Authors' objectives
To assess the clinical- and cost-effectiveness of antimicrobial agents in the prevention and healing of chronic wounds. The systematic review of diabetic foot ulceration is summarised in another DARE abstract.

Searching
Eighteen electronic databases were searched from inception to January 2000, with no restrictions on date or language. The National Research Register, the bibliographies of retrieved articles, and five specialist wound care journals were also checked and an expert panel was consulted.

Study selection
Study designs of evaluations included in the review
Clinical trials with a concurrent control group, both randomised and non-randomised, were eligible for inclusion. Patients, limbs or lesions could be the units of allocation.

Specific interventions included in the review
Studies of any systemic or topical agents with antimicrobial properties, including antibiotics, antifungals, antivirals and alternative therapies. There were 9 studies of systemic antimicrobials and 21 of topical agents.

Participants included in the review
Patients with diabetic foot ulcer, pressure ulcers, leg ulcers (various aetiologies), pilonidal sinuses, non-healing surgical wounds and chronic cavity wounds, and people at risk of developing pressure ulcers, were included.

Outcomes assessed in the review
The primary outcome measure was wound healing. This was assessed using an objective measurement such as change in ulcer size, rate of healing, frequency of complete healing, or time to healing. For pilonidal sinuses, the outcomes were healing rates and recurrence of disease. For pressure ulcer prevention, the main outcome was the incidence of new lesions.

How were decisions on the relevance of primary studies made?
The inclusion decisions were made independently by two reviewers and any disagreements were resolved by consensus.

Assessment of study quality
The validity of the studies was assessed using a checklist that covered the method of randomisation, criteria for patient selection, baseline comparability, sample size, outcome assessment, patient withdrawals and intention-to-treat analysis. The validity assessment was performed independently by two reviewers and any disagreements were resolved by consensus.

Data extraction
The data were extracted onto structured summary tables by a single reviewer and then checked by a second reviewer. Where necessary, the study authors were contacted for further information or clarification. Wherever possible, the odds ratios and effect sizes were calculated on an intention-to-treat basis.

Methods of synthesis
How were the studies combined?
The results were combined in a narrative review, with the studies grouped by wound type and intervention type (systemic or topical).

How were differences between studies investigated?
The studies were grouped by wound and intervention type, and differences between the studies were discussed in the text. The data were also displayed as forest plots (with no statistical pooling).

Results of the review
Thirty studies were included: 25 randomised controlled trials and 5 non-randomised. The total number of participants was not reported in the review.

Several methodological problems were identified; the most common was an inadequate sample size.

The studies included in this review investigated a variety of antimicrobials and a number of different wound types, with little overlap. Consequently, no single overall result could be drawn from this review.

Wounds of mixed aetiologies: ciprofloxacin in combination with a topical agent and levamisole are possibly beneficial systemic treatments (2 trials). The topical treatments that displayed some level of efficacy (5 trials) were benzoyl peroxide, collagen gel, 1% silver zinc allantoinate cream, hydrocolloid dressing, povidone iodine ointment, antiseptic spray (eosin 2% plus chloroxyphenol 0.3%) and an alternative preparation.

Pressure ulcers (5 trials): no trials of systemic agents were found. The topical treatments that demonstrated some level of efficacy were oxyquinoline ointment, hydrocolloid dressing, povidone iodine ointment, povidone iodine/sugar ointment and gentian violet. For the prevention of pressure ulcers, no difference was found between a hexachlorophane lotion and an inert preparation or a cetrimide lotion.

Diabetic foot ulcers: systemic amoxicillin plus clavulanic acid was not better than placebo, and no difference was found between systemic clindamycin and cephalaxin. One trial found that a hydrogel dressing was significantly more effective than various systemic and topical antimicrobial preparations for complete healing.

Pilonidal sinuses: pre-operative cefoxitin or peri-operative clindamycin (2 trials) did not shorten the healing time significantly, whereas oral metronidazole after excision did. Post-operative topical (impregnated sponge) gentamycin was more effective than no treatment. Silastic foam dressings, chlorhexidine and Eusol packs were equally effective.

Cost information
Yes. There were few data on the cost-effectiveness of antimicrobial agents in wound healing. Information from 6 studies suggested that certain treatments (hydrogel dressings, primary closure in pilonidal sinuses, silastic foam dressing) may be associated with reduced nurse labour time.

Authors' conclusions
There is no existing evidence to support the use of systemic antimicrobial agents for chronic-wound healing. More rigorous evaluation of promising interventions is required. Several topical agents may be beneficial but, again, further evaluation is needed before efficacy can be established.

CRD commentary
This systematic review addressed a very broad question using well-defined inclusion criteria. The searches undertaken for published studies were comprehensive, but there is a possibility that unpublished material may have been missed. Only controlled studies were included, and a quality assessment was performed and used to inform the review findings. The details of the included studies are presented in summary tables and their results in forest plots. The narrative review was entirely appropriate given the disparate interventions and indications. This level of disparity, always a potential difficulty in broad-ranging reviews, means that the review has only been able to provide an overview of the topic. This
was a very well-conducted review and the authors' conclusions are fully supported by the review findings.

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

**Practice:** The authors state that the lack of good evidence means that at present no recommendations can be made for the use of, or for the discontinuation of any systemic antimicrobial in chronic-wound prevention or healing. Some topical agents appear to be promising but, as yet, there is no available evidence on which to base firm recommendations.

**Research:** The authors state that most of the research conducted in this area needs replication with well-designed randomised controlled trials.

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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.