Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: a meta-analysis
Gieni M, Avram R, Dickson L, Farrokhyar F, Lovrics P, Faidi S, Sne N

CRD summary
This review demonstrated that there was no evidence for increased frequency of local breast cancer recurrence with immediate breast reconstruction after mastectomy surgery compared with mastectomy alone in women with primary breast cancer. Given the presence of variation and limitations in the (non-randomised) evidence presented, the authors’ conclusions may be too strong for the evidence presented.

Authors' objectives
To examine the safety of immediate breast reconstruction following mastectomy for breast cancer in terms of the frequency of recurrence.

Searching
Databases including PubMed, EMBASE, and The Cochrane Library (given as Cochrane databases) were searched up to August 2010 for English language studies; search terms were provided. Reference lists of the included studies were reviewed for potentially relevant citations. Searches were conducted by two independent investigators.

Study selection
Studies that compared breast cancer recurrence following mastectomy in women (aged 18 years or older) who had undergone immediate breast reconstruction for first-time invasive breast cancer versus those who did not undergo immediate breast reconstruction were eligible to be included. Studies of women undergoing prophylactic mastectomy or breast-conserving therapy or who had rare tumour types were excluded. Studies had to include at least 20 patients, report at least 12 months follow-up, and report American Joint Committee on Cancer (AJCC) staging. Studies with no comparator group were excluded. The primary outcome was recurrence of breast cancer. A secondary outcome was systemic recurrence.

The included studies were retrospective cohort or matched cohort studies published from 1992 to 2010. Studies were conducted in Europe, USA, Japan, China and Korea. Women underwent conventional mastectomy, radical mastectomy, extended radical mastectomy, modified radical mastectomy, nipple preserving mastectomy, or skin sparing mastectomy. Types of breast reconstruction included latissimus dorsi or transverse rectus abdominis muscle reconstruction, prosthesis, and silicone-gel implants. Adjuvant treatment included radiotherapy, chemotherapy and hormonal therapy. The age of participants was not clearly reported, but (where reported) ages ranged from 21.5 to 76 years in the intervention group and 21.5 to 97 years in the control group. Stage of breast cancer at surgery ranged from I to IV. The main primary outcome assessed was local recurrence.

The titles were reviewed independently by two authors; any discrepancies were discussed and, where agreement could not be attained, a third reviewer was consulted.

Assessment of study quality
The quality of the studies was assessed using the Methodological Index for Non-Randomised Studies (MINORS) scale, a validated 24-point tool. No information was provided on the quality assessment items included in this scale.

Quality assessment was conducted independently by two authors.

Data extraction
Data on recurrence rates, cancer stage, type of mastectomy and reconstruction, adjuvant treatments, and duration of follow-up were extracted. Odds ratios (OR) and 95% confidence intervals (CIs) were estimated for the cohort studies.

The authors do not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Methods of synthesis
Studies were analysed according to study design. Odds ratios and 95% confidence intervals from the retrospective cohort studies were pooled using a random-effects model (a fixed-effect approach was planned if no heterogeneity was identified); p<0.05 was considered statistically significant.

Heterogeneity was identified using the Cochrane Q-test (p<0.10) and I². I² values less than 25% represented low heterogeneity, 25% to 50% moderate heterogeneity, and over 50% represented high heterogeneity. A funnel plot was used to assess the presence of publication bias. The authors planned to investigate breast cancer stage as a source of heterogeneity.

The matched cohort studies were summarised narratively.

Results of the review
Ten studies were included with 4,426 women. These included eight retrospective cohort studies (2,917 women undergoing standard mastectomy and 793 women undergoing immediate breast reconstruction following mastectomy) and two matched cohort studies (with 358 pairs). Study quality was not reported. Inter-rater reliability was reported to be 74% (95% CI: 0.93%) suggesting moderate agreement. Follow-up periods ranged from 18 to 101 months.

There were no significant differences in local recurrence (3,710 women; seven studies; Q-statistic p=0.34; I²=12%) or systemic recurrence (1,393 women; six studies; Q-statistic p=0.46; I²=0%) with no evidence of study heterogeneity or publication bias.

Insufficient data were available to fully investigate breast cancer stage as a source of heterogeneity.

Similar results were observed in the matched cohort studies.

Authors’ conclusions
This meta-analysis demonstrated no evidence for increased frequency of local breast cancer recurrence with immediate breast reconstruction after mastectomy surgery compared with mastectomy alone.

CRD commentary
The aim and inclusion criteria for this review were clearly set out. Several database were searched for relevant studies, but studies were restricted to English language publications which meant there was the possibility of language bias. Two reviewers independently screened the studies for inclusion and undertook quality assessment, which limited reviewer bias; however, the authors did not describe how data extraction was performed.

Quality assessment was conducted, but the results were not reported either in summary or in full, so the quality of included studies could not be judged. Limited data on patient characteristics were provided, so the study generalisability could not be fully assessed. Although studies differed in their inclusion of early or late stage breast cancer or both, and various types of mastectomy and immediate breast reconstruction were carried out, no statistical evidence of heterogeneity was identified. Statistical pooling of studies could be justified, although it was not clear why odds ratios could not be estimated for the matched cohort studies. All of the included studies were non-randomised and would have inherent limitations.

Both the individual study results and the pooled results should be treated with considerable caution. The authors’ conclusions are likely to be too strong given the evidence presented.

Implications of the review for practice and research
Practice: The authors stated that immediate breast reconstruction may be a feasible option for women.

Research: The authors stated that further research was needed with adequate reporting of recurrence based on stage and five-year disease-free survival so that better information can be provided to women on their treatment options. The authors also stated that prospective, randomised studies, with long-term follow-up, were required to validate the results found in this meta-analysis.

Funding