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ORIGINAL RESEARCH

The burden of osteoporosis in four Latin American countries: Brazil, Mexico, Colombia, and Argentina

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ABSTRACT

Objective: Osteoporosis is under-diagnosed and under-treated worldwide. Information on the burden of osteoporosis in Latin American countries is limited. This study aimed to estimate the economic burden of osteoporosis in adults aged 50–89 years in Brazil, Mexico, Colombia, and Argentina.

Methods: Analyses were conducted using a burden of illness model. Where possible, country-specific model inputs were informed by a systematic review and expert opinion. Osteoporosis-related fracture costs were calculated for hospitalizations, testing, surgeries, prescription drugs, and patient productivity losses. Costs were expressed in 2018 USD for the annual burden, annual burden per 1,000 at risk, and projected 5-year burden. No discounting was applied.

Results: Over 840,000 osteoporosis-related fractures were predicted to occur in 2018, amounting to a total annual cost of ∼1.17 billion USD. The total projected 5-year cost was ∼6.25 billion USD. Annual costs were highest in Mexico (411 million USD), followed by Argentina (360 million USD), Brazil (310 million USD), and Colombia (94 million USD). The average burden per 1,000 at risk was greatest in Argentina (32,583 USD), followed by Mexico (16,671 USD), Colombia (8,240 USD), and Brazil (6,130 USD).

Conclusions: Over the next 5 years, ∼4,485,352 fractures are anticipated to occur in Brazil, Mexico, Colombia, and Argentina. To control and prevent these fractures, stakeholders must work together to close the care gap. Efforts to identify individuals at high fracture risk, initiate treatment, and improve long-term treatment persistence will be essential in minimizing the financial and patient burden of osteoporosis in Latin America.

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Introduction

Osteoporosis is a disease characterized by compromised bone strength, leading to greater susceptibility to fractures[1]. Osteoporosis prevalence increases with age and is particularly elevated among post-menopausal women[1]. Osteoporosis-related fractures associate with significant morbidity and mortality; moreover, the index fracture significantly contributes to risk of recurrence[2,3]. The number of elderly persons in Latin America is expected to double in the next 30 years, with corresponding increases in fracture incidence[4]. There is a strong need to prevent this excess morbidity and mortality by initiating appropriate interventions[5]. In the absence of intervention, the societal burden of osteoporosis will continue to grow.

In the US alone, the annual direct medical cost of osteoporosis is projected to rise to 25 billion USD in 2025 from 17 billion USD in 2005[6]. Direct medical costs due to incident fragility fractures were estimated at 37 billion EUR (34.5 Billion USD) during 2010 for 27 countries within the European Union[7]. In Canada, the burden of osteoporosis in 2014 was estimated to exceed 4.6 billion CAD (3.6 billion USD) annually[8,9]. For patients with osteoporosis, the pain, impaired mobility, and discomfort associated with fractures results in increased use of resources such as long-term institutional care and rehabilitation services[10]. Furthermore, despite the availability of a variety of treatment options, osteoporosis remains severely under-diagnosed and under-treated[11]. Even when treated, non-persistence and non-compliance with current therapies such as bisphosphonates and other anti-resorptives are common[12]. Early intervention and greater adherence to treatment may not only lower fracture risk and prevent mortality, but can also play a role in reducing health resource utilization and associated costs.

While the burden of osteoporosis has been well defined in the US, several European countries, and Canada, this burden is not well understood in Latin American countries[6–9]. A literature review of the burden of osteoporosis in Latin America from 2004 limited its attention to direct medical costs up to 2003 and did not perform a systematic search to gather the evidence[13]. Country-specific estimates of the burden of osteoporosis in Latin America are also lacking.

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Although a few studies have been conducted in Mexico, Brazil, Colombia, and Argentina, these studies employed heterogenous methods and primarily focused on specific sites of fracture (e.g. hip or vertebral) rather than the cumulative fracture burden[14–18]. Therefore, our objective was to estimate the current and future economic burden of osteoporosis in adults aged 50–89 years in four Latin American countries: Brazil, Mexico, Colombia, and Argentina.

Methods

Systematic review

We performed a systematic review to collect data on the four Latin American countries of interest: Brazil, Mexico, Colombia, and Argentina. We sought information on adults ($\geq$ 18 years of age) at risk of osteoporosis in these countries. More specifically, we sought information on fragility fracture incidence at all sites, as well as the frequency of fracture-related healthcare utilization. We also sought information on the direct and indirect costs of osteoporotic fractures. We did not limit by study design, or by intervention, or comparators. We focused on literature published in English, Spanish, and Portuguese from 2010 onwards. The protocol for our review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines[19]. An experienced information specialist employed peer-reviewed search strategies from December 3–7, 2017 in MEDLINE, EMBASE, and the Cochrane Library[20]. Non-English language literature was also captured by searching Latin American databases, including LILACS, Scielo, BVS, and Redalyc (see Supplementary Appendix S1). We conducted additional grey literature searches using a modified version of the tool Grey Matters: a practical tool for searching health-related grey literature (see Supplementary Appendix S2)[21].

Key opinion leader (KOL) interviews

We interviewed several key opinion leaders (KOLs) from Brazil ($n = 2$), Mexico ($n = 3$), Colombia ($n = 3$), and Argentina ($n = 3$) between January and February 2018. We interviewed KOLs with a wide range of expertise, including rheumatologists, endocrinologists, osteologists, epidemiologists, payers, and health economists, to best supplement our findings from the systematic review. As recommended by Health Technology Assessment guidance, the KOLs helped to scrutinize the credibility of alternative literature sources and clarify uncertainty regarding geographical variation[22]. We conducted the interviews in Spanish and Portuguese, and subsequently translated the transcripts into English.

Economic model

We built a cohort-level burden of illness (BOI) model for Brazil, Mexico, Colombia, and Argentina using data collected in our systematic review and KOL interviews. We sought to follow a similar format to the Tarride *et al.*[8] investigation which quantified the economic burden of osteoporosis in Canada. Wherever possible, we used country-specific inputs to parameterize the BOI model. We presented all costs in 2018 US dollars (USD). We inflated all costs to 2018 values using estimates published by the Organization for Economic Co-operation and Development (OECD) for year over year inflation[23]. We inflated costs according to the currencies in which they were reported in the primary sources. Where necessary, we converted local currencies to USD using exchange rates effective March 27, 2018, from the World Bank[24]. In accordance with the Evidence for Policy and Practice Information and Coordinating Centre costing tool, we inflated costs first before converting[25]. We did not apply any discounting in the model[26]. We included hospital costs, testing costs, surgery costs, prescription drug costs, and indirect costs resulting from patient productivity loss in our model (see Supplementary Appendix S3). We prioritized costs that were reflective of public institutions. We summed these costs to quantify the 1-year and the 5-year burden for each country, and cumulatively across all four countries. Due to the wide variation in population sizes between the countries, we also calculated the burden per 1,000 at risk to provide a better capture of the differences in per-patient expenditures in each country. We defined the population at risk as adults aged 50–89 years.

Fracture estimates

We identified hip fracture incidence rates in each country from the literature[27–30]. Where possible, we prioritized studies of incident hip fractures that excluded pathological fractures (e.g. those due to tumors, Paget's disease of bone, or neoplasia), as well as high-energy fractures resulting from automobile accidents or violent trauma[27,28,30]. This increased confidence that the fractures were related to osteoporosis. We then imputed fracture incidence at other anatomical sites (wrist, vertebral, and other) using age- and sex-specific fracture ratios reported for Sweden[31]. This approach of applying Swedish fracture ratios was used in the FRAX models for Brazil and Colombia and is a common assumption when populating models with incomplete epidemiological information[27,28]. The Swedish estimates were based on hospital admissions and fractures that came to clinical attention[31]. Only fractures associated with low bone mineral density and increased incidence after age 50 were considered osteoporotic[31]. We applied the imputed incidence rates to the population demography of each country to estimate the total number of fractures attributable to osteoporosis among adults aged 50–89 years[32]. We applied the same distribution of fracture incidence year over year. Thus, any changes in fracture burden are driven by changes in the underlying age distribution.

Cost estimates

We assumed that all patients who experienced a fracture related to osteoporosis would be hospitalized, based on our hospital length of stay data which was inclusive of same-day discharge[33]. We believe this assumption was justified because any patients who did not have a hospital encounter for any type of fracture would not have been captured in our incidence data and would, therefore, not be included in our fracture estimates[27–30]. We extracted the hospital length of stay from a Brazilian publication that listed the range of days spent in the hospital by fracture site (hip, wrist, vertebral, or other)[33]. As other countries lacked a breakdown in length of hospitalization stay by these fracture sites, we assumed that the Brazil data applied to Argentina, Colombia, and Mexico. To increase the cross-country comparability and consistency in definition of the cost description, we used primary hospital bed costs from a World Health Organization (WHO) study that included all countries of interest to inform our per diems[34]. The primary hospital bed cost is described by the WHO to represent the "hotel" component of hospital costs[34]. It excludes the cost of drugs and diagnostic tests, but includes costs related to personnel, capital, and food[34]. The costs presented by the WHO are intended to be representative of a public hospital in an urban area that is operating in the 80th percentile among a sample of institutions with similar capacity and output[34]. To calculate the costs associated with hospitalizations, we multiplied the number of fractures at each site (hip, wrist, vertebral, other) by the length of hospital stay at each site and the hospital cost per diems.

As with hospitalization costs, we assigned testing costs to all patients. We derived per-patient testing costs from four country-specific literature sources[16,17,35,36]. The per-patient testing costs included costs for bone densitometry scans, clinical laboratory tests, and radiological fracture assessments.

We used published data from Brazil to estimate the annual proportion of patients with osteoporosis-related fractures who undergo surgery (9.85%)[36]. Since these data were only available for Brazil, we assumed the proportionality of surgeries to the total number of fractures was the same across Argentina, Colombia, and Mexico. We found country-specific values in the literature to inform cost-per surgery estimates for Brazil, Mexico, and Colombia[15,17,36], but relied on a KOL estimate to inform the cost-per surgery in Argentina.

For prescription drug costs, we weighed the cost per patient of prescription drugs by the prevalence of drug usage. We did not identify any studies that reported the prevalence of osteoporosis drug usage within Latin America. However, several studies highlighted that there is a distinct "care gap" in advanced economies[37–42]. Based on the median value of several care gap studies, we assumed roughly 24% of patients with fractures received osteoporosis medications[37–42]. We informed per-patient drug costs in each country by leveraging references identified in our systematic review[16,36,43,44].

To provide a societal perspective, we estimated the patient time lost from work following an osteoporosis-related fracture. We were not able to estimate the informal care costs due to the absence of a caregiver from the workforce because the data to inform these costs were lacking. We calculated the length of time patients spent in acute care then leveraged KOL feedback to estimate the length of disability for hip fractures as an additional 120 workdays beyond acute care[33]. We assumed the length of disability for a spinal fracture was comparable to the hip (also 120 workdays), a 50% reduction in length of disability for fractures at other sites relative to the hip (60 workdays), and a 75% reduction in length of disability for forearm fractures relative to the hip (30 workdays). This assumption was verified by clinical experts. Next, we multiplied the estimated number of fractures sustained at each site by the corresponding number of workdays lost when a fracture occurred at that site, to calculate the total number of workdays lost in a year. We combined the total number of workdays lost by the average daily wage and labor force participation rate for elderly women in each country to estimate indirect costs resulting from patient productivity loss[45–52].

In addition to not capturing informal care costs due to the absence of a caregiver from the workforce, we were unable to find data on outpatient physician costs, rehabilitation, and long-term care to inform our analysis. We also excluded the costs attributable to premature mortality from our analysis to align with the methodology established by Tarride *et al.*[8]. Therefore, the societal burden estimated in our analysis could be interpreted as a conservative estimate.

Sensitivity analyses

As with any type of modeling exercise, uncertainty exists concerning the underlying assumptions and data inputs of our BOI model. To explore the impact of alternative assumptions on the economic burden of osteoporotic fractures in Latin America, we conducted several sensitivity analyses. Where possible, we obtained alternative inputs from the literature. Otherwise, we tested estimates that were higher and lower than the base-case values. We varied the following model parameters: prescription drug cost, the proportion of patients working, hospital length of stay for hip fractures, hospital per diem costs, surgery cost, and the percentage of patients with fractures who are hospitalized.

Results

We included 108 references in our systematic review: 49 Brazilian, 19 Mexican, 19 Argentinian, 11 Colombian, and 10 with multiple countries included. In 2018, we predicted 159,533 hip fractures and 840,239 total fractures (inclusive of hip) would occur among adults aged 50–89 years in Brazil, Mexico, Argentina, and Colombia. The total number of fractures was predicted to increase by ∼ 14% in 2022 vs 2018, due to the aging populations in these four countries (Table 1).

The 1-year burden was highest in Mexico (411 million USD), followed by Argentina (360 million USD), Brazil (310 million USD), and Colombia (94 million USD) (Table 2). When the four Latin American countries were considered together, the 1-year burden was 1.17 billion USD, and the cumulative 5-year burden was 6.25 billion USD.

In Argentina, the largest proportion of the burden was attributable to surgical costs (42%), followed by hospitalization costs (33%). In Brazil, the largest proportion of the burden was attributable to productivity losses (61%), followed by hospitalization costs (19%). In Colombia, the largest proportion of the burden was attributable to productivity losses (37%), followed by hospitalization costs (28%). In Mexico, the largest proportion of the burden was attributable to hospitalization costs (51%). Cumulatively, the burden in all four countries was greatest due to hospitalization costs (36%), followed by productivity losses (30%) and surgical costs (23%). Testing and prescription medication costs accounted for only 8% and 4% of the burden, respectively.

The average burden per 1,000 at risk in Latin America was 15,906 USD. As shown in Figure 1, when adjusting for the population at risk, the country with the greatest burden was Argentina (32,583 USD), followed by Mexico (16,671 USD), Colombia (8,240 USD), and Brazil (6,130 USD).

Uncertainty testing via sensitivity analyses revealed that the primary drivers in terms of model uncertainty were the hospital per diem values, with the 1-year burden approximately doubling when alternative values for hospital per diem were used (see Supplementary Appendix S4).

Table 1. Estimated number of fractures by country in 2018 and 2022 among adults aged 50 to 89 years.

Country	Number of fractures in 2018	Number of fractures in 2022	Percentage increase (from 2018–2022)
Argentina			
Hip	35,625	38,208	7.3
All fracture sites	141,164	151,457	7.3
Brazil			
Hip	73,020	85,385	17.0
All fracture sites	413,564	471,445	14.0
Colombia			
Hip	10,300	12,269	19.1
All fracture sites	64,938	75,485	16.2
Mexico			
Hip	40,586	46,793	15.3
All fracture sites	220,573	256,701	16.4
Total			
Hip	159,533	182,655	14.5
All fracture sites	840,239	955,088	13.7

Note: These estimates were not adjusted to account for variations in population size between countries.

Discussion

The results of this BOI study reaffirm the need for increased primary and secondary fracture prevention. The BOI model shows that osteoporosis among individuals aged 50–89 years is associated with a substantial economic cost in Brazil, Mexico, Colombia, and Argentina. In 2018, we estimated that over 840,000 fractures would be caused by osteoporosis in these countries, amounting to a total burden of $\sim$ 1.17 billion USD. Furthermore, as the proportion of the population who are aged 50 or over is expected to increase in the near future, this burden will increase if no intervention is taken. By 2026, the annual burden is estimated to exceed 1.51 billion (2018 USD).

Table 2. One-year burden of illness of osteoporosis in Argentina, Brazil, Colombia, and Mexico.

Cost category	1-year burden (Argentina)	1-year burden (Brazil)	1-year burden (Colombia)	1-year burden (Mexico)	1-year burden (total LATAM)
Hospital	$119,742,517	$59,966,498	$26,219,453	$211,017,074	$416,945,542
Testing	$25,204,085	$11,550,109	$16,164,221	$36,938,599	$89,857,014
Surgical	$152,881,089	$41,656,869	$10,686,123	$68,757,147	$273,981,228
Prescription drugs	$9,488,597	$8,189,659	$6,412,882	$22,549,108	$46,640,245
Productivity	$52,589,959	$188,144,113	$34,782,940	$71,477,474	$346,994,486
Total	$359,906,247	$309,507,247	$94,265,620	$410,739,402	$1,174,418,516

Abbreviation. LATAM, Latin America countries of interest (Argentina, Brazil, Colombia, Mexico).

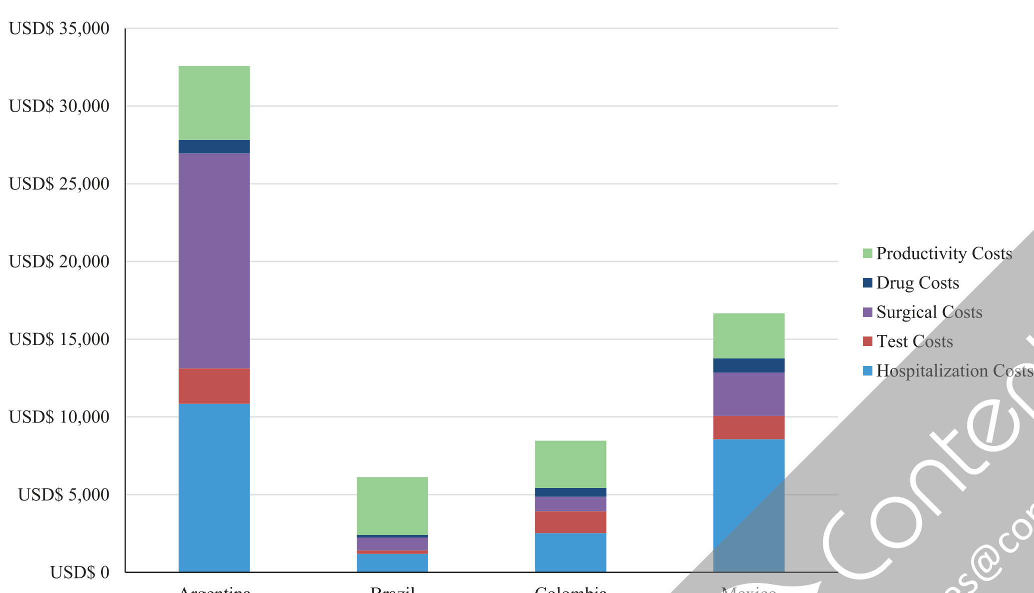

Figure 1. Burden of illness of osteoporosis per 1,000 at risk in Argentina, Brazil, Colombia, and Mexico.

There are several pharmacological and non-pharmacological strategies (e.g. exercise, smoking cessation) with proven efficacy for treating osteoporosis. Both should be considered in the care of osteoporosis patients. In our study, it was estimated that only 24% of patients with fractures receive prescription drugs to help prevent refracture. Although the value of 24% was derived from published literature out of European and North American countries[37–42], it corresponds well with the KOL estimates of a >70% treatment gap for Latin America. In the future, the use of medications and concomitant costs are anticipated to increase as patients receive more timely diagnoses, consistently initiate on appropriate therapies, and persist on therapies for longer durations. However, such a rise in medication expenditures should be considered in the context of the improved care for patients. Medications, alongside non-pharmacological interventions, will be critical in addressing the under-treatment of osteoporosis and resolving the care gap. Moreover, potential increases in medication costs are expected to be at least partially offset by substantial cost savings in hospitalizations and productivity losses.

Of note, our estimates for one-year burden do not follow the ordering of the selected countries by population size. Brazil (310 million USD) is the most populous country, followed by Mexico (411 million USD), Argentina (360 million USD), then Colombia (94 million USD). This indicates that population size is an important driver, but is not the only determinant of comparative burden. Other factors that may have contributed to variations in economic burden relative to population size include differences in hip fracture incidence and the value of cost components across countries.

Our model results generally align with other studies that have established the BOI of osteoporosis in Latin America. For example, a 2009 study estimated the BOI of osteoporosis in Argentina (considering only hip and spinal fractures) to be ∼ 190 million USD (only including hospitalization per diem, surgery, and testing costs)[16]. Adjusting for inflation, population growth, and the fact that we included other fracture types, this aligns well with our estimate of 298 million USD for the same components in 2018. Similarly, a Mexican BOI study that only considered hip fractures estimated a total burden of ∼127 million (2009 USD) by 2020 when a discounting rate of 3% was applied[53]. Given that hip fractures account for ∼ 18% of fractures we considered, but would have a larger burden due to increased hospital stay and time lost from work, this aligns well with our model which predicts a total burden due to osteoporosis of 442 million USD in 2020. A Colombian study that predicted a total burden of 342 billion COP (120 million USD) for all female-related fractures in 2015 aligns with our estimate of 268 billion COP (94 million USD) in 2018, although our estimates are slightly lower[17]. Notably, our results show a significantly lower burden for all countries compared to a Canadian BOI study which estimated the total burden at 2.3 billion CAD per year in 2010 (2.0 billion in 2018 USD)[8]. This is not surprising, given that the Canadian study included several more components of burden (e.g. costs due to rehabilitation, informal care costs, outpatient costs, and long-term care costs). Also, hospitalization costs are substantially greater in Canada compared with Latin America[34].

One of the strengths of our study was that we populated the BOI model using a rigorous evidence base (systematic review and KOL interviews). The grey literature search, performed as part of our systematic review, was critical in identifying country-specific numerical inputs. Our BOI model was further strengthened by the inclusion of multiple countries, and burden estimates standardized to population size. Lastly, unlike some previous investigations[8,9], our model had the advantage of projecting the cumulative 5-year burden of osteoporosis in addition to the 1-year burden.

There were some limitations in our analysis. When comparing estimates of the economic burden that have been adjusted for the populations at risk, it is important to keep in mind that our countries of interest demonstrated considerable differences in the relative importance of the various cost components. We do not know whether these differences are the result of a statistical artifact or if they reflect real heterogeneity in the landscape of healthcare systems, drug reimbursement policies, economic development, and resource availability in Latin America. For example, even though the hospital per diem costs all came from a single WHO source, the values used in the model varied substantially[34]. The hospital per diem cost in Mexico was over 6-times larger than the hospital per diem cost in Brazil[34]. Furthermore, this source reported costs from the perspective of a public institution. Hospital per diems in the private sector would likely be 3–4-times higher[54]. Alternative hospital per diems identified and tested in sensitivity analyses substantially altered the results for the overall burden. Accordingly, the burden due to hospital stay per 1,000 at risk was much larger in Mexico than in Brazil. Similarly, the relative burden due to surgery varied between the countries studied. Some of this may be due to the use of disparate sources, as the per surgery estimate for Argentina was an estimate from a KOL rather than a value elicited from an economic BOI study.

We were also limited by data availability. We were missing several components on healthcare utilization and country-specific costs. Owing to the lack of data around the prevalence of rehabilitation, long-term care, and continuing care usage for patients with osteoporosis in Latin America, we excluded these components. In Canada, the burden due to rehabilitation, long-term care, and continuing care was estimated at 10% of the total economic burden[8]. Similarly, the burden due to the caregiver's lost wages was estimated at 25% of the total productivity burden in Canada[9]. Therefore, by excluding these costs due to insufficiency in the data obtained in our systematic review, we likely provided a conservative estimate of the total burden of osteoporosis. Another limitation was our reliance on assumptions. For example, we did not have up-to-date incidence rates by fracture site, and had to assume that the proportionality remained constant across countries. While this approach has been used in other models examining the burden of osteoporosis, such as the FRAX models for Colombia and Brazil[27,28], a more granular account of data by fracture site and resource usage in all four of these countries would allow for a more accurate picture of the total burden of osteoporosis. In some cases, where only regional data on hip fracture incidence were available, we assumed the regional estimates were representative of the country. This assumption of generalizability requires further investigation.

Conclusions

There is a strong need to improve the diagnosis of osteoporosis and initiation of treatment for individuals at high-fracture risk in Latin America. The burden of osteoporosis in 2018 was estimated to be 1.17 billion USD in the four Latin American countries analyzed. On account of the aging population in these countries, this burden is likely to increase in the near future[55]. The prevention of osteoporotic fractures will be key to reducing the considerable human and economic burden of osteoporosis[56–58]. As this study identified several data gaps, future research should aim to accurately quantify more of the epidemiological and economic factors that contribute to osteoporosis burden in Brazil, Mexico, Colombia, and Argentina.

Transparency

Declaration of funding

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Declaration of financial/other relationships

Cornerstone received financial support from Amgen for the conduct of this study. RA, MA, MH, and JGP are employees of Amgen. RKM and KS are employees of Cornerstone, while AL and TD are subcontractors of Cornerstone. CC is an employee and shareholder of Cornerstone Research Group Inc. Cornerstone consults for various pharmaceutical, medical device, and biotech companies. JME peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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