Sensitivity Analyses

Cornfield et al. (1959)

- R_1 =risk of cancer for smokers.
- R_0 =risk of cancer for non-smokers.
- p_1 =prevalence of smokers exposed to unmeasured confounder
- p_0 =prevalence of non-smokers exposed to unmeasured confounder
- R_u =risk of cancer to those exposed by unmeasured confounder
- $R_{\overline{u}}$ =risk of cancer to those not exposed by unmeasured confounder

$$\frac{R_1}{R_0} = \frac{p_1 R_u + (1 - p_1) R_{\overline{u}}}{p_0 R_u + (1 - p_0) R_{\overline{u}}}$$

Cornfield et al. (1959)

$$\frac{R_1}{R_0} = \frac{p_1 R_u + (1 - p_1) R_{\overline{u}}}{p_0 R_u + (1 - p_0) R_{\overline{u}}}$$

$$\Rightarrow \frac{p_1}{p_0} = \frac{R_1}{R_0} + \frac{R_{\overline{u}}}{p_0 R_u} \left[(1 - p_0) \frac{R_1}{R_0} - (1 - p_1) \right]$$

- $R_1 / R_0 \equiv RR_{ED}^{obs} \approx 9$.
- Exposure to the unmeasured confounder is assumed to be higher among smokers than non-smokers (i.e., $p_1 > p_0$).
- Therefore, $(1 - p_0) R_1 / R_0 - (1 - p_1) > 0$.
- Hence, p_1 / p_0 must be greater than 9.
- $p_1 / p_0 \equiv RR_{EU}$ can be called the exposure-confounder relative risk.

Cornfield et al. (1959)

“Thus, if cigarette smokers have 9 times the risk of nonsmokers for developing lung cancer, and this is not because cigarette smoke is a causal agent, but only because cigarette smokers produce hormone X, then the proportion of hormone-X-producers among cigarette smokers must be at least 9 times greater than that of nonsmokers. If the relative prevalence of hormone-X-producers is considerably less than ninefold, then hormone X cannot account for the magnitude of the apparent effect."

Bounds

Under assumptions of binary confounder U and conditional independence between exposure E and outcome D given confounder U, Cornfield et al. (1959) showed that the exposure-confounder relative risk must be at least as large as the observed exposure-outcome relative risk:

$$RR_{EU} \geq RR_{ED}^{obs}.$$

Similarly, Schlesselman (1978) showed that the confounder-outcome relative risk ($RR_{UD} \equiv R_u / R_{\overline{u}}$) must also be as large as the observed exposure-outcome relative risk:

$$RR_{UD} \geq RR_{ED}^{obs}.$$

This makes sense, as confounders are generically defined as common causes of exposures and outcomes.

Ding and VanderWeele (2016)

Maximum amount by which unmeasured confounding could reduce an observed risk ratio (assuming $RR_{ED}^{obs} > 1$):

$$RR_{ED}^{true} \geq RR_{ED}^{obs} \bigg/ \frac{RR_{UD}RR_{EU}}{RR_{UD} + RR_{EU} - 1}.$$

Suggests a 2-parameter sensitivity analysis where RR_{UD} and RR_{EU} are specified.
Then one can see how the results vary as a function of these sensitivity parameters.

VanderWeele and Ding (2017)

Define “E-value" as the minimum strength of association, on the risk ratio scale, that an unmeasured confounder would need to have on both the treatment and the outcome, conditional on measured covariates, to explain away a treatment-outcome association."

$$\text{E-value} = RR_{ED}^{obs} + \sqrt{RR_{ED}^{obs}(RR_{ED}^{obs} - 1)}$$

They suggest routinely reporting this with all observational studies attempting to investigate causation (“that is, are not strictly about description or predictive or prognostic modeling").

Report it for the point estimate and for the confidence limit that is closest to 1.

They have alterations for different outcomes (i.e., hazard ratios, odds ratios, etc.)

General Thoughts on Sensitivity Parameters

- Used to address potential violation of assumptions.
  - These papers address ignorable treatment assignment assumption.
  - Lots of other assumptions in different causal analyses, and lots of potential sensitivity parameters.
- Not identifiable from data.
- If put a prior on it, then the posterior distribution would equal the prior. (If it changes, then your model is driving things.)
- Assumed fixed and known for purposes of the analysis.
- Chosen based on subject-matter knowledge.
- Can be thought of as compromise between worst-case scenario sensitivity analyses (extreme bounds) and making the assumption.