

## Observational cohort study in older women with early breast cancer: use of radiation therapy and impact on health-related quality of life and mortality

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**ARTICLE TYPE****Original article****TITLE****Bridging The Age Gap: an observational cohort study in older women with early breast cancer: use of radiotherapy and impact on quality of life and mortality.****AUTHORS**

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## **ABSTRACT**

### **Background**

Radiotherapy reduces the local recurrence risk in early breast cancer (EBC) in older women, but it is uncertain which patients benefit. This study determined treatment patterns according to fitness and quality-of-life (QoL) impacts.

### **Methods**

A multicentre, observational study of EBC patients aged  $\geq 70$  years was undertaken. Associations between radiotherapy use, pathological parameters, fitness and treatment centre were determined. QoL was measured using validated questionnaires.

### **Results**

Between 2013 and 2018, 2811 women in 56 UK centres underwent surgery. On multivariable analysis age and tumour risk predicted radiotherapy use. Among fitter patients with higher-risk tumours, 534/613 (87.1%) having breast conserving surgery (BCS) and 185/341 (54.2%) having mastectomy received radiotherapy. In less fit individuals with lower-risk tumours undergoing BCS, 149/207 (72.0%) received radiotherapy. Radiotherapy effects on quality-of-life domains including breast symptoms and fatigue were seen, resolving by 18 months.

### **Conclusion**

Radiotherapy use in EBC patients  $\geq 70$  years is affected by age and recurrence risk, fitness having a more limited impact. Our study suggests undertreatment of a significant number of fit, older women with high-risk tumours who do not receive radiotherapy. Conversely, some older lower-risk EBC patients risk overtreatment receiving post-BCS radiotherapy despite evidence on limited benefit. The impact of radiotherapy on QoL is small and transient.

**Keywords:** Breast cancer, older patients, frailty, comorbidity, quality of life, adjuvant radiotherapy, whole breast radiotherapy, post mastectomy radiotherapy, multivariable analysis, univariable analysis.

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## MANUSCRIPT

### BACKGROUND

Age is the most relevant primary risk factor for breast cancer and in Europe almost half of cases are diagnosed above the age of 65 years.(1) Nonetheless, outcomes are worse in older individuals(2, 3) who are also under-represented in clinical trials.(4-6) In the older age group, outcomes may be influenced by the increasing burden of competing morbidity and mortality risks, late presentation, and under-treatment. However, significant variations in treatment decisions between centres are frequently reported in older adults(7, 8) and data on fitness are crucial to predict benefits and toxicities and drive recommendations in this setting.

Whole breast radiotherapy (WBRT) is standard of care following breast conservation surgery. Post-mastectomy radiotherapy (PMRT) is selectively administered for women with a high risk of local recurrence. Radiotherapy is generally well tolerated in older women, although may cause significant inconvenience due to travel requirements and has some adverse impacts.(9) However, the risk of local breast cancer recurrences after breast conserving surgery (BCS) is lower in older patients and the benefits of radiotherapy decline with age.(10, 11)

In the setting of breast conservation surgery, the Cancer and Leukaemia Group B (CALGB) 9343 and PRIME-II trials showed that omission of radiotherapy in older women with small, node-negative, oestrogen receptor (ER)-positive tumours may be an acceptable strategy.(12, 13). In CALGB 9343 the risk of LRR was higher (8.0% versus 2.0%) after 10-year follow-up but there was no survival disadvantage. Similarly, the PRIME II trial found a LRR risk of 9.8% at 10 years in women in whom WBRT was omitted compared to 1.3% in those who were treated, but again no impact on survival(14). However, some data suggests that higher rates of local recurrence may have some detrimental impact on survival after 15 years of follow up. The Early Breast Cancer Trialist's Collaborative Group (EBCTCG) meta-analysis of WBRT after BCS found that WBRT reduced the absolute risk of local recurrence by 15.7% at 10 years of follow-up which translated into a 3.8% mortality reduction at 15 years of follow up.(15)

The EBCTCG study included women of all ages and the survival effect may be less pronounced in older cohorts due to competing risks. Therefore, selective omission of radiotherapy may well be an appropriate approach in some older women, particularly those who are less fit, and have a shorter life-expectancy (due to their co-morbidities), where there is a risk of over-treatment. Conversely, there is a risk of under-treatment in fit older patients

with early breast cancer at higher risk of recurrence, where adjuvant radiotherapy is likely to be of greater benefit.

The Bridging the Age Gap study prospectively recruited a large, real-world, cohort of older women with breast cancer and included detailed baseline geriatric assessment. Analyses examining outcomes in relation to surgery compared with primary endocrine therapy, and the impact of systemic therapy are published elsewhere.(16-19) In this analysis the age- and risk-stratified patterns of adjuvant radiotherapy use in this population, using multivariable analysis and the impact of radiotherapy on quality of life (QoL) outcomes are reported.

## **METHODS**

### **Study design**

The Age Gap study was a prospective multicentre, observational cohort study. Patients were recruited from 56 centres in England and Wales (Supplementary Table 1). Eligible patients were women  $\geq 70$  years at diagnosis of primary operable invasive breast cancer (TNM stages: T1-3 and operable T4b, N0-1, M0). Those unsuitable for surgery or with previous EBC within five years were not eligible.

### **Baseline data collection**

Patients were recruited at the time of EBC diagnosis and before commencing treatment and could participate at three levels: full, partial (no requirement to complete QoL questionnaires) or by proxy (third-party data collection for those with significant cognitive impairment).

Baseline data were collected about the primary tumour including: cancer type, grade, nodal status, tumour size, ER, progesterone (PR) and human epidermal growth factor receptor 2 (HER2) receptor status. Staging was performed if clinically indicated. Surgical, radiotherapy and systemic therapy data were collected.

At baseline, patients underwent assessments using validated tools including: comorbidities (Charlson comorbidity index [CCI]),<sup>(20)</sup> nutrition (Abridged Patient Generated Subjective Global Assessment [aPG-SGA]),<sup>(21, 22)</sup> functional status (Activities of Daily Living [ADL]),<sup>(23)</sup> advanced functional status (Instrumental Activities of Daily Living [IADL]),<sup>(24)</sup> cognitive capacity (Mini Mental State Examination [MMSE]),<sup>(25)</sup> Eastern Cooperative Oncology Group Performance Status (ECOG PS) and medication list.

QoL was assessed using the European Organisation for the Research and Treatment of Cancer QoL Questionnaires. Four validated tools were used: the generic cancer tool, the EORTC-QLQ-C30,<sup>(26)</sup> a breast cancer specific tool, the EORTC-QLQ-BR23,<sup>(27)</sup> an older patient specific tool, the EORTC-QLQ-ELD15<sup>(28)</sup> and a generic health utility tool, the EuroQol-5D-5L (EQ-5D-5L).<sup>(29)</sup> These have a range of symptom scores and domains reflecting the disease under study (Supplementary Table 2).

### **Follow-up and outcomes**

Patients were followed up at 6 weeks, and 6, 12, 18 and 24 months after recruitment. All patients were assessed for recurrence and QoL at each visit. Complications were categorised using the Common Terminology Criteria for Adverse Events system (CTCAE v4.0).

Deaths were categorised as disease-related or other causes. Deaths were reviewed by the chief investigator blind to treatment decisions. Deaths were classified as disease related if the death was related to the initial breast cancer. Patients for whom the cause could not be established were excluded from cause specific analyses.

### **Statistical methods**

Analyses were performed in IBM SPSS statistics version 24 and R version 3.6.3(30) and Stata version 16.(31) A two-sided  $p < 0.05$  was considered statistically significant.

The relationship between radiotherapy use and tumour and patient characteristics was evaluated using univariate and multivariable logistic regression for patients who had breast conserving surgery or a mastectomy separately. Characteristics found to be statistically significant in univariate models were included in the multivariable models.

Patients whose primary treatment was breast conserving surgery were considered at higher risk of recurrence if the tumour was greater than 3cm, ER negative, HER2 positive, node-positive, or grade 3. These criteria defined a population of patients who would have been too high risk to enter the PRIME II study.(13) Those whose primary treatment was a mastectomy were considered high risk if the tumour was T4, T3 >5cm, or if there were  $\geq 4$  lymph nodes involved.(32, 33) A definition of fitness was defined based on components of the geriatric assessment tool: in order to categorize women into three groups: fit, vulnerable and frail (Supplementary Table 3). The proportion of patients receiving radiotherapy by risk status and fitness was summarised.

### **Quality of life**

The EORTC-QLQ questionnaires were scored according to the EORTC Scoring Manual (3rd Edition) and reference publication.(29) Each item is scored between 0-100. A high score for a functional scale represents a high/healthy level of functioning; a high score for the global health status/QoL represents a high QoL, whilst a high score for a symptom scale represents

a high level of symptomology/problems. Missing data were managed according to the EORTC manual recommendations.

The pre-planned analysis was conducted separately for patients who had breast conserving surgery or mastectomy and patients who received chemotherapy were excluded so that clearer conclusions could be drawn from the results in the context of its significant impact on QoL outcomes in this population.(18) The mean difference (95% CI) of the domain scores at each time point, adjusted for baseline scores, was calculated with linear regression models.

The effect of radiotherapy use on the global health score over time was estimated using a mixed effect linear model. The model allowed for time, treatment, treatment-time interaction, and baseline global health status score as well as age and baseline functionality scores to adjust for baseline variation in patient characteristics, as the study was not randomised.

## RESULTS

Between January 2013 and June 2018, 3456 women were recruited from 56 breast units in England and Wales (Supplementary Table 1). This analysis included 2811 women who underwent surgery within 6 months of diagnosis (STROBE diagram [Figure 1]).(34) Surgery involved BCS in 1669 patients and a mastectomy in 1087 patients (the type of surgery was not classified in 55 patients). Patients' characteristics according to geriatric assessments, tumour characteristics, postoperative histology and surgery performed are shown in Table 1 and Supplementary Table 4 and 5.

### Use of radiotherapy

Of the 1669 patients undergoing BCS, 1385 (83.0%) received radiotherapy. Of those 1383 patients undergoing BCS where the radiotherapy site was known 1,372 (99.2%) received treatment to the breast and 154 (11.2%) to the nodal areas (62 [4.5%] to the axilla, 92 [6.7%] to the supraclavicular fossa [SCF]). Data regarding irradiation of the internal mammary chain were not recorded. Of the 1087 patients undergoing a mastectomy, 341 (31.4%) received radiotherapy. Of those 338 patients undergoing a mastectomy where the radiotherapy site was known, 247 (73.1%) received treatment to the chest wall and 221 (65.4%) to the nodal areas (68 [20.1%] to the axilla, 153 [45.3%] to the SCF). Radiotherapy fractionation is outlined in Supplementary Table 6. Radiotherapy use according to tumour and patient characteristics in patients undergoing BCS or mastectomy is shown in Supplementary Table 4.

Univariate and multivariable analyses in patients undergoing BCS or mastectomy are shown in Table 2. In the BCS cohort, younger patients with higher risk tumours (high grade, node positive) were more likely to receive radiotherapy (increasing age: odds ratio [OR] 0.95 [95% CI 0.92, 0.99],  $p$  0.008; grade 2: OR 1.87 [95% CI 1.23, 2.83],  $p$  0.003; grade 3: OR 3.68 [95% CI 2.14, 6.46],  $p$  <0.001; pN1: OR 2.55 [95% CI 1.45-4.87],  $p$  0.002).

In the mastectomy cohort, patients with larger tumours and higher nodal involvement were more likely to receive it (T1: OR 2.27 [95% CI 1.47, 3.58],  $p$  <0.001; T3: OR 7.52 [95% CI 4.42, 13.06],  $p$  <0.001; pN1: OR 4.37 [95% CI 3.12, 6.16],  $p$  <0.001; pN2: OR 14.19 [95% CI 8.48, 24.38],  $p$  <0.001; pN3: OR 14.22 [95% CI 7.59, 27.98],  $p$  <0.001).

In the BCS cohort, higher-risk (defined above) tumours were present in 820 patients (49.1%) and 709/820 (86.5%) received radiotherapy compared with 676/849 (79.6%) of patients with lower-risk tumours (Table 3a). Of those who were fit, 613 also had higher-risk tumours, and

of these patients, 534 (87.1%) received radiotherapy (Table 3b). Of those 207 vulnerable individuals with lower risk tumours, 149 (72.0%) received radiotherapy.

In the mastectomy group, higher-risk tumours were present in 479 patients (44.1%) and 255/479 (53.2%) received radiotherapy compared with 86/608 (14.1%) of patients with non-high-risk tumours (Table 3c) Of those who were fit, 341 also had higher-risk tumours, and of these patients 185 (54.2%) received radiotherapy (Table 3d).

Radiotherapy use varied from 17.6% to 90.9% between recruiting sites, although the number of patients recruited varied widely across various study sites (range: 6-153) (Figure 2; Supplementary Table 7). Of the 56 recruiting sites, 21 had radiotherapy delivery facilities directly on site and patients managed in the remaining 35 centres were required to travel for the radiotherapy.

### **Impact on QoL**

Among 2811 patients undergoing surgery, the QoL analysis was restricted to 1789/2811 (63.6%) who did not receive chemotherapy and who consented to full participation in the study. Patients who had chemotherapy were excluded as this has a marked negative impact on QoL and was disproportionately given to women in the RT group. Of these patients, 1125/1789 (62.9%) underwent BCS and 628/1789 (35.1%) underwent a mastectomy. Out of those undergoing BCS, 927/1125 (82.4%) received radiotherapy; out of those undergoing a mastectomy, 177/628 (28.2%) received radiotherapy.

### ***Breast cancer-specific QoL domains (EORTC QLQ-BR23)***

In the BCS cohort, 1042/1125 patients (92.6%) completed some or all of the EORTC QLQ-BR23 questionnaire at baseline (Supplementary Table 8). After adjustment for baseline measurements no significant declines in the questionnaire domains were observed at 6 weeks in patients receiving radiotherapy compared with those not receiving it as almost no patients received radiotherapy by this time point. Patients undergoing radiotherapy reported worse breast symptoms at 6 months (mean difference 6.27, 95% CI 3.34 to 9.19,  $p < 0.001$ ) which persisted at 12 months (mean difference = 3.89, 95% CI 1.13 to 6.64,  $p = 0.006$ ) but not thereafter (Supplementary Table 9; Figure 3).

In the mastectomy cohort, 588/628 patients (93.6%) completed some or all of the EORTC QLQ-BR23 questionnaire at baseline (Supplementary Table 8). After adjustment for baseline measurements no significant effects in these domains were seen at 6 weeks in patients receiving radiotherapy versus those not receiving it, again reflecting the fact that almost no patients had received RT by this time point. At 6 months, a significant difference was

observed in breast symptoms (5.52, 95% CI 2.67 to 8.37,  $p < 0.001$ ). At 12 months, the effect persisted in breast symptoms (7.12, 95% CI 4.07 to 10.17,  $p < 0.001$ ), along with arm symptoms (6.34, 95% CI 2.99 to 9.70,  $p < 0.001$ ). No differences were documented at 18 months, whereas at 24 months these were observed in arm symptoms (6.19, 95% CI 1.21 to 11.17,  $p = 0.015$ ) (Supplementary Table 9; Figure 2).

### **Overall QoL (EORTC QLQ-C30)**

1004/1125 patients (89.2%) undergoing BCS and 567/628 patients (90.3%) undergoing a mastectomy completed all questions included in the EORTC QLQ-C30 questionnaire at baseline (Supplementary Table 8). Following adjustment for baseline scores, in the BCS cohort the difference in the global health status score was statistically significant at 12 months (adjusted mean difference 3.19, 95% CI -0.08 to -6.29,  $p = 0.044$ ) but no significant effects were seen at the other time points. In the mastectomy cohort, patients given radiotherapy experienced a significant decline of global health at 6 weeks (-3.18, 95% CI -6.32 to -0.04,  $p = 0.047$ ) but this effect resolved subsequently (Supplementary Tables 10 and 11; Supplementary Figure 1). Radiotherapy had a significant impact on fatigue at 6 months (adjusted mean difference 4.45, 95% CI 0.77 to 8.14,  $p = 0.018$ ), 12 months (7.26, 95% CI 3.07 to 11.46,  $p = 0.001$ ), 18 months (5.44, 95% CI 0.64 to 10.23,  $p = 0.026$ ) and 24 months (6.56, 95% CI 1.76 to 11.37,  $p = 0.008$ ). No other clinically meaningful effects were observed in the remaining domains of the EORTC QLQ-C30 questionnaire.

### **Older age-specific QoL (EORTC QLQ-ELD15)**

There were 1002/1125 patients (89.1%) undergoing BCS and 559/628 patients (89.0%) undergoing a mastectomy completed all questions included in the EORTC QLQ-ELD15 questionnaire at baseline (Supplementary Table 8). In the BCS cohort, after adjustment for baseline measurements no significant impact in the questionnaire domains were observed at 6 weeks in patients receiving radiotherapy compared with those not receiving it, again because radiotherapy had not been administered by this time point. At 6 months, radiotherapy had an effect on burden of illness (5.49, 95% CI 1.33 to 9.64,  $p = 0.010$ ). At 12 and 18 months, no significant differences were observed and at 24 months radiotherapy had an effect only on worries about others (-6.21, 95% CI -11.70 to -0.71,  $p = 0.027$ ) (Supplementary Table 12; Supplementary Figure 1). In the mastectomy cohort, after adjustment for baseline measurements an effect on the burden of illness domain was documented in patients receiving radiotherapy versus not at 6 weeks (5.54, 95% CI 0.84 to 10.24,  $p = 0.021$ ), 6 months (9.66, 95% CI 4.67 to 14.66,  $p < 0.001$ ), 12 months (5.70, 95% CI 0.34 to 11.06,  $p = 0.037$ ), 18 months (8.19, 95% CI 2.64 to 13.74,  $p = 0.004$ ) and 24 months (8.34, 95% CI 1.25 to 15.43,  $p = 0.021$ ) (Supplementary Table 12; Supplementary Figure 2).

**QoL health utility score (EQ5D-5L)**

A baseline EQ-5D-5L score was calculated in 1060/1125 patients undergoing BCS (94.2%) and in 593/628 patients (94.4%) undergoing a mastectomy. No significant differences in health utilities and the visual analogue scale (VAS) measures were observed based on receipt of radiotherapy in the BCS cohort (Supplementary Table 12; Supplementary Figure 1). In the mastectomy cohort, the VAS measures were significantly worse at 6 months in patients receiving radiotherapy versus not at 18 months (adjusted mean difference -0.04, 95% CI -0.07 to -0.01,  $p=0.029$ ) and 24 months (-0.05, 95% CI -0.08 to -0.02,  $p=0.004$ ) (Supplementary Table 13; Supplementary Figure 2).

**Adverse events**

In the BCS group, skin erythema occurred in 526 patients (38.0%), pain in 216 (15.6%), breast oedema in 76 (5.5%) and breast shrinkage in 13 (0.9%) (Supplementary Table 14). In the mastectomy cohort, skin erythema occurred in 135 patients (39.6%), pain in 50 (14.7%) and chest wall oedema in 12 (3.5%) and breast pain in 18 (5.3%) (Supplementary Table 15).

**Mortality**

At 52 months of follow-up, mortality data was available for 2757 patients (98% of cohort) and cause of death data for 2738 (97% of cohort). Overall, 464 (16.8%) had died, 193 (42%) of deaths were known to be due to breast cancer (Supplementary Table 16).

In patients undergoing breast conserving surgery, mortality data were available for 1631 (98%) of patients and cause of death data for 1624 (97%) patients. Of those receiving radiotherapy: 149 (11%) died from any cause and 51 (3.8%) died from breast cancer. For those not receiving radiotherapy, 48 (17.3%) died from any cause and 9 (3.3%) died from breast cancer.

??add mastectomy and PMRT survival data as well...we have scope in the word count

## DISCUSSION

This analysis is the largest prospective cohort study describing patterns of radiotherapy use and its impact on QoL, adverse events and mortality in older women with EBC, which integrates data on tumour characteristics and geriatric assessments.

In 2016-2018 life expectancy at birth in the United Kingdom was 79.3 years for males and 82.9 years for females(35) and has been steadily increasing alongside rising rates in other Western countries.(36) Therefore even in older patients there is a risk of recurrence within projected lifetime. In these patients a breast cancer recurrence may have significant symptomatic, psychological and financial implications even in the absence of an impact on survival outcomes.(11) Therefore, ensuring that older patients are adequately treated should be a priority.

Adjuvant radiotherapy following breast conserving surgery is a standard of care treatment for patients with all but lower risk patients identified in the PRIME II study. With respect post-mastectomy radiotherapy, a previous meta-analysis did not document any differential benefit of PMRT on locoregional recurrence and any first recurrence in patients  $\geq 60$  years compared with their younger counterparts,(37) supporting its use in this population.

Nonetheless data from the UK show that rates of radiotherapy after both BCS and mastectomy decline with increasing age.(38) However, whether this decline relates to age per se or to reductions in health and fitness or patient reluctance to suffer the inconvenience of often lengthy schedules, with potentially long travelling times to RT centres, is not known. This relates to the lack of detailed health and fitness data in national datasets.

With respect those patients at higher risk of recurrence this analysis demonstrated that almost 13% of fit, higher-risk patients undergoing BCS and more than 45% of fit higher risk patients undergoing a mastectomy did not receive radiotherapy, which might suggest some degree of under-treatment in this population. The reasons for this are unclear and may relate to both patient, clinician and geographic factors.

In contrast, in lower risk patients, previous studies have demonstrated a low additional risk of ipsilateral breast recurrence(13, 39) and no survival advantage up to 10 years follow up and breast preservation benefits with the omission of radiotherapy in the older age group.(12, 40) In the PRIME II study cohort, at 10 years 93.4% of mortality was not due to BC.(14) In our analysis, in the BCS cohort only one third of mortality was due to BC. This suggests that radiotherapy might be safely omitted in some older patients, especially those with a predicted shortened life expectancy and low risk breast cancers (41). In our study, despite

849/1669 patients (50.9%) having a low risk of recurrence after BCS (some of whom were vulnerable/frail), 82.1% received radiotherapy. This suggests some degree of over-treatment in this specific group and underlines the importance of considering both risk profile and health status to inform treatment decisions and discussions with patients. Overall, the data suggests a high degree of variability of practice (ref the funnel plots figure) relating to RT use, which might be improved by strengthening existing guidelines.

Previous trials did not include data on patients' fitness which may have a significant impact on their life expectancy and mitigate the benefit in local recurrence. This study overcame these limitations, by defining risk of recurrence and fitness, and still demonstrates a low impact of fitness considerations on radiotherapy uptake. This may reflect the fact that some clinicians over-estimate the benefits of radiotherapy(42) although this does not always correspond with older patients' perceived risks, lack of benefit and inconvenience.(43) These findings also demonstrate significant variation in the use of radiotherapy which has also confirmed by many national practice surveys.(38, 44, 45) These data need to be interpreted with caution in view of the potential bias associated with case-mix (variation in patient fitness, disease characteristics, logistics and cultural issues). Geography and proximity of surgical treatment centre to radiotherapy centre may also play a part which is difficult to correct for.

This analysis also demonstrates that, where appropriate and indicated, radiotherapy has little negative long-term impact on toxicities and overall QoL, which is a meaningful endpoint in the context of the lack of survival benefits and increased risk of toxicities on anticancer treatments in this population. As expected, the most significant impact occurred on breast symptoms, although this effect was transient and resolved by two years, consistent with previous data.(46, 47)

An important strength of this analysis is that the study enrolled women from a wide range of Institutions across the UK, which suggests that these findings are applicable to a real-world population of patients and reflect contemporary practice and outcomes. The results of trials currently investigating the role of biomarkers to better select patients at low risk of recurrence that may be safely spared radiotherapy, such as PRIMETIME (ISRCTN41579286), PRECISION (NCT02653755) and LUMINA (NCT01791829), will be highly meaningful to the older EBC patient population.

This study also has some limitations. First, the study criteria to define high-risk EBC did not include data on lymphovascular invasion, which is a common considerations for the use of radiotherapy after mastectomy.(48, 49) Despite the inclusive entry criteria and low level of intervention there was still the possibility of selection bias: in a separate analysis of this

study, patients excluded at various stages of the study selection and recruitment process were older and had more frequently impaired functional status.<sup>(50)</sup> The cohort therefore has slightly skewed baseline age and health characteristics compared to the normal UK population. Also, despite the fact that we excluded patients receiving chemotherapy from the QoL analysis, we did not factor in the impact of endocrine therapy which was the most likely cause of concerns about hair loss in the QoL analysis. <sup>(51)</sup> Our findings may not be applicable to other countries, although previously published data appear comparable.<sup>(52)</sup>

In summary, this study demonstrates that fitness is not a major determinant of radiotherapy decisions for older patients with EBC and there are a significant number of vulnerable older women with both high-risk and low-risk EBC who receive adjuvant radiotherapy. Some of these patients, particularly those with competing risks of morbidity and mortality, may derive little benefit from radiotherapy. There was also a fairly low rate of PMRT in women at higher recurrence risk suggesting a degree of under treatment. Potential risks and benefits need to be discussed in the context of the risk of side effects and the transient negative impact on breast symptoms. Nonetheless, it is important that individualised treatment decisions and discussions are made to ensure the best outcomes for older adults and our findings argue for the inclusion of considerations on fitness (and not only on tumour risk of recurrence) in radiotherapy guidelines.

## **ADDITIONAL INFORMATION**

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### **Authors' contributions**

All the authors conceived and designed the work that led to the submission, drafted and revised the manuscript and approved the final version.

### **Ethics approval and consent to participate**

Ethics approval (IRAS: 12 LO 1808) and research governance approval were obtained. All patients (or their proxies, if cognitively impaired) gave written informed consent.

### **Consent for publication**

Not applicable.

### **Data availability**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare no conflict of interest. Professors Stephen Walters and Thompson Robinson are National Institute for Health Research (NIHR) Senior Investigators, Jenna Morgan is a NIHR Clinical Lecturer and Kate Lifford is funded by the NIHR as part of this project. The views expressed in this article are those of the author(s) and not necessarily those of the NIHR, or the Department of Health and Social Care.

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