Quality adjusted life years (QALYs) and dose–response models in environmental health policy analysis — methodological considerations

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Abstract

Analyses of competing risks are currently limited by the lack of empirically well-founded and generalizable quantitative methods. Specifically, quantitative methods for comparative risk analysis require the consideration of the population impacted, the duration of impact, the health endpoints at risk, and the impact on individual quality of life. Whereas risk analysis can be used to provide quantitative estimates of disease incidence, environmental health policy analyses do not often account for differences in health impact from alternative disease states. We discuss the methodological issues related to the use of quality adjusted life years (QALY) as a metric for normalizing expected disease incidence to account for health impact. Through a case study of the risks and benefits of fish consumption, we demonstrate the use of QALY weights with dose–response models for environmental health policy decision making. We suggest that, although this approach can be generalized for use in comparative risk and health policy analysis, it is informationally intensive and requires additional assumptions to those used in traditional safety/risk assessment. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: QALY; Dose–response; Fish; Comparative risk analysis; Risk-benefit analysis

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1. Introduction

Risk analysis has evolved as a central tool for environmental health decision making. In traditional risk analyses, the goal is to provide estimates with uncertainty of the predicted incidence or relative risk of disease from environmental exposure. To conduct such an analysis, the National Academy of Sciences proposed a framework for risk assessment that included hazard assessment, exposure assessment, dose–response assessment, risk characterization, and risk management (NRC, 1983, 1994). This approach has resulted in the standardization of risk assessments. Risk assessment is now widely used by government agencies, environmental and human health advocacy groups, industry, and academic researchers to identify and examine human health risks and to suggest preferred risk management options.

Because risk assessment can provide estimates of disease incidence from environmental exposures, it serves as a common basis for debate in examining alternative health policies. However, the use of disease incidence alone as a basis for decision making ignores differences in health impact between diseases in terms of duration of impact, quality of life, and related social costs. Thus, comparative analyses of policy alternatives based on the examination of disease incidence alone would leave health impact and social costs unquantified. This challenge of performing comparative health policy analysis when disparate health endpoints are at risk arises in risk–risk or risk–benefit analysis; when estimating the aggregated health impact from exposure (including mixtures) with multiple, independent health effects; and when comparing regulatory programs with disparate mandates for protecting health.

1.1. Equivalency of health impact

To circumvent the challenges that arise from the need to account for health impacts when performing comparative risk analyses, analysts have either ignored these differences or restricted the comparative analyses to those health endpoints that could be reasonably considered to have an equivalent impact. For example, in a risk–benefit analysis of fish consumption, Anderson and Wiener (1995) examined the increased lifetime fatal cancer risk from exposure to organochlorines and the benefit of coronary heart disease mortality reduction associated with fish consumption. In this analysis, they assumed that all cancers were fatal and that mortality from cancer and heart disease had an equivalent health impact and illness duration (Anderson and Wiener, 1995). Because their analysis was constrained to the simplified case wherein duration and severity were assumed to be equal for the two health effects, Anderson and Wiener simply added the excess risks of developing cancer and heart disease contributed by fish to estimate the net health impact of lifetime fish consumption. Results from their analysis suggested that while the potential excess lifetime cancer mortality risks are high, the reduction in cardiovascular mortality is 12- to 23-fold greater. Furthermore, they proposed that the benefits would be substantially greater (over 1000-fold) if the actual contaminant concentrations were used in the analysis rather than an organochlorine concentration limit assumed by the US Food and Drug Administration (FDA). This implies that there is a substantial net decrease in the risk of dying (by all considered causes) as fish intake rates increase.

As an alternative to comparative risk analysis, benefit–cost analysis and cost-effectiveness analysis can be used to examine alternative policies with disparate health endpoints. As currently applied, benefit–cost analysis is used in regulatory decision making to establish whether the benefits of a given health policy outweigh the costs. In this approach, health impacts are quantified in monetary terms, allowing the comparison of diverse health (and non-health) endpoints. However, there remains some social and ethical debate about the monetization of life and health. In contrast to benefit–cost analysis, cost-effectiveness analysis has developed non-monetary metrics for comparing diverse health endpoints including life years gained (or lost), health utilities, healthy year equivalents, quality or disability adjusted life years (QALYs or DALYs, respectively), and others (Tolley et al., 1994; Gold et al., 1996). These
metrics capture various qualities of health impacts under alternative considered scenarios and allow the identification of the most effective or efficient policy alternative.

In the end, the selection of the metric for establishing equivalency of health impacts depends on the analyst’s goals — there is no universally accepted metric for valuing and comparing diverse health endpoints and impacts. If the analyst believes that equivalency between two health endpoints exists if an individual is ambivalent between them, (s)he may choose to use QALYs, utilities, or willingness-to-pay as the most appropriate metric. If health effects are compared based on their duration of impact alone, workdays lost, hospital stay, or life years lost may be the most appropriate metric. If social cost is the preferred perspective, insurance reimbursement costs or productivity loss may be considered. Finally, if the population affected is the preferred perspective, disease incidence (i.e., risk), hospitalization rate or mortality rate may suffice. Of course, the selection of the preferred metric will require justification, and the analyst will need to consider whether the metric appropriately captures the dimensions of health so as to allow comparisons of alternative policies.

1.2. Normalizing dose–response functions to account for health effect using QALYs

We use estimates of risk (derived through risk assessment) with metrics of health impact (taken from cost-effectiveness analysis) to predict the net health impact from exposures with competing risks. We argue that this approach can be generalized to any health endpoint, allowing comparison of diverse environmental health policies using non-monetary metrics. By normalizing dose–response functions with metrics that account for health impact the analyst can: (1) aggregate normalized dose–response functions for multiple health endpoints to estimate the net population health impact; (2) directly compare normalized dose–response functions or net health impacts to identify the health policies with the lowest adverse (negative) health impact; and (3) identify distributional inequalities in terms of health impact to identify sub-populations at special risk.

We have previously conducted an analysis of the risks and benefits of fish consumption using QALYs as a metric for aggregating health risks across considered disease endpoints (Ponce et al., 2000). In that analysis, we used QALYs as an appropriate metric of health impact because they consider both quality and quantity of life as independent attributes that contribute to perceived wellbeing. In this paper, we present some of the methodological considerations and assumptions required for using QALYs to normalize dose–response functions in environmental health policy analysis.

Justification for the use of QALYs as a metric for measuring population health can be found in the cost-effectiveness literature. Originally developed to examine the cost-effectiveness of medical interventions across medical specialties, QALYs provide a means for comparing health outcomes that differ in terms of survival and quality of life (Schwartz et al., 1993; Fabian, 1994; Gold et al., 1996; Johannesson et al., 1996). Because QALYs consider both quality and quantity of life, they improve on other measures of disease impact such as life years lost, hospital stay, or survival at 5 years, which consider only duration of impact as a measure of health effect. Moreover, the use of QALYs avoids assigning a monetary cost to human life and health, which can be a controversial focus of benefit–cost analysis. Finally, by incorporating individually identified preferences for alternative health states, health policy managers may make policy decisions that maximize the occurrence of desired outcomes at the expense of undesired outcomes (Gold et al., 1996).

QALYs are estimated by weighting each year of life (T) by a weight that reflects the quality of life (Q) (Johannesson et al., 1993). When QALYs are aggregated across members of a population and mapped over years of life, a population ‘health profile’ can be derived for each considered policy. This health profile can be quantitatively estimated through definition of a utility function \( U(Q,T) \), which describes the relationship between duration of impact and quality of life in estimating the population QALYs. Under the ax-
ioms of expected utility theory, the optimal policy would be that policy that maximized the expected population health profile (i.e. that maximized the population QALYs) (Johannesson et al., 1993; Gold et al., 1996).

In the simplest case, QALYs should satisfy several assumptions (Johannesson et al., 1993):

(1) Quality of life (Q) and life years (T), which reflect the duration of impact, are mutually utility-independent. This implies that these attributes can be considered separately.

(2) A constant proportional trade-off between quality and quantity of life exists. This implies that the rate of exchange between quality and quantity of life is independent of the amount of life remaining or the individual health condition.

(3) Risk neutrality holds. This implies that the utility function for estimating QALYs is linear.

(4) All QALYs are of equal value. In other words, on a population basis, the health policy that results in the greatest quantity of population QALYs is the preferred policy regardless of how QALYs are distributed among population members.

These assumptions may not be universally applicable and they raise certain ethical and social implications. For example, assuming that all QALYs are equal ignores social perspectives regarding the distribution of QALYs among population members. Whereas one health policy might have the highest population QALYs relative to considered alternatives, these gains may derive from a very high quality of health in a minority of the population at the expense of the majority. Alternatively, improved quality of life for older population members may be achieved at the expense of the young or disabled. There is empirical evidence to suggest that although aggregated QALYs may be numerically equal between considered policies, the policies may not be actually valued equally (Russell et al., 1996).

In addition to these assumptions, several additional simplifying assumptions may be made when combining QALYs with dose–response models to estimate net population health impact, including:

(5) Independence of disease incidence holds. In other words, the presence or absence of one health effect does not alter the probability of occurrence of a second health effect.

(6) The independence of disease impact holds. In other words, on a population basis, the occurrence of two adverse health outcomes in one individual is equivalent to the occurrence of the same two adverse outcomes in separate (but otherwise comparable) individuals.

Although these latter assumptions greatly simplify the quantification of health impacts using normalized dose–response models, the analyst should only make these assumptions following studied consideration. Specifically, there is overwhelming evidence to suggest that the presence of one disease state can influence the development of others. While the relationships between considered health states may not be well-established, they cannot be ignored and the analyst should dismiss the plausibility of a relationship only with great care. Methods are available to account for non-independence (collinearity) in regression models to isolate the independent effect of one variable relative to others when assumption 5 does not hold, although this issue is not further addressed here.

2. Methods

2.1. Dose–response modeling

We have previously examined the benefits and risks of fish consumption in two populations (Ponce et al., 2000). In that analysis, we elected to use the reduced risk of fatal myocardial infarction (MI) as a result of fish consumption to model the beneficial effects of eating fish. We chose developmental delay in offspring as a result of methylmercury (MeHg) in the consumed fish as the health endpoint at risk from eating fish.

Data from existing studies were used to estimate dose–response relationships. In the case of reduced fatal MI, estimates of reduced risk were modeled by logistic regression using least squares estimation from epidemiological data from a male Chicago population (Daviglus et al., 1997). Whereas the effects of fish consumption on car-
diovascular disease are often ascribed to omega fatty acids (Kinsella et al., 1990; Kim et al., 1995; Connor and Connor, 1997), Daviglus et al. (1997) did not measure omega-3 content in consumed fish. Instead, they model the incidence of cardiovascular disease on reported fish intake. For this reason, we chose to model fish intake (0–300 g/day) as the independent variable. Use of this data set required that we assume that the data were applicable to women. Furthermore, we assumed that the change in the relative risk was comparable across all considered age categories. Although there is evidence to suggest that these assumptions do not strictly hold, we were unable to find quantitative data that could be used to modify our model. Because our model uses a life table approach (see below), the model can be easily modified to incorporate new age- and gender-specific information as it becomes available.

In the case of developmental delay, a Weibull excess risk model was fitted to data on delayed talking incidence in children with gestational exposure due to maternal consumption of MeHg contaminated grain (Marsh et al., 1987). Because dose–response information on neurodevelopmental risks was available for methylmercury, we developed dose–response models based on three plausible methylmercury concentrations in consumed fish (i.e. 0.5, 1 and 2 ppm). Thus, we assumed that the Marsh et al. (1987) data, which involved a limited term exposure to relatively high concentrations of methylmercury (and other organomercury compounds) in bread, were an appropriate basis for developing a dose–response function for modeling risks from long-term, low concentration exposures to methylmercury in fish. Such an assumption disregards potential mitigating influences on the developmental risks of methylmercury, such as selenium or other nutrients, which exist in fish.

Alternatives to both the Weibull and logistic regression models and additional or alternative health endpoints may be considered. However, the analyst should be aware of biological dependencies between considered health endpoints when adding additional health endpoints into the model. Although we assume independence between the two considered health endpoints (which is a reasonable assumption in our model), independence of health effects does not universally apply.

2.2 Populations

In the previous case study of the risks and benefits of fish consumption, we considered two plausible populations as possible target audiences for fish consumption advisories. The first population consisted of men, women and children of all ages in a population of 100,000 individuals. This population was chosen to examine the potential effects of population-wide fish consumption restrictions. Because the health endpoint at risk involved delayed development in children exposed to methylmercury in utero, the second population consisted of 100,000 women between the ages of 15 and 44, considering childbearing years, and their offspring. This population was chosen to examine the potential impact of fish consumption advisories targeted to the ‘at risk’ population.

2.3 Estimation of the net health impact

The net health impact of fish consumption can be expressed as:

\[ \text{Net health impact} = \sum (-w_i \Delta LY_i) + \sum (w_j \Delta LY_j) = \Delta QALY \] (1)

where \( \Delta LY_i \) is the life-years lost for each risk endpoint considered, \( \Delta LY_j \) is the life-years gained from each benefit considered, and \( w_i \) and \( w_j \) are the QALY weights for each risk and benefit endpoint, respectively. In this simplified case with consideration of one risk endpoint and one benefit, Eq. (1) simplifies to:

\[ \text{Net health impact} = -w_1 \Delta LY_1 + w_2 \Delta LY_2 = \Delta QALY \] (2)

where \( \Delta LY_1 \) is the life-years lost due to developmental delays, defined as the expected extra population incidence of developmental delays due
Table 1
Life table used to calculate the QALYs gained in the population due to reduced risk of fatal myocardial infarction (MI) at a fish consumption rate of 300 g/day

<table>
<thead>
<tr>
<th>Age interval (year)</th>
<th>Mortality rates (per 100000)</th>
<th>Baseline mortality rate from all causes</th>
<th>Baseline MI mortality rate</th>
<th>Mortality rate from all causes given fish consumption</th>
<th>Population at beginning of the interval</th>
<th>Deaths in the interval</th>
<th>Stationary population</th>
<th>Average number of years of life</th>
<th>QALYs gained (lost)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 1</td>
<td>854.4</td>
<td>0.0</td>
<td>854.4</td>
<td>100000</td>
<td>854.4</td>
<td>100000</td>
<td>854.4</td>
<td>1.00</td>
<td>25539.74</td>
</tr>
<tr>
<td>1 to 4</td>
<td>44.8</td>
<td>0.0</td>
<td>44.8</td>
<td>99145.6</td>
<td>1775</td>
<td>99079.0</td>
<td>3.96</td>
<td>99863.9</td>
<td>9.89</td>
</tr>
<tr>
<td>5 to 14</td>
<td>23.4</td>
<td>0.0</td>
<td>23.4</td>
<td>98968.1</td>
<td>231.3</td>
<td>98863.9</td>
<td>9.89</td>
<td>98300.4</td>
<td>9.83</td>
</tr>
<tr>
<td>15 to 24</td>
<td>98.5</td>
<td>0.2</td>
<td>98.5</td>
<td>98736.7</td>
<td>968.3</td>
<td>98300.2</td>
<td>9.83</td>
<td>97146.1</td>
<td>9.71</td>
</tr>
<tr>
<td>25 to 34</td>
<td>142.4</td>
<td>1.4</td>
<td>142.1</td>
<td>97768.5</td>
<td>1383.3</td>
<td>97744.3</td>
<td>9.71</td>
<td>95382.5</td>
<td>9.54</td>
</tr>
<tr>
<td>35 to 44</td>
<td>235.5</td>
<td>9.3</td>
<td>233.4</td>
<td>96385.1</td>
<td>2246.0</td>
<td>96331.1</td>
<td>9.54</td>
<td>92275.1</td>
<td>9.23</td>
</tr>
<tr>
<td>45 to 54</td>
<td>460.0</td>
<td>40.8</td>
<td>450.8</td>
<td>94139.2</td>
<td>4214.9</td>
<td>94105.3</td>
<td>9.22</td>
<td>85577.0</td>
<td>8.56</td>
</tr>
<tr>
<td>55 to 64</td>
<td>1154.7</td>
<td>127.4</td>
<td>1125.9</td>
<td>89897.3</td>
<td>9857.3</td>
<td>89520.0</td>
<td>8.54</td>
<td>85747.0</td>
<td>7.17</td>
</tr>
<tr>
<td>65 to 74</td>
<td>2617.1</td>
<td>299.1</td>
<td>2549.5</td>
<td>80040.0</td>
<td>18644.8</td>
<td>79135.2</td>
<td>7.12</td>
<td>48153.5</td>
<td>4.82</td>
</tr>
<tr>
<td>75 to 84</td>
<td>5951.6</td>
<td>694.9</td>
<td>5794.6</td>
<td>61395.1</td>
<td>28156.1</td>
<td>60539.0</td>
<td>4.73</td>
<td>25539.74</td>
<td></td>
</tr>
<tr>
<td>85 to 99</td>
<td>15481.7</td>
<td>1593.5</td>
<td>15121.6</td>
<td>33239.0</td>
<td>30985.5</td>
<td>31253.5</td>
<td>2.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>880</td>
<td>88.2</td>
<td>860.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The first column denotes the age interval, the second and third the mortality rates from all causes and from MI, and the fourth column is the mortality rate from all causes given the above fish consumption rate. Starting with a cohort of 100000 people, the number of deaths per age interval (columns 6, 8) can be calculated, along with the average number of people in that age interval (stationary population, columns 9, 11) and average number of years lived (columns 10, 12) for both the baseline and fish consumption populations. The difference in population life-years are the QALYs gained or lost due to fish consumption.
to fish consumption times the duration of effects (the average life expectancy at the time of birth). \( \Delta LY_2 \) is the life-years gained due to reduced fatal MI, \( w_1 \) is the QALY weight given to a fetal developmental delay, and \( w_2 \) is the QALY weight given to fatal MI.

### 2.4. Estimating the duration of impact

Using the estimates of reduced MI risk, changes in life-years gained or lost and life expectancy due to fish consumption were calculated for the population. The change in life-years was calculated using a life table approach (see Table 1). Life tables can be thought of as following a cohort of newborns through their lifetime, tabulating yearly mortality and survival (Patrick and Erickson, 1993). Life tables can be either complete (by calculating mortality and survival at every age) or abridged (by using age intervals). An abridged life table contains ranges of ages, generally 5 or 10 years, and age range-specific mortality rates. In our analysis, we developed an abridged life table using age-specific mortality rates for all causes and for MI, where the cause-specific mortality rates were derived from 1993 NCHS data (columns 2 and 3, NCHS, 1997, 1999).

The derivation of our abridged life table began with the use of age- and gender-specific mortality rates (per 100,000 population) from all causes as the baseline (no fish consumption assumed, columns 1 and 2, Table 1) and a starting cohort of 100,000 people (column 5, Table 1). Note that we have presented mortality rates for both genders considered jointly. By using the mortality rate for individuals who are <1 year old applied to the initial population, the analyst can estimate the population mortality and survival at 1 year. The population that survived at 1 year can then be used with age- and gender-specific mortality rates at 2 years of age to estimate population survival at 2 years. This process is conducted exhaustively for the entire range of considered ages, here ranging from less than 1 to 99 years.

In our abridged life table, we assumed that we had a stationary population. We used the average number of people in an age interval (column 9) and divided by the years in the age interval to estimate the average number of years of life attributable to the age interval (column 10). Life expectancy was then calculated as the sum total of the average years of life across all considered age intervals (see bottom of column 10, Table 1).

To examine the change in population life expectancy from a fish intake related reduction in fatal MI, we modified the baseline MI mortality rate by the relative risk of MI mortality derived from Daviglus et al. (1997). In this process, we first subtracted age-specific rates for MI (column 3) from age-specific mortality rates from all causes (column 2). This process can also be accomplished using gender-specific rates rather than joint mortality rates. This subtraction removed the influence of MI mortality from all cause mortality in the life table using standard methods for developing ‘cause-eliminated life tables’ (Patrick and Erickson, 1993). We then modified the age-(and gender-) specific mortality rates for MI mortality (column 3) by the relative risk of MI at a given fish consumption rate (using the dose–response modeling based on data from Daviglus et al., 1997). This fish consumption-modified MI mortality risk was then added back into the cause-eliminated MI mortality rate to develop a fish-intake modified all cause mortality rate, which is presented as column 4. Life expectancy was then calculated for the fish consumption group as described for the baseline case (see columns 7, 8, 11 and 12). The difference in population life years between the baseline case and the fish consuming population was then calculated as the population life-years gained or lost for a specific fish consumption rate due to the modified risk of MI mortality. Because the quality of life changes from 1 to 0 from MI mortality, the change in population life years is equivalent to the change in population QALYs (see bottom of Table 1).

To estimate the life-years of delayed talking in the offspring, we assumed that effects remained throughout life; therefore, life expectancy estimates were used. Note that because the population life expectancy changed with the fish intake rate, the life years of impact for a child with developmental delay was dependent on the fish consumption rate.

Discounting for effects that are expected to
occur late in life was also examined. In this analysis, we examine the effect of an assumed discount rate of 3% for each year of life beginning at birth. A number of alternative conventions are possible and are easily incorporated into the life table method if so desired.

2.5. QALY weights

In our model, QALY weights range from 0 (death) to 1 (optimal health), although some health states may also be considered ‘worse than death’ and could be valued as less than 0. For the endpoint of reduced risk of MI mortality, the QALY weight of 0 for mortality was chosen. We assumed a health-related quality of life weight of 0.9 for permanent neurobehavioral deficit according to survey data from Kind et al. (1982).

3. Results

Fig. 1 presents results of the net health impact of eating fish in the two population scenarios. As shown, across all considered fish intake rates (0–300 g/day) and fish methylmercury concentrations (0.5–2 ppm), fish consumption had a strong net positive health impact in the population consisting of 100,000 individuals of all ages and both genders. In contrast, under the same exposure conditions fish consumption had a strong net negative health impact in the population of 100,000 women of child-bearing age and their children.

The discrepancies in predicted net health impact between the two considered populations can be reconciled with examination of Table 1. As demonstrated, the risk of MI mortality increases with increasing age. Because women of child-bearing age have a very low risk of MI mortality, the health benefits of eating fish are modest. In contrast, because the risk of methylmercury-induced neurodevelopmental delay manifests itself during pregnancy, women of child-bearing age are at very high risk relative to other subgroups. For example, because there is no male-mediated reproductive toxicity associated with this health endpoint, the exclusion of males in this cohort removes a subgroup with no risk (but some benefit).

To demonstrate the application of sensitivity analysis in this model, we examine the effect of varying the fertility rate on the predicted net health impact of eating fish in the women/children cohort. As demonstrated in Fig. 2, the net health impact from eating fish in the

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Fig. 1. Predicted net population QALYs gained or lost from eating fish (0–300 g/day) contaminated with methylmercury (0.5–2.0 ppm). On the left are the net QALYs gained in a population of 100,000 individuals of all ages and both genders. On the right are the net QALYs lost in a population of 100,000 females of childbearing age (15–44 years) and their children. The net health impact estimates are bounded by estimates for 0.5 ppm (upper curve) and 2.0 ppm (lower curve) methylmercury in fish.
women/children population is sensitive to the fertility rate in the population. Whereas we chose to use the average fertility rate for the United States as the model baseline, the use of alternative fertility rates reported for other countries will either decrease (with a larger fertility rate) or increase (with a smaller fertility rate) the net health impact (see Fig. 2).

To demonstrate the effects of discounting life, we present results for predicted net health impact of eating fish (0–300 g/day, 0.5–2 ppm methylmercury) in a population of 100 000 individuals of all ages and both genders (Fig. 3). Specifically, we compare the effect of applying a 3% annual discount rate starting from birth against the baseline case wherein no discounting was applied. As demonstrated, the use of a constant 3% discount rate results in a net negative health impact of eating fish when fish consumption rates are high and the fish tissue concentration exceeds 1 ppm. The strong effect of discounting arises because the relatively large health benefits of reduced MI mortality from eating fish are realized later in life, when life years have a substantially discounted weight relative to early in life. Thus, although there is a large effect in terms of population life years gained from reduced MI fatality by eating fish, the relative contribution in terms of population QALYs following application of the 3% discount rate is low, and does not exceed the risks at high intake rates and high fish contamination levels.

4. Discussion

We have previously examined the use of QALY weights to normalize dose–response models to account for health impact (Ponce et al., 2000). The purpose of this paper was to clarify some of the methodologic considerations inherent in such an analysis. Specifically, in this paper we detail the development of life tables, describe the effects of discounting, and expand the sensitivity analysis to include an examination of the effect of fertility rate on the net health impact. We discuss these issues, and others, below.

4.1. Net health impact

As demonstrated in Fig. 1, in the absence of
discounting, the benefits of fish consumption outweigh the risks in the population of 100,000 of all ages and both genders. In contrast, the fish consumption risks outweighed the benefits in the population of 100,000 women of child-bearing age and their children. When a constant annual discount rate of 3% is applied, the risks of fish consumption outweigh the benefits at high fish intake rates and with high concentrations of methylmercury in the fish in the population consisting of all ages and both genders. These results can be understood by realizing that the first scenario consists of population members with a relatively high risk of MI (older individuals), whereas the second consists of population members at high risk of having children with neurodevelopmental delay. The effects of discounting life are shown to reduce the weight of health impacts that occur late in life.

4.2. Selection of health state preference weights

The assumed health-related quality weight of 0.9 for permanent neurobehavioral deficit, as indicated by neurodevelopmental delay, encompassed the range of weights given by 70 respondents who ranked permanent slight social disability that causes no distress (0.99) to severe distress (0.93); severe social disability and/or slight physical impairment that causes no distress (0.98) to severe distress (0.91); and severely limited physical ability with no distress (0.96) to severe distress (0.87), wherein the value in parentheses represents population median respondent preference weight (Kind et al., 1982). These health state valuations were derived using a psychometric survey that defined eight states of objective disability with four states of distress. As reported, the subjective valuations for different health states were highly variable, non-normally distributed, and correlated with the classification of the survey population, which included medical patients \( n = 10 \), psychiatric patients \( n = 10 \), medical nurses \( n = 10 \), psychiatric nurses \( n = 10 \), healthy volunteers \( n = 20 \), and doctors \( n = 10 \) (Kind et al., 1982). If we relaxed our assumption that delayed neurodevelopment manifested itself as a permanent decline in quality of life, the QALYs lost from methylmercury in fish would be reduced (data not shown).

We have conducted sensitivity analyses of the effect of alternative preference weights for permanent, delayed neurodevelopment on the predicted net health impact (see Ponce et al., 2000). Such sensitivity analyses should be conducted routinely as a means to gauge the relative influence of alternative preference weights on the expected outcome. It can be expected that the use of any subjective method for establishing preference weights for alternative health states will be influenced by true inter-individual differences in preference weights and artifactual effects related to survey design and population selection. The use of sensitivity analyses can thus help the analyst to decide whether improved information regarding the population preference weights for alternative health states could alter the identification of the preferred policy alternative.

4.3. Use of life tables

Several assumptions are inherent in the use of life tables. Specifically, the mortality rates used in the table are assumed to apply to the entire cohort, there is no migration in the population, and births are evenly distributed throughout the year (Patrick and Erickson, 1993). The mortality rates used in the life table are those observed in the actual population, whereas the cohort we examine is hypothetical. Hence, the distribution of mortality is not what would be seen in an actual population of 100,000, as mortality rates will change over the lifetime of this cohort. The latter two assumptions imply that, on any given date, there will be a constant number of persons in the age interval population (stationary population), as for every death or aging another person from the age group below will take that place. Life tables are calculated yearly by the NCHS and can also be calculated for specific races, genders, or regions. For more information see Anderson (1999).

4.4. Discounting

It is traditional to apply discount rates to model
the cost-effectiveness of health consequences that impact life at different times. The application of discount rates to examine the relative merits of health policies that impact future life years is suggested by assuming a steady-state relationship between the value of health and the cost of those health benefits and the acceptance of discounting for future money relative to present money, which suggest that the discount rate for health benefits should be in proportion to the discount rate of money. However, a number of arguments have been put forth in support of different discount rates for money and health benefits, or the dismissal of health benefit discounting altogether. The reader is referred to Gold et al. 1996 for detailed discussion of these issues. Suffice it to say that our use of life table analysis provides an easy means for incorporating discount rates. (An example comparison of model predictions of the Net Health Impact of fish consumption using a 0% or 3% discount rate is presented in Fig. 3.)

4.5. Uncertainty and sensitivity analyses

We have examined the sensitivity of the model to various input parameters such as different populations, fish intake rates, and fish methylmercury concentrations (see Ponce et al., 2000). In this paper, we demonstrate the sensitivity of the Net Health Impact to the selection of the fertility rate. For example, while we used a fertility rate of 65.0 per 1000 based on data for US women aged 15–44, different portions of the world and areas of the US have higher and lower fertility rates. Because differences in fertility rates will impact the population size of the children at risk of neurodevelopmental delay from maternal exposure to methylmercury, differences in fertility rates will alter the estimation of net health risks.

Using the life table as a basis for estimating QALYs gained or lost from implementation of a health policy easily accommodates uncertainty analysis. For example, although Table 1 incorporates deterministic values for cause-specific mortality rates by age and gender, these values can be replaced by appropriate distributions to reflect inter-individual variability in life course (i.e. latency, duration, and outcome) from disease. Alternatively, use of distributions for the quality of life weights would allow analysis of both inter-individual differences and lack-of-knowledge uncertainty in weighting of alternative health states.

5. Conclusions

The methods presented here demonstrate the use of QALYs and dose–response models for comparative risk analysis. Specifically, this quantitative method can be generalized to consider any morbidity and mortality risks for which data exist. Taken as a whole, the use of life table analysis, QALY weights and dose–response modeling provides a flexible analytical platform to explore the influence of alternative assumptions on policy preference. However, the model requires the determination of both duration and health impact of disease from an exposure. These informational requirements for using QALY weights substantially increase the informational demands compared to traditional risk assessments. Specifically, disease latency, age-of-onset, and disease duration from environmental exposures in animals and humans are generally poorly understood. This lack of information will challenge model specification and animal-to-human extrapolations, which are commonly used in traditional risk assessments. The magnitude of the uncertainty introduced into the model because of this lack of information is likely to be at least as large as uncertainties in extrapolating potencies or other factors from animals to humans.

As demonstrated here and previously (Ponce et al., 2000), both sensitivity and uncertainty analysis can be readily conducted to examine the impact of uncertainty and variable specification on the model predictions. Because sensitivity analysis can define the boundary conditions under which one health policy is preferred relative to another, this approach can create transparency in decision making and allow individuals to determine policy preferences using their own subjective weights for alternative health states. We argue that the use of a preference-based method, such as QALYs, is an
efficient means for determining resource allocation in the development of health and risk management policies.

Determination of QALY weights requires population surveys. This can be expected to limit the casual use of this method. However, development of standardized weighting factors as defaults for various health states may provide a reasonable means for conducting a first-tier analysis. In such an approach, the analyst could develop the model, incorporate the default quality of life weights, and identify the optimal policy. Next, an analysis of the sensitivity of the model to selection of the severity weight would provide information regarding whether population-specific weights would likely alter selection of the preferred policy. If warranted, a population-specific survey could then be conducted to obtain specific quality of life weights for use in the model.

In closing, any comparative risk analysis involving disparate health effects will require subjective information regarding the preferences for alternative health states. The use of risk (disease incidence) alone as the basis for decision making automatically assumes equivalence between alternative health states, and the use of disease incidence measures without consideration of the potential health impact can be expected to result in inferior health policies over the long term. We advocate the use of health impact-normalized dose–response models as a means for conducting appropriate environmental health policy analysis. Although we have demonstrated the use of QALYs as a metric to normalize dose–response models, alternative metrics exist and should be explored for this purpose.

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References


