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Revisiting the Table 2 Fallacy: A Motivating Example Examining Preeclampsia and Preterm Birth

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Abstract

Background—A "Table 2 Fallacy," as coined by Westreich and Greenland, reports multiple adjusted effect estimates from a single model. This practice, which remains common in published literature, can be problematic when different types of effect estimates are presented together in a single table. The purpose of this paper is to quantitatively illustrate this potential for misinterpretation with an example estimating the effects of preeclampsia on preterm birth (PTB).

Methods—We analysed a retrospective population-based cohort of 2,963,888 singleton births in California between 2007–2012. We performed a modified Poisson regression to calculate the total effect of preeclampsia on the risk of PTB, adjusting for previous PTB, pregnancy alcohol abuse, maternal education, and maternal socio-demographic factors (Model 1). In subsequent models we report the total effects of previous preterm birth, alcohol abuse, and education on the risk of PTB, comparing and contrasting the controlled direct effects, total effects, and confounded effect estimates resulting from Model 1.

Results—The effect estimate for previous PTB (a controlled direct effect in Model 1) increased 10% when estimated as a total effect. The risk ratio for alcohol abuse, biased due to an

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uncontrolled confounder in Model 1, was reduced by 23% when adjusted for drug abuse. The risk ratio for maternal education, solely a predictor of the outcome, was essentially unchanged.

Conclusions—Reporting multiple effect estimates from a single model may lead to misinterpretation and lack of reproducibility. This example highlights the need for careful consideration of the types of effects estimated in statistical models.

Keywords

perinatal epidemiology; preterm birth; measures of effect; Table 2 Fallacy

Introduction

In an effort to estimate the unbiased effects of a selected exposure (here referred to as the primary exposure) on an outcome of interest, researchers frequently construct multivariable statistical models. Typically, the covariates included in the model are hypothesized determinants of the primary exposure and outcome, and are selected to reduce confounding. Less often, covariates that only predict the outcome are included. At times, researchers are also interested in the effect of these covariates (here referred to as secondary exposures) as additional causal determinants of the outcome. When this occurs, they may report effect estimates for all covariates, derived from a single multivariable model, in one table. Typically, such results are displayed in Table 2 following the study population description in Table 1. However, when researchers report the effect estimates for both the primary exposure and secondary exposures estimated from the same statistical model, the results can be misleading and result in incorrect interpretation.

The practice of reporting multiple adjusted effect estimates from a single model was coined the “Table 2 Fallacy” by Westreich and Greenland in 2013.[1] This commentary, appearing in the American Journal of Epidemiology, used directed acyclic graphs (DAGs) and hypothetical examples to convey the typical fallacy in the interpretation of the primary and secondary adjusted effect estimates derived from one model. Understandably, researchers may not be familiar with causal inference language and DAG terminology, and thus the important points of caution when distinguishing between the types of effect estimates derived from a single model may not have been fully appreciated. Therefore, the purpose of this paper is to complement select points from the previous work by quantitatively illustrating this potential for misinterpretation with an example estimating the effect of preeclampsia on preterm birth. To assist readers with terminology and concepts that will be presented throughout the text, we provide a brief overview of causal modelling using DAGs (see supplemental material). Many thorough texts on the use of DAGs are also available.[2–4] Additionally, a brief introduction into direct and indirect effects, critical in understanding the Table 2 Fallacy, precedes the motivating example.

Total, direct and mediated effects

Per the hypothesized causal mechanism in Figure 1a, X affects Y directly and indirectly through M. The relationship between X and Y is confounded by Z.

If the effect of exposure X on a binary outcome Y, controlling for confounding by Z, as depicted in DAG in Figure 1a, were estimated using a log linear model in equation 1:

$$\log(P(Y = 1|X, Z)) = \beta_0 + \beta_1 X + \beta_2 Z \quad \text{(Eq. 1)}$$

the estimated coefficient for X ($\hat{\beta_1}$) would be interpreted as the conditional *total effect* of X on the log risk of Y at any given level Z.

The total effect of X on Y can be decomposed into the contributing causal components, i.e., direct effects, indirect effects, or both. *Direct effects* are the unmediated effects of the exposure on the outcome, or in Figure 1a, the causal effect of X on Y that is not mediated through M.[5,6] More specifically, when the mediator is held fixed at a given value in an attempt to estimate the direct effect, the resulting effects are termed the *controlled direct effects*.[7] *Indirect effects*, or mediated effects, are the part of the exposure effect mediated by other variables. In Figure 1a, X has an indirect effect on Y through the pathway mediated by M (the indirect path). Because M may modify the magnitude of the direct effect, the total effects cannot necessarily be decomposed into non-overlapping indirect and direct effects.[5,7]

Assuming no uncontrolled confounding of the mediator-outcome relationship, one is attempting to estimate the controlled direct effect of the exposure by conditioning on the mediator.

$$\log(P(Y = 1|X, M, Z)) = \beta_0 + \beta_1 X + \beta_2 M + \beta_3 Z \quad \text{(Eq. 2)}$$

In equation 2, the estimated coefficient for X ($\hat{\beta_1}$) would be interpreted as the conditional controlled direct effect of X on Y, or the effect of X on the log risk of Y when M is held fixed at a given level rendering it insensitive to the effects of X. The magnitude of the controlled direct effect may differ at each level of M, resulting in multiple controlled direct effect estimates dependent on the possible values of M.[5] Accordingly, it is not a recommended practice to quantify the controlled direct effects by conditioning on a mediator.[8] Further, if there are unmeasured common causes of the mediator and outcome, conditioning on the mediator will introduce collider stratification bias.[7] For example, in Figure 1B, adjusting for M to estimate the effect of X on Y would induce a collider stratification bias through X->M<-R->Y. Although beyond the scope of this paper, methodologic alternatives such as marginal structural models or g-computation to properly estimate direct and indirect effects are available.[4,8–10]

Table 2 Fallacy

Unless otherwise stated, it is assumed that researchers are estimating and presenting the total effect of the primary exposure of interest. In a table with secondary exposures of interest (some that were modelled as confounders of the primary exposure, others with effects only on the outcome) derived from the same statistical model as the primary exposure effect estimate, the total effect of the primary exposure and some secondary exposures, and the controlled direct effects of other secondary exposures are presented alongside each other.

This gives the reader the misimpression of parity across the effect estimates. There are several important problems in this approach. First, controlled direct effects and total effects are distinctly separate concepts and reporting a controlled direct effect that is easily mistaken for a total effect may lead to incorrect conclusions. Second, the primary exposure of interest may be a mediator of the secondary exposure-outcome relationship. As previously discussed, conditioning on a mediator could result in collider stratification bias and a spurious association of the secondary exposure if uncontrolled confounding remains between the mediator and outcome (Figure 1B). Third, any point estimates for secondary exposures may be biased if the relationship between the secondary exposure and outcome was not evaluated for possible additional confounding. Finally, the appropriate functional form of continuous secondary exposures may not be considered with rigor (e.g.-linear or spline terms).[1]

In order to illustrate some of these issues in the Table 2 Fallacy, we examine the risk of preeclampsia on preterm birth using a retrospective population based birth record cohort.

Motivating example

Preterm birth affects more than 1 in 10 babies born globally, and is the second leading cause of death in children under 5 years.[11] Over the past two decades, rates of preterm birth have been rising in developed countries,[12] increasingly resulting in investigations into the multifactorial causes. Preeclampsia is often investigated as a risk factor for preterm birth, typically resulting in strong relative risks between 2.5–4.5.[13–18] Preeclampsia is a pregnancy-specific disorder complicating 6–10% of all pregnancies in the United States.[19] It is diagnosed at or after 20 weeks of gestation, and defined by a combination of elevated blood pressure (diastolic blood pressure ≥90 mm Hg) and proteinuria (> 300 mg in 24 hours) or elevated blood pressure plus thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema or cerebral symptoms.[20] Preeclampsia has been associated with all three indications of preterm birth, i.e. provider initiated,[17,19] preterm premature rupture of the membranes,[21] and spontaneous preterm labor with intact membranes.[14,15,17]

Risk factors for preeclampsia include maternal obesity, older age, African-American race, low socioeconomic status, alcohol abuse, diabetes, and previous preterm birth.[16,22–25] Because these and other risk factors for preeclampsia are also associated with preterm birth, their potential for confounding the effects of preeclampsia on preterm birth must be considered. Given their association with preterm birth, authors may report effect estimates of these confounders alongside the effect estimate for preeclampsia,[13,18] and even more commonly when evaluating preeclampsia as one of multiple risk factors for preterm birth.[17,23,26–29]

Here, we provide a didactic example of an analysis to estimate the hypothesized effect of preeclampsia on preterm birth among singletons (Figure 2). In Model 1, we estimate the risk ratio for preeclampsia, adjusting for previous preterm birth, alcohol abuse, and maternal education as secondary factors. Previous preterm birth and alcohol abuse are included as potential confounders, and maternal education is included solely as a predictor of preterm birth. This and all subsequent models are further adjusted for potential confounding of maternal characteristics (pre-pregnancy body mass index (BMI), race, age, and smoking).

From Model 1, we present the mutually adjusted estimates of preeclampsia, previous preterm birth, alcohol abuse, and maternal education, illustrating the Table 2 Fallacy. In Model 2, we provide an estimate of previous preterm birth adjusted only for confounding by maternal characteristics to estimate the total effects of previous preterm birth. This estimate is then contrasted with the controlled direct effect estimate for previous preterm birth presented in Model 1. In Models 3, we estimate a biased total effect of alcohol abuse on preterm birth (failing to control for confounding by drug abuse), and then the total effect of alcohol abuse on preterm birth, adjusted for drug abuse. The estimates for alcohol abuse in Models 1 and 3 are contrasted to highlight both controlled direct effects versus total effects, as well as the need to evaluate confounding of the secondary exposures if they are to be reported from multivariable adjusted models. Finally, Model 4 estimates the total effect of maternal education to demonstrate that, given its hypothesized lack of association with preeclampsia, it should remain largely unchanged from Model 1.

Methods

Study population

Subjects in this retrospective cohort are women with a live-born singletons in the state of California between 2007–2012. Deliveries were identified from hospital discharge database maintained by the California Office of Statewide Health Planning and Development, which includes linked birth certificates, detailed information on maternal and infant characteristics, hospital discharge diagnoses and procedures recorded as early as 1 year before delivery.[30] Clinical characteristics were based on International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) four digit codes contained in the hospital discharge database.[21] Of the 3,160,268 live births, the study was restricted to singletons with gestations between 20–44 weeks of gestation (n=3,067,839), and then further restricted to mother-infant dyads with linked hospital discharge records (n=2,963,888). Methods and protocols for the study were approved by the Committee for the Protection of Human Subjects within the Health and Human Services Agency of the State of California.

Primary exposure

Preeclampsia diagnosis was obtained from administrative hospital discharge records, and was not accompanied by gestational week of diagnosis. Preeclampsia tends to occur late in pregnancy, and many women may have completed 37 weeks of gestation at the time of diagnosis, no longer at risk of preterm birth. This methodologic concern, which has been observed in other studies that our study seeks to replicate,[14,17,18,23,26] was not addressable in this didactic example. Implications are further discussed in the limitations section.

Covariates and outcome

Variables in analysis were operationalized as dichotomous variables of pre-pregnancy BMI (≥25 kg/m^2), race (African-American), alcohol abuse, drug abuse, smoking, education (<12 years), age (>34 years), previous preterm birth, and preterm birth. In a sensitivity analysis, preterm births were limited to those with an indication of spontaneous preterm birth (with intact membranes).

Statistical analyses

We estimated risk ratios and robust standard errors with log linear models and a Poisson distribution. Maternal characteristics (pre-pregnancy BMI, age, race and smoking) were included in all statistical models, but for simplicity, are denoted in the equations in the results section by “C”.

Results

Descriptive characteristics of the study population by preeclampsia status are displayed in Table 1.

Model 1

Model 1 demonstrates the typical Table 2 Fallacy. The primary exposure of interest (preeclampsia), secondary exposures, including confounders (previous preterm birth, alcohol abuse) and a predictor of the outcome (maternal education), were estimated from a single model and reported together (Table 2, Model 1).

$$\log(P(PTB = 1 | PE, PPTB, AA, EDU, C)) = \beta_0 + \beta_1 PE + \beta_2 PPTB + \beta_3 AA + \beta_4 EDU + \beta_5 C$$

(Eq. 3)

The effect estimate for preeclampsia ($\hat{\beta}_1$) is the conditional total causal effect; biasing paths through alcohol abuse and previous preterm birth were adjusted for, and no biasing paths (per the hypothesized causal mechanism in Figure 2) remained. The effect estimate is interpreted as the log risk of preterm birth at any given level of previous preterm birth and alcohol abuse comparing women with preeclampsia to women without preeclampsia.

Previous preterm birth ($\hat{\beta}_2$), presented alongside the conditional total effect estimate of preeclampsia, cannot be interpreted in the same manner as preeclampsia. Per the hypothesized DAG in Figure 2, previous preterm birth causes preterm birth directly and indirectly through preeclampsia. Given the inclusion of preeclampsia in the statistical model, we estimated a controlled direct effect of previous preterm birth. The interpretation is the effect of previous preterm birth on preterm birth when preeclampsia is held fixed at a given level, effectively blocking the mediated effects of previous preterm birth through preeclampsia.

The estimated coefficient for alcohol abuse ($\hat{\beta}_3$), also a controlled direct effect, is not a valid causal effect estimate, as the association between alcohol abuse and preterm birth is confounded by drug abuse. The estimated coefficient of alcohol abuse was not considered as an effect of primary interest and consequently confounders of the association between alcohol abuse and preterm birth were not considered. This, however, becomes problematic when the estimate of alcohol abuse is also reported as a secondary exposure of interest.

Finally, the estimated coefficient for maternal education ($\hat{\beta}_4$) is not mediated through any of the previous coefficients, and like preeclampsia, is a total effect.

Model 2

The second model (Table 2, Model 2) showed the difference between the estimate for previous preterm birth from Model 1 (the controlled direct effect not through preeclampsia) and the total effect estimated in a log-linear regression model adjusted only for maternal characteristics (Eq. 4).

$$\log(P(PTB = 1|PPTB, C)) = \beta_0 + \beta_1 PPTB + \beta_2 C \quad \text{(Eq. 4)}$$

To estimate the total effect of previous preterm birth on preterm birth, only the maternal characteristics, and not preeclampsia, confounded the relationship and needed to be included in the model. When modelled as a total effect, the risk ratio for previous preterm birth strengthened by 10%, an estimate not contained in initial confidence intervals. The weaker effect estimate of previous preterm birth in Model 1 was due to the apparent mediated effects of previous preterm birth by preeclampsia being blocked in the estimation of the controlled direct effect. It is important to note that, based on the simplistic hypothesized causal mechanism in Figure 2, previous preterm birth would only require adjustment for maternal characteristics to obtain an unbiased effect estimate. However, previous preterm birth may have been caused by previous preeclampsia, which may share common causes with the current occurrence of preeclampsia. As such, the previous preterm birth and current preterm birth association would remain a biased estimate by this uncontrolled confounding. This highlights the importance of fully considering the causal mechanisms for secondary estimates with the same rigor as primary estimates if they are also of interest to researchers.

Model 3

In Model 3 (Eq 5), we demonstrated the difference between the confounded controlled direct effect of alcohol abuse presented in Model 1 and the conditional total effect, additionally adjusting for drug abuse. When the total effects of alcohol abuse were estimated only by removing the preeclampsia covariate (not shown), a biased (over)estimate (RR 1.61, 95% CI 1.54, 1.69) was observed due to the failure to adjust for confounding from drug abuse. However, when drug abuse was subsequently added to the model for the total effect of alcohol abuse:

$$\log(P(PTB = 1|AA, DA, C)) = \beta_0 + \beta_1 AA + \beta_2 DA + \beta_3 C \quad \text{(Eq. 5)}$$

the estimated risk ratio for the total effect of alcohol abuse on preterm birth decreased by 23% as compared to the (biased) controlled direct effect estimate in Model 1. Importantly, the hypothesized causal mechanism in Figure 2, in which drug abuse is completely mediated through alcohol abuse in relation to the exposure, is a particularly strong (and perhaps unlikely) assumption.

Model 4

Finally, like the effect estimate for preeclampsia, the effect estimate for maternal education in Model 1 was a total effect. This was because maternal education was not a cause of preeclampsia, and thus was not anticipated to vary when modelled without preeclampsia (Eq 7).

$$\log(P(PTB = 1 | EDU, C)) = \beta_0 + \beta_1 EDU + \beta_2 C \quad \text{(Eq. 7)}$$

Indeed, when preeclampsia was removed from the model, the effect estimate for maternal education, as compared to Model 1, changed by less than 1% with overlapping confidence intervals.

Sensitivity analysis

There were 110,130 spontaneous preterm births in the dataset (19,146 (18.9%) among women with preeclampsia diagnosis, and 90,714 (3.2%) among women without a diagnosis of preeclampsia. When the outcome was limited to spontaneous preterm birth, results were largely unchanged with respect to the magnitude of changes in effect estimates between controlled direct effect and total effect estimates (Supplemental Table 1).

Comment

Main findings

The Table 2 Fallacy occurs when the effect estimates of secondary exposures are presented in the same manner as the primary exposure estimated from the same model. Specifically, the fallacy arises when these covariates are 1) causal determinants of the exposure (resulting in the estimation of controlled direct effects) or 2) cannot be validly estimated in the chosen model due to uncontrolled confounding. In this example, we presented a Table 2 that displayed the total effects of preeclampsia and maternal education, the controlled direct effect of previous preterm birth, and the biased controlled direct effect of alcohol abuse. This example highlights how these estimates, each uniquely a different concept, appear to the reader to be equivalent. We described a difference in risk ratios of 10% between the controlled direct effects and the total effects of previous preterm birth, which did not contain overlapping confidence intervals. Further, upon proper evaluation for confounding, the total effect estimate for alcohol abuse decreased by 23%. To be clear, in our example, previous preterm birth and alcohol abuse must be included in the model in order to estimate the unbiased effect of preeclampsia on preterm birth. The fallacy arose in two manners: 1) by presenting the secondary exposures (which were controlled direct effects) alongside the total effects of preeclampsia and maternal education, and 2) by failing to adjust for confounding of alcohol abuse by drug abuse, unnecessary when estimating preeclampsia but crucial when the reporting the effect estimate for preeclampsia. The difficulty in recognizing the differences in these types of estimates was exacerbated by including maternal education. The practice of including covariates solely as predictors of the outcome (with no causal relation with the exposure variable) has been referred to as ‘unnecessary adjustment’,[8] as they are not required to obtain a valid causal estimate of the primary exposure. Should a researcher

model and report their effect estimates, it is important to be aware of how they compare and contrast to the other estimates derived from the model. Finally, as previously noted, the causal positioning and functional form of variables used solely for confounding adjustment may not be evaluated with the same rigor as primary exposures of interest. The dichotomous effect estimate for alcohol abuse, potentially adequate for statistical control, would ideally be operationalized by timing, quantity and duration of exposure as a primary analysis. Ultimately, as our statistical packages progressively allow for ease of model creation, it is critical that researchers attempt to understand the nuances in the resulting parameter estimates.

Interpretation

Although modest, the changes we highlighted extend past an academic discussion and have practical implications. When designing intervention studies, researchers rely on published parameter estimates to hypothesize the effect sizes of intervention approaches. If researchers unwittingly make these estimates based on controlled direct effects instead of total effects, it minimizes their likelihood of demonstrating similar effects with the intervention. This issue extends to meta-analyses as well, as heterogeneity in the types of effect estimates may render summary estimates difficult to interpret. Additionally, the heterogeneity in types of effect measures may be culpable in perpetuating problems of scientific reproducibility. Table 2 fallacies often arise when researchers conduct an analysis with the intent to search for risk factors, agnostic to a primary exposure, and all effect estimates from the same multivariable model are reported. Given the complex and interdependent nature of the exposures studied for health outcomes, it is highly likely that some of the exposures will also cause other exposures, resulting in controlled direct effect estimates intermingling with total effect estimates. Finally, the degree of discrepancy between the controlled direct effect and total effect are influenced by the prevalence of the exposures and the strength of the direct and mediating paths. The larger the discrepancy between the estimates, the more problematic it becomes in practice to treat these estimates as equal. Although readers may disagree with the “significance” of the change in estimate that we have demonstrated, this is a didactic example and results could vary by much larger degrees depending on the exposures and outcomes studied. We encourage readers to investigate controlled direct effects and total effects in their own datasets in order to personalize the lessons to their own research.

Limitations

In this example highlighting the Table 2 Fallacy, we have demonstrated with empirical data the fallacy in interpreting multiple adjusted effect estimates from a single model. However, this exercise is not without limitations. The interpretation of our estimates are only as good as the underlying causal assumptions. Our hypothesized model made strong assumptions, including no uncontrolled confounding of the relation between previous preterm birth and preeclampsia. As with all observational data, further unmeasured confounding should be assumed. The authors would have liked to have more information on previous obstetric history, as well as more reliable information on obesity and alcohol and tobacco use, which is often underreported on hospital records. We would anticipate some attenuation of these estimates given these data. Readers should recognize that this remains a didactic example, and a more rigorous analysis may modify effect estimates. Also, a limitation of the data

source was that the timing of diagnoses was unavailable. Preeclampsia diagnosis often occurs after 37 weeks of gestation, resulting in a misclassification of exposure. We anticipate this would attenuate the effect estimate due to misclassification of exposure, but cannot guarantee the strength or direction of the potential bias.

Conclusions

Many diseases are multifactorial, and researchers are often interested in quantifying the effects of multiple exposures. When this is the intent, care should be taken to avoid presenting all effect estimates derived from a single model in the same manner. If researchers are interested in the effects of secondary exposures, new models should be constructed to ensure that those estimates are validly (i.e., no uncontrolled confounding) estimated total effects (i.e., excluding mediators). Further, bias assessment of the secondary exposure and outcome relation must be conducted, and, for non-binary secondary exposures, the appropriate form should be modelled. The use of DAGs with consideration to the direct and indirect paths and the desired type of effect would facilitate these efforts.

In summary, Westreich and Greenland[1] made an important contribution by describing the Table 2 Fallacy. We hope that this example complements that work and furthers the message about this topic.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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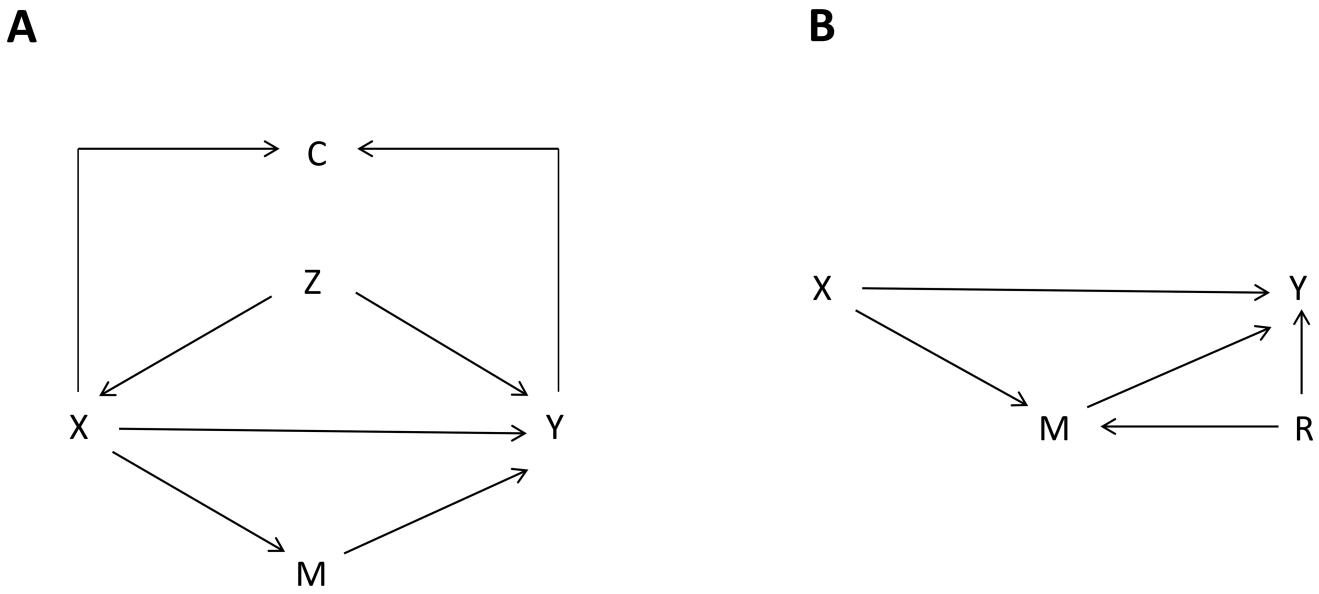

Figure 1.

Directed acyclic graph for (A) the effects of X on Y with mediation by M, confounding by Z and a collider (C); and (B) the direct and indirect effects of X on Y, with a confounder of the mediator-outcome relationship.

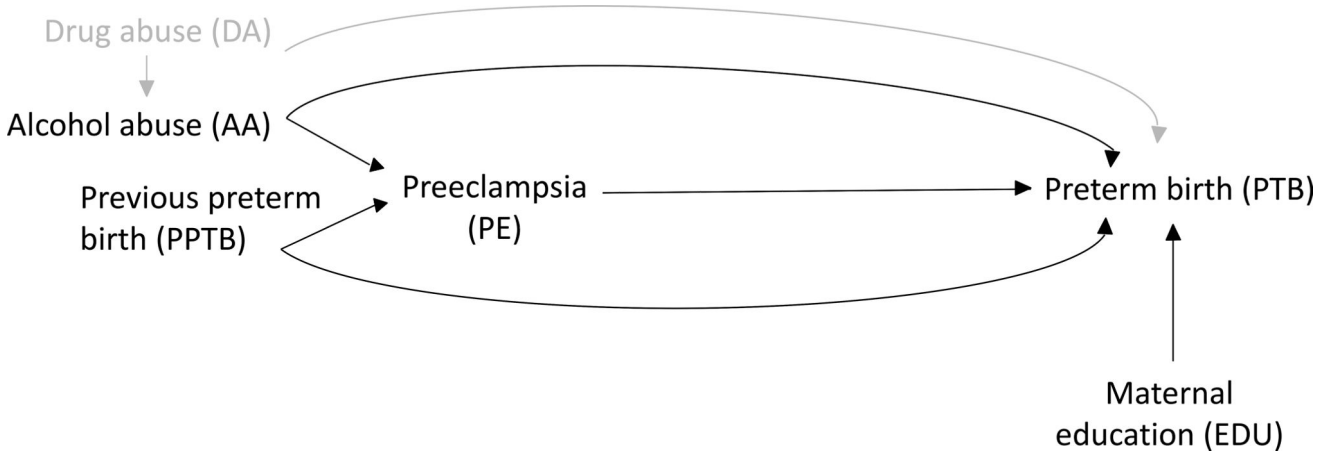

Figure 2.

Directed acyclic graph for the hypothesized effects of preeclampsia and preterm birth. Previous preterm birth and alcohol abuse in pregnancy confound this association. Drug abuse confounds the effects of alcohol abuse on preterm birth. Maternal education is a predictor of preterm birth. Maternal characteristics of pre-pregnancy body mass index, race, age, and smoking are assumed to confound all relationships between the exposure variables and the outcome variable, but not shown via individual paths for simplicity.

Table 1

Maternal characteristics of women with singleton, live births in the state of California (2007–2012)

	All births	Preeclampsia	
	n=2,963,888	Yes (n=102,545)	No (n=2,861,343)
	n (%)	n (%)	n (%)
Age (>34 years)	526,415 (17.8)	20,908 (20.4)	505,507 (17.7)
Race (African-American)	158,802 (5.4)	9,088 (8.9)	149,714 (5.2)
Pre-pregnancy overweight/obesity (≥25mg/kg^2)	1,267,392 (42.8)	58,007 (56.6)	1,209,385 (42.3)
Maternal smoking	134,682 (4.5)	5,490 (5.4)	129,192 (4.5)
Previous preterm birth	20,032 (0.7)	1,318 (1.3)	18,714 (0.7)
Alcohol abuse in pregnancy	13,214 (0.5)	672 (0.7)	12,542 (0.4)
Drug abuse in pregnancy	49,733 (1.7)	3,138 (3.0)	46,595 (1.6)
Education (<12 years)	708,807 (23.9)	24,500 (23.9)	684,307 (23.9)
Preterm birth (<37 weeks)	211,802 (7.2)	31,268 (30.5)	180,534 (6.3)

Table 2

Risk ratios for association between preeclampsia and preterm birth in a retrospective cohort of 3 million births between 2007–2012 in California

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
	RR, (95% CI)	**RR, (95% CI)**	**RR, (95% CI)**	**RR, (95% CI)**
Preeclampsia	4.65, (4.59. 4.70)			
Previous preterm birth	3.56, (3.47, 3.66)	3.91, (3.81, 4.00)		
Alcohol abuse	1.49, (1.42, 1.56)		1.15, (1.10, 1.22)	
Maternal education (<12 years)	1.12, (1.11, 1.14)			1.13, (1.12, 1.14)

All models adjusted for maternal age, race, pregnancy smoking and body mass index

[a]Total effect of preeclampsia and education, controlled direct effects of previous preterm birth and (biased) alcohol abuse

[b]Total effect of previous preterm birth

[c]Total effect of alcohol abuse, adjusted for drug abuse

[d]Total effect of maternal education

RR=risk ratio, CI=confidence interval