



# Prevalence of Osteoporosis Treatment and Its Effect on Post-Operative Complications, Revision Surgery and Costs After Multi-Level Spinal Fusion

Nikhil Jain, MD<sup>1</sup>, Lawal Labaran, MD<sup>1</sup>, Frank M. Phillips, MD<sup>2</sup>, Safdar N. Khan, MD<sup>3</sup>, Amit Jain, MD<sup>4</sup>, Khaled M. Kebaish, MD<sup>4</sup>, and Hamid Hassanzadeh, MD<sup>1</sup> 

## Abstract

**Study Design:** Retrospective cohort study.

**Objective:** To study the prevalence of pre-operative osteoporosis treatment, and its effect on risk of ORC, revision surgery and costs in osteoporotic patients undergoing  $\geq 3$ -level spinal fusion for degenerative pathology.

**Methods:** Patients and procedures of interest were included using International Classification of Diseases (ICD) and Current Procedural Terminology (CPT) coding. Our outcome measures were ORC at 1-year post-operatively and included instrumentation complications, pathological fracture, and revision surgery. Kaplan-Meier survival curves and Cox proportional hazards analysis was done to study the effect of osteoporosis treatment on risk of ORC.

**Results:** We included a total of 849 patients with documented osteoporosis undergoing  $\geq 3$ -level spinal fusion. White (85.6%), female (82.7%), and 60-79 years of age (79.9%) was the most common demographic. Of entire cohort, 121 (14.3%) were on osteoporosis treatment prior to spinal fusion. Of treated patients, 52/121 (43.0%) had continued prescriptions at 1 year post-operatively. Treated patients and not-treated patients had 1-year ORC incidence of 9.1% and 15.0%, respectively. The average 1-year reimbursement/patient for managing ORC was \$3,053 (treated) and \$21,147 (not-treated). On adjusted cox analysis, pre-operative osteoporosis treatment was associated with a lower risk of ORC (HR: 0.53, 95% CI: 0.28-0.99,  $p = 0.04$ ).

**Conclusions:** Pre-operative osteoporosis treatment is associated with lower risk of ORC and revision surgery at 1-year after  $\geq 3$ -level spinal fusion. There is a low incidence of osteoporosis treatment prior to spinal fusion, and subsequently a low rate of treatment continuation after surgery. These findings highlight the need for heightened awareness, patient education and management of osteoporosis before elective multi-level spinal fusion.

## Keywords

spinal fusion, osteoporosis, complications, bisphosphonate, teriparatide, bone density, fusion, lumbar, cervical, value

<sup>1</sup> Department of Orthopaedic Surgery, University of Virginia, Charlottesville, VA, USA

<sup>2</sup> Midwest Orthopaedics at Rush, Rush University Medical Center, Chicago, IL, USA

<sup>3</sup> Department of Orthopaedic Surgery, The Ohio State University Wexner Medical Center, Columbus, OH, USA

<sup>4</sup> Department of Orthopaedic Surgery, Johns Hopkins Hospital, Baltimore, MD, USA

## Corresponding Author:

Hamid Hassanzadeh, Department of Orthopaedic Surgery, University of Virginia, 400 Ray C. Hunt Dr, Charlottesville, VA 22903, USA.

Email: HH4XD@hscmail.mcc.virginia.edu



## Introduction

Osteoporosis is characterized by low bone mineral density (BMD), resulting in weak bone microarchitecture and higher risk of fracture. As defined by the World Health Organization (WHO), a T-score  $\leq -2.5$  standard deviation below healthy adult mean BMD on dual energy x-ray absorptiometry (DEXA) is considered osteoporosis.<sup>1,2</sup> It is estimated that 10.3% of adults more than 50 years old in the United States have osteoporosis based on this definition.<sup>3</sup>

Numerous studies have shown that there is a higher risk of compression fracture,<sup>4,5</sup> pedicle screw loosening or failure of instrumentation,<sup>4,6,7</sup> proximal junctional kyphosis,<sup>4,8,9</sup> and pseudoarthrosis<sup>7,10</sup> due to osteoporosis in patients undergoing spinal fusion. Consequently, there is growing emphasis on peri-operative medical management of osteoporosis in these patients.<sup>11</sup> While treatment of osteoporosis with bisphosphonates or teriparatide has shown to reduce vertebral fractures in nonsurgical patients, its clinical impact on osteoporosis related complications (ORC) in spinal fusion is limited.<sup>1,12-14</sup> A recent meta-analysis of 536 patients in 9 heterogeneous studies reported high fusion rates and decreased risk of ORC in medically treated osteoporosis patients undergoing spinal fusion.<sup>12</sup> However, these numbers also highlight the need for more evidence from bigger patient populations. Administrative database analyses have the advantage of studying a large cohort of patients with good accuracy and are increasingly being used to supplement evidence from clinical studies.<sup>15,16</sup>

The objective of this claims data analysis from a large national payor was to study the prevalence of pre-operative osteoporosis treatment, and its effect on risk of ORC, revision surgery and costs in osteoporotic patients undergoing  $\geq 3$ -level spinal fusion for degenerative pathology. This data will add evidence to existing clinical literature and guide pre-operative decision making in this at-risk population.

## Materials and Methods

### Data Source

The Humana national claims database (2007-Q3 2016) covering 22 million commercial and Medicare Advantage beneficiaries was used for analysis. Using this database, longitudinal research can be performed over the full data set using one or combination of identifiable fields on claims records. These include but are not limited to; International Classification of Diseases, ninth and 10th Revision (ICD-9 and 10) diagnosis and procedural coding, Diagnosis Related Group (DRG), Current Procedural Terminology (CPT), generic drug codes, prescription National Drug Code (NDC), discharge status, physician specialty, etc. Data is de-identified and HIPAA (Health Insurance Portability and Accountability Act, 1996) compliant and was accessed through the PearlDiver Technologies research platform (PearlDiver Inc., Colorado Springs, CO).<sup>17</sup>

### Data Extraction

The first occurrence of  $\geq 3$ -level spinal fusion for degenerative pathology was queried using respective ICD-9 codes (81.63 for 3-7 level, 81.64 for 8 or more level) between 2007 and Q3 2015. Procedures were queried up to Q3 2015 to allow analysis of 1-year outcome measures till Q3 2016. To reduce confounding effects of major trauma/surgery on outcomes, patients with a current/prior diagnosis of spinal fusion, spine fracture/neoplasm, infection, lower extremity arthroplasty/fracture fixation, rheumatoid arthritis, etc. were excluded. Subsequently, we queried patients with active insurance enrollment at least 1-year prior to 1-year after surgery. To create our final study cohort, we selected patients who had a diagnosis of osteoporosis (ICD 733.00, 733.01, 733.02, 733.09) and underwent dual-energy X-ray absorptiometry (DEXA) scan (CPT-77080, 77081, 77082) within 1-year before index surgery. Given the lack of ability to study DEXA scores with this database, follow-up DEXA scans were not studied in our patient cohort. The codes and definitions used for inclusion/exclusion of patients have been given in Supplemental Appendix, Table A1.

### Pharmacological Treatment of Osteoporosis

We divided our final study cohort in 2 groups: treated and not-treated, based on whether they received anti-osteoporosis treatment within the year before index surgery. However, to maintain uniformity we excluded patients who were not-treated before surgery but had anti-osteoporosis treatment after surgery. We used prescription data to identify most widely accepted pharmacological treatments for osteoporosis, which included bisphosphonates (Risedronate sodium, Ibandronate sodium and Alendronate sodium, Zoledronic Acid), and Teriparatide.<sup>1,11-14</sup> In our patient cohort, there were less than 10 patients who had Denosumab treatment. These patients were excluded from analysis to maintain consistency and include only most prevalent pharmacotherapies.

### Outcome Measures

Our primary outcome measure was occurrence of post-operative ORC. These included instrumentation complications (ICD 996.49, 996.40, 996.78) and pathological vertebral fracture (ICD 733.13). We also identified patients who underwent revision fusion (ICD 81.32, 81.33, 81.34, 81.35, 81.36, 81.37, 81.38, 78.69) for these complications within 1-year after index surgery. We ensured that these were new complications by excluding patients who already had these diagnoses or procedures prior to index surgery. The definitions for these complications have been given in Supplemental Appendix, Table A2.

### Data Analysis

Quantitative variables have been reported as frequency and percentage, and quantitative variables as mean with standard deviation. Kaplan-meier survival curves were generated to depict survival (freedom from ORC) in patients treated and

not-treated for osteoporosis before spinal fusion. To analyze significance of pre-operative osteoporosis treatment on risk of ORC, multivariate Cox proportional hazards analysis with adjustment for various demographic and clinical variables was done. Demographics such as age, gender, ethnicity, region, and clinical comorbidity burden using Charlson Comorbidity Index (CCI)<sup>18</sup> and comorbidity definitions (as defined in the Medicare Research Chronic Conditions Data Warehouse)<sup>19</sup> were used for adjustment. To adjust for the type and magnitude of spinal fusion, we identified cervical fusions (anterior, ICD 81.02, posterior, 81.03, and combined) and thoraco-lumbar fusions (81.04, 81.05, 81.06, 81.07, 81.08) in both study groups. We also distinguished patients who received osteotomies (CPT-22206, 22207, 22208, 22210, 22212, 22214, 22216). These variables are important risk factors for post-operative complications and have been included in our adjusted analysis.

For estimation of risk of ORC, adjusted hazard ratio with 95% confidence interval (CI) in treated osteoporosis patients has been reported, with not-treated patients serving as reference. The global significance of the cox model was judged by significant p-values on Likelihood ratio, Wald and score log-rank tests. For all analyses, a p-value of <0.05 has been considered statistically significant. Statistical analysis was carried out in R (The R Project for Statistical Computing) through the PearlDiver interface.

## Results

We included a total of 849 patients in our analysis. Majority of patients were white (85.6%), female (82.7%), and 60-79 years of age (79.9%). In our study cohort, 121 (14.3%) patients were on osteoporosis treatment before surgery. Univariate analysis of demographic and clinical variables among patients treated and not-treated for osteoporosis have been given in Table 1.

Out of 121 patients on osteoporosis treatment, 106 (87.6%) received bisphosphonates and 15 (12.4%) were on teriparatide. The average reimbursement for bisphosphonate and teriparatide treatment was \$596 and \$6,200 per patient in the year before spinal fusion. Of the treated patients, 52/121 (43.0%) had continued prescriptions at 1 year post-operatively.

Treated patients had a 1-year ORC cumulative incidence of 9.1% (95% CI: 3.8-14.1%), and not-treated patients had a 15.0% (95% CI: 12.3-17.5%) complication rate (Figure 1). Out of the 11/121 (9.1%) patients in the treated group who had ORC, 8 (72.7%) had a diagnosis of instrumentation related complications, 2 (18.2%) had new pathological vertebral fracture, and 1 (9.1%) had both. None of these patients underwent revision within a year after index surgery. As a sub-group analysis, the rate of ORC was 9.6% (5/52) and 8.7% (6/69) in treated patients with and without continued 1-year post-operative therapy, respectively.

In the 15.0% (109/728) not-treated patients who had ORC, 72 (66.1%) and 35 (32.1%) had instrumentation related complications and new vertebral pathological fracture, respectively. Two (1.8%) patients had diagnoses of both. In patients

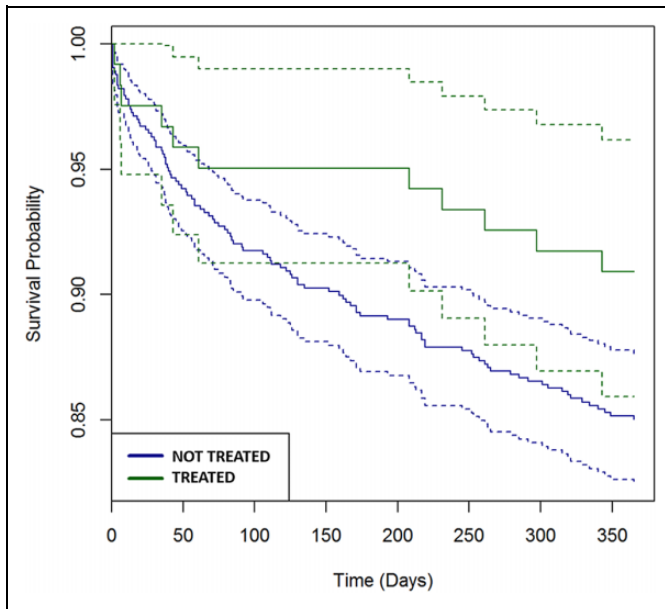
**Table 1.** Univariate Analysis of Demographic and Clinical Variables in Osteoporotic Patients Who Underwent  $\geq 3$ -Level Spinal Fusion. Humana Database (2007-Q3 2015).

	Treated n (%)	Not treated n (%)	p-value
No. of patients (N = 849)	121 (14.3)	728 (85.7)	
Age			
40-59	16 (13.2)	91 (12.5)	0.07
60-79	102 (84.3)	576 (79.1)	
80 and above	3 (2.5)	61 (8.4)	
Gender			
Female	111 (91.7)	591 (81.2)	0.004
Male	10 (8.3)	137 (18.8)	
Region			
Northeast	1 (0.8)	22 (3.0)	0.26
Midwest	26 (21.5)	133 (18.3)	
South	77 (63.6)	497 (68.3)	
West	17 (14.0)	76 (10.4)	
Ethnicity			
White	97 (80.2)	630 (86.5)	0.02
African-American	6 (5.0)	43 (5.9)	
Other	18 (14.9)	55 (7.6)	
Charlson Comorbidity Index Mean $\pm$ SD	2.52 $\pm$ 2.27	3.25 $\pm$ 3.02	0.01
Major Comorbidities			
Diabetes Mellitus	35 (28.9)	197 (27.1)	0.67
Depression	34 (28.1)	227 (31.2)	0.5
Ischemic Heart Disease	32 (26.4)	184 (25.3)	0.78
Anxiety	27 (22.3)	196 (26.9)	0.29
Chronic Lung Disease	18 (14.9)	196 (26.9)	0.004
Tobacco Use Disorder	13 (10.7)	104 (14.3)	0.3
Obesity	12 (9.9)	116 (15.9)	0.09
Chronic Kidney Disease	12 (9.9)	131 (18.0)	0.02
No. of Levels			
3-7 level	106 (87.6)	683 (93.8)	0.01
$\geq 8$ level	15 (12.4)	45 (6.2)	
Cervical	45 (37.2)	316 (43.4)	0.2
Thoracolumbar	76 (62.8)	412 (56.6)	
Osteotomy	18 (14.9)	83 (11.4)	0.27

with ORC, 20 (18.3%) patients underwent revision fusion for these complications at 1-year post-operatively.

The total and average per patient 1-year reimbursement for managing ORCs in treated patients (n = 11) was \$33,583 and \$3,053, respectively. The total cost of care for ORCs in not-treated patients (n = 109) was \$2,305,206, with an average reimbursement of \$21,147 per patient. Revision surgery in this group had an average per patient reimbursement of \$28,629 with average hospital length of stay of 9.0 days.

On adjusted cox analysis, pre-operative osteoporosis treatment was associated with a lower risk of ORC (HR: 0.53, 95% CI: 0.28-0.99, p=0.04). Cervical fusions (vs. Thoraco-lumbar) were also associated with a lower risk of ORC (HR: 0.61, 95% CI: 0.40-0.93, p=0.02), whereas spinal osteotomy (vs. no osteotomy) was significantly associated with ORC (HR: 2.52, 95% CI: 1.58-4.02, p < 0.001). While number of levels of surgery was significantly higher in the treated group on



**Figure 1.** Kaplan-Meier survival curves showing freedom from osteoporosis related complications (ORC) at 1-year among treated and not-treated osteoporotic patients undergoing multi-level spinal fusion. Humana database (2007-Q3 2015).

univariate analysis (Table 1), it was not significant for ORC on adjusted Cox analysis (HR 1.61, 95% CI: 0.62-0.94,  $P = 0.08$ ).

## Discussion

There are various recommendations to minimize risk of ORC in patients undergoing spinal fusion.<sup>1,2,11,13</sup> However, the published clinical evidence on the benefit of pharmacologic treatment of osteoporosis in spinal fusion is limited.<sup>1,12-14</sup> We have analyzed a cohort of 849 patients with osteoporosis who underwent  $\geq 3$ -level spinal fusion for degenerative pathology to study the effect of osteoporosis treatment on risk of ORC. A distinct advantage of a study such as ours is that we were able to include more patients in a single analysis than a meta-analysis of heterogeneous studies.<sup>12</sup> Additionally, we were able to describe prevalence of pre- and post-operative osteoporosis treatment in a national cohort of multi-level spinal fusion patients with data reflecting the costs to the healthcare system due to ORC. We found that pre-operative pharmacological treatment of osteoporosis is independently associated with significantly lower risk of ORC and revision surgery in patients undergoing  $\geq 3$ -level spinal fusion for degenerative pathology.

Our cohort was predominantly white, females between the age of 60 and 79 which corresponds to the most common demographic with primary senile osteoporosis.<sup>20</sup> Of the entire cohort, only 14.3% osteoporotic patients were on osteoporosis treatment before surgery. Prior studies have found low rates of osteoporosis screening and treatment in patients above 50 years of age undergoing spinal fusion.<sup>21-23</sup> There remains a gap in osteoporosis treatment with reports of low rate of initiation of anti-osteoporosis treatment after sustaining fragility<sup>20</sup> and new

vertebral compression fractures.<sup>24</sup> In patients undergoing multi-level thoracolumbar fusions, it will be beneficial to screen and treat patients for osteoporosis. This will require additional efforts on the part of the spine surgeon for coordination of care with primary care provider or endocrinologist. Due to the potential for ORC and additional costs in untreated osteoporotic patients, it seems prudent in order to improve the quality and value of care. There are some barriers to this, however. Given there is still controversy on monitoring of osteoporosis treatment,<sup>25,26</sup> it is difficult to estimate adequate duration of osteoporosis treatment before scheduling elective spinal fusion in at-risk patients. Till further clinical evidence is available, it seems reasonable to at least initiate treatment pre-operatively and maintain compliance after surgery.

In our analysis, 15% not-treated osteoporotic patients had ORC within a year after index spinal fusion. Two-third had instrumentation related complications and one-third sustained a new vertebral pathological fracture. Of patients with ORC in this group, 18.3% underwent revision surgery with an average reimbursement of \$28,629 from payors. In contrast, treated patients had a 9.1% post-operative ORC rate, and no patients underwent revision surgery within 1-year after index spinal fusion. Adjusted risk analysis revealed lower risk of ORC and revision surgery due to ORC in osteoporosis treated patients. Our results add to existing literature regarding the beneficial effects of osteoporosis treatment on spinal fusion outcomes. Bisphosphonates increase BMD by inhibiting osteoclasts, whereas intermittent teriparatide therapy works by activating osteoblasts.<sup>2,11,14</sup> Despite some concerns that bisphosphonates inhibit fusion due to its mechanism, literature suggests that both bisphosphonate and teriparatide treatment lead to good fusion. Although, fusion rates are somewhat higher with teriparatide as compared to bisphosphonates.<sup>12</sup> Limited evidence from prior literature also suggests decreased risk of cage subsidence and vertebral fractures after spinal fusion in bisphosphonate treated patients as compared to control.<sup>12</sup> A couple of studies have compared the risk of complications after spinal fusion between teriparatide and bisphosphonates, with results favoring teriparatide.<sup>27,28</sup> A comparative analysis among the 2 classes of medications was not considered feasible in our analysis given only 15 patients in the teriparatide treatment group.

The higher risk of ORC in not-treated patients also leads to significant financial burden as we found additional costs averaging over \$20,000 per patient. This is important given the increasing emphasis on healthcare cost reduction and value-based care. Given the elective nature of spinal fusion for degenerative pathology, it is certainly beneficial to manage osteoporosis pre-operatively in these patients. This is especially true in multi-level thoraco-lumbar fusions with planned osteotomies, as these were also significantly associated with ORC in our analysis.

Not only did our analysis suggest low rates of osteoporosis treatment before spinal fusion, but less than half of treated patients continued treatment in the year after surgery. We hypothesize suboptimal osteoporosis follow-up and/or care coordination postoperatively with provider managing



osteoporosis treatment. A recent review of literature found poor overall patient persistence and adherence with oral bisphosphonate therapy which drops significantly over time. Some determinants for this include medication type and frequency, age, race/ethnicity, gender, educational status and income.<sup>29</sup> Cost of medications may be another determinant of compliance. We found the average annual cost of bisphosphonate therapy before spinal fusion to be just under \$600, and teriparatide more than 10-times higher. High patient copayments for teriparatide may be a factor for poor compliance with treatment.<sup>30</sup> As mentioned above, close coordination with medical provider will be required to ensure maintenance of osteoporosis therapy after surgery.

Our study is limited by its retrospective analysis of insurance claims data. There may be inaccuracies due to coding methodology or missing data. Although we have included patients based on ICD codes for osteoporosis who underwent DEXA scans, the BMD measurement and T-scores are not available from claims data. We were unable to study clinical and surgical variables such as severity of disease, imaging studies, patient reported outcomes, surgical technique, cement augmentation, screw size/density, interbody cages, nature of instrumentation related complications, reason for revision surgery, etc. We have reported cost of medications and complications from payor reimbursement; however, we are unable to study cost-effectiveness of various treatments. We were also unable to compare risk of complications between bisphosphonates and teriparatide.

In conclusion, our analysis of osteoporosis patients undergoing multi-level spinal fusion for degenerative pathology found that pre-operative osteoporosis treatment is associated with lower risk of ORC and revision surgery at 1-year post-operatively. There is a low incidence of osteoporosis treatment prior to spinal fusion, and subsequently a low rate of treatment continuation after surgery. These findings highlight the need for heightened awareness, patient education and management of osteoporosis before elective spinal fusion. Given the higher burden of healthcare costs in these patients, there will be implications in value based and bundled payment models moving forward. Future directions include studying the adequate treatment duration before scheduling spinal fusion in osteoporotic patients, determining cost-effectiveness of bisphosphonates vs. teriparatide, identifying reasons for poor patient compliance with treatment, and improving care coordination with medical providers to ensure consistent treatment.

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### ORCID iD

Hamid Hassanzadeh, MD  <https://orcid.org/0000-0002-8224-9517>

### Supplemental Material

Supplemental material for this article is available online.

### References

- McCoy S, Tundo F, Chidambaram S, Baaj AA. Clinical considerations for spinal surgery in the osteoporotic patient: a comprehensive review. *Clin Neurol Neurosurg*. 2019;180:40-47.
- Chaudhary N, Lee JS, Wu JY, Tharin S. Evidence for use of teriparatide in spinal fusion surgery in osteoporotic patients. *World Neurosurg*. 2017;100:551-556.
- Wright NC, Looker AC, Saag KG, et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. *J Bone Miner Res*. 2014;29(11):2520-2526.
- DeWald CJ, Stanley T. Instrumentation-related complications of multilevel fusions for adult spinal deformity patients over age 65: surgical considerations and treatment options in patients with poor bone quality. *Spine (Phila Pa 1976)*. 2006;31(19 suppl): S144-S151.
- Meredith DS, Schreiber JJ, Taher F, Cammisa FP Jr, Girardi FP. Lower preoperative Hounsfield unit measurements are associated with adjacent segment fracture after spinal fusion. *Spine (Phila Pa 1976)*. 2013;38(5):415-418.
- O'Leary PT, Bridwell KH, Lenke LG, et al. Risk factors and outcomes for catastrophic failures at the top of long pedicle screw constructs: a matched cohort analysis performed at a single center. *Spine (Phila Pa 1976)*. 2009;34(20):2134-2139.
- Bjerke BT, Zarrabian M, Aleem IS, et al. Incidence of osteoporosis-related complications following posterior lumbar fusion. *Global Spine J*. 2018;8(6):563-569.
- Kim HJ, Iyer S. Proximal junctional kyphosis. *J Am Acad Orthop Surg*. 2016;24:318-326.
- Kim JS, Phan K, Cheung ZB, et al. Surgical, radiographic, and patient-related risk factors for proximal junctional kyphosis: a meta-analysis. *Global Spine J*. 2019;9(1):32-40.
- Schreiber JJ, Hughes AP, Taher F, Girardi FP. An association can be found between Hounsfield units and success of lumbar spine fusion. *HSS J*. 2014;10(1):25-29.
- Hassanzadeh H, Puvanesarajah V, Dalkin AC. Medical management of osteoporosis for elective spine surgery. *Clin Spine Surg*. 2016;29(4):134-140.
- Buerba RA, Sharma A, Ziino C, Arzeno A, Ajiboye RM. bisphosphonate and teriparatide use in thoracolumbar spinal fusion: a systematic review and meta-analysis of comparative studies. *Spine (Phila Pa 1976)*. 2018;43(17):E1014-E1023.
- Fischer CR, Hanson G, Eller M, Lehman RA. A systematic review of treatment strategies for degenerative lumbar spine fusion surgery in patients with osteoporosis. *Geriatr Orthop Surg Rehabil*. 2016;7(4):188-196.
- Stone MA, Jakoi AM, Iorio JA, et al. Bisphosphonate's and intermittent parathyroid hormone's effect on human spinal fusion: a systematic review of the literature. *Asian Spine J*. 2017;11(3): 484-493.
- Ratliff JK, Balise R, Veeravagu A, et al. Predicting occurrence of spine surgery complications using "big data" modeling of an

- administrative claims database. *J Bone Joint Surg Am.* 2016; 98(10):824-834.
16. Van Poucke S, Thomeer M, Heath J, Vukicevic M. Are randomized controlled trials the (G)old Standard? From clinical intelligence to prescriptive analytics. *J Med Internet Res.* 2016;18(7):e185.
  17. PearlDiver Healthcare Research. PearlDiver Technologies. 2019. Accessed April 25, 2019. <http://www.pearldiverinc.com/research/info.html>
  18. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47(11): 1245-1251.
  19. Condition Categories. Chronic Conditions Data Warehouse. 2019. Accessed April 25, 2019. <https://www.ccwdata.org/web/guest/condition-categories>
  20. Liu J, Curtis EM, Cooper C, Harvey NC. State of the art in osteoporosis risk assessment and treatment. *J Endocrinol Invest.* 2019;42(10):1149-1164. doi:10.1007/s40618-019-01041-6. [Epub ahead of print] Review.
  21. Wagner SC, Formby PM, Helgeson MD, Kang DG. Diagnosing the undiagnosed: osteoporosis in patients undergoing lumbar fusion. *Spine (Phila Pa 1976).* 2016;41(21):E1279-E1283.
  22. Chin DK, Park JY, Yoon YS, et al. Prevalence of osteoporosis in patients requiring spine surgery: incidence and significance of osteoporosis in spine disease. *Osteoporos Int.* 2007;18(9): 1219-1224.
  23. Dipaola CP, Bible JE, Biswas D, Dipaola M, Grauer JN, Rehtine GR. Survey of spine surgeons on attitudes regarding osteoporosis and osteomalacia screening and treatment for fractures, fusion surgery, and pseudoarthrosis. *Spine J.* 2009;9(7):537-544.
  24. Malik AT, Retchin SM, Phillips FM, et al. Declining trend in osteoporosis management and screening following vertebral compression fractures—a national analysis of commercial insurance and Medicare advantage beneficiaries. *Spine J.* 2019. pii: S1529-9430(19)31066-6. doi:10.1016/j.spinee.2019.10.020
  25. Burch J, Rice S, Yang H, et al. Systematic review of the use of bone turnover markers for monitoring the response to osteoporosis treatment: the secondary prevention of fractures, and primary prevention of fractures in high-risk groups. *Health Technol Assess.* 2014;18(11):1-180.
  26. Leslie WD, Morin SN, Martineau P, Bryanton M, Lix M. Factors associated with bone density monitoring while on antiosteoporosis treatment in routine clinical practice: a registry-based cohort study. *J Clin Densitom.* 2019. pii: S1094-6950(19)30038-1
  27. Seki S, Hirano N, Kawaguchi Y, et al. Teriparatide versus low-dose bisphosphonates before and after surgery for adult spinal deformity in female Japanese patients with osteoporosis. *Eur Spine J.* 2017;26(8):2121-2127.
  28. Ohtori S, Inoue G, Orita S, et al. Comparison of teriparatide and bisphosphonate treatment to reduce pedicle screw loosening after lumbar spinal fusion surgery in postmenopausal women with osteoporosis from a bone quality perspective. *Spine (Phila Pa 1976).* 2013;38(8):E487-E492.
  29. Fatoye F, Smith P, Gebrye T, Yeowell G. Real-world persistence and adherence with oral bisphosphonates for osteoporosis: a systematic review. *BMJ Open.* 2019;9(4):e027049.
  30. Foster SA, Foley KA, Meadows ES, et al. Adherence and persistence with teriparatide among patients with commercial, Medicare, and Medicaid insurance. *Osteoporos Int.* 2011;22(2):551-557.