Handout for Evidence Factors in Observational Studies

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Talk follows [21]. See [12] for replication, [3, 4, 14–16, 24, 25] for evidence factors.

Causal effects are not identified without random assignment of treatments An association between treatment received and outcome exhibited may reflect either an effect caused by the treatment or a bias in who is selected to receive treatment.

Biases can replicate Replication should study the same treatment, changing the likely biases, hoping the effect reappears.

Can an observational study replicate itself? If replication is not repetition, can one study replicate itself by analyzing the same data twice?

One very simple example: treatment/control matched pairs, with varied doses of treatment among the pairs A randomized experiment could randomly assign treatment/control within pairs and randomly assign doses among pairs, so the group of permutations that assigns treatments to individuals factors into the product of two subgroups.

General structure Individuals, $1, \ldots, n$, are assigned to n treatment positions by a finite group $\mathfrak{G}$ of $n \times n$ permutation matrices $\mathbf{g}$, where $\mathfrak{G}$ has a subgroup $\mathfrak{H}$. In the example, $\mathfrak{G}$ keeps the pairs intact, changes treatment/control inside pairs and permutes doses among pairs. Subgroup $\mathfrak{H}$ permutes doses among pairs, leaving treatment/control unchanged. We may always find a set $\mathfrak{K} \subseteq \mathfrak{G}$ of distinct representatives of the cosets $\{\mathfrak{H}\mathbf{g} : \mathbf{g} \in \mathfrak{G}\}$ of $\mathfrak{H}$ in $\mathfrak{G}$, so that each $\mathbf{g} \in \mathfrak{G}$ has a *unique* representation as $\mathbf{g} = \mathbf{hk}$ with $\mathbf{h} \in \mathfrak{H}$ and $\mathbf{k} \in \mathfrak{K}$.

Probability of various treatment assignments Write $|\mathcal{S}|$ for the number of elements in a finite set $\mathcal{S}$. A probability distribution on $\mathbf{k} \in \mathfrak{K}$ is a vector $\mathbf{p} = \left(p_{\mathbf{k}_1}, \ldots, p_{\mathbf{k}_{|\mathfrak{K}|}}\right)$, with $p_{\mathbf{k}_\ell} \geq 0$, $1 = \sum_{\ell=1}^{|\mathfrak{K}|} p_{\mathbf{k}_\ell}$. A distribution on $\mathbf{h} \in \mathfrak{h}$ is a vector $\mathbf{p}' = \left(p_{\mathbf{h}_1}, \ldots, p_{\mathbf{h}_{|\mathfrak{H}|}}\right)$. A distribution on the treatment assignments $\mathbf{g} \in \mathfrak{G}$ is a vector $\mathbf{p}'' = \left(p_{\mathbf{g}_1}, \ldots, p_{\mathbf{g}_{|\mathfrak{G}|}}\right)$. Randomized assignment uses $\mathbf{p}'' = \left(|\mathfrak{G}|^{-1}, \ldots, |\mathfrak{G}|^{-1}\right)$.

The null hypothesis of no treatment effect, H_0 The hypothesis H_0 of no effect asserts that changing your treatment does not change your outcome. Under H_0, write a test statistic as a function of the treatment assignment, $t(\mathbf{g})$, as outcomes are merely permuted. In a randomized experiment with realized assignment $\mathbf{G} \in \mathfrak{G}$, the P-value using $t(\mathbf{g})$ is the random variable $\left|\{\mathbf{g} \in \mathfrak{G} : t(\mathbf{g}) \geq t(\mathbf{G})\}\right| / |\mathfrak{G}|$. A level α test of H_0 may be inverted to obtain a $1-\alpha$ confidence set, an equivalence test, a 3-sided test.

Sensitivity analysis for a test of H_0 If we do not randomly assign treatments, then we do not know the distribution of treatment assignments. Consider a set $\mathcal{P}_\Gamma$ whose elements are distributions $\mathbf{p}$ on $\mathfrak{K}$. Can we reject H_0 for all $\mathbf{p} \in \mathcal{P}_\Gamma$? For each $\mathbf{p} \in \mathcal{P}_\Gamma$, we may compute a P-value as the probability that $t(\mathbf{k})$ exceeds its realized value $t(\mathbf{K})$, and we reject at level α if the largest of these, say $\overline{P}_\Gamma$, is $\overline{P}_\Gamma \leq \alpha$; then, if $\mathbf{p} \in \mathcal{P}_\Gamma$, the probability that we falsely reject H_0 is at most α. A sensitivity analysis does this for a nested sequence of $\mathcal{P}_\Gamma$'s, with $\mathcal{P}_\Gamma \subseteq \mathcal{P}_{\Gamma^*}$ if $\Gamma \leq \Gamma^*$, reporting the results to be sensitive to the smallest Γ that leads to acceptance of H_0.

Method Test H_0 twice in two separate sensitivity analyses, assuming only what each sensitivity analysis separately assumes. Assume $\mathbf{p} \in \mathcal{P}_\Gamma$, and test H_0 using a statistic $t(\mathbf{g}) = t(\mathbf{hk})$ that is invariant with respect to $\mathfrak{H}$ in the sense that $t(\mathbf{hk}) = t(\mathbf{k})$ for all $\mathbf{h}$, $\mathbf{k}$, obtaining the maximum P-value, $\overline{P}_\Gamma$. Test H_0 again using the conditional distributions $\mathbf{p}' \in \mathcal{P}'_{\Gamma'}$ of $t'(\mathbf{g}) = t'(\mathbf{hk})$ of $\mathbf{H}$ given $\mathbf{K} = \mathbf{k}$, obtaining the maximum $\overline{P}'_{\Gamma'}$ of the conditional P-values. Pointedly, *do not* assume $\mathbf{H}$ and $\mathbf{K}$ are independent.

Proposition: If H_0 is true, if $\Pr(\mathbf{K} = \mathbf{k})$ is one of the distributions $\mathbf{p} \in \mathcal{P}_\Gamma$, if $\Pr(\mathbf{H} = \mathbf{h} \,|\, \mathbf{K} = \mathbf{k})$ is one of the distributions $\mathbf{p}' \in \mathcal{P}'_{\Gamma'}$, then $\left(\overline{P}_\Gamma, \overline{P}'_{\Gamma'}\right)$ is stochastically larger than the uniform distribution on the unit square, so that $\Pr\left(\overline{P}_\Gamma \leq \alpha, \overline{P}'_{\Gamma'} \leq \alpha'\right) \leq \alpha\alpha'$ for all $0 \leq \alpha \leq 1$, $0 \leq \alpha' \leq 1$.

At the keyboard

```
library(DOS2)
data("periodontal")
attach(periodontal)
y<-pcteither[z==1]-pcteither[z==0]
x<-cigsperday[z==1]
senWilcox(y,gamma=2.75)
crosscutplot(x,y,ct=.2)
crosscut(x,y,ct=.2,gamma=1.6)
sensitivitymv::truncatedP(c(0.04651554,0.04433723))
```

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