Poster PP11

Pragmatism Meets Precision

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ABSTRACT

Pragmatic trials (PTs) provide an invaluable means of evaluating real-world interventions, but their inherent complexity demands careful statistical planning. This poster explores key statistical considerations in PTs, offering insights into best practices for study design, data analysis, and interpretation of results.

INTRODUCTION

Pragmatic trials have gained significant attention in clinical research due to their ability to provide real-world evidence on the effectiveness of medical interventions. Unlike traditional explanatory trials, which are conducted under highly controlled conditions to determine efficacy, pragmatic trials are designed to reflect routine clinical practice. This means that PTs aim to answer questions that are directly relevant to patients, clinicians, and policymakers by evaluating interventions in diverse, everyday healthcare settings.

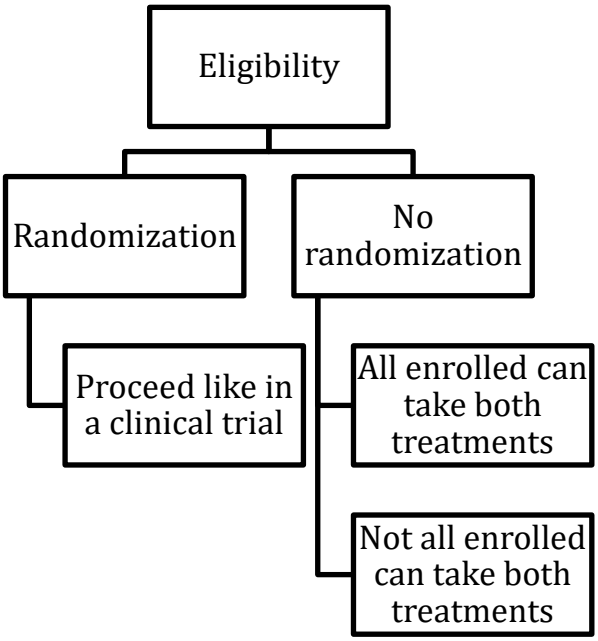
From a statistical standpoint, PTs present unique challenges and opportunities. The less restrictive inclusion criteria and the emphasis on real-world applicability lead to increased heterogeneity in study populations. This, in turn, necessitates careful consideration of statistical methodologies to ensure robust and reliable conclusions. Factors such as randomization, schedule of assessment, handling of missing data and compliance require a tailored approach that balances methodological rigor with practical feasibility.

THE PRECIS-2 TOOL

The PRECIS-2 (Proposed in the Pragmatic–Explanatory Continuum Indicator Summary 2) tool is a 9-dimension score to assess the level of pragmatism in a trial. [1]

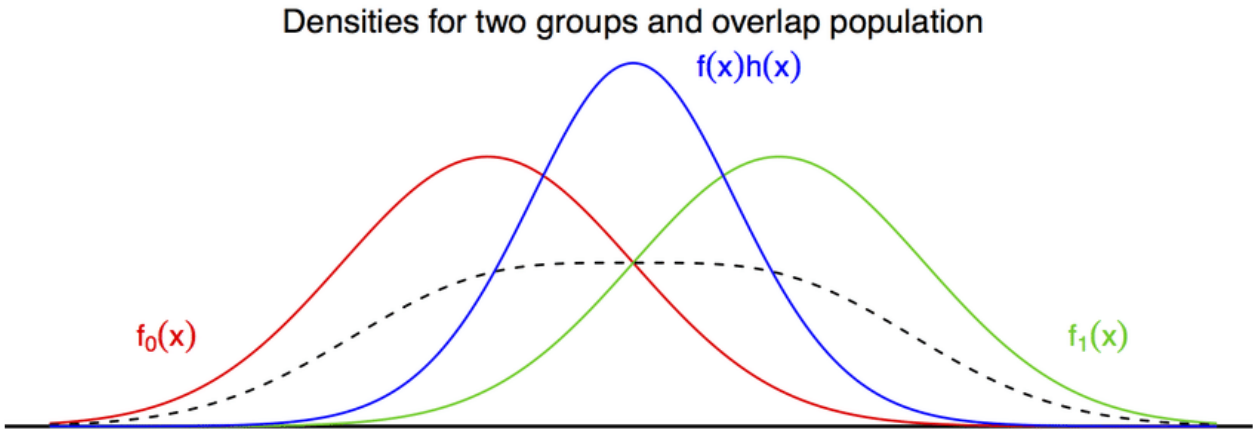
Dimension		Assessment of Pragmatism
Recruitment of investigators and participants	Eligibility	To what extent are the participants in the trial similar to patients who would receive this intervention if it was part of usual care?
	Recruitment	How much extra effort is made to recruit participants over and above what would be used in the usual care setting to engage with patients?
	Setting	How different are the settings of the trial from the usual care setting?
The intervention and its delivery within the trial	Organization	How different are the resources, provider expertise, and organization of care delivery in the intervention group of the trial from those available in usual care?
	Flexibility in delivery	How different is the flexibility in how the intervention is delivered from the flexibility anticipated in usual care?
	Flexibility in adherence	How different is the flexibility in how participants are monitored and encouraged to adhere to the intervention from the flexibility anticipated in usual care?
The nature of follow-up		How different is the intensity of measurement and the follow-up of participants in the trial from the typical follow-up in usual care?
The nature, determination, and analysis of outcomes	Primary outcome	To what extent is the primary outcome of the trial directly relevant to participants?
	Primary analysis	To what extent are all data included in the analysis of the primary outcome?

ELIGIBILITY

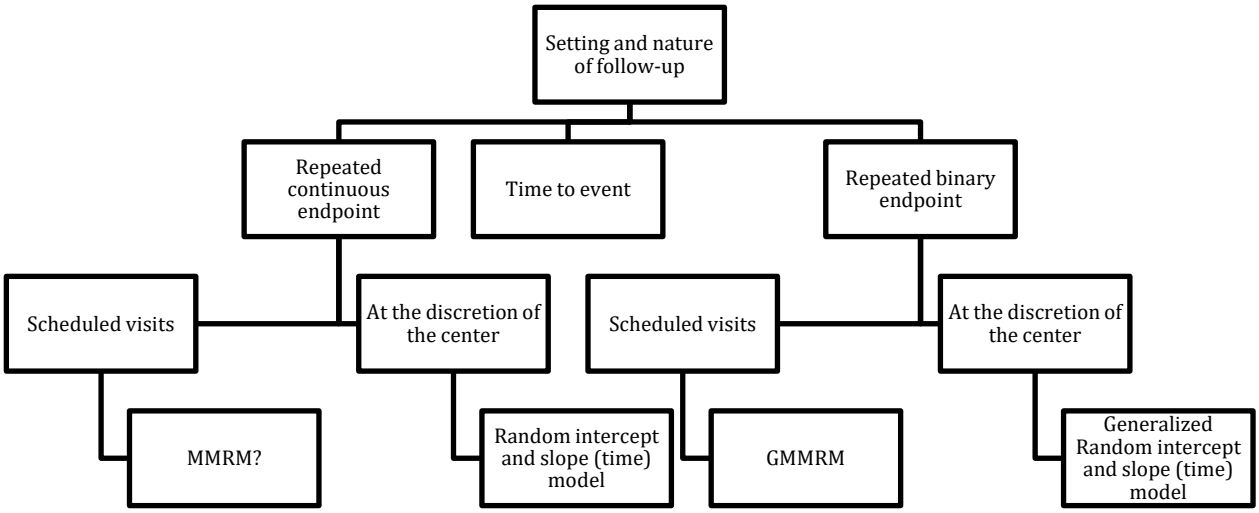


Target population	$h(x)$	Estimand	Weight (w_1, w_0)
Combined	1	ATE	$\left(\frac{1}{e(x)}, \frac{1}{1-e(x)}\right)$ [HT]
Treated	$e(x)$	ATT	$\left(1, \frac{e(x)}{1-e(x)}\right)$
Control	$1-e(x)$	ATC	$\left(\frac{1-e(x)}{e(x)}, 1\right)$
Overlap	$e(x)(1-e(x))$	ATO	$(1-e(x), e(x))$
Truncated combined	$\mathbf{1}(\alpha < e(x) < 1-\alpha)$		$\left(\frac{\mathbf{1}(\alpha<e(x)<1-\alpha)}{e(x)}, \frac{\mathbf{1}(\alpha<e(x)<1-\alpha)}{1-e(x)}\right)$
Matching	$\min\{e(x), 1-e(x)\}$		$\left(\frac{\min\{e(x),1-e(x)\}}{e(x)}, \frac{\min\{e(x),1-e(x)\}}{1-e(x)}\right)$

In absence of randomization, choose carefully all methods for balancing baseline characteristics [2]



SETTING + NATURE OF FOLLOW-UP



INTERVENTION AND ITS DELIVERY IN A TRIAL

A non-random list of random thoughts:

- For time to event endpoint use time-dependent covariates
- For models with repeated measures with continuous or binary outcomes, consider adding the compliance at each visit
- For models with outcome collection at random times with continuous or binary outcomes, consider adding the compliance at each time-point

If compliance or cumulative compliance depends on the medication type.

PRIMARY ANALYSIS

Use single/multiple imputation techniques to account for missing data, with different approaches [3], [4], [5]:

- MAR assumption
- Copy-reference
- Jump-to-reference

REFERENCES

[1] Ford, Ian, and John Norrie. “Pragmatic Trials.” The New England journal of medicine vol. 375,5 (2016): 454-63.

[2] Li, Fan, Kari Lock Morgan, and Alan M. Zaslavsky. 2017. “Balancing Covariates via Propensity Score Weighting.” Journal of the American Statistical Association 113 (521): 390–400.

[3] Rubin, D.B. “Inference and Missing Data.” Biometrika, 63(3), 1976: 581–592.

[4] White, I.R., Royston, P., & Wood, A.M. “Multiple Imputation Using Chained Equations: Issues and Guidance for Practice.” Statistics in Medicine, 30(4), 2011: 377-399.

[5] Wolbers, Marcel, et al. "Standard and reference-based conditional mean imputation." Pharmaceutical statistics 21.6 (2022): 1246-1257

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