Cost-Effectiveness Analysis with Risk Aversion

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SUMMARY

This paper discusses why, in a medical context, the standard assumption of a risk-neutral social planner is inappropriate and develops a framework for conducting cost-effectiveness (CE) analysis when social planners are risk-averse. This framework demonstrates that if new medical interventions are variance increasing (decreasing), the risk-neutral approach will approve (reject) projects that should be rejected (accepted). This methodology is applied to two medical interventions that have been previously evaluated and considered cost-effective in the published literature. Since both conclusions assumed risk neutrality we determine the level of societal risk-aversion that would be necessary to reject these new interventions and compare these levels to previous estimates of risk-aversion in the economics literature. We find that for reasonable values of the risk-aversion parameter, only one of the two interventions should be approved. It is our recommendation that the cut-off risk aversion parameter (the level of risk-aversion above which a project would be rejected) should become a standard reported figure in future CE studies. Copyright © 2001 John Wiley & Sons, Ltd.

KEY WORDS — cost-effectiveness analysis; medical interventions; risk aversion; social risk preferences

INTRODUCTION

The use of cost-effectiveness (CE) as a tool for the economic evaluation of medical interventions has increased dramatically over the last 20 years. This use has led, in turn, to a vast literature on the proper construction and use of CE ratios, with a great deal of attention focused on what constitutes a ‘cost’ and what constitutes an ‘effect’ [1–4]. In this paper, we would like to change the focus and examine the importance of uncertainty in guiding medical decision-making. Specifically, we will argue that society is risk-averse and that this risk aversion should be reflected in the effectiveness measure in CE analysis. Further, we will examine the systematic biases that are introduced when society is assumed to be risk-neutral.

Relative to the vast literature on CE analysis, the work on uncertainty in CE analysis is sparse. Until recently, the primary method for addressing uncertainty in economic evaluations of medical technologies was sensitivity analysis, where researchers specify a range of values from best case to worst case to reflect parameter uncertainty. As the collection of economic data from clinical trials has become more prevalent, statistical approaches to represent uncertainty have also been employed. Most of the work in this area is centred on techniques to estimate univariate or multivariate confidence intervals to reflect parameter uncertainty.
uncertainty [5–8]. While these outcome ranges and confidence intervals are useful as rough measures of reliability, they provide little guidance on how to utilize this information in decision making. This guidance can only come from a discussion of risk preferences and decision making under uncertainty, a point that was raised nearly a decade ago by Deber and Goel [9].

Only a few studies have taken this approach. Most of these have assumed a risk-neutral social planner, an assumption that is implicit in most studies that do not discuss risk preferences. These papers have generally concluded that the ‘ratio of means’ is sufficient to characterize the CE ratio [10,11]. There are two notable exceptions. Garber and Phelps [12] employ an expected utility framework to show how CE criterion varies by individual according to age, gender, income level and risk aversion. O’Brien and Sculpher [13] examine how risk might affect sub-societal decisions through a portfolio approach that allows decision-makers to diversify their mix of health programme investments. Neither of these papers addresses the role of risk at a societal level, i.e. the goal of this paper. As such, we will provide arguments for why a social decision-maker might be risk averse and characterize optimal decision making for such a planner. Unlike Garber and Phelps, we will derive a closed-form analytical solution for the optimal CE ratio. Further, our approach differs from O’Brien and Sculpher, as it does not require planners to make simultaneous decisions about the intensity of investment in multiple projects.

The paper is structured as follows. The first section will motivate the use of a risk-averse social planner. The second section develops a model for evaluating the CE of medical interventions under uncertainty. The biases of assuming risk-neutrality are assessed. The third section presents two case studies as a means of illustrating the analytical results. Concluding remarks are provided in the final section.

RISK PREFERENCES: INDIVIDUALS AND SOCIETY

Within the economics literature, it is generally accepted that individuals are risk averse [14–16]. Many theorists, however, argue that society as a whole should be treated as risk neutral. We are skeptical of this position for the reasons discussed below. We also note that this theoretical view stands in direct contradiction to the extreme form of societal risk aversion observed embodied in environmental health protection legislation [17].

In their seminal work on public investment, Arrow and Lind [14] demonstrate that in a world with perfect insurance, i.e. complete contingent markets, social planners should be risk neutral. Clearly, perfect or near-perfect insurance does not exist, particularly for health outcomes. In this case, Arrow and Lind show that risk neutrality may still be justified if risks from any given investment are spread over a large number of people and are not correlated across projects. In the context of health care, where outcomes are often measured in quality-adjusted life years (QALYs), an additional argument may be offered—QALYs are utility measures that reflect individual risk preferences, so the social planner need not attend to them. Lastly, even if social planners are risk averse, when risks are small, mathematical arguments of approximation suggest that planners can be treated as risk neutral.

In this section, we will discuss these three justifications in detail, and assess their validity in the context of assessment of medical interventions. We begin with a discussion of the Pareto compensation criterion and how it relates to the Arrow–Lind and QALY arguments. When the conditions for either of the two arguments do not hold, the compensation criterion will not hold, and social planners should be risk averse. In this case, social planners can be treated as risk neutral only if gambles are small. The subsection that follows describes why gambles are, in general, not small.

This is not intended to be a comprehensive discussion of the inappropriateness of social risk-neutrality in a medical context, but rather a response to major schools of thought. Other arguments may invoke statements about the inability to compensate individuals for lost health and possibly life, or on the impossibility of efficient redistribution due to state-dependent utility functions, where the marginal utility of wealth differs according to health status [18,19].

Pareto compensation criterion

The Pareto compensation criterion states that allocation $a'$ is potentially Pareto preferred to allocation $a$ if $a'$ can be reallocated such that
everyone prefers this reallocation to the original allocation \( a \). If some individuals gain from allocation \( a' \) and some individuals lose from \( a' \), the allocation \( a' \) is preferred if the winners could compensate the losers and still be better off. This argument has been extended to the medical CE literature as a justification for a risk-neutral social planner. The logic is that some people will greatly benefit from an intervention and some will not respond as well, but the intervention is worthwhile if the winners can compensate the losers.

Let us characterize an intervention with uncertainty by a mean and variance of benefits. For ease of exposition, we will assume throughout the remainder of this paper that the distribution of outcomes is perfectly symmetrical around the mean so that the mean and median are identical. If effectiveness is a truly stochastic process, probability theory indicates that some individuals will experience an above average result while others will experience a below average result, but that the total value (probability mass) of outcomes above the mean is exactly equal to those below the mean. In this case, individuals would be able to compensate one another and the only relevant measure of effectiveness is the average outcome. In other words, if an intervention is provided to many users, the winners will perfectly balance with the losers, and the social planner can behave as a risk-neutral agent.

There are two problems with applying this logic to the evaluation of medical technologies. First, it is important to think about what information is being conveyed in uncertain measures of medical performance. In general, mean-variance or confidence interval measures do not reflect a truly random process, but rather \( \text{ex ante} \) uncertainty about intervention outcomes. This uncertainty can be broken down into two constituent components: statistical uncertainty derived from the sampling variation inherent in a clinical trial; and uncertainty about the appropriate values assigned (not estimated) to various components of the analysis generally embodied in sensitivity analysis. As new treatments make the transition from a small controlled clinical setting to the general health care arena, some of both types of uncertainty will be resolved. Regardless of whether the intervention turns out, \( \text{ex post} \), to be better or worse than expected, it will not be true that half the outcomes will be above the \( \text{ex ante} \) mean, i.e. the mean as measured in the clinical trial, and half will be below it.

In the context of statistical uncertainty, this difference can be thought of as the difference between a sample and population distribution. Only when samples are very large, a prohibitively expensive proposition in the evaluation of medical technology, will the two distributions be approximately identical. For assigned parameter values, this difference between the \( \text{ex ante} \) and \( \text{ex post} \) mean represents a resolution of uncertainty gained through additional experience with the treatment. For example, conjectures about twenty-year survival from a five-year trial may be resolved over time, yielding a new mean and reducing the need for sensitivity analysis. Further, if this \( \text{ex ante} \) lack of knowledge reflects uncertainty about basic biological, chemical or even economic processes, returns across many health projects will be correlated. Thus, even when social planners invest in many projects, winners will not, necessarily, be able to compensate the losers. The maximization of mean returns does not maximize the social welfare of a society comprised of risk-averse agents. Social planners cannot act as if they are risk neutral.

Even if measurements of uncertainty about medical CE are, in fact, a reflection of true stochasticity, problems with justifying a risk-neutral social planner on the grounds of the Pareto compensation criterion persist. These problems arise because medical technology performance is measured in (quality-adjusted) life years rather than in utility terms. While QALYs are often referred to as utility measures in the health economics literature, they are only consistent with von Neumann–Morgenstern utility under very restrictive assumptions [22–24]. The least restrictive version of these assumptions is that individuals are risk neutral with respect to life years so that holding quality of life fixed, individuals are indifferent between a lottery over life years and the expected life duration of that lottery. Numerous studies have found results that are inconsistent with risk neutrality and suggest risk aversion with respect to life duration [25–27].

Thus, mean effectiveness of an intervention represents the expected number of (quality-adjusted) life years from that intervention, and risk aversion implies that the utility gained from one additional life year is less than the utility lost from one less year. This in turn implies that the half of the people who experience below average results will be made more worse off than the above average.
people are made better off, i.e. the distribution of utility from an intervention will be skewed to the left. Average life years will not correspond to average utility, so that project approval based on mean effectiveness in terms of years will not satisfy the compensation criterion.

It is important to note that even if ‘true’ measures of utility that are consistent with individual risk aversion are developed, societal risk aversion may be justified based on the ex ante argument posed earlier. That is, if either one of the arguments against the Pareto compensation criterion does not hold, then society should be treated as risk averse. This point is illustrated with an example. Suppose that utility can be appropriately measured and the social planner is deciding whether to adopt a new policy. Research results suggest a 75% cure rate and a 25% chance of serious side effects. Further suppose that an individual, based on risk preferences embodied in utility measures, finds this gamble to be worthwhile. Whether the social planner finds this gamble desirable will depend on what a 75% chance really means. Does it mean that all participants have a 75% chance of cure and a 25% chance of adverse effects? Or, does it mean that there is a 75% chance that all will be cured and a 25% chance that all will experience adverse effects? In the latter case, where the risk faced by the planner is complete success versus complete failure, the winners will not in general be able to compensate the losers. Thus when utility is properly measured but outcomes are correlated, the social planner will still be risk averse. Either of the two Pareto compensation arguments is sufficient to reject societal risk neutrality.

Small gambles

Even if planners are risk averse, the exclusion of risk concerns from societal decision-making may be justified if gambles are small. A risk-averse individual is one who strictly prefers a certainty consequence to any risky prospect whose mathematical expectation of consequences equals that certainty. Thus, a utility function represented in utility-wealth space will be concave. If gambles, or more specifically the variance of wealth outcomes, are small, then the concave utility function over that gamble is approximately linear and agents can be treated as ‘locally’ risk neutral. The validity of this argument, of course, relies on the actual size (variance) of the gamble and the curvature of the utility function.

In the medical effectiveness context, some have justified societal risk neutrality because individual interventions affect relatively few people and are fairly modest in cost, making the linear approximation a reasonable one. While this may be true for some interventions, it is not difficult to think of examples where programme costs and their variance are large, even when compared to the total health care budget. Imagine a government programme in the US to provide health insurance for the uninsured, a group that comprises roughly 15% of the total US population. Less dramatically, imagine evaluating the US legislation that mandates 48-hour maternity stays in hospitals, or modifications to any other high volume procedure.

Indeed, a long list of hypothetical interventions could be constructed to convince the reader that the costs of medical interventions are not small, but perhaps no evidence is more persuasive than the substantial resources dedicated to shape health policy. Health care dominates contemporary US political discourse; legislators devote significant amounts of time and lobbyists spend millions of dollars trying to influence the design of health policy and programmes. Clearly, such large-scale efforts suggest that the stakes are not small and that these programmes have the potential to dramatically alter social welfare. Thus, a concave utility function will not, in general, be suitably approximated by a linear one and the social planner cannot be treated as if she were risk neutral. Table 1 summarizes the results from this section.

THE MODEL

Suppose society is deliberating over the CE of medical intervention, $m$, compared to the previous standard of care. Assume that the incremental costs of the intervention are certain, $c(m)$. Let $\mu(m)$ denote the incremental mean effectiveness of the intervention and $\sigma^2(m)$ denote the incremental variance of effectiveness. Note that because all measures are net of standard treatment, $c(m)$, $\mu(m)$ and $\sigma^2(m)$ can take on both positive and negative values, i.e. the new treatment could be cost-reducing, average effectiveness reducing, or variance-reducing. Let $Y$ represent the total
### Table 1. Social risk neutrality: principal arguments and their refutation

<table>
<thead>
<tr>
<th>Argument</th>
<th>Evidence against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk spreading/diversification</td>
<td>Returns within a project are correlated, i.e. some uncertainty is resolved; the ( \text{ex ante} ) mean is not the same as the ( \text{ex post} ) mean. Returns across projects are correlated</td>
</tr>
<tr>
<td>QALYs are utilities</td>
<td>QALYs are only utilities under restrictive conditions (risk neutrality with respect to duration). Substantial evidence suggests that these conditions do not hold in practice</td>
</tr>
<tr>
<td>Small gambles</td>
<td>Gambles are not small, particularly for high volume procedures. Significant resources dedicated to shape policy indicate that policies have substantial welfare implication</td>
</tr>
</tbody>
</table>

If either one of the first two arguments for neutrality does not hold, then society should be treated as risk averse. The evidence against the third argument implies that risk neutrality will not be a good approximation in this case.

amount of money allocated to the health care budget and denote risk aversion as \( r \). In order to evaluate the benefits of intervention, a utility function must be specified. For ease of exposition we will assume a linear mean-variance utility function with constant absolute risk aversion (CARA) of the following form:

\[
U(m) = \mu(m) - \frac{r}{2} \sigma^2(m). \tag{1}
\]

The societal objective is to maximize utility from the medical intervention subject to the health budget constraint,

\[
\max_m \mu(m) - \frac{r}{2} \sigma^2(m) + \lambda [c(m) - Y].
\]

Maximization yields the following first order condition:

\[
\frac{\partial \mu}{\partial m} - \frac{r}{2} \frac{\partial \sigma^2}{\partial m} + \lambda \frac{\partial c}{\partial m} = 0.
\]

Rearranging terms:

\[
\frac{\partial \mu}{\partial m} - \frac{r}{2} \frac{\partial \sigma^2}{\partial m} \frac{1}{\lambda} = \frac{\partial c}{\partial m} \frac{1}{\lambda}.
\]

This simply states that investment in a medical intervention should occur to the point at which the incremental cost of the medical intervention divided by the utility from the intervention, which is a function of both net expected effectiveness, the net variance of effectiveness, and risk preferences, equals the inverse of the marginal utility of income. In other words, the marginal utility from an incremental $1 worth of medical intervention should equal the marginal utility of $1 worth of income, in equilibrium. This makes intuitive sense because if the 'returns' on the two investments were not equivalent, one could improve his/her welfare by diverting some funds from one investment to the other.

Note that if society is risk neutral, the risk aversion parameter is set equal to zero. In this case, the expression for the optimal CE ratio becomes:

\[
\frac{\partial c}{\partial m} = \frac{1}{\lambda}.
\]

This is the result discussed in Stinnett and Paltiel [10], who state that the CE ratio under uncertainty is represented by the 'ratio of means'. This states that the expected effectiveness of an incremental $1 worth of medical intervention should equal the marginal utility of $1 worth of income. Note that this criterion only makes sense if expected effectiveness is equivalent to expected utility, which only occurs under conditions of perfect certainty or risk neutrality.

Now it is useful to compare the two first order conditions in order to analyse the impacts of using the risk neutral criterion when, in fact, decision-makers are risk averse. Recall that the optimal CE ratio for risk-averse decision-makers is characterized in expression (2). Note that if the new medical intervention is variance increasing (i.e. \( \partial \sigma^2/\partial m > 0 \)), then the variance-related part of utility is increased (i.e. the bracketed term in (2) is increased) and the entire denominator is smaller. This suggests that the optimal CE ratio is higher, and the 'ratio of means' approach will approve projects that should be rejected based on the expected utility maximization criterion specified in (2). In other words, the 'false' assumption of risk-neutrality when interventions are variance increasing will lead to false-positive results, or Type I errors.
If the new medical intervention is variance decreasing (i.e. \( \sigma^2/c < 0 \)), then the variance-related part of utility is decreased (i.e. the bracketed term in (2) is decreased) and the entire denominator is larger. This suggests that the optimal CE ratio is smaller and that the ‘ratio of means’ approach will reject projects that should be accepted based on the expected-utility maximization criterion specified in (2). Thus, when interventions are variance decreasing, the ‘false’ assumption of risk-neutrality will lead to false-negative results, or Type II errors.

**CASE STUDIES**

This section will examine the CE ratios for two medical interventions discussed in the published literature. For each treatment in question, the CE ratio will be presented, followed by a discussion of the uncertainty-adjusted ratio. While it was argued earlier that society is risk averse, the magnitude of societal risk-aversion, \( r \), is unknown. Thus, for the purposes of illustration, a cut-off \( r \) will be determined that separates a cost-effective intervention from one that is not. This cut-off \( r \) will then be compared to previous measures of individual risk-aversion in the economics literature. It is important to note that these calculations are meant to be descriptive and, given the limitations inherent in using data from previously published studies, should not be interpreted as a mandate for action.

The difference between societal and individual risk aversion will depend, in part, on how individual utilities are aggregated, i.e. the exact form of the social welfare function. A Rawlsian social welfare function, where the objective is to maximize the utility of the person worst off, implies that social risk aversion will be greater than that of the average individual. On the other hand, when the utility of all individuals is weighted evenly, a utilitarian approach, and the government can partially pool and spread risks, social risk aversion may be lower than that of the individual. In addition to the influences of aggregation, the state, as a collective, may have interests that are independent from those of its citizens. In short, it is not clear whether societal risk aversion should be smaller or larger than individual risk aversion. The comparisons in these case studies to individual risk aversion estimates should be viewed as suggestive rather than prescriptive. As better estimates of societal risk aversion are obtained, either through empirical derivation or stated national policy, these should become the benchmark with which projects are evaluated.

Before discussing the individual interventions, we must discuss the limitations of using data from previously published studies. As one might expect, the data are often not presented in the form described in the theoretical model earlier. Often, the variance of costs and effects are not reported separately, but rather as a variance of CE. Further, some studies reflect uncertainty with 95% confidence intervals that reflect both sampling variation and sensitivity analysis. Lastly, no data are presented on the relevant budget dictating spending on these interventions. In lieu of this data, we will use a $60000 per QALY standard, a suggested figure in the literature that was chosen after a review of economic evaluations and previously suggested guidelines [29]. Thus, the empirical examination of uncertainty-adjusted CE will utilize the following expression to determine project suitability:

\[
\left( \frac{\mu(c)}{\mu(e)} - r \frac{\sigma^2}{\mu(e)} \right) \leq 60000,
\]

where \( c \) is costs in dollars, and \( e \) is effectiveness in quality-adjusted life years. Note that due to limitations in the way the case study data were reported we are forced to utilize the variance of the CE ratio rather than the ratio of the two variances. These two approaches are equivalent only when costs and effects have no covariance, which is consistent with the modeling in the studies that follow. As noted earlier, we will determine the \( r \) that solves this equation with equality. This will be the cut-off \( r \); below the absolute value of \( r \) the intervention is cost-effective and above it is not.

**Thrombolytic therapy for myocardial infarction**

The data for this case study are presented in Mark et al. [30]. In this study, the investigators examined the CE of tissue plasminogen activator (t-PA) as compared with streptokinase for acute myocardial infarction. Their results indicated that patients who received t-PA incurred higher costs ($2845) and a 1.1% higher survival rate than those treated with streptokinase. Quality of life was presumed equivalent under both treatments, thus yielding an average CE ratio of $32678 per...
QALY saved. In comparison to the industry benchmark of $60000 per QALY, this treatment should be approved.

In a subsequent section, the authors derive a 95% confidence interval on 1-year survival based on a sensitivity analysis that employed confidence interval in effects. This analysis produced CE ratios that range from $18781 to $71039 per QALY saved. Recognizing that a 95% confidence interval represents 3.92 S.D. (1.96 deviations above and below the mean), the standard deviation and thus the variance can be calculated. The standard deviation is $13331 yielding a variance of $178 million. Plugging into Equation (4) above: $32678 - r/2(178000000) = 60000$, yields a cut-off $r$ that equals $-0.00031$. This figure suggests that, due to the large variance of t-PA CE, only a very small degree of risk-aversion is necessary to overturn this project approval. In fact, this value is at the lower end of the range of estimates published in the economic literature, which vary from $-0.00047$ to $-0.00017$ [31]. Thus, once uncertainty and risk preferences are incorporated in the analysis, an intervention that is clearly cost-effective based on a 'means' approach, may in fact not be cost effective based on an uncertainty-adjusted approach.

**Chemotherapy with mitoxantrone plus prednisone for prostate cancer**

The data that form the basis of this case study are presented in Bloomfield et al. [32]. In this study, the investigators use data from a Canadian randomized trial to examine the CE of mitoxantrone plus prednisone as compared with prednisone alone for the treatment of hormone-resistant prostate cancer. Previous clinical trials demonstrated no survival differences, but there were significant changes in pain relief and health-related quality of life.

The results of this study suggest that treatment with mitoxantrone plus prednisone has lower costs and improves patient quality of life. The mean cost reduction was $1241 and an additional 13.3 quality-adjusted weeks of survival were provided. Together, these figures imply an average cost per QALY of $-5110$, and from figures on the 95% confidence interval a variance of approximately $99$ million was imputed. Following the steps outlined in the previous case study, a cut-off risk aversion parameter was derived; $r = -0.0013$. This value corresponds to a significant degree of risk aversion and is an order of magnitude larger than the most extreme estimate in the literature [31]. Thus, this cut-off $r$ is unlikely to attain for society at large, and even after adjustments for uncertainty, mitoxantrone plus prednisone appears to be cost-effective for the treatment of hormone-resistant prostate cancer.

**CONCLUSIONS**

This paper has disputed claims that while individuals are risk averse, society can be treated as risk neutral. Health outcomes are not easily insurable; intervention winners cannot, in general, compensate the losers; and net returns to medical interventions have significant variability. A framework for conducting CE analysis when social planners are risk-averse is developed. This framework is used to highlight the inappropriateness of the 'ratio of means' approach. Further, the model is used to demonstrate the repercussions of assuming risk-neutrality when society is risk-averse. If new interventions are uncertainty (variance) increasing, the risk-neutral approach will approve projects that should be rejected, i.e. will lead to false-positive results. If new interventions are uncertainty (variance) decreasing, the opposite will obtain with more false-negative results.

These analytical results are followed by a brief discussion of two case studies: thrombolytic therapy for myocardial infarction and chemotherapy with mitoxantrone plus prednisone for prostate cancer. While a ratio of means approach would suggest the approval of both projects, only the latter remains desirable after the incorporation of uncertainty. Given the wide range of results from the t-PA study, even a very modest degree of risk aversion makes the project appear undesirable. This is an important and intuitive result. Projects with large amounts of uncertainty must ‘compensate’ social investors with very strong average returns, or alternatively, investors may be willing to give up some return on average for less uncertainty.

Past research in CE analysis has focused on reporting mean CE ratios, with some recent attention being placed on reporting variance. This literature has generally treated variance as a measure of statistical uncertainty, which yields a confidence interval that allows one to determine if a
new intervention is a statistical improvement on the status quo. These variance measures are then coupled with a sensitivity analysis that varies important non-statistical parameters such as the QALY value to examine changes in the confidence interval. In this case, results may be reported as net benefit curves or acceptability curves over a range of QALY values. This paper is a departure from that literature in that we assert that, due to risk aversion, the variance directly affects the welfare gain from an intervention and has value beyond that of hypothesis testing. As such, all forms of uncertainty, including uncertainty about QALY measures, must be incorporated into the variance measure. Sensitivity analysis that allows decision-makers to choose a parameter value that seems heuristically reasonable no longer makes sense in a world of risk-aversion. Uncertainty about any parameter value has a direct impact on social welfare and the aversion. Uncertainty about any parameter value that seems heuristically reasonable no longer makes sense in a world of risk-aversion. Uncertainty about any parameter value has a direct impact on social welfare and the adoption decision that is embodied in the risk aversion parameter, \( r \). Specifying distributions for unknown parameters will be a challenge, but should highlight the costs of this uncertainty, and perhaps lead to research directed at improved knowledge in this area.

It should be noted that much of the data necessary to calculate the cut-off risk aversion level is often readily available in published CE studies. It is our recommendation that the cut-off risk aversion parameter becomes a standard reported figure in future studies. A better understanding of social risk preferences is critical to the successful implementation of the methods advocated here. Future research should focus on the form and magnitude of social risk aversion. One possible approach may be to examine environmental or health legislation enacted in the past and the information upon which these regulations were conditioned. In this manner, one could obtain a de facto estimate of social risk aversion. Further, developments in flexible utility functions that accommodate multiple forms of absolute and relative risk aversion may allow one to directly test our assumptions about the form of the social planners risk preferences [33,34]. In addition, the construction of QALY-type measures that more adequately reflect risk attitude should remain a high priority. While these measures will not eliminate concerns about societal risk aversion, insofar as returns within and across projects are not correlated, they will minimize them.

Lastly, attention should be paid to the social costs of uncertainty, so that a basis for assessing the value of uncertainty reduction can be developed. These values could then be used as a method for prioritizing research agendas and evaluating, \( ex~ante \), the expected economic returns to various lines of research [11,35,36]. The social planners’ problem would then be a simultaneous investment decision, with some monies going toward implementing medical interventions and some monies going toward reducing the uncertainty about the CE of interventions.

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**NOTES**

a. Of course, the existence of gambling suggests some individuals may be risk loving. There are two general explanations for such behaviour. First, gambling generates recreational utility, which may outweigh the disutility associated with uncertainty. Second, individuals transform probabilities so that they perceive their odds to be better than they are in actuality. In the context of medical decision making, it is unlikely that recreational pleasure would be present and the informed consent process is designed to limit the impact of probability transformation.

b. In this case, and in general, the collection of data to resolve parameter uncertainty as reflected in sensitivity analysis may result in statistical uncertainty due to sampling variation. Regardless, \( ex~ante \) and \( ex~post \) means are unlikely to be the same.

c. This result is closely related to a well-established observation in financial economics. When risks are, on average, correlated, the law of large numbers does not guarantee complete risk diversification, and the variance of returns cannot be ignored [20,21]. For a more detailed discussion of correlated returns and diversification in a medical context, see O’Brien and Sculpher [13].

d. In practice, \( Y \) could represent the budget of a health
care insurer, the federal health care administration, or society at large. This would, of course, depend on who is making the decision and who is funding the intervention.

e. Empirical tests of individual risk aversion support the notion of both constant and decreasing absolute risk aversion [28]. If one thinks about the risk aversion embodied in regulations such as the US Environmental Protection Agency’s protection of the ‘most vulnerable individual’ of the US Food and Drug Administration’s ‘do no harm’ clause in drug trials, it seems unlikely that these rules will be sensitive to national wealth changes. Thus, at a social level, CARA seems reasonable. If, however, the social planner did have CARA utility, all the basic theoretical results would remain the same. The cutoff risk aversion parameter defined in the case studies section would not have a neat analytical form, but for any given utility specification, a cutoff parameter, or pair of parameters, could be determined.

f. This figure is a suggested ‘rule of thumb’ and is not empirically derived.

g. While the 95% confidence interval is not a ‘true’ confidence interval based on statistical uncertainty, but one based on sensitivity analysis, we assume that it is a reasonable representation of 3.92 S.D.

h. The values presented here were imputed using figures on relative risk aversion and the median per capita income from 1998, $21200.

REFERENCES


