

## Appendix B: Sources of Error Involved in Measuring Socioeconomic Mortality Gradients

Sources of error in epidemiology may be considered as either random or systematic (Rothman and Greenland 1998). Regarding systematic error, these may be categorised as selection bias, confounding, and information bias.

*Selection bias* occurs ‘the relationship between exposure and disease is different for those who participate and those who should be theoretically eligible for study ...’ (Rothman and Greenland 1998, p.119). If the eligible population is the population of a country, and census data forms the study-base, then selection bias can only arise if the census data set has to be restricted for some reason (eg, availability of household income).

*Confounding* occurs when ‘the apparent effect of the exposure of interest is distorted because the effect of an extraneous factor is mistaken or mixed with the actual exposure effect ...’ (Rothman and Greenland 1998, p.120). The properties of a confounder are that it:

- must be associated with the exposure
- must be associated with the outcome
- must be independently associated with the outcome among the unexposed
- and must *not* be [exclusively] an intermediate variable between the exposure and the outcome.

Given the social structuring of society, and the fact that most socioeconomic factors are correlated, it is difficult to know when it is appropriate to consider the independent effect of some socioeconomic factor controlling for potential confounders (including other socioeconomic factors) (Kaufman and Cooper 1999).

*Information bias* (also known as misclassification bias) occurs whenever there are errors measuring exposures, outcomes and covariates. The direction of bias varies depending on whether the measurement error on one variable is correlated with that on another variable. How information bias might affect measurement of socioeconomic mortality gradients is further discussed in subsequent sections of this chapter.

It is neither feasible nor helpful to attempt a comprehensive inventory of all the possible sources of selection bias, confounding and information bias that may affect the measurement of socioeconomic mortality gradients. Indeed, most sources of systematic error will be specific to a given study design and/or a particular study. However, there are three sources of error that arise in the many studies that measure socioeconomic mortality gradients, and warrant specific mention: *confounding*, *health selection* (not ‘selection bias’; may also be considered as a special form of confounding), and *misclassification* of socioeconomic exposures, confounders, and the mortality outcome. Health selection has received considerable attention in the literature on socioeconomic determinants of health.

## 1 Confounding

Consider the association of income with mortality and the potential confounder education. Education and income are correlated, and education is associated with health outcomes. It is also probable that education is independently associated with mortality risk within strata of income (including the ‘unexposed’ income strata). Finally, for adults at least, education is prior to income in the life-course (see Figure 3 for initial framework or causal diagram used in this report), so education is unlikely to lie on the causal pathway between income and mortality risk. Thus, education is a potential confounder of the association of income with mortality.

Conversely, consider the association of education with mortality, and income as a possible confounder. As income is potentially on the causal pathway between education and mortality, adjusting for income may result in ‘over-controlling’ of the total effect of education on mortality. However, as education does not fully determine income, some of the effect of income on mortality may not be on the causal pathway from education to mortality, there will be some confounding of the education–mortality association by income. This is a critical (and largely unresolved) problem in modern epidemiology – how to control for a covariate that is in part a confounder, and in part on a causal pathway between the exposure of interest and the outcome. This issue is revisited in Section 5: Epidemiological analysis in the context of causal pathways, confounding, intermediaries, and misclassification bias.

Note that some authors use the term ‘indirect selection’ to denote confounding by variables that are prior in some causal chain – particularly causal chains over the life-course (Bartley et al 1999; Martikainen and Valkonen 1996; van de Mheen 1998). This usage of the term ‘indirect selection’ serves to remind us that many variables that satisfy the properties of a confounder are actually prior variables (in part at least) on causal pathways. For example, education is not just spuriously correlated with income. Rather, one’s income is in large part determined by education, and hence education is part of the complex of factors that ‘select’ income.

## 2 Misclassification of socioeconomic exposures and confounders

Misclassification (or mismeasurement) of independent variables occurs in all studies. Considering socioeconomic variables elicited by a census, misclassification can be thought of at two levels. First, there is misclassification compared to the correct answer for the question as written. For example, personal income data is collected by just one ‘tick-box’ question on the New Zealand census, to which most people would select a best-guess answer. Second, there is misclassification compared to the underlying socioeconomic factor of interest. For example, we may interpret the results for ‘income’ as applicable to ‘usual income’ or ‘income accumulated over the life-course’. However, the census questionnaire may only ask about income in the last year.

It is likely that such misclassification of *independent variables* (ie, exposures) is mostly non-differential with respect to the mortality outcome – but it cannot be assured. Such non-differential misclassification bias usually causes a bias to the null in the observed association of each socioeconomic exposure with the mortality outcome (Rothman and Greenland 1998).

Non-differential misclassification bias of *confounders* hampers the ability to control for confounding (Davey Smith and Phillips 1992; Greenland 1980; Liu 1988; Marshall and Hastrup 1996; Phillips and Davey Smith 1992; Phillips et al 1996). For example, if we control the association of income with mortality for the confounder education, and education is non-differentially misclassified, then there will remain residual confounding of the income–mortality association by education. Therefore, controlling for non-differentially misclassified confounders will underestimate the percentage of the association of the socioeconomic exposure with mortality that is explained by that confounding variable. However, the effect measure (eg, risk ratio) for a given socioeconomic exposure, controlled for the confounder(s), could be biased in either direction depending on the *combined effect* of misclassification of *both* the exposure and the confounder(s).

Table 52 shows a hypothetical example of the effect of non-differential misclassification of either/both the exposure (income) or confounder (education) under certain assumptions. First, assume that the mortality risk ratio for high compared to low income (exposure) was 3.0 in the absence of any non-differential misclassification bias, and controlling for the perfectly measured confounder education the risk ratio was 2.0. That is, 50% of the excess association of income with mortality was due to confounding by education. This risk ratio of 2.0 is shown for the top left cell of Table 45 where there was no (0%) misclassification of either exposure or outcome. Second, assume that non-differential misclassification of the exposure resulted in (RR-1) being underestimated by 60% – thus the crude RR is  $(1 + [(1 - 60\%) \times [\text{true crude RR} - 1]]) = (1 + ([40\%] \times [2])) = 1.8$ , where the true crude RR is 3.0 as above. Further, assuming that adjusting for the perfectly measured confounder (education) reduced the observed excess risk ratio (crude observed RR – 1) by 50% (as it does for the true crude RR), then the observed adjusted risk ratio is  $(1 + ([50\%] \times [\text{observed crude RR} - 1])) = 1.4$ . This risk ratio is shown in the top right cell of Table 52.

**Table 52:** Hypothetical example of the effect of misclassification of both exposure and confounder, where: the crude RR is 3.0 without misclassification bias of exposure; the adjusted RR is 2.0 without misclassification of either exposure or confounder

% underestimate of confounding of observed (RR-1) due to misclassification of confounder	% underestimate of (RR-1) due to misclassification of exposure			
	0%	20%	40%	60%
0%	2.0	1.8	1.6	1.4
20%	2.2	2.0	1.7	1.5
40%	2.4	2.1	1.8	1.6
60%	2.6	2.3	2.0	1.6

Third, assume there was no misclassification of the exposure, but that misclassification of the confounder caused a 60% underestimate of confounding due to education. Thus, the percentage reduction in the excess risk ratio (RR – 1) for income after controlling for education will be  $50\% \times (1 - 60\%) = 20\%$ , where 50% is the amount of the crude exposure–outcome association that is truly due to confounding by education. Consequently, the observed adjusted RR will be  $(1 + ([100\% - 20\%] \times [\text{crude RR} - 1])) = 2.6$ . This risk ratio is shown in the bottom left cell of Table 52. Finally, assume that non-differential misclassification bias affects both the exposure and the confounder, and that the percentage underestimate due to misclassification of the confounder applied to

the *observed* crude risk ratio. If the crude exposure–outcome association is underestimated by 60% due to misclassification of the exposure, and the percentage underestimate of confounding is 60%, then the observed adjusted risk ratio is now 1.6 (ie,  $(1 + ((100\% - 20\%) \times [\text{observed crude RR} - 1])) = (1 + ([80\%] \times [1.8 - 1])) = 1.64 \approx 1.6$ ).

The hypothetical example in Table 52 assumes that the percentage underestimates from misclassification of confounder and exposure act independently of each other, and that the percentage of the *observed* exposure–outcome association explained by the confounder is the same regardless of the amount of exposure misclassification. These assumptions may not hold. However, the point illustrated in Table 52 is that the observed adjusted risk ratio may be either under or overestimated with respect to the true adjusted risk ratio of 2.0 when there is misclassification bias of *both* the exposure and confounder. Put another way, the net effect of misclassification bias of both the exposure and the confounder may be to cause either an under or an overestimate of the adjusted risk ratio compared to the true adjusted risk ratio.

### 3 Misclassification of the mortality outcome

In the previous section I considered misclassification bias of the exposure and covariates. In this section I consider misclassification bias of the mortality outcome. In many cohort studies this potential bias is minor as the assessment of vital status is accurate. However, in a linked census–mortality study such as the NZCMS the bias may be more substantial. For example, not all deaths may be ascertained, and some ascertained deaths may be incorrect. Misclassification of the outcome was an issue in the NZCMS, *but it was possible to quantify the resultant bias in the cohort analyses* (unlike misclassification bias of the exposures and covariates).

Other census–mortality studies have also had limitations with the completeness and accuracy of the record linkage, for example the US 1960 Matched Records Study (Kitagawa and Hauser 1973), the Canadian study (Houle et al 1996), and the Italian study (Faggiano et al 1995). The percentage of records linked and estimated accuracy (where available) in these other linked census–mortality studies was presented in Section 1.2 of Chapter 1, Table 2).

Table 53 is a two-by-two table of the actual outcome (dead or alive at the end of the follow-up period) cross-classified by the assigned outcome (linked or unlinked) in a linked census–mortality study.

**Table 53: Two by two table of link/non-link status by vital status in a linked census–mortality study**

		True vital status at the end of follow-up		
		Died	Alive	
Output from record linkage	Linked	a	b	a + b
	Unlinked	c	d	c + d
		a + c	b + d	a + b + c + d

Where for each of the four cells in Table 53:

- a = true links, or true positives
- b = false links, or false positives
- c = false non-links, or false negatives
- d = true non-links, or true negatives.

This misclassification of the mortality outcome by the record linkage can be characterised with the following familiar terms:

Sensitivity	= Se	= a / (a+c)
Specificity	= Sp	= d / (b+d)
Positive predictive value	= PPV	= a / (a+b)
Negative predictive value	= NPV	= d / (c+d)

(Note the population distributed in Table 53 is *different* to that in Table 10. Table 10 is a two-by-two table of comparison pairs. Thus each census and mortality record is represented many times in the table. Table 53 is a two-by-two table of census records. Correspondingly, the meaning of false links and true non-links, and the specificity and the positive predictive value derived from Table 10 *differ* from that derived from Table 53.)

In most record linkage projects it is not possible to determine the actual vital status for individual census records, except perhaps for a subgroup (eg, Calle and Terrell 1993; Houle et al 1996). However, the number of linked (a+b) and unlinked records (c+b) are known. The sensitivity of the record linkage may be approximated by the percentage of submitted records linked (ie, [a+b]/[number of eligible mortality records]), but will not necessarily give a correct approximation as:

- the numerator (a+b) includes false positive links (b)
- the denominator is not necessarily the number of deaths in the cohort. For example, it may be an overestimate if many of the mortality records were for people that were absent from the country on census night or simply failed to complete the census form. Alternatively, it may be an underestimate if many of the census respondents that actually died in the eligible follow-up period emigrated before death.

It was also possible to estimate the PPV in the NZCMS – the methods to do so are presented in the Technical Report (Blakely et al 1999) and presented briefly in the Methods Chapter of this report. Thus, using these estimated values of the sensitivity and PPV it was possible to estimate each of the cell values in Table 53. Further, it would also have been possible to estimate the sensitivity and specificity by strata of socioeconomic factor (eg, small area deprivation) and covariates (eg, age) in the NZCMS. Having made these estimates, then it would have been possible to correct the observed effect measures (eg, risk differences and risk ratios) for misclassification bias of the mortality outcome using published correction formulas (Brenner and Gefeller 1993; Copeland et al 1977; Green 1983). Appendix B of my PhD thesis (Blakely 2001) (*not* Appendix C of this report) presents a number of illustrative examples of how the varying sensitivity and specificity of a record linkage project may bias the cohort analyses. Of particular note, the risk ratio may be relatively unaffected by misclassification bias of the mortality outcome while the risk difference was notably biased. The supporting material in Appendix B also helps to *understand* the linkage bias in the NZCMS. However, to actually *attempt* a sensitivity analysis of the impact of misclassification bias

of the mortality outcome in the NZCMS using the correction formula presented in Appendix B of the PhD thesis would have been cumbersome, complex and probably inaccurate. Fortunately, it also proved unnecessary – a more direct method of adjusting for linkage bias was used. The method simply used results from analyses that determined the relative risk of a mortality record being linked to a census record by demographic and socioeconomic factors, and used these relative risks to adjust the odds ratios of mortality observed in the cohort analyses.

#### 4 Health selection

Consider the association of labour force status with mortality. It is probable that people with poor health will exit the active labour force more frequently than people in good health. As poor health is associated with increased mortality, then the mortality risk among those in the non-active labour force will usually be higher than the mortality risk for those in the active labour force. This mortality difference will not be a function of any independent effect of labour force status on mortality, but rather a function of the differential mobility by health status of people between categories of labour force status – the so-called ‘healthy-worker effect’:

*‘Workers usually exhibit lower overall death rates than the general population, because the severely ill and chronically disabled are ordinarily excluded from employment.’* (Last 1995).

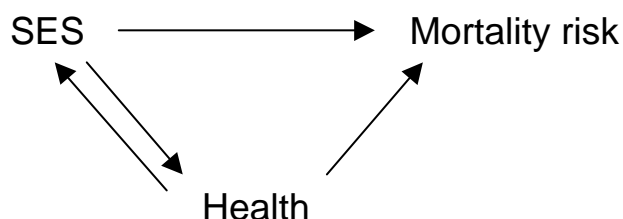
This phenomenon is not just observed with respect to labour force status. For example, people may slide down the income ladder as a result of poor health. Thus, Fox et al (1987) provide a more generalised and formal definition of health-related mobility as:

*‘... the artificial raising or lowering of the average health of people with a particular characteristic associated with the process by which that characteristic is acquired or lost. The mortality of a population with that characteristic is affected by health-related mobility if the health of people acquiring or losing the characteristic differs systematically from others with the characteristic.’* (Fox et al 1987).

This phenomenon has been given various names, eg, health selection bias, health selection, social mobility, direct selection (as opposed to ‘indirect selection’ mentioned above in Appendix B: Confounding) and health-related mobility. The default term used in this report is ‘health selection’. Note that health selection is not a ‘selection bias’ – all the eligible population may be included in the analysis (meaning there is no selection bias), yet the phenomenon persists. Rather, it is, a special form of confounding as labour force status (a proxy for health status) has an influence on measured socioeconomic position, and labour force status also influences mortality risk. But labour force status (as a proxy for health status) is also an intermediary variable on the causal pathway between socioeconomic position and mortality, thus breaching one of the properties of a (pure) confounder (Rothman and Greenland 1998).

An alternative way to consider health selection is as reverse causation. The causal diagram below represents reverse causation – socioeconomic position not only affects health (arrow from socioeconomic position to health), but health status affects socioeconomic position (arrow from health to socioeconomic position). (Labour force status can be substituted as a proxy for health in the causal diagram.) For example, poor health may cause a decrease in one’s income, as well as low income being a determinant of health status. As health status is also causally related to mortality risk

(arrow from health to mortality risk), the observed association of income with mortality risk may be 'biased' by health selection. Extending the income example, health selection may result in an increased mortality risk among those with low income and a corresponding decreased mortality risk among those with high incomes. Thus, assuming an underlying association of increasing income with lower mortality risk, health selection may exaggerate the income mortality gradient.



For the purposes of this report, it is crucial to recognise two variants of health selection, **drift health selection** and **differential health selection**. *Drift* health selection refers to the above income example – a combination of health (or labour force status as a proxy) as a confounder and an intermediary variable. Here, people drift up and down the income ladder conditional on their health status, and this in turn may cause the income mortality gradient to be overestimated. Note that this 'overestimate' occurs only if current income at the start of follow-up is used as a proxy for long-term, usual, life-time or some other longer-term measure of income. *Differential* health selection occurs when a socioeconomic mortality gradient is assessed among the active labour force only, and bias arises due to exclusion from the active labour force being differential by socioeconomic factor. Classically, differential health selection has been described for occupational class mortality gradients (Martikainen and Valkonen 1999). Here the gradient is underestimated when only *current* occupation is available for the assignment of occupational class. This underestimation is because the lower occupational classes (based on *usual* occupation) are more likely to be forced out of the labour force than the higher occupational classes when in poor health. This differential health selection out of the labour force causes the observed mortality risk/rate among the lower occupational classes (based on *current* occupation) to be underestimated more than the risk/rate among the higher occupational classes. To extend the framework of health selection in terms of classic epidemiological terms, differential health selection represents effect modification of the socioeconomic mortality gradient by labour force status.

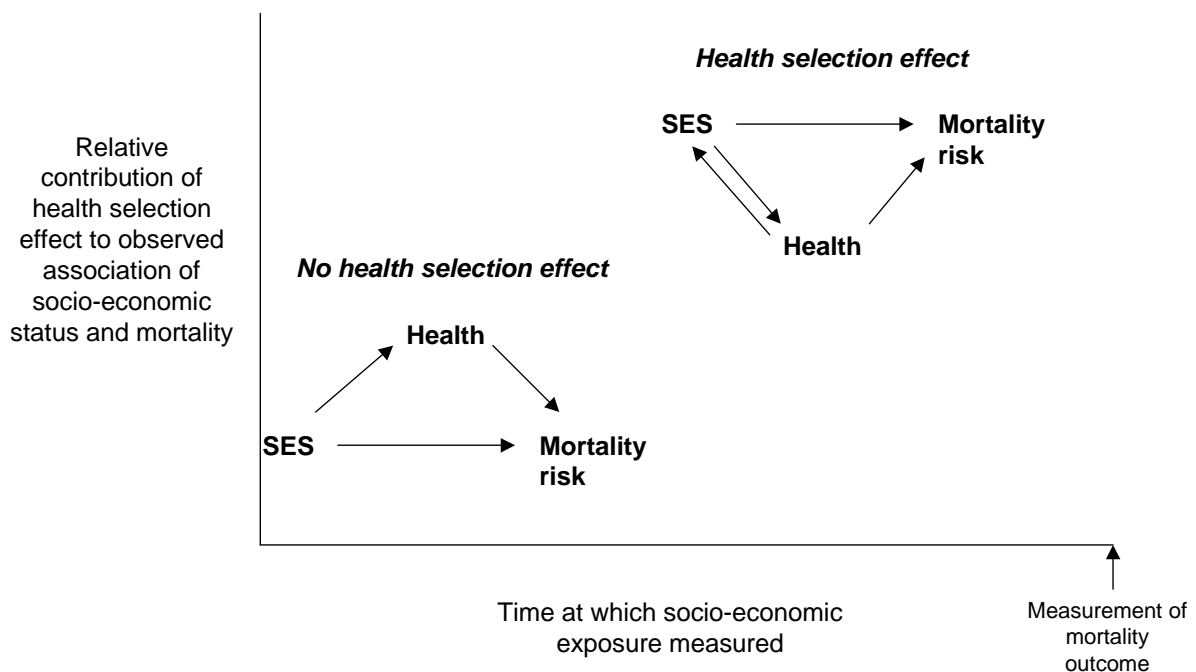
The consideration of drift versus differential health selection will be a recurrent theme in this report.

Health selection may occur over a range of time periods. It may operate in the short term such that a person's ill health precipitating exit from the workforce a year or so before death creates a spurious association between labour force status and mortality. Second, it may operate over an individual's life such that ill (or excellent) health in childhood leads to a lower (or higher) socioeconomic trajectory and, if subsequent death is related to the childhood illness, introduces an element of health selection into the relationship between socioeconomic factors and death (Bartley et al 1999; Kuh et al 1997). Third, it may operate intergenerationally with parental ill (or excellent) health influencing childhood health. For each of these three types of health selection, it is possible to argue that they are either a bias or a causal mechanism – the choice is just a matter of perspective (Blane et al 1993; van de Mheen 1998). For example, from a life-

course perspective, the influence of childhood health status on adult socioeconomic position is of causal interest.

On occasion, short-term health selection is of substantive interest, as opposed to being considered a bias. For example, the New Zealand National Health Committee (with input from J. Mackenbach, Erasmus University, Rotterdam) identified four target areas for intervention to reduce health inequalities (National Health Committee 1998). One of the four areas was the effect of ill health on socioeconomic position (reverse causation). One policy intervention might be adequate income maintenance for people who become ill, thus preventing deterioration in socioeconomic position consequent upon poor health. While acknowledging that short-term health selection may be of direct research and policy interest, the position taken in this report is that health selection over the short-term (ie, a couple of years) is a bias affecting the 'true' underlying association of socioeconomic position with health status. Intragenerational health selection is considered over many years and intergenerational health selection of causal interest, but the issue is of little direct relevance to this report as follow-up in the NZCMS was only for three years. *Unless stated otherwise, 'health selection' in this report refers to that over the short term.*

Figure 26: Possible contribution of health selection to the observed association of socioeconomic position and mortality, by time at which the socioeconomic exposure is measured relative to mortality follow-up



How can bias from short-term health selection (be it differential or drift health selection) be avoided in epidemiological analyses? Two general strategies are available. First, analyses can be restricted to those in good health at the start of follow-up. (Considering health selection as a special form of confounding, this equates to 'restriction' as a method to control for confounding.) However, as much of the 'true' association of socioeconomic position with mortality is mediated by health status, such a restriction may cause an underestimate of the socioeconomic mortality gradient. Second, the analyses can be conducted only for mortality outcomes ascertained sometime after the socioeconomic exposure is measured. For example, income could be measured in 1991, and only deaths

occurring during 1996–98 included in the analyses. The assumption here is that by delaying the ascertainment of mortality outcomes, one has allowed for all the people in poor health in 1991 (and hence also with a low income) to either have died or overcome their poor health. Obviously, there is no point in time when health selection switches on or off. Figure 26 attempts to demonstrate this by illustrating that the shorter the time period between exposure measurement and mortality follow-up, the greater the likely contribution of (short-duration) health selection to the observed association of socioeconomic position and mortality. The actual amount of bias due to health selection varies by time, socioeconomic factor, and cause of death.

Figure 26 suggests that the bias caused by health selection is a smooth linear function directly proportional to time between measure of exposure and mortality outcome. This portrayal is a simplification considering that the short-term health selection varies for acute and chronic illness. For example, Goldblatt and Fox (1979) found that people in hospital on the night of the United Kingdom 1971 census, but not usually resident at that hospital (ie, they had an acute illness), had a rapidly decreasing mortality rate. In the first year of follow-up the mortality rate was ten times higher than the general population's, but fell to a level two to three times that of the general population in the next four years (Goldblatt and Fox 1979). By comparison, people with a hospital as their usual residence (ie, they had a chronic illness) had a mortality rate about three times higher than the general population's in the first year, falling only slowly to about twice the general population's over the next four years. The implication for the NZCMS is that health selection – if any – may 'wash out' within the first year for acute illness, but not so for chronic illness.

A more detailed review of the empirical evidence for health selection with regard to each socioeconomic factor is included in the literature review in Appendix A.

## **5 Epidemiological analysis in the context of causal pathways, confounding, intermediaries, and misclassification bias**

Most studies (Davey Smith et al 1997; Gliksman et al 1995; Vagero and Leon 1994), but not all (Lynch et al 1994), demonstrate that both parental/early childhood and adult socioeconomic position contribute independently to mortality risk. Furthermore, adult socioeconomic position is itself determined in large part by a person's life-history of accumulated social (dis)advantage (Kuh et al 1997). Thus, determining the independent effect of, say, adult income on mortality risk requires controlling for all prior variables on the pathways involving income (Blakely and Woodward 2000a). Kaufman and Cooper (1999) have argued that no matter how many covariates are controlled there will still be residual differences between the exposed and unexposed socioeconomic groups on unmeasured covariates due to the non-random distribution of socioeconomic factors (Kaufman and Cooper 1999). Thus, they argue, the 'counterfactual scenario' that underpins the control of confounding in epidemiology can rarely be realised in social epidemiology, as we cannot guarantee that the exposed and unexposed are exchangeable within strata of the measured covariates. These limitations are not peculiar to social epidemiology (eg, it is unlikely that all confounders of the association of caffeine with pancreatic cancer are controlled in epidemiological analyses). However, given that socioeconomic characteristics are acquired due to common structuring of individuals within society, co-linearity is a particularly notable problem in social epidemiology. Indeed, Kaufman and Cooper argue that it is often inappropriate to consider the 'independent' effects of separate socioeconomic factors. Analyses of the association of one socioeconomic factor with mortality controlling for other socioeconomic factors are

presented in this report. These analyses must be interpreted with caution due to the relatively few measures of adult socioeconomic position available in the NZCMS and wider concerns raised by Kaufman and Cooper. Nevertheless, there is value in presenting these multivariate analyses – particularly in policy terms. For example, it is useful to have some idea whether any excess of suicide deaths among the unemployed remains after controlling for income and education.

The usual approach in epidemiology when considering variables ordered in some causal chain is to conduct a series of analyses to determine the total and residual effects of each variable (be they exposures and/or intermediaries). Specifically, Victora et al (1997) summarise a conceptual framework for the control of confounding by the use of hierarchical analyses for studies that do not have the luxury of repeated longitudinal measures (Victora et al 1997). Figure 3 is the initial framework in the NZCMS and this report. According to this framework (Victora et al 1997):

- 1 The univariate association of education with mortality in the NZCMS will represent the total effect (*direct* plus *indirect* through other socioeconomic factors) of education on mortality. (Note that ‘direct’ refers to the arrow directly from education to mortality in Figure 3, but more correctly captures the effect of education through variables other than those shown in Figure 3.)
- 2
  - (a) The association of education with mortality adjusted for labour force status, income, and car access is assumed to represent the *direct* effect only of education on mortality.
  - (b) The difference between the size of the association of education with mortality observed in 1 and 2(a) is assumed to be due to the *indirect* effect of education on mortality (ie, that mediated by labour force status, income, and car access).
- 3 The univariate association of income with mortality will be confounded by socioeconomic factors that are prior to income in causal pathways. However, the association of income with mortality controlling for the other socioeconomic factors will represent the residual unconfounded effect of income on mortality. That is, we assume counterfactually that the effect of changing an individual's income on mortality risk (but changing nothing else) is estimated by the measured effect of income in an observational study controlling for the measured confounders.

This hierarchical framework explicitly outlined by Victora et al (1997) is implicit in many studies. For example, one commonly cited finding of the Whitehall Study is that only a third of the association of occupational grade (ranking of occupations within the British civil service) with coronary heart disease mortality was ‘explained’ after adjusting for known cardiovascular risk factors (Marmot et al 1984). This finding is then usually interpreted as suggesting that other factors (eg, unmeasured and/or unknown dietary and lifestyle behaviours, psychosocial factors, or material factors consequent on occupational grade) must be responsible for the remaining two-thirds of the mortality gradient. While this type of analysis and interpretation is common in all branches of epidemiology, it is prone to error. Considering points 1 to 3 above, the sources of error (other than selection bias) might be listed as follows:

1 *'The univariate association of education with mortality represents the total education-mortality effect.'*

- Confounding. There may be uncontrolled confounders that are not on the causal pathway from education to mortality (eg, parental income, early childhood factors, ethnicity).
- Confounding. There may be variables that are both confounders *and* intermediary variables between education and mortality (eg, income, smoking). Not allowing for the confounding *component* of these variables means that the univariate total education–mortality association is confounded. Further, methods to control for just the confounding component of a variable that is both intermediary and confounder are complex, requiring longitudinal data (see Rothman and Greenland, 1998, pp.422–5).
- Information bias. Misclassification of either education or mortality may bias the observed education-mortality association.

2 (a) *'The association of education with mortality after controlling for intermediary variable(s) represents the (direct) effect of education on mortality via pathways not including the intermediary variable(s) (eg, income, labour force status and car access).'*

- Confounding. As with the first point above, there may be uncontrolled confounders that are not on the causal pathway from education to mortality (eg, parental income, early childhood factors, ethnicity).
- Confounding. Controlling for income, labour force status, and car access (if specified and measured perfectly) is often *assumed* to give the direct effect of education on mortality, by both controlling for the confounding by these variables and adjusting further for the component of the education–mortality association that is mediated by these variables. However, the latter assumption is unreliable (Poole and Kaufman 2000; Robins and Greenland 1992). Using a counterfactual model, Robins and Greenland have demonstrated that that even when the total effect of exposure on outcome is completely unconfounded (ie, by both intermediary and other confounding variables), analyses of the exposure-outcome association stratified by a true intermediary variable **does not reliably** give the residual effect of the exposure on outcome via pathways other than the intermediary (ie, stratification) variable (example 1, Robins and Greenland 1992). This finding is counterintuitive, and, simplistically, arises as while the crude exposure–outcome association is unconfounded, *within strata of the exposure the intermediary–outcome association is confounded*. Poole and Kaufman (2000) have returned to this counterfactual problem initially proposed by Robins and Greenland (1992), presenting a social epidemiology example to remind us that simply controlling intermediaries in epidemiological analyses may be an unreliable strategy (Poole and Kaufman 2000). How unreliable this method is remains unclear, and requires further methodological research. However, the counterfactual example used by these authors is noted, while being totally unconfounded by definition for the exposure has a completely arbitrary user-specified distribution of people by respondent type, and it is this arbitrary distribution that causes the lack of reliability of the method.

- Information bias. Misclassification of any of the exposure (education), outcome (death) and intermediary (income) variables may be a source of error. If the sources of error in the above two bullet points were absent, non-differential misclassification bias of income only would usually cause an overestimate of the residual direct effect of education on mortality. This overestimate would arise due to incomplete control of the intermediary–outcome association. Non-differential misclassification bias of education alone, or both education and income (but not mortality), could cause either an under or overestimate of the residual direct effect of education on mortality, depending on the net impact of misclassification of each variable as shown on page 193 (Davey Smith and Phillips 1992; Liu 1988; Phillips and Davey Smith 1992; Phillips et al 1996).
- 2 (b) *‘The difference between 1 and 2.(a) represents the (indirect) effect of education on mortality via pathways including the intermediaries (eg, income, labour force status, and car access).’*

The sources of error here are the converse of those for 2(a).

- 3 *‘The association of income with mortality after controlling for confounding variables, say education, labour force status, and car access as in Figure 3, represents the unconfounded effect of income on mortality.’*

This interpretation is as for any epidemiological analysis, and akin to Point 1 above:

- Confounding. There may be uncontrolled confounders that are not on the causal chain from income to mortality (eg, genetic endowment, component of diet not determined by income).
- Information bias. Misclassification of either income or mortality may bias the observed income–mortality association.
- Information bias. Misclassification of the confounding variables adjusted for in the analyses will mean that residual confounding remains.