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Lack of cost-effectiveness of omalizumab

To the Editor:

As health care costs continue to be a subject of much discussion, analyses such as that published in the August issue of the *Journal*¹ are of great importance. Omalizumab is one of the first high-technology and high-expense therapies approved for atopic disease. Omalizumab is clearly not cost-effective in the patient populations studied. Oba and Salzman¹ might have demonstrated this more clearly by using different outcomes than those they employed.

It is recommended that to increase comparability between studies and between diseases, cost-effectiveness analyses report their results in terms of dollars per quality-adjusted life-year (QALY) gained.² However, for some chronic diseases like asthma that typically do not result in death, economic analyses have frequently reported cost-per-event-avoided endpoints. In fact, the majority of cost-effectiveness studies in asthma do not use a QALY measure but typically report a cost-per-event-avoided endpoint (in most cases, symptom-free day [SFD]). A recent cost-effectiveness analysis applied to an asthma clinical trial used SFDs.³ This is consistent with the recommendations of the National Institutes of Health's National Asthma Education and Prevention Program Task Force on the Cost-Effectiveness of Asthma Care.⁴

The 2 outcome measures that the authors employed were the Juniper Asthma Quality of Life Questionnaire and the successfully controlled day (SCD). Neither of these measures are recognized outcomes for cost-effective analyses purposes; thus, it is difficult to determine the true meaning of the results. It is of interest to observe that it takes approximately \$140,000 per year to improve the

Juniper Asthma Quality of Life Questionnaire value by 0.5 (which represents the minimal change that is clinically relevant); however, the comparable meaning of this is unclear. This figure cannot be directly compared to the cost per QALY (as the authors made the comparison), because only utility measures that are preference-based can be used to estimate quality-adjusted life expectancy.⁵ Thus, this comparison is like comparing apples and oranges. For the other outcome measure (SCD), it is also difficult to conceptualize the comparable meaning. The authors appropriately discuss the implications for using SCD and not SFD and suggest that the cost per SFD is likely higher than their results on the basis of SCDs. This is likely true; however, these nonstandard outcome measures decrease the external validity (generalizability) of their findings.

Other measures of morbidity prevented (cost per event avoided) could have been calculated in this analysis. Specifically, an incremental cost effectiveness ratio (ICER) could be calculated for the prevention of 1 unscheduled office visit, emergency department visit, and hospitalization. This calculation is obtained by dividing the difference in treatment costs by the difference in event rates.

Table I uses data presented by Oba and Salzman¹ and describes the event rates per person calculated by dividing the total number of events by the total patient years in each treatment group. The cost estimates are calculated for a 1-year period and are derived from Table II in the study by Oba and Salzman¹ (total yearly cost difference between omalizumab and placebo, \$14,505.40 – \$753.48 = \$13,751.92). The calculated ICERs per event saved over 1 year are displayed in Table I and demonstrate the striking lack of cost-effectiveness of omalizumab.

Another issue in this analysis is that omalizumab also is effective for allergic rhinitis. Because most patients with allergic asthma also experience allergic rhinitis, the specific ICERs calculated for asthma alone likely underestimate the true effect that omalizumab would have in these patients. However, this difference is unlikely to be large enough to make a difference in the overall conclusions.

A cost-effectiveness analysis incorporating a societal perspective rather than a third-party perspective would be more appropriate, although it may or may not result in a more favorable ICER. It might better describe the specific patient who should be considered for omalizumab therapy. At present, however, omalizumab is clearly not cost-effective in the patient populations in which it has thus far been studied. The groups identified by Oba and Salzman¹ in whom omalizumab might be considered (>5 hospitalizations per year; >7 emergency department visits per

TABLE I. Medical utilization event rates and ICER by event group over a period of 1 year

Event	Event rate (# events/total patient y)		Event rate difference	ICER per event prevented
	Omalizumab (+ICS)	Placebo (+ICS)		
Unscheduled office visit	0.1647 (85/516.2)	0.3195 (150/469.5)	0.1548	\$88,836.70
Emergency department visit	0.0116 (6/516.2)	0.0298 (14/469.5)	0.0182	\$755,600.00
Hospitalization	0.0039 (2/516.2)	0.0277 (13/469.5)	0.0238	\$577,811.80

month) are extremely rare in patient populations who are already on appropriate inhaled corticosteroid (ICS) therapy. These patients with severe disease would also never be placed on an aggressive ICS tapering schedule similar to that used in the studies.

The analysis by Oba and Salzman¹ is an excellent start in our discussion of these newer, very expensive therapies. Incorporating an ICER for morbidity prevented will add to our ability to value the specific intervention, especially because the approach of QALYs is seldom used in asthma studies. It would also be helpful if measures of cost-effectiveness could be incorporated into the early clinical studies for these expensive therapies. This would only minimally increase the cost of these early studies but might not result in findings that the marketing departments of the pharmaceutical companies would be pleased with. Perhaps the Food and Drug Administration should insist on a certain level of cost-effectiveness for new drugs before they are approved and marketed for diseases in which there are already good therapeutic alternatives available.

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Reply

To the Editor:

Miller and Reeves¹ question the validity of the outcome measures used in our study. These outcome measures were

carefully chosen according to previous studies and the current guidelines as described in our article, but at the same time, we were limited by the data available to us.

The reason we used the term *successfully controlled day* as a surrogate for *symptom-free day* was to avoid overestimating the cost-effectiveness of omalizumab. This outcome measure could be described as *near-symptom-free day*. Actually, the manufacturer reported this outcome measure as *asthma-free day*, which is a misnomer, as described in our article. This is still a valid outcome measure that is comparable to symptom-free day.

Many cost-effectiveness studies have used spirometric measures (eg, FEV₁ and peak expiratory flow) to define a treatment success. We used the Asthma Quality of Life Questionnaire (AQLQ) score to define a treatment success because it is extensively used in clinical studies and better represents the perspective of patients in how successfully their asthma is being treated than spirometric measures do. Health-related quality of life scores such as the AQLQ score should be incorporated into the economic evaluation.^{2,3} Our approach makes it possible to value intangible benefits such as improvement in AQLQ scores in a monetary sense. When a cost to achieve some improvement in a disease-specific quality of life score (eg, improvement in the AQLQ value by 0.5) with a new drug is far greater than the amount of money you would pay for a cure of a disease (willingness to pay), nobody would have a problem in determining the cost-effectiveness of the new drug.

Miller and Reeves¹ report incremental cost-effectiveness ratios for the prevention of unscheduled office visit, emergency department visit, and hospitalization. Their analysis underestimates the cost-effectiveness of this agent. Because these events can happen simultaneously and repeatedly in 1 patient, an incremental cost-effectiveness ratio should be calculated per individual, not per event prevented, to reflect the true effect of this agent better.

A cost-effectiveness analysis should be an aid to decision making rather than a decision-making process, and an absolute comment such as "the striking lack of cost-effectiveness of omalizumab" should be viewed with caution.⁴ Because cost-effectiveness is relative, interventions are better described as being more or less cost-effective than others, except when actually cost-saving, as suggested by Siegel et al.⁴

We agree with Miller and Reeves¹ that cost-effectiveness analysis should be incorporated into clinical studies, especially when a new intervention is expensive and expected benefits are modest. Maybe it is time for us to emulate the efforts of the cost-conscious National Health Service in the United Kingdom to ensure the best allocation of health care resources.

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