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# Is Initiation of Atorvastatin for Employees a Good Buy for Employers?

The continually increasing share of US economic resources spent on health care has once again placed health care reform at the top of the domestic policy agenda of the Obama administration and Congress. Most of the current debate in Congress and the public press has been concerned with ways to increase health insurance coverage among uninsured individuals and has had little to do with restructuring the US health care delivery system. Fortunately, during the past 5 years, a number of new policy initiatives have attempted to improve the quality of care and the dollar value of health services purchased. One of the more promising of these efforts has focused on improving physician-patient decisions on the choice of treatment when several alternative interventions have been shown to be safe; this type of analysis is known as *comparative effectiveness research*. This approach was endorsed in an Institute of Medicine report that supports better decision making in health care.[1] Comparative effectiveness research received financial support with the passage of the American Recovery and Reinvestment Act of 2009, which allocated more than $1 billion to conduct studies in this area. Since President Obama signed this act, several federal funding agencies, including the Agency for Healthcare Research and Quality, have published prioritized lists of clinical areas for comparative effectiveness research and requested proposals to conduct studies.

In this issue of *Mayo Clinic Proceedings*, Simpson et al[2] report the results of their study that compared the cost of initiating lipid-lowering therapy between the 2 most common statin medications: atorvastatin and simvastatin. Their article discusses the type of clinical questions that comparative effectiveness studies are attempting to address. One prior head-to-head randomized clinical trial that compared the usual dose of simvastatin to high-dose atorvastatin found that atorvastatin statistically reduced nonfatal acute myocardial infarction even though there was no significant difference in the other major cardiovascular outcomes: death due to coronary heart disease or cardiac arrest with resuscitation.[3] The incremental clinical benefit of atorvastatin comes at a high cost because simvastatin is available in generic form, whereas atorvastatin is still under patent protection. A previous editorial in this journal suggested that, given the incremental benefits at increased cost, the value of atorvastatin compared with that of simvastatin can be determined only by cost-effectiveness studies.[4]

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Simpson et al[2] take a step in that direction by conducting a cost (net benefit) analysis from the employer's perspective of the 2 statin medications. They used a retrospective study design, based on administrative data from 23 health plans, to examine clinical differences in outcomes (the rates of 8 inpatient cardiovascular events), total all-cause direct medical costs, and indirect medical cost (disability payments and indirect cost through work loss) between atorvastatin and simvastatin. Their matched-cohort study sample paired each patient in the atorvastatin cohort with 1 patient in the simvastatin cohort on the basis of 4 factors: (1) initial drug dose, (2) baseline inpatient cardiovascular events, (3) average wage, and (4) the predicted probability of being a member of the atorvastatin vs simvastatin cohort. The study sample consisted of 13,584 matched pairs (98% of the original simvastatin sample) who were employed for at least 2 years after initiation of a lipid-lowering therapy. The authors used standard, appropriate statistical analysis to value all resources consumed, both direct medical and indirect cost, in 2006 US dollars. These results are reported in detail in Table 2 of their article.

Of note, since the authors conducted this study from the perspective of the employer, all health care outcome ben-

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efits and indirect medical resources consumed (disability and medically related absenteeism) were converted into costs. Results of their study showed that the net cost of initiation of atorvastatin vs simvastatin during the 2-year period was approximately $41. This suggests that employers should not pay for atorvastatin compared with simvastatin. However, because medication cost between the 2 cohorts is the single largest cost difference, atorvastatin could be the lower cost choice if its price was reduced. In fact, the authors calculated that a 9% price reduction would result in atorvastatin saving employers $44 per employee compared with simvastatin.

What should an employer do? We think that comparative effectiveness research may help the employer make a decision. Some interesting comparative effectiveness results can be made using the information presented in Table 2 in the article by Simpson et al. From the employer's perspective, assume that the primary cost between the 2 medication cohorts is the cost of direct health resources consumed by their employees: the number of health services consumed (hospitalization, emergency department visits, and outpatient visits). Data in Table 2 indicate no statistical differences in any health care resources consumed between the 2 cohorts in terms of average number of inpatient days (1.2 days in both cohorts), emergency department visits (0.7 in both cohorts), and outpatient visits (atorvastatin cohort had 0.4 fewer outpatient visits; $P$=.06). However, the employer receives 1 significant benefit of atorvastatin compared with simvastatin: a reduction in medically related absenteeism of 0.3 days ($P$=.02) per employee during the 2-year study period. At this point, one can approximate the comparative effectiveness of atorvastatin to simvastatin by dividing the difference in average direct medical cost by the difference in average benefit between the 2 study cohorts. The information in Table 2 indicates that the difference in total average cost of direct medical services between the 2 cohorts is $164 (higher cost in the atorvastatin cohort), and the average difference in medically related absenteeism between the 2 cohorts is 0.3 days (fewer missed days in the atorvastatin cohort). This suggests that an employer pays approximately $546 ($546 = $164/0.3) to reduce medically related absenteeism by 1 day when atorvastatin is initiated vs simvastatin. One could also approximate a 10% reduction in the cost of atorvastatin by reducing the average index cost of the drug during the 2-year study period by $95, which would reduce the difference in all costs of direct medical services between the 2 arms to $69, suggesting that an employer would pay approximately $203 to reduce medically related absenteeism by 1 day. When stating the data as relative comparative effectiveness research, our back-of-the-envelope estimates suggest that an employer should encourage the use of atorvastatin if its average daily wage of employees covered in their health plan exceeds approximately $200 per day, provided they receive a 10% discount on the price of atorvastatin.

One policy concern of employers using relative comparative effectiveness research (in the aforementioned manner) is that it might lead to potentially greater health care access disparities between the rich and poor because employers with higher paid employees may be more willing to cover more costly drugs that provide slightly more benefits than employers with lower paid employees. Although this is a possible outcome of using this type of analysis, we think that this already occurs in the United States. It is well documented that there are vast differences in the benefit designs of employer-based health insurance packages across different industries in the United States, and some employers in low-wage industries provide no health insurance. Looking forward, we think that comparative effectiveness research could provide analytical justification to the current drug benefit design used by many employers that place drugs into tiers with different employee deductibles and co-pays. In our example, any employer with average daily wages higher than $200 per day would want to place atorvastatin in the tier that does not have co-pays or deductibles. For employers whose average wage is less than $200 per day, they would want to place atorvastatin in the drug tier that includes the level of co-pays and/or deductibles that would make the comparative effectiveness of atorvastatin vs simvastatin approximately equal to the average daily wage. These employees would purchase atorvastatin if they perceived that the additional health benefits exceeded their out-of-pocket costs.

Of note, the comparative effectiveness research approach allows one to perform some interesting subgroup analyses among employees to determine who benefits the most from a given intervention. For example, is the relative comparative effectiveness of atorvastatin vs simvastatin different between male and female employees? Is it more or less effective for young vs older employees? Subgroup analysis is one of the advantages often highlighted in articles that discuss how comparative effectiveness research could transform medical practice.[5] Subgroup analysis adds complexity to the treatment choice for both physicians and patients because it implies that different subgroups of patients could benefit more from alternative treatment choices. In addition, determining these differences using randomized clinical trials would most likely be too costly and take too long to complete. However, once clinical trials have shown a treatment to be safe, retrospective studies using large administrative data sets (such as that used by

Simpson et al) provide a rapid and inexpensive approach for identifying potential subgroups that benefit more or less from 1 treatment vs another treatment. For example, with more than 13,000 matched pairs and a 2-year study period, the authors should be able to provide insights concerning which, if any, subgroups of employees benefit the most from being treated with atorvastatin vs simvastatin. Employers and other purchasers of health care should and are beginning to demand answers to such questions. Without the answers that comparative cost analysis can provide, purchasers are blindly spending their health care dollars hoping to help somebody.

In conducting comparative effectiveness research, it is critical to remember that the rules of science still apply.[6] Use of nonrandomized data, even after sophisticated statistical analysis, may still be subject to treatment selection bias due to imbalance between the study arms. When this is the case, results may be spurious. In addition, subgroups should be specified in advance when the study is designed because data dredging with multiple comparisons may lead to spurious conclusions. When multiple subgroups are considered with proper statistical approaches that demonstrate that the difference between the subgroups is clinically important and statistically significant, the finding must be interpreted in a critical manner. Comparative effectiveness research will be one part of improving the health care system, but the rules of good science will still apply.

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