

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 trial

Asch DA, Troxel AB, Stewart WF, Sequist TD, Hones JB, Hirsch AG, Hoffer K, Zhu J, Wang W, Hodlofski A, Frasch AB, Weiner MG, Finnerty DD, Rosenthal MB, Gangemi K, Volpp KG (2015). Effect of Financial Incentives to Physicians, Patients, or Both on Lipid Levels: A Randomized Clinical Trial. *JAMA* 314(18): 1926-35.

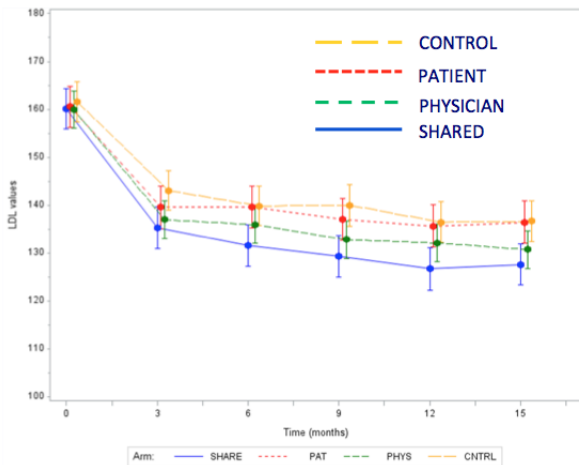
Shared incentives participants

- 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

| | Control | Patient Incentives | Physician Incentives | Shared Patient and Physician Incentives |
|--------------|-------------|--------------------|----------------------|---|
| Δ LDL | 26.6 | 26.4 | 30.0 | 36.8 |
| CI | 22.7 – 30.6 | 22.5 – 30.3 | 26.6 – 33.4 | 32.9 – 40.6 |
| <i>p</i> | – | 0.87 | 0.20 | < 0.001 |

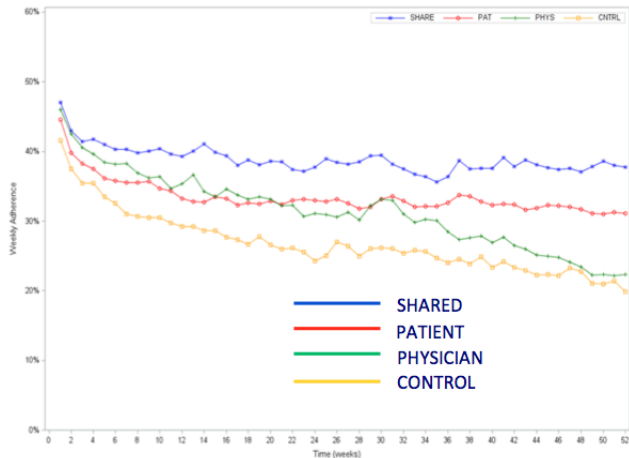
SI: Average LDL over time



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

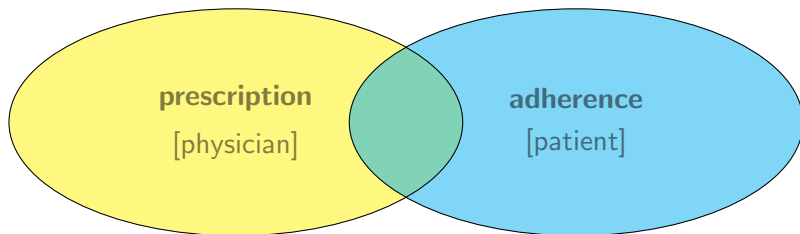


SI: Summary

- 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

SI: Summary

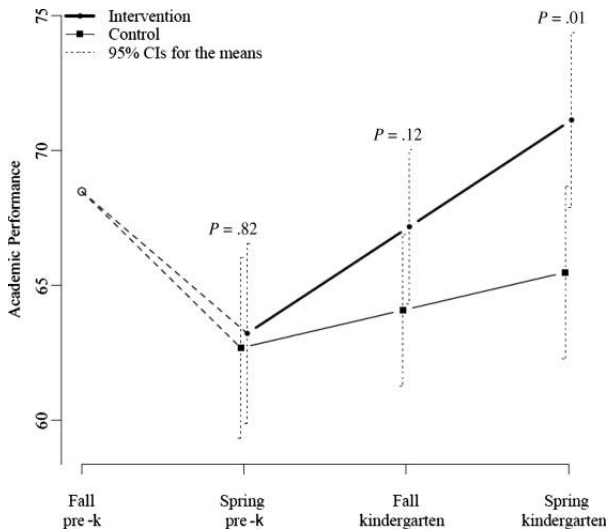
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First ParentCorps trial

Brotman LM, Dawson-McClure S, Calzada EJ, Huang KY, Kamboukos D, Palamar JJ, Pekova E. (2013). Cluster (school) RCT of ParentCorps: Impact on kindergarten academic achievement. *Pediatrics* 131(5): 1521-9.

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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