

# Occult Breast Carcinoma Is More Common in Women Undergoing Breast Reduction after Contralateral Cancer: A Systematic Review and Meta-Analysis

Siobhan E. Fitzpatrick, M.D.  
Thomas C. Lam, D.Clin.Surg.,  
F.R.A.C.S.

Westmead, New South Wales, Australia

**Background:** Occult breast carcinoma is occasionally found in breast reduction specimens. Although its incidence varies widely, there is a trend toward an increased incidence for women with a history of breast cancer. The authors performed a systematic review and meta-analysis of occult carcinoma incidence in breast reduction specimens.

**Methods:** The MEDLINE and Embase databases were searched for peer-reviewed studies with no language restrictions for studies that recorded the incidence of occult carcinoma in breast reduction specimens. Cancer incidence per specimen was pooled for women with and without a history of breast cancer.

**Results:** Forty-two studies were eligible for inclusion, of which 29 were quantitatively analyzed. The pooled incidence of carcinoma was higher within specimens from women with breast cancer (3.4 percent; 95 percent CI, 2.2 to 5.3 percent) than without (0.6 percent; 95 percent CI, 0.4 to 0.8 percent), and this increased likelihood was significant when populations were compared directly (OR, 6.02; 95 percent CI, 3.06 to 11.86;  $p < 0.0001$ ).

**Conclusions:** Women with a history of breast cancer have an increased incidence of occult breast carcinoma within their breast reduction specimens compared with women with no breast cancer history. There is a need for preoperative radiology screening, counseling, and histopathology guidelines to ensure adequate diagnosis and management of these women. (*Plast. Reconstr. Surg.* 146: 117e, 2020.)

Breast reduction, or reduction mammoplasty, is the eighth most common plastic surgery procedure performed globally, with an estimated 489,146 operations performed in 2017.<sup>1</sup> Breast reduction is typically performed bilaterally to treat symptomatic macromastia, unilaterally to correct congenital asymmetry, and in some cases as a reconstructive procedure to provide symmetry after breast cancer resection on the contralateral breast. The procedure is associated with a significant improvement in health-related quality of life.<sup>2</sup> The resected breast tissue from breast reduction surgery is often sent for histopathologic screening for breast cancer; however, this is not supported by any specific guidelines, and practice varies widely between surgeons.<sup>3–9</sup>

Breast cancer is the most commonly diagnosed malignancy in women worldwide, affecting one in eight women in their lifetime in Australia.<sup>10</sup> Occasionally, incidental findings of breast cancer are detected on histopathologic examination of breast reduction specimens, despite these being clinically or radiologically occult on preoperative screening. The incidence of occult carcinoma within breast reduction specimens has been reported in various populations since the 1960s.<sup>11,12</sup> In the current literature, this incidence is 0 to 4 percent in grouped populations,<sup>13,14</sup> 0 to 2 percent in women with no personal history of breast cancer,<sup>15,16</sup> and 0 to 5.5 percent in women with prior breast cancer of the contralateral breast.<sup>17,18</sup> Generally, the studies examining this topic are retrospective in nature and have collated their data through surveys,<sup>11,19</sup> personal<sup>9</sup> and

From the Plastic and Reconstructive Surgery Department, Westmead Private Hospital.

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national registries,<sup>20</sup> and hospital chart reviews.<sup>21,22</sup> Unfortunately, the definition of malignancy varies between studies from those that encompass in situ carcinomas and those that examine only invasive cancers. Different studies also calculate the percentage incidence of these lesions as either per specimen or per patient, making comparisons between bilateral and unilateral reduction mammoplasties inaccurate. Finally, not all studies thoroughly account for breast cancer risk factors in each study population, making conclusions problematic.

Nevertheless, throughout the literature, there is a trend toward a higher incidence of occult carcinoma within the breast reduction specimens of women undergoing symmetrization after contralateral breast cancer surgery compared with women undergoing breast reductions for macromastia.<sup>18,23</sup> This is most likely because women who have had breast cancer previously have an increased risk of having it again, relative to the general population.<sup>24</sup> The detection of occult carcinoma has important implications for these women in terms of breast cancer treatment, with probable mastectomy and need for ongoing surveillance. Furthermore, it has implications for plastic surgeons to provide appropriate preoperative counseling and radiologic screening, and it may inform the development of guidelines for the management of resection specimens. In this study, we performed a systematic review and meta-analysis to determine whether there is an increased incidence of occult carcinoma in the breast reduction specimens of women with a personal history of breast cancer compared to those without.

## PATIENTS AND METHODS

### Search Strategy

A systematic review and meta-analysis were conducted according to the Meta-Analysis of Observational Studies in Epidemiology guidelines.<sup>25</sup> The electronic databases MEDLINE and Embase were searched by means of OvidSP. Search terms included “mammoplasty” or “breast reduction” and “breast neoplasms” or “occult cancer.” Terms were searched as text word and as exploded medical subject headings where possible. The most recent search was performed on May 15, 2019. All citations were examined for their relevance to the study aims by two authors independently (S.E.F. and T.C.L.). Articles deemed relevant were subsequently read and examined in full to assess eligibility. A manual search was conducted of all the reference lists of each article from the original

search to find further studies for analysis. All publications that met the agreed inclusion criteria below were deemed potentially eligible. No language restrictions were used in either the search or study selection. A search for unpublished literature was not performed.

### Study Selection

All studies examining occult breast carcinoma in breast reduction specimens were included. Retrospective and prospective studies of patient populations and pathology databases were included, in addition to surveys of surgeons performing breast reductions. Case reports and letters to the editor were excluded. The primary outcome was breast carcinoma, defined as invasive ductal or lobular carcinoma, ductal carcinoma in situ, and lobular carcinoma in situ. Studies that examined the incidence of cancer within the specimens of women undergoing breast reduction were included in the systematic review. Studies that specified personal history of breast cancer; numbers of bilateral and unilateral procedures; and all numbers of lobular carcinoma in situ, ductal carcinoma in situ, and invasive cancer in each patient group were included in the meta-analysis. A further quantitative analysis was conducted on studies that specifically examined comparable populations of women with and without a personal history of breast cancer.

### Data Extraction

The data extraction was performed by one author (S.E.F.). The following details of each report were extracted and presented as a ratio per breast specimen: first author's name, year of publication, study design, country of origin, definition of cancer, total number of patients, number of patients undergoing unilateral and bilateral reductions, number of specimens examined, mean age, preoperative screening methods, adjustment for family history, description of histopathology protocol, history of breast cancer in population, and the percentage incidence carcinoma by type (i.e., lobular carcinoma in situ, ductal carcinoma in situ, and invasive carcinoma). Authors were not contacted if data were missing. Data were compared for between-study heterogeneity. The details are summarized in [Table 1](#).<sup>1–70</sup>

### Statistical Analysis

All analyses were performed using the “meta” package for R.<sup>26</sup> Logit transformation as outlined by Lipsey and Wilson was applied

**Table 1. Summary of Studies Measuring Incidence of Occult Carcinoma in Breast Reduction Specimens**

Reference	Country	Cancer Definition	No. of Patients	Mean Age (yr)	Breast Cancer History	Unilateral vs. Bilateral	No. of Specimens	LCIS (%)	DCIS (%)	IC (%)	Total Cancer (%)
Acevedo et al., 2019 <sup>37</sup>	U.S.	IC, DCIS	4774		No	B, 4775	9550	0.58	0.24	0.16	0.97
Ambaye et al., 2009 <sup>14*</sup> †	U.S.	IC, DCIS, LCIS	202	44	Yes	U, 21	21	0	0	0	0
Ambaye et al., 2017 <sup>32*</sup>	U.S.	IC, DCIS, LCIS	595	44.6	Grouped	B, 181	362	0.83	0.83	0.55	1.38
Ayhan et al., 2008 <sup>8*</sup>	Turkey	IC, DCIS	149	35.1	Grouped	U, 77; B, 518	1113	0.54	0.54	0.18	1.26
Aytac et al., 2013 <sup>41*</sup> †	Turkey	IC, DCIS	264	43.6	No	U, 7; B, 142	291	0	0.69	0	0.69
					Yes	B, 264	528	0	0.19	0.38	0.57
					No	U, 14	14	0	0	0	0
Blansfield et al., 1936 <sup>†</sup>	U.S.	Unclear	182	37	No	B, 168	336	0.3	0	0	0.3
Bondeson et al., 1985 <sup>22</sup>	Sweden	Unclear	200		Grouped	B, 200	400	3.5	0	0	3.5
Celik et al., 2015 <sup>15*</sup> ‡§	Turkey	IC, DCIS, LCIS	40	45.6	No	B, 40	80	0	0	0	0
Clark et al., 2009 <sup>9*</sup>	U.S.	IC	562	43	Grouped	U, 60; B, 502	1064	0.38	0.56	0	0.94
Colleau et al., 2005 <sup>42*</sup> †	France	IC, DCIS, LCIS	837	38.2	Grouped	B, 837	1674	0.06	0.24	0.12	0.42
					Yes	U, 170	170	0.59	0.59		
Colwell et al., 2004 <sup>43*</sup> †	U.S.	IC, DCIS	800	61	No	U, 19; B, 611	1241	0.16	0.16		
Cook and Fuller, 2004 <sup>7</sup> †	U.K.	IC, DCIS	1289	36.8	Grouped	NS	NS	0.16	0.31	0.08	0.54
Cruz et al., 1989 <sup>34</sup>	Puerto Rico	Unclear	100		Grouped	NS	NS	0	0	0	0
Desouki et al., 2013 <sup>44*</sup>	U.S.	IC, DCIS	2498	41	No	U, 36; B, 2462	4960	0.3	0.08	0.04	0.42
Dotto et al., 2008 <sup>45</sup> †‡	U.S.	IC, DCIS	516	35	No	B, 516	1032	0	0.1	0.1	0.19
					Yes	U, 56	56	3.57	3.57	0	7.14
Freedman et al., 2012 <sup>38*</sup> †	U.S.	IC, DCIS	700		No	B, 644	1288	0.47	0.16	0.16	0.78
Goyal et al., 2011 <sup>46*</sup>	U.K.	IC, DCIS	1588	54	Grouped	U, 341; B, 1247	2835	0.13	0.06	0.25	0.44
					Yes	U, 220	220	0.45	0.45	1.36	2.27
Hassan and Pacifico, 2012 <sup>21</sup>	U.K.	IC, DCIS	1388	43	No	U, 107; B, 1061	2229	0.09	0.34	0.09	0.51
Horo et al., 2011 <sup>17*</sup> †	France	IC, DCIS, LCIS	77	53.8	Yes	U, 77	77	0	0	0	0
Huysmans et al., 2016 <sup>47*</sup> § 47	Belgium	IC, DCIS	1045	40.2	No	U, 24; B, 1021	2066	0.1	0.19	0.19	0.48
Ishag et al., 2003 <sup>48</sup> †	U.S.	IC, DCIS	560	34.5	Grouped	U, 57; B, 503	1063	0.19	0.19	0.19	0.56
Jansen et al., 1998 <sup>19*</sup>	U.S.	Unclear	2576		Grouped	NS	NS	0	0	0	0.16
Kakagia et al., 2005 <sup>49*</sup> §	Greece	IC, DCIS	314	43	No	B, 314	628	0	0.16	0.32	0.48
Kececi et al., 2014 <sup>35*</sup>	Turkey	Unclear	95	40.9	Grouped	NS	NS	0	0	0	0
					Yes	U, 42	42	2.38	0	0	2.38
Kyriopoulos et al., 2012 <sup>33</sup> ‡§	Greece	IC, DCIS, LCIS	300	38.5	No	B, 258	516	0.39	0.19	0.19	0.78
Li et al., 2014 <sup>50*</sup>	U.S.	IC, DCIS	179	54	Yes	U, 169; B, 10	189	2.65	0.53	1.59	4.76
Merkkola-von Schantz et al., 2017 <sup>39</sup> †	Finland	IC, DCIS	317	56.3	Yes	U, 317	317	1.26	1.58	0.63	3.47
Merkkola-von Schantz et al., 2017 <sup>40*</sup>	Finland	IC, DCIS	849	44.5	No	U, 35; B, 814	1663	0.48	0.36	0.36	1.20
Petit et al., 1997 <sup>51*</sup>	France	IC, DCIS, LCIS	440	44	Yes	U, 440	440	1.82	1.82	1.59	5.23
Pitanguy et al., 2005 <sup>9*</sup>	Brazil	IC, DCIS, LCIS	2488	34.9	No	NS	NS	0.04	0.04	0.40	0.48
Ricci et al., 2006 <sup>52</sup> †	Brazil	IC, DCIS	109	39.7	Yes	U, 109	109	0	2.75	1.83	4.50
Samdanci et al., 2011 <sup>53*</sup> †	Turkey	Unclear	273	39.7	Grouped	NS	550	0.18	0	0	0.18
Slezak and Bluebond-Langner, 2011 <sup>36*</sup> †   36	U.S.	IC, DCIS	866		No	U, NS; B, 629	NS		0.48	0.32	
Snyderman and Lizardo, 1960 <sup>11</sup>	U.S.	Unclear	5008		Grouped	NS	NS				0.28
Sorin et al., 2014 <sup>54</sup>	France	IC, DCIS, LCIS	319	55	Yes	U, 319	319	0	0.94	0	0.94
Sorin et al., 2015 <sup>55*</sup>	France	IC, DCIS, LCIS	2718	54	Yes	U, 2718	2718	0.33	0.70	0.44	1.47
					Yes	U, 55	55	1.82	3.64	0	5.45
Tadler et al., 2014 <sup>18*</sup>	Switzerland	IC, DCIS, LCIS	534		No	B, 479	958	0.21	0	0	0.21
Talghini, 2013 <sup>16*</sup> ‡§	Iran	IC, DCIS, LCIS	198	37.1	No	B, 198	396	0.51	0	0.51	1.01
Tang et al., 1999 <sup>20</sup>	Canada	IC	27,500		Grouped	NS	NS			0.06	
Titley et al., 1996 <sup>5</sup>	U.K.	Unclear	157		Grouped	U, 19; B, 138	295	0	0	0	0
Usón et al., 2018 <sup>56</sup> † 56	Brazil	IC	783	40	No	U, 89; B, 694	1477	0.34		0.20	0.54
Viana et al., 2005 <sup>57*</sup>	Brazil	IC, DCIS, LCIS	274	34.8	No	B, 274	548	0.18	0.18	0.55	0.91

LCIS, lobular carcinoma in situ; DCIS, ductal carcinoma in situ; IC, invasive cancer; U.S., United States; U, unilateral; B, bilateral; NS, mammography; NS, not stated.

\*Records or implements preoperative screening protocol; physical examination.

†Outlines histopathology protocol family history.

‡Analyzed.

§Excluded.

||Recorded.

to the incidence data and weighted by inverse variance of logit transformed incidence.<sup>27</sup> Pooled incidence estimates of breast cancer per specimen were calculated by the DerSimonian-Laird method using a random effects model.<sup>28</sup> Between-study heterogeneity was examined

using the  $I^2$  statistic.<sup>29</sup> Odds ratios and 95 percent confidence intervals were calculated for populations comparing personal history of breast cancer as a risk factor using the Mantel-Haenszel method.<sup>30</sup> The Egger linear regression test was used to assess for publication bias.<sup>31</sup>

## RESULTS

Our search yielded 242 original articles, from which three duplicates were removed. Manual searching of reference lists yielded 18 additional articles for review. Records were screened based on title and abstract, and 204 articles were excluded. The 53 collated articles were read in full, and those that did not meet eligibility criteria were excluded, leaving 42 articles for qualitative analysis (Fig. 1). The extracted data from each study are summarized in Table 1.

The majority of studies were retrospective cohort studies, apart from two retrospective surveys<sup>11,19</sup> and three prospective studies.<sup>14,32,33</sup> Patient population size ranged from 40 for chart reviews<sup>15</sup> to 27,500 for national database studies.<sup>20</sup> The definition of cancer was unclear in eight studies, included lobular carcinoma in situ, ductal carcinoma in situ, and invasive cancer in 13 studies; ductal carcinoma and invasive cancer in 18 studies; and invasive cancer alone in three studies. Total incidence of cancer per specimen ranged from 0 to 7.14 percent. This value could not be calculated for eight studies because of a lack of specimen numbers.<sup>7,9,11,19,20,35,36</sup>

Synchronous lesions, either ipsilateral or bilateral, were reported in 11 studies. Acevedo et al. reported the incidence of lesions with the worst prognostic value.<sup>37</sup> When synchronous lesions were present, the authors used an estimated trumping order to determine which lesions to report. For example, if lobular carcinoma in situ and invasive cancer were present in the same specimen, they would only report invasive cancer. To account for the potential underestimation of lesions, the current authors included synchronous lesions as separate findings in the final result. There was insufficient information to carry out this adjustment for the studies by Acevedo et al. and Pitanguy et al.<sup>9,37</sup>

The mean age of patients within the studies varied from 34.5 to 61 years. Some studies did not report an average age for patients, but used age blocks to determine a relationship between chance of occult malignancy and age.<sup>38</sup> In other articles, only median age was reported. Studies varied in their inclusion of preoperative assessments. Most studies ensured that women underwent a physical breast examination and/or age-appropriate preoperative screening (mammography or ultrasound) to rule out malignancy ( $n = 28$ ); however, some did not comment on this at all ( $n = 14$ ). The histopathology protocol was outlined in 19 studies, with some specification about the number of slices, varying from two to 30. The studies by

Ambaye et al. investigated this specifically, performing analyses on the number of slices and their relation to the number of lesions detected.<sup>14,32</sup> Studies differed in their treatment of family history of breast cancer as a known risk factor. Family history was recorded and analyzed in five studies, recorded and intentionally excluded as a confounder in five, recorded but not accounted for in four studies, and simply mentioned in the discussion in 11 studies and not assessed.

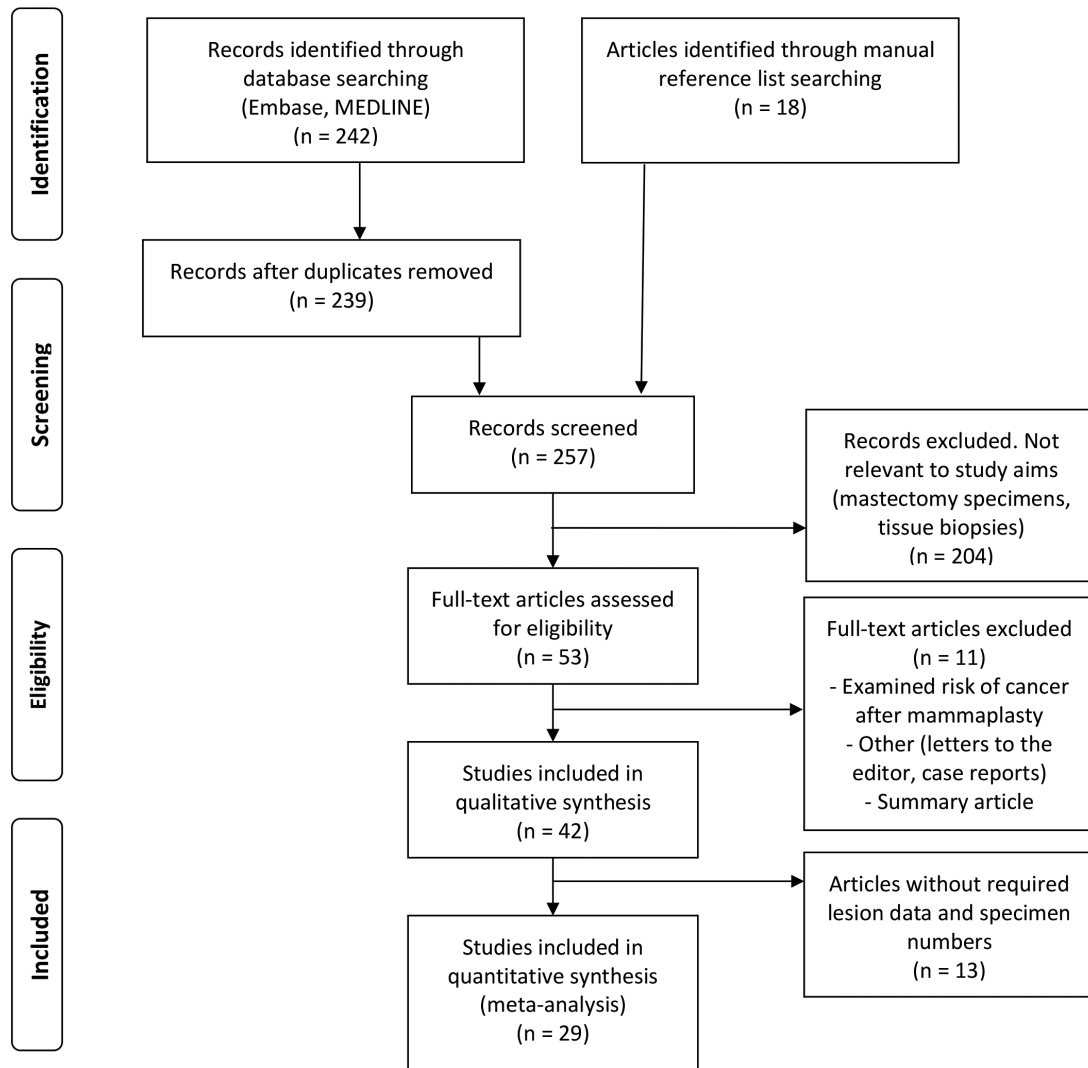
Studies that clearly specified the numbers of unilateral and bilateral procedures, history of breast cancer, and definition of malignancy in their populations were included in the meta-analysis ( $n = 29$ ). When classified into female populations with a positive history of breast cancer (14 studies, 4658 specimens), the pooled incidence of breast cancer per specimen was 3.4 percent (95 percent CI, 2.2 to 5.3 percent) (Fig. 2). There was statistically significant heterogeneity ( $I^2 = 74$  percent;  $p < 0.01$ ) and no significant publication bias (Egger test,  $p = 0.47$ ). When female populations with a negative history of breast cancer were grouped and analyzed (15 studies, 17,590 specimens), the pooled incidence of breast cancer per specimen was 0.6 percent (95 percent CI, 0.4 to 0.8 percent) (Fig. 3). There was statistically significant heterogeneity ( $I^2 = 56$  percent;  $p < 0.01$ ) and no significant publication bias (Egger test,  $p = 0.30$ ).

When further stratified into populations comparing women with a history of breast cancer (725 specimens) and those without (7352 specimens), there was a statistically significant pooled odds ratio of 6.02 (95 percent CI, 3.06 to 11.86;  $p < 0.0001$ ) (Fig. 4). It was noted that the two studies by Merkkola-von Schantz et al.<sup>39,40</sup> recruited unique patient samples from the same institution, both with and without breast cancer, so this was interpreted as one grouped population in the analysis (eight studies, seven compared populations). There was no statistically significant heterogeneity ( $I^2 = 29$  percent;  $p = 0.21$ ) or publication bias in this analysis (Egger test,  $p = 0.41$ ).

## DISCUSSION

Our systematic review and meta-analysis demonstrate that there is a higher incidence of occult carcinoma within breast reduction specimens of women with a positive history of breast cancer (3.4 percent) than in those without (0.6 percent) and that this difference is statistically significant in comparable populations of women (OR, 6.02; 95 percent CI, 3.06 to 11.86;  $p < 0.001$ ). This is





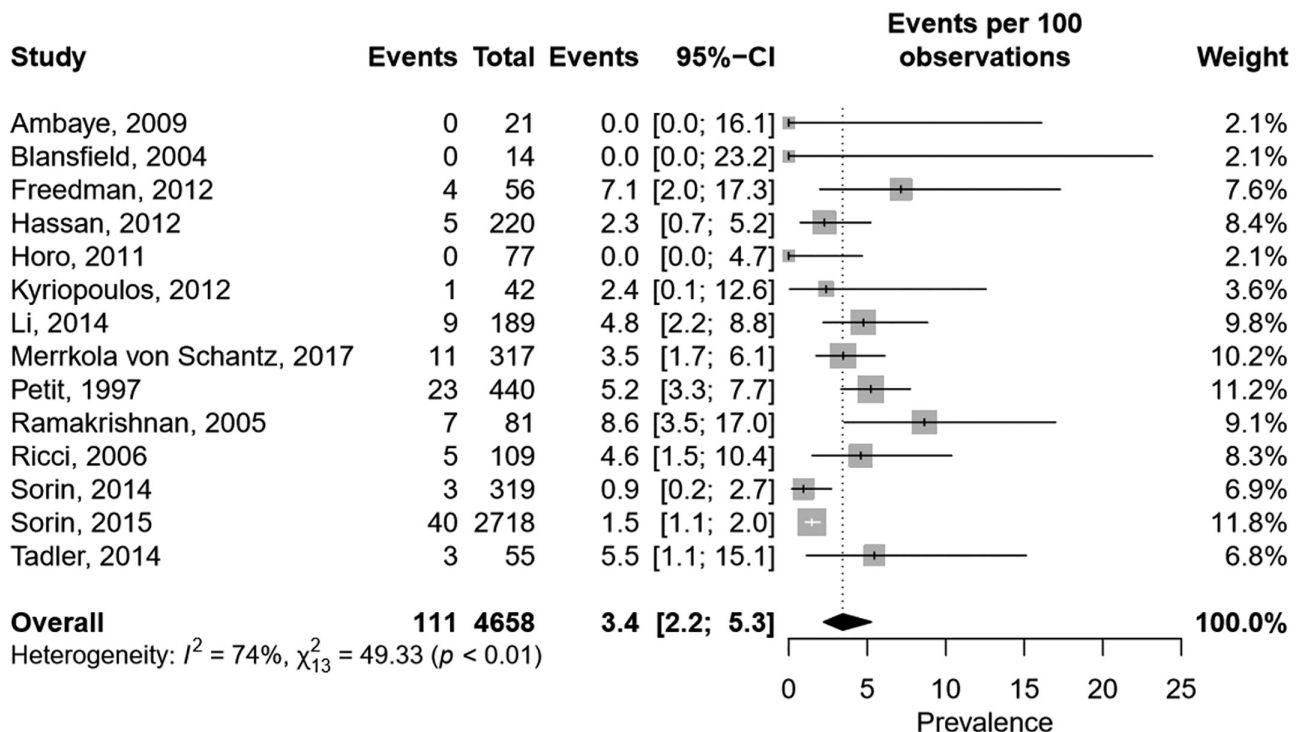
**Fig. 1.** Flow diagram of study selection.

the first systematic review and meta-analysis to examine occult breast carcinoma within breast reduction specimens and specifically analyze this relationship between personal history of breast cancer and incidence of carcinoma in reduction specimens.

In our qualitative analysis, we outlined the characteristics of 42 studies examining breast specimens from women undergoing either unilateral or bilateral breast reductions for various indications (Table 1). We found substantial variation in how cancer incidence was reported between studies, which has previously made inferences difficult to draw.<sup>21,35</sup> To improve the comparability of incidence rates, we predetermined our definition of carcinoma to include invasive carcinoma, both ductal and lobular, ductal carcinoma in situ and lobular carcinoma in situ, and directly calculated the incidence of these lesions from each

study. Ductal carcinoma in situ is well established as a form of noninvasive breast cancer with high invasive potential. As it remains impossible to predict which ductal carcinoma in situ lesions will become invasive, current guidelines recommend active treatment with surgery, radiotherapy, or hormonal therapy.<sup>58</sup>

Alternatively, the inclusion of lobular carcinoma in situ as a cancer diagnosis remains an area of controversy in the literature.<sup>21,38,47</sup> Over the past few decades, lobular carcinoma in situ has predominantly been considered a risk factor for subsequent invasive cancer rather than a precursor lesion, leading to its varied inclusion and exclusion as a cancer result in various studies (Table 1). Increasing evidence from morphologic, immunophenotypic, and molecular investigations support the idea that at least some lobular carcinomas in situ are nonobligate precursors of invasive



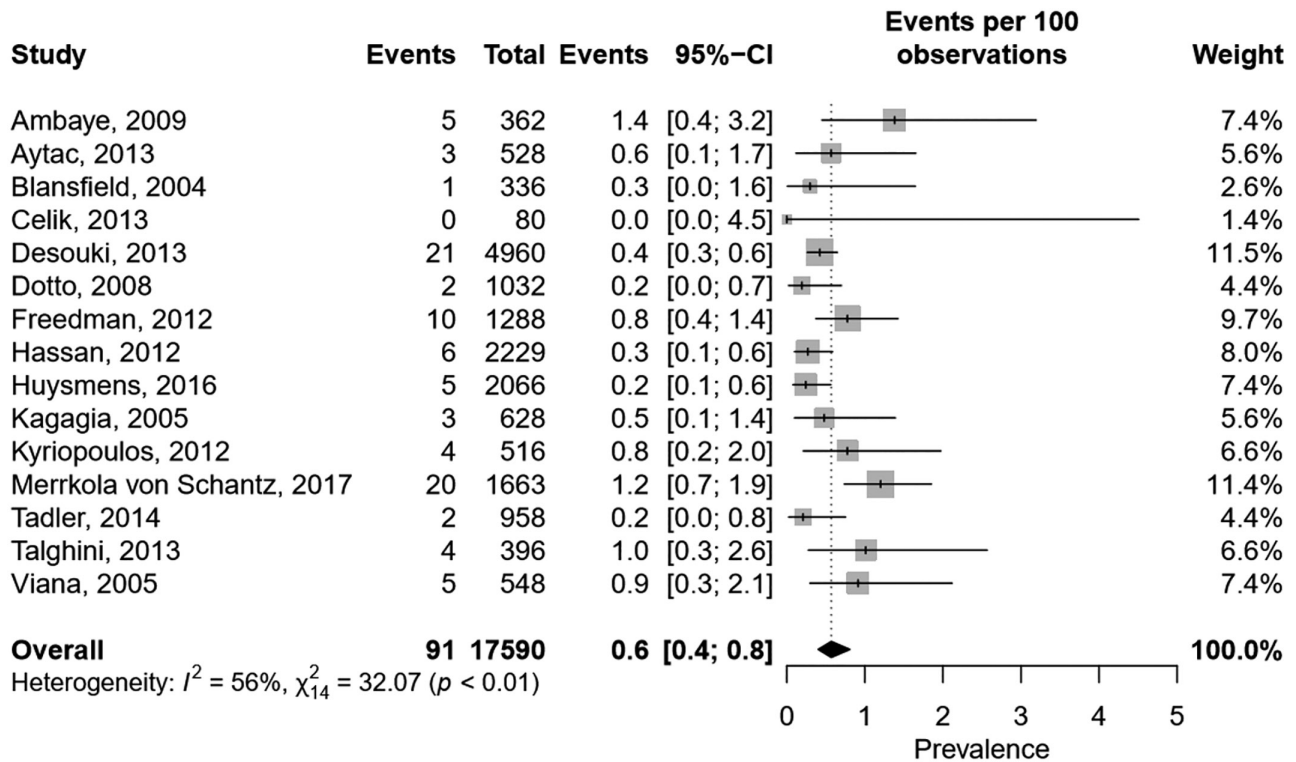
**Fig. 2.** Forest plot for incidence of occult breast carcinoma in unilateral reduction specimens in women with a history of contralateral breast cancer.

lobular carcinoma.<sup>59</sup> Cancer Australia released an updated clinical guideline in 2016 incorporating this development into its management recommendations. This guideline also outlines newly recognized subtypes of lobular carcinoma in situ for which excision is now recommended, such as pleomorphic lobular carcinoma in situ, classic lobular carcinoma in situ with comedo-type necrosis, and florid or bulky lobular carcinoma in situ.<sup>60</sup>

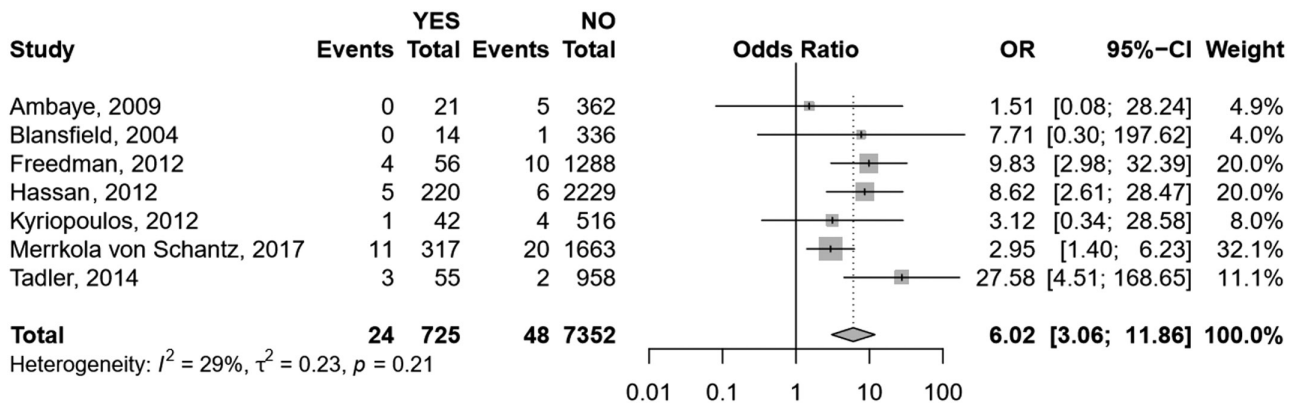
In our analysis, we intentionally calculated occult cancer lesions per specimen rather than per patient, contrary to many of the studies examined in our review. Because the majority of studies include women undergoing both unilateral and bilateral breast reductions, the calculated incidence of cancer per patient would be overestimated for women providing two breast specimens (i.e., bilateral cases) compared to the single specimen provided during a contralateral mastoplastic after cancer. In our review, 11 of the studies make reference to multiple lesions, both ipsilateral or bilateral, which grouped per patient would amplify this overestimation. We made the assumption that each breast carries an inherent risk of cancer and our results reflect a “risk per breast,” which should be doubled for a patient undergoing bilateral reduction.

Women with early-stage sporadic breast cancer have an annual risk of developing contralateral

cancer of 0.5 to 0.75 percent.<sup>24</sup> This likelihood underpins our finding that women undergoing contralateral reduction after breast cancer have a higher incidence of occult carcinoma than those with no prior cancer. Advanced age and family history are both well-known risk factors for breast cancer development. Over 75 percent of breast cancer cases in Australia occur in those older than 50 years,<sup>10</sup> and women with a first-degree relative with breast cancer have double the personal risk of breast cancer.<sup>60</sup> The studies in our analysis varied widely in their treatment of family history as a risk factor, either including it in their analysis, using it as an exclusion criterion, or failing to address it altogether (Table 1). In addition, women with a history of cancer who undergo contralateral breast reduction often have an advanced age when compared to women undergoing mastoplastic for macromastia.<sup>21,23</sup> Ambaye et al. found that when adjusted for age, history of contralateral breast cancer did not significantly predict significant pathologic findings ( $p = 0.48$ ).<sup>32</sup> However, their definition of significant pathologic findings encompassed atypical ductal and lobular hyperplasia, both of which are not included in our definition of carcinoma, making overall comparisons difficult. The lack of adjustment for potential confounders such as age and family history is an important limitation of our quantitative analysis.



**Fig. 3.** Forest plot for incidence of occult breast carcinoma in breast reduction specimens in women with no personal history of breast cancer.



**Fig. 4.** Forest plot for odds ratios of occult carcinoma incidence in specimens from women with a history of breast cancer compared to women with no history of breast cancer.

Future studies with clear adjustment for these confounders would make our findings more robust.

One of the enduring challenges lies in the management of these patients once a breast carcinoma is discovered. If a carcinoma found within a breast reduction specimen has positive margins, the potential for breast-conserving resection may be lost.<sup>21,23,62</sup> Reduction mammoplasty is a procedure that completely distorts the architecture of the breast, and the resected tissue is rarely given as a whole, orientated specimen.<sup>55</sup> Consequently, lesions with positive margins found

postoperatively warrant mastectomy,<sup>38</sup> which has significant psychological consequences for these women.<sup>63</sup> Counseling patients on the chance of diagnosing cancer on histopathology is something that should be performed preoperatively. Some authors describe elegant specimen orientation methods to facilitate reexcision,<sup>36</sup> and although it is unclear whether these change clinical outcome, the current authors feel it is no extra effort to apply orientation sutures when possible.

Nevertheless, the preoperative diagnosis of lesions is paramount. Physical examination is a

quick and inexpensive method of assessment that should not be overlooked.<sup>6,21</sup> Approximately 60 percent of breast cancers that are visible on mammography and a few that are clinically occult can be detected on a clinical breast examination.<sup>64</sup> However, this detection becomes more difficult in large-breasted women, and examination alone may be inadequate.<sup>4</sup>

Radiologic screening for breast cancer before breast reduction surgery varies widely. In a survey by Hennedige and colleagues, 92 percent of breast surgeons routinely perform radiologic screening, as opposed to only 41 percent of plastic surgeons,<sup>3</sup> emphasizing the need for shared guidelines. Mammography is the gold standard screening tool for the early detection of breast cancer in Australia<sup>65</sup> and the United States.<sup>66</sup> The American Cancer Society guidelines strongly recommend annual mammography for women with an average risk of breast cancer from the age of 45 years, and as an option from age 40 years.<sup>66</sup> As a screening modality, mammography has significantly reduced overall breast cancer mortality in women aged 50 to 60 years by 20 to 35 percent.<sup>67</sup> Unfortunately, it has a lower sensitivity for women younger than 40 years, because of a higher prevalence of dense breast tissue in this age group and a lower incidence of cancer.<sup>64</sup> The American College of Radiology appropriateness guidelines recommend ultrasound as a useful adjunct for breast cancer screening in high-risk women in addition to intermediate-risk women with dense breast tissue; however, the increased risk of false-positive findings should be elucidated to this latter group.<sup>68</sup> Magnetic resonance imaging has been demonstrated to be superior to both mammography and ultrasound in the early detection of breast cancers, and it has particular sensitivity for ductal carcinoma in situ detection.<sup>69</sup> Potentially, magnetic resonance imaging could be adopted as a screening method for high-risk women, such as those undergoing breast reduction after contralateral cancer.

There are currently no guidelines on histopathologic screening of breast reduction specimens,<sup>3-9,70</sup> although findings by Hennedige et al. report that 90 percent of plastic surgeons and 96 percent of breast surgeons routinely submit specimens for histopathologic examination.<sup>3</sup> Although the overall incidence of carcinoma in these specimens seems small (<6 percent) and histopathology can be costly, the discovery of breast cancer is significant to the individual, and delayed diagnosis may incur a greater cost for the health care system.<sup>35</sup> In their prospective study, Ambaye et

al. found a significant increase in identification of pathologic breast lesions with increased histopathologic sampling of reduction specimens in women older than 40 years.<sup>32</sup> They consequently recommended gross sampling of specimens in women younger than 35 years, microscopic examination of six to seven slices in women aged 35 to 49 years, and microscopic examination of 10 to 11 slices in women older than 50 years.<sup>32</sup> Until formal evidence-based guidelines are developed, these recommendations appear a reasonable alternative.

## CONCLUSIONS

This systematic review provides estimates for the percentage incidence of occult carcinoma within breast reduction specimens of women undergoing breast reduction. We found that women with a history of breast cancer are significantly more likely to have an occult carcinoma within their breast reduction specimen than women with no history of cancer. This has implications for preoperative counseling of risk and need for guidelines regarding radiology screening and histopathology examination. Further large, prospective cohort studies, with adequate adjustment of confounders such as age and family history of breast cancer, are required to strengthen these conclusions.

**Siobhan E. Fitzpatrick, M.D.**

4 Governor Phillip Place

West Pennant Hills, New South Wales 2125, Australia

[siobhanefitzpatrick@gmail.com](mailto:siobhanefitzpatrick@gmail.com)

Twitter: @siobhan\_fitz

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