UMC Utrecht

Methods to deal with missing data

K.G.M. Moons, PhD
k.g.m.moons@umcutrecht.nl

Methods to handle missing data

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method (See exercise)

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

Complete Case

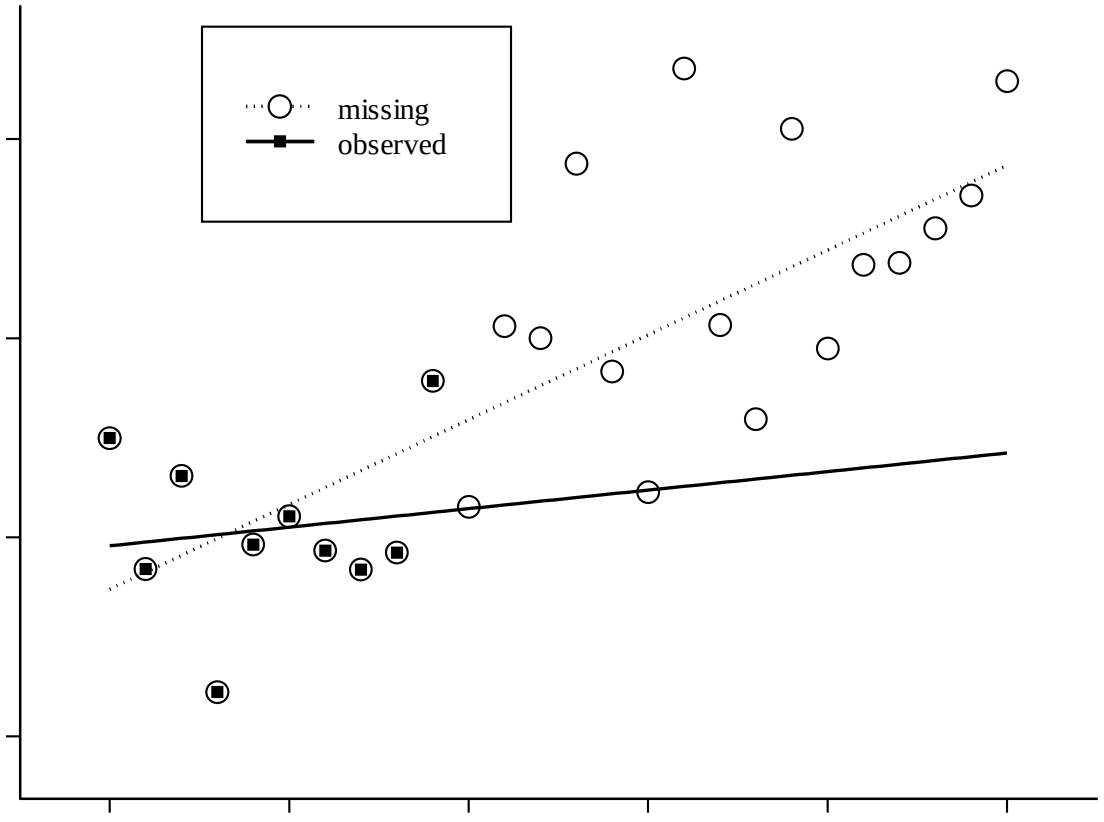
- All analyses (Y = X's models) on the same subset with completely observed X's and Y's

- See previous lecture and exercise:
  - If MCAR (though seldom):
    - Less precision
    - Unbiased/valid results

  - If MAR (as usual + more likely missing data become MAR with much documented/observed other data):
    - Less precision
    - (Very) biased/invalid results

Example correlation/regression

Clearly not MCAR - due to change in values/range → association changes



Complete Case

- CC = in fact redefinition of study sample and thus of the source/target population (domain)
  - E.g. missings in specific hospital/country → study population becomes 'all subjects in completely observed hospitals/countries'
  - E.g. missing outcomes in RCTs → 'Results apply to patients who with complete f-up'
- **Redefinition of your study sample and thus source population is not a solution to a CC analysis if missing data are not MCAR?**

Methods to handle missing data

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method (See exercise)

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

Available case

- Use in each sub-analysis (in each model Y=X's) the records with complete data on the X's and Y in that model (sub-analysis)
- Most used method to deal with missing values
- Problems similar as CC
  - Less precision – although AC more efficient → the smaller models (with less X's) use more records/data
  - Unbiased if MCAR ; biased if MAR
- In prediction modeling AC is even a bigger problem than CC: Why?
  - Number of subjects is different for each model
  - Reduced + extended prediction models compared on different subjects
    - Interpretation or even estimation problems (e.g. added value)

Methods to handle missing data
Simple methods (ad hoc)

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method (See exercise)

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

Methods to handle missing data

The imputation methods!!

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method (see exercise)

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

Imputation methods

- **Imputation is replacement** –> preferred method

- Missing participant values on one or more study variables are replaced by 'predicted values/best guesses' which are based on the observed data

- Can be done if MAR – recall previous lecture and exercise:

  - If association between missingness (yes/no) with other observed variables…
  - … These other observed variables thus convey information on missingess
  - … And can thus be used to 'guess/predict' the missing variable value.

Overall mean/median imputation

- For each missing on variable Z → overall mean of that variable Z from observed subject-values is imputed
  - Diseased (Outcome+) and Non-diseased (Outcome-) combined
- All imputations have same value for Z → Consequence?
  - Distributions of Z for Outcome+ and Outcome- merge (MORE overlap)
  - Association of Z on Outcome dilutes → Bias
  - Also: distribution of Z becomes narrower (SD too low)
    - SE's of association underestimated → too often significant

ALWAYS: ALSO IF MCAR!

Methods to handle missing data

The imputation methods!!

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

Subgroup mean/median imputation

- A priori relevant subgroups are defined → based on associations with variable (Z) with missings
  - E.g. per outcome category, sex, age groups, etc.
- Estimate mean/median for subgroup
  - For each missing on Z → subgroup mean is imputed
- More variations in imputed values than overall mean/median
  - Less bias though SE's still underestimated
  - Limited number of co-variates can a-priori be defined
  - Requires categorisation for continuous variables (loss of information)

Methods to handle missing data

The imputation methods!!

Complete case analysis (CC)

Available case analysis (AC)

Missing indicator method

Overall mean/median imputation

Subgroup mean/median imputation

Single (multivariable) regression based imputation

Multiple regression based imputation

NEXT LECTURES

References

- A gentle introduction to imputation of missing values (Donders JCE 2006)
- Handling missing data in multivariable diagnostic research: a clinical example (van der Heijden JCE 2006).
- Using the outcome variable to impute missing values of predictor variables: a self fulfilling prophecy? (Moons JCE 2006)
- To Impute is better than to ignore (Janssen JCE 2010)
- Dealing with missing values when validating a prediction model (Janssen Clin Chem 2009)
- Imputation of missing outcomes in observational and randomised studies (Groenwold AJE 2012)
- Little et al; New Engl J Med 2012
- Randomized trials with missing outcomes: what to report and how to analyze (Groenwold et al, *CMAJ 2014)*

Thank you for your attention