

ESTIMABILITY AND ESTIMATION OF EXPECTED YEARS OF LIFE LOST DUE TO A HAZARDOUS EXPOSURE

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SUMMARY

Expected years of life lost is an important concept in public-health and legal issues. We describe conditions under which the expected years of life lost due to hazardous exposure is estimable (identifiable) from epidemiologic data. We show that, in general, the average years of life lost among exposed subjects dying at a given age (the age-specific expected years of life lost) is not identifiable, although the average years of life lost among all exposed subjects (the unconditional expected years of life lost) is identifiable from an unbiased epidemiologic study. We also show that the average years of life lost among all exposed subjects dying of a specific cause (the cause-specific expected years of life lost) is not identifiable. We discuss the implications of these results for compensation schemes based on years of life lost, and compare such schemes with those based on the probability of causation.

1. INTRODUCTION

Expected years of life lost is an important parameter in public-health and legal issues, and thus it is necessary to determine the conditions under which epidemiologic data can be used to estimate this parameter. Here we will consider the latter problem in the context of tort suits. To motivate our discussion, consider the following hypothetical example.

Suppose that in 1955 one John Smith, a non-smoker born in 1925, worked for 10 months in an asbestos textile plant, and had no other asbestos exposure. At age 60, John Smith died of cancer, whereupon his spouse brought suit against the company that owned the plant. Suppose also that the cancer causing John Smith's death was peritoneal mesothelioma. Since this cancer type is incredibly rare except in asbestos-exposed individuals, it would be nearly certain that Smith's cancer was due to asbestos exposure at the plant, and so the compensation awarded to Smith's spouse by the court would depend on the extent of damages caused by exposure. The court's assessment of damage might take into account both the years of life lost by Mr. Smith and the hardships to be endured by his spouse due to loss of his earning power. If the extent of damage was measured by years of life lost and payment was to be in proportion to damages, the court's interest would be in estimating Smith's expected years of life lost. Here, we consider this estimation problem and payment schemes based on expected (average) years of life lost. Such schemes represent an important alternative to schemes that would give the same monetary award

to all former plant employees who died of peritoneal mesothelioma (such as the schemes in certain workmen's compensation laws).

We first review schemes based on the probability of causation, for the latter concept is closely related to expected years of life lost.

2. THE PROBABILITY OF CAUSATION AND PAYMENT SCHEMES

Suppose now that John Smith had died of lung cancer rather than peritoneal mesothelioma. Since death from lung cancer can occur even in the absence of asbestos exposure, we cannot be certain that asbestos played any role in Smith's lung cancer. In the face of uncertainty as to the cause of a particular individual's cancer, it has been suggested that award levels in tort suits be based on the probability of causation. (For detailed discussions of the probability of causation and the parallel concept of etiologic fraction, see References 1-3.) One such proposal is that the award should equal the product of the probability of causation and the award that would have been given if it was known with certainty that the exposure at issue had caused the cancer at issue.⁴ For a payment scheme in which awards are to be based on years of life lost, this proposal implies that compensation should be proportional to the product of the probability of causation for the cancer victim and the victim's expected years of life lost when it is known with certainty that his cancer was due to asbestos. If, on the other hand, the same award is to be paid for all lung cancer deaths known with certainty to be caused by asbestos, then, in the face of uncertainty, payment should be solely in proportion to probability of causation. To clarify the distinction between payment schemes with the awards proportional to years of life lost and those with awards proportional solely to the probability of causation, suppose a co-worker of Smith's, John Brown, died of lung cancer at age 40, and that it is known that for both Smith and Brown the probability of causation is 50 per cent. Then, under a scheme with awards proportional to the probability of causation, the estates of Smith and Brown would be equally compensated. But, in the absence of exposure, Brown's life expectancy at his age of death exceeded Smith's, so that schemes that pay in proportion to years of life lost would award greater compensation to the Brown estate.

Another proposal is to award full compensation if the probability of causation exceeds 1/2, but award nothing otherwise.⁴ This proposal is based on an interpretation of tort law that holds that no compensation should be paid unless it is 'more probable than not' that the injury was caused by the action of the defendant, but is nevertheless open to question under basic considerations of the plaintiff's welfare.⁵

Implementation of the above payment schemes requires empirical estimates of the probability of causation. Suppose an epidemiologic investigation has determined that at age 60, the lung cancer death rate among non-smoking cohort members with exposure history identical to that of Mr. Smith is twice the rate in a comparable group of non-exposed non-smoking subjects. We call this the *empirical rate ratio* and denote it R . Many epidemiologists and statisticians (for example, Reference 6) have suggested that, in the absence of bias, one can estimate the probability that John Smith's lung cancer was due to asbestos by the empirical quantity $(R - 1)/R = (2.0 - 1)/2.0 = 0.5$.

If the background rate of disease (that is, the disease rate when unexposed) is the same for *all* non-smoking cohort members, then, in the absence of confounding, selection bias or misclassification, $(R - 1)/R$ can indeed be interpreted as the probability of causation.¹ But, even if misclassification and bias are absent, variation in *unmeasured* genetic and environmental factors will lead to large within-group heterogeneity in background rates. Unfortunately, except in unusual circumstances, $(R - 1)/R$ does not equal the probability of causation in the presence of

heterogeneity. It is for this reason that Lagakos and Mosteller⁷ called $(R - 1)/R$ the 'assigned share' rather than the 'probability of causation'. In fact, we have shown that it is impossible to consistently estimate from epidemiologic data alone the average probability of causation for exposed subjects dying at a particular age; in other words, the age-specific probability of causation is not statistically identifiable (estimable) from epidemiologic data.¹ Even in an unbiased study, the empirical disease rates only determine a range of possible values for the age-specific probability of causation.

In this paper, as in Reference 1, we will focus only on questions of identifiability of parameters, rather than bias or sampling variability of estimators. We will show that the average years of life lost for exposed subjects observed to die at a particular age (that is, the age-specific expected years of life lost) is not identifiable, but that the average years of life lost by *all* exposed subjects is identifiable, that is, can be consistently estimated from an unbiased epidemiologic cohort study. In contrast, the probability of causation remains non-identifiable even when averaged over all exposed subjects.

The age-specific probability of causation and years of life lost depend on both the unknown mechanisms by which exposure causes death and the unknown degree of heterogeneity in the background disease rate. We show that, associated with various postulated biologic mechanisms and degrees of heterogeneity, there exists a 'potentially optimal' empirical payment scheme that pays in proportion to the expected number of years of life lost, and another 'potentially optimal' empirical payment scheme that pays in proportion to the probability of causation. These payment schemes are 'potentially optimal' and empirical in the sense that (in principle) they allow one to derive from epidemiologic data the optimal way to allocate awards proportional to the age-specific years of life lost and awards proportional to the age-specific probability of causation, provided that the postulated mechanism and degree of heterogeneity are the true mechanism and degree of heterogeneity.

We will also show that 'potentially optimal' empirical payment schemes that pay in proportion to years of life lost are robust to model misspecification and are economically rational in the following senses. In an unbiased study, the average payment to workers harmed by exposure under any of our 'potentially optimal' empirical payment schemes that pay in proportion to years of life lost will equal the average payment to workers harmed by exposure under the one payment scheme that is *truly optimal* under the actual (but unknown) biological mechanism and degree of heterogeneity. In this sense, these 'potentially optimal' payment schemes are robust to misspecification of the biological mechanism generating disease and to the degree of heterogeneity, although the average compensation awarded to subjects dying at a particular age, say age 60, under some particular 'potentially optimal' empirical payment scheme may differ from that awarded under the truly optimal payment scheme. In addition, the total damages assessed against the defendant (such as the owner of the asbestos textile plant) will, under any of these potentially optimal payment schemes, equal the total damages assessed under the payment scheme that is truly optimal. In this sense, these 'potentially optimal' payment schemes are economically rational.

In contrast, payment schemes that pay only in proportion to the probability of causation are neither robust nor economically rational in the above sense. Furthermore, award schemes that pay in proportion to years of life lost take into account both whether and when exposure caused death, while schemes based only on the probability of causation do not take into account when the exposure caused death. Therefore, under a payment scheme that pays only in proportion to the probability of causation, two plaintiffs could receive the same compensation even though exposure caused one to die only a few days prematurely and the other to die thirty years prematurely. Nevertheless, as discussed below and in Reference 2, in certain settings ethical, social

and legal considerations may favour making awards in proportion to the probability of causation.

3. FORMALIZATION OF THE PROBLEM

Throughout, we assume that exposure occurs only at a time $t = 0$ (start of follow-up), so that as of time zero each individual in the study cohort is either exposed or unexposed. We restrict attention to a subcohort of subjects all of whom were of a given age at $t = 0$. For now we will assume that death from any cause is the outcome, although we will later drop this assumption. We will base our development on the following formal theory of causation, which allows a precise mathematical characterization of the probability of causation for fixed exposures. We suppose that for each individual i and time t after exposure there is a certain probability $s_{1i}(t)$ of survival to time t if one is exposed at $t = 0$, and a corresponding probability $s_{0i}(t)$ of survival to time t if one is never exposed. We also assume that the $s_{ki}(t)$ are differentiable. We then define the *individual hazards* under exposure ($k = 1$) and non-exposure ($k = 0$) as $h_{ki}(t) = -ds_{ki}(t)/s_{ki}(t)dt = f_{ki}(t)/s_{ki}(t)$, where $f_{ki}(t) = -ds_{ki}(t)/dt$ is the probability density of death at time t for an individual i with exposure status k . Note that, although observing the death time of an exposed individual provides some information about $h_{1i}(t)$, we have no direct observations concerning $h_{0i}(t)$ for exposed individuals. (Likewise, we have no direct observations concerning $h_{1i}(t)$ for an unexposed individual.)

The $h_{ki}(t)$ may be interpreted as follows. If individual i is at exposure level k and still alive at time t , then the probability that this individual will die in the next short period Δt is $h_{ki}(t)\Delta t$. Thus our model is a stochastic model for individual outcomes. That is, the incidence time of individual i when exposed and when unexposed is random, rather than fixed. Some authors feel more comfortable with a deterministic model, that is, a model in which for each individual i there is a time d_{1i} at which death would occur when exposed and a time d_{0i} at which death would occur when unexposed. This deterministic model is actually a special case of the stochastic model – the special case in which $s_{ki}(t) = 1$ if $t < d_{ki}$ and $s_{ki}(t) = 0$ if $t \geq d_{ki}$. The deterministic model can also be approximated by a sequence of stochastic models (indexed by a superscript n) obeying the assumptions given above, in which $h_{ki}^{(n)}(t) = 0$ if $t < d_{ki}$ and $h_{ki}^{(n)}(t) = n$ if $t \geq d_{ki}$. Because the results we derive are inherited by the limits of such sequences, all our results will apply to deterministic models for individual outcomes, as well as stochastic models satisfying our assumptions.

We write $h_{ki}(\cdot)$ when we are referring to the entire function rather than to the particular value $h_{ki}(t)$ that the function takes at time t . We formally define a cohort study to be unconfounded if the distribution of the functions $h_{0i}(\cdot)$ in the unexposed cohort and in the exposed cohort are identical. An epidemiologic cohort study will be unconfounded if, at the time of exposure, the exposed and unexposed cohorts do not differ on unmeasured risk factors for death. In an unconfounded cohort study the expected survival curve of the unexposed cohort will equal the expected survival curve that would have been observed in the exposed cohort if that cohort had been unexposed. Until the discussion section, we consider only unconfounded studies.

We will say there is *heterogeneity of background risks* if (as is almost always the case) the functions $s_{0i}(\cdot)$ (and hence the $h_{0i}(\cdot)$) vary across individuals. A point worthy of emphasis is that in most applications one should expect such heterogeneity to be quite severe, as there are likely to be unmeasured genetic (as well as environmental) factors that vary across individuals and strongly affect individual risk (as measured by $1 - s_{0i}(t)$). Note that heterogeneity of background hazards (that is, $h_{0i}(\cdot)$ varying across individuals) is equivalent to heterogeneity of background risks.

Define $r_i(t) = h_{1i}(t)/h_{0i}(t)$ and $p_i(t) = [h_{1i}(t) - h_{0i}(t)]/h_{1i}(t) = [r_i(t) - 1]/r_i(t)$. $r_i(t)$ is the individual hazard ratio at t for individual i . If an exposed individual dies at time t , $p_i(t)$ is interpretable as the probability that individual i 's death was caused by exposure under the following causal assumptions:

Assumption 1 For each individual i and all times t after exposure, $h_{1i}(t) \geq h_{0i}(t)$.

Assumption 2 If individual i is alive at time t after exposure, then, as Δt goes to zero, the probability that the individual contracts disease in the interval $(t, t + \Delta t)$ due to a stochastic mechanism not involving exposure approaches $h_{0i}(t)\Delta t$ (or, equivalently, the probability that the individual's disease results from a mechanism involving exposure approaches $[h_{1i}(t) - h_{0i}(t)]\Delta t$).

Informally, our basic premise is that $p_i(t)$ represents the probability of causation, provided that $h_{1i}(\cdot)$ and $h_{0i}(\cdot)$ never cross, and exposure never blocks a causal mechanism leading to disease. These assumptions are satisfied by many but not all biological models. Throughout, we will suppose that Assumptions 1 and 2 are correct. We wish to stress that all of the mathematical results derived in this paper concern bounds on population averages of the $p_i(t)$ under Assumption 1. Our only use of Assumption 2 is to allow us to equate $p_i(t)$ with ordinary-language and legal notions of the probability of causation. We shall call an exposure satisfying Assumptions (1) and (2) a 'purely causative exposure'.

Let $P(t)$ denote the time-specific probability of causation, that is, the probability that the death of a randomly sampled exposed person dying at t was caused by exposure. $P(t)$ is the average of the $p_i(t)$ over all exposed subjects dying at t . We thus have two types of time-specific 'probability of causation': one, $p_i(t)$, applies to *individuals*; the other $P(t)$, applies only to *populations*. Even in the absence of confounding, $P(t)$ is not identifiable (estimable) from epidemiologic data.¹ The only identifiable quantities are the cohort survival probabilities $S_k(t) = E_k[s_{ki}(t)]$, where $E_k[\cdot]$ is the expectation over cohort k ; the cohort incidence rates (population hazard rates) $H_k(t) = -dS_k(t)/S_k(t)dt$; and the cohort-specific death densities $f_k(t) = H_k(t)S_k(t)$. Note that $S_k(t) = \exp[-\int_0^t H_k(u)du]$ is the expected proportion of cohort k surviving to time t .

Define the (population) rate ratio as $R(t) = H_1(t)/H_0(t)$ and the (population) rate fraction as $[H_1(t) - H_0(t)]/H_0(t) = [R(t) - 1]/R(t)$. If there is no confounding and no heterogeneity of background risks (that is, $s_{0i}(\cdot)$ is the same for all individuals i), then, as shown in Reference 1, $P(t) = [R(t) - 1]/R(t)$. $[R(t) - 1]/R(t)$ is sometimes called the time-specific assigned share.⁷ But, in the presence of heterogeneity, the time-specific probability of causation $P(t)$ need not equal the time-specific rate fraction, and in general will not even be identifiable from epidemiologic data.¹ The average probability of causation among all exposed subjects, $P = \int_0^\infty P(t)H_1(t)S_1(t)dt$, will also not be identifiable in the presence of heterogeneity.¹

3. YEARS OF LIFE LOST

Even if the probability of causation was identifiable, the following example suggests that one may not wish to award compensation in proportion to it.

Example 1 Consider two exposures. For every individual, exposure 1 would decrease life expectancy by 90 per cent, while exposure 2 would decrease life expectancy by 0.1 per cent. Thus the impact of exposure 1 is devastating while the impact of exposure 2 is negligible. Yet, as we have discussed elsewhere,¹⁻³ the probability of causation could be the same and arbitrarily close to one for both exposures (as would be the case if both exposures were rank preserving). The

difficulty here is that the probability of causation depends only on *whether* exposure causes a death, not on *when* the exposure causes the deaths.

A measure of exposure impact that takes into account both when and why one dies is the 'expected years of life lost due to exposure'. Specifically, for a purely causative exposure, the expected years of life lost due to exposure for an exposed individual dying at time t is defined to be the probability that the person's death was caused by exposure multiplied by that person's future life expectancy had exposure not occurred, conditional upon having survived to time t . Note that if the death was not caused by exposure, no years of life were lost because of exposure. Mathematically, the expected years of life lost for person i dying at time t are, for a purely causative exposure,

$$y_i(t) = p_i(t) \int_t^{\infty} (u - t) f_{0i}(u | u > t) du, \quad (1)$$

where $f_{0i}(u | u > t)$ is the probability density of death at u given survival to t for subject i in the absence of exposure. It follows that the expected years of life lost for a randomly sampled exposed person dying at t , which we denote $Y(t)$, is the average of $y_i(t)$ over the set of exposed subjects dying at t . Note that both $y_i(t)$ and $Y(t)$ are computed conditionally on survival to t .

We say that the effect of exposure on hazards is *additive* if, at each time t , the difference between the exposed and unexposed hazards at t is the same for all individuals; that is if, for all individuals i, j and times t ,

$$h_{1i}(t) - h_{0i}(t) = h_{1j}(t) - h_{0j}(t).$$

This condition is not identifiable from epidemiologic data, but it has important implications for the identifiability of the probability of causation and years of life lost if it can be assumed. We say the effect of exposure on time of death is *rank preserving* if each subject i has deterministic death times d_{1i} and d_{0i} and, for any subjects i and j , $d_{1i} > d_{1j}$ if and only if $d_{0i} > d_{0j}$.

We now investigate payment schemes that award compensation to an exposed subject dying at time t in proportion to $Y(t)$. Our results are based on the following three theorems. The proofs of Theorems 1 and 2 are given in the Appendix; the proof of Theorem 3 is straightforward and so is omitted here.

Theorem 1 In the absence of heterogeneity in the background rates $h_{0i}(t)$, $Y(t)$ equals the identifiable quantity

$$RY(t) = \{[R(t) - 1]/R(t)\} \int_t^{\infty} (u - t) f_0(u | u > t) du. \quad (2)$$

Theorem 2 If the effect of exposure is additive, then $Y(t) = RY(t)$ even in the presence of heterogeneity. More generally, if in the exposed study population the functions $\Delta_i(\cdot) = h_{1i}(\cdot) - h_{0i}(\cdot)$ are distributed independently of the functions $h_{0i}(\cdot)$, then $Y(t) = RY(t)$.

Theorem 3 If the effect of exposure is deterministic and rank preserving, then the expected years of life lost among exposed persons dying at t , $Y(t)$, equals the identifiable quantity $S_0^{-1}[S_1(t)] - t$. (Note that $S_0^{-1}(x)$ is the time u such that the proportion $S_0(u)$ equals x .)

Theorems 1–3 taken together show that $Y(t)$ is not completely determined by the survival curves $S_1(t)$ and $S_0(t)$, but rather depends both on the underlying biological mechanism by which exposure causes death and on the degree of background heterogeneity.

The probability of causation $P(t)$ is always one under a rank-preserving model, whereas $P(t) = [R(t) - 1]/R(t) < 1$ under an additive model.¹ Thus $P(t)$ is always greater under a rank-preserving model than under an additive model. In contrast, $Y(t) = S_0^{-1}[S_1(t)] - t$ under a rank-preserving model, whereas $Y(t) = RY(t)$ under an additive model, and the former value is *not* always greater than the latter value. This may be seen as follows. The unconditional expected years of life lost among all exposed subjects, which we denote EY , is $\int_0^\infty Y(t)f_1(t)dt$. Now, in the absence of bias and censoring, EY can be consistently estimated simply by taking the mean age of death in the unexposed cohort and subtracting the mean age of death in the exposed cohort; this follows from the fact that averaging and integration operations can be interchanged, yielding

$$EY = \int_0^\infty tf_0(t)dt - \int_0^\infty tf_1(t)dt. \tag{3}$$

When $R(t) > 1$ for all t , the true biological mechanism could be either rank preserving or additive.² Therefore, when $R(t) > 1$ for all t ,

$$EY = \int_0^\infty [S_0^{-1}[S_1(t)] - t]f_1(t)dt = \int_0^\infty RY(t)f_1(t)dt, \tag{4}$$

which immediately implies that $S_0^{-1}[S_1(t)] - t$ cannot be everywhere greater than $RY(t)$.

In an earlier paper¹ we described sufficient (but non-identifiable) conditions for the true probability of causation $P(t)$ to lie between the value it would have under a rank-preserving model and the value it would have under the additive model (that is, the conditions for $[R(t) - 1]/R(t) < P(t) < 1$). Nevertheless, under the same conditions, the true years of life lost $Y(t)$ need not lie between $S_0^{-1}[S_1(t)] - t$ and $RY(t)$.

In contrast to $P(t)$, $Y(t)$ satisfies an important robustness condition given by equation (3) and illustrated by equation (4): the expectation EY of $Y(t)$ over $f_1(t)$ is estimable (identifiable) from epidemiologic data, without any assumptions about the biological mechanism by which exposure affects disease. To see the utility of this condition, define a tort system with awards proportional to years of life lost to be *economically rational* if it requires a defendant to pay in proportion to the total number of years of life lost for which the defendant was responsible; that is, if the defendant would pay in proportion to the total number of exposed plaintiffs multiplied by EY . The robustness condition implies that an economically rational compensation payment system can be based on paying awards to exposed individuals dying at t in proportion to their expected years of life lost as computed under any model, with assurance that the average award will be insensitive to the choice of model. In particular, it follows from equation (4) that whether we pay exposed individuals dying at time t in proportion to $S_0^{-1}[S_1(t)] - t$ or $RY(t)$, our payment scheme will be economically rational regardless of the true biological mechanism or degree of heterogeneity.

If one accepts the premise that an exposed person dying at time t should be paid in proportion to the true $Y(t)$, one would assign awards in proportion to years of life lost computed under a specific biological model. Given that the actual biological mechanisms are unknown, however, such awards are likely to be biased. For example, payment would be made proportional to $S_0^{-1}[S_1(t)] - t$ under a rank-preserving model, but if the mechanism was actually additive this payment scheme would be suboptimal; depending on the biological mechanism, a randomly sampled exposed individual dying at time t may be under- or over-paid if paid in proportion to $S_0^{-1}[S_1(t)] - t$. Nevertheless this bias will not be systematic, in the sense that the under- and over-payments would balance out over all deaths occurring in the exposed.

4. THE PROBABILITY OF CAUSATION VERSUS YEARS OF LIFE LOST: SOCIAL, ETHICAL AND LEGAL CONSIDERATIONS

We have seen that award schemes that pay in proportion to years of life lost are robust and economically rational (in the sense described above); in contrast, award schemes based on probability of causation are not.¹ More generally, expected years of life lost is a more informative summary of exposure effect than the probability of causation, since it takes into account when (instead of just whether) exposure caused the death. Despite these advantages of years of life lost, in certain settings there may be ethical, social or legal reasons for preferring to base compensation on the probability of causation.

Example 2 Suppose two apparently healthy 40-year-old men were killed instantly when the brakes of the car in which they were travelling failed due to a manufacturing error. Upon autopsy, one of the men was found to have undiagnosed metastatic lung cancer. The second had no underlying medical illness. If compensation is to be paid in proportion to the probability of causation, then full compensation would be paid to the estates of both men, since the probability is 1 that their deaths were due to brake failure. On the other hand, if compensation is to be paid in proportion to years of life lost, the man with the metastatic lung cancer would receive much less compensation than the man with no underlying illness. It is clear that one could raise legal, ethical and social questions as to the propriety of differentially compensating the families of the two men in this setting.

Examples such as this show that choice of a measure can involve issues beyond science or mathematics. To further illustrate the sort of legal, social and ethical questions brought out by this example, consider the following modification.

Example 3 Suppose in the previous example that the first man had in fact a recently diagnosed localized peripheral lung cancer for which he was to be operated on in one week's time (instead of undiagnosed metastatic lung cancer). Medical experts had given him a 60 per cent chance of a complete cure and a 40 per cent chance of death from metastatic disease within 5 years. Should the damages assessed against the car manufacturer be less for the first rather than the second man if the first man had a 40 per cent chance of being dead of lung cancer in 5 years? What if, one year later, a cure for the dead person's cancer was discovered?

5. COMPETING RISKS

Suppose data on cause of death are available, and that a subject is observed to die of lung cancer t years after exposure. We now consider how to estimate the probability of causation and the expected number of years of life lost by such a subject.

We shall require some additional notation. We let d represent death from the cause of interest (that is, lung cancer) and c represent death from any other cause. Each individual i has four hazard functions $h_{1di}(t)$, $h_{1ci}(t)$, $h_{0di}(t)$, $h_{0ci}(t)$, where, for example, $h_{0di}(t)$ is individual i 's hazard from cause d in the absence of exposure. Define $s_{ci}(t) = \exp[-\int_0^t h_{kci}(u)du]$, and $h_{ki}(t) = h_{kdi}(t) + h_{kci}(t)$. Corresponding to each of the above individual quantities there is an estimable population quantity. For example, $H_{1c}(t)$ is the identifiable death rate from causes other than d at time t in the exposed cohort.

The probability of causation for an individual dying of cause d at time t is

$$p_{di}(t) = [h_{1di}(t) - h_{0di}(t)]/h_{1di}(t),$$

and the expected number of years of life lost is

$$y_{di}(t) = \{ [h_{1di}(t) - h_{0di}(t)] / h_{1di}(t) \} \int_0^{\infty} (u - t) f_{0i}(u | u > t) du,$$

[where, as in Section 3, $f_{0i}(u | u > t) = h_{0i}(u)S_{0i}(u)/S_{0i}(t)$] under a model for causation in which (a) for each subject i and all times t , $h_{1di}(t) \geq h_{0di}(t)$ and $h_{1ci}(t) \geq h_{0ci}(t)$, and (b) if subject i is alive at time t and was exposed at $t = 0$, then, as $\Delta t \rightarrow 0$, the probability that the subject dies in the interval $(t, t + \Delta t)$ from cause d and from cause c due to a stochastic mechanism not involving exposure approach $h_{0di}(t)$ and $h_{0ci}(t)$, respectively. This model formalizes, in a stochastic setting, the informal idea that *exposure does not prevent either cause of death d or c .*

For a randomly sampled exposed person observed to die at t of cause d , the expected number of years of life lost $Y_d(t)$ equals $y_{di}(t)$ averaged over those exposed individuals observed to die of cause d at t . $P_d(t)$ is the equivalent average of the $p_{di}(t)$. Given that $y_{di}(t)$ and $p_{di}(t)$ are unknown, if a subject i is observed to die of cause d at t then, in the absence of further information, payment should be in proportion to $Y_d(t)$ if compensation is in proportion to years of life lost, and in proportion to $P_d(t)$ if compensation is in proportion to the probability of causation. We assume that the joint distribution of $h_{0di}(\cdot)$ and $h_{0ci}(\cdot)$ is the same in the exposed and the unexposed cohorts; we call a study *unconfounded* if it satisfies this assumption.

In the absence of heterogeneity in the $h_{0di}(t)$ and the $h_{0ci}(t)$,

$$P_d(t) = [H_{1d}(t) - H_{0d}(t)] / H_{1d}(t) = [R_d(t) - 1] / R_d(t),$$

where $R_d(t)$ is the identifiable quantity $H_{1d}(t)/H_{0d}(t)$, $Y_d(t) = RY_d(t)$, and

$$RY_d(t) = \{ [H_{1d}(t) - H_{0d}(t)] / H_{1d}(t) \} \int_t^{\infty} (u - t) f_0(u | u > t) du.$$

(See Appendix.) In the presence of heterogeneity, $P_d(t)$ and $Y_d(t)$ will, in general, depend both on the mechanism by which exposure causes death from cause d and cause c and on the degree of heterogeneity in the background hazard functions $h_{0di}(\cdot)$ and $h_{0ci}(\cdot)$.

We define the effect of exposure on cause of death c to be additive if the additivity condition following equation (1) holds with subscript c added. We define the effect of exposure on cause of death c to be rank preserving if each subject i has deterministic death times c_{1i} and c_{0i} , and, for all subjects i and j , $c_{1j} < c_{1i}$ if and only if $c_{0j} < c_{0i}$.

We say deaths from d and c are independent if, in the population, the probability of an individual having particular functions $[h_{1di}(\cdot), h_{0di}(\cdot)]$ does not depend on his having functions $[h_{1ci}(\cdot), h_{0ci}(\cdot)]$. Under such independence, Table I gives the values for $Y_d(t)$ under four different assumptions about the biological mechanisms by which exposure causes death from causes d and c . When deaths from competing causes c are independent of deaths from cause d , we say that we have 'independent competing causes'. Note that the quantities in Table I can be evaluated using standard life-table methods.

If the effect of exposure on both d and c is additive, then $P_d(t) = [R_d(t) - 1] / R_d(t)$ and $Y_d(t) = RY_d(t)$ even if deaths from d and c are not independent; a proof of the former is given in Reference 1, a proof of the latter is given in the Appendix. On the other hand, if the effect of exposure on d is rank preserving $P_d(t)$ will be identically 1.

Unlike payment schemes with awards proportional to the probability of causation, payment schemes with awards proportional to years of life lost continue to be robust and economically rational in the competing-risks context. Suppose that we have made sufficient assumptions about

Table I. Expected years of life lost for a death from cause d at time t , under independence of competing risks and different mechanisms for the causation of d and the competing risks c^*

Mechanism by which exposure causes:		Expected years of life lost
d	c	
additive	additive	$RY_d(t)$
	RP	$RF_d(t) \left\{ \frac{S_{0d}[G_c(t)]}{S_{0d}(t)} F[G_c(t), \infty] + F_d[t, G_c(t)] \right\}$
RP	additive	$\frac{S_{0c}[G_d(t)]}{S_{0c}(t)} [G_d(t) - t] + F_c[t, G_d(t)]$
	RP	$G_d(t) - t$ if $G_c(t) \geq G_d(t)$, $\frac{S_{0c}[G_d(t)]}{S_{0c}[G_c(t)]} [G_d(t) - t] + F_c[G_c(t), G_d(t)]$ otherwise

* $RY_d(t)$ is defined in the text

RP = rank preserving: $RF_d(t) = [R_d(t) - 1] R_d(t)$;

$G_d(t) = S_{0d}^{-1}[S_{1d}(t)]$; $F_d(a, b) = \int_a^b (u - t) f_{0d}(u | u > a) du$;

$G_c(t)$ and $F_c(a, b)$ are defined analogously; and

$F(a, b) = \int_a^b (u - t) f_0(u | u > a) du$;

(a) the mechanism by which exposure leads to death from causes d and c , (b) the degree of heterogeneity in background rates ($h_{0di}(t)$, $h_{0ci}(t)$), and (c) the dependence of competing risks to allow us to compute (if our assumptions are correct) $Y_d(t)$ and $Y_c(t)$ from epidemiologic data. For example, if we assume that the effect of exposure is rank preserving for cause of death d and additive for cause of death c , and that there is independence of competing risks, then (a) $Y_d(t)$ is given by the identifiable quantity in the third row of Table I, and (b) $Y_c(t)$ is given by the second row of Table I upon interchanging the symbols d and c .

$Y_d(t)$ represents the true but unknown expected years of life lost for a randomly sampled subject observed to die at time t from cause d . For any (possibly incorrect) postulated population model for mechanisms of disease causation, background heterogeneity and independence of competing risks, there is a corresponding predicted years of life lost $\hat{Y}_d(t)$ (note that here the circumflex denotes a *population* quantity computed under a model, rather than a sample estimate). The true average number of years of life lost among all subjects observed to die of cause d is

$$EY_d = \int_0^{\infty} Y_d(t) h_{1d}(t) S_{1d}(t) S_{1c}(t) dt, \quad (5)$$

where $S_{1d}(t) = \exp(-\int_0^t H_{1d}(u) du)$ and $S_{1c}(t)$ is defined analogously. Given a particular model, one can compute the model-predicted average number of years of life lost for subjects observed to die of cause d , \widehat{EY}_d , by replacing the true but unknown $Y_d(t)$ in equation (5) by its model-based predictor $\hat{Y}_d(t)$. Similarly, the average years of life lost among persons dying of cause c is

$$EY_c = \int_0^{\infty} Y_c(t) h_{1c}(t) S_{1d}(t) S_{1c}(t) dt, \quad (6)$$

and \widehat{EY}_c may be computed by replacing $Y_c(t)$ by $\widehat{Y}_c(t)$ in equation (6). Neither EY_d nor EY_c can be robustly estimated, since in general $E\widehat{Y}_d \neq EY_d$ and $E\widehat{Y}_c \neq EY_c$ if any of the modelling assumptions are incorrect. Nevertheless, the average number of years of life lost among all exposed subjects (ignoring cause of death) is

$$EY = P_d EY_d + P_c EY_c, \quad (7)$$

where P_d and $P_c = 1 - P_d$ are the proportions of the exposed cohort that eventually die of causes d and c . EY as just defined equals EY as defined in equation (4). Of significance is that

$$EY = \widehat{EY} = P_d \widehat{EY}_d + P_c \widehat{EY}_c,$$

even if the model used to compute \widehat{EY} is incorrect.

It follows that a payment scheme with awards proportional to years of life lost remains robust and economically rational, even when the model used to estimate the cause-specific years of life lost is incorrect, in the sense that the total compensation paid by the defendant (and the average size of the individual awards) will be correct. This result must however be tempered by two limitations: first, the average awards paid to subjects dying of a particular cause may be either too great or too small, since \widehat{EY}_d need not equal EY_d ; second, the average award to subjects dying of a particular cause d at a particular time t may be either too great or too small, since $\widehat{Y}_d(t)$ need not equal $Y_d(t)$.

6. OTHER CONSIDERATIONS

Data on time-independent covariates

We define a covariate to be fixed (time independent) if, for each subject, the value of the covariate is known at the moment the subject is first exposed to the agent under study. Suppose data on a time-independent covariate Z are available (for example, Z might be age at exposure). To compute the probability of causation $P(t|z)$ or the years of life lost $Y(t|z)$ for a random subject dying of cause d at time t with level z of the covariate (under various assumptions about the effect of exposure on causes of death d and z within levels of the covariate Z), we can again use Table I. However, in constructing the identifiable parameters in Table I, whenever we use a death rate evaluated at time u , we evaluate that death rate only among subjects with the same covariate status as the subject who died.

Incomplete follow-up

Suppose follow-up is incomplete. Then, for a subject dying of disease d at time t , we can only estimate the number of years of life lost up to the time T that is the maximum observed time since first exposure among the unexposed under various assumptions about the effect of exposure on causes of death d and c . To do so, we can again use Table I, except that we replace $u - t$ by $\min(u, T) - t$ in computing $RY(t)$, $F_d(a, b)$, $F_c(a, b)$ and $F(a, b)$, and we replace $G_d(t) - t$ by $\min[G_d(t), T] - t$.

Quality years of life lost

It has often been proposed that an adverse effect of exposure should be measured in 'quality years of life lost' rather than simply in terms of 'years of life lost'. The idea is that some years of life are more valuable than others and should be given greater weight. Of course there is little agreement as to which years are more valuable. For example, one might give more weight to those years of

life lost prior to age 65 in the belief that a high proportion of individuals, had they survived past 65, would be at least partially disabled in their later years and thus life would be less enjoyable (valuable). On the other hand, one might wish to give maximum weight to those years of life lost past age 65 if one believed that the post-retirement years are a person's happiest.

Suppose that we have divided the human lifespan into equally spaced intervals, say 10-year age intervals 0–10, 10–20 etc. Suppose some official agency has determined a set of *quality weights*, one for each age interval, that are supposed to measure the relative value of life during each of these intervals. Then the quality years of life lost due to exposure are the *quality-weighted average* of the years of life lost in each of the age intervals. If, in a tort suit, one wishes to make payments in proportion to 'quality years of life lost', one needs to be able to estimate the years of life lost in each age interval after age t for a subject observed to die from cause d at age t . To do so, we can estimate the quality years of life lost in a given interval (r, s) for such a subject using Table I, under various assumptions about the effect of exposure on cause of death d and c . To do so, we compute $RY(t)$, $F_d(a, b)$, $F_c(a, b)$ and $F(a, b)$, replacing $u - t$ by $u^\dagger - t^\dagger$, and replacing $G_d(t) - t$ by $G_d(t)^\dagger - t^\dagger$, where, for any variable x , $x^\dagger = r$ if $x \leq r$, $x^\dagger = x$ if $r < x < s$ and $x^\dagger = s$ if $s \leq x$. Analogously to our earlier results, the true total quality of years of life lost by all exposed subjects will equal the total quality of years of life lost estimated under a model, even if the model is incorrect.

Multiple levels of exposure

Suppose that the asbestos exposures described in Section 1 were recorded in fibres/cm³, and let $Y_k(t)$ be the average years of life lost due to exposure for a random subject exposed to k fibres/cm³ and observed to die at time t . All our previous results concerning $Y(t)$ generalize to $Y_k(t)$. Suppose, for example, that mortality data were available only on subjects exposed to k fibres/cm³ and on unexposed subjects. Then we effectively have but a single exposed and a single unexposed group and our previous results apply. In particular, $Y_k(t)$ is given by equation (2). If data on the mortality experience of subjects exposed at levels $j \neq k$ also become available, none of our results concerning $Y_k(t)$ will be affected by these additional data. In contrast, the lower bound for the probability of causation for level k can be affected by data on other exposure levels.¹

6. DISCUSSION

In this paper we have given additional results under a formal mathematical model of causation used earlier to analyse the probability of causation.¹ We have used this model to show that, even in the absence of bias and misclassification, the expected years of life lost due to exposure by a random exposed subject observed to die of cause d at time t cannot be estimated from epidemiologic data without resorting to non-identifiable assumptions. This is because the time-specific expected years of life lost depends on (a) the unknown mechanism by which exposure causes death from both cause d and from competing causes; (b) the unknown degree of heterogeneity in the background rates of disease; and (c) the unknown degree of dependence between death from cause d and competing risks.

We derived 'potentially optimal' payment schemes for various postulated biological mechanisms, postulated degrees of heterogeneity, and degrees of dependence between competing risks. We showed that the 'potentially optimal' payment schemes with awards proportional to years of life lost are robust and economically rational, in the sense that the total damages assessed against the defendant under any of these payment schemes will equal the total damages assessed under the (unknown) payment scheme that is truly optimal. In contrast, potentially optimal payment

schemes with awards proportional to the probability of causation are neither robust nor economically rational.¹ Nevertheless, in certain settings, payments in proportion to probability of causation might be preferred to payments in proportion to years of life lost for social, ethical and/or legal reasons.

We now raise additional unresolved scientific, social and legal issues in hopes of stimulating further research and discussion. Many of these issues were raised in References 1, 2, and 7.

- (a) Who should determine whether to pay tort awards based on the probability of causation or on years of life lost? Who should decide whether such payments should be proportional or should use an 'all-or-nothing' threshold? More generally, should amount of awards be based on measures of damage (however quantified) or on measures of need?
- (b) Suppose we should decide that we prefer payments in proportion to years of life lost. Who should decide which row of Table I should be used to compute the years of life lost for a subject dying t years after exposure from cause of death d ? Or should payment in proportion to 'quality of years of life lost' be preferred to payment in proportion to total years of life lost? If so, who is to decide which years of life are the quality years?
- (c) Suppose that we should decide that we prefer payments in proportion to years of life lost in those tort suits brought by the estates of deceased subjects. What then should be the measure of the adverse effect of exposure in tort suits brought by subjects who have been injured or disabled by an exposure but are still living? That is, what quantity is analogous to years of life lost for injured or disabled subjects? Quality years of life lost would seem to be a possibility here.
- (d) In actual epidemiologic studies, confounding (that is, non-comparability of an unexposed comparison group), misclassification of exposure (and often disease) and sampling variability are inevitable, but, except for sampling variability, difficult to quantify. How should the existence of sampling variability and poorly quantified bias and misclassification affect compensation decisions?
- (e) How can years of life lost be estimated in studies with sustained and time-varying exposures and covariates?
- (f) How should we define the years of life lost due to exposure for an exposure that prevents some diseases and causes others?
- (g) How can measures such as years of life lost be partitioned into a component due solely to exposure and a component due to the joint effects of exposure and some other covariate, say cigarette smoking? If years of life lost can be partitioned into a component due solely to exposure and a component due to the joint effects of exposure and another covariate, should we or should we not modify tort awards based on the size of the respective components?

Some results bearing on question (e) are given by Robins.⁸

APPENDIX

In this appendix we assume the study is unconfounded as defined in Section 5. We define $f_{1di}(t) = h_{1di}(t) s_{1i}(t)$ and $f_{1d}(t) = H_{1d}(t) S_1(t)$. Expectation will refer to averages over subjects in the exposed cohort.

Theorem 4 If $(\Delta_{di}(\cdot), \Delta_{ci}(\cdot))$ is independent of $(h_{0ci}(\cdot), h_{0di}(\cdot))$, then $Y_d(t) = RY_d(t)$ where, for example, $\Delta_{di}(\cdot) = h_{1di}(\cdot) - h_{0di}(\cdot)$.

The theorem will be proved in a series of four lemmas.

Lemma 1 If

$$\{[R_d(t) - 1]/R_d(t)\} f_0(s|s > t) = E[p_{di}(t) f_{0i}(s|s > t) f_{1di}(t)]/f_{1d}(t), \quad (8)$$

then $Y_d(t) = R Y_d(t)$.

Proof

$$\begin{aligned} Y_d(t) &= E \left[p_{di}(t) \left\{ \int_t^\infty (s-t) f_{0i}(s|s > t) ds \right\} f_{1di}(t) / f_{1d}(t) \right] \\ &= \int_t^\infty (s-t) E[p_{di}(t) f_{0i}(s|s > t) f_{1di}(t) / f_{1d}(t)] ds, \end{aligned}$$

where the first equality is definitional and the second equality is a consequence of Fubini's theorem. But, by definition,

$$R Y_d(t) = \int_t^\infty (s-t) [\{[R_d(t) - 1]/R_d(t)\} f_0(s|s > t)] ds,$$

proving the lemma.

Lemma 2 Suppose $(\Delta_{di}(\cdot), \Delta_{ci}(\cdot))$ is independent of $h_{0i}(\cdot)$. Then equation (8) holds if and only if

$$E[\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)] = \Delta_d(t) S_1(t)/S_0(t), \quad (9)$$

where $\Delta_d(t) = H_{1d}(t) - H_{0d}(t)$.

Proof The right-hand side of equation (8) equals

$$E[\{\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)\} \{f_{0i}(s|s > t) s_{0i}(t)/f_{1d}(t)\}]. \quad (10)$$

But, by the independence assumption, expression (10) equals

$$E[\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)] E[f_{0i}(s|s > t) s_{0i}(t)/f_{1d}(t)] = E[\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)] f_0(s)/f_{1d}(t).$$

By definition, the left-hand side of equation (8) equals

$$(\Delta_d(t)/H_{1d}(t)) (f_0(s)/S_0(t)) = (f_0(s)/f_{1d}(t)) [\Delta_d(t) S_1(t)/S_0(t)],$$

proving the lemma.

Lemma 3 If $(\Delta_{di}(\cdot), \Delta_{ci}(\cdot))$ is independent of $h_{0i}(\cdot)$, then equation (9) holds if and only if

$$H_{0d}(t) S_1(t) = E[s_{1i}(t) h_{0di}(t)] \quad (11)$$

Proof

$$\begin{aligned} f_{1d}(t) &= E[f_{1di}(t)] = E[\{\Delta_{di}(t) + h_{0di}(t)\} \{s_{1i}(t)/s_{0i}(t)\} s_{0i}(t)] \\ &= E[\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)] E[s_{0i}(t)] + E[\{s_{1i}(t)/s_{0i}(t)\} s_{0i}(t) h_{0di}(t)], \end{aligned}$$

where the first two equalities are definitional and the last equality follows from independence. Therefore

$$\begin{aligned} E[\Delta_{di}(t) s_{1i}(t)/s_{0i}(t)] &= \{f_{1d}(t) - E[s_{1i}(t) h_{0di}(t)]\}/S_0(t) \\ &= \Delta_d(t) S_1(t)/S_0(t) + H_{0d}(t) S_1(t)/S_0(t) - E[s_{1i}(t) h_{0di}(t)]/S_0(t). \end{aligned}$$

Therefore, when equation (9) holds, we have,

$$H_{0d}(t) S_1(t) = E[s_{1i}(t) h_{0di}(t)] \tag{12}$$

proving the lemma.

Lemma 4 If $(\Delta_{di}(\cdot), \Delta_{ci}(\cdot))$ is independent of $(h_{0ci}(\cdot), h_{0di}(\cdot))$, then equation (12) holds:

Proof

$$E[s_{1i}(t) h_{0di}(t)] = E[\{s_{1i}(t)/s_{0i}(t)\} \{s_{0i}(t) h_{0di}(t)\}] = E[\{s_{1i}(t)/s_{0i}(t)\}] E[s_{0i}(t) h_{0di}(t)],$$

by independence. But

$$\begin{aligned} E[\{s_{1i}(t)/s_{0i}(t)\}] &= E[\{s_{1i}(t)/s_{0i}(t)\}] E[s_{0i}(t)]/E[s_{0i}(t)] \\ &= E[\{s_{1i}(t)/s_{0i}(t)\} s_{0i}(t)]/E[s_{0i}(t)] \equiv S_1(t)/S_0(t), \end{aligned}$$

where we have used independence again. Also, $E[s_{0i}(t) h_{0di}(t)] = H_{0d}(t) S_0(t)$. Upon substituting the lemma follows.

Lemma 1–4 prove Theorem 4.

Many of the results in the text are immediate corollaries of Theorem 4. As we now show, Theorem 1 and Theorem 2 are special cases in which $h_{0ci}(\cdot)$ and $\Delta_{ci}(\cdot)$ are identically 0. In Theorem 1, $h_{0di}(\cdot)$ is not a function of i . In Theorem 2, $\Delta_{di}(\cdot)$ is not a function of i . Thus the supposition of Theorem 4 is satisfied by the suppositions of Theorems 1 and 2. Similarly, in the competing risk context, the supposition of Theorem 4 is met when both the functions $h_{0ci}(\cdot)$ and $h_{0di}(\cdot)$ do not depend on i or if the functions of $\Delta_{di}(\cdot)$ and $\Delta_{ci}(\cdot)$ do not depend on i .

The proof that $(\Delta_{di}(\cdot), h_{0di}(\cdot))$ is distributed independently of $(\Delta_{ci}(\cdot), h_{0ci}(\cdot))$ implies $Y_d(t) = RY_d(t)$ is similar to that of Theorem 4 and is omitted.

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