

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective analysis of hospital episode statistics
AUTHORS	Neuburger, Jenny; MacNeill, Fiona; Jeevan, Ranjeet; van der Meulen, Jan; Cromwell, David

VERSION 1 - REVIEW

REVIEWER	Mr Tom Bates FRCS Hon. Consulting Surgeon, The Breast Unit, William Harvey Hospital, Ashford, Kent. TN24 0LZ UK
REVIEW RETURNED	20-May-2013

REPORTING & ETHICS	p5."A previous diagnosis of breast cancer was determined by checking women's hospital records" If this should read "HES records" that is acceptable but if the authors actually accessed individual patient's hospital records the ethical approval as stated would not appear to be adequate (p16)
GENERAL COMMENTS	This study shows an increase in the incidence of bilateral mastectomy in England and although this is not unexpected it appears to be previously unreported. However it does raise a number of issues: 1. The Key message that risk reducing contralateral mastectomy is not supported by the clinical evidence may well be correct but no data are provided. Some patients find psychological reassurance from a second mastectomy rather than continued surveillance, albeit the risk is very small. 2. The main weakness of the study is acknowledged, that the HES database does not distinguish between therapeutic and prophylactic bilateral mastectomy. Is it possible that the use of the code for prophylactic surgery improved over time which would accentuate the trend? 3. The use of the Swedish Cancer Registry rates (2005/2007) for synchronous breast cancers of 1% plus 0.5% for metachronous tumours within 24 months as a benchmark may well be appropriate. However there are two recent population-based studies from Australia/NZ (1) and from the Netherlands (2) which found synchronous rates of 2.3% and 2.2% respectively. The latter study (2) was of screen detected breast cancers. Bilateral breast cancer may be more common in the elderly (1) and with increasing age of the screened population and uptake of screening this may have increased the incidence of therapeutic bilateral mastectomy. (1)Roder et al. Asian Pac J Cancer Prev 2012;13:1413 (2) Setz-Pels W et al. Breast Cancer Res Treat 2011;129:955 4. Since some of the HES data for 2011/11 are incomplete these

	<p>years should be excluded.</p> <p>5. It is unclear how the cohort aged 18-80 corresponds to the age range 25-69 for the calculation of incidence. Please explain.</p> <p>6. p5."A previous diagnosis of breast cancer was determined by checking women's hospital records" If this should read "HES records" that is acceptable but if the authors actually accessed individual patient's hospital records the ethical approval as stated would not appear to be adequate (p16).</p> <p>7. Tables 1 & 2 might be better shown as graphs.</p> <p>8. There are numerous, albeit minor typographical errors.</p>
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REVIEWER	<p>Mo Keshtgar BSc, FRCSI, FRCS (Gen), PhD Consultant Surgical Oncologist and Reader in Cancer Surgery Royal Free London Foundation Trust University College London</p> <p>I have no conflict of interest.</p>
REVIEW RETURNED	01-Jun-2013

THE STUDY	I have a major concern about high rate of missing information that authors report in the paper and am unsure how representative the figures are for England.
RESULTS & CONCLUSIONS	As the authors acknowledge the main limitation of the study is that HES lacks codes for a bilateral and unilateral breast cancer diagnosis which is one of the endpoint of this study. Interpretation of some data is based on assumptions derived from Swedish Cancer Register which may not be applicable to the UK population. The authors also report that they have excluded 'FEW' NHS Trusts because of high rate of missing data but fail to state how many Trusts were excluded. This brings into question, how representative the figures are which is my main concern.

VERSION 1 – AUTHOR RESPONSE

Responses to comments from reviewer 1 (Tom Bates)

This study shows an increase in the incidence of bilateral mastectomy in England and although this is not unexpected it appears to be previously unreported. However it does raise a number of issues:

1. The key message that risk reducing contralateral mastectomy is not supported by the clinical evidence may well be correct, but no data are provided. Some patients find psychological reassurance from a second mastectomy rather than continued surveillance, albeit the risk is very small.

>> Thank you. We have revised the manuscript to clarify that a Cochrane Review in 2010 found insufficient evidence to be able to conclude that risk reducing contralateral mastectomy improved survival (Introduction, page 2, paragraph 2).

>> We have also revised the manuscript to acknowledge the reasons, other than survival benefit, that women might choose to have a contralateral mastectomy (Discussion, page 9, paragraph 1).

2. The main weakness of the study is acknowledged, that the HES database does not distinguish between therapeutic and prophylactic bilateral mastectomy. Is it possible that the use of the code for prophylactic surgery improved over time which would accentuate the trend?

>> We did not rely upon the Z40 code for prophylactic surgery to identify women who had risk-reducing BM for precisely the reason our reviewer suggests. We realise that we inadvertently introduced confusion regarding our use of Z40 codes by mentioning them in our methods section. We only used them as a "sense check" on our strategy of relying on the absence of a breast cancer diagnosis code. We have now removed this explanation (Methods, page 4, paragraph 1)

3. The use of the Swedish Cancer Registry rates (2005/2007) for synchronous breast cancers of 1% plus 0.5% for metachronous tumours within 24 months as a benchmark may well be appropriate. However there are two recent population-based studies from Australia/NZ (1) and from the Netherlands (2) which found synchronous rates of 2.3% and 2.2% respectively. The latter study (2) was of screen detected breast cancers. Bilateral breast cancer may be more common in the elderly (1) and with increasing age of the screened population and uptake of screening this may have increased the incidence of therapeutic bilateral mastectomy. (1)Roder et al. Asian Pac J Cancer Prev 2012;13:1413 (2) Setz-Pels W et al. Breast Cancer Res Treat 2011; 129:955

>> Thank you for these useful references. We have included them in our discussion of the strengths and limitations of the study. It is also a good point about the possibility of an increase in the use of therapeutic bilateral mastectomy due to an increased in detection of bilateral breast cancers among older women who are screened as part of the NHS programme. In fact, we found that the absolute increase was greater in younger women aged under 50 years, who would not have been screened under the programme for most of the study period, and the relative increase was roughly equal across the age groups. We have explicitly addressed this point in the revision of our manuscript (Discussion, page 7, paragraph 1).

4. Since some of the HES data for 2011/11 are incomplete these years should be excluded.

>> We did exclude these years from our estimated trends. However, we think presenting the actual numbers for these years in Table 2 is still useful. We have amended the note to Table 2 to clarify this.

5. It is unclear how the cohort aged 18-80 corresponds to the age range 25-69 for the calculation of incidence. Please explain.

>> We selected women aged 18-80 since we thought this age range would cover women who might consider having a risk-reducing mastectomy. After selecting our cohort, we found that the age range in healthy women who had a bilateral mastectomy for breast cancer risk was 25-69. On this basis, we used the number of women in this age range in the English population to calculate incidence rates. We have amended the description of methods (under statistical analysis section) to make this clearer (Methods, page 4, paragraph 3).

6. p5. "A previous diagnosis of breast cancer was determined by checking women's hospital records" If this should read "HES records" that is acceptable but if the authors actually accessed individual patient's hospital records the ethical approval as stated would not appear to be adequate (p16).

>> We have amended the sentence to confirm that it was HES records, not women's hospital records.

7. Tables 1 & 2 might be better shown as graphs.

>> We did previously experiment with using graphs, but we decided that tables would be clearer in the end, since they show the number and the rate side by side.

8. There are numerous, albeit minor typographical errors.

>> Thank you. We have corrected these.

Responses to comments from reviewer 2 (Mr Mo Keshtgar)

9. I have a major concern about high rate of missing information that authors report in the paper and am unsure how representative the figures are for England.

>> Previous validation work done for breast cancer surgery suggests that procedure codes in HES are accurate, with 90-93% agreement with data provided by surgeons. We have included this information and the associated reference in our manuscript (Discussion, page 7, paragraph 2).

10. As the authors acknowledge the main limitation of the study is that HES lacks codes for a bilateral and unilateral breast cancer diagnosis which is one of the endpoint of this study. Interpretation of some data is based on assumptions derived from Swedish Cancer Register which may not be applicable to the UK population.

>> This is a key point, also raised by Mr Bates, our other reviewer. We have included references to further studies from Australasia and the Netherlands that he suggested. All point to a rate of bilateral breast cancer of around 2%.

11. The authors also report that they have excluded 'FEW' NHS Trusts because of high rate of missing data but fail to state how many Trusts were excluded. This brings into question, how representative the figures are which is my main concern.

>> Missing laterality codes for whether the mastectomy was unilateral or bilateral were concentrated in four out of 162 NHS trusts. We have amended the manuscript to make this clear (Methods, page 3, paragraph 2). We were reassured to find that trends in use of BM were similar after excluding women who had surgery in these trusts from our sample (Discussion, page 7, paragraph 2).