ASSESSING THE TOTAL EFFECT OF TIME-VARYING PREDICTORS IN PREVENTION RESEARCH

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ABSTRACT

Many important prevention questions concern the consequences of individual actions on drug use and abuse. For example, consider the question, "If we could delay the initiation of alcohol, would that in turn lead to a delay in marijuana initiation?" In general, causal questions are best answered in an experimental setting, that is, a setting in which participants are randomly assigned levels of the predictor, here alcohol initiation timing. However, in this case, and frequently in prevention, it is unethical, impractical, or infeasible to conduct an experimental study. Thus we must use observational data to address prevention questions such as the above. In observational studies, unknown and known reasons why participants possess different levels of the predictors often provide alternate explanations for the differences in response. These unknown and known reasons, and the variables that measure them, are commonly called confounders. Confounders are common correlates of the predictor and the response. Thus, when using observational data, we must adjust or control for confounding in order to address the above question. For example, peer pressure resistance is a common correlate of both alcohol and marijuana initiation and thus we must adjust for peer pressure resistance in addressing the above question. When both the predictor and confounder(s) are time-varying (in our example to follow, both alcohol use initiation and peer pressure resistance are time-varying), traditional adjustments for confounders do not eliminate bias and can cause further bias (Robins & Greenland, 1994; Barber et al, 2002).

In this paper we explain and illustrate Hernán, Brumback, and Robins' (2000; 2001) method of using sample weights to adjust for confounding due to time-varying common correlates when using survival analysis. We address the above substantive question using this methodology.

INTRODUCTION

In prevention research we are often interested in assessing the total effect that delaying the timing of a predictor has on the timing of the response. This information is useful in making treatment/intervention decisions. For example, we would use the answer to the question, "If we could delay the initiation of alcohol, would that in turn lead to a delay in marijuana initiation?" to anticipate whether an alcohol use prevention study might also have effects on marijuana use. The answer to this question is provided by the total effect of the timing of alcohol use initiation on the timing of marijuana use initiation. A fundamental problem in assessing the effect of such a time-varying predictor on a response, as prevention researchers realize, is the presence of confounders. Confounders are common correlates of both the predictor and the response. In our scenario, an example of a common correlate of alcohol initiation timing and marijuana initiation timing is peer pressure resistance.

As is well known, we must control for this confounding (see Bollen, 1989 or Bohnstedt and Knoke, 1982). If confounding is not controlled, the coefficient of alcohol initiation in a regression of marijuana initiation on alcohol initiation results is a biased estimate of the total effect of alcohol use on marijuana use. This bias is due to differences in the types of individuals who choose to initiate alcohol use and who choose not to initiate. Such differences between the alcohol initiators and alcohol non-initiators are referred to as compositional differences. When compositional differences exist, the estimated effect of the timing of alcohol initiation on the timing of marijuana initiation will reflect the differences in the types of individuals who choose to initiate alcohol, in addition to the consequence of alcohol use initiation on the timing of marijuana use initiation. For example, suppose that most of the past alcohol initiators have low peer pressure resistance, whereas most of the alcohol non-initiators have high peer pressure

resistance. It is then unclear whether the estimated effect that the timing of alcohol initiation has on the timing of marijuana initiation represents the consequence that delayed alcohol timing has on the timing of marijuana initiation, or whether the estimated effect merely reflects compositional differences in peer pressure resistance, or if the estimated effect reflects a combination of the two. In experimental settings we control for confounding by randomization of the participants to different predictor levels; in observational studies statistical methods of control, along with assumptions, must be used.

In the next section (Section 2), we discuss why a traditional, standard statistical method of controlling for confounders may result in further bias in the case when both the predictor and confounders have different values through time (time-varying). This traditional method uses a standard model that includes the confounders, along with the predictor, as covariates in a regression model. As we shall see, this method does not address the desired question, "If we could delay the timing of the initiation of alcohol, would that in turn delay the timing of marijuana initiation?" An alternative to this standard method is an approach proposed by Robins (1998) that uses weights to statistically control for confounding. In Section 3, we describe the use of weights for the survival analysis setting (Hernán et al., 2000; Hernán et al., 2001). Finally, in Section 4 an illustration of the weighting methodology for the survival analysis setting as proposed by Hernán, Brumback, and Robins (2000; 2001) is presented by considering the above question using drug abuse prevention data. In section 4 we compare three methods that might be used to assess the total effect of a predictor (timing of alcohol initiation) are: 1) the naïve model that completely ignores the presence of confounders, 2) the standard model that includes confounders as covariates to control for confounding, and 3) Robins' weighting method. The Appendix contains details of the weight computation. Complete details and explanation of

SAS programming code that can be used for weight creation and the three types of response regression models are available at: http://methodology.psu.edu/pubs/tvpappen.htm.

WHY INCLUDING CONFOUNDERS IN THE RESPONSE REGRESSION MODEL FAILS

In the following, the term "response regression model" refers to a regression model of the primary response (e.g., timing of marijuana initiation) on the primary predictor (e.g., timing of alcohol initiation) and possibly other covariates. Many authors have suggested that in order to statistically control for confounding, one should include confounders as covariates in the response regression model. We refer to the response regression model that includes confounders as covariates as the standard model. George W. Bohrnstedt & David Knoke, for example, refer to "…clear-cut cases of spurious relationships which disappear when the appropriate common cause of both variables is held constant" (1982, p.73). Kenneth A. Bollen (1989) notes that, when referring to the use of structural equations modeling and confounding, "the task is to explicitly include in the analysis those characteristics suspected of influencing the dependent variable and associated with other explanatory variables." Only recently has the statistical community come to realize that, in the time-varying setting (both predictor and confounders take on different values over time), conditioning on confounders in the response regression model (i.e. using the standard model) may produce spurious correlations, thus producing bias (Robins, 1986; Robins, 1989; Robins & Greenland, 1994; Pearl, 1990; Robins et al, 2000). Because of this unexpected bias, one must find alternate ways of including the confounders in the response regression model. To make this bias clearer, consider the following scenario, pictured in Figure 1.

Here, Alc_t represents whether or not an adolescent has initiated alcohol use prior to, or at, time t; $Ppress_t$ represents a measure of the adolescent's peer pressure resistance at time t; Mj_t

represents whether or not an adolescent has initiated marijuana use prior to, or at, time t; and U_t are unmeasured predictors at time t, such as family characteristics (e.g. family functioning) or individual characteristics (e.g. hyperactivity). The arrows represent causal paths. We have omitted many arrows that naturally would be in this figure; this is for simplicity and is not an assumption (our assumptions are discussed below). In Figure 1 note that $Ppress_1$ is listed to the left of Alc_1; we are assuming that $Ppress_1$ is not an outcome of Alc_1 but occurs just before the measurement of Alc_1. Similarly, $Ppress_2$ is not an outcome of Alc_2. Note the pathways labeled by "a," "b," and "c." The "a" paths are between the peer pressure resistance measure ($Ppress_t$) and the predictor (Alc_t); the "b" path is between the predictor at time 1 (Alc_1) and the confounder at time 2 ($Ppress_2$); the "c" paths are between the unmeasured predictor (U_t), the confounder ($Ppress_t$), and the response (Mj_t).

We wish, as before, to assess the total[5] effect of alcohol use initiation on the timing of marijuana use initiation. Notice, from Figure 1, that $Ppress_2$ is a confounder because it is correlated with both subsequent alcohol use and subsequent marijuana use, via paths "a" and "c" (the correlation via path "c" occurs because U_2 is unmeasured). In order to control for this confounding, we might include both $Ppress_1$ and $Ppress_2$ as covariates in a regression of marijuana use initiation on alcohol use initiation. From the figure, however, we see that the confounder, $Ppress_2$, is also an outcome of the predictor, Alc_1, (via path "b") causing the following problem: if we condition on $Ppress_2$, by including it in the response regression model, we create a spurious correlation between Alc_1 and Mj_3, via paths "b" and "c."

To make these spurious correlation issues clear, consider an example using sprinklers, following Pearl (1998) and shown in Figure 2. This model shows relationships between a front yard sprinkler, the front yard grass, the backyard grass, and rain. The predictor, previously

alcohol use initiation, is the front yard sprinkler, which is either on or off; the confounder, previously peer pressure resistance, is the front yard grass, which is either wet or dry; the response, previously marijuana use initiation, is the backyard grass, which is also either wet or dry; and finally, U_2 is the unmeasured predictor, which in this case is rain (either yes or no; assumed unmeasured). We know that whether the front yard sprinkler is on, or not, has no effect on whether the backyard grass is wet; in other words, the predictor has no effect on the response (note the absence of an arrow from $Predict_1$ to $Resp_2$ in Figure 2). Suppose, however, that we know that the grass in the front yard at time 2 is wet ($Conf_2$=wet). Then, if the front yard sprinkler is off at time 1, we know it must be raining and thus we know that the backyard grass is also wet ($Resp_3$=wet). Knowing that the grass in the front yard at time 2 is wet is the same as including the confounder, "wet grass in the front yard," as a covariate in our response regression of the effect of the front yard sprinkler on the backyard grass. Thus, it appears that turning the front yard sprinkler off at time 1 causes wet grass in the backyard at time 3!

Including the confounder, "wet grass in the front yard at time 2," in the response regression model is equivalent to conditioning on whether the front yard grass is wet. This conditioning creates a spurious correlation from the predictor to the response; given wet grass in the front yard, having the front yard sprinkler off means that it must be raining, and so the grass must be wet in the backyard. Thus, conditional on the value of the confounder, a spurious correlation from previous values of the predictor to present values of the response is created. Consider Figure 2 for a pictorial explanation, as here the spurious correlation is depicted by the bold path from the predictor to the response via paths "b" and "c" created when conditioning on the confounder. The danger of these spurious correlations is clear: false conclusions regarding

the consequences that the timing of the predictor has on the timing of the response may be made, leading to inaccurate conclusions, treatment, and intervention decisions.

Returning to Figure 1, we see our dilemma. $Ppress_2$ is a confounder and must be controlled; it is, however, also an outcome of past values of the predictor, Alc_1. This is similar to the situation in Pearl's sprinkler example. As we have seen, outcomes of past predictors can produce spurious correlations when included as covariates in the response regression model; hence, we must find an alternative way to adjust for $Ppress_2$.

USING WEIGHTS TO ADJUST FOR CONFOUNDING IN SURVIVAL ANALYSIS

Hernán, Brumback, and Robins (2000; 2001) use a weighted survival analysis to control for time-varying confounders. The weights equalize the composition of participants with varying peer pressure resistance levels (and other confounders) within the two groups of initiators and non-initiators of alcohol. Under assumptions, this method can be used to produce an unbiased estimate of the total effect that the timing of alcohol initiation has on the timing of marijuana initiation. An intuitive discussion of the weights follows our assumptions.

Assumptions

As is well known, causal inference using observational data requires assumptions in order to control confounding. Intuitively these assumptions add information to the data, for a detailed discussion see Manski (1995) or the review paper by Winship and Morgan (1999). If a confounder is unobserved then assumptions concerning the joint distribution of the unobserved confounder, observed confounders, predictors, and response are made; for example, see the discussion of selection models in Winship and Morgan (1999). The weighting methodology assumes that good surrogates for all confounders are available and does not impose distributional assumptions on the confounders (Robins, 1989). The assumption that good surrogates for all

confounders are available is also made by the standard method; this emphasizes why scientific researchers who collect their own data strive to measure good surrogates of all confounders. In Figures 1 through 4 this assumption is implied by the absence of an arrow from the unmeasured confounder to the predictor (i.e. no unmeasured direct confounding). In the intuitive example below this means we assume that our measure of peer pressure resistance is a good surrogate for all of the confounders affecting alcohol and marijuana initiation.

The weighting methodology also assumes that past confounder patterns do not exclude certain levels of the predictor. For a more complete discussion of this assumption see Barber et al. (2002).

Intuitive Discussion

The following provides an intuitive discussion of the weights. Consider a group of high-risk adolescents who have not initiated either alcohol use or marijuana use by time t. Table 1 provides frequencies for time t alcohol use initiation by peer pressure resistance level (this table is artificially constructed for illustrative purposes). Note that one half (30/60) of the adolescents with low peer pressure resistance initiate alcohol use at time t, whereas only one fifth (10/50) of the adolescents with high peer pressure resistance initiate alcohol use at time t. This results in an under-representation of adolescents with high peer pressure resistance among the adolescents who initiate alcohol use and an over-representation of adolescents with high peer pressure resistance among the adolescents who do not initiate alcohol use.

If both one half of the adolescents with low peer pressure resistance initiate alcohol use at time t and one half of the adolescents with high peer pressure resistance initiate alcohol use at time t, then the table would be as in Table 2. This results in a representation of adolescents with high peer pressure resistance among the adolescents who initiate alcohol use that is equal to the

representation of adolescents with high peer pressure resistance among the adolescents who do not initiate alcohol use; both proportions are 25/55.

The original sample will resemble Table 1; the weighted sample will resemble Table 2. This is accomplished by weighting each subject with the inverse of the conditional probability of alcohol initiation status given peer pressure resistance status. Referring to Table 1, a weight of $(10/50)^{-1} = 5$ would be assigned to each of the 10 initiators of alcohol with high peer pressure resistance, whereas all 40 participants in the more likely group (non-initiator with high peer pressure resistance) would receive a smaller weight of $(40/50)^{-1} = 5/4$. Now, since in the low peer pressure resistance group there are equal numbers of participants initiating as well as not initiating alcohol use, each of the 60 people receive an equal weight of $(30/60)^{-1} = 2$. After weighting each subject's observations the weighted cell sizes from Table 1 become those in Table 3.

Note that in Table 3, the representation of adolescents with high peer pressure resistance among the adolescents who initiate alcohol use is equal to the representation of adolescents with high peer pressure resistance among the adolescents who do not initiate alcohol use; both proportions are 50/110 = 25/55. The only difference between Table 2 and 3 is that all cell sizes in Table 3 are double those in Table 2. In practice we weight by the ratio of the probability of alcohol initiation status divided by the conditional probability of alcohol initiation status given peer pressure resistance status, see Equation 1 (also see the appendix).

$$W = \frac{P[Alc_i]}{P[Alc_i \mid Conf_i]} \qquad (1)$$

Using this equation eliminates the elevation of the total sample size. Additionally, in the equation, the conditional probability of alcohol initiation status is given all confounders (Conf),

not just peer pressure resistance status. Ultimately, the weights adjust for peer pressure resistance's correlation with alcohol initiation, as represented pictorially by Figure 3. Now there is no correlation between peer pressure resistance and alcohol initiation, that is, pathway "a" no longer exists.

Peer pressure resistance is no longer a confounder in the weighted sample and thus we do not include peer pressure resistance as a covariate in our (weighted) response regression model. By not including peer pressure resistance we avoid the spurious correlation problem, yet we control confounding by using the weights. That is, even though the correlations indicated by paths "b" and "c" remain, we do not condition on peer pressure resistance in the model, and thus a false correlation between alcohol and marijuana is avoided. This can be seen in Figure 4.

Method

To implement the weighting procedure, we must estimate the weights; we model the initiation of alcohol at time t, among participants still at risk for marijuana use. In the models for calculating the weights the initiation of alcohol (or other predictor of interest) is the response, whereas the initiation of alcohol is a predictor in the response regression model. We begin by forming the ratio of two predicted probabilities for each time t. We calculate these predicted probabilities using discrete time survival analysis with a logistic regression model (Allison, 1995; Singer & Willet, 1993). In the logistic regression models to create the ratios, we regress the timing of alcohol use initiation on present and past values of confounders (i.e. peer pressure resistance) and baseline variables (i.e. sex and race, or other moderators) for those individuals who have not yet initiated marijuana use. The denominator of each ratio is the predicted probability of a subject's observed alcohol initiation status (initiator or non-initiator) in period t from a regression of the alcohol initiation status on confounders and baseline variables for those

who have not yet initiated marijuana use. The numerator of each ratio is the predicted probability of a subject's observed alcohol initiation status in period t from a regression of the alcohol initiation status on only the baseline variables for those who have not yet initiated marijuana use. Note that if alcohol initiation occurs prior to time t, but before marijuana initiation, then the ratio is 1 because both the numerator and denominator predicted probabilities are 1 (i.e. the predicted probability of initiating alcohol use after the initiation of alcohol use is 1 for any values of the confounders or baseline variables). The weight at time t, W_t, is the product of the ratios up to time t (i = 1,…,t). The form of the weights can be seen in Equation 2. Here Alc_t is the predictor (alcohol initiation), Sex and Race are the baseline variables, $Conf_t$ is a vector of the confounders, and Mj_t is the response (marijuana initiation). Additionally, the "over-bars" above Alc_{i-1} and Mj_{i-1} signal that the probability is conditional on the complete past predictor and response patterns. We detail the logistic regression models that are used to create the weights in the Appendix.

$$W_t = \prod_{i=1}^{t} \frac{P[Alc_i \mid \overline{Alc}_{i-1}, Sex, Race, \overline{Mj}_{i-1}]}{P[Alc_i \mid \overline{Alc}_{i-1}, \overline{Conf}_i, Sex, Race, \overline{Mj}_{i-1}]} \qquad (2)$$

Since we are interested in effects on marijuana initiation timing, we also use discrete time survival analysis, that is, a logistic regression, for the response regression model as well. After obtaining the weights, a logistic regression using these weights with marijuana initiation timing as the response and alcohol initiation timing as the predictor, is performed. We call this the weighted response regression model.

We recognize that many substantive researchers who collect their own data are justifiably unhappy with any method that appears to alter the data. It is essential to realize that this weighting method does not utilize or alter the response of marijuana initiation timing, nor does

the weighting method alter the predictor-response relationship of any particular individual. That is, at the individual level, the predictor-response relationship is unaltered. The weighting method changes the composition of participants so that certain predictor-response pairs have a higher weight and others have a lower weight. This is done in order to equalize the composition of types of participants between the various predictor levels. As referred to earlier, in an experimental study, we randomize the participants to predictor levels so as to achieve equalization of the composition of types of participants between predictor levels.

AN EXAMPLE

Data from the Lexington Longitudinal Study, a longitudinal study of etiological pathways to substance use, deviant behavior, and psychopathology, are used here to illustrate the methodology.

Participants

The participants are a subsample of a cohort (n = 481) who were part of a 10-12 year longitudinal examination of etiological pathways to substance use, deviant behavior, and psychopathology. Participants were assessed via written questionnaires beginning in the 1987-1988 school year prior to starting the 6th grade (see Clayton, Cattarello, & Johnstone, 1996 for a detailed description of the initial recruitment and assessment procedures). Follow-up data were then collected from participants over a five-year period after each school year from 6th through 10th grade. Individuals in the current study completed questionnaires on at least three of these five occasions (post 6th grade, 7th or 8th grade, and 9th or 10th grade), a mailed survey administered at age 19-20 (M = 20.1), and an extensive laboratory protocol completed at age 20-21 (M = 21.0). Data for the current study were taken from the early school-based assessments and the most recent laboratory assessment when participants were 20 to 21 years old.

Due to resource limitations, only 481 individuals out of 1,431 were assessed in the intensive phase of the above study. The 481 individuals who participated in the laboratory protocol were selected from the larger sample that had completed at least three of the school questionnaires and the mailed survey at age 20. Individuals were randomly selected for the laboratory protocol with some oversampling of heavy users in order to compensate for previous sample attrition.

Here we use 210 of the 481 individuals assessed in the intensive phase. There are 121 female and 41 non-white participants, and 5,729 person-periods. This data is a convenience sample and may not be representative of any subset of adolescents.

Confounders

There are two groups of possible confounders: time-varying and non-time-varying. Non-time-varying confounders are measured once and maintain the same value for the duration of the study. Time-varying confounders are measured at different time periods during the study and their values change throughout the study. The following are the confounders ($Conf_t$), and their related measures, that are used in forming the weights for our response regression model.

Time-Varying

Peer Pressure Resistance. This 7-item scale was designed to measure the ability to resist negative peer pressure (e.g., “If your best friend was skipping school would you skip too?” and “If a friend asks you to smoke marijuana with them, would you do it?”). Responses were made on a five-point continuum ranging from "definitely not" to "definitely would." For this variable, higher scores indicate a stronger ability to resist or ignore peer pressure.

Other Drug Use. Other drug use is a measure of the time period in which the initiation of any drug other than marijuana, alcohol, and tobacco such as cocaine, crack, inhalants, psychedelics, amphetamines, barbiturates, tranquilizers, heroin, or other analgesics occurs.

Non-Time-Varying

Sensation Seeking. Sensation Seeking was measured using 18 items that were based on Zuckerman's (1994) 40-item sensation seeking scales. Based on factor analyses, the four to six items most strongly reflective of each of the four dimensions of the scale (i.e., Thrill and Adventure Seeking, Boredom Susceptibility, Experience Seeking, and Disinhibition) were included. In order to promote understanding among the young participants, these questions were adapted from the original forced choice format to one in which the participants indicated their level of agreement with a single statement (e.g., "I like to jump off high diving boards"). Responses ranged from (1) indicating strong disagreement to (5) indicating strong agreement. To examine the comparability of the original scale and our adaptation, we administered both versions to a sample of 85 young adults; the total scale for the two versions correlated as high as the reliabilities of each scale would allow ($r = .85$), indicating equivalence between the two measures. For the present research, scores are averaged across administrations to yield one overall Sensation Seeking score[6].

IQ. IQ was assessed using two subtests from the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). Scores on the Vocabulary subtest served as indicators of Verbal IQ, whereas scores on the Block Design subtest served as indicators of Performance IQ. Previous research has shown each of these subtests is most strongly correlated with its respective IQ factor; correlations equal .89 for Vocabulary and Verbal IQ, and .81 for Block Design and Performance IQ (Wechsler, 1981).

Heart rate. Resting heart rate was obtained during the extensive laboratory assessment.

Heart rate is believed to be related to both the predictor and response (i.e. a confounder) because, although resting heart rate has not been studied often in substance use, it is one of the most consistent correlates of antisocial behavior (Raine, 1993). There are several interpretations to this relation. First, some argue that lower resting heart rate is an index of fearlessness, which would predispose individuals to any number of dangerous or harmful activities. A second related interpretation is that low resting heart rate reflects autonomic underarousal, which might facilitate stimulation-seeking behavior. Thus, heart rate is likely a confounder of the relationship between alcohol and marijuana initiation. Further, a subject's IQ measurements, desire to seek new or dangerous sensations, ability to resist peer pressure, and resistance to other types of substances have been shown to be related to substance abuse generally. For instance, we expect that these variables would all affect the subject's social life, susceptibility to situations where alcohol is present, and the subsequent ability, or rather inability, to delay the initiation of alcohol. Furthermore, these variables can be expected to be related to a subject's inability to delay the initiation of marijuana in a similar manner. Hence, since these variables are correlated with both the predictor and response they are also confounders.

In summary, the confounders used in the weight formation are:

Non Time-Varying.

- Heart Rate (Hr)
- Performance IQ (Piq)
- Verbal IQ (Viq)
- Average Sensation Seeking Scale Measurement (Asss)

Time –Varying.

- Peer Pressure Resistance (Peerpr-F4Peerpr)
- Other drug use ($Odga_t$)

Additionally, when the goal is the estimation of the total effect of alcohol initiation, the timing of cigarette initiation and conduct disorder initiation are included as possible time-varying confounders. Similarly, when the goal is the estimation of the total effect of cigarette initiation, the timing of alcohol initiation and conduct disorder initiation are included as possible time-varying confounders, and when the goal is the estimation of the total effect of conduct disorder initiation, the timing of alcohol initiation and cigarette initiation are included as possible time-varying confounders. Conduct disorder is defined as the presence of two or more different conduct problems in a single time period. Participants were asked about the presence of fourteen specific conduct problems from the following four general areas: aggression against people or animals, destruction of property, deceitfulness or theft, and serious violations of rules.

Analysis

The goal is to assess the total effect of each of three different predictors on marijuana use initiation. The response is the timing of marijuana use initiation (Mj_t). The three predictors are: alcohol use initiation (Alc_t), cigarette-smoking initiation (Cig_t), and conduct disorder initiation (Cd_t). Associated with the three predictors are three questions:

1. Does delaying alcohol use initiation lead to a delay in the initiation of marijuana use?
2. Does delaying cigarette use initiation lead to a delay in the initiation of marijuana use?
3. Does delaying conduct disorder initiation lead to a delay in the initiation of marijuana use?

In all of the cases our goal is the estimation of the total effect of a predictor on the response, marijuana use initiation.

Time is measured every third of a school year (fall, winter, and summer) beginning in the 6^{th} grade for a total of thirty intervals. The variables that are time-varying are indexed by a subscript "t". The predictor and response take on the value of zero prior to initiation, and take on the value of one in the first period after initiation and remains one thereafter.

Descriptive statistics for the non-time-varying variables are displayed in Table 4. Descriptive statistics for the time-varying variable peer pressure resistance, measured at the times denoted, are displayed in Table 5. Peer pressure resistance was measured six times over the course of the study and if a participant had a missing measurement the last available measurement was carried forward to the subsequent time.

The prevalence rates of cigarette, alcohol, marijuana, other drug use, and conduct disorder are displayed in Figure 5. In this figure the lines represent the percentage of participants at each time period that have already or are currently exhibiting the behavior. A timeline of the variables is illustrated in Table 6, where sex and race are baseline variables, denoted by $X_{0,}$ and $Conf_t$ denotes the confounders.

For illustrative purposes, we show that the confounders listed above are indeed common correlates of both marijuana initiation timing and alcohol initiation timing. Similar demonstrations can be done with the alternate predictors, timing of cigarette use initiation and conduct disorder initiation. First, we verify that there is a correlation between $Conf_t$ and the predictor (relationship "a" in Figure 1 with Conf in place of peer pressure resistance) and a correlation between $Conf_t$ and the response (relationship "c" in Figure 1 with Conf in place of peer pressure resistance). Note that all of the time-varying variables used in the models, other than marijuana initiation, (i.e. alcohol initiation, cigarette initiation, conduct disorder initiation,

etc.) are lagged by one time period. This is to ensure that we find the effect of the past predictor pattern on the current response pattern.

Correlation Between $Conf_t$ and Timing of Alcohol Initiation

To demonstrate the correlation, consider a logistic regression where $Conf_t$ is a covariate and Alc_t is the response. The covariates in the vector $Conf_t$ are $Ppress_t$, $Odga_t$, Hr, Piq, Viq, Asss, Cig_t, Cd_t. The model used is

$$\log(\frac{p_t}{1-p_t}) = \alpha' Schyr + \beta_1 * Sex + \beta_2 * Race + \theta'' Conf_t ,$$

where p_t is the conditional probability of alcohol use at time t, among those with no prior alcohol or marijuana use and with the specified sex, race, and $Conf_t$. Schyr is a vector of the dummy variables coding the participant's school year Schyr = (Schyr3=6th Grade, …, Schyr12=After High School); each School year, j, is 1 if t is an interval in school year j, and zero otherwise. Using Proc Logistic in SAS (see Allison, 1995), we find (not shown here) that the log-likelihood with the vector $Conf_t$ in the model is 968.318 and the log-likelihood with $Conf_t$ not in the model is 1086.803. This is a difference of 118.485, $p < 0.01$. Thus the variables in the confounder vector are time-varying correlates of the timing of the predictor, alcohol use initiation.

Correlation Between $Conf_t$ and Timing of Marijuana Initiation

Next, in order to establish that $Conf_t$ is a correlate of the timing of marijuana use initiation, consider a logistic regression of Mj_t on the confounders, $Conf_t$, and Alc_t. The model is similar to the one used above, but now p_t is the probability of marijuana use initiation at time t for those who have not yet initiated marijuana, and Alc_t is included as a covariate. The log-likelihood with the vector $Conf_t$ in the model is 896.856 and the log-likelihood with $Conf_t$ not in the model is 954.246. This is a difference of 57.39, $p< 0.01$. Thus, the confounders are time-varying correlates of the timing of the response, marijuana use initiation.

These results indicate that our confounder vector is indeed a common time-varying correlate of both the timing of marijuana use initiation and the timing of alcohol use initiation. We should, thus, be concerned with confounding. Similar results may be obtained when the predictor is Cig_t or Cd_t.

Response Regression Models

For each pair of response and predictor, we consider three different models:

I. Omitting confounders from the response regression model (naïve model).

II. Including confounders as covariates in the response regression model (standard model).

III. Adjusting for confounding with weights and using a weighted response regression model (weighted model).

All response regression models include sex, race, the predictor variable, and an intercept term for each school year and the standard model (the traditional method) additionally includes all measured confounders as covariates. In a particular response regression model, the two remaining predictors are treated as potential confounders. For example, with the response and predictor pair of Mj_t and Alc_t, Cd_t and Cig_t are treated as potential confounders.

Models

We will first examine the predictor Alc_t. The models are similar when we consider Cig_t or Cd_t as the predictor. We are interested in p_t, the probability of marijuana use at time t among those without previous marijuana use. The naïve model is:

$$\log(\frac{p_t}{1-p_t}) = \alpha_t Schyr + \beta_1 * Sex + \beta_2 * Race + \beta_3 Alc_t$$

and the intercept term $\alpha_t Schyr$ represents:

$$\alpha_t Schyr = \alpha_1 * Schyr_1 + \alpha_2 * Schyr_2 + \cdots + \alpha_t * Schyr_t .$$

In the standard model, the model includes the confounders as well as the baseline variables:

$$\log(\frac{p_t}{1-p_t}) = \alpha_t Schyr + \beta_1 * Sex + \beta_2 * Race + \beta_3 Alc_t + \gamma_t' Conf_t ,$$

where the confounders are represented by:

$$Conf_t = [Ppress_t, Odga_t, Hr, Piq, Viq, Asss, Cig_t, Cd_t]' ,$$

and the 8 x 1 vector of the confounder regression coefficients is represented by γ_t. The weighted model is the same as that used in the naïve model, but is fit via weighted regression.

Results

Table 7 contains the estimated odds of marijuana use for the prior-initiators versus non-initiators of alcohol, among those without prior marijuana initiation. Tables 8 and 9 contain the estimated odds of marijuana use for prior-initiators versus non-initiators of cigarettes and conduct disorder, respectively, among those without prior marijuana initiation. Note that in Tables 7, 8, and 9 the coefficients for the intercepts and baseline covariates are omitted for simplicity. We use an $\alpha = 0.05$ level of significance for all analyses.

Discussion

Question 1. Does delaying alcohol initiation lead to a delay in the initiation of marijuana?

By examining Table 7 it is clear that, depending on the response regression model used, answers are different. The naïve model implies that the estimated odds of marijuana use is significant and that prior-initiators of alcohol are much more likely to initiate marijuana use than non-initiators (odds ratio=5.10, $p<0.0001$); the odds of initiating marijuana for prior alcohol-initiators is roughly five times higher than that for non-initiators of alcohol. However, the naïve

model is almost certainly biased because it does not control for confounders, such as peer pressure resistance. Examining the results from the standard model we see that the odds are also highly significant (odds ratio=2.28, p=0.0023). Yet, although it is the convention, the use of the standard model may produce bias due to the spurious correlations discussed earlier. Hence, consider the weighted model. The weighted model is not subject to the spurious correlations via paths "b" and "c" in Figure 3, but it does control the confounding. Comparing the results of the weighted model with the other models we see that in this instance, the naïve model appears to overestimate the total effect of alcohol initiation timing on marijuana initiation timing and the standard model appears to underestimate the total effect[7]. In the weighted model, among those without prior marijuana use, the odds of initiating marijuana for prior alcohol-initiators is roughly three and a third times higher than that for non-initiators of alcohol (odds ratio=3.36, $p<0.0001$).

When alcohol is the predictor, we have a significant alcohol coefficient with all three models, but we believe that the desired interpretation of the total effect of alcohol use on marijuana initiation is best obtained from the weighted model.

Question 2. Does delaying cigarette initiation lead to a delay in the initiation of marijuana?

This question can be answered, in a similar manner as the one above, by examining Table 8. Again it is clear that the different response regression models yield very different answers. The naïve model implies that, among those without prior marijuana use, the odds of initiating marijuana for prior cigarette initiators is roughly four times higher than that for non-initiators of cigarettes, and this estimate is highly significant (odds ratio=4.16, $p<0.0001$). Yet, when we examine the standard model we see that cigarette initiation is no longer a significant predictor,

and it implies that the odds estimate is much lower (odds ratio=1.50, p=0.1560). However, because of confounding and spurious correlation issues, we again believe that the weighted model yields less biased estimates. Examining the results from this weighted model implies that cigarette initiation is a significant predictor of marijuana initiation (odds ratio=2.27, p=0.0008). The odds estimate, at roughly two and three quarter times higher for previous initiators of cigarettes in this model, appears to be overestimated in the naïve model and underestimated in the standard model.

Question 3. Does delaying the initiation of conduct disorder lead to a delay in the initiation of marijuana?

The results presented in Table 9 also illustrate that the different response regression models can lead to different answers. The naïve model implies an odds of initiating marijuana for prior conduct disorder initiators roughly three and a half times higher than that for non-initiators of conduct disorder (odds ratio=3.51, $p<0.0001$). This is a highly significant result. Using the standard model however, conduct disorder is no longer a significant predictor (odds ratio=1.44, p=0.1203). In the weighted response regression model, conduct disorder is significant, yielding an odds estimate roughly two times higher for prior conduct disorder initiators (odds ratio=2.06, p=0.0054).

In sum, a properly weighted model may result in coefficients and p-values of different magnitude when compared to the standard or naïve models. It is important to note that the method of using sample weights is not meant to increase significance, but rather to construct an unbiased estimator of the desired effect: the total effect of delaying the timing of a predictor on the timing of response initiation. Therefore, the significance of a coefficient may change when examining the weighted and unweighted coefficients. Note that across the predictors (Tables 7,

8, and 9) there is no distinguishable pattern among the p-values as to the effect of the weighting method.

SUMMARY

In this paper we are interested in assessing the consequences of delaying time-varying predictors on the timing of the response. Ideally we would answer this causal question via a randomized experiment; however, frequently, as is the case here, this is not possible. Recognizing that in absence of randomization there may be alternate explanations for the observed effects, we seek to control for these alternate explanations (i.e., confounders). As we have discussed, the most common method is to include the confounders as covariates in the regression of the response on the predictor. However, as discussed here, this method will not necessarily result in the desired total effect estimates when the confounders are time-varying. Instead we consider a weighted model. Theoretical results may be found in Robins et al. (2000) and an evaluation of this method is given by Barber et al (2002). Barber et al. (2002), demonstrated, both in simulation and via path analysis, that both the naïve model and the standard model can lead to biased estimates of the total effect of the predictor. These biases were absent in the weighed model. Furthermore, Barber et al. (2002) evaluated the robustness of the weighted model to the presence of unmeasured direct confounders. They found that even if we adjust for only a fraction of the confounders we decrease the bias in the model relative to the other methods. The strength of the relationships of pathways “a”, “b”, and “c” in Figure 1 influences the differences in results between the response regression models.

Both a drawback and an advantage of the weighting method is that, to use the weighting method, scientists must clearly specify the research question and the hypothesis, as the weights will change depending on the predictor. As always, we need to think carefully and brainstorm

about possible unmeasured confounders that may have a large influence on both the predictor and response. In particular, scientists who collect their own data have the opportunity to work toward including measurements of good surrogates for the confounders. Then the use of the weighting method allows one to appropriately control for the measured confounders.

REFERENCES

Allison, P. D. (1995). *Survival analysis using the SAS system: a practical guide*. Cary, NC: SAS Institute, Inc.

Barber, J. S., Murphy, S. A., & Verbitsky, N. (2002). Adjusting for time-varying confounding in survival analysis. Manuscript submitted for publication.

Bollen, K. A. (1989). *Structural equations with latent variables*. New York: John Wiley & Sons.

Bohrnstedt, G. W. & Knoke, D. (1982). *Statistics for social data analysis*. Itasca, IL: P. E. Peacock Publishers, Inc.

Clayton, R. R., Cattarello, A. M., & Johnstone, B. M. (1996). The effectiveness of drug abuse resistance education (project DARE): 5-year follow-up results. *Preventive Medicine*, *25*, 307-318.

Hernán, M., Brumback, B., Robins, J. M. (2000). Marginal structural models to estimate the causal effect of zidovudine on the survival of HIV-positive men. *Epidemiology*, *11*, 5, 561-570.

Hernán, M., Brumback, B., Robins, J. M. (2001). Marginal structural models to estimate the joint causal effect of nonrandomized treatments. *Journal of the American Statistical Association*, *96*, 454, 440-448.

Manski, C. F. (1995). *Identification problems in the social sciences*. Cambridge, MA: Harvard University Press.

Pearl, J. (1998). Graphs, causality, and structural equation models. *Sociological Methods and Research*, *27*, 226-284.

Raine, A. (1993). *The psychopathology of crime: Criminal behavior as a clinical disorder*. San Diego, CA: Academic Press.

Robins, J. M. (1986). A new approach to causal inference in mortality studies with sustained exposure periods – application to control of the healthy worker survivor effect. *Mathematical Modeling*, *7*, 1393-1512.

Robins, J. M. (1989). The analysis of randomized and nonrandomized AIDS treatment trials using a new approach to causal inference in longitudinal studies. In L. Sechrest, H. Freeman, & A. Mulley (Eds.), *Health Service Research Methodology: A Focus on AIDS* (pp. 113-159). Washington, DC: NCHSR, U.S. Public Health Service.

Robins, J. M. (1998). Marginal structural models. *1997 proceedings of the American Statistical Association, section on Bayesian statistical science* (pp. 1-10). Retrieved from: http://www.biostat.harvard.edu/~robins/research.html.

Robins, J. M. & Greenland, S. (1994). Adjusting for differential rates of PCP prophylaxis in high- versus low dose AZT treatment arms in an AIDS randomized trial. *Journal of the American Statistical Association*, *89*, 737-749.

Robins, J. M., Hernán, M. & Brumback, B. (2000). Marginal structural models and causal inference in epidemiology. *Epidemiology*, *11*, 5, 550-560.

Singer, J. D. & Willet, J. B. (1993). It's about time: using discrete-time survival analysis to study duration and the timing of events. *Journal of Education Statistics*, *18*, 155-195.

Wechsler, D. (1981). The psychometric tradition: Developing the Wechsler Adult Intelligence Scale. *Contemporary Educational Psychology*, *6*, 2, 82-85.

Winship, C. & Morgan, S. L. (1999). The estimation of causal effects from observational data. *Annual Review of Sociology*, *25*, 659-707.

Zuckerman, M. (1994). *Behavioral expressions and biosocial bases of sensation seeking*. Cambridge: Cambridge University Press.

APPENDIX: WEIGHT COMPUTATION

Complete details and explanation of generic SAS programming code that can be used for the weight creation, naïve model, standard model, and weighted model are available at: http://methodology.psu.edu/pubs/tvpappen.htm. Also provided are two simulated datasets that allow for practice and analysis in conjunction with a review of the SAS code.

At each measured time point, t, where the subject is at risk for response initiation a weight component is created. Each weight component is the ratio of two predicted probabilities. The numerator is the predicted probability of the subject's observed predictor initiation or non-initiation in period t, for those still at risk of response initiation, given past predictor initiation status (i.e. alcohol initiation or non-initiation) and baseline variables (i.e. sex and race). The denominator is the predicted probability of the subject's observed predictor initiation or non-initiation in period t, for those still at risk of response initiation, given past predictor initiation status, baseline variables, and confounders (i.e. common time-varying correlates of both the timing of a predictor and the timing of a response). Thus the numerator and denominator models only differ in that the confounders are present in the denominator predicted probability. The weight component at time t is 1 if t occurs after predictor initiation and before response initiation. Hence, the weight component does not need to be computed after the predictor or response initiation (whichever occurs first). Because the numerator and denominator probabilities are computed only for those still at risk of predictor and response initiation, conditioning on $\overline{\text{Alc}}_{i-1}$ and $\overline{\text{Mj}}_{i-1}$ (complete past predictor and response patterns, respectively), as is shown in Equation 2, is not necessary. Thus, the equations below do not include past Alc or Mj.

The model for the numerator regression model is:

$$\log(\frac{numpr_{ti}}{1-numpr_{ti}}) = \alpha_t Schyr + \beta_1 * Sex_i + \beta_2 * Race_i ,$$

While the model for the denominator regression model is:

$$\log(\frac{denpr_{ti}}{1-denpr_{ti}}) = \alpha_t Schyr + \beta_1 * Sex_i + \beta_2 * Race_i + \theta * Conf_{ti} .$$

Thus, the weight component for subject i before alcohol initiation is:

$$\frac{1-numpr_{ti}}{1-denpr_{ti}},$$

and the weight component for subject i at alcohol initiation is:

$$\frac{numpr_{ti}}{denpr_{ti}}.$$

The weight at time t, W_t, is the product of these weight components up to time t (i = 1,…, t). If at time t–1 subject i has yet to initiate alcohol use then the weight at time t-1 is:

$$W_{t-1} = \left(\frac{1-numpr_i}{1-denpr_i}\right)_{t-1} \cdots \left(\frac{1-numpr_i}{1-denpr_i}\right)_1 .$$

If at time t subject i initiates alcohol use then the form of the weight at time t is:

$$W_t = \left(\frac{numpr_i}{denpr_i}\right)_t \left(\frac{1-numpr_i}{1-denpr_i}\right)_{t-1} \cdots \left(\frac{1-numpr_i}{1-denpr_i}\right)_1 .$$

Here, remember that alcohol use and the confounders are lagged by one time period (as discussed earlier, see text). The weight W_s for all times, s larger than t, remains equal to W_t as each weight component is now equal to 1. Each subject has a weight for each time point until either the subject initiates the response or the study ends.

FOOTNOTES

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[5]The total effect of alcohol use initiation is represented by all paths following the directions of the arrows from Alc_1 and Alc_2 to Mj_2 and Mj_3.

[6]Given that Sensation Seeking is conceived as a relatively stable personality trait (Zuckerman, 1994), we took the average score across assessments. Empirically, Sensation Seeking is quite stable; in the larger sample from which these data are drawn, the one-year stabilities for Sensation Seeking approach the maximum correlation possible given the reliabilities of the scales (average 1-yr stability = .70).

[7]The standard model is used both to control for confounding and to also estimate the direct effect rather than total effect of the predictor (Bollen, 1989, pgs. 36-39), thus even if there were no confounding the standard model may produce a biased estimate of the total effect.

Table 1. Original frequencies – alcohol initiation by peer pressure resistance

	Alcohol Initiation Status		
	Non-Initiator	Initiator	Total
High Peer Pressure Resistance	40	10	50
Low Peer Pressure Resistance	30	30	60
Total	70	40	110

Table 2. Ideal frequencies – alcohol initiation by peer pressure resistance

	Alcohol Initiation Status		
	Non-Initiator	Initiator	Total
High Peer Pressure Resistance	25	25	50
Low Peer Pressure Resistance	30	30	60
Total	55	55	110

Table 3. Weighted frequencies – alcohol initiation by peer pressure resistance

	Alcohol Initiation Status		
	Non-Initiator	Initiator	Total
High Peer Pressure Resistance	50	50	100
Low Peer Pressure Resistance	60	60	120
Total	110	110	220

Table 4. Descriptive statistics of non-time-varying variables

Variable	N	Freq.	Percent	Mean	St. Dev.	Min.	Max.
Sex	210						
Male		89	42.38				
Female		121	57.62				
Race	210						
White		169	80.48				
Non-White		41	19.52				
Heart Rate	210			70.324	11.849	48.00	111.00
Performance IQ	210			32.829	10.154	10.00	50.00
Verbal IQ	210			42.395	12.593	11.00	70.00
Ave. Sens. Seeking	210			50.447	9.397	24.00	78.20

Table 5. Descriptive statistics of time-varying variables

Variable	N	Freq.	Percent	Mean	St. Dev.	Min.	Max.
Peer Pressure Resist.							
Pre-test	210			40.161	6.517	9.00	45.00
Post-test	210			40.881	5.633	13.00	45.00
Follow-up 1	210			38.270	7.256	9.00	45.00
Follow-up 2	210			35.801	8.618	9.00	45.00
Follow-up 3	210			34.224	9.424	9.00	45.00
Follow-up 4	210			32.532	9.435	9.00	45.00

Table 6. Temporal listing of confounders, alcohol, and marijuana

X_o	$Conf_1$	Alc_1	Mj_2	$Conf_2$	Alc_2	Mj_3	.	.	.	$Conf_{35}$	Alc_{35}	Mj_{36}
Sex	$Ppress_1$	Alc_1	Mj_2	$Ppress_2$	Alc_2	Mj_3	.	.	.	$Ppress_{35}$	Alc_{35}	Mj_{36}
Race	Cd_1			Cd_2						Cd_{35}		
	Cig_1			Cig_2						Cig_{35}		
	$Odga_1$			$Odga_2$						$Odga_{35}$		
	Piq											
	Avess											
	Viq											
	Hr											

Note. Ppress = peer pressure resistance; Cd = conduct disorder initiation; Cig = cigarette initiation; Odga = other drug use initiation; Piq = performance IQ; Viq = verbal IQ; Hr = heart rate; Alc = alcohol initiation; Mj = marijuana initiation.

Table 7. Response regression models with alcohol as the predictor[a]

	Naïve[b]	Standard	Weighted[c]
Predictor:			
Alcohol	1.6298***	0.8238**	1.2111***
Odds	5.10	2.28	3.36
	(<0.0001)	(0.0023)	(<0.0001)
Time-Varying Confounders:			
Conduct Disorder		0.3628	
		(0.1203)	
Cigarettes		0.4085	
		(0.1560)	
Other Drug Use		1.2848**	
		(0.0024)	
Peer Pressure Res.		-0.0470***	
		(0.0009)	
Non-Time-Varying Confounders:			
Heart Rate		-0.0118	
		(0.1910)	
Verbal IQ		-0.0265**	
		(0.0042)	
Performance IQ		-0.0117	
		(0.2926)	
Ave. Sen. Seeking		0.0191	
		(0.1404)	

[a]Coefficients for intercepts and baseline variables are omitted.

bThese models do not include confounders by definition, see text.

[c]p<0.05, **p<0.01, ***p<0.001, one-tailed tests

Table 8. Response regression models with cigarettes as the predictor[a]

	Naïve[b]	Standard	Weighted[c]
Predictor:			
Cigarettes	1.4255***	0.4085	1.0185***
Odds	4.16	1.50	2.77
	(<0.0001)	(0.1560)	(0.0008)
Time-Varying Confounders:			
Conduct Disorder		0.3628	
		(0.1203)	
Alcohol		0.8238**	
		(0.0023)	
Other Drug Use		1.2848**	
		(0.0024)	
Peer Pressure Res.		-0.0470***	
		(0.0009)	
Non-Time-Varying Confounders:			
Heart Rate		-0.0118	
		(0.1910)	
Verbal IQ		-0.0265**	
		(0.0042)	
Performance IQ		-0.0117	
		(0.2926)	
Ave. Sen. Seeking		0.0191	
		(0.1404)	

[a]Coefficients for intercepts and baseline variables are omitted.

bThese models do not include confounders by definition, see text.

[c]p<0.05, **p<0.01, ***p<0.001, one-tailed tests

Table 9. Response regression models with conduct disorder as the predictor[a]

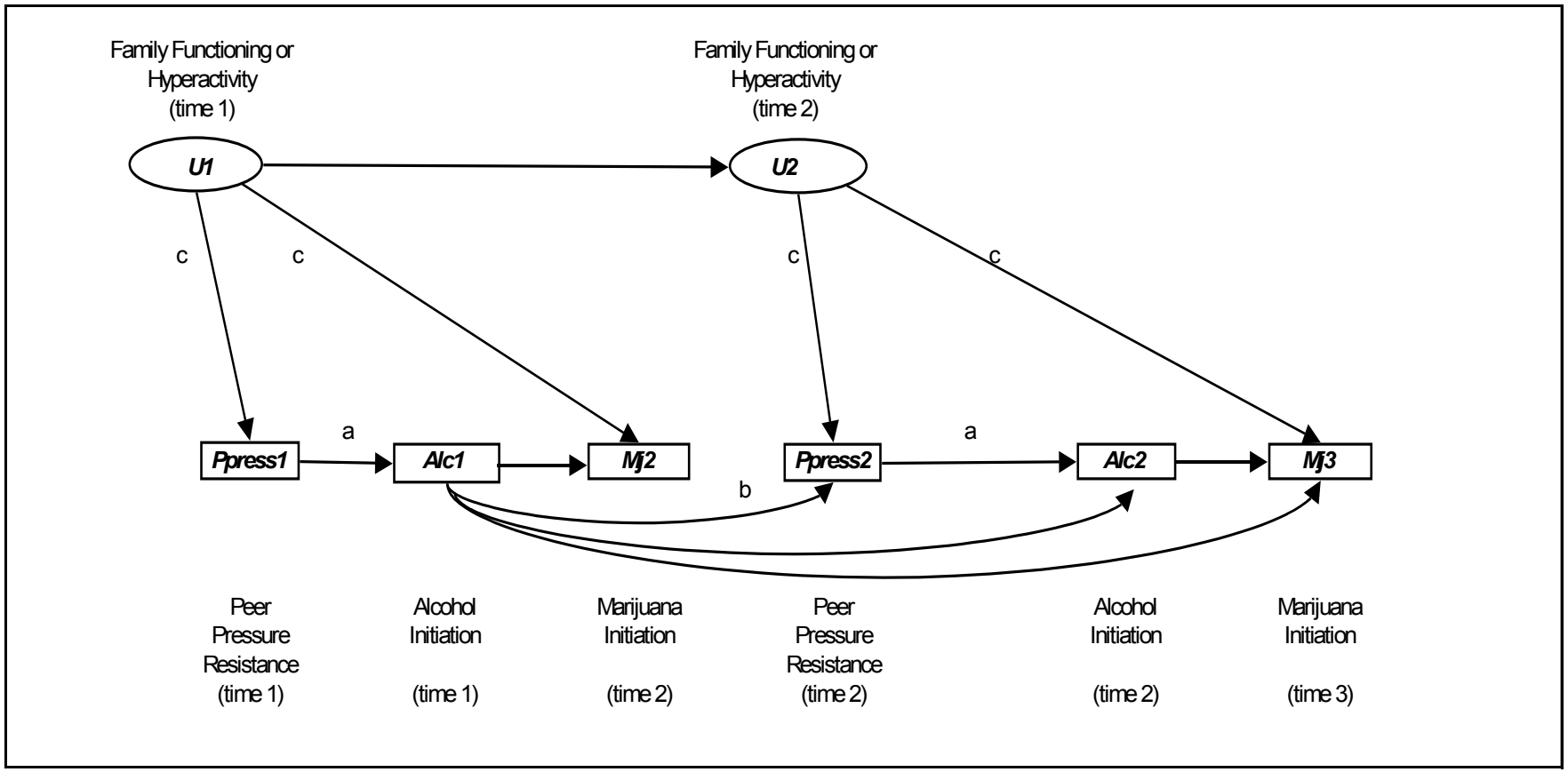
	Naïve[b]	Standard	Weighted[c]
Predictor:			
Conduct Disorder	1.2544***	0.3628	0.6565**
Odds	3.51	1.44	2.06
	(<0.0001)	(0.1203)	(0.0054)
Time-Varying Confounders:			
Cigarettes		0.4085	
		(0.1560)	
Alcohol		0.8238**	
		(0.0023)	
Other Drug Use		1.2848**	
		(0.0024)	
Peer Pressure Res.		-0.0470***	
		(0.0009)	
Non-Time-Varying Confounders:			
Heart Rate		-0.0118	
		(0.1910)	
Verbal IQ		-0.0265**	
		(0.0042)	
Performance IQ		-0.0117	
		(0.2926)	
Ave. Sen. Seeking		0.0191	
		(0.1404)	

[a]Coefficients for intercepts and baseline variables are omitted.

bThese models do not include confounders by definition, see text.

[c]p<0.05, **p<0.01, ***p<0.001, one-tailed tests

Figure 1. Some relationships among alcohol, peer pressure resistance, and marijuana



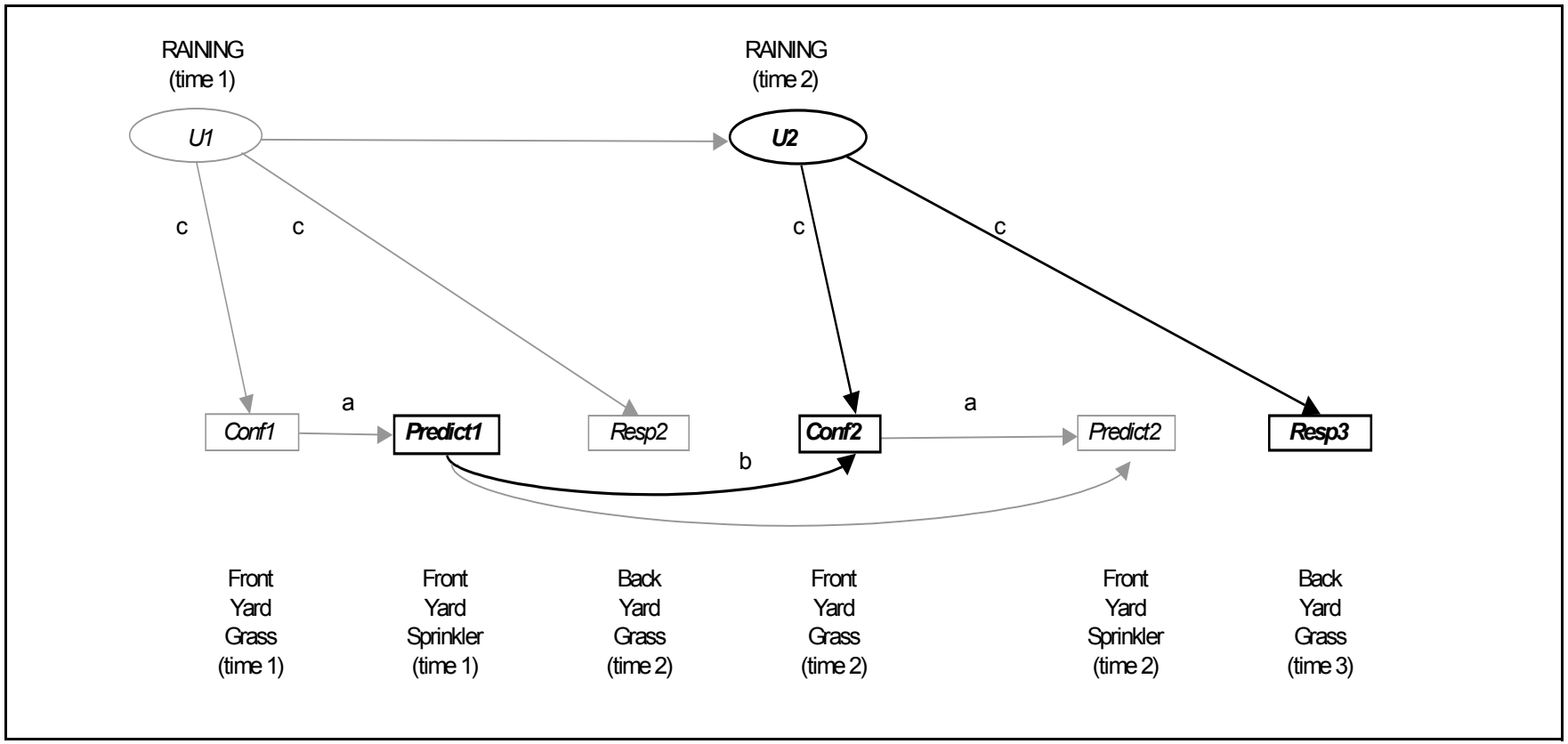
Alc = Predictor

Ppress = Confounder

Mj = Response

U = Unmeasured Predictor

Figure 2. Illustration of a spurious correlation between predictors and response in the sprinkler example.



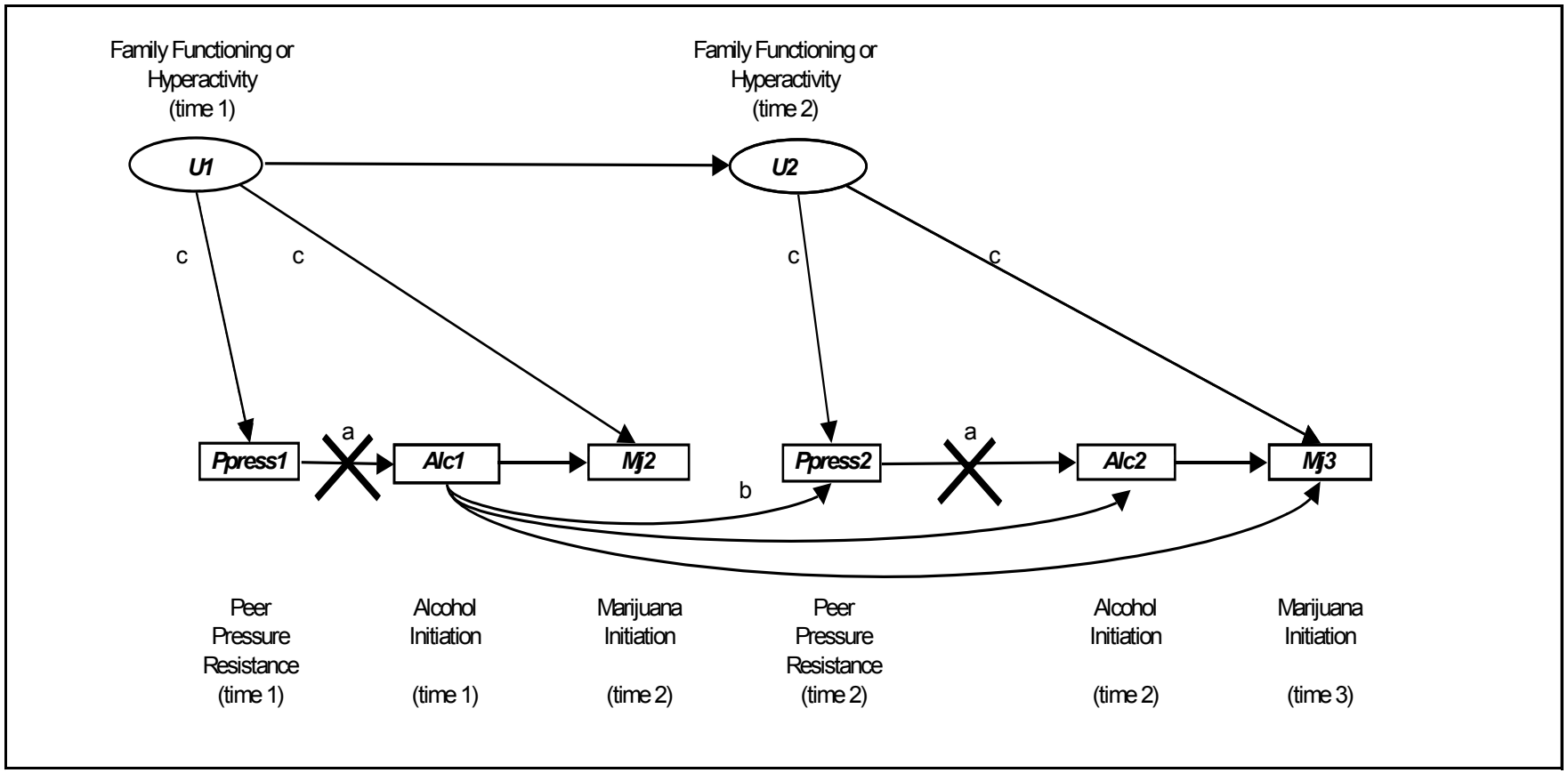
Predict = Predictor

Conf = Confounder

Resp = Response

U = Unmeasured Predictor

Figure 3. Elimination of relationship between alcohol and peer pressure resistance by using sample weights.



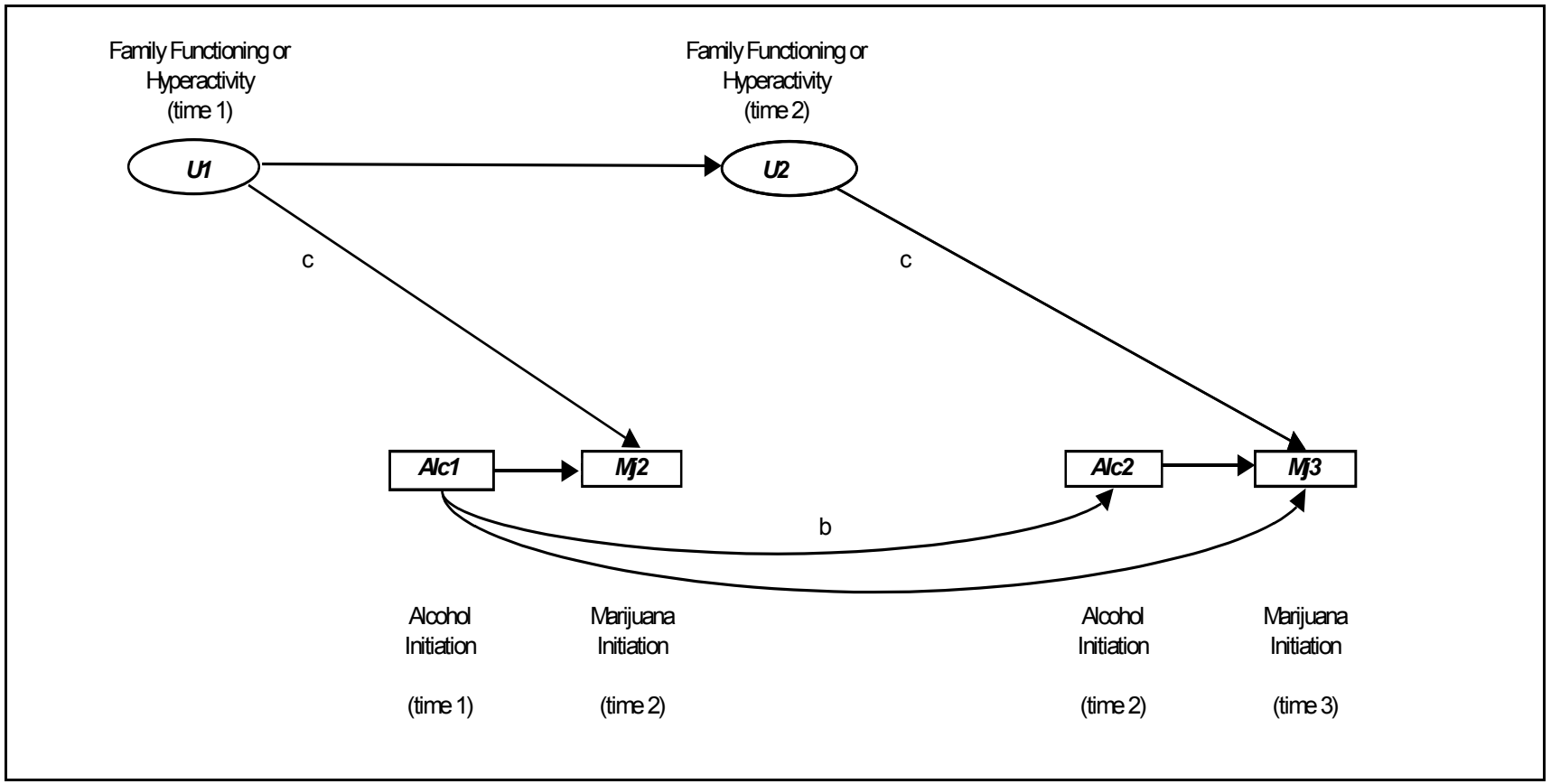
Alc = Predictor

Ppress = Confounder

Mj = Response

U = Unmeasured Predictor

Figure 4. Some relationships in a weighted sample when peer pressure resistance is omitted.



Alc = Predictor

Mj = Response

U = Unmeasured Predictor

Figure 5. Prevalence rates by time-varying behavior type.