Paclitaxel-based versus docetaxel-based regimens in metastatic breast cancer: a systematic review and meta-analysis of randomized controlled trials
Qi WX, Shen Z, Lin F, Sun YJ, Min DL, Tang LN, He AN, Yao Y

CRD summary
This review concluded that a paclitaxel-based regimen was as effective as a docetaxel-based regimen for patients with metastatic breast cancer and that a paclitaxel-based regimen was associated with less toxicity and better tolerability. In view of the limited evidence base and significant differences between study interventions and results, this conclusion may not be reliable.

Authors' objectives
To compare the safety and efficacy of paclitaxel-based versus docetaxel-based regimens for patients with metastatic breast cancer.

Searching
PubMed, EMBASE and Cochrane Register of Controlled Trials (CENTRAL) were searched up to January 2012; search terms were reported. Posters presented at annual meetings of the European Society of Medical Oncology, American Society of Medical Oncology and San Antonio Breast Cancer Symposium were searched up to 2011. Reference lists of relevant studies and review articles were checked. The search was limited to studies reported in English.

Study selection
Randomised controlled trials (RCTs) that compared paclitaxel-based with docetaxel-based regimens in patients with metastatic breast cancer were eligible for inclusion.

In three of the seven included trials patients received taxane-based regimens as first-line therapy and in four trials between 45.6% and 62.2% patients had previously received anthracycline-based regimens. Six trials included patients with metastatic breast cancer and one trial included patients with advanced breast cancer. The median age of patients ranged from 47 to 75 years. In four trials paclitaxel and docetaxel regimens were given alongside gemcitabine, doxorubicin, carboplatin or capecitabine. In most trials paclitaxel-based and docetaxel-based regimens were administered every three weeks.

The authors did not report how many reviewers selected studies for inclusion.

Assessment of study quality
Two independent reviewers assessed the quality of the included trials using the five-point Jadad scale of randomisation, blinding and treatment of withdrawals.

Data extraction
Two independent reviewers extracted intention-to-treat data on median overall survival, progression-free survival, time to progression, overall response rate and adverse events. When overall survival, progression-free survival and time to progression data were not reported, they were estimated using survival curves using the method of Parmar et al.

Methods of synthesis
Hazard ratios for overall survival, progression-free survival and time to progression, and risk ratios for overall response rate and grade 3 or 4 adverse events were pooled using a fixed-effect model (no significant heterogeneity) or a random effects model (significant heterogeneity). Heterogeneity was assessed using the Q statistic and quantified using I².

The presence of publication bias was assessed using the Begg and Egger tests.

Results of the review
Seven RCTs (1,694 participants) were included in the review. All seven RCTs scored 3 out of a possible 5 on the Jadad scale.
There was no statistically significant difference in overall survival between paclitaxel-based and docetaxel-based regimens (five RCTs) but there was significant heterogeneity for this result ($I^2=81.3\%$). In a subgroup analysis of studies in which patients received taxane-based regimens as first line therapy, the paclitaxel-based regimen significantly improved overall survival compared with the docetaxel-based regimen (HR 0.73, 95% CI 0.56 to 0.94, $I^2=0\%$; two RCTs).

There was no statistically significant difference in progression-free survival (two RCTs) or time to progression (three RCTs) between paclitaxel-based and docetaxel-based regimens but there was significant heterogeneity for these results ($I^2=65\%$ and $I^2=74.2\%$).

There was no statistically significant difference in overall response rate between paclitaxel-based and docetaxel-based regimens (seven RCTs) with no evidence of significant heterogeneity.

Grade 3 or 4 haematological toxicities, mucositis, diarrhoea and fatigue were statistically significantly more common with the docetaxel-based regimen. Incidence of Grade 3 or 4 nausea and peripheral neuropathy was not statistically significantly different between the two treatment groups. There was significant heterogeneity for most of these results.

There was no evidence of significant publication bias.

**Authors' conclusions**
Both taxane-based regimens had comparable efficacy for patients with metastatic breast cancer. The paclitaxel-based regimen was associated with less toxicity and better tolerability, especially in older patients and when used in weekly regimens.

**CRD commentary**
The review question and inclusion criteria were clear. Several relevant sources were searched, including sources of unpublished studies. Only studies in English were sought and this increased potential for language bias. Two independent reviewers undertook data extraction and quality assessment and this reduced potential for reviewer bias and error; it was unclear whether similar methods were used during study selection. Appropriate criteria were used to assess the quality of the included studies and all were adequate quality.

Clinical differences between studies (such as whether the taxane-based regimens were given as first-line therapy and the specific regimens used) it may not have been appropriate to pool the included studies. Many of the analyses included only a few studies and there was evidence of significant statistical heterogeneity for many of the outcomes.

In view of the limited evidence base and the significant heterogeneity between studies, the authors' conclusions may not be reliable. The authors' conclusions regarding older patients and the use of weekly regimens are not supported by the evidence presented.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that well designed randomised controlled trials were warranted to confirm the efficacy of weekly paclitaxel (rather than three-weekly) in patients with metastatic breast cancer. And more studies were needed to identify patients who would most likely benefit from taxane therapy.

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