

Cost-effectiveness of inhaled corticosteroids in adults with mild-to-moderate asthma: Results from the Asthma Policy Model

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Background: Inhaled corticosteroids remain underused among United States–based clinicians in treating mild-to-moderate adult asthma.

Objective: The purpose of this investigation was to estimate the clinical impact, health-related quality of life, cost, and cost-effectiveness of inhaled corticosteroid therapy in a population of patients aged 18 years and over with FEV₁ = 60% to 100% of predicted normal.

Methods: We performed a cost-effectiveness analysis of quick relievers (eg, short-acting β -agonists) on an as-needed basis plus inhaled corticosteroid therapy versus quick relievers alone. A mathematical simulation model was developed to forecast symptoms, acute exacerbations, quality-adjusted life-years (QALYs), health care costs, and cost-effectiveness, measured in both dollars per QALY gained and dollars per symptom-free day gained. All evaluation outcomes were discounted at an annual rate of 3% and measured over a 10-year planning horizon. Data on the natural history of disease, drug efficacy, patient preferences, and economic costs were obtained from a variety of observational cohorts, randomized trials, and patient surveys.

Results: Over a 10-year period, use of inhaled corticosteroids increases total health costs from roughly \$5,200 to \$8,400 and improves QALYs from 6.8 to 7.0, implying an incremental cost of \$13,500 per QALY gained. Costs per symptom-free day gained are \$7.50. Both per-person acute exacerbations and hospitalizations are reduced by 33%. The cost-effectiveness findings are sensitive to the assumed efficacy and side-effects of inhaled corticosteroid therapy.

Conclusions: Inhaled corticosteroids appear to deliver good comparative value in adults with mild-to-moderate asthma. Although more research is needed to understand their impact on preferences regarding side effects and compliance, these findings might be useful for priority-setting in limited resource situations. (*J Allergy Clin Immunol* 2001;108:39-46.)

Key words: Asthma, inhaled corticosteroids, cost-effectiveness analysis, decision analysis, Markov models

The purposes of this investigation were to evaluate the cost-effectiveness of inhaled corticosteroid (ICS) therapy in mild-to-moderate adult asthma and to propose model-based analysis as an appropriate evaluation tool for that purpose. Several considerations make this a particularly timely investigation:

1. Asthma imposes a large and growing burden on society.¹ The estimated number of Americans with self-reported disease now exceeds 17 million, direct and productivity costs for the year 2000 being forecast to be \$8.1 and \$4.6 billion, respectively.²⁻⁴
2. Clinicians have an ever-expanding range of proven therapies. Numerous studies demonstrate that ICS can prevent symptoms, improve lung function, and reduce resource utilization.^{5,6}
3. Although various professional organizations have promulgated guidelines recommending ICS therapy in persistent asthma,⁷⁻¹⁰ United States–based clinicians have been slow to adopt it as standard of care in adult patients with mild-to-moderate disease.¹¹
4. Few US studies have evaluated the costs and consequences of adherence to recommended clinical practices—to our knowledge, no economic evaluations have been conducted in conformity with the recommendations of the United States Panel on Cost-Effectiveness in Health and Medicine¹²—and this lack of evidence might contribute to practice differences between American clinicians and their foreign counterparts.¹³

Economic evaluations will likely play an increasingly influential role in asthma patient care and resource allocation. Our aim is to familiarize clinicians with both the methods and findings of a model-based analysis.

METHODS

Analytic overview

We developed a mathematical simulation model to estimate clinical outcomes, health-related quality of life (HRQOL), and costs in

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Financial support for this study was provided by a grant from AstraZeneca to the Brigham and Women's Hospital. The funding agreement ensured the independence of the authors in designing the study, interpreting the data, and writing and publishing the report without prior approval. Dr Fuhlbrigge also received support from grant 1-K08 HL03919-01 from the National Heart Lung and Blood Institute, National Institutes of Health.

Received for publication November 27, 2000; revised April 2, 2001; accepted for publication April 2, 2001.

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0091-6749/2001 \$35.00 + 0 1/81/116289

doi:10.1067/mai.2001.116289

Abbreviations used

ED:	Emergency department
HRQOL:	Health-related quality of life
ICS:	Inhaled corticosteroid
NAEPP:	National Asthma Education and Prevention Program
QALM:	Quality-adjusted life-month
QALY:	Quality-adjusted life-year

a population of adults with asthma. The model was used to compare 2 therapeutic strategies for patients with mild-to-moderate disease: (1) quick relievers (eg, short-acting β -agonists) on an as-needed basis, and (2) quick relievers plus ICS therapy. In keeping with accepted methods for cost-effectiveness analysis, we adopted a societal perspective and measured value for money in terms of both dollars per quality-adjusted life-year (QALY) gained¹² and dollars per symptom-free day gained.¹⁴ We discounted all outcomes at 3% per year.¹² Monetary values are reported in 1998 US dollars, adjusted (when necessary) using the medical care component of the Consumer Price Index.¹⁵

The Asthma Policy Model

The Asthma Policy Model is a *Markov state-transition* simulation of asthma natural history.¹⁶ Disease is characterized as a sequence of transitions through a defined set of health states. At any given time, a patient is assigned to a single health state. Patients in a particular state are assumed to resemble one another in terms of clinical history and prognosis, risk of symptoms/exacerbations, perceptions of well-being, and resource utilization patterns. The following dimensions define the model's health states:

- Disease status (*chronic/stable*, *acute/hospitalization*, *dead*): The model distinguishes between stable illness and acute exacerbations. Further distinctions are made between exacerbations involving urgent care visits, exacerbations involving emergency department (ED) visits, and exacerbations involving hospitalizations.
- Lung function impairment (*mild*, *moderate*): Reduced airflow is a known predictor of symptoms, risk for exacerbation, and HRQOL.^{17,18} FEV₁ as a percent of predicted normal (FEV₁% predicted) is a useful, objective, reproducible marker¹⁹ that is endorsed as a disease severity measure in the National Asthma Education and Prevention Program's (NAEPP) *Guidelines for the Diagnosis and Management of Asthma*.⁷ We focus on patients with mild-to-moderate lung function impairment, using the NAEPP definitions of 2 FEV₁% predicted strata: mild (>80%) and moderate (60% to 80%).
- Prior hospitalizations (*none*, *one*, *more than one*): A history of asthma-related hospitalizations is associated with higher acute event rates and different clinical care patterns, resource consumption rates, HRQOL, and survival rates.²⁰⁻²²
- Patient age (*18-35 years*, *>35 years*): Age predicts exacerbation risks, response to therapy, and cost.^{23,24} We use 2 categories, 18-35 years and >35 years, to reflect background mortality differences and to avoid misclassification of chronic obstructive pulmonary disease among younger patients.
- Cause of death (*asthma-related*, *other causes*): The model records cause of death to reflect resource consumption patterns in the final months of life.

Although additional dimensions are possible (eg, sociodemographics, risk factors, and environmental exposures), data collection burdens and computational complexities increase exponentially with greater stratification.

Patients are initially assigned to health states on the basis of published distributions of lung function, prior hospitalizations, and age.^{25,26} Each month, a number of events might trigger assignment to a new health state. For example, each month the model "ages" every member of the population; individuals reaching their 35th year advance to the higher age stratum. Transitions might also reflect the onset of an exacerbation, an event requiring hospitalization, recovery from an acute event, or death.

Input data

Symptoms. To estimate the relationship between lung function and symptom-days, we performed a review of the clinical trial literature from 1966 to 1999 and identified 5 studies that reported FEV₁% predicted and frequency of days with symptoms in adults with asthma.²⁷⁻³¹ We observed a relationship between the change in lung function and the change in symptoms within each of the studies. Accordingly, we plotted the change in FEV₁% predicted versus the change in the logit of the percent of days with symptoms for each treatment arm of the 5 studies, each treatment arm being represented by a single line. The weighted (by number of patients) average of the slopes of the lines was -0.1550. We estimated an intercept term by minimizing the vertical distances between the lines determined by each intervention and the fitted line. The resultant relationship is as follows:

$$\% \text{ symptom-days} = 1/[1 + \exp(-12.5 + 0.1550 \times \text{FEV}_1\% \text{ predicted})] \times 100.$$

This regression equation was applied in the model to translate a given increase in FEV₁% predicted into a measurable reduction in the percent of days with symptoms.

Acute event incidence. Because the definition of *acute event* varies widely, we focused on the relationship between FEV₁% predicted and observed rates of ED use. We used a retrospective study that reported ED rate and mean FEV₁% predicted for 3 severity groups: mild, moderate, and severe.³² We assumed a logistic relationship to estimate the following logit risk function:

$$\text{ED rate} = 1/[1 + \exp(-2.1872 + 0.0560 \times \text{FEV}_1\% \text{ predicted})].$$

The overall rate estimated by this function was adjusted upward or downward depending on the history of prior hospitalizations (Table I). To then determine the number of acute exacerbations that resulted only in urgent-care visits, we made use of a local patient database that has previously been used for other peer-reviewed utilization studies.^{33,34} Specifically, we estimated the ratio of the number of urgent-care visits that do not result in an ED visit (or hospitalization) to the number of asthma-specific ED visits (assuming that all ED visits are the result of an exacerbation). These ratios, which were stratified by asthma severity and age group, ranged from 3.4 to 6.1. (Milder disease and older age were associated with higher ratios). We used the same database to estimate the proportion of all asthma-related ED visits that result in an admission to the hospital, stratified by asthma severity and age group. Patients with more severe disease and older age were more likely to be admitted to the hospital from the ED (proportions ranged from 0.17 to 0.32).

Effect of ICS therapy. To quantify the relationship between ICS therapy and change in FEV₁% predicted, we performed a MEDLINE search on the following terms: *randomized clinical trial*, *asthma*, *FEV₁* (or any one of the terms *forced expiratory volume*, *spirometry*, *pulmonary function*, *lung function*, or *respiratory function*), and *beclomethasone* (or any one of the terms *flunisolide*, *triamcinalone*, *budesonide*, or *fluticasone*.) Of 352 English-language articles retrieved, 76 were deemed appropriate for full review on the basis of the following criteria: (1) the investigation was a randomized controlled trial (studies in which either the intervention arm or the "placebo" group used continuous oral steroids or other controller therapies, such as leukotriene modifiers, cromolyn sodium, nedocromil, or long-acting β -agonists were excluded); (2) the inter-

TABLE I. Monthly acute event probabilities for adults with mild-to-moderate asthma

	Age (y)	FEV ₁ % predicted					
		No prior hospitalizations		1 prior hospitalization		>1 prior hospitalizations	
		>80	60-80	>80	60-80	>80	60-80
Non-ED urgent care visits	18-35	0.0113	0.0208	0.0149	0.0275	0.0249	0.0459
	35+	0.0141	0.0277	0.0186	0.0365	0.0310	0.0608
ED visits without hospitalization	18-35	0.0019	0.0046	0.0026	0.0061	0.0043	0.0102
	35+	0.0016	0.0042	0.0022	0.0056	0.0036	0.0093
Hospitalizations	18-35	0.0004	0.0015	0.0005	0.0020	0.0009	0.0034
	35+	0.0007	0.0020	0.0009	0.0026	0.0015	0.0044

Sources: (1) Thomas P, Ross RN, Farrar JR. A retrospective assessment of cost avoidance associated with the use of nedocromil sodium metered-dose inhaler in the treatment of patients with asthma. *Clin Ther* 1996;18:939-52. (2) Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA* 1997;277:887-91.

vention was an ICS (any of the 5 currently available in the US market); (3) subjects met the individual study's criteria for asthma diagnosis; and (4) FEV₁% predicted (or the data necessary to calculate it) was reported as an outcome. Sixteen studies, yielding 26 active treatment arms, met these criteria.^{29,31,35-48}

For each treatment arm, the effect of the intervention was expressed in terms of percent change in FEV₁% predicted relative to its baseline. We subtracted the change in FEV₁% predicted for the placebo group from the change in the FEV₁% predicted for the intervention group; this gave us the expected effect of a particular treatment relative to placebo. Because our purpose was to produce a summary efficacy estimate for the model, we calculated a mean change in FEV₁% predicted weighted by the number of study subjects (both for all studies combined and stratified by baseline lung function).

From this survey of the literature, we found that improvements in FEV₁% predicted ranged from 1% to 22% of the baseline value. Because the dose range in these studies was relatively narrow (none of the trials compared low-dose therapy with high-dose therapy) and the absolute improvement in FEV₁% predicted associated with the highest versus the lowest dose was negligible or small (0% to 3%), we assumed equivalency across dose ranges. We estimate that ICS therapy produces baseline relative increases in FEV₁% predicted of 7.6% for patients with mild disease and 11.6% for patients with moderate asthma. Mindful of the limitations of our approach, however, we explored efficacy values ranging from 1% to 22% in sensitivity analysis.

It should be noted that we assumed that the impact of therapy on an acute event was mediated entirely through lung function. No benefits independent of FEV₁ effect were assumed. Moreover, we assumed equivalency across all ICS preparations. Although the model can be used to simulate the effects of a given agent, our approach is consistent with the most recent version of the NAEPP guidelines (which acknowledge differences on a per-inhalation or microgram basis but do not currently define any implications of these differences for purposes of clinical dosing recommendations⁷).

Mortality. Because no published estimates of asthma mortality that were stratified by lung function could be located, age-specific death rates were applied across severity strata. Estimated monthly probabilities of asthma-related death were 10⁻⁵ for patients aged 18 through 35 years and 2.0 × 10⁻⁵ for patients over 35 years.⁴⁹ Non-asthma-related mortality rates were taken from the US life tables.⁵⁰

Costs. Costs were estimated from published resource utilization studies.⁵¹⁻⁵⁷ Baseline monthly chronic care costs (medications, routine office visits, laboratory testing) were \$35 and \$57 for patients with mild asthma and patients with moderate asthma, respectively. Acute event costs included \$63 for non-ED urgent care visits, \$242

for ED visits, and \$3,200 for hospitalizations. A \$38/month ICS drug cost was estimated from the manufacturer's reported number of inhalations per container, the average wholesale cost per container, and the estimated number of inhalations required to achieve the desired daily dose over 30 days.⁵⁸ Recognizing the demographic and clinical variation across studies, we explored the effects of varying costs by as much as 50% to 200% of their baseline values.

Quality of life. The US Panel on Cost-effectiveness in Health and Medicine recommends that community preferences for health states be used whenever feasible to value morbidity consequences.¹² However, the Panel acknowledges the difficulties of adhering to this recommendation and suggests various practical approximations. In the case of the relationship between lung function and values (utilities), published evidence is limited.^{59,60} No studies have considered a sufficiently rich set of symptomatic health states to be suitable for our use. Moreover, we know of no studies that have directly collected community-based preferences in asthma. We therefore chose to collect our own preference weights in a companion, cross-sectional study of 100 adults (≥18 years of age) with asthma in the Lexington, Kentucky, area.⁶¹ Data collection took place between November 1999 and January 2000. Inclusion criteria for all patients in the study were (1) drug therapy indicative of asthma in the pharmacy computer system and (2) self-report of asthma. Basic patient population characteristics included the following: female, 76%; white, 90%; and annual income below \$10,000 (\$20,000), 43% (60%).

Several instruments were administered to patients to obtain preference scores, including direct utility assessments with time trade-off (TTO), standard gamble, and rating scale questions,⁶² and multi-attribute utility scores via the Health Utilities Index⁶³ and the Asthma Symptom Utility Index.⁶⁰ For each patient, information was also collected on FEV₁% predicted. The relationship between FEV₁% predicted and preference scores was obtained separately for each preference assessment technique using ordinary least-squares regression. Our baseline analysis uses the TTO preferences (a choice that is consistent with the Panel's recommendations¹²) as given by the following function:

$$\text{TTO} = 0.521 + 0.003958 \times \text{FEV}_1\% \text{ predicted}$$

Cognizant of the small size and demographic homogeneity of our sample, we used preferences obtained using the other elicitation instruments (most notably, the community-weighted Health Utilities Index) for sensitivity analysis.

Disutility of ICS therapy. Documented side effects of ICS therapy in adults include dysphonia and thrush, cataracts and intraocular pressure, adrenal suppression, and the development of osteoporosis.

sis.⁶⁴⁻⁶⁶ There is concern that these weigh heavily in patients' and clinicians' decision making. In the absence of any data on the subject, we conducted a "what-if" analysis, the impact of side effects being modeled as an across-the-board percent reduction in the HRQOL adjustment value for any patient receiving ICS therapy, regardless of dose. The baseline value for this reduction was 0%; values up to 3% were considered in sensitivity analysis.

RESULTS

Natural history

Over a 10-year horizon, patients receiving quick relievers alone will live for an average of 81.2 quality-adjusted life-months (QALMs). Undiscounted and unadjusted for HRQOL effects, this equates to 110 months of life, with virtually all deaths attributable to non-asthma-related causes (Table II). The model predicts a population average of 36.7% symptom-days, 4.5 acute episodes per person over the 10-year period, and \$5,200 in per person, discounted, total direct costs. As expected, the model predicts more serious outcomes for patients with more severe disease. For example, a patient with mild asthma will experience 3.4 acute exacerbations and will incur costs of \$4,200 over a 10-year period; patients with moderate illness would be predicted to experience, on average, 7.4 acute exacerbations and incur \$7,800 in costs over the same period.

Cost-effectiveness of ICS

Addition of ICS increases discounted, quality-adjusted life over the 10-year planning period to 84.0 QALMs and costs to \$8,400. (Additional costs are almost all attributable to drug outlays.) Symptom-days are reduced to 21.7%, and the average patient experiences only 3.0 acute events. Compared with quick relievers alone, we estimate an incremental cost of \$13,500 per QALY gained and \$7.50 per additional symptom-free day.

Sensitivity analysis

To explore uncertainties in our results, we conducted a number of 1-way sensitivity analyses (wherein a single input parameter was varied over the range of plausible values). A selection of outputs from these efforts is presented in Fig 1. In most instances, the policy conclusions were robust over reasonable parameter uncertainty; there were some exceptions, however. Most notable among these was the effect of ICS efficacy. As the percent change in FEV₁% predicted was varied from 1% to 21%, the cost-effectiveness ratio ranged from \$5,000 to \$128,000 per QALY gained.

Most of the evidence used for this analysis relates to less than 5 years of data. To address concerns that our choice of a 10-year planning horizon was somewhat arbitrary and that our understanding of the natural events might not be strong enough to project beyond actual data, we also explored the results of the model over a shorter, 5-year planning horizon. Costs and effects were reduced roughly by one half. The resultant \$13,600/QALY ratio was virtually identical to the ratio obtained over the 10-year horizon.

Finally, we explored the impact of ICS side-effects by assuming an across-the-board, percentage decrement in

HRQOL. In the absence of side effects (ie, at 0% quality decrement), the baseline cost-effectiveness ratio was \$13,500/QALY. This value rose to \$19,200 at 1% decrement, \$33,200 at 2%, and \$121,700 at 3%. HRQOL decrements greater than 2.9% produced cost-effectiveness ratios exceeding \$100,000/QALY gained.

Targeted intervention

We considered 4 possible approaches to targeted intervention: (1) quick relievers alone ("No ICS"), (2) ICS targeted to patients with mild asthma ("Mild Only"), (3) ICS targeted to patients with moderate asthma ("Moderate Only"), and (4) the original intervention in which all patients receive ICS ("Mild and Moderate"). In keeping with accepted methods,¹² we arrayed results in order of increasing cost and eliminated from consideration any "dominated" strategies (ie, strategies that were more expensive and delivered fewer benefits than some other approach or combinations of approaches). As described in Table III, the "Mild Only" approach was dominated. We computed cost-effectiveness ratios for the remaining strategies. Compared with use of quick relievers alone, the Moderate Only strategy conferred additional QALYs at an incremental cost of \$10,300. In comparison with the "Moderate Only" strategy, scaling up to the "Mild and Moderate" approach had a cost-effectiveness ratio of \$15,000/QALY gained.

DISCUSSION

Although practice guidelines strongly endorse the use of ICS in mild-to-moderate adult asthma, United States-based clinicians vary in their adherence to these recommendations. To promote empirically based decision-making, we adopted a model-based framework to assemble the accumulated clinical, epidemiologic, and economic evidence on the subject.⁶⁷ Such an approach has been used successfully by collaborative teams of clinicians, epidemiologists, economists, and statisticians to guide policy decisions in other chronic conditions, including coronary heart disease,^{68,69} hypertension and hypercholesterolemia,^{70,71} Alzheimer's disease,⁷² AIDS,⁷³ acute nonlymphocytic leukemia,⁷⁴ gallstones,⁷⁵ and chronic lymphocytic leukemia.⁷⁶ However, we believe that ours is the first effort to apply these methods to the care of patients with asthma.

In contrast to the use of quick relievers alone, we estimate that ICS therapy confers benefits at an incremental cost of \$13,500/QALY (or \$7.50 per symptom-free day gained). Although targeting therapy first to patients with more severe lung function impairment might be most efficient, Table III suggests that even ICS intervention in adults with mild asthma compares favorably with a host of life-saving and health promotion alternatives in chronic disease. (Examples include the following: (1) ticlopidine vs aspirin in 65-year-olds with high risk of stroke, \$48,000/QALY; (2) chemotherapy vs no chemotherapy in 75-year-olds with breast cancer, \$58,000/QALY; and bypass surgery vs medical management in patients with moderate angina and triple vessel disease, \$30,000/QALY.⁷⁷) These findings

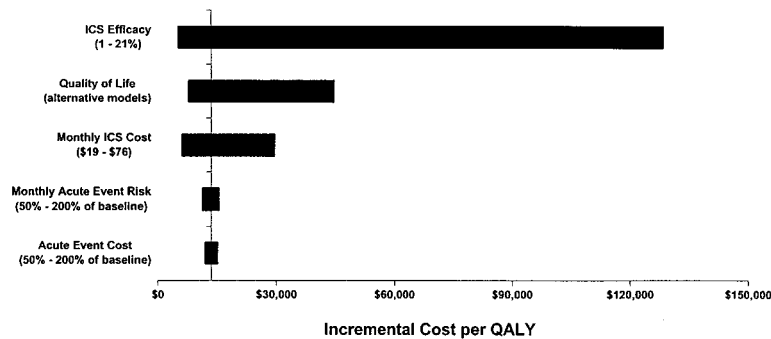


FIG 1. Incremental cost-effectiveness. A “tornado diagram” summarizes the results of a series of 1-way sensitivity analyses. Each horizontal bar represents a given model parameter. The vertical axis sits at the base-case incremental cost-effectiveness estimate (\$13,500/QALY). The length and position of a given horizontal bar denote the range of cost-effectiveness outcomes produced by varying that specific parameter over its plausible range.

TABLE II. Baseline clinical and cost-effectiveness results for adults with mild-to-moderate asthma

	No ICS	ICS
Average months of life	110.0	110.0
Asthma-related deaths/100,000/y	0.037	0.025
Non-asthma-related deaths/100,000/y	1700	1700
Percent symptom-days	36.7	21.7
Average no. of ED visits	0.55	0.37
Average no. of hospitalizations	0.21	0.14
Average no. of acute episodes	4.5	3.0
Discounted QALMs	81.2	84.0
Discounted symptom-days	1,051	622
Discounted chronic state costs (\$)	3,900	3,900
Discounted hospital costs (\$)	600	400
Discounted nonhospital acute event costs (\$)	700	500
Discounted drug costs (\$)	—	3,600
Discounted total costs (\$)	5,200	8,400
Cost per QALY gained (\$)*	—	13,500
Cost per symptom-free day gained (\$)	—	7.500

*Because of rounding, reported cost-effectiveness ratios might not be precisely equal to the ratio of costs and effects.

should be interpreted with some caution, however, inasmuch as they hinge on a number of uncertainties, most notably the efficacy of ICS therapy and its impact on patient perceptions of HRQOL. That efficacy should be the primary source of uncertainty makes intuitive sense, given both the variance that surrounds our baseline estimate and the fact that efficacy mediates both clinical and economic outcomes. We note that we have defined side effects crudely as an across-the-board reduction in HRQOL to represent the average decrement over the population. In reality, only a fraction of patients experience side effects. Better published data on the long-term adverse effects of ICS (especially osteoporosis and cataracts) and their impact on HRQOL would help clarify the importance of these considerations. Although we have conducted sensitivity analyses to explore the potential impact of across-the-board decrements in HRQOL due to the effects of therapy, we acknowledge that our findings in this regard are specula-

TABLE III. Sensitivity analysis: cost-effectiveness of targeted intervention for adults with mild-to-moderate asthma

Strategy	Cost (\$)	QALM	Cost per QALY* (\$)
1. No ICS	5,200	81.2	—
2. Moderate asthma only	6,000	82.1	10,300
3. Mild asthma only	7,600	83.1	Dominated†
4. Mild and moderate asthma	8,400	84.0	15,000

*All cost-effectiveness ratios are incremental compared with the next-least-costly, undominated alternative. Because of rounding, reported ratio might not be precisely equal to the ratio of costs and effects.

†A strategy is said to be *dominated* if an alternative allocation of resources can produce greater benefit at lower cost. Strategy 3 is dominated because a 40/60 allocation of resources to strategies 2 and 4 produces $(0.4 \times \$5,961) + (0.6 \times \$8,392) = \$7,420$ in costs and $(0.4 \times 82.08) + (0.6 \times 84.02) = 83.24$ QALMs.

tive. They provide thresholds for the *average* HRQOL decrements that would be required to produce a material change in the cost-effectiveness of ICS therapy. They do not reflect the HRQOL experienced by those persons suffering side effects. Finally, we have assembled cost data from a variety of sources, reflecting different patient populations and particular size, quality, and design limitations.

These cautionary notes notwithstanding, our results suggest that ICS therapy delivers good value and is an appropriate use of scarce resources. However, the present analysis is only a first step. It is our intention to continue to refine the model to explore questions that—given both the inevitability of difficult choices and severe time, data, and financial constraints—only a simulation-based approach can currently address. These include: Which steroid ought to be the first choice? Are combination products cost-effective in comparison with single agent controllers? Do results change materially when attention is focused on children or switched to the European setting? Are leukotriene additivity, disease management, and/or patient education cost-effective? What are the incremental effects of specialist versus generalist care? How much more cost-effective

would ICS therapy be if the substantial time and productivity losses of adult asthma were included in the analysis? By providing a formal evaluation framework, we believe that the Asthma Policy Model offers a new tool in setting priorities in asthma patient care.

We gratefully acknowledge the help of colleagues at AstraZeneca, including Drs Fredrik Andersson, Gillian Black-Noller, Evi Hatzianandreu, and Edwin Hedblom. We thank our project research assistant, Ms Jody Wilson. We are also indebted to the members of our International Project Advisory Panel, including Drs Harry Burns, Tommy Ekstrom, Dirkje Postma, Klaus Rabe, and Kevin Weiss.

GLOSSARY^{12,78,79}

Markov model. A decision-analytic framework that characterizes the prognosis of a cohort of patients by assigning them to a fixed number of health states and modeling transitions among those states.

Quality-adjusted life-years (QALYs). A health outcome measure that combines quality of life, as determined by some valuation process (eg, time tradeoff [see below]), and length of life. One year in perfect health equals 1 QALY or 12 **quality-adjusted life-months (QALMs)**. One year in a health state that is rated by the patient as 40% of perfect health equals 0.4 QALY (or 4.8 QALMs).

Cost-effectiveness ratio. The added cost of attaining a unit of health effect. The numerator represents the cost difference between the health care intervention and its alternative, whereas the denominator is the difference in health effect (ie, clinical or quality of life outcome), measured in natural units, between the intervention and its alternative. In this study, cost-effectiveness ratios are reported in cost per QALY and cost per symptom-free day.

Time tradeoff (TTO). A quality of life (utility) measure derived by asking patients a series of questions; the responses result in an expression of the value of time spent in the current health state in terms of time spent in perfect health.

Direct cost. The value of all goods, services, and other resources that are consumed in the provision of an intervention or in dealing with the side effects or other current and future consequences linked to it.

Indirect costs (also known as *productivity costs*). The value of lost time or reduced productivity resulting from morbidity or premature mortality due to a medical condition or treatment as well as the value of informal care-giving costs.

Annual discount rate. The rate used to convert both future costs and future health effects to their present values.

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Appendix: How the Asthma Policy Model works

A.1 OVERVIEW

This appendix introduces the mechanics of the current version of the Asthma Policy Model and illustrates its capabilities, limitations, input data requirements, computations, and output formats. The intent is to acquaint the reader with all of the following:

- the various components of the spreadsheet implementation
- how data and events are recorded
- the computations used to translate input data into usable output
- how the model can be used to evaluate interventions and to ask “what-if” questions
- sample output formats.

A.2 THE SPREADSHEET

The model comprises 8 linked worksheets: *Decision*, *Input*, *Severity*, *Exacerbations*, *Cost-QoL*, *Transition*, *Tally*, and *Results*. The first 5 of these worksheets contain and manage user-specified decision variables and input data. It is by means of these worksheets that the user can record data, specify scenarios, and explore the effects of alternative assumptions and parameter values. All blue-shaded cells in these worksheets can be modified by the user. The remaining 3 worksheets perform the necessary computations to produce and report results.

This section describes and illustrates each of the 8 worksheets.

A.2.1 Worksheet 1: *Decision*

This worksheet (Fig A1) summarizes basic decision variable settings and assumptions about the costs and effects of intervention. The user can supply or alter information regarding the implementation, efficacy, and cost of either therapy or education programs for patients at any or all of 4 levels of disease severity.

The various parameters in the worksheet are defined as follows:

Yes/no. Assumes a value of 1 if the intervention is provided to patients in a particular disease severity level; assumes a value of 0 otherwise. (For the example presented in Fig A1, the intervention is set to be implemented for patients with Mild-Persistent and Moderate disease.)

Efficacy—disease progress. Represents the efficacy of the intervention as a percent reduction in the rate of disease progression. (Because it is assumed that Education interventions cannot alter disease progression, the user is not permitted to assign a value to this parameter. The cells representing this kind of efficacy are assigned a value of *n/a*.)

Efficacy—acute events. Represents the efficacy of the intervention as a percent reduction in the incidence of acute exacerbations.

Efficacy—downstream utilization. Represents the efficacy of the drug as a percent reduction in the likelihood that a given exacerbation will result in further resource consumption, such as an emergency department (ED) visit, urgent care visit, or hospitalization. (Because it is assumed that drug therapy interventions cannot directly alter downstream utilization, the user is not permitted to assign a value to this parameter. The cells representing this kind of efficacy are assigned a value of *n/a*.)

Efficacy—FEV increase. Represents the efficacy of the drug as a percent improvement in FEV level. (Because it is assumed that Education interventions cannot alter disease progression, the user is not permitted to assign a value to this parameter. The cells representing this kind of efficacy are assigned a value of *n/a*.) In Fig A1 the intervention is set to produce FEV increases of 7.6% and 11.63% in patients with Mild-Persistent and Moderate disease, respectively.

Monthly cost. Represents the monthly, per patient cost of the intervention, as specified by the user. (In Fig A1 the intervention is set to cost \$38 per month.)

Discount. Represents the annual rate at which all costs and consequences are discounted in the model to account for time preference. This value is set to 3% per annum in Fig A1.

A.2.2 Worksheet 2: *Input*

This worksheet (Fig A2) records assumptions about the progress of disease and the likelihood of various clinical events. The parameters in the worksheet are defined as follows:

Smoking. Represents the likelihood (measured in probability values between 0 and 1), as specified by the user, that a given patient will change his or her smoking status in a given month.

Aging. Represents the monthly probability of transition from one age stratum in the model to another. Data in these fields are fixed by the age strata used in the model and should not be changed unless new strata are defined.

Disease progression. Represents monthly rates of progression from one disease severity level to another. The sample provided above assumes no disease progression. Hence the probability of remaining in a given severity level from one month to the next is set to 1; all other values are set to 0.

Death probabilities. Represents the monthly likelihoods of asthma-related and non-asthma-related death. Non-asthma-related deaths are stratified by age and smoking behavior; asthma-related deaths are stratified by age and disease severity level. This part of the sheet also includes fields to assign costs to the various causes of death.

Initial population distribution. Denotes the severity, disease history, age, and smoking distribution of the population entering the model. This makes it possible for the user to determine the breadth of the population cohort to be examined.

BASIC DECISION PARAMETERS		EFFICACY			
Therapy		Disease progression yes/no	Acute Downstream events	Utiliza Increase	FEV Monthly Costs
	<i>mild</i>	0 0.00%	0 0.0%	n/a	0 0.0%
	<i>mild-pers</i>	1 0.00%	0 0.0%	n/a	7 6.6%
	<i>moderate</i>	1 0.00%	0 0.0%	n/a	11 6.3%
	<i>severe</i>	0 0.00%	0 0.0%	n/a	0 0.0%
Education					
	<i>mild</i>	0 n/a	0 0.0%	0 0.0%	n/a
	<i>mild-pers</i>	0 n/a	0 0.0%	0 0.0%	n/a
	<i>moderate</i>	0 n/a	0 0.0%	0 0.0%	n/a
	<i>severe</i>	0 n/a	0 0.0%	0 0.0%	n/a
Discount rate		3.00%			

FIG A1. Worksheet 1: *Decision*.

CLINICAL INPUT DATA ADOXA

1) Smoking Behaviour

Probability that non-smoker begins smoking

Probability that smoker quits

2) Ageing

3 age net

SDS

3) Disease progression rate

ADJUSTED FOR DIRECT PROGRAM EFFECTS
ON DISEASE PROGRESSION RATES

ADJUSTED FOR DIRECT PROGRAM EFFECTS
ON DISEASE PROGRESSION RATES

4) Deaths

Non-oncath-related death probabilities

Non-oncath-related death counts

(He may want to break these out by smoking and age)

Acute event-related death probability

Acute event-related death counts

5) Initial population distribution

Used to assign the population to the various states at time =0

6) X days and nights with symptoms

% days

% nights

Effective

Mean, STD

FIG A2. Worksheet 2: *Input*.

Severity	Classification and assumed FEV levels			
				Effective
Stratum Number	Stratum Name	FEV Category	Mean FEV	Mean FEV
1	<i>Incipient</i>	???	100	100
2	<i>Mild</i>	>80	90	96.836
3	<i>Moderate</i>	60-80	70	78.1383
4	<i>Severe</i>	<60	50	50

FIG A3. Worksheet 3: *Severity*.

% days and nights with symptoms. Represents the symptom rates assigned to a given FEV level. Although these values can be adjusted directly by the user, the current values are computed from the risk equations for FEV and symptom-days and symptom nights. The Effective mean FEV figure comes from the Severity worksheet (see below).

A.2.3 Worksheet 3: *Severity*

This worksheet (Fig A3) records assumptions about disease severity and how this translates into a mean FEV level. The user controls the Mean FEV level in a given severity stratum. The “effective mean FEV” is then obtained by adjusting the Mean FEV level upward to

reflect the user's assumption (in the *Decision* worksheet) about the impact of intervention. (In the example provided here, the intervention is directed only at patients with Mild and Moderate disease. Thus, the Effective FEV value for these 2 severity levels is improved by 7.6% and 11.63%, respectively; there is no change in the Effective Mean FEV for patients with Incipient or Severe disease.)

A.2.4 Worksheet 4: *Exacerbation*

The purpose of this worksheet (Fig A4) is to produce acute event probabilities, stratified by patient age, disease severity, smoking behavior, and prior acute event history. Unfortunately, the literature does not provide such data in the form required by the model. To generate the input data in the form that we need, we begin with observed rates of ED use among patients with asthma and then adjust upward or downward depending on patients' histories of prior hospitalizations. To then determine the number of acute exacerbations that result only in an urgent-care visit, we make use of a local patient database to estimate the ratio of the number of urgent-care visits that do not result in an ED visit (or hospitalization) to the number of asthma-specific ED visits (assuming that all ED visits are the result of an exacerbation). We use the same database to estimate the proportion of all asthma-related ED visits that result in an admission to the hospital. The input data fields are as follows:

AE₀ factor: This is a ratio comparing the number of exacerbations that do not result in an ED visit or hospitalization to the number of exacerbations that do include an ED visit or hospitalization.

Probability of hospitalization (given ED visit). This is the conditional probability that an ED visit will result in hospitalization.

Acute event pathway probabilities. These values are computed from the AE_0 values specified in step 1 and are not available for user specification.

ED visit (hosp and non-hosp) probabilities. The user may specify ED likelihoods here. The values currently in the spreadsheet are based on our preliminary studies to estimate risk equations relating disease severity to ED visit rates. In this section of the worksheet, users may also choose a “multiplier” to denote the additional risk posed by smoking.

Prior event multipliers. This represents the additional risk of exacerbation posed by a prior history of acute exacerbations.

A.2.5 Worksheet 5: *Cost-QoL* [not shown]

In this worksheet, the user may define state-specific quality of life and cost levels. The quality adjustment levels are intended to reflect preferences for various health states, with 1 denoting states equivalent to perfect health and 0 representing states equivalent to death. In the current version of the model, users can assign a quality adjustment value to each of the 4 disease severity levels. This value can then be further adjusted on the basis of both the assumed toxicity of therapy and/or the assumed disutility associated with hospitalization. Once these val-

ues are specified, the model proceeds to assign a utility to each of the 123 health states.

This spreadsheet also invites the user to specify severity-, age-, and event-specific resource consumption costs. These are assigned to individual states in the same manner as the quality of life adjustments just described.

Together, worksheets 1 through 5 contain all the input data required by the analysis. The remaining worksheets manage and transform this data into usable output.

A.2.6 Worksheet 6: *Transition* [not shown]

The flows of patients into and out of each of the health states in the model can be formalized as a sequence of state-to-state transitions. This worksheet summarizes the input data and calculations into a “transition probability matrix,” a 123×123 matrix whose entries govern these flows. The cell in row i and column j of this matrix contains the monthly probability of a transition from health state i to state j . There are several things to note about this matrix:

- Because each row in this matrix denotes a set of mutually exclusive and collectively exhaustive events, the entries in each row must sum to 1.
- Most of the entries in the matrix are assigned a value of 0. In many instances, these denote transitions that cannot logically occur. (For example, a patient cannot logically progress from having a history of 2 prior acute events to having a history of 0 prior events.)
- Because death is a “trapping” state, all death state rows assign a value of 1 to the likelihood that the individual will remain in that state.

A.2.7 Worksheet 7: *Tally* [not shown]

This worksheet is where the work of the model is done. Each row represents a month. The first row represents time 0. At time 0, an initial population of 100,000 patients are distributed across various ages, severity levels, and smoking behaviors, in keeping with the initial population distributions specified in the Input sheet. Using the transition probability matrix as its guide, the worksheet then proceeds to keep a running tally of population levels, resource consumption, life years, and quality-adjusted life years as they accrue:

- Column B keeps track of the time, from month 0 to month 120.
- Columns C through DU record the population level in each of the 123 model compartments.
- Columns DW through EI report life-months in various sectors and under various quality adjustment and discount factors.
- Columns EJ through ES track important patient events, such as symptoms-days, symptom-nights, hospitalizations, and ER visits.
- Columns ET through FF track resource consumption in various sectors and under various discount factors.
- Column FG monitors the discount rate.

The population cohort is followed for 10 years. The final row (row 128) computes totals and averages. This is

ACUTE EXACERBATIONS CALCULATIONS											
1) "AED Factor"		This figure represents the ratio of exacerbations with an ER or hospitalization vs. exacerbations that include an ER visit or hospitalization									
	Severity										
Age		mild	moderate	severe							
1	0	0.45	0.45	0.45							
2	0	0.45	0.45	0.45							
3	0	0.45	0.45	0.45							
2) Probability of hospitalization (given ER visit)											
	Severity										
Age		mild	moderate	severe							
1	0	0.27	0.27	0.27							
2	0	0.27	0.27	0.27							
3	0	0.27	0.27	0.27							
3) Computed acute event pathway probabilities		These are conditional probabilities of various pathways given that an acute exacerbation takes									
N Recent Visits											
	Severity										
Age		mild	moderate	severe	place						
1	0	0.00	0.00	0.00	0.00						
2	0	0.00	0.00	0.00	0.00						
3	0	0.00	0.00	0.00	0.00						
N ER/hosp											
	Severity										
Age		mild	moderate	severe							
1	0	0.00	0.00	0.00							
2	0	0.00	0.00	0.00							
3	0	0.00	0.00	0.00							
N ER only											
	Severity										
Age		mild	moderate	severe							
1	0	0.00	0.00	0.00							
2	0	0.00	0.00	0.00							
3	0	0.00	0.00	0.00							
4) ER visit (hosp and non-hosp) probabilities											
Non-Smoker											
	Severity										
Age		mild	moderate	severe							
1	0	0.0045	0.0173	0.0447							
2	0	0.0045	0.0173	0.0447							
3	0	0.0045	0.0173	0.0447							
Smoker											
	Severity										
Age		mild	moderate	severe							
1	0	0.0112	0.0433	0.1118							
2	0	0.0112	0.0433	0.1118							
3	0	0.0112	0.0433	0.1118							
Elixhauser Mean PEY		100	97	78	50						
Elixhauser Multipliers		0	1.43	2.07	1.55						
Smoker Multiplier		2.500									
ADJUSTED FOR DIRECT PROGRAM EFFECTS ON EXACERBATION RATES											
Non-Smoker											
	Severity										
Age		mild	moderate	severe							
1	0	0.0045	0.0173	0.0447							
2	0	0.0045	0.0173	0.0447							
3	0	0.0045	0.0173	0.0447							
Smoker											
	Severity										
Age		mild	moderate	severe							
1	0	0.0112	0.0433	0.1118							
2	0	0.0112	0.0433	0.1118							
3	0	0.0112	0.0433	0.1118							
6) Prior event multipliers											
	Prior hospitalizations										
Age		1	2								
1	0	0.729645	0.974331	1.627219							
2	0	0.729645	0.974331	1.627219							
3	0	0.729645	0.974331	1.627219							

FIG A4. Worksheet 4: *Exacerbation*.

the source for the performance statistics reported in the Results section of the spreadsheet.

A.2.8 Worksheet 8: *Results*

This worksheet collects values from the Tally sheet to report on average survival, quality-adjusted survival, time spent in various health states, symptom-days and symptom-nights, and costs for the current parameter settings. These results are tabulated along with comparative cost-effectiveness statistics.

Examples of the *Results* worksheet format are contained in the illustrative analyses that follow.

A.3 ILLUSTRATIVE ANALYSES

What follows is a series of illustrative analyses designed to demonstrate the model's ability to explore alternative assumptions, test a variety of parameter choices, and entertain “what-if” type questions.

A.3.1 Scenario 1: *Natural history*

This first scenario reports the costs and consequences of allowing the disease to run its course without any interventions. All “yes/no” variables in the Decision worksheet are set to 0, and we consider only patients with mild and moderate disease. Other input parameters are assigned the default values that they assume in the illustrative tables presented above.

The results are shown in Fig A5. Over a 120-month planning horizon, patients receiving no additional inter-

SUMMARY RESULTS			CEA RESULTS		
	Current	Base	Net discounted costs	\$	
Undiscounted Life Years	5,17	5,17	Net discounted life-years	-	
Discounted Life Years	7,95	7,95	Net discounted QALYs	-	
Discounted QALMs	81,18	81,18	Symptom-days averted	-	
Discounted Symptom Days	1,851	1,851	Symptom nights averted	-	
Discounted Symptom Nights	462	462			
Discounted Chronic State Costs	\$ 3,888	\$ 3,888	CostLY	18,518	
Discounted Hospital State Costs	\$ 594	\$ 594	CostQALY	18,518	
Discounted Non Resp AE Costs	\$ 782	\$ 782	CostSymptom Day averted	18,518	
Discounted Death Costs	\$ -	\$ -	CostSymptom Night averted	18,518	
Discounted Information Costs	\$ -	\$ -			
Discounted Total Cost	\$ 5,165	\$ 5,165			
			Current	Base	
% time in Severity level 1	0.88%	0.88%	while in severity level 1	4.2%	4.2%
% time in Severity level 2	22.68%	22.68%	while in severity level 2	19.88%	19.88%
% time in Severity level 3	27.32%	27.32%	while in severity level 3	83.88%	83.88%
% time in Severity level 4	0.88%	0.88%	while in severity level 4	99.14%	99.14%
% time in chronic sector	99.81%	99.81%	% symptom nights	14.88%	14.88%
% time in hospital sector	0.19%	0.19%	while in severity level 1	1.17%	1.17%
Lifetime acute episodes (undiscounted)	4.47	4.47	while in severity level 2	4.33%	4.33%
while in severity level 1	-	-	while in severity level 3	39.94%	39.94%
while in severity level 2	2.46	2.46	while in severity level 4	98.72%	98.72%
while in severity level 3	2.82	2.82	Asthma related deaths per 100,000	0.37	0.37
while in severity level 4	-	-	acute events	8.47	8.47
Lifetime hospitalizations (undiscounted)	0.21	0.21	ER visits	8.55	8.55
while in severity level 1	-	-	hospitalizations	8.21	8.21
while in severity level 2	0.09	0.09	Non-asthma related deaths per 100,000	16,591	16,591
while in severity level 3	0.12	0.12			
while in severity level 4	-	-			

FIG A5. Worksheet 8: Natural history results.

SUMMARY RESULTS			CEA RESULTS		
	Current	Base	Net discounted costs	\$	(88)
Undiscounted Life Years	5,17	5,17	Net discounted life-years	8,88	
Discounted Life Years	7,95	7,95	Net discounted QALYs	8,218	
Discounted QALMs	81,18	81,18	Symptom-days averted	428	
Discounted Symptom Days	622	1,851	Symptom nights averted	223	
Discounted Symptom Nights	159	462			
Discounted Chronic State Costs	\$ 3,888	\$ 3,888	CostLY	Cost saving	
Discounted Hospital State Costs	\$ 401	\$ 594	CostQALY	Cost saving	
Discounted Non Resp AE Costs	\$ 426	\$ 782	CostSymptom Day averted	Cost saving	
Discounted Death Costs	\$ -	\$ -	CostSymptom Night averted	Cost saving	
Discounted Information Costs	\$ -	\$ -			
Discounted Total Cost	\$ 4,708	\$ 5,165			
			Current	Base	
% time in Severity level 1	0.88%	0.88%	while in severity level 1	4.2%	4.2%
% time in Severity level 2	22.68%	22.68%	while in severity level 2	19.88%	19.88%
% time in Severity level 3	27.32%	27.32%	while in severity level 3	83.88%	83.88%
% time in Severity level 4	0.88%	0.88%	while in severity level 4	99.14%	99.14%
% time in chronic sector	99.81%	99.81%	% symptom nights	14.88%	14.88%
% time in hospital sector	0.19%	0.19%	while in severity level 1	1.17%	1.17%
Lifetime acute episodes (undiscounted)	3.83	4.47	while in severity level 2	4.33%	4.33%
while in severity level 1	-	-	while in severity level 3	39.94%	39.94%
while in severity level 2	1.18	2.46	while in severity level 4	98.72%	98.72%
while in severity level 3	5.33	2.82	Asthma related deaths per 100,000	0.26	0.37
while in severity level 4	-	-	acute events	3.83	8.47
Lifetime hospitalizations (undiscounted)	0.14	0.21	ER visits	8.37	8.55
while in severity level 1	-	-	hospitalizations	8.14	8.21
while in severity level 2	0.07	0.09	Non-asthma related deaths per 100,000	16,591	16,591
while in severity level 3	0.08	0.12			
while in severity level 4	-	-			

FIG A6. Worksheet 8: Perfect drug results.

vention enjoy an average of 81.2 quality-adjusted life-months (QALMs). Undiscounted and unadjusted for health-related quality of life effects, this equates to 110 months of life, virtually all deaths being attributable to non-asthma-related causes. The model predicts a population average of 36.7% symptom-days, 14.1% symptom-nights, 4.5 acute episodes per person over the 10-year period, and \$5,200 in per-person discounted, total direct costs. (Users who change the initial population parameters in the *Input* worksheet will find that, as one might expect, the model predicts more serious outcomes for patients with more severe disease. For example, a population composed entirely of patients with mild asthma will experience an average of 3.4 acute exacerbations and will incur costs of \$4,200 over a 10-year period, whereas a population of patients with moderate illness would be predicted to experience, on average, 7.4 acute exacerbations and to incur \$7,800 in costs over the same period.)

A.3.2 Scenario 2: A perfect drug

Consider a cost-free, zero-toxicity drug that is 100% effective in preventing acute exacerbations. (To create such a scenario, set all therapy “yes/no” variables in the *Decision* worksheet equal to 1, set the Acute Event Efficacy parameters to 100%, and set the costs to \$0.) Results for this “best-case” scenario are reported in Fig A6. Although this “perfect” drug saves money and prolongs life, the absolute survival gain is small, amounting

SUMMARY RESULTS			CEA RESULTS		
	Current	Base	Net discounted costs	\$	3,287
Undiscounted Life Years	5,17	5,17	Net discounted life-years	8,88	
Discounted Life Years	7,95	7,95	Net discounted QALYs	8,218	
Discounted QALMs	81,18	81,18	Symptom-days averted	428	
Discounted Symptom Days	622	1,851	Symptom nights averted	223	
Discounted Symptom Nights	159	462			
Discounted Chronic State Costs	\$ 3,888	\$ 3,888	CostLY	71,430,844	
Discounted Hospital State Costs	\$ 401	\$ 594	CostQALY	13,529	
Discounted Non Resp AE Costs	\$ 426	\$ 782	CostSymptom Day averted	7,48	
Discounted Death Costs	\$ -	\$ -	CostSymptom Night averted	14,28	
Discounted Information Costs	\$ -	\$ -			
Discounted Total Cost	\$ 8,382	\$ 5,165			
			Current	Base	
% time in Severity level 1	0.88%	0.88%	while in severity level 1	4.2%	4.2%
% time in Severity level 2	22.68%	22.68%	while in severity level 2	19.88%	19.88%
% time in Severity level 3	27.32%	27.32%	while in severity level 3	83.88%	83.88%
% time in Severity level 4	0.88%	0.88%	while in severity level 4	99.14%	99.14%
% time in chronic sector	99.81%	99.81%	% symptom nights	14.88%	14.88%
% time in hospital sector	0.19%	0.19%	while in severity level 1	1.17%	1.17%
Lifetime acute episodes (undiscounted)	3.83	4.47	while in severity level 2	4.33%	4.33%
while in severity level 1	-	-	while in severity level 3	39.94%	39.94%
while in severity level 2	1.18	2.46	while in severity level 4	98.72%	98.72%
while in severity level 3	5.33	2.82	Asthma related deaths per 100,000	0.26	0.37
while in severity level 4	-	-	acute events	3.83	8.47
Lifetime hospitalizations (undiscounted)	0.14	0.21	ER visits	8.37	8.55
while in severity level 1	-	-	hospitalizations	8.14	8.21
while in severity level 2	0.07	0.09	Non-asthma related deaths per 100,000	16,591	16,591
while in severity level 3	0.08	0.12			
while in severity level 4	-	-			

FIG A7. Worksheet 8: Inhaled corticosteroid results.

SUMMARY RESULTS			CEA RESULTS		
	Current	Base	Net discounted costs	\$	778
Undiscounted Life Years	5,17	5,17	Net discounted life-years	8,88	
Discounted Life Years	7,95	7,95	Net discounted QALYs	8,218	
Discounted QALMs	81,18	81,18	Symptom-days averted	198	
Discounted Symptom Days	851	1,851	Symptom nights averted	128	
Discounted Symptom Nights	217	462			
Discounted Chronic State Costs	\$ 3,888	\$ 3,888	CostLY	35,684,449	
Discounted Hospital State Costs	\$ 401	\$ 594	CostQALY	15,129	
Discounted Non Resp AE Costs	\$ 588	\$ 782	CostSymptom Day averted	6,88	
Discounted Death Costs	\$ -	\$ -	CostSymptom Night averted	4,57	
Discounted Information Costs	\$ -	\$ -			
Discounted Total Cost	\$ 5,961	\$ 5,165			
			Current	Base	
% time in Severity level 1	0.88%	0.88%	while in severity level 1	4.2%	4.2%
% time in Severity level 2	22.68%	22.68%	while in severity level 2	19.88%	19.88%
% time in Severity level 3	27.32%	27.32%	while in severity level 3	83.88%	83.88%
% time in Severity level 4	0.88%	0.88%	while in severity level 4	99.14%	99.14%
% time in chronic sector	99.81%	99.81%	% symptom nights	14.88%	14.88%
% time in hospital sector	0.19%	0.19%	while in severity level 1	1.17%	1.17%
Lifetime acute episodes (undiscounted)	3.79	4.47	while in severity level 2	4.33%	4.33%
while in severity level 1	-	-	while in severity level 3	39.94%	39.94%
while in severity level 2	2.46	2.46	while in severity level 4	98.72%	98.72%
while in severity level 3	1.33	2.82	Asthma related deaths per 100,000	0.38	0.37
while in severity level 4	-	-	acute events	3.79	8.47
Lifetime hospitalizations (undiscounted)	0.17	0.21	ER visits	8.46	8.55
while in severity level 1	-	-	hospitalizations	8.17	8.21
while in severity level 2	0.09	0.09	Non-asthma related deaths per 100,000	16,591	16,591
while in severity level 3	0.08	0.12			
while in severity level 4	-	-			

FIG A8. Worksheet 8: Targeted steroid results.

to less than 1 additional day of life expectancy. On a discounted, quality-adjusted basis, however, the gain is almost 3 months.

A.3.3 Scenario 3: Inhaled corticosteroids

Fig A7 presents the results of our analysis of inhaled corticosteroids (ICSs) in mild-to-moderate asthma. Here we assume that ICS treatment costs \$38 per patient per month and that its only efficacy is a 7.6% and 11.6% improvement in FEV among patients with mild and moderate disease, respectively. The results, as shown in Table 8, suggest that the addition of ICS to the therapy regimen increases discounted, quality-adjusted life time over the 10-year planning period to 84.0 QALMs and increases costs to \$8,400. (Additional costs are almost all attributable to drug outlays.) Patient symptom-days are reduced to 21.7%, symptom-nights fall to 6.3%, and the average patient experiences only 3.0 acute events. In comparison with no intervention (the Base Case), we estimate an incremental cost of \$13,500 per quality-adjusted life-year (QALY) gained and \$7.50 per additional symptom-free day.

A.3.4 Scenario 4: Targeted steroids

Suppose that ICS therapy is targeted only to patients with Moderate disease. (In other words, all “yes/no” values are set to 0 in the *Decision* worksheet except for that representing Moderate disease.) Fig A8 reports that this would confer additional QALYs at an incremental cost of \$10,300.