Ding and VanderWeele, "Sensitivity Analysis without Assumptions"[1]

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Sociology Statistics Reading Group
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[1]Conversations with Brandon Stewart and Ian Lundberg helped improve these slides and clarify my thinking on sensitivity analysis.

Outline

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3. Work through the notation in the paper
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5. Share some of my thoughts on the paper and sensitivity analysis in general

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- Today we'll be talking about sensitivity analysis for unmeasured confounding in observational studies, also known as **bias analysis**
- We typically use sensitivity analysis to answer the following questions:
  - How much would some hypothetical level of unmeasured confounding change our causal estimates?
  - How strong would unmeasured confounding have to be to render our causal estimates substantively and statistically insignificant?

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- **Whenever we try to estimate causal effects using a selection-on-observables approach**
- When we try to estimate the effect of some treatment on some outcome by conditioning on a set of **observed** confounders, we should always worry about **unobserved** confounding

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4. Alternatively, we can calculate what the strength of the confounding would have to be to reduce our causal estimate to a substantively and statistically insignificant value
   - This approach also relies on assumptions we make about the unobserved confounding

Origins of Sensitivity Analysis

Cornfield, et al. 1959. "Smoking and Lung Cancer: Recent Evidence and a Discussion of Some Questions." *Journal of the National Cancer Institute.*

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- The association between lung cancer and smoking is **spurious** rather than causal

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- Let's say this unobserved Hormone X causes both smoking and cancer
- But if you believe this confounder explains the entire association between smoking cancer, you also have to believe that this biological trait is **nine times more prevalent** among smokers than among non-smokers, and **sixty times more prevalent** among people who smoke two packs a day than among non-smokers

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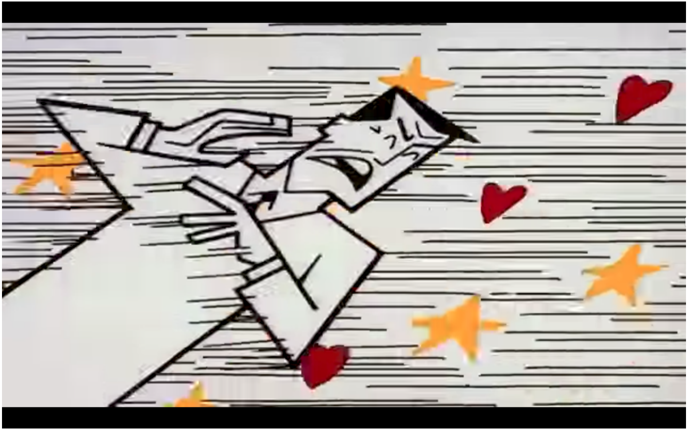

Why use sensitivity analysis?

- Sensitivity analysis can be a powerful tool that allows you to make the case for causality even in the presence of potential unobserved confounding
- We might not be convinced by Cornfield's sensitivity analysis—it's not entirely implausible that Hormone X really **is** sixty times more prevalent among those who smoke two packs a day
- But at the very least, I think sensitivity analysis can **boost our confidence** that an effect is causal even if it fails to **completely convince us**

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- But in order to relax this assumption, we have to make **other** assumptions about the nature of the confounding!
- What if our readers don't buy our assumptions about the unobserved confounding?
- What if we're really uncertain about the nature of the confounding?

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- This technique allows us to make claims like:
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  - "For unmeasured confounding alone to reduce an observed association to [a given level], two sensitivity analysis parameters must satisfy [another specific inequality]."

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- Plotting all the values of the parameters that satisfy the particular inequality helps communicate your sensitivity analysis results

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- For continuous outcomes, we use the ratio by which the treatment increases the expected outcome:
  - E.g., "Completing a job training program increases future earnings by a factor of 1.3 on average."

Notation

- E - Treatment (binary)
- D - Outcome (binary)
- C - Measured confounders
- U - Unmeasured confounder (categorical with levels $0, 1, \ldots, K-1$)

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- Intuition:
  - $\text{RR}^{\text{obs}}_{ED|c} = \dfrac{\text{Probably of observing the outcome among \textbf{treated} units in stratum } C = c}{\text{Probably of observing the outcome among \textbf{control} units in stratum } C = c}$

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- Intuition:
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- If U is a vector of unobserved confounders, then $\text{RR}_{EU|c}$ refers to the maximum relative risk comparing any two categories of the vector U

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- Intuition:
  - The largest "effect" of U on D across **all** levels of the treatment E **within a given stratum** of measured confounders C
  - "Effect" refers to the ratio of the highest probability of the outcome across all levels of U to the lowest probability of the outcome across all levels of U

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  - **This looks deceptively similar to the Law of Total Probability (LOTP)**
  - But in order for our numerator to sum to $\Pr(D = 1 \mid E = 1)$ by LOTP, it would have to read:
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- Intuition:
  - Our **numerator** represents a weighted average of the probabilities of observing the outcome **among treated units in stratum** $C=c$ where the weights are the probabilities of U taking different values of k **across the entire stratum** $C=c$ (i.e., among both treated and control units)

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  - **Note:** the ratio of weighted averages is numerically equivalent to the ratio of weighted sums, since $\frac{1}{K}$ would be present in both the numerator and denominator and would thus cancel out

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- E.g., we replace $\text{RR}^{\text{obs}}_{ED|c}$ with $\text{RR}^{\text{obs}}_{ED}$

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- If we redefine RR_{EU} as $\max_k \text{RR}_{EU,k}^{-1}$, and our observed $\text{RR}_{ED}^{\text{obs}} < 1$ we can obtain an **upper bound** on the true causal relative risk:

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- We can also show that for unmeasured confounding to reduce our observed relative risk $\text{RR}_{ED}^{\text{obs}}$ to a true causal relative risk of $\text{RR}_{ED}^{\text{true}}$, RR_{EU} and RR_{UD} must satisfy the following inequality:

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- We can use this inequality to show how strong confounding would have to be to completely explain away the observed effect if we let $\mathrm{RR}_{ED}^{\mathrm{true}} = 1$
- Note that we are using the original definition of RR_{EU}

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- What if we want a more general inequality for our sensitivity analyses?

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- All of the results covered up until now apply within a given stratum $C = c$
- What if we want a more general inequality for our sensitivity analyses?
- If we're interested in true causal relative risks averaged over observed covariates C, then our sensitivity analysis parameters must satisfy the following inequality:
  - $\text{RR}_{ED}^{\text{true}} \geq \min_c \left(\text{RR}_{ED|c}^{\text{obs}} \div \frac{\text{RR}_{EU|c} \times \text{RR}_{UD|c}}{\text{RR}_{EU|c} + \text{RR}_{UD|c} - 1} \right)$

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  3. Plug your observed $\text{RR}_{ED}^{\text{obs}}$ and your chosen values for RR_{EU} and RR_{UD} into this expression to get a **lower bound** for the true causal relative risk:
     - $\text{RR}_{ED}^{\text{obs}} \div \dfrac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1}$

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    - We might opt for this more conservative upper bound if we're very uncertain about the degree of confounding or if we're trying to convince a skeptical audience
  - Alternatively, we could use this inequality to obtain an upper bound, again plugging in the **lowest plausible values** for RR_{EU} and RR_{UD}:
    - $\text{RR}_{ED}^{\text{true}} \leq \text{RR}_{ED}^{\text{obs}} \times \dfrac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1}$

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    - Recall that for this inequality, we redefine RR_{EU} as $\max_k RR_{EU,k}^{-1}$, and our RR_{ED}^{obs} must be less than 1

Implementation

One drawback to the upper- and lower-bound techniques—in my view—is that it can be difficult to think about what the highest and lowest plausible values for our relative risks are without coming up with a concrete example of a confounder and making assumptions about it.

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  2. Calculate RR^{obs}_{ED} and a 95% confidence interval
  3. Plug in the **lower confidence limit** of RR^{obs}_{ED} and our hypothetical RR^{true}_{ED} to find the values of RR_{EU} and RR_{UD} that satisfy the inequality:
     - $$\frac{RR_{EU} \times RR_{UD}}{RR_{EU} + RR_{UD} - 1} \geq \frac{RR^{obs}_{ED}}{RR^{true}_{ED}}$$

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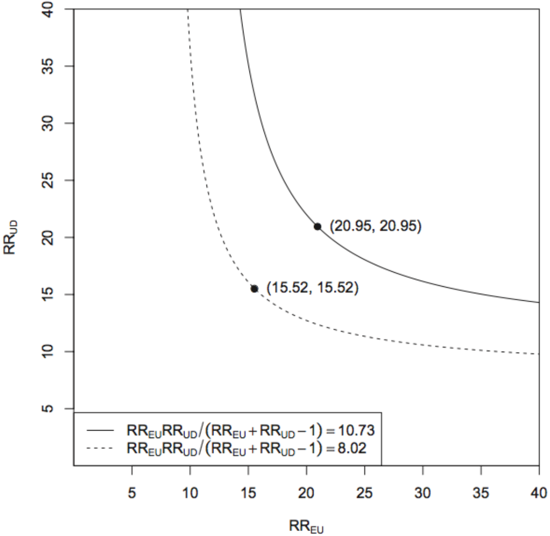
     - $$\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} \geq \frac{\text{RR}_{ED}^{\text{obs}}}{\text{RR}_{ED}^{\text{true}}}$$
  4. Plot the values of RR_{EU} and RR_{UD} that satisfy the inequality
- What I like about this approach is that you can leave it to your audience to decide how plausible the resulting level of confounding is

Example Plot from Ding and VanderWeele



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- You could conduct separate analysis for positive and negative values
  - If our outcome is net worth, we could run separate analyses for net debtors and net asset holders

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- We compare those who enrolled and completed a job training program with those who didn't, controlling for observed covariates like **race** and **education** (C)
- But we're worried about unmeasured confounders like **ambition** or **work ethic** (U)

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  - I.e., those who completed the program are 2.3 times more likely to be employed one year later compared with those who never enrolled
- The lower bound of our confidence interval for $\text{RR}_{ED}^{\text{obs}}$ is 2.1
- We want to find and plot the smallest values of RR_{EU} and RR_{UD} that would reduce the lower bound of our confidence interval to 1

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- $$\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} \geq \frac{\text{RR}_{ED}^{\text{obs}}}{\text{RR}_{ED}^{\text{true}}}$$

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- $\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} \geq \frac{\text{RR}_{ED}^{\text{obs}}}{\text{RR}_{ED}^{\text{true}}}$
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- $$\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} \geq \frac{\text{RR}_{ED}^{\text{obs}}}{\text{RR}_{ED}^{\text{true}}}$$
- $$\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} \geq \frac{2.1}{1}$$
- Set $\frac{\text{RR}_{EU} \times \text{RR}_{UD}}{\text{RR}_{EU} + \text{RR}_{UD} - 1} = \frac{2.1}{1}$ to find the smallest values of RR_{UD} and RR_{EU} that satisfy the inequality

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- Rearrange:
  - $$\text{RR}_{UD} = \frac{21(\text{RR}_{EU} - 1)}{10\text{RR}_{EU} - 21}$$

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- In R:

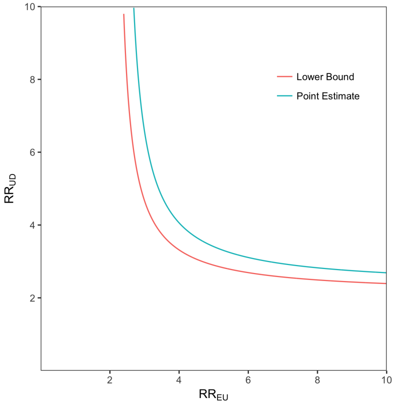
```
x <- seq(from = 1, to = 40, by = .01)
y <- (21 * (x - 1)) / (10 * x - 21)
y.2 <- (23 * (x - 1)) / (10 * x - 23)
x <- rep(x, 2)
y <- c(y, y.2)
type <- c(rep("lower", length(x) / 2), rep("point", length(x) / 2))

data <- data.frame(x, y, type)

data <- data[data$y > 0, ]
```

Example

- Plot values of the sensitivity analysis parameters needed to explain away your effect estimate:



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- In order to explain away the effect estimate among white men with no college degrees:
  1. Those who complete the job training would have to be around four times more likely to possess **some level** of work ethic compared with those who don't enroll, **and**
  2. The maximum of the **relative risks** of work ethic on future employment comparing any two levels of work ethic would have to be around four

My Thoughts on Ding and VanderWeele

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- These are **my** thoughts on the paper
- You don't have to agree with them!

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- The main advantage of this approach is that the results of your sensitivity analysis hold without having to make any assumptions about the nature of the confounding
- But in my view, the sensitivity analysis parameters lack straightforward interpretations
- While we don't have to make any assumptions about the nature of the confounding, it's a lot harder to think through how plausible different levels of confounding are because the sensitivity parameters are just—frankly—**weird**

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  - That said, **you should give your readers concrete examples** of potential confounders and **provide substantive interpretations** of your parameter values using those examples

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- I'm not sure that Ding and VanderWeele's approach has this advantage

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    4. But when they present their results, they emphasize that their models are **"descriptive"** and caution that they should not be interpreted causally

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- What I think these authors are suggesting is that even if they don't have unbiased estimates of treatment effects, their results should still boost our confidence that there is some underlying causal relationship
- I think that's correct!
- But I think that sensitivity analysis gives us a sense of **how much more confident** we should be that there is a causal relationship

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- So instead of saying:
  - "There is unmeasured confounding between the treatment and the outcome, but that's okay because my results are merely descriptive."
- We should say:
  - "Look, we're interested in this causal relationship, and we know our methods give us biased causal estimates, but we did this sensitivity analysis to show you how different levels of unmeasured confounding would change our results and how bad the confounding would have to be to render our results insignificant."

What are your thoughts?