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Structure and Control of Healthy Worker Effects in Studies of Pregnancy Outcomes

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Much of the literature on the healthy worker effect focuses on studies of chronic disease and mortality; however, when studying pregnancy outcomes, these effects might differ because of the short, defined risk periods of most pregnancy outcomes. Three pregnancy-specific healthy worker effects have also been described, but the structure of these effects has not yet been investigated when occupational exposure, and not employment status, is the exposure of interest. We used directed acyclic graphs to examine healthy worker effects in studies of occupational exposures and pregnancy outcomes: the healthy hire effect, the healthy worker survivor effect, the desperation/privilege effect (differential workforce reentry after pregnancy), the reproductively unhealthy worker effect (women with live births leave the workforce, while women with nonlive births do not), and the insecure pregnancy effect (women with adverse pregnancy outcomes reduce their exposures in subsequent pregnancies). Given our assumptions, we conclude that the healthy hire effect, the desperation/privilege effect, the reproductively unhealthy worker effect, and the insecure pregnancy effect result from confounding that can be addressed if data on measured confounders, such as employment status, are available. The presence of the healthy worker survivor effect, however, varies by study design. Different types of healthy worker effects can be present in studies of occupational exposure and pregnancy outcomes, and many of them are easily addressed analytically.

bias (epidemiology); healthy worker effect; occupation; pregnancy

Abbreviation: DAG, directed acyclic graph.

Healthy worker effects are caused by differential entry into and exit from the workforce according to health status (1, 2). The healthy hire effect and the healthy worker survivor effect are the most common types described.

Differential entry into the workforce by health status causes the healthy hire effect (3). The healthiest people are the most likely to enter the workforce, meaning that workers have better health (i.e., lower disease risk), on average, than nonworkers (4). When comparing workers with populations that include nonworkers (e.g., the general population), disease risk appears lower among workers, potentially masking the effects of hazardous occupational exposures. The healthy hire effect is therefore confounding by factors related to employment and can be addressed by conditioning on employment. Two common strategies are to replace the nonworker comparison population with either an internal referent group or an external worker population with similar characteristics (2, 5).

Differential departure from the workforce causes healthy worker survivor bias (3). Workers in worse health (including those more susceptible to the outcome) leave the workforce at higher rates than workers in better health. The healthiest workers have the highest cumulative exposures because they “survived” longest in the workforce. The result is often a downward bias in the association between cumulative exposure and disease (2). The healthy worker survivor effect is caused by time-varying confounding affected by prior exposure or selection bias. These biases can be addressed through a combination of g-methods and study design (6).

Much of the literature on the healthy worker effect focuses on studies of chronic diseases or mortality and not on pregnancy outcomes, even though pregnancy outcomes are commonly studied in occupational epidemiology (7–9). For pregnancy outcomes, the etiologically relevant risk period (when the fetus or pregnant woman is at risk for the outcome) is typically short and defined. In contrast, chronic diseases and mortality often have a long risk period. Because healthy worker effects arise from differential entrances and exits from the workforce during the risk period, the length of the risk period could affect their occurrence.

Healthy worker effects specific to employment status and pregnancy outcomes have been previously described: the desperation/privilege effect, the reproductively unhealthy worker effect (also called the infertile worker effect or the unhealthy pregnant worker effect), and the insecure pregnancy effect (10–13). Although some of these effects cause biases in directions similar to those of the healthy hire and healthy worker effects, others cause biases in the opposite direction.

There is little guidance on how to address these biases analytically when occupational exposure (and not employment status) is the exposure of interest. Our aims were to illustrate the structures of healthy worker effects in studies of occupational exposures and pregnancy outcomes using directed acyclic graphs (DAGs) and to discuss how to account for resultant biases.

METHODS

We created DAGs for relationships between an occupational exposure (Exposure$_i$) and an adverse pregnancy outcome (Outcome$_i$) (14, 15). The subscript i denotes whether the variable's value was determined during the index pregnancy's risk period ($i = 1$), before the index pregnancy's risk period ($i = 0$), or during a prior pregnancy's risk period ($i = -1$). For ease of interpretation, we superimposed dashed vertical lines on the DAGs to demarcate these periods.

The risk period is the period in which the fetus is at risk for the outcome; its timing and length vary by outcome. For example, the risk period for cleft lip is the fifth through eighth weeks of gestation, but the risk period for preterm birth is commonly defined as the 20th–36th gestational weeks (16). In occupational epidemiology, the risk period is also defined by employment status. For example, if a woman starts work during her 25th week of pregnancy, she is at risk for an occupation-related preterm birth starting in the 25th week (instead of the 20th week).

We assumed a study in which the exposure of interest occurs during the index pregnancy's risk period (Exposure$_1$). Similar DAGs could be constructed for studies in which the exposure occurred before the risk period, studies in which cumulative exposures were of interest, or studies of reproductive outcomes without discrete risk periods, such as infertility. The conclusions, however, could differ from those we describe.

We assumed that all variables were measured without error and the DAGs included all relevant arrows. Unless otherwise indicated, our estimand of interest was the causal effect of Exposure$_1 = 1$ versus Exposure$_1 = 0$ on Outcome$_1$. Our goal was to draw inference about the exposed population (women who have the occupational exposure of interest), not the total or unexposed population; the presence of confounding can vary by choice of target population (17).

The original description of healthy worker effects in studies of pregnancy outcomes addressed these biases when employment status is the exposure of interest (10). We build on that work by evaluating how these biases apply to occupational exposures, another common exposure in reproductive occupational epidemiology (7–9). Because we focus on occupational exposures rather than employment, our results will differ from the original proposed methods for addressing these biases.

We used DAGitty, version 2.3, to identify minimally sufficient sets of variables for adjustment to estimate the total effect of the exposure on the outcome (18). Table 1 summarizes each healthy worker effect, its structure, and methods of analysis. These are discussed in detail below.

TYPES OF HEALTHY WORKER EFFECTS

Healthy hire effect

The healthy hire effect is caused by confounding of the exposure-disease association by variables related to employment at study entry (5). Although study entry is often the employment start date or the cohort enrollment date, we also considered the start of the pregnancy risk period to be another definition of "study entry."

Consider a study of occupational chemotherapy exposure (Exposure$_1$) and miscarriage (Outcome$_1$) in which investigators compare miscarriage prevalence between pregnant nurses working at a network of oncology clinics in Ohio (a proxy for exposure) and pregnant women in Ohio using administrative data from a health insurance provider. Figure 1 illustrates assumed relationships between variables. Job$_1$ indicates whether the woman was in the oncology clinic cohort at any time during the pregnancy risk period. U_0 and U_1 (unknown or unmeasured variables) affect Job$_1$ and Outcome$_1$.

Suppose that information on smoking status (U_i) is unavailable in the administrative data. Further suppose that women who smoke are less likely to be nurses and more likely to miscarry than nonsmokers. Even without a causal association between chemotherapy and miscarriage, the 2 variables would be associated because nurses are more likely to be exposed, less likely to smoke, and less likely to miscarry than the general population. In the DAG, this is represented by the open backdoor path (a noncausal association indicating confounding) Exposure$_1$ ← Job$_1$ ← U_0 → U_1 → Outcome$_1$ (Figure 1).

We can close this confounding path by conditioning on (controlling for) Job$_1$: using an internal reference group or an external reference population of similar workers. For the first strategy, we could restrict the study to oncology clinic nurses and compare miscarriage prevalence between nurses who do and do not administer chemotherapy. For the second, we could compare miscarriage prevalence between oncology clinic nurses and dialysis clinic nurses in Ohio.

This example illustrates the healthy hire effect through confounding by (unmeasured) smoking status, but the healthy hire effect can also occur through confounding by other unknown or unmeasured health behaviors related to employment (U_i). Because these confounders are unmeasured, we have to control for Job$_1$ instead. Even if some confounders are measured, there are enough sociodemographic differences between workers and the general population to make residual confounding likely (11, 19).

Table 1. Types of Healthy Worker Effects and Strategies for Their Control in Studies of Occupational Exposures and Pregnancy Outcomes

Effect	Description	Method of Control[a]	When Does it Arise?
Healthy hire effect	Risk factors differ between employed and nonemployed women. When risk is compared between workers and a population that includes nonworkers, this results in confounding.	Restrict the analysis to women who were employed in the job of interest at any time during the risk period.	Before the risk period starts
Desperation and privilege effects[b]	Socioeconomic factors affect who returns to the workforce following pregnancy. This results in differences in the prevalence of risk factors for the outcome among employed women compared with women out of the workforce.	Restrict the analysis to women who were employed in the job of interest at any time during the risk period.	Before the risk period starts
Reproductively unhealthy worker effect[b,c]	Women with live births leave the workforce, and women with nonlive births return to work. Women in the workforce therefore have a higher prevalence of risk factors for the outcome than women out of the workforce.	Restrict the analysis to women who were employed in the job of interest at any time during the risk period.	Before the risk period starts
Insecure pregnancy effect			
Type 1: change in job status before the risk period[b]	Women with a history of adverse pregnancy outcomes (i.e., higher prevalence of risk factors for adverse outcomes) leave the workforce before the risk period, creating differences in risk between working and nonworking women.	Restrict the analysis to women who were employed in the job of interest at any time during the risk period.	Before the risk period starts
Type 2: change in exposure before the risk period[b]	Women with a history of adverse pregnancy outcomes (i.e., higher risk for subsequent adverse outcomes) take precautions to lower their occupational exposures before the risk period, resulting in an apparent association between low exposures and adverse outcomes.	Restrict the analysis to women who were employed at any time during the risk period and condition on prior pregnancy outcome.	Before the risk period starts
Type 3: change in job during the risk period[b]	Women with a history of adverse pregnancy outcomes (i.e., higher prevalence of risk factors for adverse outcomes) leave the workforce during the risk period, creating differences in risk between women who leave the workforce and women who continue working.	Restrict the analysis to women who were employed in the job of interest at any time during each measured segment of the risk period.	During the risk period
Type 4: change in exposure during the risk period[b]	Women with a history of adverse pregnancy outcomes (i.e., higher risk for subsequent adverse outcomes) take precautions to lower their occupational exposures during the risk period, resulting in an apparent association between low exposures and adverse outcomes.	Restrict the analysis to women who were employed at any time during each measured segment of the risk period and condition on prior pregnancy outcome (or restrict the analysis to first pregnancies instead of conditioning on prior pregnancy outcome).	During the risk period
Healthy worker survivor effect			
Type 1: time-varying confounding affected by prior exposure	Workforce exit is differential by exposure status, creating time-varying confounding by prior exposure.	G-methods are needed to control for confounding. Restrict the analysis to women who worked during all segments of the risk period.	During the risk period
Type 2: selection bias	Participants are enrolled partway through the risk period, raising the possibility of bias if timing of enrollment is differential by exposure.	Enroll participants at the beginning of the risk period.	During participant selection

[a] Given the assumptions made in this article.
[b] Because this effect depends on a prior pregnancy outcome, conducting the analysis in a cohort of women with first pregnancies will avoid the occurrence of this effect.
[c] Also referred to as the infertile worker effect or the unhealthy pregnant worker effect.

Desperation and privilege effects

Desperation and privilege effects affect return to work following pregnancy (10). The desperation effect occurs when economic constraints like lack of income or lack of maternity leave drive a woman's return to work. The privilege effect occurs when women have other sources of income, supportive workplace policies, fulfilling jobs, or flexible schedules or job tasks that provide greater freedom to decide whether to

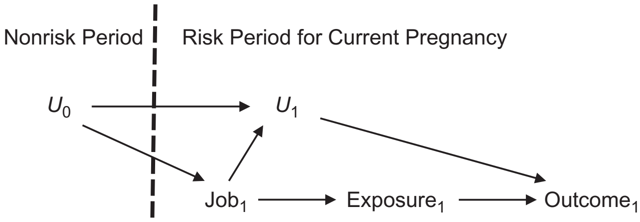

Figure 1. Directed acyclic graph illustrating the healthy hire effect. Variable subscripts denote whether values are determined during the nonrisk period ($i = 0$) or the pregnancy risk period ($i = 1$); the dashed line demarcates these periods. U_i are unknown or unmeasured variables. As an example, let Exposure_1 represent working in an oncology clinic (a proxy for chemotherapy exposure) and let Outcome_1 represent miscarriage. Miscarriage risks are compared between nurses working at an oncology clinic and the general population (Job_1), which in turn affects exposure to chemotherapy (Exposure_1). Smoking (U_i) affects both the likelihood of being a nurse and the likelihood of miscarriage. The open backdoor path, corresponding to the healthy hire effect, can be closed by conditioning on Job_1.

return to work (10). As a result, women with certain demographic characteristics are more likely to reenter the workforce after pregnancy, altering the demographic profiles of workers and nonworkers.

Consider a longitudinal cohort study of occupational chemotherapy exposure and preterm birth. At recruitment, all women are nurses; as time passes, some leave the workforce but remain enrolled in the study. Unlike in the previous example, here we compare the prevalences of preterm birth between exposed and unexposed nurses within the same cohort.

The same DAG (Figure 1) represents relationships between variables. Nurses who returned to work after a prior birth will likely be working as nurses and could be exposed to chemotherapy during their current pregnancy risk period (Job_1). Nurses who did not return to work will remain unexposed. Suppose that single parenthood (U_i) increases the likelihood of both returning to work and preterm birth (through sociodemographic mechanisms). The chemotherapy–preterm birth association is confounded by single parenthood: Single mothers are more likely to be in the workforce, be exposed, and have a preterm birth. Desperation/privilege effects are therefore specific examples of the healthy hire effect—we compare risk between exposed worker populations (nurses) and unexposed populations that include nonworkers (nurses out of the workforce) who have different health characteristics.

To control for confounding, one option is to enter Job_1 (employment status in the risk period) into a multivariable model. However, this would cause nonpositivity and violate modeling assumptions. Nonpositivity occurs when 1 or more strata of a covariate include only exposed or unexposed people (20). Here, 1 stratum of Job_1 (women not currently working) is unexposed to chemotherapy. Instead, restricting the analysis to employed women ($\text{Job}_1 = 1$) avoids violation of the positivity assumption.

Because desperation and privilege effects are caused by differences in returning to work following a prior pregnancy, conducting the study in a cohort of women with their first pregnancies is another option for addressing this bias. We might still need to condition on Job_1 to account for the healthy hire effect.

Reproductively unhealthy worker effect

The reproductively unhealthy worker effect occurs when women with live births leave the workforce to provide child care, leaving women with nonlive births overrepresented in the workforce (11–13, 21). As a result, the prevalence of risk factors for adverse outcomes is higher among women in the workforce versus out of the workforce. In the absence of a causal association, occupational exposure is associated with an adverse outcome.

Consider the study of chemotherapy exposure (Exposure_1) and miscarriage (Outcome_1). We assume that exposure before the risk period (Exposure_0) has no causal effect on Outcome_1. Nurses with prior live births are more likely to leave the workforce, remain out of the workforce during their current pregnancy (Job_1), and be unexposed to chemotherapy (Figure 2). Nurses with miscarriages or early pregnancy losses probably return to work or stay at work and therefore are more likely to be exposed to chemotherapy. As a result, the prevalence of unmeasured risk factors for miscarriage in the exposed population is higher than that in the unexposed. This is an example of the healthy hire effect (confounding by health factors related to employment status): We compare risks of miscarriage between exposed workers and an unexposed population that includes nonworkers (nurses who left the workforce). Again, we should restrict the analysis to women employed at any time during the risk period.

We could also address this bias by conducting the study in a cohort of women with their first pregnancies, guaranteeing that prior pregnancy outcome has no effect on employment. We might still need to condition on Job_1 to account for the healthy hire effect.

Insecure pregnancy effect

The insecure pregnancy effect occurs when women with adverse pregnancy outcomes leave the workforce or alter behaviors (e.g., change job tasks, use personal protective equipment) in a later pregnancy to prevent occupational exposures that might increase risk for another adverse outcome (10). This causes lower occupational exposures among women at the highest risk for an adverse outcome in the absence of a causal association.

The timing (before or during the risk period) and reason for the change in occupational exposures (leaving the workforce, reducing exposures) affect how we address the insecure pregnancy effect. We explore 4 combinations of these factors: 1) women leaving the workforce before the risk period, 2) women reducing exposure before the risk period, 3) women leaving the workforce during the risk period, and 4) women reducing exposure during the risk period.

Consider the study of chemotherapy exposure (Exposure_1) and miscarriage among nurses. We assume that exposures incurred prior to the risk period (Exposure_0, Exposure_{-1}) have no causal effect on Outcome_1.

In scenario 1, nurses with a prior miscarriage are more likely to leave work and to be unexposed during the risk period. Women with prior live births are more likely to keep working and to be exposed. This is similar to the reproductively unhealthy worker effect, but the direction of the bias is reversed (Figure 2). We control for confounding by conditioning on Job_1.

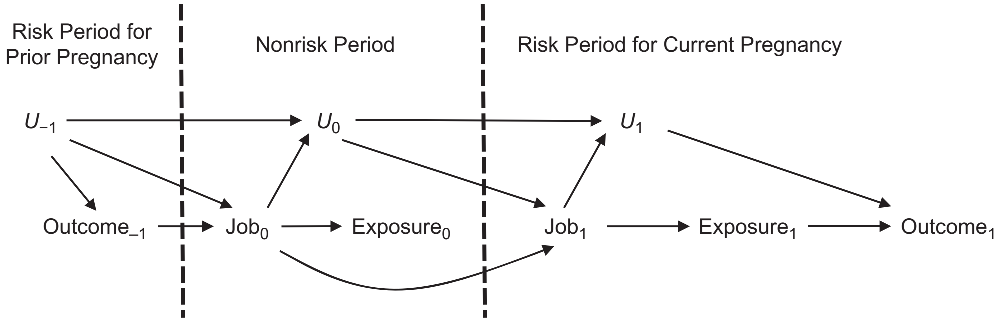

Figure 2. Directed acyclic graph (DAG) illustrating the reproductively unhealthy worker effect. A prior pregnancy outcome (Outcome_{-1}) affects the likelihood that a woman is working and is exposed to an occupational hazard during the index pregnancy. For example, women with a live birth are more likely to leave the workforce than women who have a miscarriage ($\text{Outcome}_{-1} \rightarrow \text{Job}_0$). As a result, there are more women with risk factors for miscarriage (U_i) in the workforce than out of the workforce at the time of the index pregnancy (Job_1). This confounding can be addressed by restricting the analysis to women who worked at any time during the risk period (Job_1). This same DAG represents insecure pregnancy effect type 1: Women with adverse pregnancy outcomes are more likely than women without these outcomes to leave the workforce prior to the index pregnancy risk period.

In scenario 2, nurses with prior miscarriages remain at work but reduce their chemotherapy exposure before the risk period (Figure 3). We can address the resulting confounding by conditioning on Job_1 and Outcome_{-1}. To condition on Job_1, we restrict the analysis to nurses working at any time during the risk period. Options for conditioning on Outcome_{-1} include multivariable modeling or restriction (nonpositivity is less likely when adjusting for Outcome_{-1} vs. Job_1).

When job (scenario 3) or exposure (scenario 4) changes during the risk period, we need multiple measurements to capture this change. For simplicity, we assume 2 measurements during the risk period, denoted with the subscripts $i = 1.1$ and $i = 1.2$.

In scenario 3, nurses with prior miscarriages leave their job partway through the risk period. Figure 4A illustrates this with an arrow pointing from Outcome_{-1} to $\text{Job}_{1.2}$. With 2 measurements, our exposure of interest is the combined effects of $\text{Exposure}_{1.1}$ (before the job change) and $\text{Exposure}_{1.2}$ (after the change). To control for the resultant confounding, we can restrict the analysis to nurses who worked in at least part of both segments of the risk period (conditioning on $\text{Job}_{1.1}$ and $\text{Job}_{1.2}$).

In scenario 4, nurses with prior miscarriages reduce their exposures during the risk period. In Figure 4B, Outcome_{-1} affects $\text{Exposure}_{1.2}$. To control for the resultant confounding, we can restrict the analysis to nurses who worked during both segments of the risk period (condition on $\text{Job}_{1.1}$ and $\text{Job}_{1.2}$) and additionally condition on Outcome_{-1} through multivariable modeling or restriction.

Studying a cohort of women with first pregnancies would eliminate the insecure pregnancy effect, because no one would alter her behaviors based on a prior pregnancy outcome.

The insecure pregnancy effect could also be caused by an early warning, such as bleeding or preeclampsia, which causes women to leave work or reduce exposures (10). In the DAGs, we would replace Outcome_{-1} with Warning_i; this variable's value would be determined before or during the risk period ($i = 0$ or $i = 1$) rather than before the risk period ($i = -1$). Assuming that the warning symptom is not a component of Outcome_1 itself, we could analytically treat Warning_i identically to Outcome_{-1} to control for confounding.

Healthy worker survivor effect

The healthy worker survivor effect can be caused by time-varying confounding affected by prior exposure ("time-varying confounding") or selection bias (6).

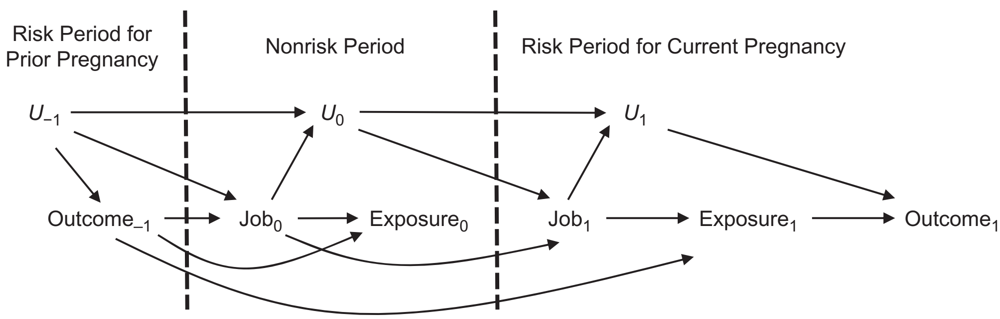

Figure 3. Directed acyclic graph illustrating insecure pregnancy effect type 2 (a prior adverse pregnancy outcome affects exposure before the risk period). For example, a prior miscarriage (Outcome_{-1}) causes women to reduce their occupational exposures in anticipation of their next pregnancy and continuing into the pregnancy risk period (Exposure_0 and Exposure_1). Conditioning on Job_1 and Outcome_{-1} will block the open backdoor paths.

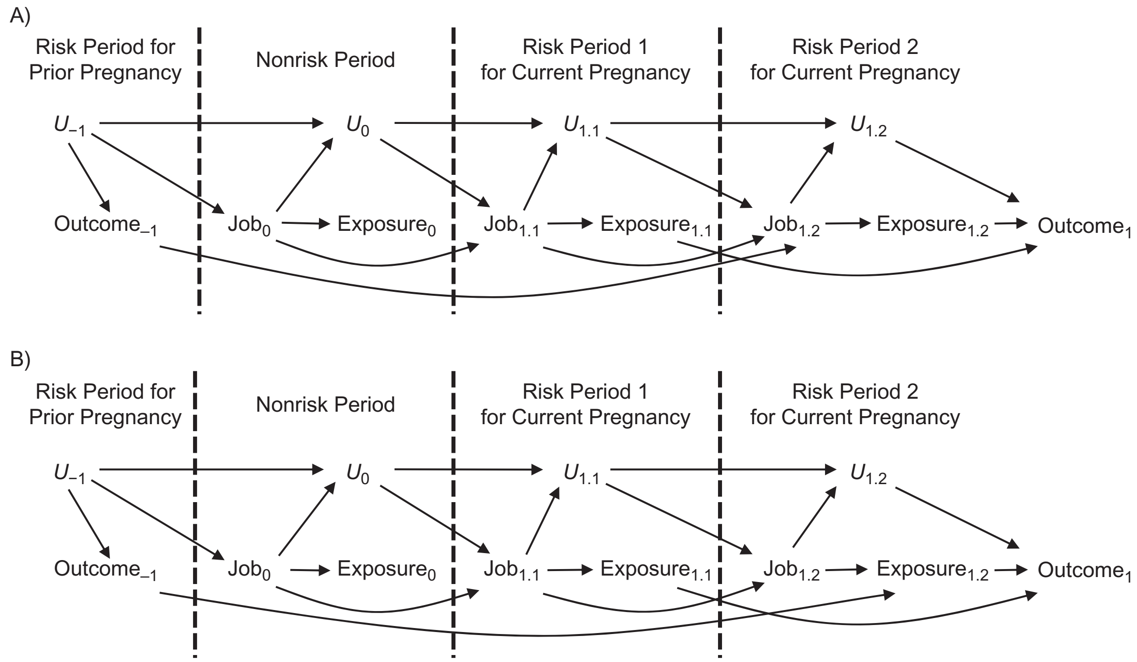

Figure 4. Directed acyclic graphs illustrating insecure pregnancy effect types 3 (A) and 4 (B). In insecure pregnancy effect type 3, a prior pregnancy outcome (Outcome_{-1}) causes women to leave their jobs during the latter part of the risk period ($\text{Job}_{1.2}$). We need to condition on $\text{Job}_{1.1}$ and $\text{Job}_{1.2}$ to control for confounding. In insecure pregnancy effect type 4, a prior outcome causes women to reduce their exposure during the latter part of the risk period ($\text{Exposure}_{1.2}$). We need to condition on $\text{Job}_{1.1}$, $\text{Job}_{1.2}$, and Outcome_{-1} to control for confounding.

Time-varying confounding (Figure 5) occurs when 4 conditions are met: 1) Job_i causes Exposure_i, 2) Job_i and Outcome_1 are associated (e.g., through confounding by U_i), 3) multiple exposure measurements or cumulative effects are of interest, and 4) exposure earlier in the risk period ($\text{Exposure}_{1.1}$) affects workforce exit later in the risk period ($\text{Job}_{1.2}$) (22, 23).

The first condition is met if working in a given job affects the likelihood of exposure. The second is met if there are common risk factors between holding that job and adverse pregnancy outcomes. In our cohort study examples, condition 1 is met because many nurses are exposed to chemotherapy. Condition 2 is met because there are common risk factors between being a nurse and reproductive outcomes (e.g., socioeconomic status).

Condition 3 (multiple exposure measurements or cumulative effects are of interest) might only apply in a subset of studies. It might not be commonly met in retrospective studies, for example, which often define exposure as "ever/never."

Condition 4 (workforce exit is differential by exposure) is commonly assumed to occur in studies of chronic disease or mortality: Exposure causes or exacerbates poor health, causing susceptible workers to leave the workforce. Because the risk period for pregnancy outcomes is short, few workers exit the workforce during the pregnancy risk period because of poor health. However, other factors could cause differential exit. For example, exposed women could be more likely to take leave or bed-rest near delivery. Women with physically

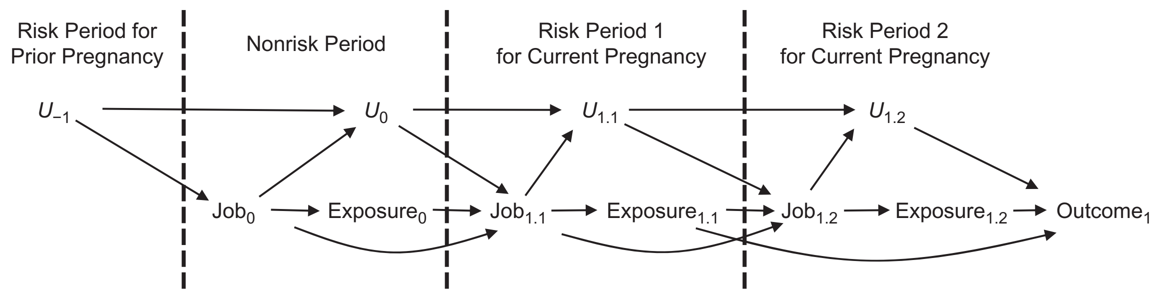

Figure 5. Directed acyclic graph illustrating the healthy worker survivor effect from time-varying confounding affected by prior exposure. $\text{Job}_{1.2}$ is both an intermediate on the causal pathway and a confounder of the association of interest, meaning that g-methods are required for data analysis. We must condition on $\text{Job}_{1.1}$ and $\text{Job}_{1.2}$ in the analysis.

demanding jobs leave work earlier in pregnancy than women with less demanding jobs, creating this differential workplace departure (24).

When these 4 conditions are met, time-varying confounding and the healthy worker survivor effect are probably present (Figure 5). G-methods, a class of statistical models used to account for time-varying confounding, must be used to control for confounding by $\mathrm{Job}_{1,2}$, which is both an intermediate factor on the causal pathway and a confounder (23). These methods are increasingly being used in occupational epidemiology (6, 25–27).

Cohort selection can also cause the healthy worker survivor effect (6). Cohort follow-up ideally begins on the first day of the risk period. However, if follow-up begins partway through the risk period (i.e., the beginning of the risk period is unobserved), left-truncation might be present (28). Participants with outcomes occurring before commencement of follow-up are missing because only those experiencing the outcome after follow-up are observed (29). In studies of chronic disease or mortality, this favors inclusion of the healthiest workers with the longest job tenures (higher exposures) and exclusion of ill workers who have already left work (lower exposures), resulting in the healthy worker survivor effect. Similar effects can occur in studies of pregnancy outcomes.

Suppose we conduct a prospective cohort study of chemotherapy exposure and miscarriage by enrolling nurses at the time of their first prenatal visits, but exposed nurses seek prenatal care earlier than unexposed nurses. This differential study entry means that exposed nurses are more likely to have a miscarriage after enrollment than unexposed nurses, causing bias (29). In such studies, left-truncation can be addressed using survival analysis (29).

Multiple effects

Some of these healthy worker effects probably occur simultaneously, but they can still be addressed using the methods we described (see Web Figure 1, available at https://academic.oup.com/aje). Condition on Job_i and sometimes $\mathrm{Outcome}_i$; use g-methods if time-varying confounding is present.

DISCUSSION

Healthy hire effects (including the desperation/privilege and reproductively unhealthy worker effects) and the insecure pregnancy effect are caused by confounding—differences in disease risk between exposed and unexposed women at the start of the pregnancy risk period. Because of substantial differences in unknown and unmeasured sociodemographic factors related to employment between women in and out of the workforce, we can control for Job_i instead of trying to control for all variables that differ (11, 19). Our DAGs confirm that restricting the analysis to women working at any time during the risk period can minimize this confounding, given our assumptions.

The insecure pregnancy effect might be less common than the healthy hire effect, but there is evidence that some women with prior adverse outcomes reduce occupational exposures. For example, flight attendants with a prior miscarriage were the most likely to avoid flying in early pregnancy, reducing their occupational exposures (30). However, reduced exposure is not always a result of prior adverse pregnancy outcomes. Workplace policies designed to protect pregnant women decrease exposures for all workers. This would not create an insecure pregnancy effect because the policy does not depend on prior pregnancy outcome. In a study of veterinary personnel, 93% of women took precautions to reduce occupational exposures while pregnant, suggesting that reducing occupational exposures during pregnancy is common among workers, regardless of prior outcome (31). Health-conscious women might also reduce their exposures regardless of prior pregnancy outcome. However, these women probably also alter other behaviors that increase or decrease risk for adverse outcomes, confounding the exposure-outcome relationship.

The healthy worker survivor effect might be less common in studies of pregnancy outcomes than in studies of chronic diseases or mortality. There are data-based methods to check for whether time-varying confounding is present, and study design will dictate whether left-truncation is a concern (22). The likelihood of bias is also determined by the definition of the target parameter, the choice of analysis method (which corresponds to a hypothetical intervention in the worker population), and the structure of the hypothetical intervention (6). We refer readers interested in an in-depth discussion of target populations, target parameters, and healthy worker survivor effects to the work of Brown et al. (6).

Several healthy worker effects are consequences of behaviors undertaken because of prior pregnancy outcomes. The relative importance of these effects therefore depends on the prevalence of prior pregnancies in the population. A population with many nulliparous women would probably be minimally affected by these effects.

Investigators should determine whether the relationships between their variables are consistent with our structures before applying our conclusions. For example, when studying early-pregnancy exposures and preterm birth, we might assume that exposures in pregnancy before the risk period can cause the outcome. In addition, various research groups represent healthy worker effects differently in DAGs (2, 5, 23, 32). Using other representations might result in different conclusions.

We have described structures of healthy worker effects in studies of occupational exposures and pregnancy outcomes. Using DAGs could help researchers to identify biases in their studies and methods for their control.

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