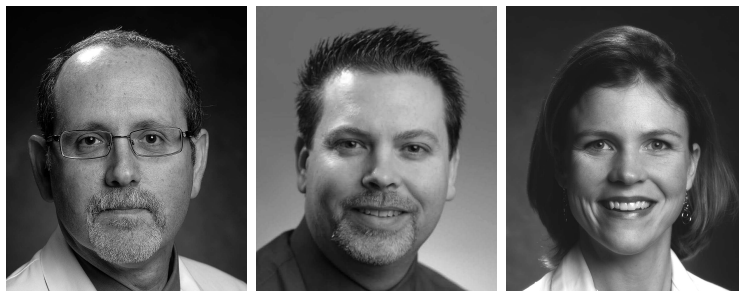


Challenges in Defining Quality of Care for Glucocorticoid-induced Osteoporosis: Defending Good Against Perfect



In an era of increasing preventive care complexity coupled with progressively shorter doctor visits, asymptomatic conditions such as osteoporosis (OP) can easily be neglected. Despite a reported reduction in fracture burden in the United States and Canada^{1,2}, OP continues to be a condition that is both underdiagnosed and undertreated. In the United States, the Healthcare Effectiveness Data and Information Set statistics from the National Committee on Quality Assurance estimates that less than 25% of persons who incur fracture receive a bone-specific medication; a proportion that has remained essentially stagnant over the past 10 years. These US findings are quite similar to the low rates of OP treatment in Canada, as highlighted in the paper in this issue of *The Journal* by Majumdar and colleagues³. Glucocorticoids constitute the most commonly administered drugs that are associated with bone loss and higher fracture risk. Despite a clear time- and dose-dependent association of glucocorticoids with fracture risk^{4,5} and international guidelines that support a variety of pharmacotherapies for both primary and secondary prevention^{6,7,8,9}, the prevention and treatment statistics are also rather dismal for glucocorticoid-induced OP (GIOP). Curtis and colleagues observed temporal improvement in the rates of treatment with nonestrogen bone-acting agents among chronic glucocorticoid users of an Aetna managed-care plan over a 5- to 6-year period¹⁰. However, even among postmenopausal women, the group at highest fracture risk, less than two-thirds were being treated in the early 2000s. Majumdar and colleagues, using much newer data from Canada, reported that only 25% of over 15,000 older adults receiving supraphysiologic prednisone were managed in accord with the latest guidelines. Thus, an underuse gap persists for GIOP prevention and treatment.

Underuse of many evidence-based therapeutics for chronic conditions such as OP constitutes one of the most common types of medical errors¹¹. Defining what is the optimal quality of care in these areas involves translating clinical practice guidelines into performance or quality measures. Historically, most indicators of quality have been

“process measures,” which define necessary clinical services and procedures, such as drugs and tests that are warranted under specific circumstances. The numerator of a quality indicator represents the proportion receiving the measure, and the denominator defines the eligible population with certain per-specified exclusions, such as persons who might have known contraindications to a recommended drug or a very limited life expectancy. For better and for worse, physicians and health plans often are graded and compared to their peers based on their performance on these quality measures. National quality reporting initiatives like the Physician Quality Reporting System in the United States allow physicians to receive “credit” for care that was considered but not delivered for patient, health system, or medical reasons¹². This provision is able to overcome some shortcomings of administrative claims data that are frequently used in reporting quality measures for processes of care.

Majumdar and colleagues address this interesting and timely controversy in quality measurement for GIOP in an observational study of a large sample of adults newly initiating glucocorticoids. The findings of this nicely conducted and thoughtful study are provocative and, as the authors themselves acknowledge, counterintuitive. They found that adherence to the GIOP guidelines advocating OP prevention and treatment with pharmacotherapies was associated with worse fracture outcomes. A natural question raised by the Majumdar paper is why is there a focus on the processes of healthcare in GIOP if the real goal is to improve health outcomes? The reasons that most quality measurement is directed at processes rather than outcomes of care are multifold. Process measures are directly actionable and generally easier to measure¹³. Measuring outcomes is limited by the difficulties of case-mix and channeling. “Sicker” patients may be preferentially offered a given treatment (the process of care), but they are the very patients who, on the basis of their more severe condition (i.e., worse OP risk), are more likely to have the bad outcome (i.e., fracture) that the treatments defined in the

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quality measure seek to prevent. This type of susceptibility bias, or confounding by indication, is the greatest threat to validity of any observational study of therapeutics. Other epidemiologic studies have also found that those preferentially treated for OP also have higher fracture rates¹⁴. In addition to susceptibility bias as a reason to measure process over outcomes, more socioeconomically disadvantaged patients might not have access to certain recommended services, and they too will have worse outcomes, irrespective of whether the “right thing” was done by the healthcare provider. Therefore, it is necessary to take into account patient demographics and disease characteristics, as the authors rigorously attempted to do in this study. For these reasons and more, clinicians and outcomes researchers are often left applying a somewhat “transitive property of quality measurement”; whereby, if a well-done clinical trial demonstrates efficacy of a particular process of care (i.e., an OP treatment) on a clinical outcome (i.e., fracture reduction), often with added support from rigorously developed clinical guidelines, then improving the process measure should ultimately lead to an improvement in the outcome.

Majumdar and colleagues’ findings are contrary to this transitive property since GIOP clinical trial of several agents including alendronate, risedronate, zoledronic acid, and teriparatide have all showed reductions or trends toward reductions in vertebral fracture risk^{15,16,17,18,19}. It is worth noting that the GIOP clinical trials were not statistically powered to show a reduced risk of either vertebral or nonvertebral fractures. However, metaanalysis suggests the magnitude of the effect for bisphosphonates on nonvertebral fractures may be similar to that seen in postmenopausal OP¹⁹. Evidence is less compelling, however, for any fracture risk reduction with calcitonin and raloxifene in GIOP^{21,22}. Both these treatments were medications considered as satisfying receipt of high-quality GIOP care in Majumdar’s study, but both likely had limited usefulness based on international trends. To address the issue of the small effects size for fracture risk reduction with GIOP drugs, the authors enriched their population for those more likely to experience fracture by conducting a restricted analysis of only the highest-risk subgroup (those most likely to fracture). However, even among those persons, the findings were consistent with the main result. This suggests that either the study was underpowered to detect small efficacy or that the effectiveness for nonvertebral fractures with antiosteoporotic medication in GIOP may not exist in the general community, at least over the time period measured in this study. Indeed, patients generally need at least 6-12 months of OP therapy to demonstrate beneficial effect on clinical fracture risk reduction²¹. Therefore, the finding of no benefit with a 1-year outcome is somewhat expected. Moreover, a high proportion of patients treated with prescription medications to prevent GIOP have suboptimal adherence²³, further

retarding any fracture benefit. Another limitation the authors highlight with GIOP process-of-care quality measures are the challenges intrinsic to the use of administrative claims data. Claims data can lead to nondifferential misclassification of who was or was not an appropriate candidate for a particular service; yield imperfect risk stratification needed to evaluate truly comparable patients; underestimate fractures; and misclassify OP treatment effectiveness because of an expected lag in treatment benefit. Therefore, it is much more difficult in routine clinical settings, such as those used in this study, to disentangle an OP treatment benefit from actual fracture outcomes.

Despite the international proclivity to use process over outcome measures, because they are certainly more convenient and less costly to measure, they are not without limitations, as this article highlights. Process measures become potentially problematic if the clinical trials supporting them do not generalize to persons in whom the measures are applied, or if there is reason to suspect the processes may have unintended consequences. The authors provide an example of early aggressive treatment of pneumonia where adherence to a process measure could have unintended consequences. However, it is difficult to make this case with GIOP testing and treatment. Specifically, unless adhering to the process measures (initiating OP treatment) actually leads to more short-term fractures (again, contrary to the clinical trials, and very unlikely because a major difference in fracture rates in the Majumdar article is seen within 1 year but attenuates by 3 years, suggesting channeling) by some unintended consequence (not easy to conceptualize), then there is a limited argument to not use these process measures at all. In other words, without making a case that adherence to the process of care is causal in the increased fracture outcome, it is hard to argue (on the basis of this study alone) that these measures are not useful as quality-of-care indicators but more likely that their perceived lack of validity is the result of a confounded study or too short a followup to appreciate a small fracture protective effect. To test this further in clinical practice would require access to even more granular data containing information on many of the currently unmeasured confounders; accounting for any preferential losses due to death; censoring the not-screened/treated group if they were screened/treated after 6 months, or allowing people to contribute person-time to both groups; even larger sample size; and/or longer durations of followup. While the availability of linked T scores from a dual-energy x-ray absorptiometry (DEXA) database is a unique strength of this Canadian data source, even that may not be enough to overcome confounding because as many as three-quarters of these patients were never tested with DEXA.

A major concern in the current quality measurement field highlighted by Majumdar and colleagues is the use of imper-

fectly measured or inadequately validated process-of-care indicators to provide financial reward, or more commonly financial punishments, to physicians. Given the imperfect nature of the evidence base as well as the measurement issues that limit such metrics, we agree that measure adoption should be sequential and judicious before rewards or penalties are applied. Ultimately, quality improvement efforts have a cost-outcome consideration. If the intervention aimed at improving quality through the process measure is reasonably low-cost and safe, then even a very small effect size may be of societal value. For now, we are left with imperfect process measures for GIOP quality-of-care that have not been tightly linked to beneficial fracture outcomes in a well-done population-based study. However, we believe that requiring perfection in demanding this evidence base should not be the enemy of the good. We continue to support the current GIOP process measures with hopes that some of this debate ultimately will be attenuated by future OP drugs of greater potency, easier adherence, and in turn more effectiveness, thereby creating less discordance between process-of-care and real-world clinical outcomes.

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REFERENCES

1. Brauer CA, Coca-Perrillon M, Cutler DM, Rosen AB. Incidence and mortality of hip fractures in the United States. *JAMA* 2009;302:1573-9.
2. Leslie WD, O'Donnell S, Jean S, Lagacé C, Walsh P, Bancej C, et al. Trends in hip fracture rates in Canada. *JAMA* 2009;302:883-9.
3. Majumdar SR, Lix LM, Morin SN, Yogendran M, Metge CJ, Leslie WD. The disconnect between better quality of glucocorticoid-induced osteoporosis preventive care and better outcomes: a population-based cohort study. *J Rheumatol* 2013;40:1736.
4. Van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Use of oral corticosteroids and risk of fractures. *J Bone Miner Res* 2000;15:993-1000.
5. van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Oral corticosteroids and fracture risk: relationship to daily and cumulative doses. *Rheumatology* 2000;39:1383-9.
6. Brown JP, Josse RG, Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167 Suppl:S1-34.
7. Grossman JM, Gordon R, Ranganath VK, Deal C, Caplan L, Chen W, et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. *Arthritis Care Res* 2010;62:1515-26.
8. Lekamwasam S, Adachi JD, Agnusdei D, Bilezikian J, Boonen S, Borgström F, et al. A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis. *Osteoporos Int* 2012;23:2257-76.
9. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. *CMAJ* 2010;182:1864-73.
10. Curtis JR, Westfall AO, Allison JJ, Becker A, Casebeer L, Freeman A, et al. Longitudinal patterns in the prevention of osteoporosis in glucocorticoid-treated patients. *Arthritis Rheum* 2005;52:2485-94.
11. Institute of Medicine. To Err Is Human: Building a Safer Health System. The National Academy of Sciences; 1999 [Internet. Accessed August 12, 2013.] Available from: <http://www.iom.edu/~media/Files/Report%20Files/1999/To-Err-is-Human/To%20Err%20is%20Human%201999%20%20report%20brief.pdf>
12. Curtis JR, Sharma P, Arora T, Bharat A, Barnes I, Morrissey MA, et al. Physicians' explanations for apparent gaps in the quality of rheumatology care: results from the US Medicare Physician Quality Reporting System. *Arthritis Care Res* 2013;65:235-43.
13. Mant J. Process versus outcome indicators in the assessment of quality of health care. *Int J Qual Health Care* 2001;13:475-80.
14. Curtis JR, Yun H, Lange JL, Matthews R, Sharma P, Saag KG, et al. Does medication adherence itself confer fracture protection? An investigation of the healthy adherer effect in observational data. *Arthritis Care Res* 2012;64:1855-63.
15. Cohen S, Levy RM, Keller M, Boling E, Emkey RD, Greenwald M, et al. Risedronate therapy prevents corticosteroid-induced bone loss: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. *Arthritis Rheum* 1999;42:2309-18.
16. Reid DM, Devogelaer JP, Saag K, Roux C, Lau CS, Reginster JY, et al. Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet* 2009;373:1253-63.
17. Reid DM, Hughes RA, Laan RF, Sacco-Gibson NA, Wenderoth DH, Adami S, et al. Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. *European Corticosteroid-Induced Osteoporosis Treatment Study. J Bone Miner Res* 2000;15:1006-13.
18. Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, et al. Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. *N Engl J Med* 1998;339:292-9.
19. Saag KG, Shane E, Boonen S, Marín F, Donley DW, Taylor KA, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med* 2007;357:2028-39.
20. Kanis JA, Stevenson M, McCloskey EV, Davis S, Lloyd-Jones M. Glucocorticoid-induced osteoporosis: a systematic review and cost-utility analysis. *Health Technol Assess* 2007;11:iii-iv, ix-xi, 1-231.
21. Crandall CJ, Newberry SJ, Diamant A, Lim YW, Gellad WF, Suttrop MJ, et al. Treatment to prevent fractures in men and women with low bone density or osteoporosis: update of a 2007 report. Rockville: Agency for Healthcare Research and Quality; 2012.
22. Cranney A, Welch V, Adachi JD, Guyatt G, Krolicki N, Griffith L, et al. Calcitonin for the treatment and prevention of corticosteroid-induced osteoporosis. *Cochrane Database Syst Rev* 2000:CD001983.
23. Curtis JR, Westfall AO, Allison JJ, Freeman A, Saag KG. Channeling and adherence with alendronate and risedronate among chronic glucocorticoid users. *Osteoporos Int* 2006;17:1268-74.

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