What magnitude of HTE is sufficiently large to merit attention?

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Overview

- HTE is never 0, so testing is irrelevant
- The point estimate doesn't tell the whole story about magnitude; uncertainty is equally, possibly more, important
  - Ideally, report and use the full posterior distribution
  - Otherwise, report and use $_{2.5}\,_{25}\,50\,_{75}\,_{97.5}$, see [1]
- Calibrate HTE magnitude (including uncertainty) relative to goals
  - Quantitative/Qualitative
  - Regulatory decisions
  - Clinical decisions
  - Patient communication (snapshots)
  - Therapeutic effects and side effects, (S)AEs
- Need sufficient stability

[1] Louis TA, Zeger SL (2009). Effective Communication of Standard Errors and Confidence Intervals. *Biostatistics*, 10: 1-2.

Design & Analysis

For a single study

- $\widehat{HTE}$ = difference of differences; $V\left(\widehat{HTE}\right) \approx 4 \times V\left(\widehat{TE}\right)$

  $\Longrightarrow$ Combining/borrowing information is usually necessary
- Need to estimate/accommodate the between-context variance component
- Small number of clusters/clinics or small n for each $\Longrightarrow$ need to stabilize
  - Within study, hierarchical models with regressors/strata, possibly Bayesian with an informative prior

Across studies

- Prospective harmonization/alignment
  - data definitions
  - regressors
  - design, follow-up
  - censoring policy: no news is no news vs no news is good news
  - .....

It's complicated

- Therapeutic effects and side effects, (S)AEs
- Cost
- Complicated, multivariate decision regions,
  best structured by a utility function
  - Inputs are underlying truths
  - **The Bayesian formalism is essential**
  - Sensitivity analysis, including threshold utility boundaries
- Transportation [2,3]
  - Pay attention to the reference population and to the next study
  - Measure baseline attributes you may not need for the current study, but that can help transport

[2] Keiding N, Louis TA (2016). Perils and potentials of self-selected entry to epidemiological studies and surveys (with discussion and response). *J. Roy. Statist. Soc., Ser. A*, 179: 319–376.

[3] Keiding N, Louis TA (2018). Web-based Enrollment and other types of Self-selection in Surveys and Studies: Consequences for Generalizability. *Annual Review of Statistics and Its Application*, 5: 25–47.