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¹ Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

² Oxford University Hospitals NHS Foundation Trust, Oxford, UK

³ Cancer Sciences, University of Southampton and University Hospitals Southampton, Southampton, UK

⁴ Nuffield Department of Population Health, University of Oxford, Oxford, UK

⁵ Department of Breast Surgery, St James's Hospital, Leeds, UK

⁶ Division of Cancer Sciences, School of Medical Sciences, University of Manchester, Manchester, UK

⁷ Nightingale Breast Centre, Manchester University NHS Foundation Trust, Manchester, UK

⁸ Independent Cancer Patients' Voice, London, UK

Correspondence to: T Gathani
toral.gathani@ndph.ox.ac.uk

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Age and sex can predict cancer risk in people referred with breast symptoms

Toral Gathani and colleagues argue that risk stratification by age and sex should be used to help manage demand on breast clinics efficiently to minimise delays in diagnosis

Toral Gathani,^{1,2} Ramsey Cutress,³ David Dodwell,^{2,4} Kieran Horgan,⁵ Cliona Kirwan,^{6,7} Hilary Stobart,⁸ Sau Wan Kan,¹ Gillian Reeves,¹ Sian Sweetland¹

Breast cancer is the most common malignancy in women globally.¹ Improvements in breast cancer survival over several decades are partly attributed to population based breast screening programmes and rapid access to specialist diagnostic services for patients with breast symptoms. These facilitate diagnosis at early stages and prompt access to treatment. Even delays as short as a month in diagnosis and starting treatment can be associated with poorer outcomes.²⁻⁴

Population based breast screening programmes have been the subject of much international comparison, investigation, and debate. However, less is known about the performance of healthcare services that assess women and men referred from primary care with symptoms that may indicate breast cancer, even though these services identify a large proportion of people with breast cancer. In England, six out of 10 people with breast cancer are diagnosed after referral with symptoms.⁵

Services for breast symptoms are under increasing pressure. Over five million people with breast symptoms have been referred for urgent or routine assessment over the past decade in England, making it the highest volume cancer referral service in the NHS.⁶ With such high overall volumes, small mismatches between capacity and demand rapidly lead to large numbers of patients waiting for assessment and may delay the diagnosis of breast cancer in some patients. In 2021-22, four out of 10 patients referred urgently or routinely waited longer than the recommended 14 days for assessment, the lowest performance for timely assessment among all cancers.⁷

The challenge of managing the volume of referrals has led to calls for a review of breast services, including the development and evaluation of safe models of care for patients who are at low risk of cancer.⁸⁻¹⁰ Drawing on data from the NHS in England, we argue that age and sex, as key predictors of a breast cancer diagnosis, can be used to optimise the efficient use of finite resources.

Breast service under pressure

In England, women and men presenting to primary care with breast symptoms are referred to rapid access breast clinics in secondary care for further assessment (box 1). Those known to be at high risk because of family history or presence of predisposing BRCA gene mutations are usually offered annual screening. Similar models exist in Scotland, Wales, Northern

Ireland, several other European countries, Canada, and New Zealand.¹³⁻¹⁵

Box 1: Referral guidance, quality statements, and performance standards for breast cancer services in 2022

NICE guidance on recognition and referral of suspected breast cancer (2015)¹¹

- *Urgent referral criteria*
- Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer if they are:
 - Aged ≥ 30 and have an unexplained breast lump with or without pain or
 - Aged ≥ 50 with any of the following symptoms in one nipple only:
 - Discharge
 - Retraction
 - Other changes of concern
- Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer in people:
 - With skin changes that suggest breast cancer or
 - Aged ≥ 30 with an unexplained lump in the axilla
- *Routine referral criteria*
- Consider non-urgent referral in people aged < 30 with an unexplained breast lump with or without pain

NICE breast cancer quality statements (2016)¹²

- *Quality statement 1: Timely diagnosis*
- People with suspected breast cancer referred to specialist services are offered the triple diagnostic assessment in a single hospital visit

Cancer waiting time performance standards for assessment and diagnosis

- *Time to assessment (introduced 2009)*
- 93% of patients referred urgently with suspected cancer symptoms or patients referred routinely for investigation of breast symptoms, even if cancer is not initially suspected, to see a specialist within 14 days of referral
- *Faster diagnosis standard (for implementation 2023-24)*
- 75% of patients referred urgently with suspected cancer symptoms or patients referred routinely for investigation of breast symptoms, even if cancer is not initially suspected, to have a cancer diagnosis confirmed or excluded within 28 days of referral

The internationally accepted model for assessment of breast symptoms is a combination of clinical examination, breast imaging (mammography or ultrasonography, or both), and, when indicated, needle biopsy.⁴ In the UK, this assessment is usually done in a single visit to a hospital breast clinic.¹² The model is associated with high levels of patient satisfaction¹⁶ but is resource intensive and challenging because of workforce shortages across the required specialty roles.¹⁷

The number of referrals to breast clinics has increased over the past decade, largely driven by urgent referrals. In 2021-22, nearly 500 000 people were referred urgently to the breast service (roughly 20% of all urgent cancer referrals), and around 150 000 were referred for routine assessment.⁷ The number of annual urgent breast referrals more than doubled from 185 601 to 433 306 between 2009-10 and 2019-20, while the proportion of these referrals that resulted in a cancer diagnosis halved (10.5% to 5.5%).⁶ Over the same time, the volume of routine referrals has remained around 150 000, with a consistently lower cancer diagnosis rate (<2%) (fig 1).

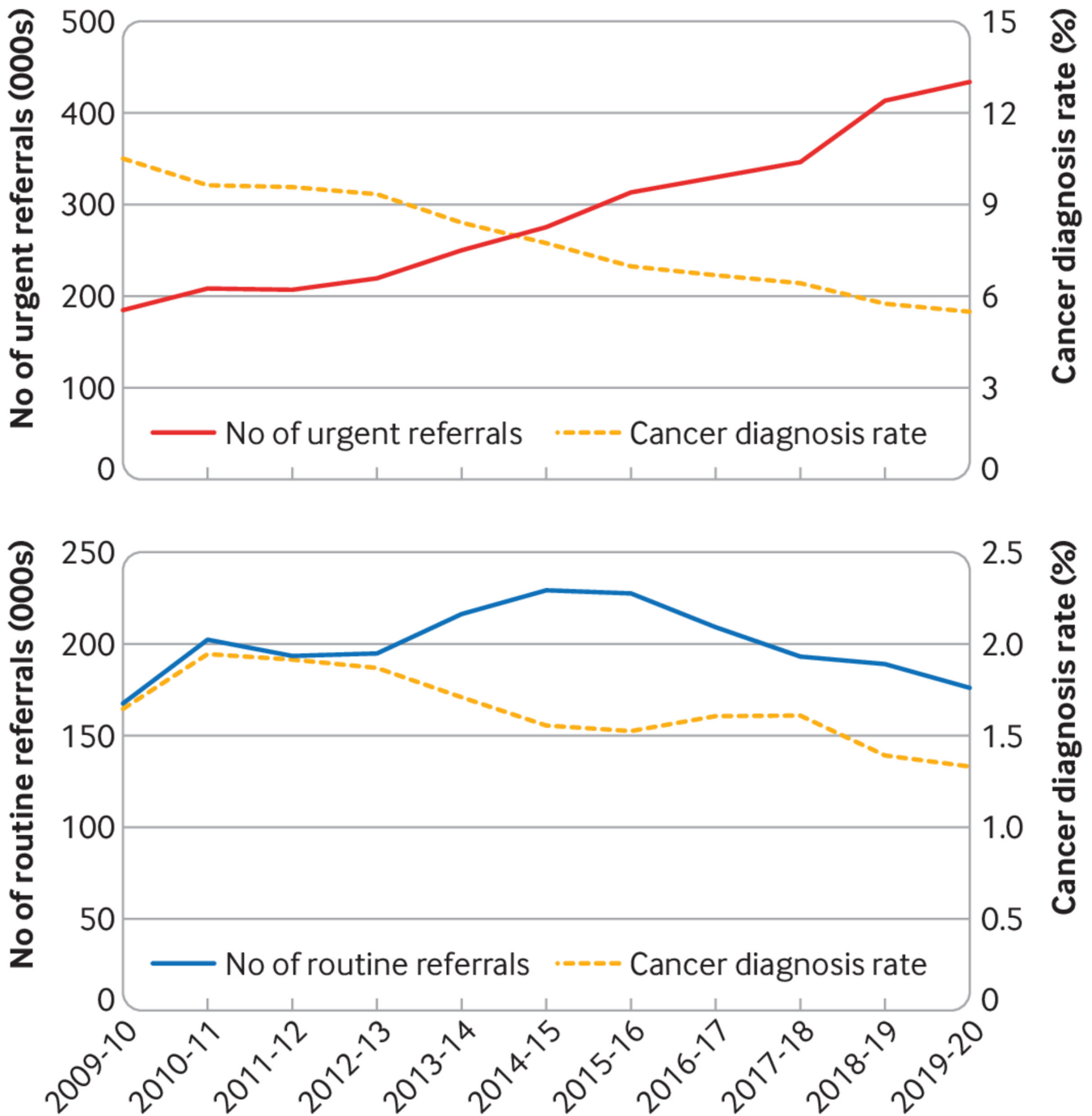


Fig 1 | Rates of cancer diagnosis among people referred for urgent and routine assessment, 2009-20⁶

Urgent referrals increased steeply after 2015, especially in women and men aged 30-59 (fig 2).⁶ One factor behind this rise is almost certainly the referral guidance published that year by the National Institute for Health and Care Excellence (NICE),¹¹ which advises that patients should be referred urgently if their risk of breast cancer is considered to be over 3% (box 1).¹¹ Although the guidance recognised that the 3% risk threshold could lead to increased referral

volumes, service pressures, and possible over-investigation, these concerns were justified by the potential benefit of expediting breast cancer diagnoses.^{18 19} Other factors that may have influenced referral patterns include national breast cancer awareness campaigns^{20 21} (which are relatively untargeted), fear of diagnostic delay and subsequent potential litigation among healthcare professionals, and patient perceptions of their cancer risk.²²

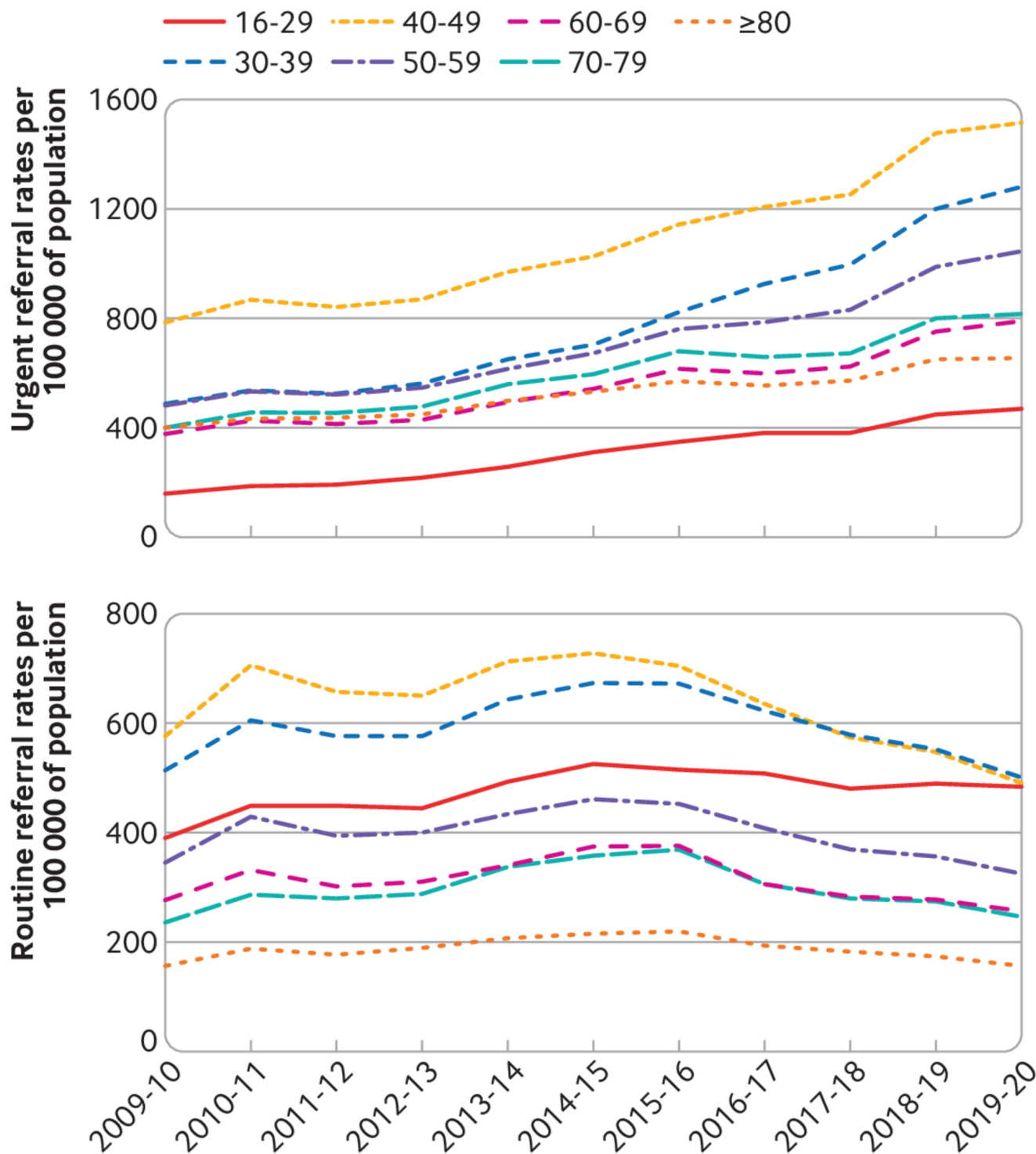


Fig 2 | Urgent and routine referrals for suspected breast cancer in England by age, 2009-20⁶

In April 2023, the NHS introduced the 28 day faster diagnosis standard to replace the 14 day target for time to specialist assessment after referral with breast symptoms (referred urgently or routinely).²³ Setting a target for time to diagnosis rather than initial assessment is clinically beneficial and also provides an opportunity to introduce flexibility in timescales to assessment for different groups of patients.

Risk adapted approach using age and sex

Several changes have been proposed to support breast clinics to deliver timely assessment for those referred with breast symptoms. Existing initiatives to expand the multidisciplinary workforce—for example, by recruiting more advanced clinical practitioners for assessment²⁴ and training radiologists through the national breast imaging academy²⁵—are likely to continue and be scaled up. Wider national recruitment and retention challenges for consultants in breast radiology and pathology are recognised.

Efforts to fortify the healthcare workforce are essential but will not alleviate pressure on the breast symptomatic service in the short term.¹⁷ Other approaches to managing the volume of referrals in the short term based on presenting symptoms are being evaluated.

However, symptom based approaches have limited effect because symptoms that are individually considered low risk (eg, breast pain) are often associated with higher risk symptoms such as a lump or nodularity.²⁶ National data on referral and cancer diagnostic rates by age and sex suggest an alternative approach to assessing risk that could be used to alleviate pressure on the service while longer term structural changes are under way.

The low cancer diagnosis rates among some patient subgroups who are urgently referred highlight the limitations of, and lack of compliance with, existing guidance (table 1). For example, roughly 50% of referrals of women aged under 30 are classed as urgent, but these women have a low cancer diagnosis rate (<0.5%). For these young women, referral on a suspected cancer pathway can cause anxiety and over-investigation.¹⁰ Similarly, men represent 5% of all referrals to breast clinics. Two thirds of these men are referred urgently but have a breast cancer diagnosis rate of <3% across all age groups. By contrast, women older than 70 years of age have a cancer diagnosis rate of >4% even when referred routinely. Women in this age group account for one in three breast cancer diagnoses and have a more advanced stage at diagnosis and experience poorer outcomes.²⁷

Table 1 | Urgent and routine referrals and cancer diagnosis rates for breast cancer by age among women and men in England in 2019-20*

Sex and age (years)	No (%) of referrals	No (%) diagnosed with cancers	Referral rate/100 000	Cancer diagnosis rate (%)
Urgent referrals				
Women:				
All	411 836	23 514	1753	5.7
<30	43 210 (10.5)	123 (0.5)	853.0	0.3
30-39	93 225 (22.6)	1398 (5.9)	2458.5	1.5
40-49	105 262 (25.6)	4116 (17.5)	2931.6	3.9
50-59	75 403 (18.3)	4107 (17.5)	1962.8	5.4
60-69	43 190 (10.5)	3643 (15.5)	1426.1	8.4
70-79	35 081 (8.5)	5046 (21.5)	1409.4	14.4
≥80	16 465 (4.0)	5081 (21.6)	977.5	30.9
Men:				
All	21 473	232	95.0	1.1
<50	8544 (39.8)	23 (9.9)	67.8	0.3
50-59	3792 (17.7)	33 (14.2)	101.5	0.9
60-69	3557 (16.6)	48 (20.7)	123.5	1.3
70-79	3466 (16.1)	82 (35.3)	155.4	2.4
≥80	2 114 (9.8)	46 (19.8)	183.4	2.2
Routine referrals				
Women:				
All	164 906	2301	702.0	1.4
<30	43 601 (26.4)	76 (3.3)	860.7	0.2
30-39	36 124 (21.9)	150 (6.5)	952.7	0.4
40-49	33 641 (20.4)	458 (19.9)	936.9	1.4
50-59	23 405 (14.2)	418 (18.2)	609.3	1.8
60-69	13 963 (8.5)	333 (14.5)	461.0	2.4
70-79	10 460 (6.3)	450 (19.6)	420.2	4.3
≥80	3712 (2.3)	416 (18.1)	220.4	11.2
Men:				
All	10 837	30	47.9	0.3
<50	6493 (59.9)	3 (10.0)	51.5	0.0
50-59	1281 (11.8)	7 (23.3)	34.3	0.5
60-69	1208 (11.1)	6 (20.0)	41.9	0.5
70-79	1187 (11.0)	10 (33.3)	53.2	0.8
≥80	668 (6.2)	4 (13.3)	58.0	0.6

* Data from the National Cancer Registration and Analysis Service. Population denominators are the numbers of women and men aged ≥16 years and resident in England from the Office of National Statistics Census 2011.

These data confirm there are groups of people with an overall risk of cancer diagnosis of <3%, for whom routine referral is compliant with current guidance. Based on national data for 2019-20 (table 1), referring women younger than 30 years of age and all men on routine pathways would result in nearly 65 000 fewer urgent referrals annually. If all women older than 70 years of age were referred urgently, this would add around 14 000 urgent referrals each year, resulting in a net transfer of 50 000 urgent referrals to routine referrals.

The April 2023 change in emphasis to diagnosis within 28 days rather than assessment within 14 days provides an opportunity to introduce flexibility in the timescales for specialist assessment for different patient groups.²³ A risk adapted approach could reduce time to diagnosis for those at highest risk of breast cancer by prioritising their assessment. For example, women older than 70 could be offered appointments within a week of referral, while lower risk younger women and men could be assessed less urgently but still within the 28 day diagnosis standard. This would alleviate

pressures in the existing service and adhere to the 3% cancer risk threshold for urgent referrals. Surveillance and management of people at increased risk of breast cancer because of family history or predisposing genetic variants would continue through separate services.

Risk adapted approaches have potential downsides. For example, breast cancer awareness campaigns advocate urgent assessment of breast symptoms at all ages. Prioritising appointments based on age and sex as key determinants of breast cancer risk would contrast with this messaging. It could also exacerbate diagnostic delays among the small number of young women at low risk of a cancer diagnosis and increase fear and anxiety among those waiting longer for assessment, albeit within the 28 day faster diagnosis standard.

Improving timely diagnosis

Ultimately, adequate resources are needed to invest in and expand the healthcare workforce for long term sustainability in breast care. In the short term, however, a coordinated effort to improve time to

diagnosis for people referred with breast symptoms would start with an update of national referral guidance to further differentiate between high and low risk patient groups. Specifically, all men and women younger than 30 with breast symptoms should be referred routinely, whereas all women older than 70 should be referred urgently. All patients should be assessed and receive a diagnosis within 28 days, but breast clinics could prioritise appointments by age and sex—for example, offering older women earlier appointments for assessment.

The development and delivery of consistent public health messages about low risk of breast cancer in men and the differences in risk between women of different ages requires coordinated action of relevant professional groups and representatives from patients, the public, and third sector organisations. This work must be supported by existing evidence and regularly evaluated to provide reassurance of safety for patients and practitioners.

Clear and transparent mechanisms for ongoing evaluation of referral patterns and patient outcomes will also be necessary. These evaluations should be led by the professional groups involved in the delivery of the service and would need to include measures of service activity and performance as well as the collation and analysis of user experience feedback. For example, existing patient experience surveys could be expanded to include patients who are found not to have breast cancer to provide information about the acceptability of the proposed changes.²⁸ Regular evaluation should ensure the early identification of increases in diagnosis times for the low risk patient groups and allow for subsequent mitigation.

Increasing referral numbers are challenging the capacity of breast clinics in England. It is critical to address the potential fears of patients who might experience longer waiting times and to ensure that mechanisms for evaluation of implementation are in place. The importance of age and sex in predicting a diagnosis of breast cancer merits greater consideration to improve efficiency in secondary care breast services safely.

Key messages

- Breast cancer is the most common malignancy in women globally
- In England, over a third of hospital trusts are failing to meet national targets for timely assessment of women and men referred with breast symptoms
- Breast cancer diagnosis rates vary by age and sex among patients with breast symptoms, and these factors could be better used to optimise the use of finite resources
- Non-urgent referral of people with a risk of a cancer diagnosis consistently under 3% could allow prioritisation of those with higher risk

Contributors and sources: TG, RIC, DD, CK, and KH are clinical academics and have wide collective experience of breast health services research and delivering secondary care breast services. TG, GR, SWK, and SS are epidemiologists and data analysts and have wide experience in using routinely collected national data for research purposes. TG conceived the idea and wrote the manuscript. SWK and SS extracted the data used in the article and prepared the table and figures. All authors reviewed and contributed to the final article.

Public and patient involvement: Hilary Stobart, as a coauthor, and Lesley Turner provided input from their experience as breast cancer patients and are members of Independent Cancer Patients' Voice (ICPV).

Competing interests: We have read and understood BMJ policy on declaration of interests and have the following interests to declare. TG is a member of the Academic and Research Committee for the Association of Breast Surgery, the Clinical Advisory Panel for Cancer Research UK, and National Audit of Primary Breast Cancer Audit Advisory Committee. RIC is a trustee and chair of the Academic and Research Committee for the Association of Breast Surgery, a committee member for the National Institute for Health and Care Excellence, joint lead investigator for the EndoNET Trial, and has received research support from SECA and Astra-Zeneca. DD and KH are the oncology and surgical leads for the National Audit of Primary Breast Cancer. KH is the chair of the EndoNET Trial Steering Committee. GKR

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