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ESTIMATING MEDIATED EFFECTS IN HEALTH AND EPIDEMIOGICAL RESEARCH

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ABSTRACT

A central objective in health and epidemiological research is to examine the processes by which explanatory variables yield certain outcomes. For example, two overarching, policy-relevant issues are (1) the pathways through which various socio-demographic, attitudinal, and behavioural risk factors lead to particular health outcomes (e.g., death, disease), and (2) the mechanisms through which intervention and treatment programs produce their desired effects (e.g., increasing screening rates for serious illness, as well as reducing drug, alcohol, and tobacco use). Such issues can be addressed empirically via estimation of mediated (i.e., indirect) effects; however, the required statistical procedures are complex and not yet widely applied in the fields of health and epidemiology. The purpose of this paper is to provide an overview of the major theoretical and methodological concepts involved in mediated effects analysis, as well as present some illustrative applications using Structural Equation Modeling (SEM) and data from the 2003 Canadian Health Services Access Survey (HSAS).

KEY WORDS: Mediated Effects; Health; Structural Equation Modeling.

1. INTRODUCTION

1.1 Studying Causal Processes in Health and Epidemiology

A principal research aim in the health and epidemiology fields (and other disciplines) is to understand the processes by which hypothesized explanatory (i.e., causal) variables produce certain outcomes. In this regard, two overarching, policy-relevant issues are (1) the pathways through which various socio-demographic, attitudinal, and behavioural risk factors lead to particular health outcomes (e.g., death, disease), and (2) the mechanisms through which intervention and treatment programs produce their desired effects (e.g., increasing screening rates for serious illness, as well as reducing drug, alcohol, and tobacco use). Evidently, empirical examination of these issues requires gathering high-quality data on a number of key variables, as well as informed, *a priori* specification of complex sequences of behaviours and events. In other words, addressing such questions requires developing and testing explicit "causal stories" about the relations among variables. The validity of these causal stories can then be addressed via statistical analysis of mediated or indirect effects, which represent the impact that an explanatory variable has on an outcome variable through one or more intervening variables. These analyses can be informative from a policy perspective, since they assist in evaluating hypothesized pathways among risk factors, disease, and health outcomes, as well as help determine if treatment and intervention programs are actually successful at modifying the variables they are designed to modify.

However, estimation of mediated effects requires specific, complex statistical procedures that are not yet widely applied in health and epidemiological research. The purpose of the current paper is to give an overview of theoretical concepts and statistical methods involved in mediated effects analysis. In addition, a set of illustrative examples is presented, based on *Structural Equation Modeling* (SEM) of data from the 2003 Canadian Health Care Services Access Survey (HSAS).

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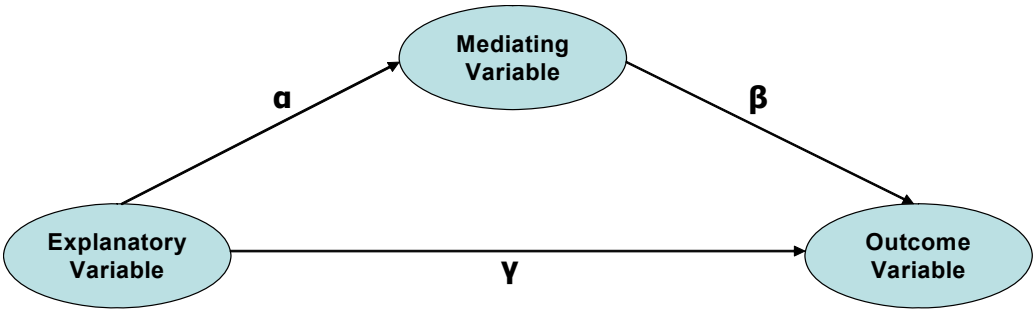
Figure 1: An Illustration of Mediated Effects



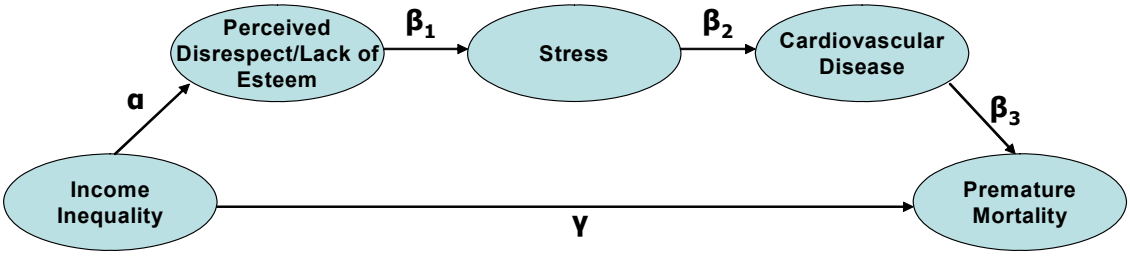
1.2 Mediated Effects Analysis: Basic Concepts

The basic concepts underlying an analysis of mediated effects are presented in Figure 1, which contains the simplest generic causal model possible: one explanatory variable, one mediating variable, and one outcome variable (see Baron & Kenny, 1986). Essentially, the model depicts an hypothesized chain reaction among the variables; in other words, the model tells a "causal story" about how an explanatory variable produces an outcome. The explanatory variable causes the mediator (quantified by path **α**); and in turn, the mediator causes the outcome (quantified by path **β**). Thus, the mediator is seen as at least partly responsible for the association between the explanatory variable and the outcome variable. The mediated effect, or what is often called the indirect effect, is defined as the product of these two **α** and **β** pathways linking the explanatory variable to the outcome variable: **α*β**.

Further, given that the explanatory variable may have an impact on the outcome variable over and above that accounted for by the mediator, a direct pathway (**γ**) is also included in the model. This direct pathway captures the effects of any mediators not formally specified in the model. We can thus define the total effect of the explanatory variable on the outcome mediator as the sum of the direct and indirect effects:
α*β + **γ**.

In a mediated effects analysis, the "ideal" analytical situation is where there is no direct effect (i.e., **γ** = 0), while the remaining pathways, including the direct effect itself, are significant. Such a result supports full mediation, meaning that the mediator completely explains the association between the explanatory and outcome variable. This situation rarely arises, particularly in social science research, as the investigator typically does not have the requisite substantive knowledge or empirical data available to include all possible mediators in the analysis. Therefore, partial rather than complete mediation, where one has a total effect consisting of both significant mediated and direct effects, is a much more common research situation. Further examples of these types of models, derived from different research areas, are presented below for illustrative purposes.

Figure 2: Mediated Effects of Income Inequality on Premature Mortality

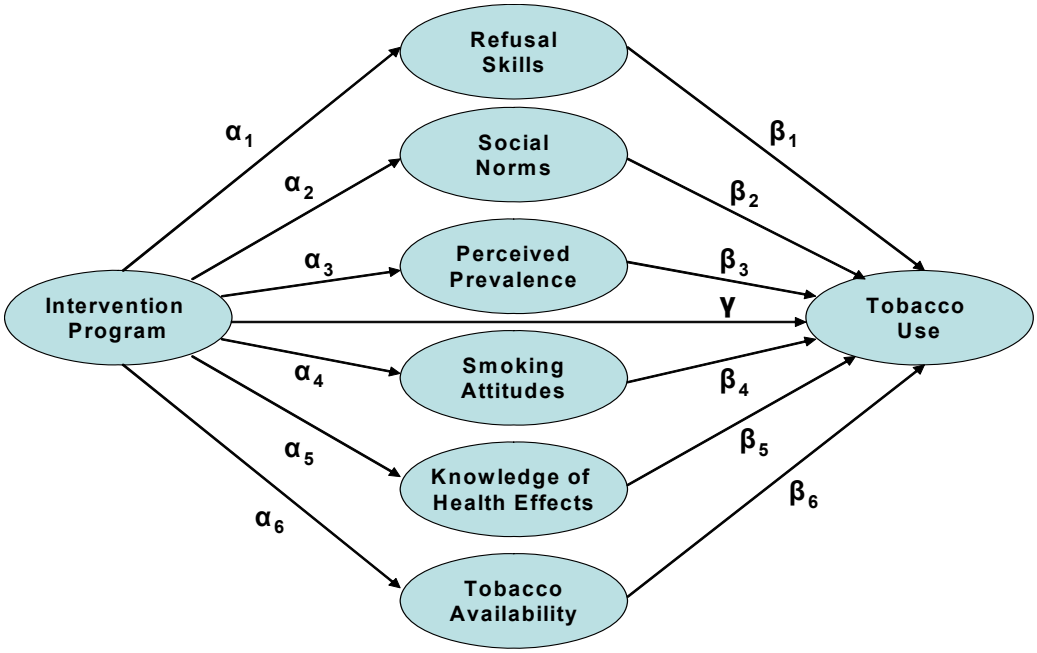


A specific example of a "causal story", taken from the work of Richard Wilkinson (2005) on the population health impact of income inequality, is shown in path diagram form in Figure 2. In this model, income inequality is hypothesized to lead to premature mortality via three mediating variables. First, income inequality causes perceived

disrespect and lack of esteem, given the perception of being "lower down in the pecking order). Next, this psychological damage leads to stress, which in turn contributes to the development of cardiovascular disease (supposedly through increasing levels of the stress hormone cortisol), which results in premature mortality. The mediated or indirect effect is slightly more complex than in the previous example, but is still represented quantitatively by a straightforward multiplicative combination of the parameters lying along the sequence of paths, that is, $\alpha*\beta_1*\beta_2*\beta_3$. A direct path from income inequality to premature mortality is also included, to acknowledge the possibility that not all of the potential mediating variables have been included in the model.

Overall, the model provides an explicit account of how income inequality contributes to premature mortality, which is of course superior to simply stating that there is a connection between these two variables. However, to the author's knowledge, there has not yet been a formal, simultaneous test of the proposed system of pathways, possibly due to the difficulty inherent in obtaining high-quality data on each of the variables involved.

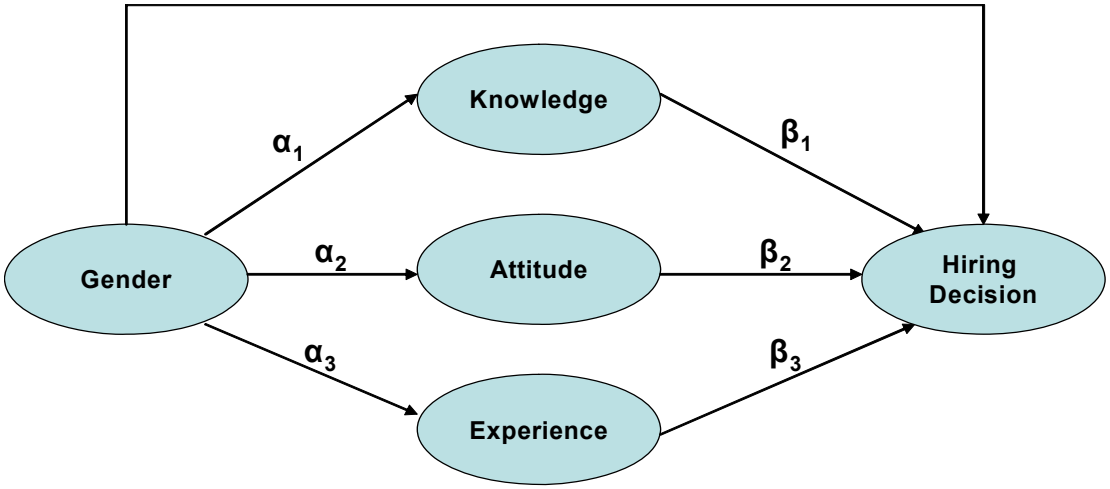
Figure 3: Mediated Effects of a Tobacco Use Intervention Program for Adolescents



The path diagram in Figure 3 is another example of a mediational model; it represents how a hypothetical intervention program for reducing tobacco use among adolescents is supposed to operate (see MacKinnon, Taborga, & Morgan-Lopez, 2002). Specifically, according to MacKinnon et al. (2002), the following six mediating variables are first modified by the program: (1) *refusal skills* (e.g., adolescents are instructed in social techniques for dealing with peer pressure to smoke), (2) s*ocial norms* (e.g., a media campaign could be directed at making the social norm seem less accepting of tobacco use), (3) *perceived prevalence* (e.g., the program could attempt to alter perceptions of high smoking prevalence, that is, deconstructing a potential myth among teenagers that "most people do it, so it must not be that bad"), (4) s*moking attitudes* (e.g., the program could try and convince adolescents that they make little or no social "gain" from smoking), (5) *knowledge of health effects* (e.g., there could be strategic dissemination of knowledge regarding the links among smoking, lung cancer, and heart disease), and (6) *tobacco availability* (e.g., continue to develop stricter policies regarding selling tobacco products to minors, as well as impose tighter controls on tobacco advertising). These mediators then supposedly act in concert to modify tobacco use. Thus the indirect effect of the program on tobacco use is quantified by multiplying the appropriate pairs of coefficients and summing their products, as follows: $(\alpha_1*\beta_1)+ (\alpha_2*\beta_2) + (\alpha_3*\beta_3) + (\alpha_4*\beta_4) + (\alpha_5*\beta_5) + (\alpha_6*\beta_6)$. As with the previous example, the direct path from the intervention program to the outcome accounts for any program effects not transmitted by the set of mediators.

This model is also provides a good illustration of the nature of mediated effects, as it details the specific pathways through which an intervention program is hypothesized to reduce tobacco use. Obtaining high-quality data on all the variables would help assess which aspects of the program were working as hypothesized, and which ones required refinement or might be abandoned altogether.

Figure 4: Mediated Effects of Gender on Hiring Decisions



The final example shown in Figure 4 comes from the business rather than the health and epidemiology fields, but illustrates well the potential practical uses of a mediated effects analysis. In this example, let us suppose that a firm is called upon to empirically demonstrate that they have no gender preferences in hiring (see Pearl, 2001). As Pearl (2001) notes, what the firm would want to show is that if gender had any effect at all on hiring, it would be solely through qualifications, represented in the model by the following mediators: knowledge, attitude and experience. In other words, it would be hoped that only the indirect effect, $(\boldsymbol{\alpha}_1*\boldsymbol{\beta}_1) + (\boldsymbol{\alpha}_2*\boldsymbol{\beta}_2) + (\boldsymbol{\alpha}_3*\boldsymbol{\beta}_3)$, would be significant. The existence of a direct effect of gender on hiring, above and beyond that accounted for by qualifications, might indicate that the firm had gender preferences in hiring.

1.3 Mediated Effects Analysis: Methodological Approaches

For assessing mediated effects in practice, there are a number of requirements. First, reliable data on each of the modeled variables is essential. Next, the typical analytical approach is to estimate a series of regression models, from which one obtains all necessary coefficients (and their standard errors) for computing and testing the mediated effect (Baron & Kenny, 1986). For example, for a simple 3-variable model with a continuous explanatory variable (**X**), mediator variable (**M**), and outcome variable (**Y**), the set of linear regression equations is written as follows:

$$\mathbf{M} = \boldsymbol{\tau}_1 + \boldsymbol{\alpha}*\mathbf{X} + \boldsymbol{\varepsilon}_1 \qquad [1]$$

$$\mathbf{Y} = \boldsymbol{\tau}_2 + \boldsymbol{\gamma}*\mathbf{X} + \boldsymbol{\beta}*\mathbf{M} + \boldsymbol{\varepsilon}_2, \qquad [2]$$

where $\boldsymbol{\tau}_1$ and $\boldsymbol{\tau}_2$ are intercept terms, $\boldsymbol{\alpha}$ represents the effect of **X** on **M**, $\boldsymbol{\beta}$ denotes the effect of **M** on **Y**, $\boldsymbol{\gamma}$ is the effect of **X** on **Y**, and $\boldsymbol{\varepsilon}_1$ and $\boldsymbol{\varepsilon}_2$ are error terms (i.e., unexplained variance). After separately estimating equations 1 and 2 above, the indirect effect $\hat{\alpha} * \hat{\beta}$ can be computed and then evaluated using a popular asymptotic z-test (Sobel, 1982):

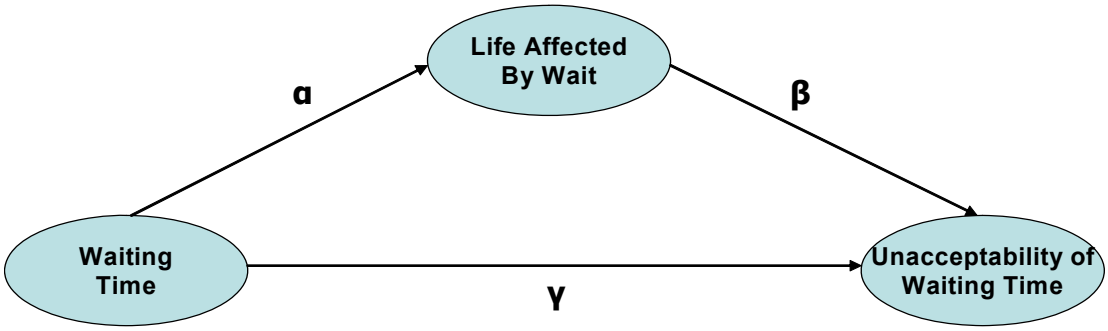
$$z = (\hat{\alpha} * \hat{\beta}) / [(\hat{\alpha}^2 * \mathrm{var}(\hat{\beta})) + (\hat{\beta}^2 * \mathrm{var}(\hat{\alpha}^2))]^{1/2} \qquad [3]$$

However, it should be noted that the regression-based approach quickly becomes labour-intensive and tedious with complex mediated models, especially when the researcher is dealing with multiple explanatory, mediator, and outcome variables. In such cases, more versatile statistical techniques such as Structural Equation Modeling (SEM)

allow a mediated model to be evaluated conveniently in a single analytical step. Despite its flexibility, SEM has not been widely applied in health and epidemiological research. To demonstrate the potential of SEM for addressing research questions in these fields, an application is presented below.

2. MEDIATED EFFECTS ANALYSIS: AN ILLUSTRATIVE APPLICATION

Figure 5: Mediated Effects of Waiting Times for Medical Services on Judgments of Wait Time Acceptability Among Canadians Insert Figure 5 about here



2.1 The Conceptual Model

Figure 5 contains the conceptual model to be evaluated. The general research question guiding the development of this model was: "What leads Canadians to view their waiting times for medical services as unacceptable?" The primary hypothesis was that the longer patients waited for a given medical service, the more likely the wait would affect their lives; and in turn, there would be greater likelihood of judging the waiting time as unacceptable. A direct path was also specified between waiting time and judgments of acceptability, given that people may judge a wait to be unacceptable simply because it was too long, independent of whether it actually had some other specific impact on their lives. The model examined here is therefore quite simple in form, but one will easily see that the methods described below readily extend to the evaluation of more complex models.

2.2 Data Source and Variable Definitions

The data source for this study was the 2003 Health Services Access Survey (HSAS), which collects information on waiting times for key diagnostic and treatment services and access to 24/7 first contact health services, including patient experiences, acceptance and perceptions of waiting for care. The HSAS 2003 was a supplement to cycle 2.1 of the Canadian Community Health Survey (CCHS). In total, there were 32,005 respondents aged 15 and older (for a response rate of 87.1%). The current study focused on those who had received a specialized service (i.e., diagnostic tests, specialist visits, and non-emergency surgery) in the 12 months prior to HSAS 2003.

Waiting time was defined as the time between the decision to go ahead with a particular service (diagnostic test, specialist visit, non-emergency surgery) and the time when the service was received; it was based on self-report and coded in weeks. *Life Affected by Waiting* had two categories: waiting for the service was reported as not affecting the patient's life in any way (0), or it was indicated as affecting the patient's life in some way (1). *Acceptability of Waiting Time* also had two categories: waiting time for the service was judged to be either acceptable (0) or unacceptable (1). Finally, the following covariates were included in the model: age, sex, education, income, rural versus urban residency, activity limitation, and self-perceived health. These were permitted to correlate freely with *waiting time*, as well as directly predict both *life affected by waiting* and *acceptability of waiting time*. In this way, all model estimates were adjusted for the covariates.

2.2 Statistical Specification of the Model

Given that both dependent variables in this analysis (*life affected by waiting* and *acceptability of waiting time*) were dichotomous, a logit model was specified. Let **WT** = *waiting time*, **LA** = *life affected by waiting*, and **AW** = *acceptability of waiting time*. Further, let $\boldsymbol{\pi}_1$ = Pr(**LA** = 1| **WT**) and $\boldsymbol{\pi}_2$ = Pr (**AW** = 1| **WT**, **LA**). The core of the full conceptual model can then be expressed in terms of the following simultaneous two-equation system:

$$logit(\boldsymbol{\pi}_1) = \boldsymbol{\tau}_1 + \boldsymbol{\alpha}*\mathbf{WT} \quad [4]$$

$$logit(\boldsymbol{\pi}_2) = \boldsymbol{\tau}_2 + \boldsymbol{\gamma}*\mathbf{WT} + \boldsymbol{\beta}*\mathbf{LA}, \quad [5]$$

where $\boldsymbol{\tau}_1$ and $\boldsymbol{\tau}_2$ are intercept terms, $\boldsymbol{\alpha}$ represents the effect of **WT** on **LA**, $\boldsymbol{\beta}$ is the effect of **LA** on **AW**, and $\boldsymbol{\gamma}$ denotes the effect of **WT** on **LA**.

2.3 Parameter Estimation

The M*plus* software package (version 3.13; Muthén & Muthén, 1998-2005) was used to estimate the model with respect to all three service types (i.e., diagnostic tests, specialist visits, and non-emergency surgery). It should be noted that most SEM programs are based on a mathematical framework that requires a variance-covariance matrix as input. For coarsely categorized variables, however, a variance-covariance matrix is not a theoretically appropriate statistic for parameter estimation. Sample variances and covariances tend to most biased when the observed variables are binary, as was the case in the present study. However, M*plus* does allow raw data as input as well as the specification of logit links in path models; whereas in the majority of SEM software packages, linear additive identity link functions are the sole option. Parameter estimates were obtained here via the Maximum-Likelihood technique. Further, only complete cases were retained for the analysis, and the data were weighted using the normalized CCHS sampling weights. The final sample sizes for each service type were as follows: diagnostic tests = 2249, specialist visits = 3526, and non-emergency surgery = 1879.

2.4 Results

Table 1: Parameter Estimates for Models

Service Type	$\hat{\alpha}$	$\hat{\beta}$	$\hat{\alpha} * \hat{\beta}$	$\hat{\gamma}$
Diagnostic Tests	.12 (1.12)**	2.71 (14.97)**	.33 (1.39)**	.02 (1.02)
Specialist Visits	.17 (1.19)**	3.18 (24.14)**	.54 (1.72)**	.02 (1.02)*
Non-Emergency Surgery	.08 (1.08)**	3.71 (23.83)**	.25 (1.28)**	-.02 (.98)

Note. Odds ratios are in brackets.
** Estimate is significant at the .01 level
* Estimate is significant at the .05 level

The parameter estimates for all three models are shown in Table 1. Across all models, every one-week increase in waiting time increased the odds of the wait affecting the patient's life. In turn, if the wait affected a patient's life, the odds of judging the wait as unacceptable were substantially increased, with respect to all service types. Further, the indirect effect of waiting time on judgments of acceptability was reliable in all three cases. Through its effect on patients' lives, waiting time significantly increased the odds of judging the wait as unacceptable. Further, non-emergency surgery was the only service type where a significant direct effect of waiting time on acceptability was observed. However, the direct effect itself was quite small (O.R. = 1.02).

3. CONCLUSIONS

3.1 Theoretical and Practical Implications

Overall, the above analysis appears to yield reasonably sound evidence for a mediated effect of waiting times for medical services on judgements of the acceptability of the wait. For the most part, it does not appear to be the length of the waiting time *per se* that leads patients to view their waiting times as unacceptable; rather, these judgments seem to depend to a larger extent on whether the wait actually had an impact on patients' lives. These results could therefore be useful for health policy makers wanting more information about how waiting for medical services affects the lives and views of Canadians. However, it is critical to remember that no statistical analysis can ever *prove* a model to be true, especially when using correlational and cross-sectional data. Another limitation of the present analysis is that a rather general approach was taken to evaluate the model (i.e., with respect to diagnostic tests, specialist visits, and non-emergency surgery). Therefore, one possible avenue for future research is examining the model with regard to more specific types of medical services and procedures (e.g., hip and knee replacement surgery), in order to see if the hypothesized linkages still hold among the key variables.

3.2 Future Directions

On a more general level, the present results suggest that analysis of mediated effects can increase understanding of phenomena in health and epidemiological research; and can therefore help identify areas for possible intervention. Further, SEM and versatile software packages such as M*plus* might be useful additions to the methodological arsenals of health and epidemiological researchers. Further, it seems possible that enhanced collaboration between health and epidemiological researchers and population-level survey developers might be beneficial, potentially helping to guide and refine the collection of data required for testing complex models of health-related phenomena. Lastly, it is important to emphasize that any statistical modeling endeavour should always be accompanied by sound theory and/or prior empirical evidence in support of a given model specification.

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