Published in final edited form as:

Spine (Phila Pa 1976). 2011 December 15; 36(26): 2354–2362. doi:10.1097/BRS.0b013e31820bc9e5.

Outcomes for Single-Level Lumbar Fusion: The Role of Bone Morphogenetic Protein

Kevin S. Cahill, MD, PhD, John H. Chi, MD, MPH, Michael W. Groff, MD, Kevin McGuire, MD, MS, Christopher C. Afendulis, PhD, and Elizabeth B. Claus, PhD, MD

Department of Neurosurgery, Brigham and Women's Hospital, Boston, MA (KSC, JC, EBC), Department of Epidemiology and Public Health (EBC), Yale University School of Medicine, New Haven, CT, Departments of Surgery, Division of Neurosurgery (MG) and Orthopedic Surgery (KM), Beth Israel Medical Center, Boston, MA, and the Department of Health Care Policy (CCA), Harvard Medical School, Boston, MA

Abstract

Study Design—Retrospective analysis of a population-based insurance claims dataset.

Objective—To determine the risk of repeat fusion and total costs associated with bone morphogenetic protein (BMP) use in single-level lumbar fusion for degenerative spinal disease.

Summary of Background Data—The use of BMP has been proposed to reduce overall costs of spinal fusion through prevention of repeat fusion procedures. Although radiographic fusion rates associated with BMP use have been examined in clinical trials, little data exists regarding outcomes associated with BMP use in the general population.

Methods—Using the MarketScan[®] claims dataset, 15,862 patients that underwent single-level lumbar fusion from 2003 to 2007 for degenerative disease were identified. Propensity scores were used to match 2,372 patients that underwent fusion with BMP to patients that underwent fusion without BMP. Logistic regression models, Kaplan-Meier estimates, and Cox proportional hazards models were used to examine risk of repeat fusion, length of stay, and 30-day readmission by BMP use. Cost comparisons were evaluated with linear regression models using logarithmic transformed data.

Results—At one year from surgery, BMP was associated with a 1.1% absolute decrease in the risk of repeat fusion (2.3% with BMP vs 3.4% without BMP, $p=.03$) and an odds ratio for repeat fusion of 0.66 (95% confidence interval 0.47-0.94) after multivariate adjustment. BMP was also associated with a decreased hazards for long-term repeat fusion (adjusted hazards ratio =0.74, 95% confidence interval 0.58-0.93). Cost analysis indicated that BMP was associated with initial increased costs for the surgical procedure (13.9% adjusted increase, 95% confidence interval 9.9%-17.9%) as well as total one year costs (10.1% adjusted increase, 95% confidence interval 6.2%-14.0%).

Conclusions—At one year, BMP use was associated with a decreased risk of repeat fusion but also increased healthcare costs.

Introduction

Significant resources are devoted to the evaluation and treatment of back pain. The average expenditure for medical care by US adults with spine problems such as back pain has been

shown to be 73% higher than adults without spine problems¹. Utilization of spinal fusion procedures as a treatment for back pain has seen a dramatic increase in the past 15 years, with a greater than 100% increase in the number of fusion procedures performed for degenerative spine disease seen from 1996 to 2001². The yearly total number of fusion procedures has stabilized since 2002, although the performance of complex surgical fusions has increased³.

Bone morphogenetic protein (BMP) is a novel fusion technology that has also experienced a rapid increase in utilization. BMPs have been used in spinal surgery to improve the process of bony fusion through the effects of BMPs on osteo-induction^{4,5}. Recombinant human BMP-2 (INFUSE[®], Medtronic) was first FDA approved in 2002 for anterior lumbar interbody fusion followed by the approval of BMP-7 (OP-1, Stryker) in 2003 for revision posterolateral fusion^{6,7}. It has previously been reported that BMPs have experienced a rapid nationwide increase in utilization since 2002 and is estimated that BMPs were used in approximately 25% of all spinal fusions nationally in 2006⁸.

BMP use in spinal fusion has been reported to increase the immediate costs of the initial fusion procedure⁸⁻¹². Less is known about the long-term costs associated with BMP use and it has been suggested that BMP use may actually lower overall costs associated with the fusion procedure¹²⁻¹⁴. The ability of BMP use to prevent repeat fusion procedures has been proposed as one mechanism for overall cost reduction^{9,12}. However, although the effect of BMP use on radiographic fusion rates has been documented in many clinical trials, the impact of BMP use on the need for repeat fusion remains less well defined¹⁵. Given the rapid increase in BMP utilization nationally, the goal of this analysis was to evaluate the association of BMP use with post-operative repeat fusion rates and healthcare costs in a population-based analysis. This study was accomplished through an analysis of patients that underwent single-level lumbar spinal fusion in a national commercial insurance claims dataset.

Materials and Methods

This was a retrospective cohort study using data from the MarketScan[®] Commercial Claims and Encounters database (Thomson Reuters Inc.), a longitudinal health insurance claims dataset drawn from inpatient and outpatient settings as well as yearly enrollment data. This database includes administrative claims from approximately 100 different insurance companies and large employers including fee-for-service, preferred provider organizations, and capitated health plans representing over 69 million unique patients since 1996¹⁶. The MarketScan[®] databases have been extensively used for analysis of outcomes and costs in many different surgical fields¹⁷⁻²⁰. For spinal fusions, the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) and Current Procedural and Terminology, 4th Edition (CPT-4) codes have been continually updated to reflect technical changes and advances in spine surgery. Data from 2003, the first complete year after BMP-2 was approved, until year 2008, the latest database available, was utilized for this analysis.

Patients over the age of 18 that underwent a single-level lumbar fusion were identified using CPT-4 codes from the surgeon inpatient procedure claims and the corresponding ICD-9-CM procedural codes from the inpatient hospitalization claims. Lumbar fusions were classified as interbody, posterolateral, or circumferential fusions. An interbody fusion included cases with lumbar interbody fusion codes (22558 or 22630) without posterolateral codes (22612). A circumferential fusion was defined as any lumbar fusion that included codes for both an interbody and posterolateral fusion. The fusions that utilized BMP were identified by the secondary procedure code for insertion of recombinant bone morphogenetic protein (ICD-9-CM code 84.52). Posterior instrumentation was identified by the code 22840 and anterior

instrumentation by the code 22845. Cases that included codes for pelvic instrumentation (22848), multi-level instrumentation (22842, 22843, 22844, 22846, or 22847), or revision fusion (22830, 22849, 22850, 22852, or 22855) were excluded. Autologous bone graft harvested from a separate incision was identified by codes 20937 and 20938.

The clinical diagnoses associated with the fusion procedure were identified using ICD-9-CM codes as listed in Table 2. Patients with clinical diagnoses related to spinal cancer, infectious processes, or trauma were excluded. Medical co-morbidity stratification was performed using the Charlson co-morbidity index²¹⁻²³. Individual Charlson scores were calculated by averaging all inpatient admissions during the immediate 3 months prior to and including the index procedure. Other clinical co-morbidities relevant to spinal fusion outcomes such as osteoporosis, obesity, diabetes and tobacco use were identified from inpatient and outpatient records. Age, gender, health insurance plan type, employment status, and geographic region of the enrollee were also included in the analysis. Health plan type was categorized into capitated, non-capitated plans, or unknown health plan type. Only patients with continuous post-operative enrollment for at least one year were included in the analysis.

Study Cohort

Propensity scores were used to match patients that underwent fusion with BMP to controls with a similar probability of undergoing a fusion with BMP²⁴. Propensity scores were calculated using the final probability of a multivariate logistic regression model that estimated the probability of undergoing a fusion with BMP. The final model used a backward selection strategy with a requirement of $p < .1$ to remain in the model. All variables were eligible for inclusion with the exception of autograft use as BMP is often used as a substitute for autograft. One to one matching of cases to controls with a maximum difference less than .005 in propensity scores was achieved using the SAS macro with the greedy algorithm²⁵.

Outcome measures

The primary outcome measures were occurrence of repeat lumbar fusion and the total cost of healthcare services in the first 12 months following the lumbar fusion procedure. A repeat fusion was defined as any subsequent lumbar fusion including revision fusion, supplemental fixation, and any other lumbar fusion performed in the first year following surgery. The need for repeat fusion was evaluated at the one year time point as a binary variable and the long-term repeat fusion estimates were calculated using the Kaplan-Meier estimation and Cox proportional hazards models. Due to variable durations of insurance enrollment, patients were censored according to the dates of insurance termination contained in the annual enrollment summary file. Secondary outcomes included the post-operative inpatient length of stay and the risk of 30-day repeat inpatient admission.

The post-operative cost analysis included the total cost of the initial procedure, all post-operative inpatient admissions, and all post-operative outpatient care. Costs were inflated to 2008 dollars using the medical component of the consumer price index²⁶. The costs used in this analysis were the actual settled amounts paid by the insurance providers and any deductibles or co-payments by the patient. Matched pairs with patients in capitated health plans or with unknown health plan type were not included in the cost analysis due to lack of fee-for-service payment equivalents for capitated encounter data.

Statistical Analysis

Descriptive statistics used means, proportions and standard deviations. Bivariate comparisons were examined using the Chi square test, T test, or Wilcoxon non-parametric test. Univariate and multivariate logistic regression models were constructed to evaluate the

association of the operative variables with the outcome of need for repeat lumbar fusion and 30 day re-admission. Odds ratios and 95% confidence intervals were calculated. Long-term repeat fusion estimates were compared with the Log-rank test after examination via Kaplan-Meier analyses and a Cox proportional hazards model. Hazard ratios (HR) were estimated with 95% confidence intervals. Variables found to be significant at $P < 0.10$ in unadjusted analyses were included as candidates in multivariate analyses. Linear regression using logarithmic transformed data was performed to examine the association between BMP use and the total one year healthcare costs. Statistical significance was defined as a type 1 error less than 5%. All analyses were two-sided and performed using SAS version 9.2 (SAS Institute, Cary, NC).

Results

For the years 2003 to 2007 there were 21,216 single-level, primary lumbar fusions performed for degenerative spine disease. Of these cases, 15,862 had at least one year of post-operative follow-up and were included in the study. There were 2,373 fusions performed using BMP and 13,489 fusions without BMP. Figure 1a displays the use of BMP according to year and type of fusion. Use of BMP increased each year for all categories of single-level lumbar fusions ($p < .01$). The highest rate of use was seen for interbody fusions performed in 2007 (24.5% of cases with BMP use). Over this same time period the utilization of autologous bone graft declined (Figure 1b). Fusions performed with BMP had lower rates of utilization of autologous bone graft (6% with BMP vs 26% without BMP, $p < .01$). The use of autologous graft from a separate incision has declined for all fusions irrespective of BMP use ($p < .01$) from 2002 to 2007. In 2003, 41.9% of fusions that did not use BMP used autologous bone graft compared to 18.9% of fusions in 2007.

Table 1 gives descriptive characteristics of the matched study cohort by BMP usage. Of the 2,373 patients undergoing fusions with BMP, 2,372 (99%) were successfully matched to controls using propensity scores. The mean age of patients was 48 for fusions with and without BMP ($p = .6$) and there were no differences in the gender distribution (49% vs 51% females, $p = .4$) or mean number of medical co-morbidities ($p = .2$). Likewise, the percentage of patients with a diagnosis of obesity, tobacco use, diabetes, or osteoporosis, the geographic region, the year the fusion was performed, and the percentage of patients in capitated health plans were equally distributed per group. The percentage of patients with clinical diagnoses of spinal stenosis, spondylolithesis, back pain, disc degeneration, disc herniation, and spondylosis were similar for patients that underwent fusions with and without BMP. Circumferential fusions were the most common type of fusion performed (48%) in both groups. The use of instrumentation was comparable ($p = .2$) as was the use of allograft ($p = .1$) in both groups. The significant difference in the use of autologous bone graft was preserved with use seen in 19% of cases without BMP compared to use in 6% of cases that used BMP ($p < .01$).

The use of BMP was associated with a lower risk of repeat fusion in the first post-operative year (3.4% without BMP vs 2.3% with BMP, $p = .03$, Table 2), corresponding to an unadjusted odds ratio of 0.65 (95% CI 0.47-0.90) for BMP use. After multivariate adjustment for the other significant predictors the odds ratio for repeat fusion was 0.66 (95% CI 0.47-0.94). On unadjusted analyses the significant predictors of increased repeat fusion risk were the type of lumbar fusion performed and the diagnosis of lumbar degenerative disc disease, while the use of spinal instrumentation and the diagnosis of spondylolithesis were associated with a decreased risk for repeat fusion. Circumferential fusions had the lowest risk of repeat fusion (2.4%) compared to interbody and posterolateral fusions (4.0% and 3.3% respectively, $p = .01$), OR=2.13 (95% CI 1.42-3.17) and OR=2.14 (95% CI 1.34-3.42), respectively. The use of instrumentation was associated with a decreased odds of repeat

lumbar fusion on unadjusted and adjusted analyses (Adjusted OR=.45, 95% CI 0.30-0.69). After multivariate adjustment the diagnosis of degenerative disc disease remained a significant predictor of repeat fusion risk but a diagnosis of spondylolithesis did not. None of the other clinical or demographic variables was a significant predictor of the need for repeat lumbar fusion.

The use of BMP was associated with a decrease in the overall long-term need for repeat lumbar fusion ($p=.01$ log rank test) (Figure 2), corresponding to an unadjusted hazards ratio of 0.75 (95% CI 0.59-0.95) associated with BMP use. After multivariate adjustment, the use of BMP remained associated with a decreased hazards for post-operative repeat fusion (HR=0.74, 95% CI 0.58-0.93). The estimated need for repeat fusion by 2 years was 5.2% (95% CI, 4.6%-6.4%) for cases with BMP and 6.6% (95% CI, 5.6%-7.8%) without BMP. The 3 year estimated need for repeat lumbar fusion was 6.8% (95% CI, 5.6%-8.3%) with BMP and 9.2% (95% CI, 7.7%-10.9%) without BMP.

The median length of stay for patients was 3 days regardless of BMP use ($p=.5$, Wilcoxon test). The 30 day risk of readmission was 3.9% with BMP compared to 5.0% without BMP ($p=.08$), corresponding to an unadjusted odds ratio of 0.77 (95% CI 0.58-1.02). After multivariate adjustment the odds ratio decreased to 0.72 (95% CI 0.54-0.95).

Costs were analyzed for patients not enrolled in capitated health plans (Table 3). In this subset of patients the one year repeat fusion risk was 2.5% for fusions with BMP and 3.4% for fusions without BMP ($p=.08$). The median payment for fusions performed with BMP was higher than that for fusions without BMP (\$42,627 with BMP vs. \$38,686 without BMP, $p<.01$). After multivariate adjustment for demographic and operative characteristics, the use of BMP was associated with a 13.9% (95% CI: 9.9%-18.2%) increase in the payments for the initial fusion surgery. The median total payments for post-operative care in the first year for patients that underwent fusion with BMP was not significantly different compared to fusions performed without BMP (\$5,512 with BMP vs \$5,732 without BMP, $p=.07$). Likewise, after multivariate adjustment BMP was not associated with a decrease in the one year post-operative costs. Finally, evaluation of the total of the payments for the fusion procedure and the first post-operative year (initial surgical costs + one year post-operative costs) indicated that the use of BMP was associated increased total payments of 10.1% (95% CI: 6.2%-14.0%).

Discussion

Recent interest has focused on the costs, complications, and utilization of spinal fusion procedures and associated fusion technologies, such as BMP, which offer the potential to improve surgical outcomes but may also be associated with increased costs. Consistent with a previous study reporting a rapid increased in BMP use over the last decade, the current analysis indicates that the use of BMP in single-level lumbar fusion has increased each year since 2007⁸.

The current analysis reveals an inverse association between BMP use and autologous bone graft use over time for single-level lumbar fusions. Interestingly, the use of autologous bone graft in fusions not using BMP decreased from approximately 50% of cases in 2003 to less than 20% of fusions in 2007. These findings may suggest a general trend away from autologous bone graft regardless of BMP usage. This also suggests that the evaluation of the outcomes comparing BMP to autologous bone graft may not be the only relevant comparison as approximately 80% of the fusions that did not use BMP did not use autologous bone graft.

It is important to consider that this study only evaluated BMP use in primary, single-level fusions in relatively young patients with few medical co-morbidities. In this cohort, there was a statistically significant difference in the one year risk of repeat lumbar fusion as well as the long-term overall need for repeat fusion associated with BMP use. The one year risk of repeat fusion in patients that underwent a fusion with BMP was 2.3% compared to 3.4% in fusions without BMP ($p=.03$), corresponding to an odds ratio for repeat fusion of 0.66 on adjusted analyses. Although this represents a reduction in the odds of repeat fusion of almost 40%, the absolute risk reduction is 1.1%. The effect of BMP on the need for repeat fusion has not been previously well defined. Clinical trials have demonstrated improvements in radiographic fusion success with BMP; however less is known about repeat fusion rates. One meta-analysis of the clinical trial data of anterior lumbar interbody fusion indicated that BMP was associated with decreased reoperation rates while a meta-analysis of posterolateral lumbar fusion with BMP did not find a significant difference in the reoperation risks 27-28. Our results based on a larger sample size suggest that there may be a statistically significant reduction in the repeat fusion risk albeit of a relatively small absolute magnitude.

Other operative factors were also predictors of repeat fusion risk including the type of fusion performed and the use of instrumentation. The lowest risk for repeat fusion was seen in circumferential fusions. There has been recent interest in the proliferation of complex fusion procedures such as circumferential fusions and the associated outcomes³. Our findings on repeat fusion risk agree with other clinical studies that have indicated decreased reoperation rates with circumferential fusion²⁹⁻³⁰. A randomized trial comparing circumferential fusion with cage placement to posterolateral fusion alone demonstrated fewer reoperations with circumferential fusion³⁰. The use of instrumentation in lumbar fusion has been shown in several randomized trials to increase radiographic fusion rates, although others have not shown a difference in fusion rates, and, in general, there is little data available on repeat fusion rates associated with instrumentation use³¹⁻³⁴.

The cost analysis in this study confirmed that the initial costs for fusions that incorporated BMP were approximately 14% higher than fusions without BMP. A prior analysis using a different national dataset also indicated that BMP use is associated with increased initial costs for the spinal fusion procedure⁸. In our current report, the total one year cost increase associated with BMP use was 10.1%. In general, there has been limited data on the effect of BMP use on the total costs related to a spinal fusion procedure. One prior study of posterolateral lumbar fusions suggested BMP use may decrease 3 month overall costs through a reduction in post-operative rehabilitation costs¹¹. Likewise, using modeling strategies it has been estimated that the prevention of the need for repeat fusion procedures and the elimination of donor site pain are direct effects of BMP that may lower overall costs⁹⁻¹².

There are several potential limitations to our current analysis. First, this study was a retrospective analysis of insurance claims data and it is possible that there were unbalanced unmeasured confounders that influenced the outcomes in this analysis despite the use of propensity score matching. For example, it may be possible that BMP was selectively used by surgeons in more complex fusion cases thus contributing to increased costs in the BMP group. The inclusion of only single-level fusions and the exclusion of revision procedures were attempts to uniformly limit the complexity of the cases in the analysis; however there were likely other clinical factors that could not be accounted for in this analysis. Likewise, the use of post-operative bracing or other measures such as external bone growth stimulators may have also influenced the outcomes. Second, this study was limited to costs and repeat fusions incurred in the first post-operative year. It is possible that cost savings may not be appreciated until later time points. We selected the one year time point as we believed repeat fusions during this time would represent problems related to the initial procedure and not

adjacent segment disease. Finally, as an analysis based on insurance claims it is possible that there could be bias introduced from inappropriately coded fusion procedures. To minimize this risk we used the CPT-4 codes from the surgeon claims to classify the fusion procedures. There is data indicating that the use of CPT-4 codes more accurately reflect the level of surgical complexity than ICD-9 codes from hospital discharge records³⁵.

In conclusion, this study allowed for the analysis of usage patterns, post-operative repeat fusion risks, and costs associated with BMP use in single-level lumbar fusion in patients with private health insurance. It is evident that the use of BMP has increased from 2003 to 2007 and autologous bone graft use has decreased irrespective of BMP utilization. We have shown that in this cohort, the use of BMP was associated with an approximate 1.1% absolute decrease in the risk of repeat fusion if the first post-operative year. The cost analysis indicated that the initial increases in costs associated with BMP use were not entirely offset by associated cost reductions in the first post-operative year following surgery. More work is needed to incorporate functional outcomes to further define the cost-effectiveness profile of BMP use in single-level lumbar fusion.

Acknowledgments

Funding: This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (NIH Award #UL1 RR 025758 and financial contributions from Harvard University and its affiliated academic health care centers). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, the National Center for Research Resources, or the National Institutes of Health.

The study was approved by the Partners Human Research Committee.

References

1. Martin BI, Deyo RA, Mirza SK, et al. Expenditures and health status among adults with back and neck problems. *JAMA*. 2008; 299:656–64. [PubMed: 18270354]
2. Deyo RA, Mirza SK. Trends and variations in the use of spine surgery. *Clin Orthop Relat Res*. 2006; 443:139–46. [PubMed: 16462438]
3. Deyo RA, Mirza SK, Martin BI, et al. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. *JAMA*. 2010; 303:1259–65. [PubMed: 20371784]
4. Hsu WK, Wang JC. The use of bone morphogenetic protein in spine fusion. *Spine J*. 2008; 8:419–25. [PubMed: 18375186]
5. Urist MR, Huo YK, Brownell AG, et al. Purification of bovine bone morphogenetic protein by hydroxyapatite chromatography. *Proc Natl Acad Sci U S A*. 1984; 81:371–5. [PubMed: 6320184]
6. OP-1 FDA Approval. Available from: <http://www.fda.gov/cdrh/pdf2/H020008a.pdf>
7. INFUSE FDA APPROVAL. Available from: <http://www.fda.gov/cdrh/mda/docs/p000058.pdf>
8. Cahill KS, Chi JH, Day A, et al. Prevalence, complications, and hospital charges associated with use of bone-morphogenetic proteins in spinal fusion procedures. *JAMA*. 2009; 302:58–66. [PubMed: 19567440]
9. Polly DW Jr, Ackerman SJ, Shaffrey CI, et al. A cost analysis of bone morphogenetic protein versus autogenous iliac crest bone graft in single-level anterior lumbar fusion. *Orthopedics*. 2003; 26:1027–37. [PubMed: 14577525]
10. Buttermann GR. Prospective nonrandomized comparison of an allograft with bone morphogenetic protein versus an iliac-crest autograft in anterior cervical discectomy and fusion. *Spine J*. 2008; 8:426–35. [PubMed: 17977799]
11. Glassman SD, Carreon LY, Campbell MJ, et al. The perioperative cost of Infuse bone graft in posterolateral lumbar spine fusion. *Spine J*. 2008; 8:443–8. [PubMed: 17526436]

12. Ackerman SJ, Mafilios MS, Polly DW Jr. Economic evaluation of bone morphogenetic protein versus autogenous iliac crest bone graft in single-level anterior lumbar fusion: an evidence-based modeling approach. *Spine*. 2002; 27:S94–9. [PubMed: 12205426]
13. Carreon LY, Glassman SD, Djurasovic M, et al. RhBMP-2 versus iliac crest bone graft for lumbar spine fusion in patients over 60 years of age: a cost-utility study. *Spine*. 2009; 34:238–43. [PubMed: 19179918]
14. Cardoso MJ, Sciubba DM. Is use of bone-morphogenetic proteins for spine fusion surgery cost-effective? *Arch Surg*. 2009; 144:996–7. [PubMed: 19917933]
15. Burkus JK, Sandhu HS, Gornet MF, et al. Use of rhBMP-2 in combination with structural cortical allografts: clinical and radiographic outcomes in anterior lumbar spinal surgery. *J Bone Joint Surg Am*. 2005; 87:1205–12. [PubMed: 15930528]
16. Health research Data for the Real World: The MarketScan Databases [Thomson Healthcare], 2008. [May 27, 2010]. 2010 Available from: http://thomsonreuters.com/products_services/healthcare/healthcare_products/pharmaceuticals/epidemiology_res/mktscan_res_db
17. Kutikova L, Bowman L, Chang S, et al. Utilization and cost of health care services associated with primary malignant brain tumors in the United States. *J Neurooncol*. 2007; 81:61–5. [PubMed: 16773215]
18. MacKenzie EJ, Jones AS, Bosse MJ, et al. Health-care costs associated with amputation or reconstruction of a limb-threatening injury. *J Bone Joint Surg Am*. 2007; 89:1685–92. [PubMed: 17671005]
19. Encinosa WE, Bernard DM, Steiner CA, et al. Use and costs of bariatric surgery and prescription weight-loss medications. *Health Aff (Millwood)*. 2005; 24:1039–46. [PubMed: 16012144]
20. Krupski TL, Foley KA, Baser O, et al. Health care cost associated with prostate cancer, androgen deprivation therapy and bone complications. *J Urol*. 2007; 178:1423–8. [PubMed: 17706711]
21. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987; 40:373–83. [PubMed: 3558716]
22. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992; 45:613–9. [PubMed: 1607900]
23. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005; 43:1130–9. [PubMed: 16224307]
24. Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. *Am J Epidemiol*. 1999; 150:327–33. [PubMed: 10453808]
25. Bergstralh, E.; Kosanke, J. %match, 2004. [June 1, 2010]. Available from: <http://mayoresearch.mayo.edu/mayo/research/biostat/sasmacros.cfm>
26. Bureau of Labor Statistics. United States Department of Labor. [May 1, 2010]. Available from: <http://www.bls.gov/cpi/>
27. Burkus JK, Heim SE, Gornet MF, et al. Is INFUSE bone graft superior to autograft bone? An integrated analysis of clinical trials using the LT-CAGE lumbar tapered fusion device. *J Spinal Disord Tech*. 2003; 16:113–22. [PubMed: 12679664]
28. Papakostidis C, Kontakis G, Bhandari M, et al. Efficacy of autologous iliac crest bone graft and bone morphogenetic proteins for posterolateral fusion of lumbar spine: a meta-analysis of the results. *Spine (Phila Pa 1976)*. 2008; 33:E680–92. [PubMed: 18758349]
29. Han X, Zhu Y, Cui C, et al. A meta-analysis of circumferential fusion versus instrumented posterolateral fusion in the lumbar spine. *Spine (Phila Pa 1976)*. 2009; 34:E618–25. [PubMed: 19644321]
30. Christensen FB, Hansen ES, Eiskjaer SP, et al. Circumferential lumbar spinal fusion with Brantigan cage versus posterolateral fusion with titanium Cotrel-Dubousset instrumentation: a prospective, randomized clinical study of 146 patients. *Spine (Phila Pa 1976)*. 2002; 27:2674–83. [PubMed: 12461393]
31. Zdeblick TA. A prospective, randomized study of lumbar fusion. Preliminary results. *Spine (Phila Pa 1976)*. 1993; 18:983–91. [PubMed: 8367786]

32. Fischgrund JS, Mackay M, Herkowitz HN, et al. 1997 Volvo Award winner in clinical studies. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. *Spine (Phila Pa 1976)*. 1997; 22:2807–12. [PubMed: 9431616]
33. Bjarke Christensen F, Stender Hansen E, Laursen M, et al. Long-term functional outcome of pedicle screw instrumentation as a support for posterolateral spinal fusion: randomized clinical study with a 5-year follow-up. *Spine (Phila Pa 1976)*. 2002; 27:1269–77. [PubMed: 12065973]
34. Bridwell KH, Sedgewick TA, O'Brien MF, et al. The role of fusion and instrumentation in the treatment of degenerative spondylolisthesis with spinal stenosis. *J Spinal Disord*. 1993; 6:461–72. [PubMed: 8130395]
35. Faciszewski T, Jensen R, Berg RL. Procedural coding of spinal surgeries (CPT-4 versus ICD-9-CM) and decisions regarding standards: a multicenter study. *Spine (Phila Pa 1976)*. 2003; 28:502–7. [PubMed: 12616165]

Figure 1.
a+b. a. Use of BMP according to type of lumbar fusion and year. B. Use of autograft according to year and BMP use

Figure 2. Kaplan-Meier estimate (presented as a failure curve) of the long-term need for repeat lumbar fusion according to BMP use.

Table 1

Demographics of propensity score matched study cohort.

	Propensity Score Matched		
	With BMP n=2,372	Without BMP n=2,372	P value
Mean Age (median)	48 (49)	48 (50)	0.6
Gender: Female	1394 (49%)	1425 (51%)	0.4
Region			1.0
Northeast	55 (2%)	52 (2%)	
North Central	562 (24%)	566 (24%)	
South	1404 (59%)	1409 (60%)	
West	349 (15%)	344 (15%)	
Unknown	2 (<1%)	1 (<1%)	
Insurance type			0.8
Non-capitated	2039 (86%)	2025 (85%)	
Capitated	300 (13%)	310 (13%)	
Unknown	33 (1%)	37 (2%)	
Charlson Comorbidity Score, mean, median	0.3 (0)	0.3 (0)	0.2
Osteoporosis	19 (1%)	17 (1%)	0.7
Tobacco abuse	633 (27%)	613 (26%)	0.5
Obesity	326 (14%)	329 (14%)	0.9
Diabetes	268 (11%)	248 (10%)	0.4
Year			0.3
2003	100 (4%)	80 (3%)	
2004	262 (11%)	290 (12%)	
2005	355 (15%)	343 (15%)	
2006	798 (34%)	771 (33%)	
2007	857 (36%)	888 (37%)	
Days enrollment post-op, mean (std)	795 (359)	799 (360)	0.7
Diagnosis *			
Lumbar disc herniation	1104 (47%)	1055 (44%)	0.2
Degenerative disc disease	1507 (64%)	1501 (63%)	0.9
Spondylosis	528 (22%)	544 (23%)	0.6
Spinal stenosis	946 (40%)	960 (40%)	0.7
Spondylolithesis	814 (34%)	844 (36%)	0.4
Back pain	670 (28%)	686 (29%)	0.6
Fusion type			0.7
Interbody	809 (34%)	830 (35%)	
Posterolateral	429 (18%)	412 (17%)	
Circumferential	1134 (48%)	1130 (48%)	
Instrumented fusion	2051 (86%)	2083 (88%)	0.2

	Propensity Score Matched		
	With BMP n=2,372	Without BMP n=2,372	P value
Autograft			
Different-incision	139 (6%)	453 (19%)	<.01
Allograft	655 (28%)	626 (26%)	0.3

* lumbar spondylosis codes: 721.3, 721.42, 721.90, 721.91, lumbar disc herniation: 722.1, 722.10, 722.2, degenerative disc disease: 722.5, 722.51, 722.52, 722.7, 722.70, 722.73, 722.90, 722.93, spinal stenosis: 724.0, 724.02, 724.09, non-specific back pain: 724.1, 724.3, 724.4, 724.5, 724.9, and spondylolysis or spondylolithesis: 738.4, 756.11, 756.11.

osteoporosis codes: 733.0, 733.02, 733.03, 733.09, obesity: 278.0, 278.01, diabetes: 250, and tobacco use disorder: 305.1, V15.82.

Table 2

Effect of BMP use and other clinical and demographic variables on risk of one year post-operative repeat lumbar fusion. Adjusted odds ratios are from the final multivariate model that included all significant predictors on univariate analysis with $p < .2$.

	Repeat operation	P value	OR (unadjusted)	OR (adjusted)
BMP Use				
With BMP	55 (2.3%)	.03	0.65 (0.47-0.90)	0.66 (0.47-0.94)
Without BMP	80 (3.4%)			
Age (per year increase)			NS	
Gender				
Male	56 (2.9%)	.8	NS	
Female (reference)	79 (2.8%)			
Charlson co-morbidity score (per unit increase)			NS	
Tobacco abuse				
Present	36 (2.9%)	.9	NS	
Absent (reference)	99 (2.8%)			
Obesity				
Present	22 (3.4%)	.4	NS	
Absent (reference)	113 (2.8%)			
Osteoporosis				
Present	2 (5.6%)	.3	NS	
Absent (reference)	133 (2.8%)			
Diabetes				
Present	16 (3.1%)	.7	NS	
Absent (reference)	119 (2.8%)			
Lumbar disc herniation				
Present	66 (3.0%)	.4	NS	
Absent (reference)	69 (2.7%)			
Lumbar degenerative disc disease				
Present	104 (3.5%)	<.01	1.97 (1.31-2.95)	1.98 (1.28-3.07)
Absent (reference)	31 (1.8%)			
Spondylosis				
Present	25 (2.3%)	.3	NS	
Absent (reference)	110 (3.0%)			
Spinal stenosis				
Present	51 (2.7%)	.6	NS	
Absent (reference)	84 (3.0%)			
Spondylolithesis				
Present	35 (2.1%)	.03	0.64 (0.43-0.95)	0.85 (0.56-1.29)
Absent (reference)	100 (3.2%)			

	Repeat operation	P value	OR (unadjusted)	OR (adjusted)
Back pain				
Present	38 (2.8%)	.9		
Absent (reference)	97 (2.9%)			
Year				
2003	5 (2.8%)	.8	NS	
2004	15 (2.7%)			
2005	25 (3.6%)			
2006	44 (2.8%)			
2007 (reference)	46 (2.6%)			
Region				
Northeast	4 (3.7%)	.8	NS	
North Central	33 (2.9%)			
South	83 (3.0%)			
West (reference)	15 (2.2%)			
Unknown	0%			
Insurance type				
Capitated	19 (3.1%)	.7	NS	
Non-capitated (reference)	115 (2.8%)			
Unknown	1 (1.4%)			
Fusion type				
Interbody	4.0%	.01	2.13 (1.42-3.17)	1.50 (0.97-2.32)
Posterolateral	3.3%		2.14 (1.34-3.42)	2.12 (1.29-3.47)
Circumferential (reference)	2.4%		Ref	Ref
Instrumented fusion				
Present	97 (2.4%)	<.01	0.36 (0.24-0.53)	0.45 (0.30-0.69)
Absent (reference)	38 (6.2%)			
Autograft (separate incision)				
Present	13 (2.2%)	.3	NS	
Absent (reference)	122 (2.9%)			
Allograft				
Present	42 (3.3%)	.3	NS	
Absent (reference)	93 (2.7%)			

Table 3

One-year post-operative healthcare costs according to BMP use (in 2008 dollars) in the matched cohorts of patients in non-capitated health plans.

	With BMP n=1752	Without BMP n=1752	P value
Initial lumbar fusion			
Median costs (IQ range)	42,627 (32,014-60,406)	38,686 (27,504-54,653)	<.01
% increase with BMP (unadjusted)	14.0% (9.9%-18.2%)		
% increase with BMP (adjusted)	13.9% (9.9%-17.9%)		
Post-op care: inpatient and outpatient claims			
Median costs (IQ range)	5,512 (2,194-13,220)	5,732 (2,387-14,417)	.07
% increase with BMP (unadjusted)	-7.4% (-15.7% to +1.8%)		
% increase with BMP (adjusted)	-8.1% (-16.3% to +1.0%)		
Total one year costs, median (IQ range)	53,624 (38,746-76,215)	49,315 (34,788-69,214)	<.01
% increase with BMP (unadjusted)	10.4% (6.4%-14.4%)		
% increase with BMP (adjusted)	10.1% (6.2%-14.0%)		

* adjusted for gender, age, Charlson score, clinical diagnosis, obesity, tobacco use, osteoporosis, year, region, type of fusion, allograft use, and autograft use