Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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In Reply: Drs Grey and Cundy indicate their dissatisfaction with the intervention thresholds for osteoporosis treatment recommended by the National Osteoporosis Foundation (ie, 3% absolute risk of hip fracture or 20% risk of major osteoporotic fracture during a 10-year period).[1] We understand that intervention thresholds will vary by practitioner, patient, and country, and we agree that a robust discussion about appropriate thresholds is important. We do believe, however, that cost-effectiveness analyses can be helpful in setting public health policy.

Furthermore, using the same assumptions of Grey and Cundy, the number needed to treat to prevent a major osteoporotic fracture for patients at the lowest-risk intervention threshold is only 25 during a 5-year period, and will decrease further as absolute fracture risk increases. Nevertheless, we are happy that Grey and Cundy accept our premise that absolute fracture risk, which takes into account individualized risk factors, be used to determine treatment instead of relying solely on bone density T-score.

The survey cited by Grey and Cundy reported that patients are willing to accept an extraordinarily high absolute risk of hip fracture (50% risk during a 10-year period) before they would consider osteoporosis treatment.[2] We believe that the large discrepancy between public and physician assessment of the risk-to-benefit ratio for osteoporosis treatment is due to the medical community's failure to educate the public properly about the serious consequences of osteoporotic fractures as well as misperceptions of the potential risks.

We advocate arming patients with information about the rates of permanent disability and excess mortality associated with osteoporotic fractures,[3] as well as providing a fair assessment of the ability of osteoporosis treatments to effectively prevent fractures at relatively low risk.[4] Perhaps then the discrepancies in perception about osteoporosis treatment can be resolved and adherence to treatment can be improved.

Dr Gourlay and colleagues provide follow-up information from their longitudinal study of bone density from the Study of Osteoporotic Fractures cohort.[5] Their additional calculations more accurately define the decline in T-scores over time for our example patient. Because we did not have access to the primary data, we had assumed a constant rate of bone loss over the period (as stated in our Viewpoint). Nevertheless, the fundamental point remains that incorporating clinical risk factors into an intervention decision would result in more frequent bone density screening intervals to identify women who are at risk of fracture prior to reaching an osteoporotic T-score of −2.5.

We agree with Gourlay and colleagues that ideally a randomized controlled trial should be performed to validate the efficacy of osteoporosis therapies in patients identified using absolute fracture risk thresholds. Unfortunately, such a trial is unlikely to occur due to the considerable size and expense that would be required. Given that T-score cutoffs for the diagnosis of osteoporosis are arbitrary and insensitive,[6] we instead advocate a more individualized and we believe rational approach for risk stratification, incorporating age and other clinical risk factors in addition to bone density.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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RESEARCH LETTER

Off-Label Use of Bone Morphogenetic Proteins in Pediatric Spinal Arthrodesis

To the Editor: Arthrodesis of the spine is frequently performed in children. Although nonunion occurs frequently in adults, children rarely experience nonunion.[1] We are aware of no evidence to support the need for augmentation beyond instrumentation and autograft bone grafting in pediatric spinal arthrodesis.

Bone morphogenetic proteins (BMPs) are approved for limited use in adults when healing may be suboptimal.[2,3] In addition to concerns about possible carcinogenesis, complications include wound dehiscence, spinal stenosis, and respiratory complications.[4] The US Food and Drug Administration has not approved the use of BMPs in children.

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Table. Adjusted Factors Associated With Use of Bone Morphogenetic Proteins (BMPs)

	With Use of BMPs		Without Use of BMPs		
	No.	Weighted % (95% CI)[a]	No.	Weighted % (95% CI)[a]	AOR (95% CI)[b]
Age, mean (SD), y	771	14.75 (14.38-15.11)	7518	13.71 (13.59-13.82)	1.09 (1.05-1.13)[c]
Sex					
Male	325	42.1 (38.5-45.6)	2826	37.6 (36.3-38.9)	1 [Reference]
Female	446	57.9 (54.4-61.5)	4679	62.4 (61.1-63.7)	1.04 (0.89-1.23)
Race/ethnicity[d]					
White	456	58.6 (51.4-65.8)	4126	54.7 (49.7-59.7)	1 [Reference]
Black, Hispanic, Pacific Islander, or Asian	140	18.4 (13.6-23.2)	1817	24.1 (21.2-27.0)	0.98 (0.71-1.34)
Other or unknown	175	22.9 (15.3-30.6)	1575	21.2 (15.7-26.7)	0.96 (0.62-1.50)
Income quartile, $					
<39 999 (or not reported)	189	25.0 (20.6-29.3)	1815	24.4 (21.9-26.8)	0.96 (0.73-1.25)
40 000-49 999	169	22.1 (19.1-25.0)	1802	24.0 (22.4-25.7)	0.80 (0.62-1.03)
50 000-65 999	180	23.4 (20.0-26.8)	1857	24.7 (23.1-26.4)	0.84 (0.65-1.08)
≥66 000	233	29.5 (24.3-34.8)	2043	26.9 (24.0-29.8)	1 [Reference]
Diagnoses					
Spondylolisthesis					
Yes	71	9.2 (7.0-11.4)	224	3.0 (2.5-3.5)	1.64 (1.16-2.33)
No	700	90.8 (88.6-93.0)	7294	97.0 (96.5-97.5)	1 [Reference]
Neurofibromatosis					
Yes	13	1.7 (0.8-2.7)	80	1.1 (0.9-1.3)	2.25 (1.20-4.21)
No	758	98.3 (97.4-99.2)	7438	98.9 (98.7-99.1)	1 [Reference]
Congenital spine anomaly					
Yes	40	5.2 (3.6-6.8)	355	4.8 (4.2-5.4)	1.28 (0.85-1.91)
No	731	94.8 (93.2-96.4)	7163	95.2 (94.6-95.8)	1 [Reference]
Idiopathic scoliosis					
Yes	290	37.9 (32.2-43.7)	4297	57.3 (55.1-59.5)	0.61 (0.44-0.84)
No	481	62.1 (56.3-67.8)	3221	42.7 (40.5-44.9)	1 [Reference]
Associated curves, muscular dystrophy, cord injury, osteodystrophies, achondroplasias					
Yes	142	18.7 (15.5-21.9)	1483	19.9 (18.3-21.6)	0.93 (0.71-1.22)
No	629	81.3 (78.1-84.5)	6035	80.1 (78.4-81.7)	1 [Reference]
Neuromuscular					
Yes	105	13.8 (11.1-16.5)	1186	15.9 (14.6-17.2)	0.92 (0.72-1.18)
No	666	86.2 (83.5-88.9)	6332	84.1 (82.8-85.4)	1 [Reference]
Bone graft					
Yes	452	58.8 (51.9-65.7)	4192	56.1 (52.1-60.0)	1.17 (0.89-1.55)
No	319	41.2 (34.3-48.1)	3326	43.9 (40.0-47.9)	1 [Reference]
Trauma					
Yes	141	17.8 (13.1-22.6)	724	9.4 (8.1-10.6)	0.66 (0.32-1.36)
No	630	82.2 (77.4-86.9)	6794	90.6 (89.4-91.9)	1 [Reference]

(continued)

We determined the prevalence of BMP use, associated complications, costs, and potential predictors of use in pediatric spinal arthrodesis in the United States.

Methods. The Kids´ Inpatient Database, Healthcare Cost and Utilization Project, a sample of 4121 US hospitals containing 10% of uncomplicated births and 80% of complicated pediatric admissions representing approximately 30% of total pediatric admissions, is weighted to allow calculation of national estimates.[5] We included children aged 18 years or younger who had undergone primary or revision spine arthrodesis in 2009 using *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnoses and procedure codes as previously described by Cahill et al.[6]

SAS version 9.2 (SAS Institute Inc) was used, accounting for the complex survey design to calculate appropriate standard errors and *P* values and to provide nationally representative weighted estimates of prevalence of BMP use, in-hospital complications, length of stay, and in-hospital costs. Costs were estimated from supplied charges data using hospital-specific cost-to-charge ratios from the Healthcare Cost and Utilization Project.

Multivariable logistic regression was used to determine the independent association of diagnoses, comorbidities, demographic factors, and insurance status with BMP use (TABLE). Complications assessed included medical, neurological, wound healing, infectious, and those related to breath-

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Table. Adjusted Factors Associated With Use of Bone Morphogenetic Proteins (BMPs) (continued)

	With Use of BMPs		Without Use of BMPs		
	No.	Weighted % (95% CI)[a]	No.	Weighted % (95% CI)[a]	AOR (95% CI)[b]
Primary payer					
Private	565	72.9 (68.6-77.3)	4814	63.8 (60.8-66.8)	1 [Reference]
Medicare or Medicaid	152	20.2 (16.6-23.8)	2085	27.9 (25.4-30.4)	0.70 (0.56-0.89)
Other	54	6.9 (4.5-9.3)	619	8.3 (5.9-10.8)	0.73 (0.48-1.10)
Charlson Comorbidity Index, mean (SD)	771	0.18 (0.15-0.22)	7518	0.17 (0.15-0.18)	1.05 (0.94-1.17)[c]
Elective admission					
Yes	549	71.5 (60.6-82.4)	6323	84.5 (81.0-87.9)	0.50 (0.20-1.21)
No	217	28.5 (17.6-39.4)	1173	15.5 (12.1-19.0)	1 [Reference]
Revision fusion					
Yes	62	7.9 (5.5-10.2)	260	3.4 (2.8-4.1)	2.14 (1.48-3.11)
No	709	92.1 (89.8-84.5)	7258	96.6 (95.9-97.2)	1 [Reference]
Segment of fusion					
Cervical	90	11.9 (8.9-14.9)	661	8.8 (7.7-9.8)	1 [Reference]
Thoracolumbar	443	58.2 (52.5-63.8)	5587	75.0 (73.1-76.8)	1.20 (0.80-1.80)
Lumbosacral	230	29.9 (25.5-34.4)	1223	16.3 (14.8-17.7)	1.47 (1.01-2.12)
Vertebral levels					
2-3	303	38.7 (32.7-44.7)	1564	20.5 (19.0-22.1)	1.34 (1.05-1.72)
≥4	468	61.3 (55.3-67.3)	5954	79.5 (77.9-81.0)	1 [Reference]
Hospital type					
Teaching	584	75.8 (67.6-84.0)	6194	82.3 (77.0-87.6)	0.97 (0.60-1.56)
Nonteaching or unknown	187	24.2 (16.0-32.4)	1324	17.7 (12.4-23.0)	1 [Reference]
Hospital location					
Northeast	95	11.2 (5.5-16.8)	1461	18.2 (11.7-24.6)	1 [Reference]
Midwest	246	32.5 (20.7-44.3)	1786	23.9 (17.1-30.7)	2.33 (1.11-4.87)
South	248	33.7 (23.4-44.0)	2518	34.8 (27.2-42.3)	1.72 (0.87-3.43)
West	182	22.6 (15.2-30.1)	1753	23.2 (16.0-30.3)	1.50 (0.76-2.96)
Type of hospital					
All ages	294	36.9 (27.9-45.9)	1597	20.0 (15.9-24.2)	1.76 (1.23-2.51)
Pediatric center	477	63.1 (64.1-72.1)	5921	80.0 (75.8-84.1)	1 [Reference]

Abbreviation: AOR, adjusted odds ratio.
[a] Unless otherwise indicated.
[b] Adjusted for all other factors in this table and weighted to be representative of the US population of hospital discharges in 2009.
[c] The AOR represents a relative increase in the odds of BMP use for each unit increase in the independent variable.
[d] Data supplied to the Healthcare Cost and Utilization Project by the hospital or state administration and may have been self-reported or reported by the hospital. Race/ethnicity was included as a socioeconomic measure.

ing and dysphagia.[6] The institutional review board at the Hospital for Sick Children approved the study and waived participant consent.

Results. In 2009, 8289 pediatric spinal arthrodeses were in the Kids´ Inpatient Database. Nationally, BMP was estimated to be used in 9.2% (95% CI, 7.3%-11.0%; unweighted n=771) of cases. The estimated prevalence of in-hospital complications in those who received BMP was 3.0% (95% CI, 2.0%-4.1%; unweighted n=24) and in those who did not receive BMP was 3.6% (95% CI, 3.0%-4.2%; unweighted n=271) (Rao-Scott χ^2=0.74; P=.39 for comparison across BMP groups).

The median total in-hospital adjusted costs for patients receiving BMP was $47 136 (interquartile range [IQR], $30 692-$73 848) and in those not receiving BMP was $43 126 (IQR, $31 246-$59 849) ($P<.001$). Adjusted analysis of log-transformed costs showed that surgeries using BMP were 19% (95% CI, 10%-28%) more costly than those not using BMP. Median length of stay for patients receiving BMP was 4.6 days (IQR, 3.2-6.9 days) and for those not receiving BMP was 4.6 days (IQR, 3.5-6.1 days) (P=.70).

Use of BMP was associated with older age, lumbosacral arthrodeses, fewer vertebrae fused, spondylolisthesis, neurofibromatosis, revision fusions, and surgeries performed in the Midwest. Use of BMP was less frequent in idiopathic scoliosis, specialized pediatric hospitals, and in patients with Medicare or Medicaid health coverage (Table).

Comment. Given the lack of indication for augmentation of pediatric spinal arthrodesis, the use of BMP in 9.2% of patients is surprising. Although no difference in the rate of in-hospital complications was demonstrated, most complications previously reported with BMP are late complications and would not be expected to occur during hospitalization. While it is possible that some unmeasured factors account for the increase in costs associated with BMP use, our adjusted analysis showed that surgeries using BMP were 19% more costly than those that did not involve BMP use. Although BMP was used for diagnoses considered higher

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risk for nonunion, such as neurofibromatosis, BMP was still used frequently in idiopathic scoliosis and for other low-risk diagnoses.

This study was limited by lack of longitudinal data in the Kids´ Inpatient Database, as well as lack of details on dosage and type of BMP. Use of BMP should not be routine in pediatric spine arthrodesis until it has been shown to be safe and beneficial.

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Author Contributions: Dr Dodwell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Dodwell, Snyder, Wright.
Acquisition of data: Dodwell.
Analysis and interpretation of data: Dodwell, Snyder, Wright.
Drafting of the manuscript: Dodwell, Wright.
Critical revision of the manuscript for important intellectual content: Dodwell, Snyder, Wright.
Statistical analysis: Dodwell.
Study supervision: Snyder, Wright.
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CORRECTIONS

Incorrect Metric Conversion: In a Viewpoint entitled, "Bone Density Screening Intervals for Osteoporosis: One Size Does Not Fit All," published in the June 27, 2012, issue of *JAMA* (2012;307[24]:2591-2592), the metric conversion describing the height of an average-sized woman should have read as 165 cm. This article has been corrected online.

Incorrect Data and Conflict of Interest Disclosures: In the Research Letter entitled "Number and Order of Whole Cell Pertussis Vaccines in Infancy and Disease Protection" published in the August 1, 2012, issue of *JAMA* (2012;308[5]: 454-456), incorrect data appear in 2 places. The first sentence of the Results section should be "Of 58 233 children born in 1998 identified in the QVR, 40 694 (69.9%) received at least 3 doses of any pertussis-containing vaccine during the first year from a Queensland vaccine service provider and were included in the analysis." In the Table, the footnote "a" should be "A primary vaccination course is defined as 3 or more doses of a pertussis-containing vaccine for infants younger than 12 months of age. Analysis excludes records for infants with no vaccination history recorded before 12 months of age (n=6806), those with vaccination history provided by outside source (not a Queensland vaccine service provider; n=4129), those with irregularity of the vaccine dose by number or description (n=192), and those with less than 3 vaccination doses recorded (n=6412)." The second sentence of the Conflict of Interest Disclosures section should be "Drs Grimwood and Lambert reported receiving honoraria for serving on the GlaxoSmithKline advisory boards for pneumonia and pneumonia conjugate vaccine. Dr Lambert also reported serving as an investigator on clinical studies sponsored by GlaxoSmithKline and sanofi-pasteur (both manufacturers of pertussis-containing vaccines), and serving on GlaxoSmithKline and sanofi-pasteur advisory boards for pneumococcal and influenza vaccines, respectively." This article has been corrected online.

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