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Cost-Effectiveness of Migraine Treatment: A Commentary

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Migraine headaches impart substantial personal and financial costs on individuals, health systems, and employers. We have known for nearly two decades that one-tenth or more of the population suffers from migraines in a given year [1]. For persons experiencing migraines, multiple episodes consume an average of more than 2 weeks per year [2]. For health systems, persons with migraines use significantly more physician services and pharmaceutical services than persons without migraines. For employers, missed days of work, or absenteeism, and reduced productivity at work, presenteeism, cost one-half percent of total labor productivity, a figure that translates to one-tenth of net corporate profits in 2000. Clearly, the appropriate treatment of migraines is a substantial societal concern.

With the introduction of selective serotonin receptor agonists (triptans), pharmaceutical treatment has more effectively addressed the burden of migraines. Studies of triptans have demonstrated their ability to reduce the duration of migraines and, in some cases, reduce other medical costs and time lost from work. Among the questions facing pharmaceutical benefit decision makers are, should triptans be included on preferred drug lists, such as formularies, subsidy schedules, etc., and if so, which ones? Decision makers are obviously concerned with the effectiveness of each migraine medication. So too are they increasingly concerned with its cost and cost-effectiveness. The use of particular measures of effectiveness and costs may vary with the role of the decision maker, pharmacy benefit manager, health plan manager, employer, etc., and the relative weight the decision maker places on effectiveness of treatment and a line item in a budget.

In the case of migraines, the standard measure of effectiveness has been improvement at 2 hours. Improvement is typically measured as moving from some patient-reported level of pain to a lower level of pain. Recent investigations have pushed the measures of effectiveness to more precisely address the complaints of migraine sufferers. A contribution made by Wells et al. [3] in this issue of *Value in Health* is the use of two measures of treatment effectiveness that go beyond improvement at 2 hours. Specifically, they compare eletriptan and sumatriptan using 1) pain-free, not just improvement, at 2 hours, with no recurrence within 24 hours of the first dosing and no requirement for rescue medication, and 2) improvement at 1 hour, followed by pain-free status at 2 hours and sustained at 4 hours and the absence of recurrence within 24 hours of the first dosing.

The differences in the percentage of patients successfully treated with eletriptan and sumatriptan diminishes as increasingly stringent measures are evaluated, from 64% to 67% versus 50% to 53% for improvement at 2 hours to 16% to 17% versus 14% to 16% for improvement at 1 hour for eletriptan and sumatriptan, respectively. Since the data for this study were not generated for the purpose of the specific analyses conducted, the statistical significance of certain comparisons is modest, but do not qualitatively affect results. Findings are similar to a comparison among other triptans with alternative effectiveness measures that are also more stringent than improvement at 2 hours [4].

The two additional effectiveness measures more clearly define patients concerns with migraines. The results also suggest three avenues for future research. First, the added measures address areas of concern to patients, but the relative importance of such concerns, improvement at 2 hours versus pain-free at 1 hour, has yet to be measured. As an ultimate measure of patient well-being, a quality-of-life measure transformed into quality-adjusted life-years (QALYs) might be appropriate. There are available quality-of-life measures specifically applied to migraine that could be used to address the added value of more detailed effectiveness measures [5]. Further, standardizing outcomes into QALYs would permit comparisons across illnesses. Decision makers are required to make trade-offs among illnesses demanding scare resources.

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Second, the relative effectiveness of treatments among subpopulations has yet to be addressed. In the determination of differences in effectiveness between eletriptan and sumatriptan, logistic regressions were performed with treatment as the only regressor. Age and gender were similar between the two groups of patients, which was taken as an indicator that the randomization procedure worked appropriately and that these variables could be subsequently ignored. The later indication may not be appropriate. It is possible that one medication is more effective for one particular subgroup, with less than half of the patients, and still the average would favor the other medication. Future analyses should include independent variables such as age, gender, and comorbidities and specifically look for subpopulation effects.

Third, the relevance to the employer of alternative measures of effectiveness merits attention. Logically, there should be correlations among patient-reported effectiveness measures and time lost from work, which constitutes two-thirds of total migraine costs. One study in a managed care setting found that improvement at 2 hours with a triptan was associated with a two-thirds reduction in migraine-related absenteeism, but a minimal change in presenteeism [6]. Another managed-care organization found that productivity benefits exceeded triptan costs by 10-fold [7]. An interesting question remains unanswered: what is the gain to the employer from improvement at 1 hour or improvement to pain-free? A quick response might further reduce absenteeism, address presenteeism, and make migraine treatment a priority for workplace wellness programs.

A second contribution made by this study is the evaluation of cost-effectiveness of treatment. The study takes a health-care system perspective on costs—but only includes drug costs. There is an expectation that other medical services costs would be proportional to drug costs and future research should consider total medical cost, including physician services costs and costs associated with adverse events. Such research would be particularly useful to pharmacy benefit managers and health plans. Cost-effectiveness analysis permits decision makers to go beyond consideration of only unit costs of medications.

The preferred drug lists of many entities include multiple drugs in a single class. In part, inclusion of multiple drugs reflects suspected or verified differences in effectiveness of drugs among subgroups of patients. An analysis of migraine trials recommended that almotriptan, eletriptan, and rizatriptan be included on preferred drugs lists, each addressing a specific concern [8]. Inclusion of multiple drugs also reflects lack of sound evidence for the selection of a single drug or subset of drugs. Improvements and perhaps narrowing of preferred drugs lists is possible through research such as what we see for migraines. Truly preferred drugs lists will come about though a process of refining effectiveness measures to reflect what is important to patients and decision makers, presenting head-to-head trials and including evidence of cost, effectiveness, and cost-effectiveness.

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