



Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective analysis of hospital episode statistics

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3 **Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective**
4 **analysis of hospital episode statistics**
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ABSTRACT

Objectives For healthy women at high risk of developing breast cancer, a bilateral mastectomy can reduce future risk. For women who already have unilateral breast cancer, removing the contralateral healthy breast is more difficult to justify. We examined trends in the number of women who had a bilateral mastectomy in England between 2002 and 2011.

Design Retrospective cohort study using the Hospital Episode Statistics.

Setting NHS hospitals in England.

Participants Women aged between 18 and 80 years who had a bilateral mastectomy (or a contralateral mastectomy within 24 months of unilateral mastectomy) with or without a diagnosis of breast cancer.

Main outcome measures Number and incidence of women without breast cancer who had a bilateral mastectomy; number and proportion who had a bilateral mastectomy as their first operation, and the proportion of those undergoing bilateral mastectomy who had immediate breast reconstruction.

Results Among women without breast cancer, the number who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011 (annual incidence rate ratio 1.16, 95% confidence interval 1.13 to 1.18). In women with breast cancer, the number rose from 529 to 931, an increase from 2.0% to 3.1% of first operations (odds ratio for annual increase 1.07, 95% CI 1.05 to 1.08). Across both groups, rates of immediate breast reconstruction roughly doubled and reached 90% among women without breast cancer in 2011.

Conclusion The number of women who had a bilateral mastectomy nearly doubled over the last decade, and more than tripled among women without breast cancer. This coincided with an increase in availability of breast reconstruction.

2,622 words, excluding article summary, figures, tables and references

ARTICLE SUMMARY

Article focus

In the US, there has been substantial increase in the use of bilateral mastectomy among women with unilateral breast cancer. The operation is intended to reduce the risk of developing contralateral breast cancer, but the survival benefits are unclear. We speculated that a similar increase may have occurred in England.

Among healthy women with a high risk of developing breast cancer, a bilateral mastectomy can reduce their future breast cancer risk and is supported by NICE guidelines in England.

We examined trends in use of bilateral mastectomy in English NHS hospitals among women with and without breast cancer between 2002 and 2011.

Key messages

Over the last decade in England, the number of women having a bilateral mastectomy increased both among women with and without breast cancer.

Among women with breast cancer, the apparent increase in use of risk reducing contralateral mastectomy is not supported by the clinical evidence.

Among women without breast cancer, the increase in use of bilateral mastectomy was proportionately greater and is clinically justified for risk reduction. Among this group, 90% of women have immediate breast reconstruction.

Strengths and limitations of study

Ours is the first English study to examine trends in use of bilateral mastectomy at the national level using a large, administrative database, the Hospital Episode Statistics (HES).

The HES database does not contain diagnosis codes that distinguish unilateral from bilateral breast cancer, so we were not able to exclude women who had a therapeutic bilateral mastectomy from our study. However, by checking the use of codes for prophylactic surgery, we were able to confirm that a large fraction of mastectomies among women with breast cancer were intended as risk reducing operations.

INTRODUCTION

There are two distinct groups of women who undergo bilateral mastectomy (BM): those without breast cancer but with familial breast cancer or known genetic mutations (BRCA1 or BRCA2) and those with breast cancer in one or both breasts. Guidelines produced by the UK National Institute for Health and Clinical Excellence (NICE) recommend that risk-reducing BM is appropriate for high-risk women without breast cancer. High-risk is defined as a lifetime risk of 30% or higher, compared to an average risk of 11% in the UK female population.[1] This advice is consistent with clinical evidence that removal of both healthy (non-cancerous) breasts can reduce the future incidence of breast cancer in high-risk women.[2-5]

Some women with unilateral breast cancer have the healthy breast removed to reduce their risk of contralateral breast cancer. Both breasts can be removed simultaneously or the contralateral healthy breast can be removed at a later date. Although the contralateral mastectomy may reduce the risk of developing a future malignant breast tumour and the need for further breast cancer treatments, it is uncertain whether it improves survival, even in BRCA carriers.[3,4]

Over the last two decades in the United States, there has been an increase in contralateral risk-reducing mastectomy from 1-2% to around 5% of women having breast cancer surgery.[6-9] Several reasons have been suggested for this increase, including wider availability of genetic testing, avoidance of long-term breast surveillance and increased availability of immediate breast reconstruction. Patients and health professionals may also overestimate the risk of contralateral breast cancer.[10] However, trends in the UK and rest of Europe may be different as a result of different medical and cultural attitudes toward extensive ablative surgery and aesthetic surgery in general. [11]

Our aim was to investigate trends in bilateral mastectomy for women without and with a breast cancer diagnosis in England between 2002 and 2011. We also examined trends in immediate breast reconstruction to assess the role that this might have played.

METHODS

Data definitions and selection of cohort

We used data extracted from the Hospital Episode Statistics (HES) database, [12] which covers all admissions to English National Health Service (NHS) hospitals. A unique patient identifier allows same patient admissions to be linked. Each HES record captures up to 24 procedures, using the UK Office of Population Censuses and Surveys (OPCS) classification, version 4.4. Diagnoses are recorded using the International Classification of Diseases, 10th Revisions (ICD-10). Our extract from HES covered the period from 2002 to 2011, using financial years (1st April to 31st March).

Bilateral mastectomy performed as a single operation was identified with the OPCS codes B27 (mastectomy) and Z94.1 (bilateral). Unilateral mastectomy was identified with the codes B27 plus Z94.2 (right sided), Z94.3 (left sided) or Z94.4 (unilateral). We excluded women with missing information on uni or bi-laterality. Because high rates of missing information were concentrated in a few NHS trusts, we re-ran our analyses after excluding these trusts to check the robustness of the estimated trends. Breast-conserving operations were identified with OPCS codes B28.1, B28.2, B28.3, B28.8 and B28.9.

Breast reconstruction was identified using OPCS codes B29 (breast reconstruction, excluding B29.5 revision), B38 (reconstruction using buttock flap), B39 (reconstruction using abdominal flap), B30.1 (insertion of prosthesis) and S48.2 (insertion of skin expander).

We identified women with breast cancer using the ICD-10 diagnosis codes C50 (malignant neoplasm) and D05 (carcinoma-in-situ). The ICD-10 codes do not distinguish bilateral from unilateral breast cancer so it was not possible to identify how many women had a therapeutic BM for bilateral breast cancer. The number of women diagnosed with synchronous bilateral breast cancer is thought to be extremely small and stable since the 1980s, based on Swedish Cancer Register data. [13,14]

We selected women aged 18 to 80 years who fulfilled one of the following two inclusion criteria: 1) they had a BM between 2002 and 2011; or 2) they had a first breast cancer operation between 2002 and 2011 and had a current or previous diagnosis of breast cancer. A previous diagnosis of breast cancer was determined by checking women's hospital records going back to April 2000.

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3 From this cohort, we distinguished between two groups of women who underwent BM. The
4 first group comprised of women who did not have a current or previous diagnosis of breast
5 cancer. To ensure appropriate allocation to this non-cancer group, we checked the frequency
6 with which ICD-10 codes associated with breast cancer risk were used, such as Z40
7 (prophylactic surgery) or Z80 (Family history of malignant neoplasm). All women in this
8 group had BM as a simultaneous procedure.
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14 The second group included women who had a current or previous diagnosis of breast cancer.
15 Women in this group underwent simultaneous BM or had a contralateral mastectomy as a
16 separate procedure within 24 months of the unilateral mastectomy. This approach is referred
17 to in this paper as BM (two procedures). Removal of a contralateral breast may be decided at
18 the time of the initial cancer diagnosis but only be performed after completion of adjuvant
19 therapies (chemotherapy or in particular radiotherapy). Alternatively, the decision for
20 contralateral mastectomy may be made after genetic assessment/testing during or after
21 adjuvant treatment.
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27 **Statistical analysis**

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30 We calculated the number of women who underwent BM each financial year from 2002 to
31 2011.
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35 Among women without breast cancer, we calculated the incidence of BM per 100,000
36 women in the English population aged 25-69, using figures published by the Office for
37 National Statistics as the denominator.[15] This corresponds to the age range in the study
38 cohort. We then used poisson regression to estimate an annual trend in the use of BM,
39 including year as a linear term.
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45 Among women with breast cancer, we calculated the BM rate as a proportion out of all
46 women who had a first breast cancer operation that year. We used multivariable logistic
47 regression to estimate the annual trend in the proportion undergoing BM, including year as a
48 linear term, with and without adjusting for age. We report average trends for the period
49 2002-2009. This is because the number of contralateral mastectomies is underestimated for
50 2010 and 2011 because our extract from the HES database extended only up to 31st March
51 2012.
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We calculated the percentage of women who underwent immediate breast reconstruction following BM each year, along with their 95% confidence intervals.

In all cases, we tested for a change in trends using spline terms, but only describe linear trends for simplicity of presentation. Reported p values are based on likelihood ratio tests. All analyses were carried out in Stata version 11.

RESULTS

Bilateral mastectomy in women without breast cancer

Between 2002 and 2011, the number of women without breast cancer who underwent simultaneous BM increased from 71 to 255 (Table 1). The population incidence increased from 0.4 to 1.3 per 100,000 women aged 25-69 years with an estimated annual increase around 16% (incidence rate ratio 1.16, 95% CI 1.13 to 1.18, $P < 0.001$), although increases were less in more recent years ($P < 0.001$).

Women without breast cancer comprised an increasing fraction of all women who had a BM, from 11.8% (71 / (71 + 529)) in 2002 to 19.9% in 2009 (232 / (232 + 931)) (Tables 1 and 2). The average age at surgery was 40 years and did not change over this time period.

Bilateral mastectomy in women with breast cancer

Between 2002 and 2009, the number of women with breast cancer who underwent BM increased from 521 to 931, representing an increase from 2.0% to 3.1% of all women undergoing their first breast cancer surgery (Table 2). The estimated annual increase was around 7% (odds ratio 1.07, 95% CI 1.05 to 1.08, $P < 0.001$), with no strong evidence of a change in trends over the period.

The average age for first breast cancer operation was 58 years, for BM in two procedures it was 51 years, and for simultaneous BM the average age fell from 57 years to 54 years.

Around two-fifths of BMs were carried out as separate operations, with the contralateral mastectomy being performed within 24 months.

Rates of immediate breast reconstruction 2002-2011

Among women without breast cancer immediate breast reconstruction rates increased substantially from 59.2% (95% CI 46.8 to 70.7) to 90.6% (95% CI 86.3 to 93.9) (Table

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3 3).Reconstruction rates were higher among younger than older women, particularly those
4 under 40 years ($P < 0.001$).
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7 Among women with breast cancer who had simultaneous BM, immediate breast
8 reconstruction rates increased from 18.2% (95% CI 14.0 to 23.0) to 40.8% (95% CI 36.9
9 to 44.8). Reconstruction among women who underwent BM in two procedures increased
10 from 27.1% (95% CI 21.4 to 33.5) to 53.8% (95% CI 43.1 to 64.2).
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14 **DISCUSSION**

15 **Summary of results**

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18 Over the last decade the total number of women in England who had a bilateral mastectomy
19 nearly doubled, from around 600 to 1,000 women per year. Proportionally the largest increase
20 in BM was seen in women without breast cancer whose numbers tripled from 71 to 255,
21 representing an increase in use among women aged 25-69.
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27 Overall, the majority of women who underwent BM had breast cancer. In this group there
28 was an increase in the number who underwent BM (in one or two procedures) between 2002
29 and 2009, representing a modest increase from 2% to 3% of women who had their first breast
30 cancer operation.
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34 Between 2002 and 2011, rates of breast reconstruction after BM roughly doubled to nearly
35 50% for women with cancer and over 90% for women who did not have breast cancer.
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39 **Strengths and limitations of study**

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41 The comprehensiveness of HES enabled us to identify different hospital admissions for the
42 same woman over a long period of time. Because HES links separate episodes of care for the
43 same patient, we could reliably identify contralateral mastectomies performed within 24
44 months of having a first unilateral mastectomy.
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48 The main limitation of HES is the lack of codes for a bilateral or unilateral breast cancer
49 diagnosis. This meant that we were unable to exclude women with bilateral breast cancer at
50 initial diagnosis from our study, or women diagnosed with an occult or new contralateral
51 breast cancer within 24 months of the index cancer. As a result, among women with breast
52 cancer, those who underwent a therapeutic BM will be included in our figures. In the
53 Swedish Cancer Register, around one percent of women were first diagnosed with bilateral
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3 breast cancer and less than half a percent were diagnosed with contralateral breast cancer
4 within 24 months of a first diagnosis, [13] rates that have remained stable since the 1980s.
5 [14] Assuming trends in the UK are comparable; it is therefore unlikely that a change in
6 incidence could explain the observed increase in BM rates. Improved MRI-detection of
7 occult contralateral breast cancers could have contributed to the increase in the rate of
8 contralateral mastectomy following a unilateral mastectomy,[16] but upon checking the use
9 of codes for prophylactic surgery within our database, we were able to confirm that, at
10 minimum, half of these were intended as risk-reducing operations, and more than 60% since
11 2009.

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13 A further limitation of HES, common to administrative databases, is the potential for
14 inaccuracies and omissions in coding. We carried out a separate analysis to check the impact
15 of missing procedure codes for whether a mastectomy was bilateral, right-sided or left-sided.
16 The rate of missing codes decreased over the study period from around 5.6% to 1.4% of first
17 mastectomies among women with breast cancer. However, underuse of these codes was
18 concentrated in a few NHS trusts, so we re-estimated trends after excluding these trusts from
19 our analysis and were able to confirm that the observed increase in the rate of BM was
20 similar, ie, an increase from 2% to 3% among women with breast cancer.

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22 Ideally, to estimate changes in BM use among women without breast cancer, the denominator
23 would be the number of women with a high risk of breast cancer. Based on a single study,
24 NICE estimated that up to 2,500 women aged 30-49 in England and Wales could be assessed
25 each year as having a genetic risk of breast cancer,[17] but actual numbers are not published.

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27 By looking at rates of immediate breast reconstruction, we are likely to underestimate the
28 total number of women with breast cancer who underwent breast reconstruction, which will
29 include some women who underwent delayed reconstruction.[18] Delayed reconstruction
30 may be recommended in women with breast cancer when radiotherapy is anticipated, since
31 radiotherapy can impair the long-term aesthetic results of breast reconstruction.

32 33 **Comparison with bilateral mastectomy trends in the US**

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35 The dramatic increase in BM among women without breast cancer in England has not been
36 noted in the US over the last two decades, although an increase could have occurred earlier in
37 the US. [6] In contrast, several US studies have identified an increase in contralateral risk-
38 reducing mastectomy among women with breast cancer.[6-9] Although the definitions and
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3 populations studied are not exactly the same as ours, the evidence points toward a larger
4 increase in risk-reducing contralateral mastectomy in the US than in England.
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7 Various reasons have been suggested for the increase in contralateral risk-reducing
8 mastectomy in the US. One reason may be increased awareness of hereditary risk and
9 associated use of genetic testing. Additional drivers may be higher screening re-call rates, the
10 need for additional breast assessment including biopsies and other uncertainties arising from
11 annual surveillance mammography and magnetic resonance imaging (MRI).[19]
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14 Refinements of mastectomy techniques, (skin and nipple-sparing) as well as increased access
15 to breast reconstruction may also have contributed to the increase of contralateral
16 mastectomy. Wider acceptance of aesthetic surgery with higher immediate breast
17 reconstruction rates in the US (up to 40% in 2008 compared to around 20% in the UK) may
18 also partly account for the relatively greater increase in contralateral risk-reducing
19 mastectomy, compared to the UK.[11, 18]
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27 **Implications for clinical practice**

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29 In women at high risk of developing breast cancer, there has been an increase in BM since the
30 publication of NICE guidance (2004 and 2006). [1] In an otherwise healthy woman, a BM is
31 a radical approach to risk reduction, but has been estimated to reduce the incidence of breast
32 cancer in BRCA carriers by up to 90%.[3] NICE emphasises the importance of patient-led
33 decision making and provides detailed recommendations regarding the need for a specialist
34 multidisciplinary approach including psychological counselling, with clear information
35 provision on extent of risk reduction and options for breast reconstruction.
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42 The high rate of immediate breast reconstruction after BM among women without breast
43 cancer suggests that reconstruction is widely available for these patients. This seems
44 appropriate as women who undergo breast reconstruction report higher levels of satisfaction
45 with their post-surgery appearance than women who undergo mastectomy alone.[18]
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49 In women with a personal history or new diagnosis of unilateral breast cancer the value of
50 contralateral mastectomy for risk reduction is more controversial. For this group of women,
51 decision-making is complicated. It is likely that the risk of dying or need for further cancer
52 treatment is determined by the biology and stage of the index rather than by a subsequent
53 cancer in the contralateral breast.[5] The risk of subsequent cancers is likely to be reduced by
54 the treatment of the index cancer [20] and any future cancers are likely to be surveillance
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3 detected with a correspondingly better prognosis.[21] Consequently, a risk-reducing
4 contralateral mastectomy may not confer any benefit.
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7 **CONCLUSION**

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9 Over the last decade, the number of women who had a bilateral mastectomy in England
10 increased. The increase was proportionately greater in women without breast cancer and
11 within this group, 90% have breast reconstruction at the time of their bilateral mastectomy.
12 However, the majority of women who had a bilateral mastectomy appear to have had
13 unilateral breast cancer. The evidence to support contralateral risk reducing mastectomy in
14 women with breast cancer is limited.
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What is already known on this topic

Among healthy women with a high risk of developing breast cancer, a bilateral mastectomy can reduce their future risk

Among women with unilateral breast cancer, there is not strong evidence that a contralateral risk reducing mastectomy improves survival

In the US, there has been an increase in use of contralateral risk reducing mastectomy over the last two decades from 1-2% to around 5% of women having breast cancer surgery

What this study adds

In England, the number of women without breast cancer who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011

The number of women with breast cancer who had a bilateral mastectomy (including a contralateral mastectomy after a unilateral mastectomy) increased from 529 in 2002 to 931 in 2009, an increase from 2% to 3% of women having first breast cancer surgery

Rates of immediate breast reconstruction roughly doubled over this period, reaching 90% among women without breast cancer in 2011

Table 1 Number of women without breast cancer who had a bilateral mastectomy (BM) in England, 2002-2011

	Number of women who had a BM	Incidence per 100,000 females aged 25-69	Annual trend	
			IRR (95% CI)	P value
2002	71	0.4	1.16 (1.13 to 1.18)	<0.001
2003	72	0.4		
2004	101	0.6		
2005	131	0.7		
2006	147	0.8		
2007	201	1.1		
2008	186	1.0		
2009	232	1.2		
2010	238	1.3		
2011	255	-		

Table 2 Number (%) who had a bilateral mastectomy (BM) out of women with breast cancer having their first operation, 2002-2011

	All women who had first breast cancer operation	No of women who had a BM			Annual trend (2002-2009)	
		Performed as same operation	Performed as two operations	Total (%)	OR (95% CI)	P value
2002	25,844	308	221	529 (2.0)	1.07 (1.05 to 1.08)	<0.001
2003	27,303	332	263	595 (2.2)		
2004	27,643	335	269	604 (2.2)		
2005	29,179	369	312	681 (2.3)		
2006	28,645	407	307	714 (2.5)		
2007	28,702	432	336	768 (2.7)		
2008	29,629	493	384	877 (3.0)		
2009	29,745	546	385	931 (3.1)		
2010	30,760	528	263*	-		
2011	31,240	617	93*	-		

*These numbers are underestimates since the HES database only covers the period up to 31st March 2012. Some women will have had a contralateral mastectomy after this date, but within 24 months of their first mastectomy in 2010 or 2011.

Table 3 Number (%) of women who underwent immediate breast reconstruction at the time of a bilateral mastectomy (BM), by presence of a breast cancer diagnosis, 2002-2011

	Women without breast cancer		Women with breast cancer			
	No	% (95% CI)	BM in same operation		BM in two operations	
	No	% (95% CI)	No	% (95% CI)	No	% (95% CI)
2002	42	59.2 (46.8 to 70.7)	56	18.2(14.0 to 23.0)	60	27.1(21.4 to 33.5)
2003	47	65.2 (53.1 to 76.1)	43	13.0 (9.5 to 17.0)	80	30.4 (24.9 to 36.3)
2004	70	69.3 (59.3 to 78.1)	58	17.3 (13.4 to 21.8)	83	30.9 (25.4 to 36.7)
2005	87	66.4 (57.6 to 74.4)	80	21.7 (17.6 to 26.2)	105	33.7 (28.4 to 39.2)
2006	106	72.1 (64.1 to 79.2)	93	22.9 (18.9 to 27.2)	142	46.3 (40.6 to 52.0)
2007	160	79.6 (73.4 to 84.9)	103	23.8 (19.9 to 28.1)	155	46.1 (40.7 to 51.6)
2008	151	81.2 (74.8 to 86.5)	135	27.4 (23.5 to 31.5)	173	45.1 (40.0 to 57.3)
2009	203	87.5 (82.5 to 91.5)	185	33.9 (30.0 to 38.0)	201	52.2 (47.1 to 57.3)
2010	207	87.0 (82.0 to 91.0)	188	35.6 (31.5 to 40.0)	132	50.2 (44.0 to 56.4)
2011	231	90.6 (86.3 to 93.9)	252	40.8 (36.9 to 44.8)	50	53.8 (43.1 to 64.2)

review only

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11 DAC is the guarantor.
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37 Ethical approval: The study is exempt from UK National Research Ethics Committee
38 approval as it involved secondary analysis of an existing dataset of anonymised data for
39 service evaluation. Approvals for the use of hospital episode statistics data were obtained as
40 part of the standard hospital episode statistics approval process.
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45 Data sharing: No additional data available.
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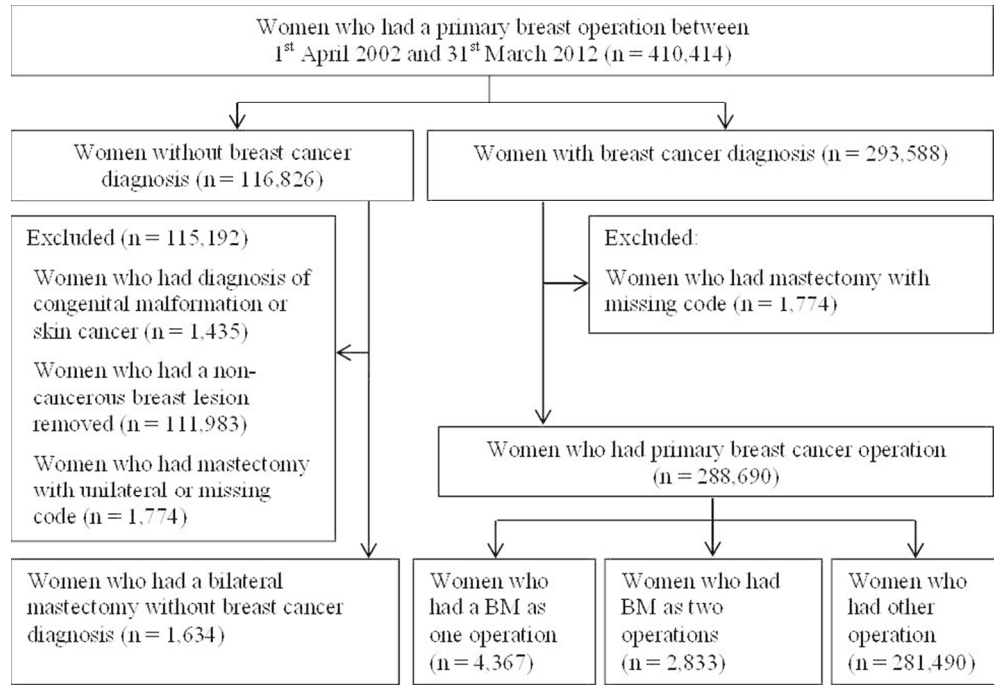


Figure 1 Inclusion of women in the study
166x113mm (150 x 150 DPI)



Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective analysis of hospital episode statistics

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3 **Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective**
4 **analysis of hospital episode statistics**
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Abstract

Objectives For healthy women at high risk of developing breast cancer, a bilateral mastectomy can reduce future risk. For women who already have unilateral breast cancer, removing the contralateral healthy breast is more difficult to justify. We examined trends in the number of women who had a bilateral mastectomy in England between 2002 and 2011.

Design Retrospective cohort study using the Hospital Episode Statistics database.

Setting NHS hospital trusts in England.

Participants Women aged between 18 and 80 years who had a bilateral mastectomy (or a contralateral mastectomy within 24 months of unilateral mastectomy) with or without a diagnosis of breast cancer.

Main outcome measures Number and incidence of women without breast cancer who had a bilateral mastectomy; number and proportion who had a bilateral mastectomy as their first breast cancer operation, and the proportion of those undergoing bilateral mastectomy who had immediate breast reconstruction.

Results Among women without breast cancer, the number who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011 (annual incidence rate ratio 1.16, 95% confidence interval 1.13 to 1.18). In women with breast cancer, the number rose from 529 to 931, an increase from 2.0% to 3.1% of first operations (odds ratio for annual increase 1.07, 95% CI 1.05 to 1.08). Across both groups, rates of immediate breast reconstruction roughly doubled and reached 90% among women without breast cancer in 2011.

Conclusion The number of women who had a bilateral mastectomy nearly doubled over the last decade, and more than tripled among women without breast cancer. This coincided with an increase in the use of immediate breast reconstruction.

2,744 words, excluding figures, tables and references

INTRODUCTION

There are two distinct groups of women who undergo bilateral mastectomy (BM): those without breast cancer but with familial breast cancer or known genetic mutations (BRCA1 or BRCA2) and those with breast cancer in one or both breasts. Guidelines produced by the UK National Institute for Health and Clinical Excellence (NICE) state that risk-reducing BM may be appropriate for high-risk women without breast cancer. High-risk is defined as a lifetime risk of 30% or higher, compared to an average risk of 11% in the UK female population.[1] This advice is consistent with clinical evidence that removal of both healthy (non-cancerous) breasts can reduce the future incidence of breast cancer in high-risk women.[2-5]

Some women with unilateral breast cancer have the healthy breast removed to reduce their risk of contralateral breast cancer. Both breasts can be removed simultaneously or the contralateral healthy breast can be removed at a later date. Although the contralateral mastectomy may reduce the risk of developing a future malignant breast tumour and the need for further breast cancer treatments, a 2010 Cochrane Review found insufficient evidence of improved survival.[5]

Over the last two decades in the United States the use of contralateral risk-reducing mastectomy has increased, from 1-2% to around 5% of women having breast cancer surgery.[6-9] Several reasons have been suggested for this increase, including wider availability of genetic testing, avoidance of long-term breast surveillance and increased availability of immediate breast reconstruction. Patients and health professionals may also overestimate the risk of contralateral breast cancer.[10] However, trends in the UK and rest of Europe may be different as a result of different medical and cultural attitudes toward extensive ablative surgery and aesthetic surgery. [11]

Our aim was to investigate trends in bilateral mastectomy for women without and with a breast cancer diagnosis in England between 2002 and 2011. We also examined trends in immediate breast reconstruction to assess the role that this might have played.

METHODS

Data definitions and selection of cohort

We used data extracted from the Hospital Episode Statistics (HES) database, [12] which covers all admissions to English National Health Service (NHS) hospital trusts. A unique patient identifier allows same patient admissions to be linked. Each HES record captures up to 24 procedures, using the UK Office of Population Censuses and Surveys (OPCS) classification, version 4.4. Diagnoses are recorded using the International Classification of Diseases, 10th Revisions (ICD-10). Our extract from HES covered the period from 2002 to 2011, using financial years (1st April to 31st March).

Bilateral mastectomy performed as a single operation was identified by the OPCS codes B27 (mastectomy) and Z94.1 (bilateral). Unilateral mastectomy was identified by the code B27 in addition to Z94.2 (right sided), Z94.3 (left sided) or Z94.4 (unilateral). We excluded women with missing information on laterality. Because high rates of missing information were concentrated in four out of 162 NHS trusts, we re-ran our analyses after excluding these NHS trusts to check the robustness of the estimated trends. Breast-conserving operations were identified by the OPCS codes B28.1, B28.2, B28.3, B28.8 and B28.9.

Breast reconstruction was identified using OPCS codes B29 (breast reconstruction, excluding B29.5 revision), B38 (reconstruction using buttock flap), B39 (reconstruction using abdominal flap), B30.1 (insertion of prosthesis) and S48.2 (insertion of skin expander).

We identified women with breast cancer using the ICD-10 diagnosis codes C50 (malignant neoplasm) and D05 (carcinoma-in-situ). The ICD-10 codes do not distinguish bilateral from unilateral breast cancer so it was not possible to identify how many women had a therapeutic BM for bilateral breast cancer. The number of women diagnosed with synchronous bilateral breast cancer is thought to be extremely small and relatively stable since the 1980s, based on Swedish Cancer Register data and studies from Australasia and the Netherlands. [13-16]

We selected women aged 18 to 80 years who fulfilled one of the following two inclusion criteria: 1) they had a BM between 2002 and 2011; or 2) they had a first breast cancer operation between 2002 and 2011 and had a current or previous diagnosis of breast cancer. A

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3 previous diagnosis of breast cancer was determined by checking women's HES records going
4 back to April 2000.
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7 From this cohort, we distinguished between two groups of women who underwent BM. The
8 first group comprised of women who did not have a current or previous diagnosis of breast
9 cancer. All women in this group had BM as a simultaneous procedure.
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12 The second group included women who had a current or previous diagnosis of breast cancer.
13 Women in this group underwent simultaneous BM or had a contralateral mastectomy as a
14 separate procedure within 24 months of the unilateral mastectomy. This approach is referred
15 to in this paper as two procedure BM. Removal of a contralateral breast may be decided at
16 the time of the initial cancer diagnosis but only be performed after completion of adjuvant
17 therapies (chemotherapy or in particular radiotherapy). Alternatively, the decision for
18 contralateral mastectomy may be made after genetic assessment/testing and appropriate
19 counselling, during or after any adjuvant treatments.
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27 **Statistical analysis**

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29 We calculated the number of women who underwent BM each financial year from 2002 to
30 2011. Of the women without breast cancer we identified, all were aged from 25 to 69 years.
31 We therefore calculated the incidence of BM per 100,000 women in the English population
32 aged 25-69 as a denominator, using figures published by the Office for National
33 Statistics.[17] We then used Poisson regression to estimate an annual trend in the use of BM,
34 including year as a linear term.
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40 Among women with breast cancer, we calculated the BM rate as a proportion out of all the
41 first breast cancer operations undertaken that year. We used multivariable logistic regression
42 to estimate the annual trend in the proportion undergoing BM, including year as a linear term,
43 with and without adjusting for age. We report average trends for the period 2002-2009. This
44 is because the number of two procedure BMs is underestimated for 2010 and 2011 because
45 our extract from the HES database extended only up to 31st March 2012, allowing 24 months
46 of follow up only for women who had a mastectomy before 1 March 2010.
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53 We calculated the percentage of women who underwent immediate breast reconstruction
54 following BM each year, along with the 95% confidence intervals.
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3 In all cases, we tested for a change in trends using spline terms, but only describe linear
4 trends for simplicity of presentation. Reported P values are based on likelihood ratio tests.
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6 All analyses were carried out in Stata version 11.
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8 9 **RESULTS**

10 11 **Bilateral mastectomy in women without breast cancer**

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13 Between 2002 and 2011, the number of women without breast cancer who underwent
14 simultaneous BM increased from 71 to 255 (Table 1). The population incidence increased
15 from 0.4 to 1.3 per 100,000 women aged 25-69 years with an estimated annual increase of
16 around 16% (incidence rate ratio 1.16, 95% CI 1.13 to 1.18, $P < 0.001$), although increases
17 were smaller in more recent years ($P < 0.001$).
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21 Women without breast cancer comprised an increasing fraction of all women undergoing
22 BM, from 11.8% ($71 / (71 + 529)$) in 2002 to 19.9% in 2009 ($232 / (232 + 931)$) (Tables 1
23 and 2). The average age at surgery was 40 years and did not change over this time period.
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28 29 **Bilateral mastectomy in women with breast cancer**

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31 Between 2002 and 2009, the number of women with breast cancer who underwent BM
32 increased from 521 to 931, representing an increase from 2.0% to 3.1% of all women
33 undergoing their first breast cancer operation (Table 2). The estimated annual increase was
34 around 7% (odds ratio 1.07, 95% CI 1.05 to 1.08, $P < 0.001$), with no strong evidence of a
35 change in trends over the period.
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40 The average age at first breast cancer operation was 58 years, for two procedure BM it was
41 51 years, and for simultaneous BM it fell from 57 years to 54 years during the study period.
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45 Around two-fifths of BMs were carried out as two procedures, with the contralateral
46 mastectomy being performed within 24 months.
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48 49 **Rates of immediate breast reconstruction 2002-2011**

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51 Among women without breast cancer, the immediate breast reconstruction rate increased
52 substantially from 59.2% (95% CI 46.8 to 70.7) to 90.6% (95% CI 86.3 to 93.9) (Table 3).
53 Reconstruction rates were higher among younger women, particularly those under 40 years
54 ($P < 0.001$).
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3 Among women with breast cancer who had simultaneous BM, the immediate breast
4 reconstruction rate increased from 18.2% (95% CI 14.0 to 23.0) to 40.8% (95% CI 36.9 to
5 44.8). The immediate reconstruction rate among women who underwent BM in two
6 procedures increased from 27.1% (95% CI 21.4 to 33.5) to 53.8% (95% CI 43.1 to 64.2).
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10 **DISCUSSION**

11 **Summary of results**

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15 Over the last decade the total number of women in England who had a bilateral mastectomy
16 nearly doubled, from around 600 to 1,000 women per year. Proportionally, the largest
17 increase in BM incidence was seen in women without breast cancer. Their number tripled
18 from 71 to 255 between 2002 and 2009, representing an increase in uptake among women
19 aged 25-69.
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24 Overall, the majority of women who underwent BM had breast cancer. In this group there
25 was an increase in the number who underwent BM (in one or two procedures) between 2002
26 and 2009, representing a modest increase from around 2% to 3% of women undergoing their
27 first breast cancer operation.
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32 Between 2002 and 2011, rates of immediate breast reconstruction after BM roughly doubled
33 to nearly 50% for women with cancer and over 90% for women who did not have breast
34 cancer.
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38 **Strengths and limitations of study**

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40 The comprehensiveness of HES enabled us to identify different hospital admissions for the
41 same woman over a long period of time. Because HES links separate episodes of care for the
42 same patient, we could reliably identify contralateral mastectomies performed within 24
43 months of a first unilateral mastectomy.
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48 The main limitation of HES is the lack of codes indicating whether a breast cancer diagnosis
49 is unilateral or bilateral. This meant that we were unable to exclude from our analysis
50 women with bilateral breast cancer at initial diagnosis, or diagnosed with an occult or new
51 contralateral breast cancer within 24 months of the index cancer. As a result, among women
52 with breast cancer, those who underwent a therapeutic BM are included in our figures. Of
53 women diagnosed with breast cancer in the Swedish Cancer Register, around one percent of
54 women were first diagnosed with bilateral breast cancer and less than half a percent were
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3 diagnosed with contralateral breast cancer within 24 months of a first diagnosis, [13] and
4 these rates have remained stable or decreased since the 1980s. [14] Two recent population-
5 based studies from Australasia and the Netherlands reported comparable bilateral breast
6 cancer rates of 2.3% and 2.2% respectively.[15,16] Assuming trends in the UK are
7 comparable, it is unlikely that a change in incidence alone could explain the observed
8 increase in BM rates. Increased detection of bilateral breast cancers through the NHS Breast
9 Screening Programme is also unlikely to explain the increase in BM rates, since we found
10 higher rates and larger increases in rates among women aged under 50 years, who would not
11 have been routinely screened over the study period. Improved MRI-detection of occult
12 contralateral breast cancers could have contributed to the increase in the rate of contralateral
13 mastectomy following a unilateral mastectomy.[18] However, upon checking the use of
14 codes for prophylactic surgery within our database, we were able to confirm that, at a
15 minimum, half of these procedures were intended as risk-reducing operations, and more than
16 60% since 2009.

17
18 A further limitation of HES, common to administrative databases, is the potential for
19 inaccuracies and omissions in coding.[19] Validation work done for breast cancer surgery
20 suggests that procedure codes in HES are accurate, with 90-93% agreement with data
21 provided by surgeons.[20] We carried out a separate analysis to check the impact of missing
22 procedure codes that indicated whether a mastectomy was bilateral, right-sided or left-sided.
23 The rate of missing laterality codes decreased over the study period from around 5.6% to
24 1.4% of first mastectomies among women with breast cancer. However, underuse of these
25 codes was concentrated in four NHS trusts, so we re-estimated trends after excluding these
26 trusts from our analysis and were able to confirm that the observed increase in the rate of BM
27 was similar, i.e., an increase from 2% to 3% among women with breast cancer.

28
29 Ideally, to estimate changes in BM use among women without breast cancer, the denominator
30 would be the number of women at a high risk of developing breast cancer. Based on a single
31 study, NICE estimated that up to 2,500 women aged 30-49 years in England and Wales could
32 be identified each year as having a genetic risk of breast cancer,[21] but actual numbers are
33 not published.

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35 By looking at rates of immediate breast reconstruction, we have underestimated the total
36 number of women with breast cancer who underwent breast reconstruction because many
37 women undergo delayed reconstruction following their mastectomy.[22] Delayed
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3 reconstruction may be recommended when post-mastectomy radiotherapy is anticipated,
4 since this can impair the long-term aesthetic results of breast reconstruction.
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7 **Comparison with bilateral mastectomy trends in the US**

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10 The dramatic increase in BM among women without breast cancer in England has not been
11 noted in the US over the last two decades, although an increase could have occurred earlier in
12 the US. [6] In contrast, several US studies have identified an increase in contralateral risk-
13 reducing mastectomy among women with breast cancer.[6-9] Although the definitions and
14 populations studied are not exactly the same as ours, the evidence points toward a larger
15 increase in risk-reducing contralateral mastectomy in the US than in England.
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20 Various reasons have been suggested for the increase in contralateral risk-reducing
21 mastectomy in the US. One reason may be increased awareness of hereditary risk and the
22 associated use of genetic testing. Additional drivers may be higher screening re-call rates and
23 the need for additional breast assessment arising from annual surveillance mammography and
24 magnetic resonance imaging (MRI) undertaken routinely in the US.[23]
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29 Refinements of mastectomy techniques (skin- and nipple-sparing) and increased access to
30 breast reconstruction may also have contributed to the increase of contralateral mastectomy.
31 Higher immediate breast reconstruction rates in the US (up to 40% in 2008 compared to
32 around 20% in the UK) may also partly account for the relatively greater increase in
33 contralateral risk-reducing mastectomy.[11, 22]
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39 **Implications for clinical practice**

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41 In women at high risk of developing breast cancer, there has been an increase in BM since the
42 publication of NICE guidance (2004 and 2006).[1] In an otherwise healthy woman, BM is a
43 radical approach to risk reduction, but has been estimated to reduce the incidence of breast
44 cancer in BRCA carriers by up to 90%.[3] NICE emphasises the importance of patient-led
45 decision making and provides detailed recommendations regarding the need for a specialist
46 multidisciplinary approach that includes psychological counselling, with clear information
47 provided on the extent of risk reduction and the options for breast reconstruction.
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53 The high rate of immediate breast reconstruction after BM among women without breast
54 cancer suggests that reconstruction is widely available for these patients. This seems
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3 appropriate as women who undergo breast reconstruction report higher levels of satisfaction
4 with their post-surgery appearance than women who undergo mastectomy alone.[22]
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7 In women with a personal history or new diagnosis of unilateral breast cancer the value of
8 contralateral mastectomy for risk reduction is more controversial. For this group of women,
9 decision-making is complicated. It is likely that the risk of dying or the need for further
10 cancer treatment is determined primarily by the biology and stage of the index cancer, rather
11 than by a subsequent cancer in the contralateral breast.[5] The risk of subsequent cancers is
12 likely to be reduced by the treatment of the index cancer [24] and any future cancers are
13 likely to be surveillance-detected with a correspondingly better prognosis.[25] Consequently,
14 a risk-reducing contralateral mastectomy may not confer any benefit. Some women may still
15 prefer to have a contralateral mastectomy to avoid the stress of long-term regular surveillance
16 and risk of a subsequent cancer and related treatment.
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24 **CONCLUSION**

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26 Over the last decade, the number of women having a bilateral mastectomy in England has
27 increased. The increase was proportionately greater in women without breast cancer and
28 within this group, 90% have breast reconstruction at the time of their bilateral mastectomy.
29 However, the majority of women who undergo bilateral mastectomy appear to have had
30 unilateral breast cancer. The evidence to support contralateral risk reducing mastectomy in
31 women with breast cancer is limited.
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What is already known on this topic

Among healthy women with a high risk of developing breast cancer, a bilateral mastectomy can reduce their future risk

Among women with unilateral breast cancer, there is not strong evidence that a contralateral risk reducing mastectomy improves survival

In the US, there has been an increase in use of contralateral risk reducing mastectomy over the last two decades from 1-2% to around 5% of women having breast cancer surgery

What this study adds

In England, the number of women without breast cancer who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011

The number of women with breast cancer who had a bilateral mastectomy (including a contralateral mastectomy after a unilateral mastectomy) increased from 529 in 2002 to 931 in 2009, an increase from 2% to 3% of women having first breast cancer surgery

Rates of immediate breast reconstruction roughly doubled over this period, reaching 90% among women without breast cancer in 2011

Table 1 Number of women without breast cancer who had a bilateral mastectomy (BM) in England, 2002-2011

	Number of women who had a BM	Incidence per 100,000 females aged 25-69	Annual trend IRR (95% CI)	P value
2002	71	0.4	1.16 (1.13 to 1.18)	<0.001
2003	72	0.4		
2004	101	0.6		
2005	131	0.7		
2006	147	0.8		
2007	201	1.1		
2008	186	1.0		
2009	232	1.2		
2010	238	1.3		
2011	255	-		

Table 2 Number (%) who had a bilateral mastectomy (BM) out of women with breast cancer having their first operation, 2002-2011

	All women who had first breast cancer operation	No of women who had a BM			Annual trend (2002-2009)	
		Performed as same operation	Performed as two operations	Total (%)	OR (95% CI)	P value
2002	25,844	308	221	529 (2.0)	1.07 (1.05 to 1.08)	<0.001
2003	27,303	332	263	595 (2.2)		
2004	27,643	335	269	604 (2.2)		
2005	29,179	369	312	681 (2.3)		
2006	28,645	407	307	714 (2.5)		
2007	28,702	432	336	768 (2.7)		
2008	29,629	493	384	877 (3.0)		
2009	29,745	546	385	931 (3.1)		
2010	30,760	528	263*	-		
2011	31,240	617	93*	-		

*These figures are incomplete since our version of the HES database only covers the period up to 31st March 2012.

Table 3 Number (%) of women who underwent immediate breast reconstruction of those who had a bilateral mastectomy (BM), by presence of a breast cancer diagnosis, 2002-2011

	Women without breast cancer		Women with breast cancer			
	No	% (95% CI)	BM in same operation		BM in two operations	
			No	% (95% CI)	No	% (95% CI)
2002	42	59.2 (46.8 to 70.7)	56	18.2 (14.0 to 23.0)	60	27.1 (21.4 to 33.5)
2003	47	65.2 (53.1 to 76.1)	43	13.0 (9.5 to 17.0)	80	30.4 (24.9 to 36.3)
2004	70	69.3 (59.3 to 78.1)	58	17.3 (13.4 to 21.8)	83	30.9 (25.4 to 36.7)
2005	87	66.4 (57.6 to 74.4)	80	21.7 (17.6 to 26.2)	105	33.7 (28.4 to 39.2)
2006	106	72.1 (64.1 to 79.2)	93	22.9 (18.9 to 27.2)	142	46.3 (40.6 to 52.0)
2007	160	79.6 (73.4 to 84.9)	103	23.8 (19.9 to 28.1)	155	46.1 (40.7 to 51.6)
2008	151	81.2 (74.8 to 86.5)	135	27.4 (23.5 to 31.5)	173	45.1 (40.0 to 57.3)
2009	203	87.5 (82.5 to 91.5)	185	33.9 (30.0 to 38.0)	201	52.2 (47.1 to 57.3)
2010	207	87.0 (82.0 to 91.0)	188	35.6 (31.5 to 40.0)	132	50.2 (44.0 to 56.4)
2011	231	90.6 (86.3 to 93.9)	252	40.8 (36.9 to 44.8)	50	53.8 (43.1 to 64.2)

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40 approval as it involved secondary analysis of an existing dataset of anonymised data for
41 service evaluation. Approvals for the use of hospital episode statistics data were obtained as
42 part of the standard hospital episode statistics approval process.
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47 Data sharing: No additional data available.
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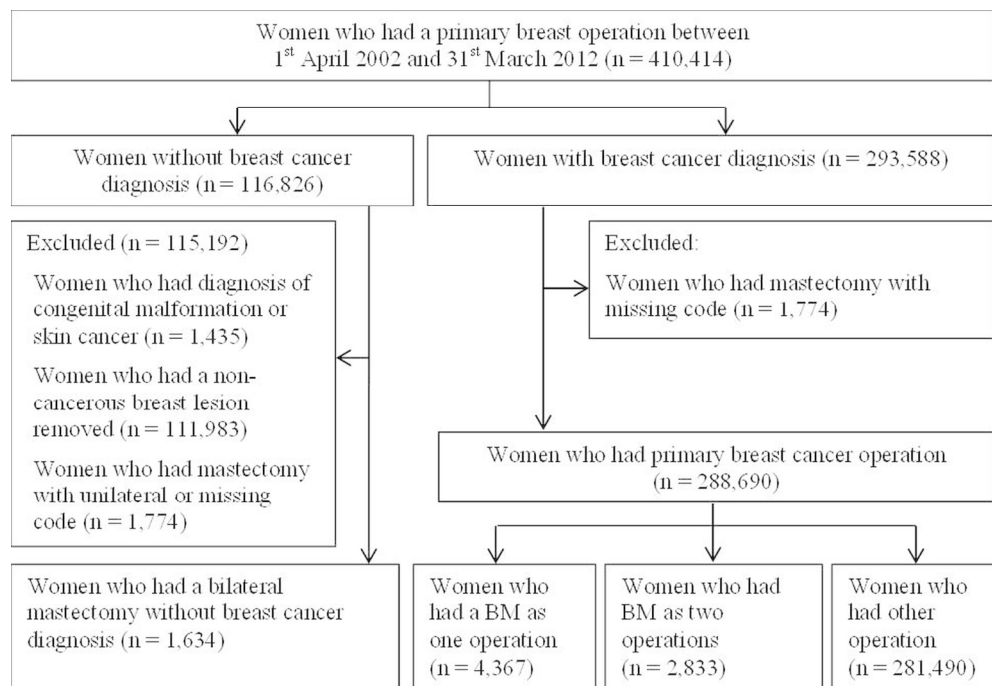


Figure 1 Inclusion of women in the study
131x90mm (300 x 300 DPI)

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3 **Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective**
4 **analysis of hospital episode statistics**
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Abstract

Objectives For healthy women at high risk of developing breast cancer, a bilateral mastectomy can reduce future risk. For women who already have unilateral breast cancer, removing the contralateral healthy breast is more difficult to justify. We examined trends in the number of women who had a bilateral mastectomy in England between 2002 and 2011.

Design Retrospective cohort study using the Hospital Episode Statistics database.

Setting NHS hospital trusts in England.

Participants Women aged between 18 and 80 years who had a bilateral mastectomy (or a contralateral mastectomy within 24 months of unilateral mastectomy) with or without a diagnosis of breast cancer.

Main outcome measures Number and incidence of women without breast cancer who had a bilateral mastectomy; number and proportion who had a bilateral mastectomy as their first breast cancer operation, and the proportion of those undergoing bilateral mastectomy who had immediate breast reconstruction.

Results Among women without breast cancer, the number who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011 (annual incidence rate ratio 1.16, 95% confidence interval 1.13 to 1.18). In women with breast cancer, the number rose from 529 to 931, an increase from 2.0% to 3.1% of first operations (odds ratio for annual increase 1.07, 95% CI 1.05 to 1.08). Across both groups, rates of immediate breast reconstruction roughly doubled and reached 90% among women without breast cancer in 2011.

Conclusion The number of women who had a bilateral mastectomy nearly doubled over the last decade, and more than tripled among women without breast cancer. This coincided with an increase in the use of immediate breast reconstruction.

2,744 words, excluding figures, tables and references

INTRODUCTION

There are two distinct groups of women who undergo bilateral mastectomy (BM): those without breast cancer but with familial breast cancer or known genetic mutations (BRCA1 or BRCA2) and those with breast cancer in one or both breasts. Guidelines produced by the UK National Institute for Health and Clinical Excellence (NICE) state that risk-reducing BM may be appropriate for high-risk women without breast cancer. High-risk is defined as a lifetime risk of 30% or higher, compared to an average risk of 11% in the UK female population.[1] This advice is consistent with clinical evidence that removal of both healthy (non-cancerous) breasts can reduce the future incidence of breast cancer in high-risk women.[2-5]

Some women with unilateral breast cancer have the healthy breast removed to reduce their risk of contralateral breast cancer. Both breasts can be removed simultaneously or the contralateral healthy breast can be removed at a later date. **Although the contralateral mastectomy may reduce the risk of developing a future malignant breast tumour and the need for further breast cancer treatments, a 2010 Cochrane Review found insufficient evidence of improved survival.[5]**

Over the last two decades in the United States the use of contralateral risk-reducing mastectomy has increased, from 1-2% to around 5% of women having breast cancer surgery.[6-9] Several reasons have been suggested for this increase, including wider availability of genetic testing, avoidance of long-term breast surveillance and increased availability of immediate breast reconstruction. Patients and health professionals may also overestimate the risk of contralateral breast cancer.[10] However, trends in the UK and rest of Europe may be different as a result of different medical and cultural attitudes toward extensive ablative surgery and aesthetic surgery. [11]

Our aim was to investigate trends in bilateral mastectomy for women without and with a breast cancer diagnosis in England between 2002 and 2011. We also examined trends in immediate breast reconstruction to assess the role that this might have played.

METHODS

Data definitions and selection of cohort

We used data extracted from the Hospital Episode Statistics (HES) database, [12] which covers all admissions to English National Health Service (NHS) hospital trusts. A unique patient identifier allows same patient admissions to be linked. Each HES record captures up to 24 procedures, using the UK Office of Population Censuses and Surveys (OPCS) classification, version 4.4. Diagnoses are recorded using the International Classification of Diseases, 10th Revisions (ICD-10). Our extract from HES covered the period from 2002 to 2011, using financial years (1st April to 31st March).

Bilateral mastectomy performed as a single operation was identified by the OPCS codes B27 (mastectomy) and Z94.1 (bilateral). Unilateral mastectomy was identified by the code B27 in addition to Z94.2 (right sided), Z94.3 (left sided) or Z94.4 (unilateral). We excluded women with missing information on laterality. **Because high rates of missing information were concentrated in four out of 162 NHS trusts, we re-ran our analyses after excluding these NHS trusts to check the robustness of the estimated trends.** Breast-conserving operations were identified by the OPCS codes B28.1, B28.2, B28.3, B28.8 and B28.9.

Breast reconstruction was identified using OPCS codes B29 (breast reconstruction, excluding B29.5 revision), B38 (reconstruction using buttock flap), B39 (reconstruction using abdominal flap), B30.1 (insertion of prosthesis) and S48.2 (insertion of skin expander).

We identified women with breast cancer using the ICD-10 diagnosis codes C50 (malignant neoplasm) and D05 (carcinoma-in-situ). The ICD-10 codes do not distinguish bilateral from unilateral breast cancer so it was not possible to identify how many women had a therapeutic BM for bilateral breast cancer. The number of women diagnosed with synchronous bilateral breast cancer is thought to be extremely small and relatively stable since the 1980s, based on Swedish Cancer Register data and studies from Australasia and the Netherlands. [13-16]

We selected women aged 18 to 80 years who fulfilled one of the following two inclusion criteria: 1) they had a BM between 2002 and 2011; or 2) they had a first breast cancer operation between 2002 and 2011 and had a current or previous diagnosis of breast cancer. A

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3 previous diagnosis of breast cancer was determined by checking women's HES records going
4 back to April 2000.
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7 From this cohort, we distinguished between two groups of women who underwent BM. The
8 first group comprised of women who did not have a current or previous diagnosis of breast
9 cancer. All women in this group had BM as a simultaneous procedure.
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12 The second group included women who had a current or previous diagnosis of breast cancer.
13 Women in this group underwent simultaneous BM or had a contralateral mastectomy as a
14 separate procedure within 24 months of the unilateral mastectomy. This approach is referred
15 to in this paper as two procedure BM. Removal of a contralateral breast may be decided at
16 the time of the initial cancer diagnosis but only be performed after completion of adjuvant
17 therapies (chemotherapy or in particular radiotherapy). Alternatively, the decision for
18 contralateral mastectomy may be made after genetic assessment/testing and appropriate
19 counselling, during or after any adjuvant treatments.
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27 **Statistical analysis**

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29 We calculated the number of women who underwent BM each financial year from 2002 to
30 2011. Of the women without breast cancer we identified, all were aged from 25 to 69 years.
31 We therefore calculated the incidence of BM per 100,000 women in the English population
32 aged 25-69 as a denominator, using figures published by the Office for National
33 Statistics.[17] We then used Poisson regression to estimate an annual trend in the use of BM,
34 including year as a linear term.
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40 Among women with breast cancer, we calculated the BM rate as a proportion out of all the
41 first breast cancer operations undertaken that year. We used multivariable logistic regression
42 to estimate the annual trend in the proportion undergoing BM, including year as a linear term,
43 with and without adjusting for age. We report average trends for the period 2002-2009. This
44 is because the number of two procedure BMs is underestimated for 2010 and 2011 because
45 our extract from the HES database extended only up to 31st March 2012, allowing 24 months
46 of follow up only for women who had a mastectomy before 1 March 2010.
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53 We calculated the percentage of women who underwent immediate breast reconstruction
54 following BM each year, along with the 95% confidence intervals.
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3 In all cases, we tested for a change in trends using spline terms, but only describe linear
4 trends for simplicity of presentation. Reported P values are based on likelihood ratio tests.
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6 All analyses were carried out in Stata version 11.
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8 9 **RESULTS**

10 11 **Bilateral mastectomy in women without breast cancer**

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13 Between 2002 and 2011, the number of women without breast cancer who underwent
14 simultaneous BM increased from 71 to 255 (Table 1). The population incidence increased
15 from 0.4 to 1.3 per 100,000 women aged 25-69 years with an estimated annual increase of
16 around 16% (incidence rate ratio 1.16, 95% CI 1.13 to 1.18, $P < 0.001$), although increases
17 were smaller in more recent years ($P < 0.001$).
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21 Women without breast cancer comprised an increasing fraction of all women undergoing
22 BM, from 11.8% ($71 / (71 + 529)$) in 2002 to 19.9% in 2009 ($232 / (232 + 931)$) (Tables 1
23 and 2). The average age at surgery was 40 years and did not change over this time period.
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28 29 **Bilateral mastectomy in women with breast cancer**

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31 Between 2002 and 2009, the number of women with breast cancer who underwent BM
32 increased from 521 to 931, representing an increase from 2.0% to 3.1% of all women
33 undergoing their first breast cancer operation (Table 2). The estimated annual increase was
34 around 7% (odds ratio 1.07, 95% CI 1.05 to 1.08, $P < 0.001$), with no strong evidence of a
35 change in trends over the period.
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40 The average age at first breast cancer operation was 58 years, for two procedure BM it was
41 51 years, and for simultaneous BM it fell from 57 years to 54 years during the study period.
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45 Around two-fifths of BMs were carried out as two procedures, with the contralateral
46 mastectomy being performed within 24 months.
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48 49 **Rates of immediate breast reconstruction 2002-2011**

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51 Among women without breast cancer, the immediate breast reconstruction rate increased
52 substantially from 59.2% (95% CI 46.8 to 70.7) to 90.6% (95% CI 86.3 to 93.9) (Table 3).
53 Reconstruction rates were higher among younger women, particularly those under 40 years
54 ($P < 0.001$).
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3 Among women with breast cancer who had simultaneous BM, the immediate breast
4 reconstruction rate increased from 18.2% (95% CI 14.0 to 23.0) to 40.8% (95% CI 36.9 to
5 44.8). The immediate reconstruction rate among women who underwent BM in two
6 procedures increased from 27.1% (95% CI 21.4 to 33.5) to 53.8% (95% CI 43.1 to 64.2).
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10 **DISCUSSION**

11 **Summary of results**

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15 Over the last decade the total number of women in England who had a bilateral mastectomy
16 nearly doubled, from around 600 to 1,000 women per year. Proportionally, the largest
17 increase in BM incidence was seen in women without breast cancer. Their number tripled
18 from 71 to 255 between 2002 and 2009, representing an increase in uptake among women
19 aged 25-69.
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25 Overall, the majority of women who underwent BM had breast cancer. In this group there
26 was an increase in the number who underwent BM (in one or two procedures) between 2002
27 and 2009, representing a modest increase from around 2% to 3% of women undergoing their
28 first breast cancer operation.
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33 Between 2002 and 2011, rates of immediate breast reconstruction after BM roughly doubled
34 to nearly 50% for women with cancer and over 90% for women who did not have breast
35 cancer.
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38 **Strengths and limitations of study**

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40 The comprehensiveness of HES enabled us to identify different hospital admissions for the
41 same woman over a long period of time. Because HES links separate episodes of care for the
42 same patient, we could reliably identify contralateral mastectomies performed within 24
43 months of a first unilateral mastectomy.
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48 The main limitation of HES is the lack of codes indicating whether a breast cancer diagnosis
49 is unilateral or bilateral. This meant that we were unable to exclude from our analysis
50 women with bilateral breast cancer at initial diagnosis, or diagnosed with an occult or new
51 contralateral breast cancer within 24 months of the index cancer. As a result, among women
52 with breast cancer, those who underwent a therapeutic BM are included in our figures. Of
53 women diagnosed with breast cancer in the Swedish Cancer Register, around one percent of
54 women were first diagnosed with bilateral breast cancer and less than half a percent were
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3 diagnosed with contralateral breast cancer within 24 months of a first diagnosis, [13] and
4 these rates have remained stable or decreased since the 1980s. [14] Two recent population-
5 based studies from Australasia and the Netherlands reported comparable bilateral breast
6 cancer rates of 2.3% and 2.2% respectively.[15,16] Assuming trends in the UK are
7 comparable, it is unlikely that a change in incidence alone could explain the observed
8 increase in BM rates. Increased detection of bilateral breast cancers through the NHS Breast
9 Screening Programme is also unlikely to explain the increase in BM rates, since we found
10 higher rates and larger increases in rates among women aged under 50 years, who would not
11 have been routinely screened over the study period. Improved MRI-detection of occult
12 contralateral breast cancers could have contributed to the increase in the rate of contralateral
13 mastectomy following a unilateral mastectomy.[18] However, upon checking the use of
14 codes for prophylactic surgery within our database, we were able to confirm that, at a
15 minimum, half of these procedures were intended as risk-reducing operations, and more than
16 60% since 2009.

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27 A further limitation of HES, common to administrative databases, is the potential for
28 inaccuracies and omissions in coding.[19] Validation work done for breast cancer surgery
29 suggests that procedure codes in HES are accurate, with 90-93% agreement with data
30 provided by surgeons.[20] We carried out a separate analysis to check the impact of missing
31 procedure codes that indicated whether a mastectomy was bilateral, right-sided or left-sided.
32 The rate of missing laterality codes decreased over the study period from around 5.6% to
33 1.4% of first mastectomies among women with breast cancer. However, underuse of these
34 codes was concentrated in four NHS trusts, so we re-estimated trends after excluding these
35 trusts from our analysis and were able to confirm that the observed increase in the rate of BM
36 was similar, i.e., an increase from 2% to 3% among women with breast cancer.

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45 Ideally, to estimate changes in BM use among women without breast cancer, the denominator
46 would be the number of women at a high risk of developing breast cancer. Based on a single
47 study, NICE estimated that up to 2,500 women aged 30-49 years in England and Wales could
48 be identified each year as having a genetic risk of breast cancer,[21] but actual numbers are
49 not published.

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By looking at rates of immediate breast reconstruction, we have underestimated the total
number of women with breast cancer who underwent breast reconstruction because many
women undergo delayed reconstruction following their mastectomy.[22] Delayed

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3 reconstruction may be recommended when post-mastectomy radiotherapy is anticipated,
4 since this can impair the long-term aesthetic results of breast reconstruction.
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7 **Comparison with bilateral mastectomy trends in the US**

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10 The dramatic increase in BM among women without breast cancer in England has not been
11 noted in the US over the last two decades, although an increase could have occurred earlier in
12 the US. [6] In contrast, several US studies have identified an increase in contralateral risk-
13 reducing mastectomy among women with breast cancer.[6-9] Although the definitions and
14 populations studied are not exactly the same as ours, the evidence points toward a larger
15 increase in risk-reducing contralateral mastectomy in the US than in England.
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20 Various reasons have been suggested for the increase in contralateral risk-reducing
21 mastectomy in the US. One reason may be increased awareness of hereditary risk and the
22 associated use of genetic testing. Additional drivers may be higher screening re-call rates and
23 the need for additional breast assessment arising from annual surveillance mammography and
24 magnetic resonance imaging (MRI) undertaken routinely in the US.[23]
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29 Refinements of mastectomy techniques (skin- and nipple-sparing) and increased access to
30 breast reconstruction may also have contributed to the increase of contralateral mastectomy.
31 Higher immediate breast reconstruction rates in the US (up to 40% in 2008 compared to
32 around 20% in the UK) may also partly account for the relatively greater increase in
33 contralateral risk-reducing mastectomy.[11, 22]
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38 **Implications for clinical practice**

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41 In women at high risk of developing breast cancer, there has been an increase in BM since the
42 publication of NICE guidance (2004 and 2006).[1] In an otherwise healthy woman, BM is a
43 radical approach to risk reduction, but has been estimated to reduce the incidence of breast
44 cancer in BRCA carriers by up to 90%.[3] NICE emphasises the importance of patient-led
45 decision making and provides detailed recommendations regarding the need for a specialist
46 multidisciplinary approach that includes psychological counselling, with clear information
47 provided on the extent of risk reduction and the options for breast reconstruction.
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54 The high rate of immediate breast reconstruction after BM among women without breast
55 cancer suggests that reconstruction is widely available for these patients. This seems
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3 appropriate as women who undergo breast reconstruction report higher levels of satisfaction
4 with their post-surgery appearance than women who undergo mastectomy alone.[22]
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7 In women with a personal history or new diagnosis of unilateral breast cancer the value of
8 contralateral mastectomy for risk reduction is more controversial. For this group of women,
9 decision-making is complicated. It is likely that the risk of dying or the need for further
10 cancer treatment is determined primarily by the biology and stage of the index cancer, rather
11 than by a subsequent cancer in the contralateral breast.[5] The risk of subsequent cancers is
12 likely to be reduced by the treatment of the index cancer [24] and any future cancers are
13 likely to be surveillance-detected with a correspondingly better prognosis.[25] Consequently,
14 a risk-reducing contralateral mastectomy may not confer any benefit. **Some women may still
15 prefer to have a contralateral mastectomy to avoid the stress of long-term regular surveillance
16 and risk of a subsequent cancer and related treatment.**
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24 CONCLUSION

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27 Over the last decade, the number of women having a bilateral mastectomy in England has
28 increased. The increase was proportionately greater in women without breast cancer and
29 within this group, 90% have breast reconstruction at the time of their bilateral mastectomy.
30 However, the majority of women who undergo bilateral mastectomy appear to have had
31 unilateral breast cancer. The evidence to support contralateral risk reducing mastectomy in
32 women with breast cancer is limited.
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What is already known on this topic

Among healthy women with a high risk of developing breast cancer, a bilateral mastectomy can reduce their future risk

Among women with unilateral breast cancer, there is not strong evidence that a contralateral risk reducing mastectomy improves survival

In the US, there has been an increase in use of contralateral risk reducing mastectomy over the last two decades from 1-2% to around 5% of women having breast cancer surgery

What this study adds

In England, the number of women without breast cancer who had a bilateral mastectomy increased from 71 in 2002 to 255 in 2011

The number of women with breast cancer who had a bilateral mastectomy (including a contralateral mastectomy after a unilateral mastectomy) increased from 529 in 2002 to 931 in 2009, an increase from 2% to 3% of women having first breast cancer surgery

Rates of immediate breast reconstruction roughly doubled over this period, reaching 90% among women without breast cancer in 2011

Table 1 Number of women without breast cancer who had a bilateral mastectomy (BM) in England, 2002-2011

	Number of women who had a BM	Incidence per 100,000 females aged 25-69	Annual trend IRR (95% CI)	P value
2002	71	0.4	1.16 (1.13 to 1.18)	<0.001
2003	72	0.4		
2004	101	0.6		
2005	131	0.7		
2006	147	0.8		
2007	201	1.1		
2008	186	1.0		
2009	232	1.2		
2010	238	1.3		
2011	255	-		

Table 2 Number (%) who had a bilateral mastectomy (BM) out of women with breast cancer having their first operation, 2002-2011

	All women who had first breast cancer operation	No of women who had a BM			Annual trend (2002-2009)	
		Performed as same operation	Performed as two operations	Total (%)	OR (95% CI)	P value
2002	25,844	308	221	529 (2.0)	1.07 (1.05 to 1.08)	<0.001
2003	27,303	332	263	595 (2.2)		
2004	27,643	335	269	604 (2.2)		
2005	29,179	369	312	681 (2.3)		
2006	28,645	407	307	714 (2.5)		
2007	28,702	432	336	768 (2.7)		
2008	29,629	493	384	877 (3.0)		
2009	29,745	546	385	931 (3.1)		
2010	30,760	528	263*	-		
2011	31,240	617	93*	-		

*These figures are incomplete since our version of the HES database only covers the period up to 31st March 2012.

Table 3 Number (%) of women who underwent immediate breast reconstruction of those who had a bilateral mastectomy (BM), by presence of a breast cancer diagnosis, 2002-2011

	Women without breast cancer		Women with breast cancer			
	No	% (95% CI)	BM in same operation		BM in two operations	
			No	% (95% CI)	No	% (95% CI)
2002	42	59.2 (46.8 to 70.7)	56	18.2 (14.0 to 23.0)	60	27.1 (21.4 to 33.5)
2003	47	65.2 (53.1 to 76.1)	43	13.0 (9.5 to 17.0)	80	30.4 (24.9 to 36.3)
2004	70	69.3 (59.3 to 78.1)	58	17.3 (13.4 to 21.8)	83	30.9 (25.4 to 36.7)
2005	87	66.4 (57.6 to 74.4)	80	21.7 (17.6 to 26.2)	105	33.7 (28.4 to 39.2)
2006	106	72.1 (64.1 to 79.2)	93	22.9 (18.9 to 27.2)	142	46.3 (40.6 to 52.0)
2007	160	79.6 (73.4 to 84.9)	103	23.8 (19.9 to 28.1)	155	46.1 (40.7 to 51.6)
2008	151	81.2 (74.8 to 86.5)	135	27.4 (23.5 to 31.5)	173	45.1 (40.0 to 57.3)
2009	203	87.5 (82.5 to 91.5)	185	33.9 (30.0 to 38.0)	201	52.2 (47.1 to 57.3)
2010	207	87.0 (82.0 to 91.0)	188	35.6 (31.5 to 40.0)	132	50.2 (44.0 to 56.4)
2011	231	90.6 (86.3 to 93.9)	252	40.8 (36.9 to 44.8)	50	53.8 (43.1 to 64.2)

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40 approval as it involved secondary analysis of an existing dataset of anonymised data for
41 service evaluation. Approvals for the use of hospital episode statistics data were obtained as
42 part of the standard hospital episode statistics approval process.
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47 Data sharing: No additional data available.
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