Contribution of time-varying measures of health behaviours to socioeconomic inequalities in mortality: how to understand the underlying mechanisms?

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ABSTRACT

A higher prevalence of unhealthy behaviours in lower socioeconomic groups contributes to socioeconomic inequalities in mortality. Recent cohort studies suggest that the contribution of health behaviours to socioeconomic inequalities in mortality is larger when measured repeatedly over time ('time-varying') instead of once only ('time-fixed'). Explanations for a larger contribution of health behaviours, however, are hardly discussed in the current literature, and appear to be more complex than a widening of inequalities in health behaviours over time alone. We describe the use of time-varying health behaviours to examine socioeconomic inequalities in mortality, systematically listing underlying mechanisms that may cause differences between time-varying and time-fixed models, and show that these mechanisms may be specific for each health behaviour. The use of time-varying health behaviours advances our understanding of the explanation of socioeconomic inequalities in mortality, but underlying mechanisms must be carefully examined.

INTRODUCTION

Studies investigating explanations for socioeconomic inequalities in mortality have usually added material, behavioural and psychosocial factors to a model linking socioeconomic position to mortality during follow-up. They suggest that maximally half of these inequalities are due to health behaviours.[1–7] This contribution of health behaviours to socioeconomic inequalities in mortality is determined by the percentage reduction in the estimated association between socioeconomic position and mortality after inclusion of the mediating health behaviours in the model. Generally, the behavioural factors included in such mediation analyses are measured once (often at baseline) and therefore treated as 'time-fixed' mediators. In these cases, the underlying assumption is that health behaviours are fairly stable over time, and that the initial baseline measurement is a good indicator for lifelong exposure. Since this is often not the case, some recent papers have started including behavioural factors measured repeatedly during follow-up. In these models, health behaviours were treated as so-called 'time-varying' mediators.[8–14] An initial study suggested that the contribution of health behaviours is greater when measured multiple times,[8] which is in line with findings in some but not all studies published ever since.[9–14] The main explanation given to a more prominent role of health behaviours is that repeated measures are able to account for an increasing socioeconomic gradient in unhealthy behaviour over time. However, an increasing socioeconomic gradient is not the only possible explanation for differences in results between time-fixed and time-varying models. For example, the role of physical activity in the explanation of socioeconomic inequalities in mortality has been shown to increase when multiple measurements of physical activity are used, even in the presence of a declining socioeconomic gradient in physical activity.[8] Also, while inequalities in smoking increased over time, some studies have found no difference in the contribution of smoking between time-fixed and time-varying models.[8 11] We argue that several mechanisms may cause differences in results between time-fixed and time-varying models, and that the extent to which they do so may vary by mediator. In this paper, we briefly introduce the concept of time-varying covariates, systematically describe potential mechanisms that may lead to different results between time-fixed and time-varying models, and recommend how to report results of studies using time-varying models in order to advance our understanding of socioeconomic inequalities in mortality.

TIME-DEPENDENT MODELS

Socioeconomic inequalities in mortality are usually explored with a Cox proportional hazards regression where all covariates are only measured once, often at baseline:

$$h(t|SES, M, C) = h_0(t)\exp(\beta_1 SES + \beta' M + \beta'' C) \quad (1)$$

In this model, h_0 is the baseline hazard, *SES* the indicator for socioeconomic status, *M* a vector of potential mediators, *C* a vector of potential confounders, and the β's a vector of regression coefficients. The HR of the mediators $exp(\beta' M)$ is independent from time *t*. This implies that the health behaviours are assumed to be fixed over the entire follow-up period, for example, a smoker at baseline will be treated as a smoker during follow-up, even if the person quit soon after the baseline measurement. This may cause misclassification of the exposure. A solution to reduce this misclassification is to measure smoking several times over the follow-up period, and take behaviour changes into account.

The role of repeatedly measured health behaviours can be explored with an expansion of the

Cox proportional hazards regression in which time-dependent covariates are allowed in the model:

$$h(t|SES, M(t), C(t)) = h_0(t)\exp(\beta_1 SES + \beta' M(t) + \beta'' C(t)) \quad (2)$$

In this model, the hazard at time t depends on the value of the mediators M and confounders C at time t. While SES is still measured at baseline only, repeatedly measured mediators and confounders are entered into the model as time-dependent covariates.

In studies that used this model to explain socioeconomic inequalities in mortality, the mediating health behaviours were measured as categorical variables (ie, non-smoker, former smoker and current smoker). According to the technique, participants are then reclassified as exposed or non-exposed at every assessment.[8–13] Since people changed their behaviours over time (some quit smoking, others became inactive), accounting for these changes should reduce misclassification and provide a more accurate measure of the exposure. Further, the quality of measurement could be increased by using time-varying behaviours, especially for behaviours that are difficult to measure (eg, physical activity).

It is important to realise that exposure to a risk factor in time-varying models as described here is not equivalent to cumulative exposure in accumulation models.[15–17] For instance, a participant who quit smoking at the last assessment is grouped together with all former smokers at that point in time regardless of when the other participants quit. Thus, accumulation of unhealthy behaviour at more than one point in time is not modelled; exposure is only reclassified at every assessment. Formally, statistical methods do allow the modelling of time-varying mediators as more complex functions over time, but these methods are often not employed since they also increase the potential for erroneous inference.[18] Preferably, the modelling of the mediators should be consistent with the hypothesis. So, when the causal process of health behaviours is hypothesised as a cumulative effect (eg, supposed in some life course models), one should try to model the mediators accordingly.

CAUSAL PATHWAYS OF THE MEDIATION ANALYSIS

Differences in the estimated contribution of health behaviours measured once only or measured multiple times can be caused by changes in one or both of the causal pathways of the mediation analysis (figure 1): (1) the association between socioeconomic position and health behaviours has changed over time, and/or (2) the association between health behaviours and mortality has changed when behaviours are measured repeatedly over time instead of once only.

Although socially patterned changes in health behaviours may have instigated this line of research and dominate the explanation, our main message is that the second pathway may be just

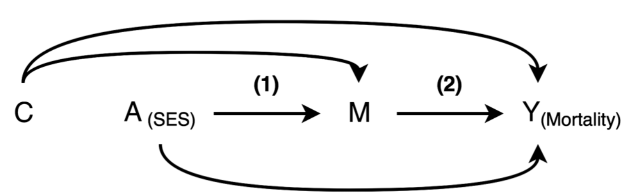

Figure 1 Mediation diagram with mediators M measured only once, exposure A (assumed to be effectively randomised), outcome Y, and confounders C. (1) Association between socioeconomic status (SES) and risk factor. (2) Association between risk factor and mortality.

as important in understanding differences in results between models with time-fixed and time-varying risk factors.

Changing socioeconomic gradients in risk factors

The first pathway of interest ((1) in figure 1) is a change in the association between socioeconomic position and mediators (ie, changes in the socioeconomic gradient of the health behaviours). A larger gradient in health behaviours will, ceteris paribus, lead to a larger contribution of the behaviours to health inequalities. Evidence of widening inequalities in health behaviours (and other cardiovascular disease risk factors)[19–23] makes this a likely and dominant explanation. Changing gradients can be related to progress in a behavioural epidemic over time, to a differential impact of policies and interventions between higher and lower socioeconomic groups or to different life course progressions between socioeconomic groups. First, trends in behaviours have been shown to be socially patterned.[24–26] For instance, smoking was first adopted by more advantaged groups, but the social distribution of smoking has reversed over time and smoking is now more prevalent among disadvantaged groups. Second, it has also been shown that policies and interventions targeted at promoting healthy behaviour are often more effective among higher socioeconomic groups, resulting in a widening of health behaviour inequalities.[27–30] Third, disparities in health behaviours may widen with increasing age. For instance, owing to an accumulation of socioeconomic disadvantage over time, it may be more difficult for lower socioeconomic groups to quit smoking at a later stage in life than it is for higher socioeconomic groups.

Some studies, however, have reported a larger contribution of behaviours to inequalities in mortality even when the socioeconomic gradient in health behaviours reduced, for instance with regard to physical activity.[8] Clearly, the second pathway cannot be neglected.

Changing associations between risk factors and mortality

The second pathway of interest ((2) in figure 1) is a change in the estimated association between mediating risk factors and mortality. We list four mechanisms that may be responsible for changes in the estimates. The first and second are related to actual changes in the association between health behaviour and mortality, while the third and fourth are related to the methodological properties of the time-varying models.

First, taking changes in health behaviours into account reduces exposure misclassification and provides a better estimate of the association between health behaviours and mortality. Reducing misclassification in most cases leads to an increase in the observed association.[31]

Second, mortality risks of health behaviours may change over time. For example, better treatment of lifestyle-related chronic diseases (eg, the treatment of obese patients)[32 33] or an improvement in the early detection of diseases caused by unhealthy behaviour (eg, lung cancer screening) will, ceteris paribus, decrease the association between behaviours and mortality. Those who become exposed in times of better treatment or more effective screening will thus have a lower mortality risk than those exposed at baseline, resulting in a decreased association in time-varying models. The impact of this mechanism will be even greater when such changes in relative risks differ between socioeconomic groups. This may be especially relevant with regard to health-related innovations, which are often adopted earlier by higher socioeconomic groups.[27 34 35] Mortality risks may also increase in time-varying models. For instance, the health benefit of light or moderate physical activity in leisure time may increase after retirement,[36–38] since work-related physical activity no longer protects older adults from a sedentary lifestyle.

Third, the time lapse that is needed for changes in behaviour to have an effect on mortality may affect the differences in the estimates.[9 18] This concerns the time it takes for a risk exposure to increase a participant's mortality risk as well as the time it takes to lower a participant's mortality risk after changing from being exposed to being non-exposed. Importantly, these time periods differ by health behaviour and require insights into the aetiology of the risk factor. For changes that require a long time to affect mortality risks, and which are not captured in time-varying models, there is a large potential for exposure misclassification. For instance, a person who quit during follow-up after 20 years of smoking will be reclassified as a former smoker at the first follow-up measurement, but will remain at an increased risk of dying for many years.[39] If the person dies soon after the follow-up measurement, the event will be attributed to the 'former smoker' level of the exposure. While death may have been caused by smoking, it is not attributed to smoking in the model, resulting in an underestimation of the effect of smoking.

Fourth, if changes in the mediators are associated with confounders, bias will be introduced in the time-varying models (figure 2).[10 18] For example, the role of repeatedly measured physical activity can be confounded by the participant's health status. If poor health results in less physical activity among initially active persons, and if poor health results in shorter survival, the association between physical activity and mortality will be larger in the time-varying models due to confounding. It may also be that perceived or diagnosed poor health triggers favourable behavioural changes, such as quitting smoking or increasing physical activity. Again, for the purpose of understanding inequalities in mortality, this is even more relevant because the first example may occur more often among persons in lower socioeconomic groups, and the second example more often among higher socioeconomic groups. Potential time-varying confounding can be checked when data are available (ie, examine the association between confounders and subsequent health behaviour). Controlling for time-varying confounding, however, is not possible with conventional regression methods and requires the use of more sophisticated methods, such as marginal structural models or G-estimation.[10 40 41]

CONCLUSION AND IMPLICATIONS

Some recent studies have analysed health behaviours as time-varying mediators and estimated that they contribute up to 75% to socioeconomic inequalities in mortality depending on the context.[8–13] Moreover, these studies suggest a tendency that the contribution of health behaviours is larger when longitudinal data of health behaviours are used.[8 11 13] We have argued that several mechanisms may be responsible for differences between time-fixed and time-varying models and that the extent to which they do so may vary by health behaviour. Interpreting these results requires examination of possible changes in both pathways of the mediation analysis and cannot solely be attributed to socially patterned behavioural changes. Clearly, the same applies to studies on other groups of mediators, such as material and psychosocial factors.

The mechanisms listed here are relevant for the general adult populations and some may gain in importance if populations are getting older (eg, time-varying confounding by health status). The choice of either a time-fixed or time-varying model depends on the context of the study. In some studies, the time-fixed approach would be preferable (eg, because time lapse and confounding may seriously impact on the results); in others, the time-varying approach may be preferred (eg, when inequalities in the risk factors widen over time and it is reasonable to assume that time lapse and confounding are not an issue). To aid the interpretation, we recommend future studies in this field to explicitly discuss possible explanations for changes over time both in the socioeconomic gradient in risk factors and in the association between risk factors and mortality. Since mechanisms may differ between risk factors, these results should also be provided for separate risk factors.

In sum, the use of time-varying mediators advances understanding of the explanation of socioeconomic inequalities in mortality, but underlying mechanisms must be carefully examined.

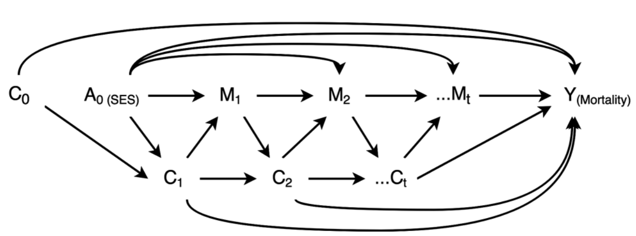

Figure 2 Mediation diagram with time-varying mediators M, exposure A (assumed to be effectively randomised), outcome Y, and time-varying confounders C. SES, socioeconomic status.

What is already known on this subject

A higher prevalence of unhealthy behaviours in lower socioeconomic groups contributes to socioeconomic inequalities in mortality. Recent studies suggest that the contribution of health behaviours in mediation models examining socioeconomic inequalities in mortality is larger when measured repeatedly over time instead of once only.

What this study adds

While explanations for the larger contribution of health behaviours have been mostly attributed to changing socioeconomic gradients in health behaviours over time, other mechanisms probably play a more prominent role. Several mechanisms can cause differences in results between models with time-varying and time-fixed mediators, perhaps most notably related to a change in the association between health behaviours and mortality. Moreover, mechanisms can differ between risk factors. A systematic examination of the most likely mechanisms will help ascertain the causes that drive socioeconomic inequalities in mortality.

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