topic guide

Breast awareness/behaviours

1. What is your understanding of being breast aware?
   - Probe: Can you tell me more about that?

2. How aware and well informed do you think women in your age group are about being breast aware?
   - Prompt: How aware do you think women in your age group are of the current statistics of breast cancer? Remind of stats if needed
   - Probe: Can you tell me more about that?

3. How confident are you in being breast aware?
   - Prompt: What information sources, if any, do you look at for breast health?
   - Prompt: Awareness of what to look for, confidence in carrying out self-examination (behaviours)
   - Probe: What are your reasons for feeling that way?

Acceptability of risk and process of risk assessment

As stated earlier, future breast cancer risk can be measured by completing a risk assessment which combines results from three pieces of information. These three things are a questionnaire, a spit sample and a mammogram (breast x-ray).

4. What's your initial reaction to offering women the opportunity to find out their future breast cancer risk?
   - Prompts: Benefits, concerns, questions
   - Probe: Can you tell me more about that?

5. How would finding out this information make you feel?
   - Probe: What are your reasons for feeling that way?

6. To find out risk, women would need to answer questions about family history of breast & ovarian cancer, hormonal factors such as age at first period and personal information such as weight and number of pregnancies.
   - How would you feel about answering these sorts of questions?
     Probe: What are your reasons for feeling that way?
     Prompt: Mention the different categories of questions if not addressed
   - What could stop women completing the questions?

Prompt: How could these barriers be minimised?
- What could be done to help women complete the questions?
  Prompt: What would be your preferred route (online, telephone etc) for accessing help?

7. To find out risk, women would need to provide a spit sample so that their DNA could be analysed.
   - How would you feel about providing a spit sample?
     Probe: What are your reasons for feeling that way?
   - What could stop women providing a spit sample?
     Probe: How could these barriers be minimised?
   - What could be done to help women provide a spit sample?
     Prompt: What would be your preferred route (online, telephone etc) for accessing help?

8. To find out risk, women would need to have a mammogram (breast x-ray). This will allow assessment of the different types of tissue in the breast which is known to be related to breast cancer risk.
   - How would you feel about having a breast x-ray?
     Probe: What are your reasons for feeling that way?
   - What could stop women attending a breast x-ray?
     Probe: How could these barriers be minimised?
   - What could be done to help women attend a breast x-ray?
     Prompt: What would be your preferred route (online, telephone etc.) for accessing help? How could non-attenders be encouraged to attend?

9. Depending on answers to the questionnaire, completing a breast cancer risk assessment will not be the right option for every woman. In these cases, women will be directed to another healthcare pathway.
   - How would you feel if you were invited but later found out you could not complete a risk assessment?
     Probe: What are your reasons for feeling that way?
   - What could be done to help women in this situation?

Communication of risk

10. Results from the questionnaire, spit sample and breast x-ray will be combined to give a risk score and category.
    - How would you like to receive your risk assessment results?
    - How do you think risk information should be presented?
      Prompts: numerically, graphically, labelling of categories
    - What information would you like in the risk feedback?

Prompt: would the information you like differ according to level of risk received e.g. low vs high?

- If you had any queries about your results, how and with whom would you like to discuss this with?
- What information about your breast cancer risk do you think would be important for your GP to know?

11. Women identified at increased risk of developing breast cancer would be invited to attend an appointment at a risk and prevention clinic. During this appointment, care pathways to reduce breast cancer risk such as earlier access to breast screening and medication to prevent cancer from developing will be discussed.
    - How would you feel about this?
      Probe: What are your reasons for feeling that way?
    - How would you feel about using breast cancer risk to determine access to healthcare pathways?
      Probe: What are your reasons for feeling that way?
      What are your thoughts about risk management strategies such as chemoprevention or lifestyle changes?
      Probe: What are your reasons for feeling that way? Do you believe in prevention?
    - What could stop women attending an appointment at the risk and prevention clinic?
      Prompt: How could these barriers be minimised?
    - What could be done to help women attend the appointment?
      Prompt: What would be your preferred route (online, telephone etc.) for accessing help?

12. Can you think of any additional issues which are relevant for women as they turn 30 which we should consider when designing this breast cancer risk assessment pathway/that might impact engagement with a breast cancer risk assessment programme?

Finishing comments

Thanks for your time today. We really do appreciate it.

- Is there anything else you want to add?
- Is there anything you thought you would talk about today that you haven't had a chance to say and want to mention?
- Do you have any questions for me?

Appendix E: Chapter 6 supplementary materials

Appendix E.1: BCAN-RAY risk feedback letters (average, increased)

INSERT LOGOS

Nightingale Centre, Wythenshawe Hospital
Manchester University NHS Foundation Trust
Southmoor Road
Manchester
M23 9LT
Tel: INSERT NUMBER

INSERT PARTICIPANT NAME
INSERT ADDRESS
INSERT ADDRESS
INSERT ADDRESS

INSERT POSTCODE

Date: **INSERT DATE**

Dear **[INSERT NAME]**,

RE: BCAN-RAY Study
NHS number: INSERT

Thank you for taking part in the BCAN-RAY study. This is your first risk feedback letter. A second letter will follow when the study is complete for all women (probably in 2025). It is possible that the second letter may change your risk level.

We have calculated your risk of developing breast cancer in the next 10 years from the following information collected in this study:

- Breast cancer risk factors as assessed from the information you provided on the risk factor questionnaire
- Breast density (the amount of tissue in your breast that is not fat) as assessed from your mammogram
- DNA as assessed from your saliva (spit) sample

Your risk of developing breast cancer in the next 10 years was calculated to be:

Average for the population – that is less than 3 in 100 chance of developing breast cancer in the next 10 years.

More detailed information about your risk result is given in the enclosed document. This information is also available on the study web-based application, which can be accessed by scanning this QR code:

INSERT QR CODE FOR WEB BASED APPLICATION

We also confirm that no pathological variants (mutations) were identified in the 9 risk genes analysed in your saliva sample DNA.

Further information and support resources

There are things that all women can do to reduce their risk of breast cancer, such as maintaining a healthy weight through diet and exercise and limiting alcohol intake. More information on the ways to reduce your risk is provided in the accompanying leaflet. It is also important to regularly check your breasts and report anything new or unusual to a GP. A guide explaining how to check your breasts is enclosed.

Additionally, you may find the following sources of information and support useful if you have any breast health concerns.

CoppaFeel!

Website: https://coppafeel.org/

Breast Cancer Now

Website: https://breastcancernow.org/

They have a section where you can ask any questions you have relating to breast health:

https://forum.breastcancernow.org/t5/Ask-Our-Nurses/ct-p/Asknurses

They also offer a free, confidential helpline to answer questions about breast cancer or breast health – 0808 800 6000 (Text relay prefix – 18001)

Should you have any questions about the study please get in touch with the study team on INSERT NUMBER.

Yours sincerely,

INSERT SIGNATURE
INSERT NAME

INSERT LOGOS

Nightingale Centre, Wythenshawe Hospital
Manchester University NHS Foundation Trust
Southmoor Road
Manchester
M23 9LT
Tel: INSERT NUMBER

INSERT PARTICIPANT NAME
INSERT ADDRESS
INSERT ADDRESS
INSERT ADDRESS

INSERT POSTCODE

Date: **INSERT DATE**

Dear **[INSERT NAME]**,

RE: BCAN-RAY Study
NHS number: INSERT

Thank you for taking part in the BCAN-RAY study. This is your first risk feedback letter.

A second letter will follow when the study is complete for all women (probably in 2025). It is possible that the second letter may change your risk level.

Your result:

You are at **increased** risk of breast cancer

This means that you are more likely to develop breast cancer than other women your age in the general population.

The details of your 10 year risk and lifetime risk of breast cancer compared to the general population are provided in the attached document and are also available on the study web-based application, which can be accessed by scanning this QR code:

INSERT QR CODE FOR WEB BASED APPLICATION

The factors that may have increased your personal risk were:

- Breast cancer risk factors as assessed from the information you provided on the risk factor questionnaire
- Breast density (the amount of tissue in your breast that is not fat) as assessed from your mammogram
- DNA as assessed from your saliva (spit) sample

At this level of risk you will be eligible to start breast screening earlier than the general population and will have access to breast cancer risk reducing approaches.

Gene mutation search

We did not identify a pathological variant (mutation) in any of the 9 risk genes tested.

OR

We have also identified a pathological variant (mutation) in one of the 9 risk genes tested. We would like to give you the opportunity to discuss the potential implications of this for yourself and your family in more detail and the planned risk review appointment (see below) will be with a geneticist (a doctor who specialises in gene mutations and what they mean for families).

Risk review appointment

We would like to offer you a face-to-face appointment at the Family History Risk and Prevention Clinic at The Nightingale Centre to discuss your risk result further. During this appointment, your breast cancer risk will be explained to you along with information about additional breast screening and when this can begin in addition to ways to reduce your risk.

This appointment is part of NHS care and not part of the study itself. As such, a referral into the clinic will be made by your GP and an appointment will be arranged. This should be within 8-12 weeks so if you have not received an appointment 8 weeks after receiving your risk result, please contact the Nightingale team on **INSERT NUMBER**.

Further information and support resources

There are things that all women can do to reduce their risk of breast cancer, such as maintaining a healthy weight through diet and exercise and limiting alcohol intake. More information on the ways to reduce your risk is provided in the accompanying leaflet. It is also important to regularly check your breasts and report anything new or unusual to a GP. A guide explaining how to check your breasts is enclosed.

Additionally, you may find the following sources of information and support useful if you have any breast health concerns.

CoppaFeel!

Website: https://coppafeel.org/

Breast Cancer Now

Website: https://breastcancernow.org/

They have a section where you can ask any questions you have relating to breast health:

https://forum.breastcancernow.org/t5/Ask-Our-Nurses/ct-p/Asknurses

They also offer a free, confidential helpline to answer questions about breast cancer or breast health – 0808 800 6000 (Text relay prefix – 18001)

Should you have any questions about the study please get in touch with the study team on INSERT NUMBER.

Yours sincerely,

INSERT SIGNATURE
INSERT NAME

Appendix E.2: Detailed description of self-reported measures of potential harms and benefits of participation in breast cancer risk assessment

Measures	Description
State anxiety (36) and cancer worry (37)	To determine whether increased distress is a harm of participating in breast cancer risk assessment, we will compare levels of general anxiety and breast cancer worry between average and increased risk women and across time to evaluate short as well as longer term effects. One might expect changes in distress, particularly amongst women being identified as increased risk, as the result may be unexpected because of a lack of family history of the disease. General state anxiety will be assessed using the six-item short-form of the state scale of the State Trait Anxiety Inventory (STAI) (36), with participants responding to six statements (e.g. "I feel tense") about how they currently feel by selecting one of the following response options "not at all", "somewhat", "moderately" and "very much". Breast cancer worry will be assessed using the Lerman Cancer Worry Scale (37). The scale consists of six statements such as: "how often do you worry about developing breast cancer?". Participants will endorse one of the following response options for items 1-3 and 5: "never", "rarely", "sometimes", and "almost all the time". For items 4 and 6, participants

	select one option from “not at all”, “a little”, “somewhat”, and “a lot”. Both scales have previously been used in similar studies evaluating the psychological impact of receiving breast cancer risk estimates (26, 27).
Risk perception (38)	Perceived comparative risk of developing breast cancer will be assessed using a single item whereby women will be asked to rate their risk of developing breast cancer in the next 10 years, compared with other women of their age (38). Participants will select one of the following response options: “much higher”, “a bit higher”, “about the same”, “a bit lower”, and “much lower”.
Attitudes towards breast cancer risk assessment (39)	Attitudes towards breast cancer risk assessment will be assessed following a standard approach (39). Three items will be used to assess affective (feelings towards the behaviour) and instrumental (evaluation of the behaviour’s outcomes) attitudes. Women will be asked to indicate the extent to which they view risk assessment as good/beneficial/important, with response options including: “entirely good”, “mainly good”, “neither good nor bad”, “mainly bad”, and “entirely bad”.
Knowledge	No validated measure has been developed for the assessment of breast cancer risk assessment knowledge. Therefore, we decided to create a measure focusing on knowledge of the breast cancer risk assessment process to assess the potential benefit of increased knowledge and inform future implementation. The measure is informed by data on potential misunderstandings of the breast cancer risk assessment process identified from a content analysis of qualitative data

	collected in the context of optimising the delivery of breast cancer risk assessment in the BCAN-RAY study (28). The measure consists of three questions that map onto the potential misunderstandings identified, namely eligibility for risk assessment, the purpose of the mammogram and access to screening and preventive strategies. Subjective knowledge will be assessed with a single item that asks women to rate how informed they feel about their breast cancer risk, from "very well informed", "quite well informed", "quite uninformed", and "not very informed at all".
Satisfaction with risk feedback information (40)	Satisfaction with risk feedback information will be assessed using four items from a published scale (40) that has been used previously in breast cancer risk stratification research (26, 27). Women will be asked how well informed they feel about their breast cancer risk, how satisfied they are with the amount of information given, how confusing they found it, and how clear they found the information. Participants will select one of the following response options for each item: "strongly agree", "agree", "agree somewhat", "undecided", "somewhat disagree", "disagree", and "strongly disagree.
Satisfaction with decision to participate in breast cancer risk assessment (41)	Participants' remorse or distress over their decision to take part in breast cancer risk assessment will be assessed using a single item adapted from the Decision Regret Scale (41): "The decision to participate in breast cancer risk assessment was a good decision for me". Response options will be "strongly agree", "agree", "neither agree nor disagree", "disagree", and "strongly disagree".

Appendix E.3: Participant questionnaires (baseline, 6 weeks post risk feedback and 6 months post risk feedback)

Breast **CAN**cer – **R**isk Assessment in **Y**ounger Women **(BCAN-RAY):** Acceptability survey (baseline)

Please enter your unique identifier and date of birth. Your unique identifier can be found on your study invite letter.

Unique study identifier:

Date of birth:

SECTION A – YOUR MENTAL WELL-BEING

A number of statements which people have used to describe how they feel are given below. Please read each of the 6 statements and then circle the most appropriate number below the statement to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

A1 **I feel calm**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A2 **I am tense**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A3 **I feel upset**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A4 **I am relaxed**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A5 **I feel content**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A6 **I am worried**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

SECTION B – YOUR WORRIES ABOUT DEVELOPING BREAST CANCER

Please read the statements below and circle the number below each statement that best indicates your current level of worry about getting breast cancer someday:

B1 **How often have you thought about your chances of getting breast cancer?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B2 **How often have these thoughts affected your mood?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B3 **How often have these thoughts interfered with your ability to do daily activities?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B4 **How concerned are you about the possibility of getting breast cancer one day?**

Not at all	A little	Somewhat	A lot
1	2	3	4

B5 **How often do you worry about developing breast cancer?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B6 **How much of a problem is this worry?**

Not at all	A little	Somewhat	A lot
1	2	3	4

SECTION C – YOUR PERCEPTION OF BREAST CANCER RISK

Please tick **ONE** of the statements below that best describes your breast cancer risk in relation to other women of a similar age:

C1 **Compared to other women my age, I believe my risk of developing breast cancer in the next 10 years is…**

- ❑ Much higher
- ❑ A bit higher
- ❑ About the same
- ❑ A bit lower
- ❑ Much lower

SECTION D – YOUR ATTITUDES TOWARD BREAST CANCER RISK ASSESSMENT

Please read the statement and items below and circle the number that best indicates how you feel about participating in breast cancer risk assessment right now, at this moment:

D1 **Taking part in breast cancer risk assessment will be…**

Entirely good	Mainly good	Neither good nor bad	Mainly bad	Entirely bad
1	2	3	4	5
Entirely beneficial	Mainly beneficial	Neither beneficial nor harmful	Mainly harmful	Entirely harmful
1	2	3	4	5
Entirely important	Mainly important	Neither important nor unimportant	Mainly unimportant	Entirely unimportant
1	2	3	4	5

SECTION E – INTEREST IN INTERVIEW

We would like to hear more about your experience of participating in breast cancer risk assessment as part of the BCAN-RAY study. Please tick one box to indicate whether you are happy to be contacted about participating in an interview (over the phone or face-to-face).

E1 **I am happy to be contacted about participating in an interview following receipt of my risk results**

YES ❑ NO ❑

Thank you for completing this questionnaire.
Please return your completed questionnaire to the study team in the pre-paid envelope provided.

Sources of information and support

You may find some of the following sources of information and support useful if you have any concerns about breast health.

CoppaFeel!

Website: https://coppafeel.org/

They have a section that provides guidance on checking your breasts: https://self-checkout.coppafeel.org/onboarding

Breast Cancer Now

Website: https://breastcancernow.org/

They have a section where you can ask any questions you have relating to breast health:

https://forum.breastcancernow.org/t5/Ask-Our-Nurses/ct-p/Asknurses

They also offer a free, confidential helpline to answer questions about breast cancer or breast health – 0808 800 6000 (Text relay prefix – 18001)

Breast **CAN**cer – **R**isk Assessment in **Y**ounger Women **(BCAN-RAY):** Acceptability survey (6 weeks post risk feedback)

Please enter your unique identifier and date of birth. Your unique identifier can be found on your study invite letter.

Unique study identifier:

Date of birth:

SECTION A – YOUR MENTAL WELL-BEING

A number of statements which people have used to describe how they feel are given below. Please read each of the 6 statements and then circle the most appropriate number below the statement to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

A1 **I feel calm**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A2 **I am tense**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A3 **I feel upset**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A4 **I am relaxed**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A5 **I feel content**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A6 **I am worried**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

SECTION B – YOUR WORRIES ABOUT DEVELOPING BREAST CANCER

Please read the statements below and circle the number below each statement that best indicates your current level of worry about getting breast cancer someday:

B1 **How often have you thought about your chances of getting breast cancer?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B2 **How often have these thoughts affected your mood?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B3 **How often have these thoughts interfered with your ability to do daily activities?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B4 **How concerned are you about the possibility of getting breast cancer one day?**

Not at all	A little	Somewhat	A lot
1	2	3	4

B5 **How often do you worry about developing breast cancer?**

Never	Rarely	Sometimes	Almost all the time
1	2	3	4

B6 **How much of a problem is this worry?**

Not at all	A little	Somewhat	A lot
1	2	3	4

SECTION C – YOUR PERCEPTION OF BREAST CANCER RISK

Please tick **ONE** of the statements below that best describes your breast cancer risk in relation to other women of a similar age:

C1 **Compared to other women my age, I believe my risk of developing breast cancer in the next 10 years is…**

- ❑ Much higher
- ❑ A bit higher
- ❑ About the same
- ❑ A bit lower
- ❑ Much lower

SECTION D – YOUR BREAST CANCER RISK KNOWLEDGE

Please read the statement below and then circle the most appropriate number below the statement to indicate how informed you feel about your breast cancer risk at this moment:

D1 **How informed do you feel about your breast cancer risk?**

Very well informed	Quite well informed	Quite uninformed	Not very informed at all
1	2	3	4

SECTION E – YOUR KNOWLEDGE

For each question please place ONE tick in the box that corresponds with your knowledge/understanding of breast cancer risk assessment being offered in the BCAN-RAY study.

E1 **Who are the intended participants of breast cancer risk assessment in the BCAN-RAY study?**

- ❑ Women who have been told by a healthcare professional that they have a strong family history of breast cancer

❑ Women who have not been told by a healthcare professional that they have a strong family history of breast cancer

E2 **What is the purpose of the low dose mammogram in the BCAN-RAY study?**

❑ To assess breast density (the amount of tissue in your breast that is not fat)

❑ To detect breast cancer

E3 **Who will be given the opportunity to discuss additional breast screening and risk reducing measures with a clinician in the BCAN-RAY study?**

❑ Only women identified as being at increased risk of breast cancer

❑ All women who participate in the study

SECTION F – YOUR PERCEPTIONS OF THE BREAST CANCER INFORMATION ENCLOSED WITH YOUR RISK FEEDBACK

Thinking about the letter and leaflets you received when you were provided with your risk of developing breast cancer in the next 10 years, please read each statement and then circle the most appropriate number below the statement to indicate how you feel about the information *(please circle **only one number**)*.

F1 **I feel well informed about my breast cancer risk.**

Strongly agree	Agree	Somewhat agree	Undecided	Disagree somewhat	Disagree	Strongly disagree
1	2	3	4	5	6	7

F2 **I feel satisfied with the amount of information I have been given.**

Strongly agree	Agree	Somewhat agree	Undecided	Disagree somewhat	Disagree	Strongly disagree
1	2	3	4	5	6	7

F3 **I am confused by the information I have been given.**

Strongly agree	Agree	Somewhat agree	Undecided	Disagree somewhat	Disagree	Strongly disagree
1	2	3	4	5	6	7

F4 **The information was clear.**

Strongly agree	Agree	Somewhat agree	Undecided	Disagree somewhat	Disagree	Strongly disagree
1	2	3	4	5	6	7

Thank you for completing this questionnaire.
Please return your completed questionnaire to the study team in the pre-paid envelope provided.

Sources of information and support

You may find some of the following sources of information and support useful if you have any concerns about breast health.

CoppaFeel!

Website: https://coppafeel.org/

They have a section that provides guidance on checking your breasts: https://self-checkout.coppafeel.org/onboarding

Breast Cancer Now

Website: https://breastcancernow.org/

They have a section where you can ask any questions you have relating to breast health:

https://forum.breastcancernow.org/t5/Ask-Our-Nurses/ct-p/Asknurses

They also offer a free, confidential helpline to answer questions about breast cancer or breast health – 0808 800 6000 (Text relay prefix – 18001)

Breast **CAN**cer – **R**isk Assessment in **Y**ounger Women **(BCAN-RAY):** Acceptability survey (6 months post risk feedback)

Please enter your unique identifier and date of birth. Your unique identifier can be found on your study invite letter.

Unique study identifier:

Date of birth:

SECTION A – YOUR MENTAL WELL-BEING

A number of statements which people have used to describe how they feel are given below. Please read each of the 6 statements and then circle the most appropriate number below the statement to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

A1 **I feel calm**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A2 **I am tense**

Not at all	Somewhat	Moderately	Very much
1	2	3	4

A3 **I feel upset**

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SECTION B – YOUR WORRIES ABOUT DEVELOPING BREAST CANCER

Please read the statements below and circle the number below each statement that best indicates your current level of worry about getting breast cancer someday:

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B4 **How concerned are you about the possibility of getting breast cancer one day?**

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B5 **How often do you worry about developing breast cancer?**

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B6 **How much of a problem is this worry?**

Not at all	A little	Somewhat	A lot
1	2	3	4

SECTION C – YOUR PERCEPTION OF BREAST CANCER RISK

Please tick **ONE** of the statements below that best describes your breast cancer risk in relation to other women of a similar age:

C1 **Compared to other women my age, I believe my risk of developing breast cancer in the next 10 years is…**

- ❑ Much higher
- ❑ A bit higher
- ❑ About the same
- ❑ A bit lower
- ❑ Much lower

SECTION D – YOUR ATTITUDES TOWARD BREAST CANCER RISK ASSESSMENT

Please read the statement and items below and circle the number that best indicates how you feel about participating in breast cancer risk assessment right now, at this moment:

D1 **Taking part in breast cancer risk assessment was…**

Entirely good	Mainly good	Neither good nor bad	Mainly bad	Entirely bad
1	2	3	4	5
Entirely beneficial	Mainly beneficial	Neither beneficial nor harmful	Mainly harmful	Entirely harmful
1	2	3	4	5
Entirely important	Mainly important	Neither important nor unimportant	Mainly unimportant	Entirely unimportant
1	2	3	4	5

SECTION E – YOUR SATISFACTION WITH DECISION TO PARTICIPATE IN BREAST CANCER RISK ASSESSMENT

Please read the statement below and then circle the most appropriate number below the statement to indicate how satisfied you are with your decision to participate in breast cancer risk assessment.

E1 **The decision to participate in breast cancer risk assessment was a good decision for me**

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
1	2	3	4	5

Thank you for completing this questionnaire.
Please return your completed questionnaire to the study team in the pre-paid envelope provided.

Sources of information and support

You may find some of the following sources of information and support useful if you have any concerns about breast health.

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Website: https://coppafeel.org/

They have a section that provides guidance on checking your breasts: https://self-checkout.coppafeel.org/onboarding

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They have a section where you can ask any questions you have relating to breast health:

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They also offer a free, confidential helpline to answer questions about breast cancer or breast health – 0808 800 6000 (Text relay prefix – 18001)

Appendix E.4: Interview topic guide

Opening questions

As you know, we are interested in what women think about the offer of finding out their breast cancer risk as part of the BCAN-RAY study. To start, can you tell me anything about whether breast cancer risk is something you have thought about before being invited to join the BCAN-RAY study?

I understand you were invited to have your breast cancer risk assessed; can we go back to that point and tell me what that was like? What did you think at that point?

How did you make the decision to take part in breast cancer risk assessment?
Prompts:

- Were there are aspects of the BCAN-RAY study that made you question whether to take part (any concerns)?
- Can you tell me anything about why you wanted to know your risk? Anything personal to you?
- How did you receive the invite (as a letter from GP practice if no recall)? What do you think about receiving it that way? How do you think that influenced your decision to have your breast cancer risk assessed?
- (if not already come up) When you were deciding, did you discuss it with anyone (friend / family / study team / GP)?
- Did you feel you had all the information you needed to make a decision about whether to take part? If not, what would have been helpful to know?

Questions relating to risk assessment process

Can you tell me what you had to do once you joined the study? Could you tell me about what happened when you had your breast cancer risk assessed?
Probes: What was it like / can you tell me anything about it
Prompts:

- Completing the risk factors questionnaire e.g. how easy was it to access, can you remember what it was asking you to do, were any questions unclear, ability to answer the questions more generally, did you find any questions uncomfortable to answer, did you get any support to help with this part of the study
- What happened once you completed the questionnaire? What was that time-period like?
- Attending the appointment at the hospital (spit sample, mammogram) e.g. what did you think about how the appointment was arranged
- Waiting for the risk feedback results (6-8 week turnaround) e.g. how were you feeling during this time, what did you think about the length of time you

had to wait, did you look for any information related to breast cancer during this time
- Receiving the risk feedback (a letter if no recall)
- Contents/wording of the letter (thoughts, feelings and understanding) e.g. did the feedback you received match your expectations in terms of what you thought you would be told
- Logging back into the app to view detailed risk feedback (if not, why not)
- Personal meaning of risk category received e.g. what do you remember about your risk result, how would you describe the risk, how do you feel about the factors that contributed to your risk (increased risk), how did it make you feel, was it something you expected, how do you feel about your risk today/now
- Discussing risk feedback with others (friends / family / healthcare professionals)
    - Did you talk about your risk feedback with anyone in the study team / outside the study team? If yes/no, why? What did you discuss?
    - What did you think of the support provided at this point?
- (increased risk) Experience of risk consultation
    - What did you think about the option to receive an appointment to discuss your risk if it was increased?

After you received your risk feedback, did you do anything differently that you thought might reduce your breast cancer risk?
Prompts:
- (all) Health behaviours
- (increased risk) Recommendation to contact medical doctors to discuss risk reducing medication / additional screening
- (increased risk) Deciding whether to have risk reducing medication
- (increased risk) Deciding whether to have additional screening

Looking back, was there anything that caused any concerns during the risk assessment process? Is there anything you would have preferred to happen in a different way?

Looking back, how do you feel about having made the decision to take part in breast cancer risk assessment?
Prompts:
- Did you understand what was involved when you made the decision to participate?
  Probe: did you have sufficient information?

The way breast cancer risk is calculated changes over time as we learn more about new risk factors. As we are trying to find out whether using a low dose mammogram

helps to identify younger women at risk of developing breast cancer, towards the end of the study you will receive updated risk feedback. At this point, your risk might change. What are your thoughts about this? Why?

We are trying to figure out whether introducing a breast cancer risk assessment service for women aged 30 to 39 years is a good or bad idea. What are your thoughts about this? Why? Would you recommend a breast cancer risk assessment service to friends and family members of a similar age?

Finishing comments

Thanks for your time today. We do really appreciate it.

- Is there anything else you want to add?
- Is there anything you thought you would talk about today which you haven't had a chance to say and want to mention?
- Do you have any questions for me?