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Research Paper

Mastectomy patterns among older women with early invasive breast cancer in England and Wales: A population-based cohort study

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ABSTRACT

Introduction: Older women with early invasive breast cancer (EIBC) are more likely to receive a mastectomy compared with younger women. This study assessed factors associated with receiving a mastectomy among older women with EIBC, with a particular focus on comorbidity and frailty.

Materials and Methods: Women diagnosed with EIBC (stages I-IIIa) aged ≥50 years from 2014 to 2019 in English and Welsh NHS organisations who received breast surgery were identified from cancer registration datasets linked to routine hospital data. Separate multivariable logistic regression models explored factors associated with mastectomy use, within each tumour stage (T1-T3). For each tumour stage, risk-adjusted rates of mastectomy were calculated for each NHS organisation and displayed using funnel plots.

Results: We included 106,952 women with EIBC: 23.4% received a mastectomy as their first breast cancer surgery. Receipt of mastectomy was more common among patients with a higher tumour stage (T1: 12.3%; T2: 37.6%; T3: 77.5%), and mastectomy use increased with age within each tumour stage category (50–59 vs 80 + years: 11.8% vs 26.3% for T1; 31.5% vs 56.9% for T2; 73.4% vs 90.3% for T3). Results from a multivariable regression model showed that more severe frailty was associated with mastectomy use for women with T1 ($p = 0.002$) or T2 ($p = 0.003$) tumours, but may not be for women with T3 tumours ($p = 0.041$). There was no association between comorbidity and mastectomy use after accounting for frailty (all $p > 0.1$). Adjusting for clinical and patient factors only slightly reduced the association between age and mastectomy use. Variation in mastectomy use between NHS organisations was greatest for women with T2 EIBC (unadjusted range: 17.7% to 68.4%).

Discussion: Older women with EIBC are more commonly treated with mastectomy. This could not be explained by tumour characteristics or physical fitness, raising questions about whether surgical decision-making inconsistently incorporates information on patient fitness and functional age.

1. Introduction

Surgical options for early invasive breast cancer (EIBC) include breast conserving surgery (BCS), where the tumour is excised along with a margin of breast tissue, or a mastectomy, involving removal of the whole breast. Randomised controlled trials (RCTs) have demonstrated BCS followed by post-operative radiotherapy has equivalent local recurrence rates and long-term survival compared with mastectomy [1–5].

The decision to offer BCS or mastectomy is influenced by multiple factors [6], including characteristics of the breast cancer tumour, patient preferences [7], availability of healthcare resources such as access to immediate breast reconstruction [8], and local surgical practice [9].

UK guidelines from the National Institute for Health and Care Excellence do not make recommendations on type of initial surgery [10] but the European Society for Medical Oncology guidelines for early breast cancer state BCS is the preferred treatment option for most patients [11]. According to the 2021 Getting It Right First Time

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Programme report on breast surgery in England, between 2015 and 2018, 68.5% of patients who had surgery for breast cancer received BCS as their initial operation [12].

When discussing surgical options with older patients, clinicians must balance the desire to perform the most suitable oncological operation with other factors including perioperative morbidity, patient preference, the risk of needing further surgery for incomplete excision and the need for radiotherapy. Previous reports from the US [13] and UK [14] suggest older women are more likely to receive a mastectomy as their initial operation compared with younger women. This may be due to older women presenting with larger tumours, or patient choice to avoid radiotherapy [15]. Studies have also reported that higher levels of existing comorbidity are associated with greater use of mastectomy which may be associated with a desire to decrease the risk for further excisional surgery [13,16–18]. Differences in surgical treatment by age require investigation, as women who receive mastectomy compared with BCS are reported to have worse body image [19] and higher rates of major post-operative complications [20]. Decision-making for treatment should not be guided by chronological age alone but should consider competing risks of mortality such as frailty and comorbidity, alongside the risk of breast cancer recurrence [11,21].

The objectives of this study are to understand the factors associated with receipt of mastectomy among older women with EIBC in England and Wales, with a particular focus on age, comorbidity, and frailty; and to assess variation in mastectomy rates between NHS (National Health Service) organisations.

2. Methods

This study was performed as part of the National Audit of Breast Cancer in Older Patients (NABCOP), a national clinical audit which investigated the treatment and outcomes of older women (≥70 years) compared with younger women (50–69 years). The NABCOP received pseudonymised patient and tumour-level data for women ≥50 years newly diagnosed with breast cancer from 2014 to 2019 in England and Wales, from the National Cancer Registration and Analysis Service and the Wales Cancer Network respectively. National cancer registration data provided information on patient demographics and tumour details. The cancer registration dataset was linked to other national datasets, including the Cancer Outcomes and Services Dataset (England only), hospital admissions data (Hospital Episode Statistics [HES] in England; Patient Episode Database for Wales [PEDW]), radiotherapy treatment data (national radiotherapy dataset in England; Cancer Network Information System Cymru [Canisc] in Wales), and chemotherapy treatment data (Systemic Anti-Cancer Therapy dataset in England; Canisc in Wales). Linked mortality information (vital status, date, and cause of death) was provided from the Office for National Statistics death register. This study was exempt from NHS Research Ethics Committee approval because it involved analysis of pseudonymised linked data collated for the purpose of service evaluation as part of the NABCOP. Further information on specific inclusion criteria for the NABCOP can be found in the Annual Reports and methodology documents [22,23]. The NABCOP has approval for processing health care information under Section 251 (reference number: 16/CAG/0079).

2.1. Patient Population

This study included women who met the following criteria: (1) aged ≥50 years diagnosed with EIBC (overall stage I-IIIa) in England and Wales between 1 January 2014 and 31 December 2019, (2) received breast surgery in NHS organisations, and (3) date of surgery was at least seven days, and no more than 12 months, after the date of diagnosis.

Women were excluded if they (1) died within least 31 days of the date of surgery, or (2) had missing or incongruent values in key variables (tumour stage and size, nodal stage, estrogen receptor [ER] status, human epidermal growth factor receptor 2 [HER2] status, tumour grade, comorbidity index, referral source).

2.2. Definition of Study Variables

Women were classified into groups according to the type of first breast operation (BCS or mastectomy) recorded within HES/PEDW. If a patient received mastectomy after BCS, they were recorded as having received BCS (the 'intention to treat' principle). Within HES/PEDW, admissions for surgical procedures were identified using the OPCS Classification of Interventions and Procedures (OPCS-4) codes for BCS, mastectomy, axillary surgery and breast reconstruction (Table S1). Women were classified as having received immediate breast reconstruction (IR) when the date of mastectomy and date of reconstruction matched. Neoadjuvant chemotherapy (NACT) was defined as chemotherapy which began within six months of diagnosis and occurred before the date of initial surgery. Referral source was categorised as screened and non-screened.

Patient demographics included age, deprivation level, comorbidities, and level of frailty. Deprivation was defined using the Index for Multiple Deprivation (IMD), which is a measure of deprivation at a local area level in England and Wales [24,25]. Based on their IMD score, local areas were assigned to national deprivation quintiles with Q1 being the most deprived and Q5 the least. The Royal College of Surgeons of England Charlson Comorbidity Index (CCI) was used to identify specific comorbidities and is based on International Classification of Diseases 10th Revision (ICD-10) codes within inpatient HES/PEDW records at diagnosis or in the two years prior to diagnosis [26]. The Secondary Care Administrative Records Frailty (SCARF) index, which maps 'deficits' to ICD-10 codes within the HES/PEDW datasets, was used to assess frailty. The SCARF index is also derived from records that occurred within two years prior to diagnosis [27].

Tumour characteristics included tumour stage (T1-T3), nodal stage (N0−N2), whole tumour size (<1 cm, 1–1.99 cm, 2–4.99 cm, ≥5 cm), grade (G1-G3), ER status (positive [including borderline], negative) and HER2 status (positive, borderline, negative). Pre-treatment information on individual tumour, nodal and metastasis stage was used where available (proportion of patients in final cohort with pre-treatment information: T stage 37.4%; N stage 37.1%, M stage 37.0%). Where data existed, biopsy and cytology results were used to define grade and ER/HER2 status. For patients who did not have pre-treatment, biopsy or cytology information, final pathology results were used. Tumour size was available as whole tumour size (final pathology).

2.3. Statistical Analysis

The primary outcome for analysis was receipt of mastectomy. Descriptive statistics summarised the percentage of patients who received mastectomy according to patient, tumour, and treatment factors, stratified by tumour stage (T1-T3). The Cochran-Armitage trend test was used to examine if mastectomy rates had changed over time.

A multivariable logistic regression model was used to investigate the relationship between use of mastectomy and all relevant variables (age, SCARF index, CCI, IMD, referral source, nodal stage, ER status, HER2 status, grade, receipt of NACT, year of diagnosis). Separate models were fitted to the data in each tumour stage group, to understand the determinants of mastectomy among women with different invasive tumour sizes. Age was included in the model as a restricted cubic spline, with knots placed at the 1st, 50th and 90th percentiles of age for each tumour stage. Model discrimination and calibration were assessed using the area under the receiver operating characteristic (ROC) curve, and a plot of observed versus expected values, respectively [28].

Further analyses explored the impact of age on mastectomy use. First, the percentage of women who received a mastectomy according to tumour stage and age at diagnosis were examined graphically using symmetric nearest neighbour smoothing. Second, the average adjusted prediction of receiving a mastectomy was estimated for each observed value of age, also known as the 'marginal effect' [29]. For each tumour stage, univariable (containing age alone) and multivariable (all explanatory variables) models were fitted, with the marginal effect of age calculated using predictions from the logistic regression model [30]. The results allow the effect of age on receipt of mastectomy to be assessed after accounting for other patient, tumour, and treatment factors.

For analysis of geographical variation, patients were grouped according to the NHS organisations at which they were diagnosed (defined as NHS trusts in England; local health boards in Wales). Funnel plots visually assessed the variation in risk-adjusted rates of mastectomy between NHS organisations, stratified by tumour stage. These plots are valuable in understanding the outcome rate in relation to unit volume, as they contain 95.0% and 99.8% control limits around the mean rate [31]. NHS organisations which had a unit volume of ≤10 patients receiving breast surgery within each tumour stage across the study period were excluded. For each tumour stage, the risk-adjusted mastectomy rate for each NHS organisation was calculated by dividing the observed mastectomy rate by expected (predicted from the multivariable model) mastectomy rate, and multiplying this by the overall average mastectomy rate. To assess if variation existed in mastectomy rates across all patients at a regional level, NHS trusts in England were grouped into the 21 Cancer Alliances and all Welsh health boards were grouped together [32]. All statistical tests were two sided and *p*-values <0.001 were considered to demonstrate strong evidence of statistical significance. Analyses were performed using Stata 17.

3. Results

This study included 106,952 women aged ≥50 years diagnosed with EIBC in England and Wales between 1 January 2014 and 31 December 2019 who received breast surgery (Fig. S1). Table 1 describes the distribution of clinical and pathological characteristics of the cohort, stratified by age at diagnosis. A greater proportion of older women had tumours with unfavourable prognostic characteristics, such as larger tumour size, higher nodal stage, or grade, and were more likely to have a greater comorbidity or frailty burden. Women ≥70 years were less likely to have screen detected cancer compared with women ≤70 years, reflecting the upper age limit of the NHS breast cancer screening programme.

Most patients received BCS as their initial surgery (76.6%), and 23.4% received a mastectomy. The percentage of women who had a mastectomy decreased over the study period, from 25.7% in 2014 to 21.8% in 2019 ($p < 0.001$). This small reduction in mastectomy rates was seen across all age groups and tumour stages (Fig. S2).

3.1. Factors Associated with Receipt of Mastectomy

There were differences in the percentage of patients who received mastectomy according to patient, tumour, and treatment characteristics, when stratified by tumour stage (Table 2). Receipt of mastectomy was more common among patients with a higher tumour stage (T1: 12.3%; T2: 37.6%; T3: 77.5%), and within each of these groups, mastectomy rates increased with age. Among women aged 50–59 years, the rates for T1, T2 and T3 stages were 11.8%, 31.5% and 73.4%. Among women aged 80+ years, the corresponding rates were 26.3%, 56.9% and 90.3%. Within each tumour stage group, higher mastectomy rates were also observed among women with ER negative, HER2 positive, higher grade tumours, those with a higher degree of comorbidity or frailty, and those diagnosed via non-screening pathways.

Further analyses investigated any relationship between receipt of mastectomy and the number of comorbidities or level of frailty, among different age groups (Table S2). Within each age group, mastectomy rates increased with higher levels of comorbidity or frailty. This was most apparent among women aged 50–59 years; 20.7% among women classified as fit (according to the SCARF index) had a mastectomy,

Table 1
Patient and tumour characteristics of women aged 50 and over diagnosed in England and Wales with EIBC who received surgery within 12 months from diagnosis, stratified by age at diagnosis.

	Total	Age group			
	N (%)	50–59 yrs	60–69 yrs	70–79 yrs	80+ yrs
Total	106,952	34,346	38,568	24,947	9091
IMD					
1 - Most deprived	16,129 (15.1%)	17.0%	14.8%	13.5%	13.4%
2	18,780 (17.6%)	18.2%	17.8%	16.6%	16.8%
3	22,440 (21.0%)	20.6%	21.3%	21.3%	20.2%
4	24,440 (22.9%)	21.9%	22.9%	23.5%	24.3%
5 - Least deprived	25,163 (23.5%)	22.3%	23.2%	25.1%	25.3%
Referral source					
Screened	54,586 (51.0%)	56.4%	66.0%	36.5%	7.5%
Non-screened	52,366 (49.0%)	43.6%	34.0%	63.5%	92.5%
Comorbidity index					
0	94,535 (88.4%)	93.1%	89.7%	83.9%	77.5%
1	8860 (8.3%)	5.5%	7.6%	11.1%	14.0%
2	2598 (2.4%)	1.1%	2.1%	3.7%	5.6%
3+	959 (0.9%)	0.3%	0.7%	1.4%	2.9%
SCARF index					
Fit	87,552 (81.9%)	89.6%	83.8%	74.5%	64.3%
Mild	11,244 (10.5%)	7.1%	10.0%	13.9%	16.2%
Moderate	6269 (5.9%)	2.7%	5.0%	8.9%	13.0%
Severe	1887 (1.8%)	0.6%	1.1%	2.7%	6.5%
Tumour size					
<1	16,386 (15.3%)	15.3%	19.6%	12.5%	4.9%
1–1.99	43,735 (40.9%)	42.3%	43.7%	38.6%	30.0%
2–4.99	41,841 (39.1%)	37.3%	33.0%	44.1%	58.1%
≥5	4990 (4.7%)	5.1%	3.6%	4.7%	7.0%
T stage					
T1	66,139 (61.8%)	63.3%	68.9%	56.6%	41.0%
T2	36,768 (34.4%)	32.5%	28.2%	39.5%	53.4%
T3	4045 (3.8%)	4.2%	2.9%	3.9%	5.6%
N stage					
N0	84,442 (79.0%)	77.2%	81.6%	78.8%	74.7%
N1	19,534 (18.3%)	20.1%	16.2%	18.0%	20.9%
N2	2976 (2.8%)	2.7%	2.2%	3.2%	4.5%
ER status					
Positive	92,991 (86.9%)	87.7%	88.6%	86.1%	79.7%
Negative	13,961 (13.1%)	12.3%	11.4%	13.9%	20.3%
HER2 status					
Positive	11,630 (10.9%)	12.2%	10.2%	9.9%	11.5%
Negative	89,159 (83.4%)	82.3%	84.3%	84.0%	81.7%
Borderline	6163 (5.8%)	5.6%	5.5%	6.1%	6.8%
Grade					
G1	20,563 (19.2%)	21.3%	20.7%	16.5%	12.7%
G2	61,490 (57.5%)	54.6%	58.5%	59.6%	58.2%
G3	24,899 (23.3%)	24.2%	20.7%	23.9%	29.1%
Axillary surgery					

(*continued on next page*)

Table 1 (*continued*)

	Total	Age group			
	N (%)	50–59 yrs	60–69 yrs	70–79 yrs	80+ yrs
SNB	85,395 (79.8%)	78.4%	82.9%	80.0%	71.9%
AND	10,536 (9.9%)	10.1%	8.1%	10.5%	14.4%
SNBAND	8325 (7.8%)	9.5%	7.1%	7.1%	6.2%
None	2696 (2.5%)	1.9%	1.9%	2.4%	7.5%
IR					
Mx	21,048 (84.0%)	65.8%	82.1%	95.8%	99.4%
Mx and IR	3996 (16.0%)	34.2%	17.9%	4.2%	0.6%
NACT					
No	102,966 (96.3%)	93.7%	96.5%	98.2%	99.9%
Yes	3986 (3.7%)	6.3%	3.5%	1.8%	0.1%

Table 2
The percentage of women with EIBC receiving mastectomy according to patient, tumour and treatment characteristics, stratified by tumour stage.

	No. of patients			% Mastectomy		
	T1	T2	T3	T1	T2	T3
Total	66,139	36,768	4045	12.3%	37.6%	77.5%
Age group						
50–59 yrs	21,729	11,173	1444	11.8%	31.5%	73.4%
60–69 yrs	26,569	10,888	1111	9.8%	32.3%	72.6%
70–79 yrs	14,112	9851	984	13.8%	40.7%	82.2%
80+ yrs	3729	4856	506	26.3%	56.9%	90.3%
IMD						
1 - Most deprived	9666	5819	644	13.3%	39.9%	80.7%
2	11,468	6579	733	12.3%	38.9%	77.5%
3	13,977	7594	869	11.7%	36.7%	76.1%
4	15,324	8291	825	12.6%	37.5%	78.2%
5 - Least deprived	15,704	8485	974	11.7%	35.7%	75.9%
Referral source						
Screened	42,633	11,031	922	8.3%	25.7%	67.9%
Non-screened	23,506	25,737	3123	19.4%	42.6%	80.3%
Charlson Index						
0	58,831	32,155	3549	11.8%	36.7%	77.1%
1	5302	3224	334	14.8%	41.3%	79.3%
2	1508	980	110	16.8%	47.6%	83.6%
3+	498	409	52	18.7%	50.6%	76.9%
SCARF index						
fit	54,685	29,573	3294	11.7%	36.4%	77.3%
mild	6888	3933	423	13.4%	38.4%	74.9%
moderate	3576	2461	232	15.7%	44.7%	81.0%
severe	990	801	96	22.0%	53.2%	86.5%
N stage						
N0	57,942	24,579	1921	10.9%	32.8%	73.1%
N1	7551	10,390	1593	20.6%	45.8%	79.8%
N2	646	1799	531	32.4%	55.6%	86.3%
ER status						
Positive	59,583	30,121	3287	11.7%	36.8%	77.0%
Negative	6556	6647	758	17.1%	41.0%	79.6%
HER2 status						
Positive	5869	5134	627	20.9%	44.0%	81.0%
Negative	56,541	29,404	3214	11.4%	36.5%	76.9%
Borderline	3729	2230	204	12.0%	37.0%	74.5%
Grade						
G1	17,210	3160	193	7.7%	28.0%	78.8%
G2	37,793	21,137	2560	13.0%	38.5%	77.5%
G3	11,136	12,471	1292	16.7%	38.4%	77.1%
NACT						
No	65,316	34,200	3450	12.0%	37.5%	78.4%
Yes	823	2568	595	31.2%	37.9%	72.1%
Year of diagnosis						
2014	9420	5160	498	14.1%	41.7%	80.3%
2015	10,572	5638	606	13.9%	39.9%	78.5%
2016	11,452	6417	674	12.3%	38.1%	78.0%
2017	11,389	6666	722	11.7%	36.3%	78.0%
2018	12,158	6758	836	11.0%	35.1%	78.3%
2019	11,148	6129	709	11.0%	35.4%	72.4%

increasing to 37.9% among women classified as severely frail. The smallest difference in mastectomy rates was seen for women aged ≥80 years, where the proportion of patients who received a mastectomy was almost equivalent across frailty categories (fit 46.2% vs severe frailty 49.8%). Age and patient fitness were also influential in the receipt of IR (Fig. S3). IR rates were low among women aged ≥70 years, regardless of overall fitness ($N = 313$; 2.9%). Among younger women (50–59 years), the proportion who had IR decreased as levels of frailty or comorbidity increased.

Table 3 summarises the adjusted odds of receiving a mastectomy, for each patient and clinical factor, stratified by tumour stage group. The regression model exhibited good calibration in each tumour stage (Fig. S4). The results confirm a strong association between age and mastectomy use. Receipt of mastectomy was also associated with referral source and nodal stage. Higher grade (≥G2 vs G1) and earlier year of diagnosis were associated with increased mastectomy use for women with T1/T2 EIBC, but there was no evidence of an association for women with T3 tumours. There was evidence that severe frailty was associated with increased odds of receiving mastectomy for women with T1 (adjusted odds ratio [aOR] [95% confidence interval (CI)]: 1.48 [1.21, 1.81]) or T2 (aOR: 1.29 [1.06, 1.55]) tumours, and the estimate for women with T3 tumours was imprecise (aOR: 1.84 [0.79, 4.28]). No evidence of an association was found between comorbidity and mastectomy for any tumour stage group. A sensitivity analysis was performed where tumour size was added to the model as a covariate. The results were similar to those of the main analysis (data not shown), demonstrating no change in associations of age, comorbidity and frailty with receipt of mastectomy, for each of the tumour stages.

Further analysis investigated whether the associations of patient and tumour characteristics with receipt of mastectomy were mediated by age. Patterns of mastectomy use by age were similar across tumour stage groups between the ages of 50–70 but steadily increased after the age of 70 (Fig. 1). Second, adjusted odds ratios were plotted for categorical variables from the multivariate logistic regression model, for each tumour stage (Fig. 2), to visualise how factors were associated with the odds of receiving a mastectomy after adjusting for age. Women with N1/N2 tumours, severe frailty, and those diagnosed via non-screening pathways had increased odds of receiving a mastectomy, across each tumour stage group. Finally, the predicted probability of receiving a mastectomy was plotted from a univariable (age alone) and multivariable logistic regression model, stratified by tumour stage. Despite adjusting for explanatory variables, the predicted probability of receiving a mastectomy rose with increasing age although the relationship was not as marked for women with T1 tumours (Fig. 3).

3.2. Regional Variation

The observed overall mastectomy rate varied between NHS organisations from 11.7% to 53.4%. The between-organisation variation in observed rates was largest among women with T3 tumours and smallest among those with T1 tumours (T1: 3.1% to 35.4%; T2: 17.7% to 68.4%; T3: 47.3% to 100%). For women with T3 tumours, this variation was consistent with expected level of random variation due to the smaller volumes of cases, but for women with T1 and T2 tumours, the differences between organisations exceeded the expected range (based on 99.8% control limits; data not shown). After adjusting for differences in the case-mix of patients, the variation between organisations in mastectomy rates was reduced (Fig. 4), but excess variation (outside the expected range) remained. For women with T3 EIBC (risk-adjusted range 45.8% to 100.0%), four of 107 NHS organisations had adjusted mastectomy rates outside the 99.8% funnel limit. The variation in mastectomy rates was mainly at the level of NHS organisations, with little difference in unadjusted rates seen between Cancer Alliances (Fig. S5).

Table 3
Adjusted odds ratio (aOR) estimates for the likelihood of receiving a mastectomy according to patient characteristics, tumour characteristics and treatment.

	T1		T2		T3	
	aOR (95% CI)	*P* value	aOR (95% CI)	P value	aOR (95% CI)	P value
Age spline 1	1.13 (1.10, 1.16)	0.000	1.25 (1.23, 1.28)	0.000	1.35 (1.24, 1.47)	0.000
Age spline 2	0.82 (0.80, 0.84)	0.000	0.86 (0.84, 0.88)	0.000	0.81 (0.75, 0.88)	0.000
SCARF Index		0.002		0.003		0.041
Fit	1.00		1.00		1.00	
Mild	1.02 (0.93, 1.11)		0.93 (0.85, 1.00)		0.73 (0.55, 0.97)	
Moderate	1.11 (0.98, 1.26)		1.05 (0.94, 1.18)		1.03 (0.67, 1.60)	
Severe	1.48 (1.21, 1.81)		1.29 (1.06, 1.55)		1.84 (0.79, 4.28)	
Comorbidity Index		0.462		0.468		0.207
0	1.00		1.00		1.00	
1	1.08 (0.98, 1.20)		1.05 (0.95, 1.16)		1.06 (0.75, 1.52)	
2	1.06 (0.89, 1.26)		1.13 (0.96, 1.33)		0.96 (0.51, 1.81)	
3+	0.98 (0.74, 1.29)		1.11 (0.87, 1.42)		0.40 (0.16, 1.00)	
IMD		0.000		0.000		0.083
1 - Most deprived	1.00		1.00		1.00	
2	0.92 (0.85, 1.00)		0.98 (0.90, 1.05)		0.82 (0.63, 1.07)	
3	0.87 (0.80, 0.94)		0.88 (0.82, 0.95)		0.75 (0.58, 0.97)	
4	0.93 (0.86, 1.01)		0.91 (0.84, 0.97)		0.85 (0.65, 1.10)	
5 - Least deprived	0.85 (0.79, 0.92)		0.83 (0.78, 0.90)		0.71 (0.55, 0.91)	
Referral source		0.000		0.000		0.000
Screened	1.00		1.00		1.00	
Non-screened	2.00 (1.89, 2.10)		1.65 (1.57, 1.74)		1.58 (1.33, 1.89)	
N stage		0.000		0.000		0.000
N0	1.00		1.00		1.00	
N1	1.76 (1.65, 1.87)		1.73 (1.65, 1.82)		1.59 (1.35, 1.88)	
N2	2.84 (2.39, 3.38)		2.47 (2.24, 2.73)		2.21 (1.68, 2.91)	
ER status		0.527		0.046		0.416
Positive	1.00		1.00		1.00	
Negative	1.03 (0.95, 1.11)		1.07 (1.00, 1.14)		1.10 (0.88, 1.38)	
HER2 status		0.000		0.000		0.020
Positive	1.00		1.00		1.00	
Negative	0.58 (0.54, 0.63)		0.75 (0.70, 0.80)		0.73 (0.57, 0.92)	
Borderline	0.62 (0.55, 0.71)		0.78 (0.70, 0.86)		0.66 (0.44, 0.98)	
Grade		0.000		0.000		0.055
G1	1.00		1.00		1.00	
G2	1.54 (1.44, 1.65)		1.49 (1.37, 1.63)		0.84 (0.58, 1.22)	
G3	1.59 (1.46, 1.73)		1.27 (1.15, 1.39)		0.69 (0.47, 1.02)	
NACT		0.000		0.622		0.008
No	1.00		1.00		1.00	
Yes	1.85 (1.57, 2.17)		1.02 (0.93, 1.12)		0.74 (0.59, 0.92)	
Year of diagnosis		0.000		0.000		0.061
2014	1.00		1.00		1.00	
2015	0.98 (0.91, 1.07)		0.93 (0.86, 1.01)		0.89 (0.66, 1.20)	
2016	0.88 (0.81, 0.95)		0.87 (0.80, 0.94)		0.90 (0.67, 1.21)	
2017	0.80 (0.74, 0.87)		0.81 (0.75, 0.88)		0.91 (0.68, 1.22)	
2018	0.74 (0.68, 0.81)		0.76 (0.70, 0.82)		0.95 (0.71, 1.26)	
2019	0.76 (0.69, 0.82)		0.78 (0.72, 0.84)		0.68 (0.51, 0.91)	

Note: For each tumour stage, estimates were obtained using a logistic regression model. The model was adjusted for age (using a restricted cubic spline), comorbidity, frailty, Index of Multiple Deprivation, referral source, nodal stage, ER status, HER2 status, grade, neoadjuvant chemotherapy and diagnosis year. An odds ratio of >1 favours receipt of mastectomy versus breast conserving surgery. For the restricted cubic spline of age, knots were placed at 50, 64 and 76 years for T1; 50, 66 and 81 years for T2; and 50, 65 and 81 years for T3.

4. Discussion

This population-based study of over 100,000 women aged ≥50 years diagnosed with EIBC between 2014 and 2019 investigated the relationships of age, comorbidity, and frailty with receipt of mastectomy in NHS organisations in England and Wales. After adjusting for influential factors, increasing age at diagnosis was associated with higher odds of receiving a mastectomy, across all tumour stages. Whilst we found some evidence that severe frailty was associated with higher odds of receiving a mastectomy, the number of comorbidities did not appear to impact on mastectomy use, within any tumour stage. Among all women, there was little regional variation across Cancer Alliances in mastectomy rates, but there was variation at the level of NHS organisations for women with T1/T2 EIBC.

A principal factor which influences the recommendation of BCS or mastectomy is tumour size in relation to breast size, with mastectomy recommended for women with smaller tumour-to-breast volume ratio. We found that women aged ≥75 years had significantly higher odds of receiving a mastectomy compared with younger women, even among patients with T1/T2 tumours, and after adjusting for other influential factors.

The reasons behind this discrepancy are likely to be complex, multifactorial, and related to patient and clinician factors [6,9,33]. Due to higher levels of frailty and comorbidities, older patients may be less likely to receive NACT for potential tumour down-staging which could facilitate breast conservation. There is no evidence that the grief and loss of physical self-esteem associated with a mastectomy is age-related. In a

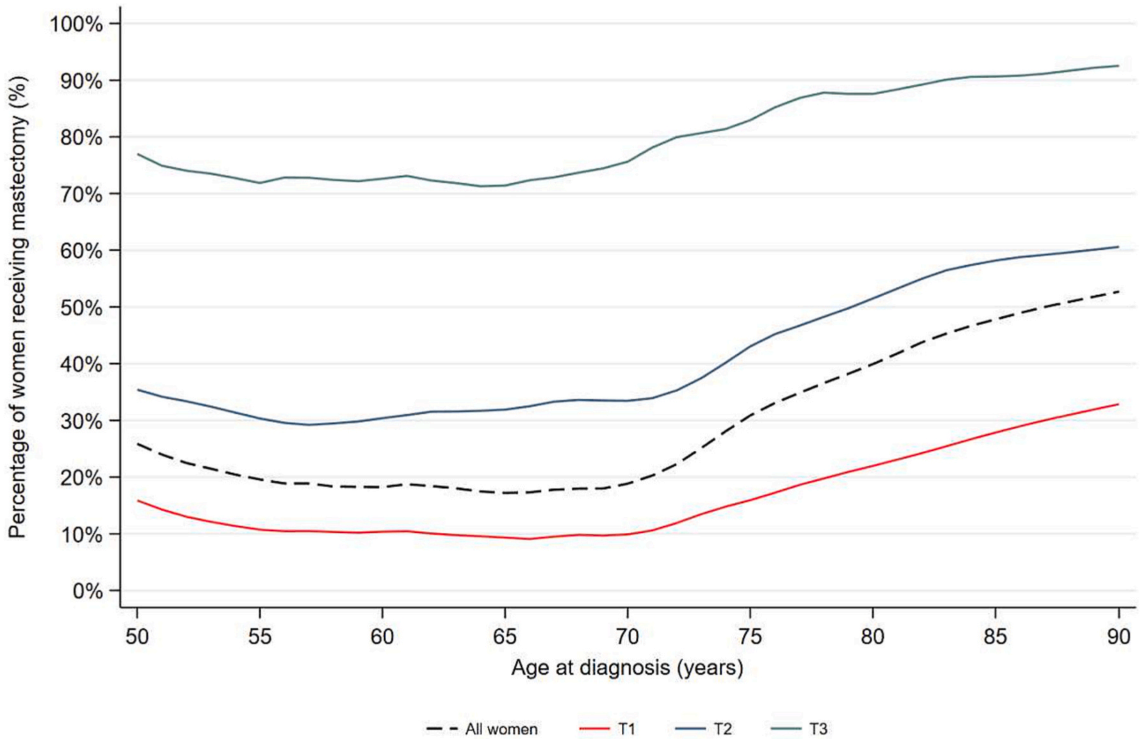

Fig. 1. The percentage of women receiving mastectomy according to age at diagnosis, overall and stratified by tumour stage.
Note: Estimates were obtained used symmetric nearest neighbour smoothing.

systematic review which assessed the impact of patient-reported factors on choice of breast surgery, body image was the main influence affecting patient preference for BCS, whilst survival and treatment-related factors (e.g., the requirement with BCS for radiotherapy) impacted decision-making the most for patients who had a mastectomy [34]. Given the option, older women may be more likely to opt for mastectomy over BCS [14] in order to avoid the potential for further cancer excisional surgery or requirement for radiotherapy [15]. In a regional survey of 339 patients aged ≥70 years in England, 38% of women were worried about the cosmetic effect of mastectomy, with 55% concerned a mastectomy would lead to psychological harm [35], highlighting the importance of discussing these aspects during surgical treatment consultations with older women. In addition, clinician factors such as female sex of surgeon and higher volume of cases performed are associated with greater use of BCS over mastectomy [6,16].

The results demonstrated that severe frailty was associated with receipt of mastectomy, but the number of comorbidities was not, when accounting for each other and other important factors. Among the younger age group (50–59 years), higher rates of mastectomy were seen with increasing comorbidity or frailty, but in the oldest group (≥80 years) comorbidity and frailty made little difference to mastectomy rates. While some studies have found greater comorbidity burden is associated with greater use of mastectomy [13,16–19], others have found the opposite [36,37], reflecting a lack of consensus as to which surgical treatment should be offered. Higher rates of mastectomy among frailer women or those with more comorbidities may indicate clinician preference to not offer radiotherapy or to reduce the need for further surgery due to involved surgical margins [19]. In a US study of breast cancer surgery among long-term nursing home patients, 30-day all-cause mortality was highest for women who received BCS alone (8.2%), which likely suggests patient selection for any breast surgery was inadequate in that cohort, considering most patients tolerate breast surgery well with negligible mortality [38]. All treatment decision-making should consider functional rather than chronological age, both to identify individuals who can progress with surgery as normal and also those who may require additional support (such as anaesthetic optimisation or geriatric assessment) or are at such an increased risk of adverse outcomes to require further consideration by the patient and surgeon [21]. The capture of accurate data on patient frailty at the time of diagnosis within national datasets will be informative to understand the impact of fitness on decision-making for breast cancer patients in greater detail [22].

There is substantial variation in mastectomy rates between NHS organisations for women with T1/T2 EIBC and there is not an evident explanation within the data. In a previous report, moderate regional variation in BCS rates across English NHS trusts was demonstrated, but this observed variation was reduced when trusts that provided regional IR services (with higher rates of mastectomy on average) were removed [12]. International differences in rates of BCS versus mastectomy for older women with EIBC have been reported [39,40], which may represent differences in either patient/surgeon preference or tumour stage at diagnosis between countries [40]. Rates of BCS and mastectomy for EIBC should be a source of audit and inquiry for NHS organisations, to understand and address potential barriers to breast conservation.

4.1. Implications for Research and Clinical Practice

Formulating options for changing these patterns of surgery requires a clear understanding of the surgical decision-making process among older patients and clinicians, including the type and amount of information provided and preferences of both patients and surgeons. This may highlight age-related biases about particular types of surgery and surgical decision-making and identify opportunities to challenge misperceptions. Qualitative studies on decision-making around breast cancer surgery have described the information requirements of women and their preferences, and how these differ between younger and older women [6,7,9,15,35,36,41–43]. A common finding of studies that focus on older women is the openness of women to consider BCS [35]. The dynamic between patient and surgeon is known to influence decision-making for surgery [7]. Several studies have shown no difference

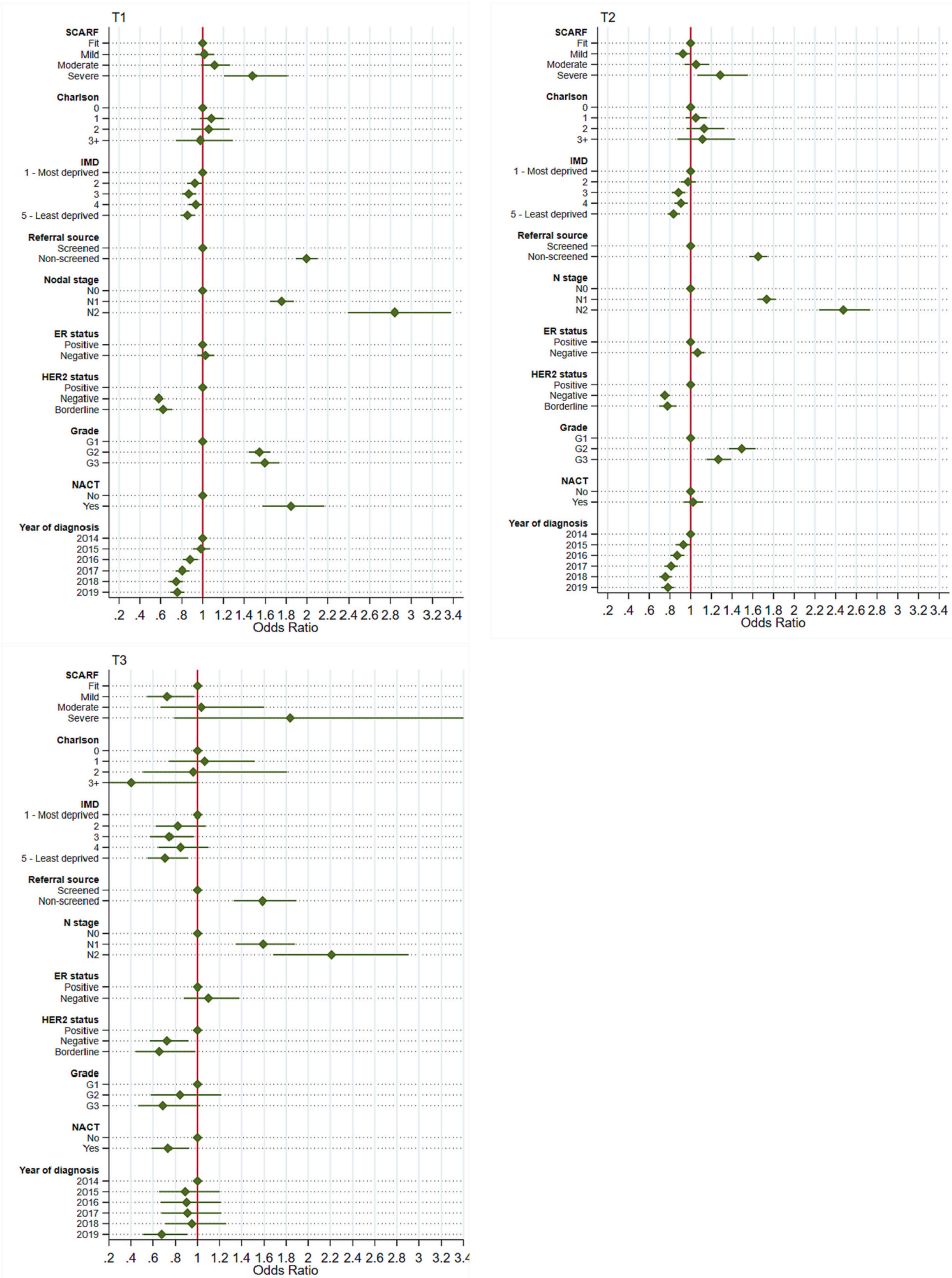

Fig. 2. The likelihood of receiving a mastectomy stratified by tumour stage. Odds ratios are plotted from a multivariate logistic regression model containing age, frailty index, comorbidity index, Index of Multiple Deprivation, referral source, nodal stage, ER status, HER2 status, grade, use of neoadjuvant chemotherapy and year of diagnosis.

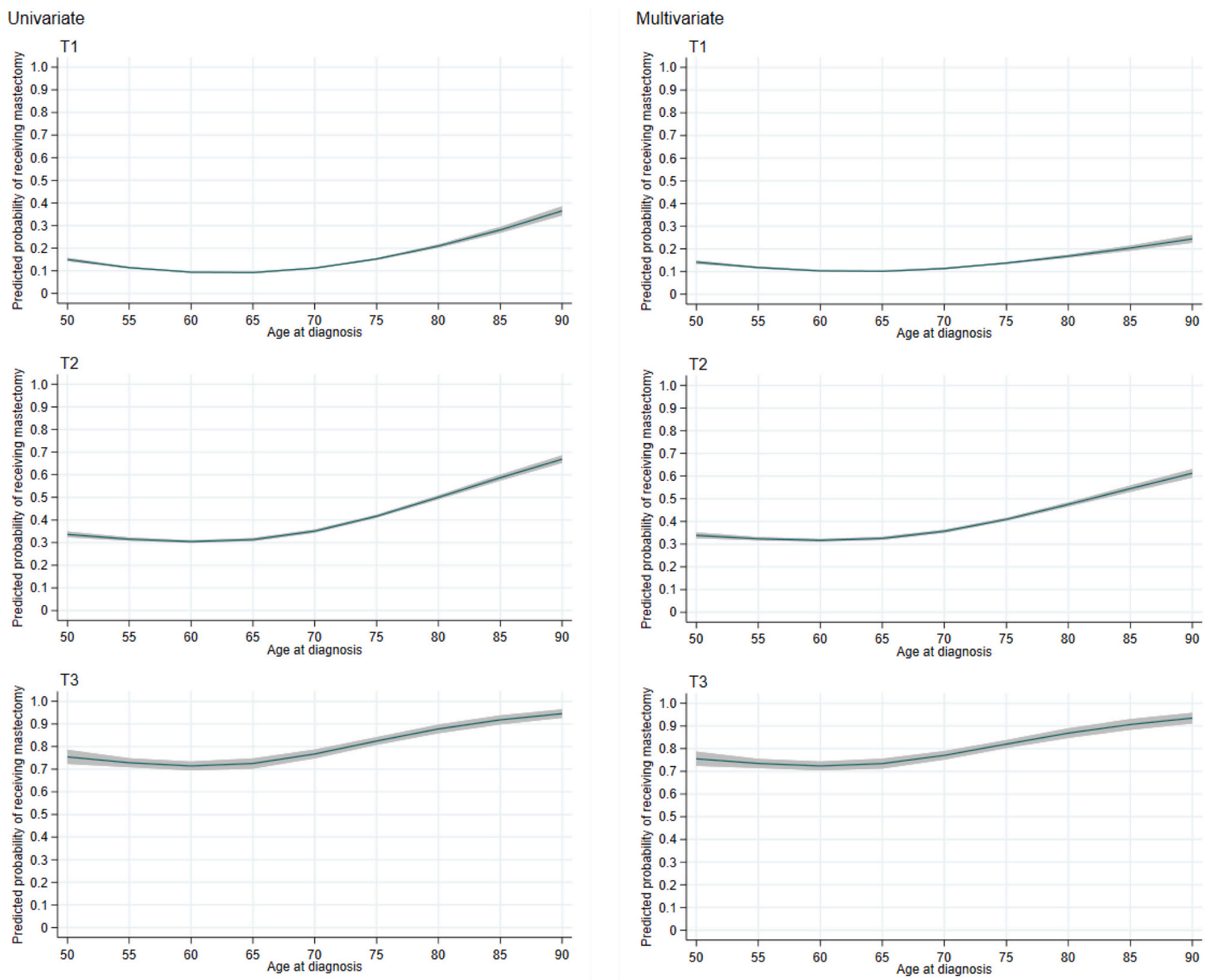

Fig. 3. Marginal plots of the effect of age on the probability of receiving a mastectomy, estimated from a univariable logistic regression model (containing age alone) and a multivariable model (containing all explanatory variables), for each of the tumour stages.
Note: shaded area represents the 95% confidence interval. Plots were created using the *marginscontplot* command in Stata.

according to age in the preferred consultation 'role' (e.g., collaborative, patient, or surgeon based) for surgery decision-making, with evidence suggesting older women feel as confident as younger women in decision-making [36,42]. The evidence is difficult to synthesise, though, because it has been generated from different populations or countries using different study designs. Consequently, there is currently no accepted framework to guide the development of initiatives to support decision-making and reduce the variation in treatment selection observed between organisations.

4.2. Strengths and Limitations

The strengths of this study include the large sample size, which provides 'real-world' evidence of clinical practice through the use of routine national data sources. In addition, this study offers a contemporary insight into surgical decision-making for women of varying comorbidity and frailty levels in England and Wales, including those traditionally excluded from RCTs [44,45].

Limitations include incomplete information about pre-treatment TNM staging in the routine datasets, which required the use of post-surgery tumour characteristics to allocate tumour stage, and impaired the ability to determine true pre-operative stage which informs the initial decision for surgery. Compared with the other frailty groups, patient numbers in the severe frailty group were smaller, which may have impaired the ability to identify evidence of an association with receipt of mastectomy. Furthermore, there is a risk of residual confounding as routine national datasets do not collect data on key variables known to influence type of surgery, such as patient preference, breast volume-to-tumour ratio, and clinician or multidisciplinary team meetings' treatment recommendations. Finally, characteristics of each NHS organisation (such as available resources, experience of staff or ability to offer immediate reconstruction) were not available. This meant we were unable to adjust for organisation level characteristics within our analysis, which may influence surgical decision-making, and some variation in mastectomy rates will be explained by these factors. Despite these limitations, our study provides a novel insight into the association of patient and tumour factors with surgical treatment selection among older patients with EIBC across England and Wales.

5. Conclusions

Older women with EIBC were more likely to receive mastectomy over BCS compared with younger women, regardless of invasive tumour size. Women with severe frailty were more likely to undergo mastectomy. There was substantial variation in mastectomy rates particularly in T2 disease. Surgical treatment decision-making should be informed

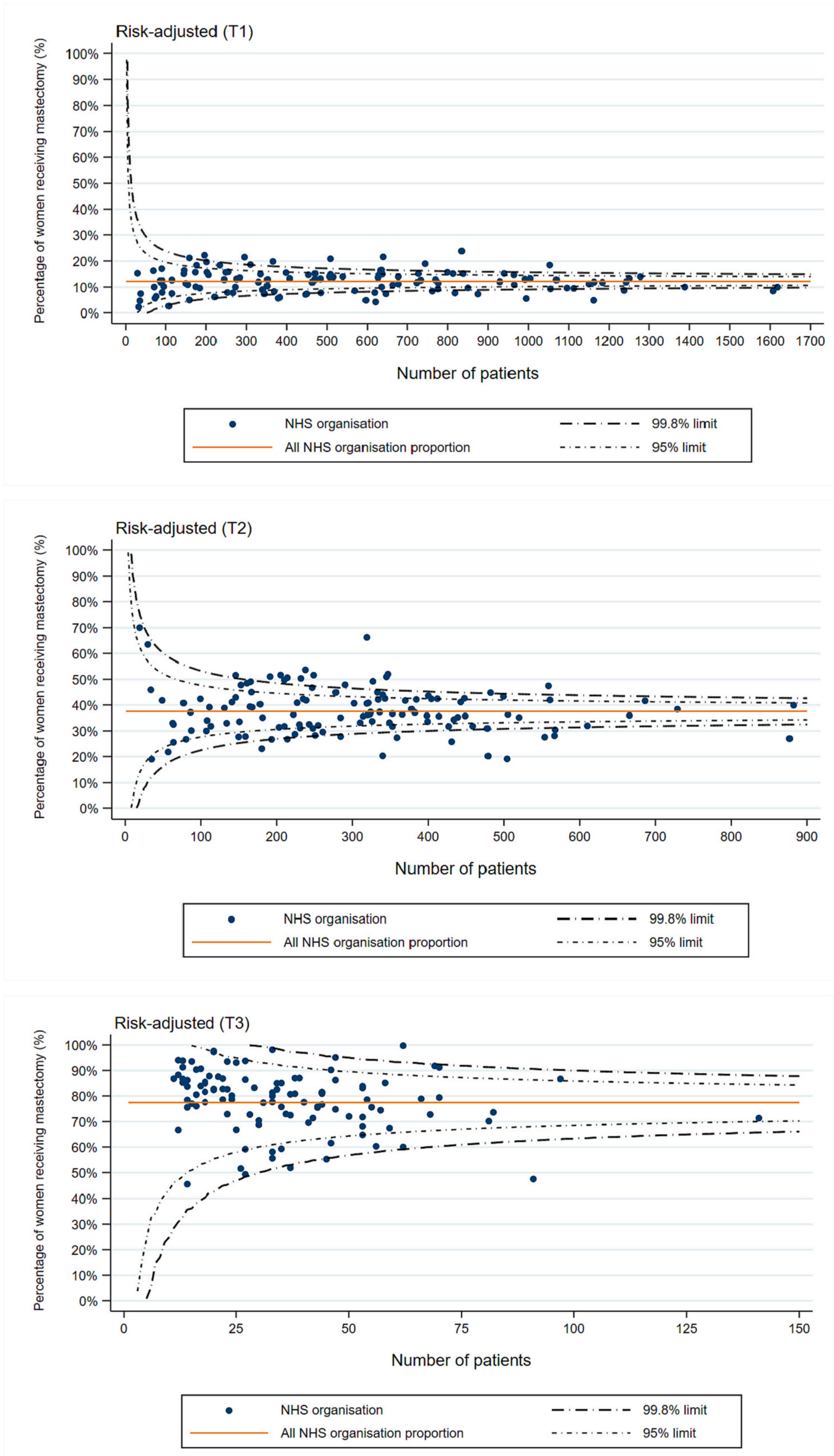

Fig. 4. Funnel plots demonstrating risk-adjusted mastectomy rates among women in NHS organisations in England and Wales, stratified by tumour stage.
Note: Risk-adjusted mastectomy rates were plotted for 123 NHS organsations in the T1 and T2 groups. 16 NHS organisations were excluded from the funnel plot for T3 (N = 13 with ≤10 patients; N = 3 with risk-adjusted rates >100%).

by functional age, as well as relevant tumour characteristics and patient preferences, to avoid age-biased management. Future efforts should encourage NHS organisations to regularly review their data and increase the completeness of pre-treatment staging returns as well as items on patient fitness in national datasets, to allow a more granular evaluation and understanding of surgical treatment among older women. Evidence from qualitative research on the perceptions of both older patients and surgeons on types of breast surgery would provide a clearer framework for decision making, which could help to reduce barriers to breast conservation among older patients with breast cancer.

Ethical Considerations

This study was exempt from NHS Research Ethics Committee approval because it involved analysis of pseudonymised linked data collated for the purpose of service evaluation as part of the National Audit of Breast Cancer in Older Patients. The NABCOP has approval for processing health care information under Section 251 (reference number: 16/CAG/0079).

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Author Contributions

Katie Miller: Conceptualization, Methodology, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Melissa Ruth Gannon:** Methodology, Writing – review & editing. **Jibby Medina:** Writing – review & editing. **Karen Clements:** Writing – review & editing. **David Dodwell:** Writing – review & editing. **Kieran Horgan:** Conceptualization, Methodology, Writing – review & editing. **Min Hae Park:** Conceptualization, Methodology, Writing – review & editing. **David Alan Cromwell:** Conceptualization, Methodology, Writing – review & editing.

Declaration of Competing Interest

Karen Clements has a breast cancer research manager role within NHS England as part of the Cancer Grand Challenges PRECISION team. David Cromwell has received funding grants from the Healthcare Quality Improvement Partnership, and is on the trial steering committee for the Pregnancy Outcome Prediction Study (POPS2). Kieran Horgan is the chair of the trial steering committee for Endonet.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2023.101653.

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