

## Use of Randomized Controlled Trials in Organizational Decision Making: A Cost-Minimization Approach

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### **Abstract**

**Objective:** To determine whether conducting a randomized controlled trial (RCT) of an optimal size could result in a net reduction in regret costs to an organization in a policy decision regarding drug coverage.

**Study Design:** Probabilistic decision model and cost-minimization analysis.

**Patients and Methods:** We used a probabilistic decision model and cost-minimization analysis to estimate overall 5-year regret costs (ie, the financial loss associated with making an incorrect decision) to a health plan of performing an RCT for a new asthma medication and making the coverage decision using the results from the RCT. Our analyses were based on a hypothetical cohort of 10,000 patients with moderate to severe asthma enrolled in the health plan.

**Results:** An RCT with 150 patients per group would decrease the expected 5-year regret costs by \$568,000. Under the baseline assumptions, the sample size resulting in the greatest reduction in losses was about 400 per group, with a loss reduction of \$697,000. The cost-minimizing sample size and amount of loss reductions varied substantially with assumptions regarding baseline rates of hospitaliza-

tion for asthma, cost of hospitalization for asthma, and drug utilization rates and costs. Moderate-sized RCTs, however, nearly always resulted in loss reductions.

**Conclusions:** Randomized controlled trials can be a useful organizational decision-making tool to reduce financial regret.

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Randomized controlled trials (RCTs) are the keystone to evaluations of the efficacy of medical interventions. Most RCTs are performed in academic medical centers, often with the intent of determining the efficacy of new drugs or medical devices. They are usually perceived as expensive and time consuming, but most of the expense is for the intervention and the collection of substantial amounts of outcome data. When a health plan decides to cover the expense of an intervention and routinely collects financial outcome data, the cost of an RCT can be very low. The use of RCTs as an organizational decision-making tool has not been explored in great detail. Typically, information used for organizational decision making derives from historical data, or, when these data are not available, intuition. In this article, we explore the concept of using RCTs to enhance informed organizational decision making. In a previous study, we used a decision-analytic approach to examine the effect of the use of RCTs in organizational decision-making regarding quality improvement initiatives.<sup>1</sup> Here, we take the cost-minimization approach to organizational RCTs used by Hornberger et al<sup>2</sup> and apply it to

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coverage decisions in a managed care organization. We show that intelligent use of moderate-sized RCTs can result in substantial reductions in expected financial losses to an organization. The method can be adapted to many different organizational settings.

... METHODS ...

Cost-minimization analyses can be used to determine an organization's expected losses with and without the information derived from an RCT. Information gained from an RCT can be used to make better decisions and minimize financial losses. The information, however, can come at a substantial price. The goal is to balance the reduction in losses resulting from the expected gain in information derived from the RCT against the trial's cost. We demonstrate this method using an example of a hypothetical health plan faced with different options for cost sharing of a new asthma drug.

**Description of the Problem**

The Food and Drug Administration (FDA) has recently approved a set of asthma drugs that affect the leukotriene pathway.<sup>3</sup> Clinical trials to date suggest that these drugs are promising in patients with chronic moderate to severe asthma, reducing both physiologic measures of asthma (eg, forced expiratory volume in 1 second [FEV<sub>1</sub>]) and use of rescue treatment with both beta-adrenergic agonists and glucocorticoids. No published trials, however, have assessed either the reduction in risk of hospital admissions for status asthmaticus or the overall reductions in

medical care costs attributable to the new drugs. Faced with these data, physicians at the health plan believe that one of the drugs should be available for their patients as an adjunctive treatment to inhaled steroids and adrenergic agents and have pushed to have it added to the plan formulary and the plan treatment guidelines.

The health plan administrators must decide how to cover the drug. We focus on 2 extreme coverage options: the plan can cover the drug fully, offering it at a low cost to its patients but at a high cost to the organization, or the plan can refuse to cover the drug and require its patients to pay retail prices.] The plan's physicians and organizational decision makers agree that coverage for the drug will affect drug utilization in their patients with asthma. Full coverage will probably result in higher utilization than no cov-

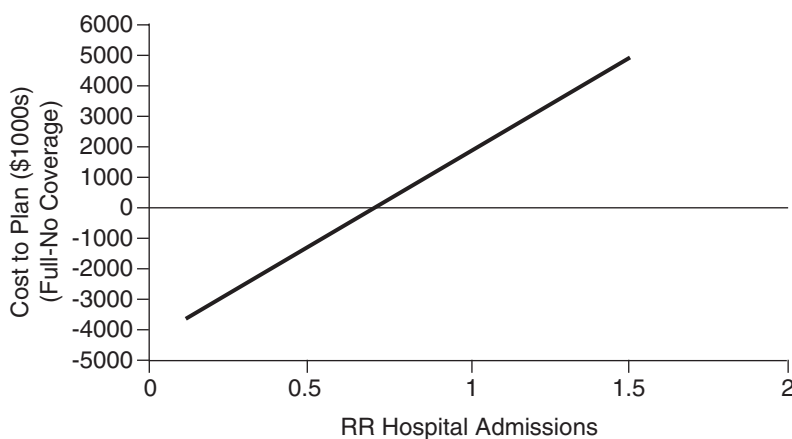
**Table 1.** Health Plan Cost and Clinical Estimates Used in Analysis

Variable	Most Likely Estimate	Plausible Range
Number of patients with moderate to severe asthma in health plan	10,000	8000 - 15,000
Baseline rate of hospital admission per year	30%	20% - 40%
Cost of hospital admission for status asthmaticus	\$5000	\$3000 - \$8000
Drug cost per month with full coverage	\$25	\$15 - \$40
Drug cost per month with no coverage	\$0	—
Drug utilization rate with full coverage	60%	40% - 70%
Drug utilization rate with no coverage	20%	10% - 30%
Estimated relative risk of hospital admissions attributable to drug use	0.8	0.6 - 1.0
Fixed cost of performing an in-plan randomized controlled trial (including design, implementation, and analysis)	\$200,000	\$150,000 - \$300,000
Variable per-patient cost of an in-plan randomized controlled trial	\$250	\$150 - \$400
Discount rate	10%	5% - 15%
Weighting of prior distribution	50%	0% - 100%

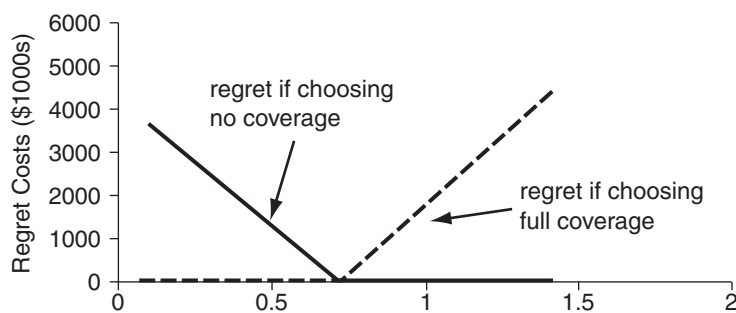
erage, giving rise to increased drug costs but potential cost savings owing to drug-related decreases in the risk for asthma hospitalizations. Based on review of hospital admissions and pharmacy data and discussion among plan physicians, pharmacists, and managers, the pricing decision

makers obtain the health plan cost and clinical estimates shown in Table 1. The plan's physicians believe that drug use will, on average, lower the risk of hospital admissions for status asthmaticus; however, they acknowledge that available data are limited and do not support an accurate estimate of this relative risk (RR) reduction.

**Figure 1.** Net Difference in 1-Year Costs if a New Asthma Drug Is Covered Fully Versus No Coverage as a Function of the Relative Risk (RR) for Hospital Admissions Conferred by the Drug



**Figure 2.** One-Year Regret Costs if a New Asthma Drug Is Covered Fully Versus No Coverage as a Function of the Relative Risk (RR) for Hospital Admission Conferred by the Drug



With full coverage, the health plan experiences regret costs if the RR is more than 0.7. With no coverage, the health plan experiences regret costs if the RR is less than 0.7.

### Cost-Minimization Analysis

Figure 1 shows an analysis of net costs to the organization if the drug is fully covered versus not covered as a function of the degree of effectiveness of the drug, plotted as the RR for hospital admissions conferred by the drug. The figure takes into account use (at different utilization rates) of the drug by the health plan's 10,000 (hypothetical) asthmatic patients, the cost of full versus no coverage of the drug, the baseline and drug-modified yearly hospital admission rates for asthma exacerbations, and the mean cost of hospital admissions for asthma. If the drug does not decrease hospital admissions for asthma (RR = 1) for the plan's asthmatic patients, then compared with no coverage, full coverage for an ineffective drug is quite expensive. On the other hand, if the drug is very effective in reducing hospital admissions (RR = 0.5, a 50% reduction), then full coverage is beneficial because even if the drug utilization rate is higher, it results in fewer hospital admissions, offsetting the cost of the drug itself. Net costs are equal at an RR of 0.7.

The analysis presented here takes the perspective of what has been termed organizational losses or "regret." Regret is the loss associated with a particular decision if that decision is wrong. If a health plan chooses to cover the drug fully but the drug does not substantially decrease hospital admissions (RR > 0.7), the plan

suffers financial losses (regret costs). If the RR for hospital admissions is less than 0.7, however, the plan incurs no regret from full coverage. Similarly, if the drug is very effective in reducing hospital admissions ( $RR < 0.7$ ), the plan suffers losses only if partial coverage is chosen; there is no regret if full coverage is offered. Figure 2 shows a plot of organizational regret given full coverage or no coverage for the new drug as a function of the RR for hospital admissions conferred by the drug.

The true RR for hospital admissions related to the new asthma drug is not known, and published data are unavailable to guide the decision. Without data from an in-plan RCT, there is substantial uncertainty as to where the true RR lies. After some discussion, the health plan physicians provide educated guesses, using one of several different techniques,<sup>4,8</sup> about the probability distribution for the RR of interest. In Bayesian statistics, this distribution is referred to as a prior distribution. Table 2 shows this distribution, and Figure 3 plots a smoothed version. The figure demonstrates that physicians' beliefs regarding the drug's efficacy are somewhat vague, consistent with the lack of knowledge regarding the ability of the drug to decrease hospital admissions. The RR value with the highest probability is 0.8.

Without better information from a clinical trial, the prior distribution regarding the RR for hospital admissions forms the baseline basis for the coverage decision. The regret resulting from the decision to cover fully can be calculated by multiplying the prior distribution curve by the regret for full coverage; this "expected regret," plotted as the curved line in the lower right of Figure 3, is a financial summary of the organization's expected regret if it chooses full coverage.\* The regret resulting from no coverage is shown as the curved line in the lower left of Figure 3. Whichever expected regret is

lower forms the basis for the coverage decision. In this case, the yearly regret from no coverage is \$455,000 and that from full coverage is \$526,000, so no coverage is chosen.

In the setting of perfect information, the true RR would be known with complete certainty, the correct coverage decision would be made without the potential for error, and the expected loss associated with the decision would be 0. In lieu of perfect information, the health plan could consider performing an RCT of the drug in its patients, the outcome of interest being the RR for hospital

**Table 2.** Plan Physicians' Estimates of the Prior Distribution for the Relative Risk (RR) of Hospitalization With Use of the New Asthma Drug

RR	Subjective Probability*	Normalized Probability
0	0	0
0.1	0.001	0.000442
0.2	0.01	0.004417
0.3	0.04	0.017668
0.4	0.1	0.04417
0.5	0.2	0.088339
0.6	0.3	0.132509
0.7	0.4	0.176678
0.8	0.45	0.198763
0.9	0.4	0.176678
1	0.2	0.088339
1.1	0.1	0.04417
1.2	0.05	0.022085
1.3	0.01	0.004417
1.4	0.002	0.000883
1.5	0.001	0.000442
1.6	0	0
1.7	0	0
1.8	0	0
1.9	0	0
2	0	0

\*Plan physicians used a 0 to 1 scale to estimate the relative chance of observing the listed RR values. For example, physicians believe that an RR of 0 is impossible and an RR of 0.1 is highly unlikely. Relative risk values between 0.7 and 0.9 are most likely. There is a small chance of observing RR values of 1 or greater, but there is no chance of observing values of greater than 1.5. In the third column, values are normalized such that the total probability sums to 1.

\*This calculation takes advantage of the Bayesian paradigm, in which the probability of parameters can be interpreted directly. It is not possible to perform such a calculation from a "frequentist" statistical perspective.

admissions among patients assigned to treatment with the active drug versus those assigned no drug (or a placebo pill or even delayed use of the drug). Applying standard Bayesian methods, the health plan would use the RCT results as the Bayesian likelihood function to revise the prior distribution of RR estimates (the beliefs of the plan's physicians), yielding a posterior distribution describing the RR. Given the posterior distribution, the net expected regret of each coverage decision can be recalculated, and the decision made on the basis of which regret is lower.

Once the RCT is performed and the posterior RR estimate obtained, the health plan makes its coverage decision. Regret costs after the RCT is performed also include the cost of the RCT itself. In our model, we assumed that the decision would be relevant for the following 4 years, with 5 years being the total expected lifetime of the drug. This period was selected because 5 years hence, new drugs may become available, drug prices may decrease

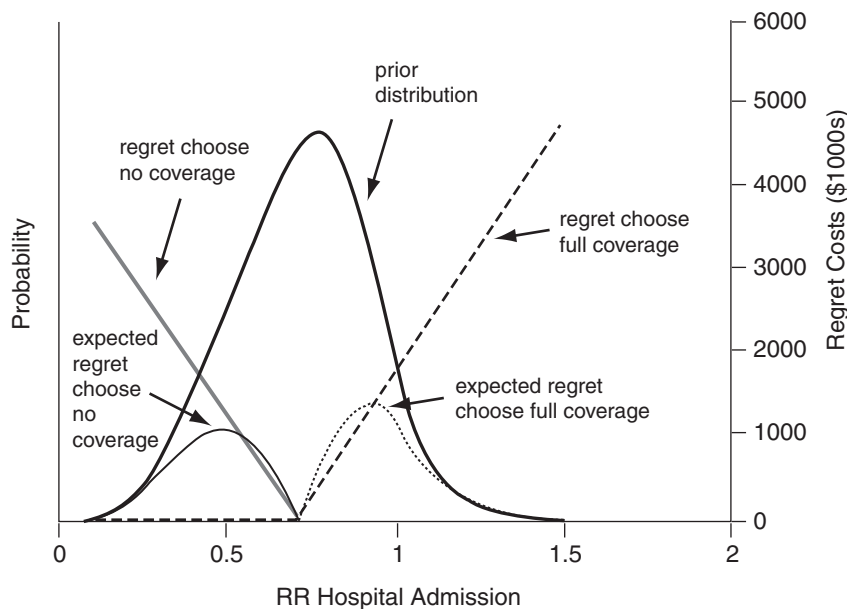
because of competition from other drugs in the same class, and forecasting costs beyond 5 years can be viewed as too uncertain.

What sample size should be chosen for the trial? Larger trials are more expensive, but smaller trials may yield insufficient information. We modeled the expected impact of different sample sizes on net losses by assuming a true underlying RR value. Suppose that the true RR is 0.8. With 200 total patients in a 1-year RCT (100 per group) and a baseline admission rate of 30% per year, we expect, on average, 30 admissions in the placebo group ( $X_p = 30$ ) and 24 in the drug treatment group ( $X_d = 24$ ). The likelihood function describing this finding is conveniently estimated by assuming that the natural log of the RR is distributed normally<sup>9</sup> with a mean  $\ln(L_{RR}) = \ln([X_d/N_d]/[X_p/N_p])$  and standard deviation

$$SD(\ln[L_{RR}]) = \sqrt{1/X_d - 1/N_d + 1/X_p - 1/N_p}$$

Because of sampling error alone, the RCT may show different numbers of admissions than those listed above (eg, 32 in the placebo group and 29 in the drug group). We used Monte Carlo simulation (500 simulations) to model the set of possible results from running an RCT with a given sample size and underlying RR. Although several different distributions were available, we selected the binomial distribution to model the occurrence of different numbers of hospital admissions among patients treated with either placebo or drug:  $p(X_i) = \text{binom}(N_i, p_i)$ , where  $X_i$  is the (integer) number of hospital admissions among  $N_i$  patients followed up for 1 year with yearly probability of admission  $p_i$ . In our model, patients receiving placebo have  $p_i = 30\%$  while those taking the drug have  $p_i = RR \times 30\%$ . With each Monte Carlo simulation, we calcu-

**Figure 3.** Expected Regret Costs of Choosing Full Coverage Versus No Coverage



The straight lines show the regret associated with no coverage or full coverage as a function of the relative risk (RR) for hospital admissions conferred by the new asthma drug. The upper curved line shows the prior distribution of the RR estimate. The 2 lower curved lines show the expected regret (before a clinical trial is conducted) of either decision, calculated as the product of the prior distribution for the RR and the regret lines.



lated the expected regret cost of each coverage decision, noting which decision was favored (ie, which had the lower regret cost) and the actual regret value for the decision. We then calculated the 5-year expected regret costs of the entire process, which takes into account the cost of the 1-year RCT, the no-coverage regret cost during the first year for patients not participating in the RCT (\$455,000), and the regret cost for the entire population of asthmatic patients in the health plan during the remaining 4 years after the RCT is complete and the coverage decision has been made.

The larger the number of patients assigned to each group, the more likely the "expected" number of hospital admissions will be obtained, and the more likely the likelihood function will be tightly centered on the underlying RR value. Larger RCT sample sizes therefore result, on average, in tighter, more precise posterior distributions, with consequently smaller regret costs. The goal of our analysis was to determine whether the organizational costs of performing an in-plan RCT are outweighed by the potential reductions in expected regret costs resulting from this gain in information and improvement in organizational decision making.

*Computer Programming.* We performed all programming using Excel 2000 (Microsoft Corporation, Redmond, WA); the spreadsheet is available on request. All future costs were discounted by 10% per year. We used Excel's "critbinom" function, along with the software's random number generator ("rand()") to simulate  $X_i$ .

... RESULTS ...

For a health plan with 10,000 patients with moderate to severe asthma that attempts to make the coverage decision without use of RCT, the 1-year regret costs are \$455,000 for no coverage and \$526,000 for full coverage. The plan chooses no coverage, and its 5-year regret cost for that decision is \$1.72 million (discounted by 10% over 5 years). This figure takes into account the prior distribution for the RR of hospital admission resulting from drug use, different utilization rates for the drug given different coverage decisions, drug costs, and costs of hospital admissions because of asthma exacerbations. In contrast, if the true but unknown RR was 0.8, conducting a small RCT (eg, with 150 patients in each arm) would result in the following: the

overall cost of the trial is about \$329,000; about 85% of the time, the regret cost for partial coverage is lower than that for full coverage. The expected regret cost after the trial is about \$154,000; and the 5-year net expected regret cost associated with conducting the RCT and use of its results to make the coverage decision is \$1.16 million, a reduction of about \$568,000 in expected regret costs. The reduction occurs because after 1 year the RCT has provided additional information regarding the true effectiveness of the drug in the health plan's population of asthmatic patients, enabling a more informed decision about coverage. As the number of trial participants increases, additional reductions in expected regret costs accrue. Figure 4 shows reductions in expected regret to the plan given different assumptions about the drug's true effectiveness and the number of patients to include in an RCT. In the base case (RR = 0.8), the critical sample size per group resulting in minimum organizational regret costs is about 400, with a maximal regret reduction of \$697,000. There is a 93% chance that the trial will support choosing no coverage for the drug.

We explored the effect of perturbations in the model's input values on critical sample size and regret cost reductions using sensitivity analysis. Table 3 shows the reductions in regret costs at optimal RCT sample sizes for the ranges of values given in Table 1. Note that changes in some of the parameters result in a change in the decision threshold, which affects expected regret. For example, if the baseline hospitalization rate for patients with asthma is lowered from 30% to 20%, the decision threshold changes to an RR value for hospital admissions of 0.55. This change was taken into account in the values listed in Table 3. Regret cost reductions ranged from none to more than \$2.8 million. The critical regret-minimizing RCT sample size per group and the reduction in expected regret costs were sensitive to changes in most variables; they were least sensitive to changes in the fixed cost of performing an RCT and changes in the discount rate. Under several situations, conducting an RCT did not result in reductions in 5-year regret costs. For example, if the baseline yearly rate of hospital admissions was decreased from 30% to 20%, the expected regret cost reduction did not outweigh the cost of performing a trial with as few as 200 participants. Other situations in which performing an RCT resulted in no regret reduction were cost of hospitalization of \$3000 (baseline \$5000), drug utilization under full coverage of 40% (baseline

60%), and drug cost under full coverage of \$40 (baseline \$25).

It is useful to compare the critical sample sizes calculated by the model with those generated by typical sample size calculations for randomized trials (performed with StatCalc [EpiInfo, version 6], Centers for Disease Control and Prevention, 1993). With a type I error rate of 10% (ie, 1-sided alpha = .05), a type II

error rate of 80%, and a baseline 30% annual rate of hospital admission, the required sample size to detect an RR of 0.8 is 709 patients per group. This figure is substantially higher than many of the cost-minimizing sample sizes listed in Table 3. The reason for the difference is that the cost-minimization model we constructed takes into account the different consequences of concluding, with or without an RCT, that

**Table 3.** One-Way Sensitivity Analysis of Critical Sample Size and Reduction of Expected Regret Costs When a Randomized Controlled Trial (RCT) Is Performed

Variable	Low Estimate	No. per Group*	Regret Cost Loss Reduction (\$1000s)	High Estimate	No. per Group*	Regret Cost Loss Reduction (\$1000s)
No. of asthmatic patients	8000	400	470	15,000	700	1253
Baseline rate of hospital admission per 100 patients per year	20%	200	-88	40%	400	1812
Cost of hospitalization	\$3000	150	-140	\$8000	400	2811
Drug cost per month with full coverage	\$15	450	1676	\$40	150	1
Drug utilization rate with full coverage	40%	150	-36	70%	500	1097
Drug utilization rate with no coverage	10%	550	1456	30%	250	103
Relative risk of hospital admissions conferred by drug	0.6	450	608	1.0	250	934
Fixed cost of performing RCT	\$150,000	400	785	\$300,000	350	672
Variable cost of performing RCT	\$150	550	799	\$400	250	596
Discount rate	5%	500	878	15%	400	573

Base case: reduction in regret of \$697,000 with regret-minimizing sample size of about 400 patients per group.

\*An increase of 50 patients per group decreased losses.

the drug's effectiveness is great or small rather than taking into account standard error rates.

... DISCUSSION ...

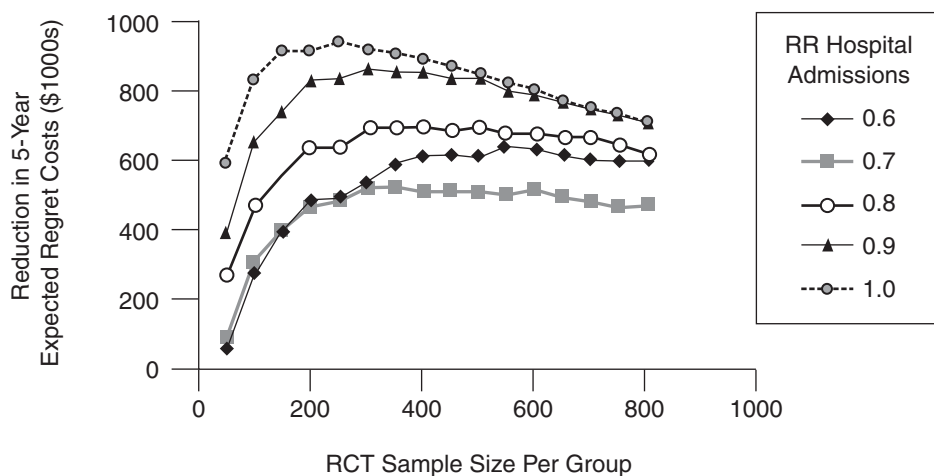
We used a Bayesian approach combined with a simple economic model to explore the use of RCTs as an organizational decision-making tool for reducing expected regret costs. Often, decisions must be made in a setting of little or no knowledge regarding an intervention's effectiveness or its potential impact on overall costs. In addition, an organization must consider that the results of any published trial, if available, might not be generally applicable to the plan's own patients. Data gained from conducting an in-plan RCT can help to sufficiently decrease uncertainty regarding the intervention so as to positively affect health or financial considerations. Of interest, then, is whether the gain in certainty is worth the cost and trouble of performing the trial.

We selected regret costs as one of several potential measures of value to a health plan. Other met-

rics could have been chosen, such as decreases in hospitalizations, improvements in quality of life, or cost effectiveness. We chose regret costs because costs of health outcomes can be determined more easily than effects on health quality and can be performed using electronically available data rather than individual patient interviews or chart review.

Regret costs represent the expected loss, based on current knowledge, of making an incorrect decision. In the example presented in this article, deciding to cover the drug fully when it does not substantially decrease hospital admissions results in regret costs but deciding not to cover the drug in this situation results in no regret costs. As certainty regarding the parameters describing regret costs increases, the chance of making the correct decision increases, and the expected regret cost decreases. In theory, perfect information regarding all of the parameters results in the correct decision 100% of the time and no regret. Thus when, as in our example, we consider uncertainty only regarding the RR of hospitalization conferred by the drug, the value of perfect information is approximately \$1.7 million.

**Figure 4.** Decrease in Expected 5-Year Regret Given Different Assumptions About the True Effectiveness of a New Asthma Drug to Decrease Hospital Admissions and the Number of Patients in to Include Each Group in a Randomized Controlled Trial (RCT)



Five hundred Monte Carlo simulations were done for each sample size and relative risk (RR) value.



Our modeling of a decision regarding coverage for a new asthma drug showed that within the ranges of uncertainty given in Table 1, performing an RCT at or near the critical sample size usually resulted in a decrease in expected regret costs to the organization by allowing better decision making. Moreover, in the example examined here, the sample sizes required were typically smaller than those usually required by standard sample size calculations with classical statistics. Other models (not shown), in which the hypothetical number of asthmatic patients in the health plan was raised substantially, resulted in critical, regret-minimizing sample sizes that were larger than those dictated by classical statistics.

Calculating appropriate sample sizes using the modeling approach we took will almost always yield different results than that using classical statistics. In the latter, a trial can be designed to detect a particular reduction in risk (eg, an RR of 0.8) with 80% certainty and with an error rate of 5% or less. The Bayesian approach we chose directly evaluates the posterior distribution of RR and determines the economic consequences of decisions based on this distribution using a simple cost model. It also adds the costs of performing the RCT. Optimal sample sizes in our model were smaller because the added benefit of certainty in reducing expected regret is outweighed by the cost of adding more patients. When target populations are large, regret costs from decisions can be large. Therefore, when using the analytic approach described here, regret-minimizing sample sizes may be larger than those determined by classical statistics.

There is precedent for using cost modeling in determining potential savings from performing RCTs. Raiffa and Schlaifer initially described cost modeling in business decisions.<sup>9</sup> Berry describes calculation of the expected value of a function of a variable<sup>10</sup> and its use in Bayesian modeling to determine optimal sample sizes in medical device trials.<sup>11</sup> Lindley<sup>12</sup> described methods consistent with those used here. Hornberger and Wrone<sup>13</sup> used similar methods to calculate whether a health organization can decrease losses by performing an internal RCT rather than waiting for a similar study to be published in the medical literature. Hornberger<sup>14</sup> also used such methods to show that conducting a large-scale RCT of folic acid could result in net savings from a public health perspective. Woodward et al<sup>15</sup> have investigated the conditions under which pro-

ject evaluations (eg, an RCT) can be cost effective. The model we present extends this theory to continuous outcomes, not just “successes” or “failures,” and also takes into account the exact statistical nature and cost of the project evaluation effectiveness estimate. In addition, our model specifically estimates the effect of different coverage decisions on the potential utilization rate of the drug, which would affect its potential effectiveness.

The Bayesian methodology used in our analysis is similar to that used in previous studies. This approach is advantageous in that information from previous trials or input from expert physicians can be used to enhance the calculation of the posterior distribution resulting from conducting the RCT. The calculations used in our model are not complex and can be implemented in standard spreadsheet programs.

### Limitations

The approach used in our study makes several assumptions about health plans, cost modeling, and RCTs. First, it assumes that a health plan can model expected events and their associated costs with various alternatives. Data from analysis of electronic databases are often available to aid in setting up models. Often, however, models must rely on the opinion of experts from risk management, finance, and clinical medicine. The more data available to the health plan on which to base the models, the more valid the analysis becomes; the more input from all of the players involved in the decision, the more likely the analysis will be seen as acceptable.

Second, our model assumed that the plan will make the drug coverage decision based on cost estimates alone independent of other factors. In theory, a plan could be criticized for not covering a drug that decreases hospital admissions substantially (eg, 20% reduction) because it does not meet a critical economic threshold. Our model could be updated to include these alternative decision thresholds.

Third, for the sake of simplicity, the model assumed that the plan's RCT did not suffer from loss to follow-up. Loss to follow-up would decrease expected loss reductions resulting from performing the trial. This occurs because the posterior distribution for the RR estimate becomes wider as the effective sample size decreases.

Fourth, the plan's RCT must be designed to be generalizable to the entire target population (ie,

all patients with moderate to severe asthma). If entry criteria for the study are limited, the trial's results may be applicable only to that set of patients; the true effect in the remaining population may be greater or less, resulting in decreased cost savings because decisions were based on biased data.

Fifth, the approach assumes that a health plan is willing to perform RCTs in its target population. Several obstacles can prevent a plan from pursuing this approach. Physicians or other organizational leaders may oppose a clinical trial when published results appear reasonably provocative. In such a case, however, the expected regret from one decision may be substantially lower than from another, obviating the need for an RCT. Randomizing patients to a control intervention may make some physicians uncomfortable. Adopting protocols that randomize patients to immediate versus delayed drug administration can facilitate performance of the trial. Fully covering the drug for trial participants, offering enhanced follow-up with preapproved state-of-the-art treatment for the disease, and rewarding trial participants in other ways can help the health plan sell the trial to its patients and physicians. It is plausible that a drug that has been shown to improve surrogate endpoints (eg, an improvement in pulmonary function test findings) may have no effect or prove detrimental when assessed using clinically meaningful endpoints such as hospitalizations. This supports performance of an RCT.

There is precedent for plan-wide RCTs to support reimbursement decisions for medications. British Columbia's Pharmacare (the province's pharmacy benefits management organization) recently implemented a plan-wide RCT of delisting nebulized asthma medications, with a randomized control group given an optional 6-month exemption from the policy. The results of this trial can be used to make policy decisions.

Sixth, the plan must accept that conducting a limited-scale RCT is reasonably inexpensive. Chalmers, the preeminent trialist in the United States, said: "Randomization costs a few cents per patient. What is expensive is observation and recording data."<sup>16</sup> Published clinical trials sponsored by pharmaceutical or medical device companies tend to be expensive primarily because they are often multicentered and require close follow-up, and the interventions are often themselves expensive. The focus of a health plan's study is quite dif-

ferent. For the plan, the only outcome of relevance in its own RCT is effectiveness in its patient population. Because hospital admission rates (or outpatient visits) are routinely tracked for financial reasons, data collection for the trial involves only a reprocessing of data from the plan's administrative databases.

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... CONCLUSION ...

Use of limited RCTs in organizational decision making can substantially decrease expected financial regret. The models required to determine the regret-minimizing sample size are straightforward but require input from several different areas of expertise, including risk management, finance, and clinical specialists. A Bayesian approach allows flexibility in clinical trial design that incorporates other outcomes.

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