Modeling Adherence and Implementation:

Understanding Intervention Effects by Going Beyond Intent to Treat Analyses

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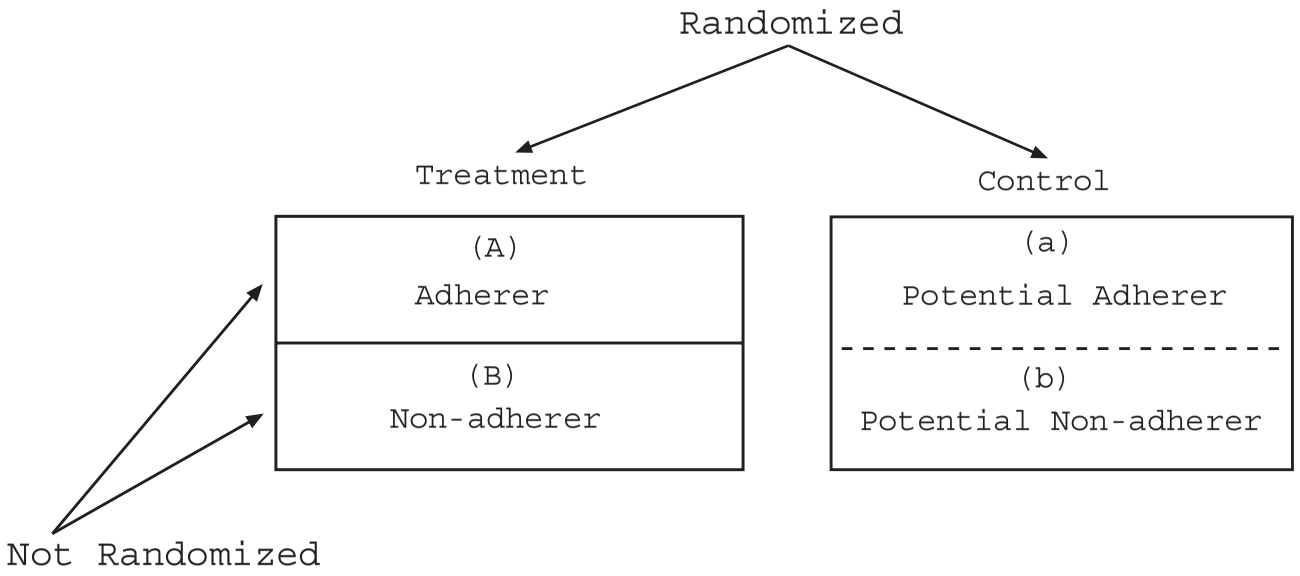
Modeling Difficulties with Non-Adherence in Randomized Field Experiments

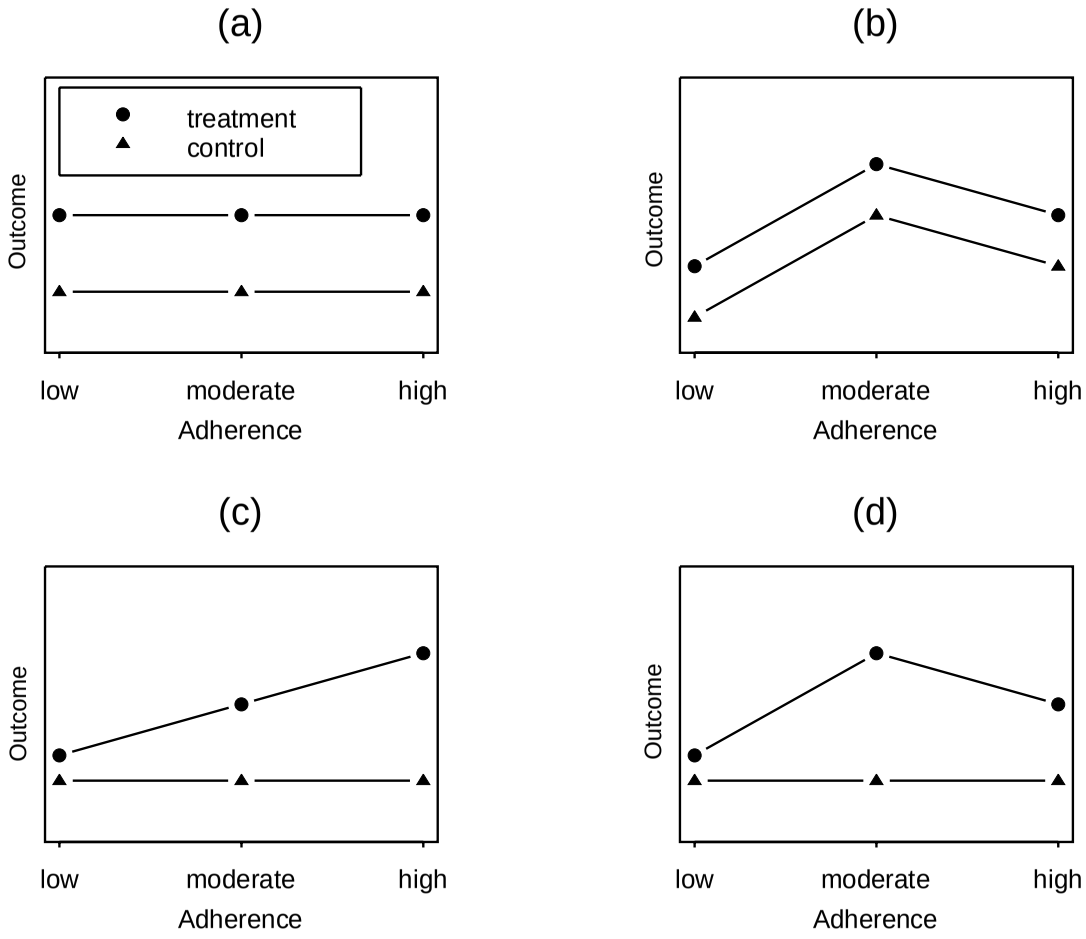
- Non-adherence affects intervention effect estimates and statistical power (Jo, in press-b).
- Efficacy of intervention trials is usually understated when ITT (intent to treat) analysis is applied (Frangakis & Baker, 2000; Sheiner & Rubin, 1995).
- Adherence among individuals assigned to the control group is usually unknown – handled as missing (latent) in CACE (complier average causal effect) estimation (Angrist, Imbens, & Rubin, 1996; Imbens & Rubin, 1997; Little & Yau, 1998).
- Treatment assignment may affect non-adherers (Hirano et al., 2000; Jo, 2001, in press-a).
- Dosage effects – Treatment effects may vary depending on the level of adherence (Jo, 2001), and may have a non-linear relationship with the level of adherence.
- Multilevel structures of data (e.g., cluster randomized trials, contextual effects) may affect intervention effect estimates and power (Frangakis, Rubin, & Zhou, 1998; Jo, Muthén, Ialongo, & Brown, 2002).
- Non-adherence can be related to non-response (non-ignorable missingness).

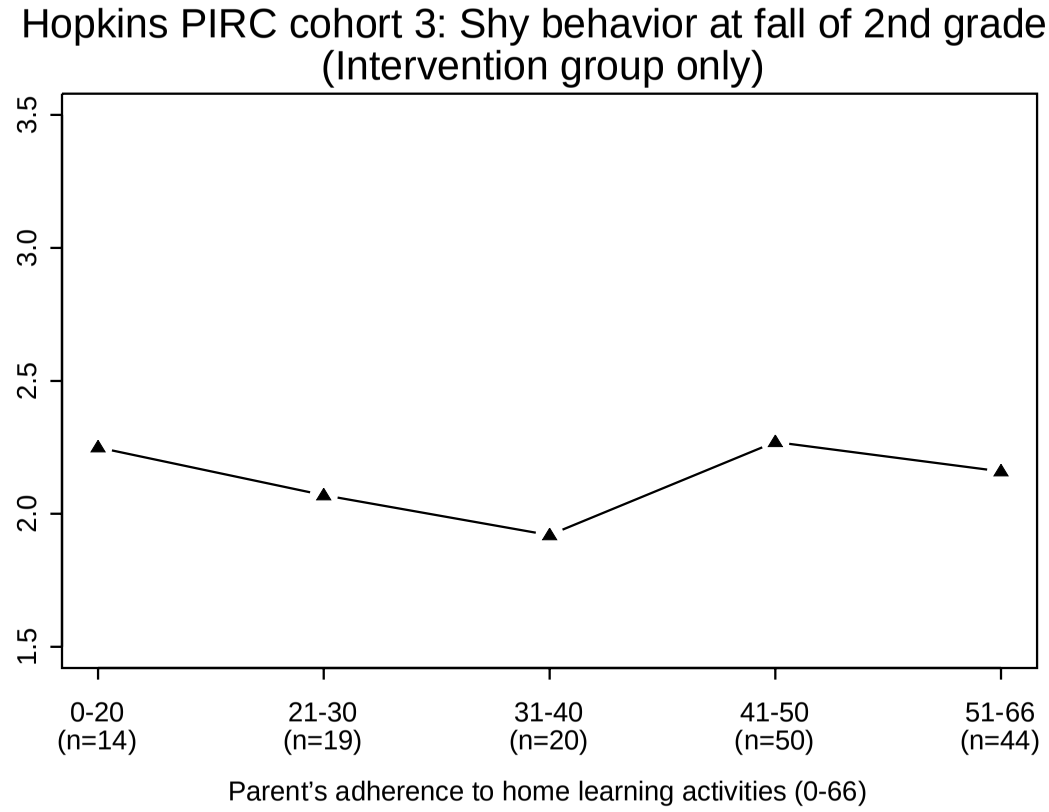
Non-Adherence



- Intent to Treat (ITT) analysis: (A+B) vs. (a+b)
- As-Treated (AT) analysis: (A) vs. (B+a+b)
- Per-Protocol analysis: (A) vs. (a+b)
- CACE estimation: (A) vs. (a)

Varying Levels of Adherence and Dosage Effects





- Which underlying assumptions should we impose?
- How do we classify individuals in the control group (identifiability)?
- How do we decide cut-points (is the choice of cut-points reasonable)?

Causal Effect Estimation with Varying Levels of Adherence

- In the standard CACE estimation method, causal effects of treatments are estimated assuming that the level of compliance is binary (none or all).
- In practice, intervention trials often include several treatment sessions or doses, and individuals may have varying levels of compliance.
- Statistical models should be carefully selected based on the most plausible assumptions.

– Dose Response Curve Analysis (Efron & Feldman, 1991)

– ALICE model (Holland, 1988)

– Ordinal Compliance Analysis (Goetghebeur & Molenberghs, 1996)

– Two-Stage Least Squares Estimation (Angrist & Imbens, 1995)

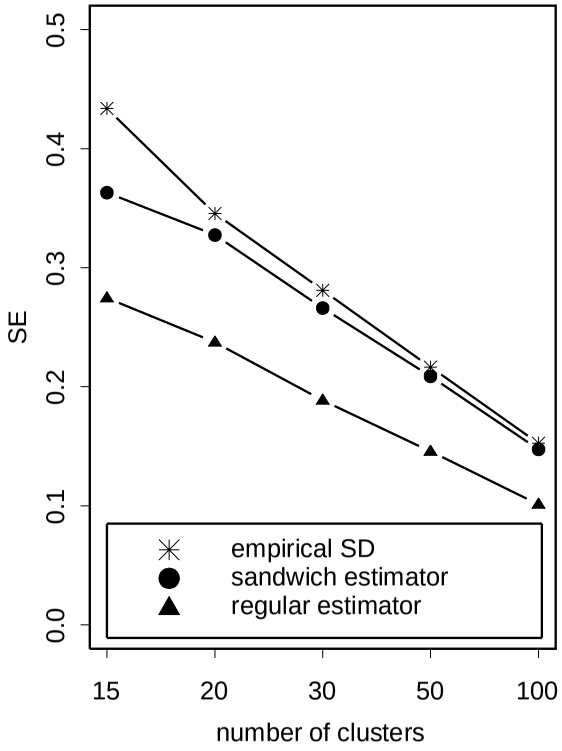
– Extensions of CACE approaches based on auxiliary information (Bayesian approach – Hirano et al., 2000; ML-EM approach – Jo, 2001)

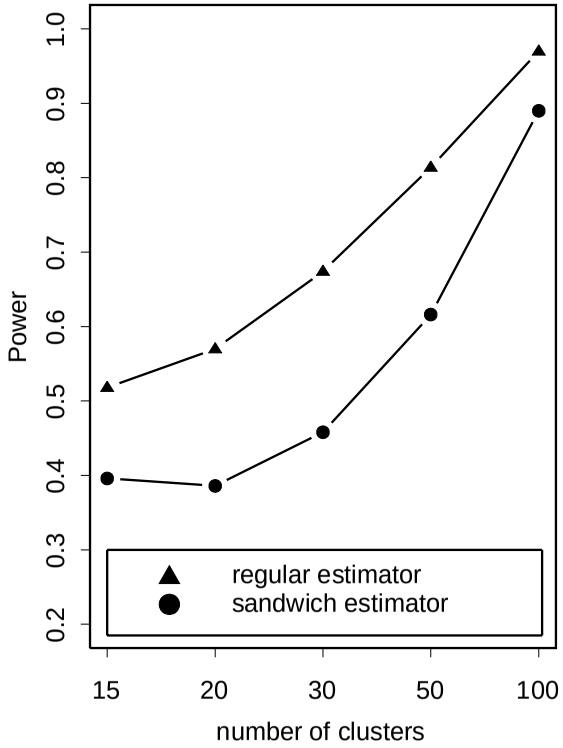
Cluster Randomized Trials (CRT) with Non-Adherence

- CRT is often used in field experiments for ethical/practical reasons, treating a group of individuals as the unit of randomization (e.g., patients within clinics, students within classrooms).
- Statistical challenges arise in CRT because inferences are often made at the individual level while randomization is carried out at the cluster level.
- If clustering is ignored in CRT, standard errors are usually underestimated, which results in inflation of statistical power (type I error).
- Adjustment of parameter estimates and standard errors is more complicated when CRT is accompanied by non-adherence.
- The unit of adherence can be a group (i.e., implementation), not an individual – a larger number of clusters is necessary. Covariate information that describes group (contextual) characteristics needs to be collected.

Standard Error and Power in CRT Using CACE Estimation

(ICC = 0.10, cluster size = 15, Simulations with 500 rep's, Mplus 2.01)





Example: Ialongo et al. (1999)
Hopkins PIRC cohort 3 Shy behavior at fall of 2nd grade

(N=277, 18 classrooms, raw ICC=0.154, average cluster size=15.3,
8 covariates included. Additive effect of treatment assumed. Mplus 2.01)

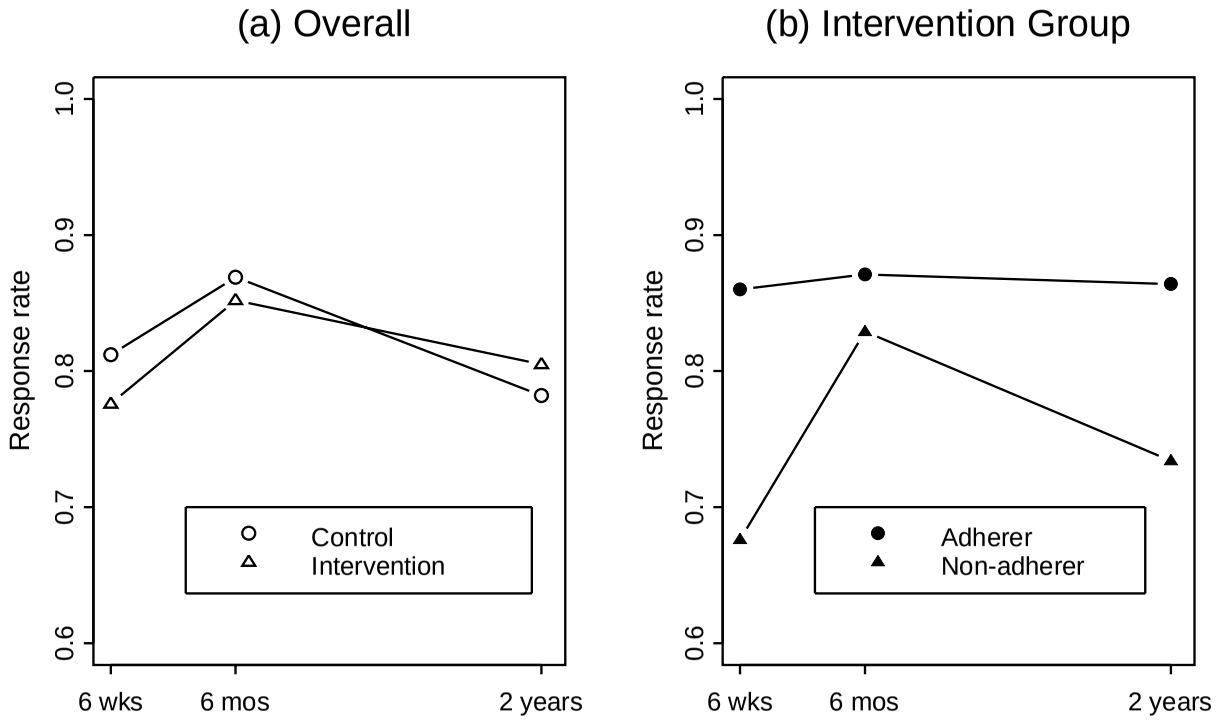
ITT Analysis

	Estimate	SE (regular)	SE (sandwich)
Overall (everybody)	-0.351	0.112	0.202

CACE Estimation

	Estimate	SE (regular)	SE (sandwich)
High Adherers (45-66: 50%)	-0.563	0.220	0.276
Low Adherers (0-44: 50%)	-0.106	0.188	0.350

Non-Adherence and Non-Response: JOBS II (Vinokur, Price, & Schul, 1995)



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