Published in final edited form as:

Clin Trials. 2014 June ; 11(3): 380–381. doi:10.1177/1740774514524650.

Letter to the Editor: Principal stratification: all-or-none versus partial compliance

Stuart G. Baker

EPN 3118 Bethesda Maryland 20892, United States

Keywords

principal stratification; noncompliance; randomized trial

I would like to add another perspective to that in Shrier et al [1] on the application of principal stratification [2] to all-or-none versus partial compliance. With all-or-none compliance in randomized trials [3] or all-or-none changes in availability in the paired availability design [4, 5], the assumptions needed for identifiability of the principal stratification model are often reasonable. Consider a binary outcome and suppose participants are randomized to either group 0 (assigned T0) or group 1 (assigned T1). The principal strata partition participants into pairs defined by (treatment received if in group 0, treatment received if in group 1), namely (T0,T0), (T0,T1), (T1,T0), and (T1,T1). Assuming rational decision making so no (T1,T0), persons receiving T0 in group 0 are a mixture of (T0,T0) and (T0,T1); persons receiving T1 in group 0 are (T1,T1); persons receiving T0 in group 1 are (T0,T0); and persons receiving T1 in group 1 are a mixture of (T0,T1) and (T1,T1). With the additional assumption that probabilities of outcome not depend on group for (T0, T0) and (T1, T1), one can estimate the effect of receipt of T0 versus T1 (treatment efficacy) in the principal stratum (T0,T1) for compliers, a result which can be elucidated graphically [5, 6]. In essence, this estimation peels away the irrelevant (T0,T0) and (T1,T1) strata [7] to obtain a more informative estimate of treatment efficacy (if the assumptions hold) than an intent-to-treat estimate. This identifiability of treatment efficacy in principal stratification under all-or-none compliance extends to missing binary outcomes [7, 8] and survival outcomes [9].

In contrast an application of principal stratification to partial compliance requires strong assumptions for identifiability. Consider treatment received initially and later yielding 16 principal strata, each of the form (initial treatment if randomized to group 0: later treatment if randomized to group 0, initial treatment if randomized to group 1: later treatment if randomized to group 1). Strong assumptions are needed to estimate treatment efficacy via the stratum of most interest, namely (T0:T0,T1:T1) [10]. However, under reasonable assumptions, the study can still yield an approximate estimate of treatment efficacy. The rational decision-making assumption implies no (T0:T1, T0:T0), (T1:T0,T0:T0), (T1:T0,T0:T1), (T1:T1,T0:T0), (T1:T1,T0:T1), or (T1:T1,T1:T0). Persons receiving T0:T0 in group 0 are (T0:T0,T0:T0) and persons receiving T1:T1 in group 1 are (T1:T1,T1:T1). We call the remaining persons partial compliers as they are a mixture of (T0:T0,T0:T1), (T0:T0,T1:T0), (T0:T0, T1:T1), (T0:T1,T0:T1), (T0:T1,T1:T0), (T0:T1,T1:T1), (T1:T0,

T1:T0), and (T1:T0,T1:T1). With the additional assumption that probabilities of outcome not depend on group for (T0:T0,T0:T0) and (T1:T1,T1:T1), the estimate of treatment efficacy when applying the usual principal stratification analysis under all-or-none compliance is an approximate estimate of treatment efficacy (with mixtures of initial and late treatments) among partial compliers. This approximate estimate of treatment efficacy in partial compliers, while not ideal, is still more informative than an intent-to-treat estimate with respect to treatment efficacy (if the assumptions hold) because it peels away strata (T0:T0,T0:T0) and (T1:T1,T1:T1). Another approach to estimating treatment efficacy under partial compliance involves a third randomization group and a modified principal stratification model [10].

Acknowledgments

This research was supported by the National Institutes of Health. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Shrier I, Steele RJ, Verhagen E, Herbert R, Riddell CA, Kaufman JS. Beyond intention to treat: What is the right question? *Clin Trials*. 2013 Oct 3. Epub ahead of print.
2. Frangakis CE, Rubin DB. Principle stratification in causal inference. *Biometrics*. 2002; 58:21–29. [PubMed: 11890317]
3. Angrist JD, Imbens GW, Rubin DB. Identification of causal effects using instrumental variables. *J Am Stat Assoc*. 1996; 92:444–455.
4. Baker SG, Lindeman KS. The paired availability design: a proposal for evaluating epidural analgesia during labor. *Stat Med*. 1994; 13:2269–2278. [PubMed: 7846425]
5. Baker SG, Lindeman KL. Revisiting a discrepant result: a propensity score analysis, the paired availability design for historical controls, and a meta-analysis of randomized trials. *J Causal Inference*. 2013; 1(1):51–82.
6. Baker SG. Causal inference, probability theory, and graphical insights. *Stat Med*. 2013; 32:4319–4330. [PubMed: 23661231]
7. Baker SG. Analyzing a randomized cancer prevention trial with a missing binary outcome, an auxiliary variable, and all-or-none compliance. *J Am Stat Assoc*. 2000; 95:43–50.
8. Frangakis CE, Rubin DB. Addressing complications of intention-to-treat analysis in the combined presence of all-or-none treatment-noncompliance and subsequent missing outcomes. *Biometrika*. 1999; 86:365–379.
9. Baker SG. Analysis of survival data from a randomized trial with all-or-none compliance: estimating the cost-effectiveness of a cancer screening program. *J Am Stat Assoc*. 1998; 93:929–934.
10. Baker SG, Frangakis C, Lindeman KS. Estimating efficacy in a proposed randomized trial with initial and later noncompliance. *J Roy Stat Soc, Ser C*. 2007; 56:211–221.