Dear Editor,

We read with interest the article by Fivenson and colleagues on the total burden of illness associated with atopic dermatitis. The study is important in that it provides a perspective from payer costs to individual productivity. We agree with their conclusion that atopic dermatitis “imposes a financial burden on the health care system.”

Using a claims-based approach that included comorbidities associated with atopic dermatitis and eczema, we estimated direct payer costs within a managed care population to average $580 per patient per year (n=35,000), significantly higher than the $167 per patient per year (n=298) found by Fivenson et al.

The difference in annual direct payer cost per patient appears mainly to be the result of different cost-accounting methods. We incorporated costs for comorbid conditions; the validity and accuracy of our use of expert opinion to incorporate disease comorbidities were confirmed in a separate study. It appears that Fivenson et al. included direct costs only if they could be tied directly to atopic dermatitis. Although data in the 2 studies are not directly comparable, direct costs in Fivenson et al. are in the range of those in our study if costs for comorbid conditions that we examined are excluded.

Other factors might also explain the disparate results. First, we included patients with eczemas as well as atopic dermatitis; however, we would surmise that the average annual direct payer cost would be even higher than $580 if we restricted our study to patients with atopic dermatitis, which is often chronic and difficult to treat. Second, Fivenson et al. report that 7% to 12% of their patients had severe disease. Yet, a recent report estimates the prevalence of severe disease in atopic dermatitis to be 16% of patients. Therefore, average annual direct costs likely would have been higher if more severe patients were included.

Regardless, the study by Fivenson et al. is particularly valuable because it quantified various costs associated with atopic dermatitis including out-of-pocket expenses and productivity. Those costs were obtained by survey of patients and families who, although asked about “eczema,” may not ascribe their time and expenses so specifically; therefore, those costs may, in fact, include the effects of at least some comorbidities. Thus, an annual cost burden of $1,022 per patient with atopic dermatitis may be a conservative total (using our total of $580 for payer direct costs plus the Fivenson et al. total of $442 for out-of-pocket expenses and productivity).

In addition, neither study attributes a cost to patients’ decreased quality of life. Thus, we still have not captured completely the financial burden of having atopic dermatitis, which is indeed substantial. Further research will be required to fully understand the burden of illness as well as the cost-effectiveness of patient management and intervention programs.

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DISCLOSURES

There was no specific funding for the preparation of this letter. Ms. Prendergast approved this letter on behalf of Fujisawa Healthcare, Inc. The study to which we refer (reference 2) was funded by Fujisawa Healthcare, Inc., Deerfield, Illinois. Dr. Ellis serves as a consultant to Fujisawa Healthcare, Inc., and to other companies that make treatments for atopic dermatitis, including Novartis Pharmaceuticals Corp., that funded the study by Fivenson et al. (reference 1). Quorum Consulting, Inc. has research contracts with Fujisawa Healthcare, Inc.

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The Authors Respond

We thank JMCP for the opportunity to comment on the letter by Ellis and colleagues in response to the recent publication of our study. We concur that it is difficult for patients to specifically ascribe their out-of-pocket costs to atopic dermatitis (AD). However, since our study showed that approximately 50% of the total burden of illness associated with AD resulted from days lost from work, it is most important that the patient’s perception of his or her illness, in addition to the health care provider’s perception, be taken into consideration. We admire Ellis et al.’s examination of 35,000 claims and understand their use of comorbidities in their evaluation, especially since one of the most common comorbidities in our population (occurring in approximately 8% of our prospective cohort) was “dermatitis not otherwise specified.” However, we too, examined the population over a 3-year period (n=6,609) and found mean annual per-patient direct expenditures ranging from $123 (in 1995) to $128 (in 1997). Therefore, the $167 per-patient-per-year direct expenditure we found would not appear to be an artifact of our relatively smaller sample size. Certainly, as we have found, it is important to directly query a representative sample of the dataset to gain an understanding of the error inherent in claims analyses.

Moreover, we used different insurance systems and not stan-
standard costs applied to health care resource use. The Ellis manuscript is not very transparent on how costs were attributed except that a panel determined it. They may have attributed costs to AD/E based on ICD-9 codes other than those we used. Furthermore, we most probably used a different method of assessing severity than the method used in the international study cited. Also, we included individuals with private insurance in our study; thus, our study population probably had different characteristics from the sample used in the ISAAC study. Therefore, it is difficult to compare our findings to those of Ellis et al.

Lastly, our previous analyses did attempt to quantify the effects of this illness on quality of life. Indeed, using Pearson correlation coefficients, we found that visit count correlated moderately well with the results of the Dermatology Life Quality Index ($r=0.33; P=0.0006$).

Taken together, all of our results, in concert with those of Ellis and colleagues, would indeed indicate that AD might impose a significant financial and humanistic burden on society.

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2. Arnold RJG, Kotsanos JG. Proceedings of the Advisory Panel Meeting and Conference on Pharmacoeconomic Issues: Panel 3: methodological issues in the international study cited. Also, we included individuals with private insurance in our study; thus, our study population probably had different characteristics from the sample used in the ISAAC study. Therefore, it is difficult to compare our findings to those of Ellis et al.

Dear Editor,

This letter is in response to the article on the relative cost-effectiveness of triptans by Dr. Adelman and Mr. Belsey that appeared in the January/February 2003 issue of JMCP. I believe their conclusions may be misleading because they are based on an oversimplified analysis of cost-effectiveness.

In order to calculate comparative triptan costs, the authors evaluated only 1 efficacy endpoint: the percentage of patients who were pain-free at 2 hours. Their rationale for focusing on this endpoint alone was that IHS guidelines identify the 2-hour pain-free endpoint as the most important endpoint and that patients have identified complete pain relief as their most important concern. However, patients rate “no recurrence of migraine” almost as high as they rate initial pain relief.

Furthermore, when doing a cost analysis, there is a need to focus on other endpoints. At a minimum, the total cost of treating a migraine attack for 24 hours (not just 2 hours) should be evaluated. Most patients who have a recurrence of moderate or severe migraine will remedicate with either a repeat dose of triptan or with another medication, thus increasing the overall 24-hour cost.

Recurrence rates from published double-blind studies range from 7% to 47%, depending on the particular triptan and study. The authors, based on an analysis of 2-hour pain-free response rates alone, suggest that rizatriptan (10 mg) is the most cost-effective triptan, but rizatriptan has been associated with recurrence rates in the 35% to 47% range. They also suggest, based on 2-hour pain-free response, that frovatriptan (2.5 mg) is the least cost-effective triptan; however, frovatriptan has lower recurrence rates in the 7% to 25% range.

Migraine recurrence is costly from a number of perspectives. A second or a third dose of a triptan (or other medication) taken within a single 24-hour period increases the “out-of-pocket” medication costs to patients and the reimbursement costs to insurers. Office visits and even emergency room visits may be required for particularly long-lasting, refractory attacks. Employers bear some of the costs from an extended migraine attack in the form of lost productivity. For most migraine sufferers, hours 3 through 24 of the attack (and beyond) can be more costly than the initial 2 hours in terms of both the financial and physical burden of migraine.

Variability in recurrence and remedication rates must be taken into account in order to obtain a reasonable estimate of triptan cost-effectiveness. If a single endpoint is to be used to calculate cost-effectiveness, the 24-hour response endpoint may be most appropriate. The impact of remedication as a result of recurrence is accounted for in measures of 24-hour sustained relief (moderate or severe pain reduced to no or mild pain with no recurrence or remedication within 24 hours) or 24-hour sustained pain freedom (moderate or severe pain reduced to no pain with no recurrence and no remedication). These endpoints.
are now recognized as the most important clinical and pharmacoeconomic endpoints.\textsuperscript{3}

Neither of these endpoints has been consistently reported in the clinical-trial literature.\textsuperscript{3,6} Two recent meta-analyses have attempted to evaluate them. In a meta-analysis of 24-hour sustained relief,\textsuperscript{3} only 3 of the currently marketed triptans (rizatriptan 10 mg, sumatriptan 50 mg and 100 mg, and zolmitriptan 5 mg) were included. At the time this meta-analysis was performed, the other triptans did not have published data available on sustained relief. In a separate meta-analysis that evaluated 24-hour sustained pain-free response, all but one of the triptans (frovatriptan) were included.\textsuperscript{6} However this endpoint could only be calculated for some of the 53 trials that were identified for the primary meta-analysis; the actual number of trials included is not reported. Therefore it would not be appropriate to make comparisons across the entire triptan class based on either of these meta-analyses.

It is currently not reasonable to undertake a single endpoint meta-analysis in order to determine relative cost-effectiveness of the triptans. In addition, the cost of adverse events should be included. Some triptans have higher adverse-event rates than others.\textsuperscript{7} A sensible approach to cost-effective migraine treatment requires stratification based on the patient’s migraine history and particular attack characteristics. Patients with short-duration migraine do well using triptans that deliver freedom from pain within 2 hours. Patients who are more susceptible to recurrence and adverse events might find it more cost effective to use triptans with less recurrence and fewer adverse events.

**References**


**The Authors Respond**

We thank Dr. Silberstein for his carefully constructed comments regarding our article on the relative cost-effectiveness of triptans.\textsuperscript{1} His criticism of the piece offers some interesting notes concerning the methodology of cost-effectiveness analyses.

Silberstein writes that our paper is “misleading” due to “an oversimplified analysis of cost-effectiveness.” His argument rests on 3 pivots: (a) the choosing of an inappropriate endpoint, (b) the excluding of recurrence rates, and (c) the ignoring of adverse events. Responding to these points will allow us to clarify our methodological motivations.

Silberstein criticizes the choice of the 2-hour pain-free endpoint, the industry standard. It does not take into account recurrence, the return of a moderate or severe headache within 24 hours.\textsuperscript{2} Recurrence, as Silberstein points out, is a persistent problem from the perspective of effectiveness of treatment as well as cost.

Recurrence data derived from randomized controlled trials should be used with caution. Although comparing recurrence rates appears to offer clinically useful information, the lack of a consistently used definition of recurrence invalidates such comparisons. Recurrence figures also tend to be derived from a selected subset of patients—those who initially responded to treatment—rather than the entire intention-to-treat population.\textsuperscript{3} The resultant corruption of randomization means that any conclusions will be prone to significant bias.\textsuperscript{3}

Silberstein suggests using the “24-hour sustained pain-free” endpoint instead of 2-hour pain free. We agree that the 24-hour data is a quality gauge of sustained migraine relief. We explained in the original paper, “The endpoint of ‘24-hour sustained pain free’ could also have been used in this meta-analysis. It would have produced data similar to the ‘pain-free’ data presented.”\textsuperscript{3} We based this statement on the strong correlation (\(R^2=0.89\)) for Ferrari’s meta-analysis\textsuperscript{5} between the 2 endpoints.

Unfortunately, sustained response only constitutes a primary outcome measure in a very small number of triptan studies. Estimates of these rates found in the literature generally relate to post hoc analyses of previously published data rather than results derived from primary data gathering.\textsuperscript{3} The potential for bias is therefore considerable.\textsuperscript{4} Although Ferrari’s analysis confirms a strong concordance between these 2 outcomes, when examining older studies, the 2-hour response offers the more statistically rigorous results.

Recently, Reeder conducted a cost-effectiveness study based on the 24-hour sustained pain-free endpoint, which confirmed our prediction of parallel cost-effectiveness for the 2 endpoints.\textsuperscript{6} In both studies, almotriptan and rizatriptan were the most cost effective, while naratriptan was the least cost effective (among the triptans included in both; frovatriptan did not have published 24-hour sustained pain-free data).

Reeder’s analysis indicates that sustained pain-free status depends more heavily on response than on recurrence. Lack of initial effect, therefore, would be expected to cause more multi-

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ple dosing than would recurrence. Pascual’s triptan per-attack study verifies this idea. His results indicate that rizatriptan, with its large response rates, has a significantly lower incidence of attacks treated with multiple tablets than does sumatriptan, zolmitriptan, and naratriptan in spite of relatively high recurrence rates.

Simply, recurrence is a poor endpoint. We would recommend that studies not report recurrence rates; instead, they should use 24-hour sustained pain relief or 24-hour sustained pain free to indicate the long-term efficacy of acute medications.

Like recurrence, adverse events were not included in the original analysis because they do not clarify or alter the cost-effectiveness of the medications. In addition, it would not have been statistically valid to include the measure in our analysis. No published triptan study has measured adverse events as a primary outcome. Although it is certainly possible to pool such data as exists in order to define a “number needed to harm,” inconsistent recording of adverse events and very wide confidence intervals mean that these findings are of limited value when comparing alternative treatments.

Triptans are consistently well tolerated. Most adverse effects are mild and have no related costs. Even the once-feared side effects of neck and chest tightness do not trigger cardiac evaluation as they once did. These side effects are not thought to be related to cardiac events.

There seems to be no correlation between the adverse effects and safety of triptans, nor is there any evidence of safety differences among triptans. The impact of side effects on cost is consequential compared to migraine disability considerations.

To conclude, we chose the 2-hour pain-free data because it was the industry standard, matched the desires of patients, mirrored 24-hour sustained pain-free results, and minimized the risk of introducing bias into our conclusions. Including recurrence rates and adverse events in the analysis would not have significantly altered the results, only added complicating factors.

Again, we thank Dr. Silberstein for his comments.

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Provider Perspective on HIPAA

Dear Editor,

I had some thoughts about the Health Insurance Portability and Accountability Act of 1996 (HIPAA) subsequent to the recent article1 and editorial1 in the Journal. There are real and presumably unintended consequences of the HIPAA statute and regulations.

I was looking for a new car. I decided to be patriotic and avoid German cars—the Russians and French long ago sinking into the oblivion of instant lemons—due to the antiwar stances being taken by our former enemies/charity recipients/allies. However, before I could leave the office, I had an inch-thick pile of HIPAA compliance policies and forms to review and frantic administrators calling in panic and fear about the impending invasion of trial lawyers and bureaucrats looking for HIPAA compliance gotchas over which to sue. Also, in the local paper, Los Angeles County announced it was closing a dozen or more primary care clinics to save money, while, in another article in a trade rag, there was mention of the fact that L.A. County had just announced it had signed agreements with consultants totaling $16 million to prepare the county for HIPAA. The more I thought, the more angry I became over the fed’s heavy-handed, dogmatic, and ignorant approach to confidentiality.

Here we are with literally hundreds of years of experience with the doctor-patient relationship and its spillover, and relatively stringent laws in almost every state governing the use and aftereffects of the federal mandates. Suddenly, I had a little empathy for the Germans. While I agree with our stance toward Iraq, I can’t help thinking that the Europeans’ complaints about Bush’s foreign policy sound all too familiar when walking the
hospital and health plan hallways. Unfortunately, we providers don’t have veto power over HIPAA at the United Nations.

While we chafe at the dictatorial approach of HIPAA, try to put HIPAA in perspective. In most states, HIPAA changes are bothersome, but they don’t need to be the huge and expensive problem some consultants are making it out to be. All HIPAA does is formalize what is being done, hopefully, in practice. Yes, it adds some costs and bureaucratic and unnecessary steps to the health care process, but common sense should still prevail. I think HIPAA really only requires a written notice of privacy practices that is available to patients, on the Web and in the facility or office or store; some kind of acknowledgment from the patient in writing, like signing a log book; care in the use of medical information and tracking its disclosure outside regular health care operations (meaning sending a bill to a payer is not trackable); and patient access to his or her record, with the right to request the ability to alter or comment on the record, which the provider doesn’t have to agree to.

There are stupid sides to HIPAA, like requiring a provider to obtain written privacy agreements from vendors who obtain protected information. They are already required to keep the information confidential, but we will waste millions of dollars nationwide in legal, printing, and postage costs just to comply with this make-work, unnecessary requirement. I guess I should get over it and feel sorry for the thousands of people in Los Angeles who have lost access to primary care while the county fattens the pockets of consultants and feels that it has somehow done something to protect patients’ privacy. I am sure the sick who show up at shuttered clinics will suddenly be cured knowing that if they can find a provider, their information will be protected.

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HIPAA on the Edge
Dear Editor,

My job takes me to many different types of health care settings. I have been painfully watching the HIPAA evolution in the places I visit. It spurs me to share a few stories.

Last month, I was in a local hospital. The hospital was challenged to figure out how to dispose of their used IV bags. Each IV bag is labeled with the patient’s name. Evidently, the local hospital association sent this hospital a news-flash informing them that they would be in violation of HIPAA if they simply threw the empty IV bag in the patient’s waste paper basket—a practice that has been done forever. Emptying the trash 3 times a day is simply not adequate anymore—absolute paradise for a HIPAA consultant!

Last week, one of my friends told me of a heated battle he observed in the academic medical center. Legal counsel had informed the medical staff that all specialists, unless they were the admitting physician, could not look at a patient’s chart until the patient had given informed consent. Yes, another potential HIPAA violation. Can you imagine a teaching hospital full of specialists who can’t look at a chart until the patient provides informed consent? HIPAA on the edge!

Closer to home, I am coordinating a 40-site, 4,000-patient benchmarking study. It involves a retrospective review of the patient’s medical record and data collection by a clinician who works in the study site. No patient-identifying information is transferred to me to perform the benchmarking—no name; no geographic subdivision of the patient’s address smaller than a state; no elements of date (birth, admission, discharge, initiation of therapy, etc.); and no identifying numbers (social security, medical record, prescriber number, etc.).

I coordinated a conference call earlier this week, and one site (and I am thankful it was only one) inquired about locating patients who had previously been discharged from the hospital to obtain informed consent to retrospectively review their medical record. The reason cited—HIPAA. Eeeeks, I quietly thought, HIPAA on the edge again—it has finally happened to me!

Quickly, though, I discovered the valuable HIPAA consultants—those other pharmacists on the conference call. They profoundly dismissed the notion that this practice would constitute a HIPAA violation. Their logic was as simple as one…two…three: (1) no patient identifying information, (2) the hospital’s own staff collecting the data, (3) therefore, no need for informed consent. Patient privacy can be a good thing—but not on the edge!

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