Imperial College London

EFSPI

European Federation of Statisticians in the Statistical Industry

Promoting professional standards in Europe

BBS

Basel Biometric Society

Discussion on treatment policy strategy

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Key take-aways for estimation

- Design trial to maximise data collection after IE's

- The most appropriate estimation tool depends on proportion of data obtained post IE

None/minimal missingness

-Standard MMRM/MI

-Retrieved drop out MI/MMRM; time independent

-Retrieved drop out MI/MMRM; time dependent

-Reference based analysis

(i) via MI

(ii) via conditional mean imputation + jackknifing

High missingness

Reference based analysis

- MI vs. conditional mean imputation + jackknife:
  - Comparable point estimate
  - But variance estimator will be quite different!!...

- MI + Rubin's rules provides **information anchored inference**:
  - the increase in variance due to missing data is approx. the same as that seen under the MAR assumption
  - variance estimate logically larger than if could fully observe the reference-based behaviour
  - the more missing data the larger the variance estimate

- Conditional mean imputation + jackknife provides **traditional frequentist long-run inference**:
  - variance < variance when observe data under reference-based behaviour
  - the more missing data the smaller the variance

Stata software

- **Mimix** implements the reference-based MI procedures of Carpenter, Roger, Kenward 2013 (MAR, CR, J2R, CIR, LMCF)

- Extensively tested against James Rogers' SAS macro **miwithd**

Reference: Cro S, Morris TP, Kenward MG, Carpenter JR. Reference-based sensitivity analysis via multiple imputation for longitudinal trials with protocol deviation. *Stata J*. 2016 Apr;16(2):443-463. PMID: 29398978; PMCID: PMC5796638.