Sex and Gender Analysis within a Demonstration of Effect Measure Modification versus Confounding

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Appropriate HSPH Core Courses:
This teaching example is meant to be used in introductory biostatistics and epidemiology courses, such as BIO201, EPI201, and EPI202 that teach the difference between confounding and effect measure modification on a potential causal pathway.

Brief Background:
Our teaching example examines the relationship between gender, sex, and suicide risk. Many studies have shown that depression is correlated with suicide risk and that while more women than men are diagnosed with depression, more men than women successfully commit suicide (1, 2). What contributes to this difference is complicated, but involves both elements of effect modification and confounding. The literature suggests that, at least in the western context, components of masculine norms affect both the risk of men becoming diagnosed with depression and the risk of men committing suicide. These components of masculinity include anti-femininity, competitiveness, emotional stoicism, self-reliance, physical toughness and strength, and valuing self-worth through monetary success (1). The research hypothesizes that these traits cause men to both seek out care for depression and to be diagnosed with depression under the current diagnoses tools less often than women. In addition, there is a known link between substance abuse and suicide. Men are more likely than women to engage in substance abuse, such as drinking alcohol, which may exacerbate their suicide risk (3). The research thus makes a compelling argument for how gender could be a confounding variable on the association between depression and suicide.

Sex differences and similarities further complicate research on depression and suicide risk. Multiple studies examining neurobiological risk factors for suicide and aggression have found an association between low serotonergic activity and risk. In particular, multiple studies have focused on the serotonin metabolite 5-HIAA measured in cerebrospinal fluid. Lower levels of CSF 5-HIAA have been shown to be correlated with increased suicide risk, independent of the neurobiology of specific psychiatric disorders (4, 5). Furthermore, it has been shown that baseline serotonin activity varies by sex, with males demonstrating lower levels of CSF 5-HIAA (6). Given similar findings in human and other mammalian findings, this relationship thus suggests how biological differences between males and females can affect suicide risk, independent of depression diagnosis, and thus demonstrates effect modification by sex.

Learning Objectives for Students:
The learning objectives for students are: 1) to clarify the differences between effect measure modification and confounding and to show how they could work simultaneously in one example, 2) to clarify the concepts of sex and gender, especially since the two concepts are often represented by one variable in a dataset, and demonstrate their use in an epidemiology example, and 3) to highlight the importance of focusing on these effects within men's health specifically.

Teaching Methods:
The learning objectives will be communicated through an in-class example that can be inserted into any set of lecture slides on confounding and effect measure modification. The in-class example reviews the definitions of effect measure modification and confounding as well as showing how they can be modeled through directed acyclic graphs (DAGs). Then the slides show a graph demonstrating the stark differences in suicide risk among depression men and women. The slides prompt questions for the class on whether this phenomenon could be due to effect measure modification, confounding, or both, and whether the data analysis should be stratified or adjusted by gender/sex. The slides unpack the difference between gender as a reflection of socially constructed norms for men and women and sex as a confluence of biological differences between men and women. Then the slides present how male status, as a social phenomenon, could act as a confounder of the relationship between depression and suicide as shown in Figure 1. Finally, the slides demonstrate how male status, as a biological phenomena, could act as an effect modifier as shown in Figure 2. Ultimately, the slides conclude that both effect measure modification and confounding are involved in this one causal relationship between depression and suicide risk. These results should thus be stratified due to the presence of effect measure modification. Public health implications are that suicide prevention programs should take into account the differing societal and biological contexts that differentiate suicide risk in men versus women.

FIGURE 1

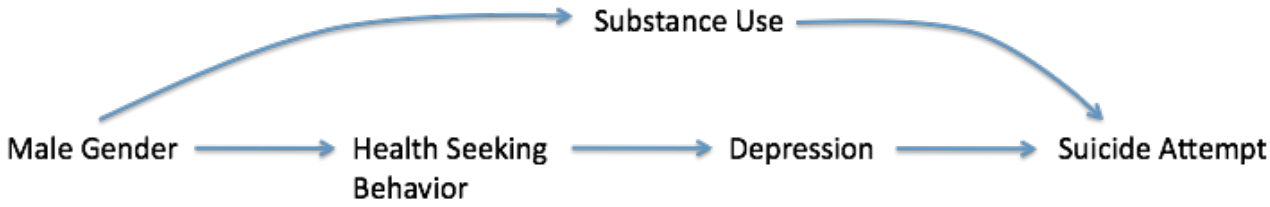
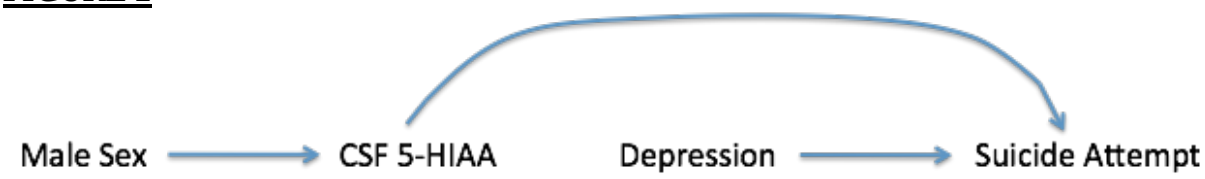


FIGURE 2



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