Estimands, Missing Data, and Sensitivity Analysis

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Speakers’ Key Points

• Emerson
  ▶ comprehensive overview of current landscape
  ▶ prevention is critical
  ▶ sensitivity analyses are important
  ▶ there is no substitute for careful thought

• Scharfstein
  ▶ consider treatment strategies
  ▶ such strategies are defineable and include contingency plans
  ▶ define adherence precisely

• Ibrahim
  ▶ panitumumab: real example of treatment switching
  ▶ develop a class of “average” hazard ratios
Moving Forward

- Apply these principles to **pragmatic trials**
- Learn from evaluation of **treatment regimes** in adaptive settings
  - design treatment strategies to mimic clinical practice
  - maintain randomization to facilitate, if not guarantee, causal inference
Some Examples

- **Shared incentives** trial
- **ParentCorps** trials
Shared incentives participants

- 238 primary care physicians at 3 health systems
- 1,503 patients
  - age 18 – 80
  - high cardiac risk
  - high LDL cholesterol
- Four interventions
  - “control”
  - patient incentives: daily lottery for statin adherence
  - physician incentives: direct payments to physicians for quarterly goal achievement
  - shared incentives: both patient and physician, each at half value
- Primary outcome: change in LDL over 12 months
## SI: LDL reduction at 12 months

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Patient Incentives</th>
<th>Physician Incentives</th>
<th>Shared Patient and Physician Incentives</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta \text{LDL} )</td>
<td>26.6</td>
<td>26.4</td>
<td>30.0</td>
<td>36.8</td>
</tr>
<tr>
<td>CI</td>
<td>22.7 – 30.6</td>
<td>22.5 – 30.3</td>
<td>26.6 – 33.4</td>
<td>32.9 – 40.6</td>
</tr>
<tr>
<td>( p )</td>
<td>–</td>
<td>0.87</td>
<td>0.20</td>
<td>&lt; 0.001</td>
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</tbody>
</table>

\( p \)-value 0.87, 0.20, < 0.001
SI: Average LDL over time
SI: Interpretation

- This is an ITT estimate
- This is appropriate here
  - the interventions are *supplementary* to the primary treatment (daily statin)
  - we want to know what happens *system-wide* with these different programs
- How to explain the result?
  - adherence
  - medication initiation/intensification
SI: Average adherence over time
SI: Summary

- Physician incentives are no better than control
- Patient incentives are no better than control
- Shared incentives are better than control
  - each at half value
- Adherence is disappointingly low
• Physician incentives are no better than control
• Patient incentives are no better than control
• Shared incentives are better than control
  ▶ each at *half value*
• Adherence is disappointingly low
First ParentCorps trial

First ParentCorps trial
Ongoing ParentCorps trials

- Randomized evaluation of three tiers of services
  - professional learning for teachers
  - ParentCorps classroom program
  - ParentCorps family engagement program
- 80 NYC public schools and early education centers
  - high poverty
  - high minority population
- Enormous heterogeneity
  - leader engagement/enthusiasm
  - school/center capacity
  - degree of implementation
Ongoing ParentCorps trials: Questions

- What is the impact on early education achievement of implementing ParentCorps at scale?
- Does ParentCorps perform differently when implemented in schools and centers?
- What affects fidelity of implementation?
- How does fidelity of implementation affect results?
Final Thoughts

- **Clear specifications** are critical
  - interventions
  - outcomes
  - hypotheses
  - target population

- We have a **moral imperative** to get this right
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