CRD summary
The review found no statistically significant differences for recurrence or anal incontinence between fibrin glue versus conventional surgery for the treatment of perianal fistula. The authors' conclusions should be treated with caution due to the low number of studies identified and high variability between studies.

Authors' objectives
To compare fibrin glue versus conventional surgery in the treatment of perianal fistula.

Searching
MEDLINE, EMBASE, Science Citation Index, Conference Proceedings Citation Index, CINAHL, Zetoc, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched to January 2010 with no language restrictions; search terms were reported. Abstracts of The American College of Surgeons, The American Society of Colon and Rectal Surgeons, The Italian Society of Surgery, The Italian Society of Colorectal Surgery and The Courrier de Coloproctologie were also searched to 2009. The bibliographies of included studies were handsearched for additional studies.

Study selection
Eligible randomised controlled trials (RCTs) and non-randomised controlled trials compared conventional surgery against fibrin glue in patients aged 18 years or older with cryptoglandular and Crohn's perianal fistulae. For studies to be eligible: the fibrin glue used had to be from commercial kits (details reported); the fistula tract had to be irrigated with hydrogen peroxide solution; and fibrin glue inserted in the fistula tract by the external opening, while the internal opening was closed with a suture or a "blob" of instant solid glue. To be eligible, conventional surgery had to consist of fistulotomy, or placement of a cutting or loose latex seton, or performing an advancement mucosal flap closure.

Primary outcome was fistula healing with a main outcome of recurrence rate. Secondary outcomes included: anal incontinence; clinical healing rate; complications; changes in baseline incontinence score and maximum resting and satisfaction scores; pain scores; and days off work. Studies were excluded: if they did not report outcomes for both patient groups; if fibrin glue was used in the flap repair of anal fistula; if they were of rectovaginal and trauma anal fistulae; if there was considerable overlap between authors, centres or patient cohorts.

The conventional surgery performed in the included studies was fistulotomy in one RCT and cutting setons in another RCT. In the non-randomised controlled trials the alternative treatments to fibrin glue were fistula plugs, seton drains and flap advancements. It was only possible to assess results for one secondary outcome (anal incontinence) since other results were too heterogeneous. Patients in two studies had trans-sphincteric anal fistulas and had both simple and complex anal fistulas in the third study. All patients underwent surgery with general or spinal anaesthesia and were followed up at six and 12 weeks.

Three reviewers performed the study selection.

Assessment of study quality
Criteria assessed included: randomisation method; allocation concealment; sample size calculation; and intention-to-treat analysis.

Three independent reviewers performed the quality assessment, with disagreements resolved by discussion or via a fourth reviewer.

Data extraction
The numbers of events were used to calculate odds ratios (OR) or relative risk (RR) with 95% confidence intervals (CI) and risk differences were calculated for absolute results. The authors did not specifically report how many reviewers performed the data extraction.
Methods of synthesis
Results were pooled giving odds ratios with 95% CIs (Mantel-Haenzel) using a random-effects model if there was significant heterogeneity and a fixed-effect model if there was not. Between study heterogeneity was determined using $\chi^2$ and $I^2$. Forest and funnel plots were provided. Subgroup meta-analyses were performed for the RCTs and for patients with complex anal fistulae in the RCTs.

Results of the review
Three studies were identified (338 patients, range 42 to 232), with two RCTs (106 patients) and one non-randomised controlled trial (232 patients). The longest follow-up was six months.

There was a lower recurrence rate for conventional surgery versus fibrin glue but the result was not significant (OR 0.44, 95% CI 0.12 to 1.68; $I^2=75%$; three studies). For the two RCTs alone, the effect was not significant with greater heterogeneity ($I^2=85%$), and the result was not significant with even higher heterogeneity ($I^2=93%$) when the meta-analysis was performed for the RCT patients with complex anal fistulae alone. Random-effects meta-analyses were used.

For post-operative anal incontinence there was no significant difference for conventional surgery versus fibrin glue (OR 1.00, 95% CI 0.43 to 2.34; $I^2=0%$; three studies) with no significant heterogeneity. The cases identified had minor incontinence.

Individual study results were reported for Wexner's score for incontinence and anal manometry.

Authors' conclusions
These meta-analyses did not show any statistically significant differences between fibrin glue treatment compared with conventional surgical treatment for all perianal fistulae in terms of recurrence and anal incontinence.

CRD commentary
The review addressed a well-defined question in terms of study design, participants, interventions and relevant outcomes. The search appeared to be extensive and there were no language restrictions so it was unlikely that any relevant studies would have been missed. Study quality was assessed using relevant criteria but little relevant data was provided, which would enable the reader to assess study quality. Efforts were made to reduce error and bias in the validity assessment and study selection but they were less clearly reported for data extraction.

Some relevant study details were reported but the authors did not differentiate clearly between inclusion criteria and study characteristics. No details were provided for patient's age or gender. The methods of synthesis seemed appropriate but the authors referred to results for patients receiving an anal fistula plug in one study but provided no relevant data. The authors’ conclusions should be treated with caution due to the low number of studies identified and high variability between studies.

Implications of the review for practice and research
Practice: The authors noted one study's result implied that the anal fistula plug might be superior to fibrin glue because it eradicates the problem of slippage of the material from the fistula tract and acts as a good bridging medium or matrix for human tissue regeneration (data not reported).

Research: The authors recommended further RCTs with higher numbers of patients and adequate follow-up (for at least six months) to provide definitive evidence of the advantage of new technologies compared to traditional interventions. Studies should include other secondary outcomes such as Wexner's scores for incontinence and the results of anal manometry (mean pre and postoperative resting and squeezing anal pressure).

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