CRD summary
The review concluded that alendronate was associated with development of oral ulcers as healing occurred when the drug was either withdrawn or administered correctly. Due to very limited evidence and substantial risk of bias in the review process, the authors’ conclusions cannot be considered reliable.

Authors' objectives
To review the published data on the relationship of mucosal ulcers in the oral cavity with the use of alendronate.

Searching
PubMed was searched for relevant published studies from 1966 to August 2010. There were no language restrictions. Limited search terms were reported. Reference lists of selected reports were searched.

Study selection
Studies that reported ulceration of the oral mucosa in patients who used alendronate were eligible for the review. Studies were required to show an association between the drug and the ulcer as a result of healing occurring after withdrawal of the drug or after changing the method of drug administration. Studies were excluded if they described osteonecrosis of the jaw as a result of alendronate or if the ulcers were not limited to the oral mucosa.

In the included studies, the average age of patients was 70 years (range 49 to 90 years) and 62% were women. Most had osteoporosis and all had systemic disease. About half of the patients had removable dentures. Seventy-three percent of patients used alendronate once a day at a dosage of 10mg per day, where reported; three patients used a dosage of 70mg per week. All patients except one were reported to misuse alendronate by sucking on tablets or keeping within the mouth for a long time. Duration of the oral ulcers ranged from two days to 12 months. The most common symptom was pain.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
The included studies were not assessed for quality.

Data extraction
Data were extracted on dosage and duration of alendronate, appearance and duration of oral ulcers, treatment received and healing rates.

The authors did not state how many reviewers extracted data.

Methods of synthesis
The results of the studies were combined in narrative synthesis.

Results of the review
Twelve case reports (13 patients) were included in the review. Two studies appeared to report on the same patient and were considered as representing one case.

In 12 patients withdrawal of alendronate was associated with ulcer healing. In the remaining case, correct administration of alendronate was associated with ulcer healing. In seven patients, healing occurred within 15 days of withdrawal of the drug, in three patients healing occurred within three to four months and in three patients healing required 11 to 13 months.

Authors' conclusions
Alendronate was associated with development of oral ulcers as healing occurred when the drug was either withdrawn or
administered correctly.

CRD commentary
The research question was not entirely clear. The inclusion criteria meant that not all evidence relevant to the relationship between alendronate and oral ulcers was included. As a result, it was not possible to determine how many patients did not develop ulcers when taking alendronate or whether there were characteristics of an alendronate regimen that made it more likely for ulcers to occur. A very limited search without language restriction was performed and it was possible some studies were missed. The included studies were case series of only one or two patients. The authors did not state how many reviewers selected studies or extracted data, so reviewer error and bias could not be excluded. All the cases involved patients who had misused alendronate so the results provided no information about the frequency or severity of ulcers with correct use.

Very limited evidence and substantial risk of bias in the review process mean that the authors’ conclusions cannot be considered reliable.

Implications of the review for practice and research
Practice: The authors stated that all patients taking alendronate should be followed up for the first year and patients seeking care for oral ulcers should be asked about their medication use.

Research: The authors did not state any implications for research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.