



Title	Clinical Effectiveness and Cost Effectiveness of Bone Morphogenetic Proteins in the Non-Healing of Fractures and Spinal Fusion: A Systematic Review
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Aim

To determine the effectiveness and cost effectiveness of bone morphogenetic protein (BMP) in treating spinal fusions and fracture healing.

Conclusions and results

The review included 8 randomized controlled trials (RCTs) assessing BMP in treating fracture healing and 10 RCTs assessing BMP in treating spinal fusions. BMP is more effective than surgery alone for patients with acute open tibial fractures. BMP is more effective than autograft bone for patients with single-level degenerative disc disease. The evidence was insufficient to determine effectiveness of BMP in other diagnoses. BMP treatment also reduced pain, the number of secondary interventions, and eliminated donor site morbidity for patients with acute fractures. BMP reduced operative time and hospital length of stay, improved clinical outcomes, and eliminated donor site morbidities for patients with spinal fusions.

Only one economic evaluation was included, which suggested that the initial cost of BMP is likely to be offset by the costs of autograft bone grafting, complications, and increased fusion rates.

The modified economic modeling suggests that for fracture healing the cost per QALY ranges from GBP 13 791 to GBP 66 209 and for spinal fusions the cost per QALY is GBP 54 890.

Recommendations

BMP improves union and fusion rates in patients with acute fractures and single-level degenerative disc disease, respectively. Evidence for other diagnoses is weak, and further research is required.

Methods

Data sources included: electronic searches of MEDLINE, EMBASE, Science Citation Index, Cochrane Library and NeLH, default start dates to 2006; hand-searches of frequently cited journals, 1995 to 2006;

relevant industry; and authors. The searches were not restricted by language or publication status. Because it was anticipated that there would be a limited amount of relevant studies and the BMP treatment would vary considerably including fracture or fusion, degree of fracture or fusion, location, previous failed interventions, dosage, standard of care treatment method, BMP delivery system etc, we included all varying BMP interventions for treatment of fracture or fusion in humans.

Data were extracted by one reviewer and checked by another. Where appropriate, overall event rates were calculated by pooling results from the included studies. Economic evaluations were assessed. Economic models, provided by industry, were assessed and modified to determine the cost effectiveness of BMP compared with standard of care treatments.

Further research/reviews required

1. Large and properly designed RCTs of patients with nonunions are to compare BMP (as primary treatment) and standards of care.
2. RCTs of acute fractures other than tibia fractures to assess BMP effectiveness in other fracture locations.
3. Compare different BMP products (BMP-2 and BMP-7), the combination of BMP-2 and BMP-7, and different doses.
4. Trials that compare BMP and autogenous bone graft for spinal fusion with a control of intensive rehabilitation without surgery.
5. Large, well-designed RCTs on BMP for treating other spinal conditions for which efficacy is not well established, eg, spinal stenosis or spondylolisthesis.
6. Future trials should use more clinically relevant and patient targeted outcomes, and economic evaluation should be an integral part of clinical trials of BMP.