Statistical Methods for Analysis with Missing Data

Lecture 3: naïve methods: complete-case analysis and imputation

Mauricio Sadinle

Department of Biostatistics

UNIVERSITY of WASHINGTON
Previous Lecture

Universe of missing-data mechanisms:

- **MCAR**: $p(R = r \mid z) = p(R = r)$
  - Unreasonable in most cases

- **MAR**: $p(R = r \mid z) = p(R = r \mid z_{(r)})$
  - Hard to digest, in general
  - $R \perp \perp Z_1 \mid Z_2$, if $Z_2$ fully observed

- **MNAR**: $p(R = r \mid z) \neq p(R = r \mid z_{(r)})$
  - Most realistic, but hard to handle
Today’s Lecture

Naïve or ad-hoc methods

- Complete-case / available-case analyses
- Different types of (single) imputation

Reading: Ch. 2, of Davidian and Tsiatis
Naïve or Ad-Hoc Methods

- Motivation: we know how to run analyses with complete (rectangular) datasets

- Idea: somehow “fix” the dataset so that the analysis for complete data can be run
Outline

Complete-Case and Available-Case Analysis
Complete-Case Analysis
Available-Case Analysis

Imputation
Mean Imputation
Mode Imputation
Regression Imputation
Hot-Deck Imputation
Last Observation Carried Forward

Summary
Outline

Complete-Case and Available-Case Analysis
  Complete-Case Analysis
  Available-Case Analysis

Imputation
  Mean Imputation
  Mode Imputation
  Regression Imputation
  Hot-Deck Imputation
  Last Observation Carried Forward

Summary
Complete-Case Analysis

- Idea: ignore observations with missingness, run intended analysis with remaining data
## Complete-Case Analysis

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... ... ... ...
Assumption for Complete-Case Analysis

Complete-case analysis implicitly assumes

\[ p(z) = p(z \mid R = 1_K) \]  \hfill (1)

where \( 1_K \) represents a vector \((1, 1, \ldots, 1)\) of length \( K \)

- By Bayes’ theorem

\[
p(z \mid R = 1_K) = \frac{p(R = 1_K \mid z)p(z)}{p(R = 1_K)}
\]

- Therefore, (1) is equivalent to

\[
p(R = 1_K \mid z) = p(R = 1_K)
\]

- This doesn’t require any assumptions on \( p(R = r \mid z) \) for \( r \neq 1_K \)

- MCAR \((Z \perp \!\!\!\perp R)\) is a sufficient condition for (1)
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Complete-Case Analysis is Wasteful/Inefficient

Clearly, there can be a huge waste of information

- Observed data with response patterns \( r \neq 1_K \) should be informative about the distribution of \( Z_r \), which is informative about the distribution of \( Z \)

\[
p(z_r) = \int p(z) \, dz_r, \quad r \in \{0, 1\}^K
\]

- We might end up with very little data

  - Say the \( R_1, \ldots, R_K \) i.i.d. Bernoulli(\( \pi \))

  - \( p(R = 1_K) = \pi^K \xrightarrow{K \to \infty} 0 \)
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Example: Estimating a Mean

We’ll see an alternative presentation of Example 1 in Section 1.4 of Davidian and Tsiatis

- \( \{(Y_i, R_i)\}_{i=1}^{n} \sim F \)
- \( Y_i \): numeric variable for individual \( i \)
- \( R_i \): indicator of \( Y_i \) being observed
- If \( Y_i \) was always observed, we could estimate the mean of \( Y \), \( \mu = E(Y) \), as

\[
\hat{\mu}_{full} = \frac{1}{n} \sum_{i=1}^{n} Y_i
\]
Example: Estimating a Mean

With missing data, we could use the complete cases

\[ \hat{\mu}^{cc} = \frac{\sum_{i=1}^{n} Y_i R_i}{\sum_{i=1}^{n} R_i} \]

Is this any good?

HW1: show that the following holds

\[ E(\hat{\mu}^{cc}) = E(Y \mid R = 1) \]

for all sample sizes, provided that at least one \( Y_i \) is observed.

Hint: write \( E(\hat{\mu}^{cc}) = E \left[ E \left( \frac{\sum_{i=1}^{n} Y_i R_i}{\sum_{i=1}^{n} R_i} \mid R_1, \ldots, R_n \right) \right] \)
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\[ E(\hat{\mu}^{cc}) = E(Y \mid R = 1) \]

Therefore

- Complete-case estimator of the mean requires assuming
  \[ E(Y) = E(Y \mid R = 1) \]

- In particular, valid under MCAR

- Otherwise, \( \hat{\mu}^{cc} \) is not valid for \( \mu \), as it estimates the wrong quantity

- HW1: if \( p(R = 1 \mid y) \) is an increasing function of \( y \), show that
  \[ E(Y \mid R = 1) > E(Y) \]
Example: Estimating a Mean

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Available-Case Analysis

Sometimes what we need to estimate doesn’t really require a “rectangular” dataset

- If you can, just use whatever data are available for computing what you need

- Davidian and Tsiatis talk about generalized estimating equations (GEEs) and their Example 3 in Section 1.4 (we’ll cover this when we get to Chapter 5)

- \( K \) normal random variables: under some missing-data assumption, it seems we could still obtain a good estimate of the distribution as it only depends on univariate and bivariate quantities (means, variances, covariances)
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Example of Available-Case Analysis

Say the data are

- $Z_i = (Y_{i1}, \ldots, Y_{iK})$
- $R_i = (R_{i1}, \ldots, R_{iK})$

Available-case estimators:

\[
\hat{\mu}_{ac}^j = \frac{\sum_{i=1}^{n} Y_{ij} R_{ij}}{\sum_{i=1}^{n} R_{ij}}, \quad j = 1, \ldots, K
\]

\[
\hat{\sigma}_{jk}^{ac} = \frac{\sum_{i=1}^{n} (Y_{ij} - \hat{\mu}_{ac}^j)(Y_{ik} - \hat{\mu}_{ac}^k)R_{ij}R_{ik}}{\sum_{i=1}^{n} R_{ij}R_{ik} - 1}; \quad j, k = 1, \ldots, K
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Better than complete-case analysis

Valid under MCAR, but what are the minimal assumptions on the missing-data mechanism for this to be valid?
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Better than complete-case analysis

Valid under MCAR, but what are the minimal assumptions on the missing-data mechanism for this to be valid?
Complete-Case and Available-Case Analysis

The moral:

- Complete-case analysis is wasteful and, most likely, invalid

- Available-case analysis is better, but still requires MCAR or possibly a weaker assumption depending on what we need to compute
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Imputation
  Mean Imputation
  Mode Imputation
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  Last Observation Carried Forward

Summary
Imputation

- Idea: plug something “reasonable” into the holes of the dataset, then run intended analysis with completed data
## Imputation

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Summary
Mean Imputation

- Numeric variables
  - Impute mean of observed values
  - Corresponds to imputing an estimate of $E(Y_j \mid R_j = 1), j = 1, \ldots, K$
  - Leads to valid point estimates of means under MCAR
  - Underestimates true variance of estimators
Mean Imputation

Say the data are

- $\{(Z_i, R_i)\}_{i=1}^n \sim F$
- $Z_i = (Y_{i1}, \ldots, Y_{iK})$
- $R_i = (R_{i1}, \ldots, R_{iK})$

Mean imputation:

- Compute

$$\hat{\mu}_j^1 = \frac{\sum_{i=1}^n Y_{ij} R_{ij}}{\sum_{i=1}^n R_{ij}}, \quad j = 1, \ldots, K$$

- Impute $Y_{ij}$ with $\hat{\mu}_j^1$ whenever $R_{ij} = 0$

- Run your analysis as if your data were fully observed
Mean Imputation

Say the data are

\[ \{ (Z_i, R_i) \}_{i=1}^{n} \sim F \]

\[ Z_i = (Y_{i1}, \ldots, Y_{iK}) \]

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Mean imputation:

\[ \text{Compute} \]

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\[ \text{Impute } Y_{ij} \text{ with } \hat{\mu}_j^1 \text{ whenever } R_{ij} = 0 \]

\[ \text{Run your analysis as if your data were fully observed} \]
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- Impute \( Y_{ij} \) with \( \hat{\mu}_j^1 \) whenever \( R_{ij} = 0 \)

- Run your analysis as if your data were fully observed
Mean Imputation

Say the data are

\[ \{(Z_i, R_i)\}_{i=1}^{n} \sim \text{i.i.d. } F \]

\[ Z_i = (Y_{i1}, \ldots, Y_{iK}) \]

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Mean imputation:

\[ \widehat{\mu}_{ij} = \frac{\sum_{i=1}^{n} Y_{ij} R_{ij}}{\sum_{i=1}^{n} R_{ij}}, \quad j = 1, \ldots, K \]

Impute \( Y_{ij} \) with \( \widehat{\mu}_{ij} \) whenever \( R_{ij} = 0 \)

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\[
\hat{\mu}_{\text{Age}} \quad \hat{\mu}_{\text{Income}} \\
\]
Example: Estimating a Mean

- Estimating a mean after mean imputation corresponds to using the estimator

\[
\hat{\mu}_j^{\text{mimp}} = \frac{1}{n} \sum_{i=1}^{n} [Y_{ij} R_{ij} + \hat{\mu}_1^j (1 - R_{ij})]
\]

- \(\hat{\mu}_j^{\text{mimp}}\) is the mean of the imputed data, so its naively estimated variance is

\[
\hat{\sigma}_\text{naïve}(\hat{\mu}_j^{\text{mimp}}) = \hat{\sigma}_\text{naïve}(Y_j)/n
\]

where

\[
\hat{\sigma}_\text{naïve}(Y_j) = \frac{1}{n - 1} \sum_{i=1}^{n} [R_{ij}(Y_{ij} - \hat{\mu}_j^{\text{mimp}})^2 + (1 - R_{ij})(\hat{\mu}_1^j - \hat{\mu}_j^{\text{mimp}})^2]
\]

- HW1: show that \(\hat{\mu}_j^{\text{mimp}} = \hat{\mu}_1^j\)
Example: Estimating a Mean

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\[
\hat{V}_{\text{naive}}(\hat{\mu}_j^{\text{mimp}}) = \frac{\hat{V}_{\text{naive}}(Y_j)}{n}
\]

where

\[
\hat{V}_{\text{naive}}(Y_j) = \frac{1}{n-1} \sum_{i=1}^{n} [R_{ij}(Y_{ij} - \hat{\mu}_j^{\text{mimp}})^2 + (1 - R_{ij})(\hat{\mu}_j^1 - \hat{\mu}_j^{\text{mimp}})^2]
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- HW1: show that \(\hat{\mu}_j^{\text{mimp}} = \hat{\mu}_j^1\)
Example: Estimating a Mean

- Estimating a mean after mean imputation corresponds to using the estimator

\[ \hat{\mu}_{j}^{\text{mimp}} = \frac{1}{n} \sum_{i=1}^{n} [Y_{ij}R_{ij} + \hat{\mu}_{1j}(1 - R_{ij})] \]

- \( \hat{\mu}_{j}^{\text{mimp}} \) is the mean of the imputed data, so its naïvely estimated variance is

\[ \hat{\text{V}}_{\text{ naïve}}(\hat{\mu}_{j}^{\text{mimp}}) = \frac{\hat{\text{V}}_{\text{ naïve}}(Y_{j})}{n} \]

where

\[ \hat{\text{V}}_{\text{ naïve}}(Y_{j}) = \frac{1}{n - 1} \sum_{i=1}^{n} [R_{ij}(Y_{ij} - \hat{\mu}_{j}^{\text{mimp}})^2 + (1 - R_{ij})(\hat{\mu}_{1j} - \hat{\mu}_{j}^{\text{mimp}})^2] \]

- HW1: show that \( \hat{\mu}_{j}^{\text{mimp}} = \hat{\mu}_{1j}^{1} \)
Example: Estimating a Mean

As a consequence, using the mean imputation method we:

- Underestimate the variance of each variable:
  \[ \hat{V}_{\text{naïve}}(Y_j) = \frac{1}{n-1} \sum_{i=1}^{n} R_{ij} (Y_{ij} - \hat{\mu}_j)^2 \]

- Compare with an estimate based on the available cases:
  \[ \hat{V}^1(Y_j) = \frac{\sum_{i=1}^{n} R_{ij} (Y_{ij} - \hat{\mu}_j)^2}{\sum_{i=1}^{n} R_{ij} - 1} \]

\[ \implies \hat{V}_{\text{naïve}}(Y_j) \leq \hat{V}^1(Y_j) \]
Example: Estimating a Mean

As a consequence, using the mean imputation method we:

▶ Underestimate the variance of $\hat{\mu}_j^{\text{mimp}}$:

$$\hat{V}_{\text{naïve}}(\hat{\mu}_j^{\text{mimp}}) = \frac{1}{n(n-1)} \sum_{i=1}^{n} R_{ij}(Y_{ij} - \hat{\mu}_j^1)^2$$

▶ Compare with an estimate based on the available cases:

$$\hat{V}^1(\hat{\mu}_j^{\text{mimp}}) = \frac{\sum_{i=1}^{n} R_{ij}(Y_{ij} - \hat{\mu}_j^1)^2}{(\sum_{i=1}^{n} R_{ij})(\sum_{i=1}^{n} R_{ij} - 1)}$$

▶ $\implies \hat{V}_{\text{naïve}}(\hat{\mu}_j^{\text{mimp}}) \leq \hat{V}^1(\hat{\mu}_j^{\text{mimp}})$

▶ HW1: comment on the implications of mean imputation for the construction of confidence intervals
Example: Estimating a Mean

As a consequence, using the mean imputation method we:

- Underestimate the variance of $\hat{\mu}_j^{\text{mimp}}$:

  $$\hat{V}_{\text{naïve}}(\hat{\mu}_j^{\text{mimp}}) = \frac{1}{n(n-1)} \sum_{i=1}^{n} R_{ij} (Y_{ij} - \hat{\mu}_j^1)^2$$

- Compare with an estimate based on the available cases:

  $$\hat{V}^1(\hat{\mu}_j^{\text{mimp}}) = \frac{\sum_{i=1}^{n} R_{ij} (Y_{ij} - \hat{\mu}_j^1)^2}{(\sum_{i=1}^{n} R_{ij})(\sum_{i=1}^{n} R_{ij} - 1)}$$

  $$\Rightarrow \hat{V}_{\text{naïve}}(\hat{\mu}_j^{\text{mimp}}) \leq \hat{V}^1(\hat{\mu}_j^{\text{mimp}})$$

- **HW1**: comment on the implications of mean imputation for the construction of confidence intervals
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Summary
Mode Imputation

- Categorical variables
  - Impute mode of observed values
  - Artificially inflates frequency of mode
  - Leads to valid point estimates of marginal modes under MCAR
  - Underestimates true variance of estimators
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  Last Observation Carried Forward

Summary
Regression Imputation

- Regress one variable on others based on observed data, then impute predicted values from model

- Corresponds to imputing an estimate of $E(Y_j | y_{-j}, R = 1_K)$, where $y_{-j} = (y_1, \ldots, y_{j-1}, y_{j+1}, \ldots, y_K)$

- Valid for means under MCAR

- Underestimates true variance of estimators

- Validity depends on model used for imputation
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Example of Regression Imputation in Davidian and Tsiatis

- \( Z = (Y_1, Y_2) \), baseline and follow-up, \( Y_1 \) always observed

- \( R \) indicator of response for \( Y_2 \)

- Goal: to estimate \( \mu_2 = E(Y_2) \)

- Say we posit a linear model \( E(Y_2 | y_1) = \beta_0 + \beta_1 y_1 \)

- Impute \( Y_{i2} \) with \( \hat{Y}_{i2} = \hat{\beta}_0 + \hat{\beta}_1 Y_{i1} \) when \( R_i = 0 \), with \( \hat{\beta}_0 \) and \( \hat{\beta}_1 \) obtained via least squares among complete cases

- The regression imputation estimator for \( \mu_2 \) is

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\hat{\mu}_2^{imp} = \frac{1}{n} \sum_{i=1}^{n} [Y_{i2} R_i + \hat{Y}_{i2} (1 - R_i)]
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- When is this valid? (when does \( \hat{\mu}_2^{imp} \xrightarrow{n\to\infty} \mu_2 \)?)
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Davidian and Tsiatis show that for $\hat{\mu}_2 \xrightarrow{n \to \infty} \mu_2$ ($\hat{\mu}_2 \xrightarrow{p} \mu_2$) we need these two requirements to hold simultaneously:

- $E(Y_2 | y_1, R = 1) = E(Y_2 | y_1)$ (implied by MAR)

- $E(Y_2 | y_1)$ is correctly specified, i.e., there really exist $\beta_0^*$ and $\beta_1^*$ such that $E(Y_2 | y_1) = \beta_0^* + \beta_1^* y_1$

However, even if these two conditions hold, single imputation leads to underestimation of variances, as seen with mean imputation.
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Complete-Case and Available-Case Analysis
  Complete-Case Analysis
  Available-Case Analysis

Imputation
  Mean Imputation
  Mode Imputation
  Regression Imputation
  Hot-Deck Imputation
  Last Observation Carried Forward

Summary
Hot-Deck Imputation

- Replace missing values of a non-respondent (called the recipient) with observed values from a respondent (the donor)

- Recipient and donor need to be similar with respect to variables observed by both cases
  - Donor can be selected randomly from a pool of potential donors
  - Single donor can be identified, e.g. “nearest neighbour” based on some metric

- Andridge & Little (2010, Int. Stat. Rev.) reviewed this approach and concluded that
  - General patterns of missingness are difficult to deal with (“swiss cheese pattern”)
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Last Observation Carried Forward

- Common in settings where a variable is measured repeatedly over time and there is dropout

- If there is dropout at time $j$, we don't observe $Z_j, Z_{j+1}, \ldots, Z_T$

- LOCF: replace all of $Z_j, Z_{j+1}, \ldots, Z_T$ with $Z_{j-1}$
Last Observation Carried Forward

Example from Davidian and Tsiatis:

Solid lines: observed data. Dashed lines: extrapolated data with LOCF.
Attempts to justify LOCF

- Interest in the last observed outcome measure (reasonable in some context??)

- Under some assumptions, will lead to conservative analysis
  - Say we have a clinical trial, outcome under treatment is expected to improve over time
  - If treatment is found to be superior even with LOCF, then true effect should be even larger
  - Relies on assumption of monotonic improvement over time!
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Example of LOCF in Davidian and Tsiatis

Study participants’ characteristic to be measured at $T$ times

- $Y_j$: measurement taken at time $t_j$
- $D$: participant dropout time

Interest: $\mu_T = E(Y_T)$

The LOCF estimator of the mean is

$$\hat{\mu}_T^{LOCF} = \frac{1}{n} \sum_{i=1}^{n} \sum_{j=1}^{T} I(D_i = j + 1) Y_{ij}$$

The expected value of the LOCF estimator of the mean is

$$E(\hat{\mu}_T^{LOCF}) = \mu_T - \sum_{j=1}^{T-1} E[I(D = j + 1)(Y_T - Y_j)]$$

so $\hat{\mu}_T^{LOCF}$ is biased, in general
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▶ Available-case analyses make a better use of the available data but still requires MCAR (weaker assumptions possibly depend on model/quantity being used/estimated)

▶ Imputation methods might be valid for some quantities under MCAR but variances are underestimated $\Longrightarrow$ overconfidence in your results!

Next lecture:

▶ R session 1: imputation methods, some simulation studies

▶ Bring your laptops!
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