

# Breast health screening: a UK-wide questionnaire

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## ABSTRACT

**Background** Currently, there is an unmet clinical need in identifying and screening women at high risk of breast cancer, where tumours are often aggressive and treatment intervention is too late to prevent metastasis, recurrence and mortality. This has been brought into sharp focus by the SARS-CoV-2 global pandemic, constantly changing hospital policies and surgical guidelines in reducing access to established screening and treatment regimens. Nipple aspirate fluid (NAF), is thought to provide a unique window into the biological processes occurring within the breast, particularly in the context of a developing neoplasm. Evaluation of NAF in asymptomatic women, for novel chemical biomarkers of either early disease and/or cancer risk offers tremendous promise as a tool to facilitate early detection and to supplement screening. However, its acceptability as a method of collection and screening by women is critical and yet unknown. A breast health questionnaire was disseminated to women through breast cancer charities, patient support groups and social media platforms, with the aim of collecting opinions on the acceptability of use of NAF as a potential screening tool. **Method** Following ethical approval a questionnaire was prepared using online surveys consisting of four parts: (a) introduction on breast health screening in the UK, (b) core demographic data, (c) questions regarding screening and the acceptability of using NAF and (d) opinions about the process of collecting and using nipple fluid for screening. The voluntary and anonymous questionnaire was disseminated through social media, professional networks, charity websites and by individuals between October 2019 and December 2020. Survey responses were collected electronically, and the data analysed using online surveys statistical tools.

**Results** A total of 3178 women completed the questionnaire (65.9% Caucasian, 27.7% Asian/British Asian, 0.6% black and 5.0% other). Of these, 2650 women (83.4%) had no prior knowledge of NAF and 89.4% were unaware that NAF can be expressed in up to 90% of all women. Concerning their risk of breast cancer, 89.8% of women were keen to know their future risk of breast cancer, 8.5% were unsure whether they wanted to know their risk and a further, 1.6% did not want to know. Regarding screening, 944 women (29.8%) were unaware of the lack of routine National Health Service Breast Screening for those under the age of 47 years. Furthermore, 53.0% of women were unaware that mammographic screening is affected by breast density. In terms of the acceptability of home testing for breast health, 92.0% were keen to undergo a home test. Both 79.7% and 70.9% stated they would consider hand massage and a breast pump to acquire nipple fluid samples, respectively.

## What this paper adds

- ▶ The concept of self-testing of nipple fluid, with either hand massage or a breast pump was well received by the majority of women.
- ▶ Public awareness regarding breast screening protocols and limitations of mammography could be improved.
- ▶ Efforts should be made to increase awareness of the benefits of alternative and supplementary tests, especially in the context of high-risk individuals and younger patients.

A further 48.6% of women would consider the use of a hormonal nasal spray for the same purpose. However, with regards to acquiring results from NAF testing, 42.6% of women would prefer to receive results at home and 34.2% in a medical facility. Finally, 91.6% of women believed that breast health should be incorporated as part of school education curriculum.

**Conclusion** Public awareness regarding breast screening protocols and limitations of mammography could be improved. Many women were unaware that NAF might be a useful biofluid for future risk prediction, and yet the concept of self-testing of nipple fluid, with either hand massage or a breast pump was well received. Efforts should be made to increase awareness of the benefits of alternative and supplementary tests, especially in the context of high-risk individuals and younger patients.

## INTRODUCTION

The majority of the 55 000 new breast cancer cases in the UK each year derive from women deemed to be at low or average risk. However, women at high risk constitute ~6% of the female population between 40 and 75 years of age.<sup>1</sup> A relative risk of 3–8, or higher, is defined as high risk and is associated with a plethora of features including significant family history of breast or ovarian cancers,<sup>2</sup> very high breast density and those previously treated for breast and cancer with ≥1% risk of recurrence.<sup>3</sup> While certain high-risk individuals may be identified from attending family genetic clinics, for the vast majority there is no mechanism to quantify breast cancer risk. This is critical, since identification of risk status facilitates adaptation of screening

schedule intensity on the basis that early detection improves survival.<sup>4</sup>

In terms of current screening pathways, in addition to mammograms from the age of 47 years, those at higher risk are offered 12–18 monthly mammograms from the age of 40 years, and MRI screening, which has high sensitivity for breast cancer detection,<sup>5</sup> but which is expensive, time consuming and has its contraindications.<sup>6</sup> Similarly, the diagnostic accuracy of mammography is inferior in premenopausal women (eg, only 30%–48% sensitive).<sup>7–8</sup> This is, in part due to high breast density.<sup>9–10</sup> In addition, although able to detect breast cancer at an early stage, some lobular invasive cancers are notoriously occult on mammography, while other screen-detected cancers may have already metastasised at the time of diagnosis due to their aggressive nature.<sup>11</sup> Moreover, ductal carcinoma in situ (DCIS) constitutes 20%–25% of all cases and if detected results in surgical excision often combined with radiotherapy. However, with such a small percentage of low-grade and intermediate-grade DCIS developing into an invasive carcinoma, overtreatment is a significant concern.<sup>7–12</sup> Radiation exposure may also contribute to an increased incidence in breast cancer, particularly in high-risk populations, rendering mammography unsuitable for more frequent screening.<sup>7–12</sup>

Consequently, there is an unmet clinical need to provide high risk women with a safe, convenient breast health diagnostic and screening tools.<sup>13</sup> Furthermore, in the midst of a SARS-CoV-2 global pandemic, with ever changing hospital policies and surgical guidelines,<sup>14</sup> restrictions being placed on the number of diagnostic modalities offered to patients and the need to avoid unnecessary hospital admissions and surgical intervention—a single non-invasive, screening test to exclude breast carcinoma has become increasingly important and would pave the way towards proactive rather than reactive breast health management.

When considering novel screening tests, there has been a shift towards organ-specific biofluids.<sup>15–17</sup> Exclusive to the breast, nipple aspirate fluid (NAF), is thought to provide a unique window into the biological processes occurring within the mammary ducts, particularly in the context of a developing neoplasm. Evaluation of NAF in asymptomatic women, for novel chemical biomarkers of disease offers tremendous promise as a tool to supplement screening and facilitate early detection, as well as the potential to offer a more tailored personalised risk profile.<sup>17–18</sup> Early work has identified proteins,<sup>17–18</sup> lipids,<sup>19</sup> DNA promotor hypermethylation,<sup>20</sup> hormones and tumour markers,<sup>21</sup> as well as microbiome features<sup>22</sup> that carry diagnostic potential. However, it is acceptability to women as a method of screening is unknown. In terms of the acquisition of NAF, over the years, a variety of methods have been used including: manual breast suction pumps, automated aspiration devices (similar to breast pumps for lactating women),<sup>23</sup> nipple ductoscopy, ductal lavage<sup>24</sup> and manual compression.<sup>25</sup> These techniques carry success rates from 38% to

76%,<sup>26–27</sup> increasing to up to 94% with oxytocin-assisted NAF collection.<sup>28–29</sup>

## AIM

A breast health questionnaire was disseminated to women through breast cancer charities, patient support groups and social media platforms, with the aim of evaluating opinions on the acceptability of use of NAF as a potential screening tool.

## METHODS

The survey was prepared using online surveys (<https://www.onlinesurveys.ac.uk/>) and comprised four parts: (a) introduction on breast health screening in the UK; (b) core demographic data; (c) questions regarding screening and the acceptability of use of NAF and (d) opinions about the process of collecting and using nipple fluid for screening. Having read the background information, respondents were required to consent to participate in the survey. The inclusion criteria encompassed: being 18 years old or over, female, no known diagnosis of dementia and able to understand English. After consenting, respondents created a confidentiality code to protect their anonymity, before proceeding to complete the survey. No personal identifiable information was included to ensure privacy of patients.

The survey was launched in October 2019 and responses collected until December 2020 (<https://bradford.onlinesurveys.ac.uk/breast-health-screening-uk>). It was disseminated through social media (Facebook, Instagram, HealthUnlocked, Mumsnet), charity websites (CRUK, Breast Cancer Now), medical, cancer and professional networks (Bosom Friends, Soroptimists, British Society of Proteomics Research), institution newsletters (University of Bradford) and through correspondence of individuals. The social media platforms of doctors, professional groups and women were used to distribute the survey through all untargeted channels that encouraged participation of healthy women, along with patients with cancer in the past through the CRUK distribution mailing list and website.

Survey responses were electronically collated, processed and analysed using online survey statistical tools. Free text answers were subcategorised into themes and then grouped using Microsoft Excel (Excel 2019, V.16.30). Those respondents who did not consent were excluded from analysis.

## RESULTS

A total of 3178 completed the questionnaire with consent, providing a response rate of 74.0% (4305 respondents interacted with the survey to the point of creating a confidentiality code prior to commencing the survey). Of these, 65.9% were white, 27.7% Asian or British Asian and 5.0% other (undefined). Only 0.6% (19 respondents)

**Table 1** Demographics of patients, including: age, ethnicity, professional qualifications and relationship status

Demographics of respondents	Number of respondents (/3178) (percentage of respondents)
<b>Age (years)</b>	
<20	80 (2.5)
21–30	988 (31.1)
31–40	1693 (53.5)
41–50	247 (7.8)
51–60	87 (2.7)
61–70	61 (1.9)
≥71	11 (0.3)
Prefer not to say	3 (0.1)
<b>Ethnicity</b>	
White	2083 (65.9)
Asian/Asian British	877 (27.7)
Black/African/Caribbean/black British	18 (0.6)
Other	159 (5.0)
Prefer not to say	25 (0.8)
<b>Professional qualification</b>	
Bachelor's degree	1317 (41.6)
Master's degree	532 (16.8)
Professional degree	606 (19.2)
6th Form, A levels or equivalent (diploma)	299 (9.5)
Doctorate degree	192 (6.1)
Secondary school (GCSEs)	91 (2.9)
Trade/technical vocational training	75 (2.4)
Prefer not to say	50 (1.6)
<b>Relationship Status</b>	
Married, domestic partnership	2337 (74.9)
Single, never married	687 (22.0)
Divorced	49 (1.6)
Separated	19 (0.6)
Widowed	9 (0.3)
Prefer not to say	19 (0.6)

were of black African, black American, black British or black Caribbean ethnicity while 0.8% preferred not to say (table 1). In terms of educational background, 2647 women (83.3%), had a higher degree, either in the form of a bachelor's degree (41.6%), a master's degree (16.6%), a professional degree (19.2%) or a doctorate degree (6.1%).

Regarding breast cancer risk, the vast majority of women (89.8%) were keen to know their risk, although a small proportion (8.5%) were unsure whether they wanted to know their risk and very few (1.6%) did not

**Table 2** Summary of questionnaire answers, detailing overall response to non-free text questions

Question	Number of respondents (/3178) (percentage of respondents)	
Would you want to know your risk of breast cancer?	Yes	2850 (89.8)
	No	51 (1.6)
	Not sure	271 (8.5)
Have you heard of nipple aspirate fluid (NAF)?	Yes	392 (12.3)
	No	2650 (83.4)
	Not sure	134 (4.2)
Did you know that NAF can potentially be expressed in up to 90% of all women?	Yes	135 (4.3)
	No	2837 (89.4)
	Not sure	200 (6.3)
Are you aware that currently there is no routine NHS test for breast cancer under the age of 47 years?	Yes	1954 (61.7)
	No	944 (29.8)
	Not sure	271 (8.6)
Do you know that breast density affects the success of mammography testing?	Yes	1284 (40.5)
	No	1679 (53)
	Not sure	205 (6.5)
If the opportunity was given to you, would you like an 'at-home' test for breast health?	Yes	2918 (92)
	No	63 (2)
	Not sure	192 (6.1)
If you were required to produce an NAF sample at home, would you be willing to consider using	Hand massage	2523 (79.7)
	Breast pump	2245 (70.9)
	Hormonal nasal spray	1539 (48.6)
Would testing at home be preferable to testing in a medical facility?	Yes	1884 (59.4)
	No	478 (15.1)
	Not sure	811 (25.6)
Would you prefer to find out the results of a breast health test at home or a medical facility?	At home	1348 (42.6)
	Medical facility	1082 (34.2)
	Not sure	737 (23.3)
Do you think the subject of breast health should be initiated as part of the school education curriculum?	Yes	2903 (91.6)
	No	79 (2.5)
	Not sure	188 (5.9)

NHS, National Health Service.

want to know (table 2). Free text responses revealed that most women wanted to know their risk because of a family history of breast cancer (29.2%), a personal history of breast cancer/previous breast disease (11.5%), or they were undecided between wanting to know their risk and

**Table 3** Summary of free text answers about whether women would want to know their risk of breast cancer, detailing common themes expressed

Themes	Number of responses (/253)	Percentage
<b>Question 3— Would you want to know your risk?</b>		
Family history of breast cancer	61	24.1
Personal history of breast cancer	17	6.7
History of breast disease	7	2.8
Torn between wanting to know and anxiety of knowing	9	3.6
Want to know if high risk/early intervention/increased testing/screening	13	5.1
Would want to know (miscellaneous)	53	20.9
Other comments	49	19.3
No/not sure/anxiety	44	17.4

concern that it would cause undue anxiety especially if there no acceptable treatment (4.3%) (table 3). Respondents who wanted to know did so in order to proactively managing their health, especially since they have known family members or friends who had breast cancer or died from it at a relatively early age (less than 60 years old). For those unsure, it was important for health services to have a support strategy in place should they find out they are at high risk. Those who said no, generally had no family history of breast cancer and therefore saw no reason for unnecessary alarm.

In terms of screening, 1954 women (61.7%) were aware of the lack of routine National Health Service Breast Screening for those under the age of 47 years, with 29.8% stating they were completely unaware. Furthermore, 53.0% of women were unaware that mammographic screening is affected by breast density, with further comments focusing on wanting to reduce the age of screening, drawing on personal experiences of their breast cancer diagnoses and comparisons to breast screening pathways in other countries (both good and bad). Many respondents who were aware of their breast density, were particularly enthusiastic for an alternative screening approach.

The majority of respondents (83.4%) were unaware of nipple fluid production in the breast other than for milk production, and consequently most were also oblivious to the fact that up to 90% of women can express NAF. Free text responses ranged from alarm to curiosity, with many requesting more information. A few commented on having expressed an infrequent discharge but as it did not persist, they ignored it. Many thought that expression of NAF might be restricted to those women who were pregnant (producing colostrum) or had breast fed and some comments reflected a concern that NAF expression might be uncomfortable or even painful.

In terms of the acceptability of home testing for breast health, 92.0% were keen to undergo a home test. Free text comments were subcategorised between the empowerment of a home-based test (citing convenience, flexibility, privacy, safety and timesaving when managing work and family commitments) versus trust in health professionals to

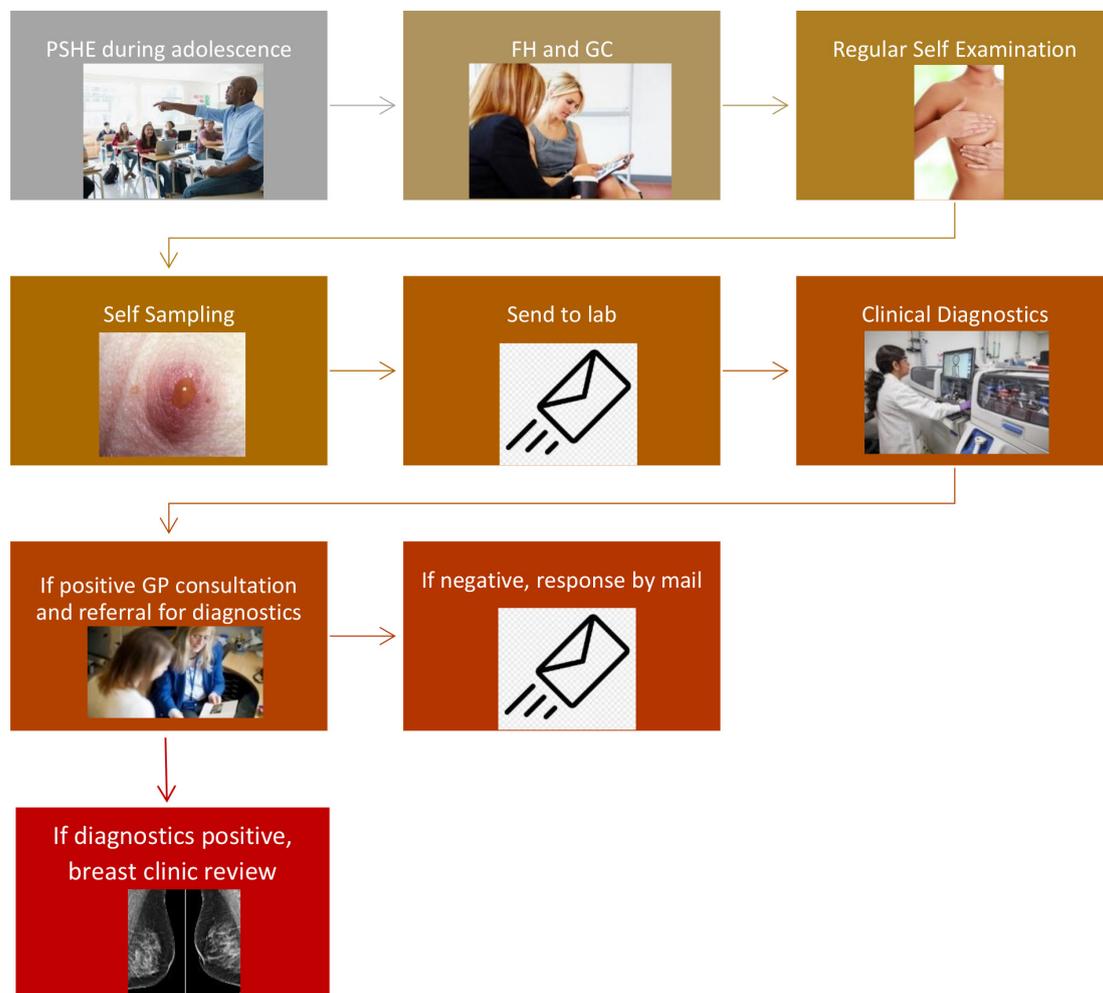
do a better job (in clinic or general practitioner surgery). Some concerns were expressed regarding performing the test correctly, that it needs to be simple, provide an accurate diagnosis and be able to reflect the importance of the result in terms of next steps that is, further investigations, whether surgery was required, or whether the patient could indeed, be discharged. Many observed the benefits of a home test during the SARS-CoV-2 global pandemic rather than screening in a hospital.

79.7% and 70.9%, respectively stated they would consider hand massage and a breast pump to acquire nipple fluid samples, respectively, particularly if the respondent had successfully breast fed in the past. A further 48.6% of women would consider the use of a hormonal nasal spray for the same purpose. A negative response to the hormonal nasal spray approach from some respondents was based on the assumption that it was a steroid administration (whereas it is in fact a peptide, oxytocin, used to assist milk production in mothers with preterm babies) and that further steroid treatments (in addition to the pill and hormone replace therapy) would not be acceptable. However, with regards to acquiring results from home testing, 42.6% of women would prefer to receive results at home, 34.2% in a medical facility and 23.3% were undecided.

Finally, 91.6% of women believed that breast health should be incorporated as part of school education curriculum. Some of those respondents who felt it should not be included based their view on an already full curriculum.

## DISCUSSION

The results of this questionnaire illustrate that overall, a large majority of women (92%) would be keen to try an 'at-home' test, with 80% and 71% willing to trial either manual compression or a breast pump, respectively, to acquire a nipple fluid sample. From this, we demonstrate what appears to be a large shift in mindset following years of mammographic screening within the hospital setting. It can also be concluded that public awareness of at-home test has been raised by the SARS-CoV-2 crisis, whereby home-testing kits have been publicised and implemented



**Figure 1** Summary of pathway for management of breast screening with nipple aspirate fluid. FH, family history; GC, genetic counselling; GP, general practitioner; PSHE, physical and sexual health education.

successfully, with a turnaround time for 48 hours in some cases.<sup>30</sup> Moreover, fear of attending a hospital for a non-urgent test during this time has been substantial.<sup>31</sup> Other home-testing kits such as faecal occult blood testing<sup>32</sup> for colorectal cancer and postal kits for sexually transmitted diseases (STDs) have helped this become the new norm for diagnostic as well as cancer screening tests.<sup>33</sup> Although groups such as Suijkerbuijk *et al*,<sup>29</sup> de Groot *et al*<sup>34</sup> and Proctor *et al*,<sup>27</sup> have conducted questionnaires on patients enrolled in their studies evaluating NAF collection, to the author’s knowledge, this is the first questionnaire of its kind, seeking opinion on the acceptability of acquisition of NAF within the general untested population, focusing on the implementation of home-testing for breast health. Unsurprisingly, knowledge of NAF was limited, with 83% and 89% not having heard of NAF before or unaware that nipple fluid can be expressed in women. This was regardless of age, education or relationship status. Despite this, their willingness to try new methods of testing was significantly higher than those who were not interested, with 92% of women keen to both try this means of testing for breast health and improve baseline knowledge through the introduction of breast education into curriculums.

From this, the conclusions drawn are threefold. First, women are concerned about their risk of developing breast cancer and are willing to go above and beyond current means to reassure themselves. Second, women are aware of the gaps in their own knowledge and understanding and third, there is a desire to change this for future generations.

While exploring the demographic of those who responded to the questionnaire, it was interesting to note that 85.8% of respondents were aged between 21 and 40 years. This reflects the currently ‘unscreened’ population of women. Targeting this cohort of women was considered a strength as it reflects the opinions of future service users, rather than only those who are considering their experience of screening retrospectively, which can carry bias for a number of reasons including personal history of breast disease, family history of breast cancer and of course, their past experience of screening. In addition, 28% of women who completed the questionnaire were of either an Asian or British Asian background. This is disproportionately high compared with the 8% represented within the UK population, and contradicts the engagement barriers often encountered with breast screening services within

these communities.<sup>35</sup> Reasons for high engagement may include: a higher distribution by word-of-mouth through these communities; marketing within doctors' groups on social media, with a larger percentage of Asian followers/subscribers, an ability to express their views anonymously through the survey and an increasing desire to self-educate as the incidence of more aggressive subtypes of breast cancer perpetuate within ethnic minority groups in the western world.<sup>36</sup> Moreover, engagement from these communities in this way demonstrates that the use of social media may enable clinical researchers to connect with populations that have been historically difficult to study.<sup>35</sup> Another important point to note is that only 8% of respondents were aged 41–50 years. This age group includes current screening users, particularly in high-risk groups and it would have been interesting to equally compare differences in opinions between this group and the younger cohort. Screening guidelines for this group differ internationally and therefore future questionnaires would seek to target this group of women to explore their ideas about screening for breast health.

In terms of the response rate, we documented that the number of people who progressed to the point of creating a confidentiality page on the questionnaire, compared with those who went on to complete it, was 74%. An important consideration is that there is no agreed methodology for calculating response rates in questionnaires which have been distributed on social media platforms. This is because, for example, a link to the study posted on a person's account, may then be shared by another person, leading to an exponential and incalculable rise in the number of viewers, making the denominator impossible to calculate. However, validity can be assumed from the large absolute number of responses from the survey. It is rare for surveys of this nature to attract so many responses, with a recent meta-analysis demonstrating that the average response rate in web-based patient-studies is 59.3%.<sup>37</sup> This potential limitation is therefore also one of the greatest strengths of the questionnaire and signifies a change in the way we look at public engagement.

Another key finding was the willingness of participants to improve public knowledge of breast cancer and self-examination through school education (91.6%). Free text answers echoed this, with 12.4% reiterating that education should be for both sexes. This finding reflects the increasing interest in breast health awareness in general, especially when compared with similar diseases such as cervical cancer, vaccinations, STDs and so on. With this in mind, we have suggested a potential pathway for breast education, self-examination and NAF screening, based on responses from the questionnaire (figure 1).

## CONCLUSION

This questionnaire highlights that the concept of self-testing of nipple fluid, with either hand massage or a breast pump, is well received. Public awareness regarding breast screening protocols and limitations of mammography

could be improved, with many women understandably unaware that analysis of nipple fluid might be useful for future risk prediction. The use of social media for public engagement creates endless possibilities for similar research in the future. Efforts should be made to increase awareness of the benefits of alternative and supplementary tests, especially in the context of high-risk individuals and younger patients. Consequently, there is a case to initiate a programme of research to determine the diagnostic value of NAF for the early detection of breast cancer in women at highest risk. Future work would need to further explore the themes identified within this questionnaire in the form of patient interviews. Opinions on methods of collection of nipple fluid, as well as how best to disseminate patient education and improve public awareness across all demographics is the key to improving pathways for breast cancer screening in the years to come.

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**Contributors** NJ: disseminated the questionnaire, cleaned and analysed the data and prepared the draft and revised manuscript. As the guarantor, NJ accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. ZT: prepared the manuscript and provided a supervisory role. DRL: Prepared the draft and revised iterations of the manuscript. He also provided a supervisory role. CS: responsible for overall design, acquired ethical approval, designed and disseminated the questionnaire. He cleaned and analysed the data and prepared the draft and revised iterations of the manuscript. He was overall lead supervisor of project.

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**Data availability statement** Data are available upon reasonable request. The authors are happy to share all data of individual participants with the BMJ if required.

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## REFERENCES

- Public health England. Protocols for surveillance of women at very high risk of developing breast cancer; 2020.
- Cobain EF, Milliron KJ, Merajver SD. Updates on breast cancer genetics: clinical implications of detecting syndromes of inherited increased susceptibility to breast cancer. *Semin Oncol* 2016;43:528–35.
- Robertson C, Arcot Ragupathy SK, Boachie C, et al. The clinical effectiveness and cost-effectiveness of different surveillance mammography regimens after the treatment for primary breast cancer: systematic reviews registry database analyses and economic evaluation. *Health Technol Assess* 2011;15:1–322.
- Saadatmand S, Bretveld R, Siesling S, et al. Influence of tumour stage at breast cancer detection on survival in modern times: population based study in 173,797 patients. *BMJ* 2015;351:h4901.
- DeMartini W, Lehman C, Partridge S. Breast MRI for cancer detection and characterization: a review of evidence-based clinical applications. *Acad Radiol* 2008;15:408–16.
- Mann RM, Balleyguier C, Baltzer PA, et al. Breast MRI: EUSOBI recommendations for women's information. *Eur Radiol* 2015;25:3669–78.
- Drukteinis JS, Mooney BP, Flowers CI, et al. Beyond mammography: new frontiers in breast cancer screening. *Am J Med* 2013;126:472–9.
- DeSantis C, Siegel R, Bandi P, et al. Breast cancer statistics, 2011. *CA Cancer J Clin* 2011;61:408–18.
- Bertrand KA, Tamimi RM, Scott CG, et al. Mammographic density and risk of breast cancer by age and tumor characteristics. *Breast Cancer Res* 2013;15:R104.
- Bertrand KA, Scott CG, Tamimi RM, et al. Dense and nondense mammographic area and risk of breast cancer by age and tumor characteristics. *Cancer Epidemiol Biomarkers Prev* 2015;24:798–809.
- Provencher L, Hogue JC, Desbiens C, et al. Is clinical breast examination important for breast cancer detection? *Curr Oncol* 2016;23:332–9.
- Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology* 2002;225:165–75.
- Ryser MD, Worni M, Turner EL, et al. Outcomes of active surveillance for ductal carcinoma in situ: a computational risk analysis. *J Natl Cancer Inst* 2016;108. doi:10.1093/jnci/djv372. [Epub ahead of print: 17 12 2015].
- Dietz JR, Moran MS, Isakoff SJ, et al. Recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic. The COVID-19 pandemic breast cancer Consortium. *Breast Cancer Res Treat* 2020;181:487–97.
- Widlak MM, Thomas CL, Thomas MG, et al. Diagnostic accuracy of faecal biomarkers in detecting colorectal cancer and adenoma in symptomatic patients. *Aliment Pharmacol Ther* 2017;45:354–63.
- Kumar S, Huang J, Abbassi-Ghadi N, et al. Mass spectrometric analysis of exhaled breath for the identification of volatile organic compound biomarkers in esophageal and gastric adenocarcinoma. *Ann Surg* 2015;262:981–90.
- Shaheed S-ul, Tait C, Kyriacou K, et al. Evaluation of nipple aspirate fluid as a diagnostic tool for early detection of breast cancer. *Clin Proteomics* 2018;15:3.
- Pavlou MP, Kulasingam V, Sauter ER, et al. Nipple aspirate fluid proteome of healthy females and patients with breast cancer. *Clin Chem* 2010;56:848–55.
- Do Canto LM, Marian C, Varghese RS, et al. Metabolomic profiling of breast tumors using ductal fluid. *Int J Oncol* 2016;49:2245–54.
- de Groot JS, Moelans CB, Elias SG, et al. DNA promoter hypermethylation in nipple fluid: a potential tool for early breast cancer detection. *Oncotarget* 2016;7:24778–91.
- Wang G, Qin Y, Zhang J, et al. Nipple discharge of CA15-3, CA125, CEA and TSGF as a new biomarker panel for breast cancer. *Int J Mol Sci* 2014;15:9546–65.
- Chan AA, Bashir M, Rivas MN, et al. Characterization of the microbiome of nipple aspirate fluid of breast cancer survivors. *Sci Rep* 2016;6:28061.
- Zonta M, Velame F, Hyppolito P. The use of halo breast test (Halo Mamo Cito Test) to improve cytology examination of breast nipple aspirate samples reserved in surepath medium. *J Am Soc Cytopathol* 2012;1:S13.
- Tice JA, Miike R, Adduci K. Nipple aspirate fluid cytology and the Gail model for breast cancer risk assessment in a screening population. *Cancer Epidemiology Biomarkers & Prevention* 2005;14:324–8.
- Su S, Tait C, Kyriacou K, et al. Nipple aspirate fluid—a liquid biopsy for diagnosing breast health 2017;11:1700015.
- Shaheed S-U, Tait C, Kyriacou K, et al. Evaluation of nipple aspirate fluid as a diagnostic tool for early detection of breast cancer. *Clin Proteomics* 2018;15:3.
- Proctor KAS, Rowe LR, Bentz JS. Cytologic features of nipple aspirate fluid using an automated non-invasive collection device: a prospective observational study. *BMC Womens Health* 2005;5:10.
- Suijkerbuijk KPM, van der Wall E, van Diest PJ. Oxytocin: bringing magic into nipple aspiration. *Ann Oncol* 2007;18:1743–4.
- Suijkerbuijk KPM, van der Wall E, Meijrink H, et al. Successful oxytocin-assisted nipple aspiration in women at increased risk for breast cancer. *Fam Cancer* 2010;9:321–5.
- Care DoHaS. COVID-19 home test: step-by-step guide (adults and children) 2020.
- Giles GCC. Is it safe to go to hospital or visit my GP—patients want to know 2020.
- Chapple A, Ziebland S, Hewitson P, et al. What affects the uptake of screening for bowel cancer using a faecal occult blood test (FOBT): a qualitative study. *Soc Sci Med* 2008;66:2425–35.
- Cook RL, Østergaard L, Hillier SL, et al. Home screening for sexually transmitted diseases in high-risk young women: randomised controlled trial. *Sex Transm Infect* 2007;83:286–91.
- de Groot JS, Moelans CB, Elias SG, et al. Repeated nipple fluid aspiration: compliance and feasibility results from a prospective multicenter study. *PLoS One* 2015;10:e0127895.
- Woof VG, Ruane H, Ulph F, et al. Engagement barriers and service inequities in the NHS breast screening programme: views from British-Pakistani women. *J Med Screen* 2020;27:130–7.
- John EM, Hines LM, Phipps AI, et al. Reproductive history, breast-feeding and risk of triple negative breast cancer: the breast cancer etiology in minorities (BEM) study. *Int J Cancer* 2018;142:2273–85.
- Meyer VM, Benjamens S, Moumni ME, et al. Global overview of response rates in patient and health care professional surveys in surgery. *Ann Surg* 2020;Publish Ahead of Print.