# Should We Be Considering a Different Study Design?

Patrick Heagerty, PhD
Professor, Department of Biostatistics
University of Washington

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# “How to approach the design of an ePCT based on our collective experience?”

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# Multiple Considerations…

| | |
|---|---|
| **Embedded** | Healthcare context = different organizational levels/elements; clusters/complexity |
| **Pragmatic** | Sources of variation = setting; subjects; intervention delivery; study conduct; (and bias!) |
| **Longitudinal** | Time = changes in background; standard of care; intercurrent forces that impact study |
| **Design Structure** | Consider PICOTS (estimand) |
| **Design Process** | Consider peer/expert input (“cores”) |

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# Question → Design

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### *A.3.3. Estimand attributes*

The attributes below are used to construct the estimand, defining the treatment effect of interest.

The **treatment** condition of interest and, as appropriate, the alternative treatment condition to which comparison will be made (referred to as "treatment" through the remainder of this document). These might be individual interventions, combinations of interventions administered concurrently, e.g. as add-on to standard of care, or might consist of an overall regimen involving a complex sequence of interventions. (see Treatment Policy and Hypothetical strategies under A.3.2.).

The **population** of patients targeted by the clinical question. This will be represented by the entire trial population, a subgroup defined by a particular characteristic measured at baseline, or a principal stratum defined by the occurrence (or non-occurrence, depending on context) of a specific intercurrent event (see Principal Stratum strategies under A.3.2.).

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# Question → Design

The **variable** (or endpoint) to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event (see Composite Variable and While on Treatment strategies under A.3.2.).

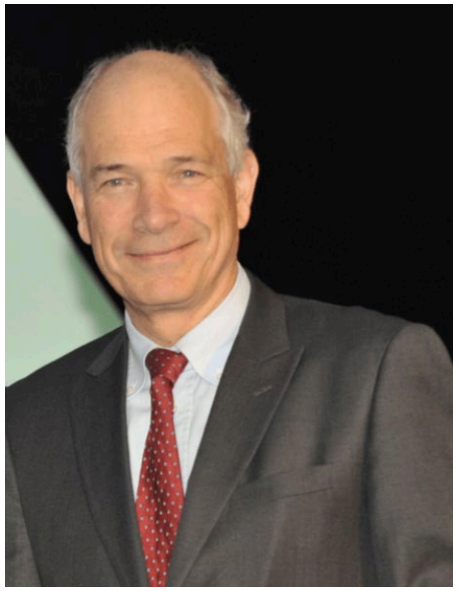
Precise specifications of treatment, population and variable are likely to address many of the intercurrent events considered in sponsor and regulator discussions of the clinical question of interest. The clinical question of interest in respect of any **other intercurrent events** will usually be reflected using the strategies introduced as treatment policy, hypothetical or while on treatment.

Finally, a **population-level summary** for the variable should be specified, providing a basis for comparison between treatment conditions.

# Some Key Discussion Points

- What were the initial considerations that motivated your chosen study design?
- How, if at all, did your perspective change after the trial began?
- What alternative designs would you consider in the future?

**Doug Zatzick, MD**
Professor,
Department of
Psychiatry and
Behavioral Sciences
University of
Washington School
of Medicine



**Vince Mor, PhD**
Professor of Health Services,
Policy & Practice
Florence Pirce Grant
Professor
Brown University School of
Public Health

**Myles Wolf, MD, MMSc**
Charles Johnson, MD,
Professor of Medicine
Chief, Division of Nephrology
Professor, Population Health
Sciences
Duke University School of
Medicine

**Susan Shortreed, PhD**
Senior Biostatistics Investigator
Kaiser Permanente Washington
Health Research Institute
Affiliate Professor, Biostatistics
University of Washington