Missing Values in Repeated Measurement Designs

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- In simple words, missing data are defined as values that are not observed and would be meaningful if they are observed.
- Missing data can be anything from missing sequence, incomplete feature, files missing, information incomplete, data entry error etc. Most datasets in the real world contain missing data.

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- ► Clinical trials comparing different treatments on participants often involve repeated measures of the outcome over time.
- ▶ It is common in clinical trials for studies comparing the efficacy of several noncurative treatments because they can effectively remove within subject variances.
- ▶ However, by the very nature of taking repeated measurements, they also suffer from the common problem of missing values on one or more occasions.

Reasons For Missing Data

- Patients are in very critical conditions.
- Patients wants to change the treatment.
- Missing due to the breakdown of machines .
- Failed in continuing the follow up.
- Failed to answer some questionnaires.
- Patients are cured or died before study.
- Investigators forgot to collect the data.
- Family migrated.
- Patients' profile might be missing.

Effects of Missing Data

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- Inaccurate results.

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- ▶ In most studies unobserved data are treated as "missing" in the sense that their underlying values that could have been observed but were not.
- Depending on how the data have become missing, treating unobserved data simply as missing can lead to serious estimation bias.
- The most appropriate way to handle missing data or incomplete data depends on how the data points became missing.

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 - 1. MCAR: Missing completely at random.
 - 2. MAR: Missing at random.
 - 3. MNAR: Missing not at random.

▶ Missing completely at random (MCAR) is defined as when the probability that the data are missing is not related to either the specific value which is supposed to be obtained or the set of observed responses, i.e MCAR situation assumes that the reasons why the data are missing is completely unrelated to the data (both covariates and response).

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- ► MCAR is an ideal but unreasonable assumption for many studies performed in the field of anesthesiology.
- However, if data are missing by design, because of an equipment failure or because the samples are lost in transit or technically unsatisfactory, such data are regarded as being MCAR.

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- ► MCAR causes enlarged standard errors due to the reduced sample size, but does not cause bias.
- ► Thus, power may be lost in the design, but the estimated parameters are not biased by the absence of the data.

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- For example, when we take a sample from a population, where the probability to be included depends upon some known property.
- ➤ Another example of MAR is that males are less likely to fill in a depression survey but this has nothing to do with their level of depression, after accounting for maleness.

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- Consequently, there is no way to test the MAR mechanism or to verify that scores are MAR.
- ► This represents an important practical problem for missing data analyses because maximum likelihood estimation and multiple imputation (the two techniques that methodologists currently recommend) assume an MAR mechanism

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- ▶ The cases of MNAR data are problematic.
- ► The only way to obtain an unbiased estimate of the parameters in such a case is to model the missing data.
- ► The model may then be incorporated into a more complex one for estimating the missing values.

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- Three broad catagories of methods for handeling missing data are,
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 - 2. Imputation.
 - 3. Augmentation.
- ► For any missing data methods to be effective, it is important for them to incorporate a specific missing data mechanism in its development.

Data deletion

▶ Data deletion methods such as list-wise and pair-wise deletion are efficient ways of dealing with missing data as long as missing data are MCAR.

1. Complete Case Analysis (Listwise Deletion)

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Example: Here we are deleteing the incomplete units of data.

Gender	8 th grade math test score	12 th grade math score
F	45	
M		22
F	55	86
F	85	88
F	80	75
	81	82
F	75	80
M	95	
М	86	90
F	70	75
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- ▶ listwise deletion can produce unbiased estimates of regression slopes under any missing data mechanism, provided that missingness is a function of a predictor variable and not the outcome variable (Little, 1992). This relatively esoteric scenario is the only situation in which listwise deletion is likely to outperform maximum likelihood estimation and multiple imputation with missing not at random (MNAR) data.

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- listwise deletion is potentially very wasteful, particularly when the discarded cases have data on a large number of variables. Deleting the incomplete data records can produce a dramatic reduction in the total sample size.
- ► These shortcoming led to investigators to develop the following second approach .

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- This uses all available data to estimate parameters of the model.
- ▶ When a researcher looks at univariate descriptive statistics of a data set with missing observations, he or she is using available case analysis, examining the means and variances of the variables observed throughout the data set.

Advantages

▶ When the data are MCAR, when the remaining observations are representative of the originally identified data set shows that available case analysis provides consistent estimates when variables are moderately correlated in regression models.

► The primary problem with pairwise deletion is that it requires MCAR data and can produce distorted parameter estimates when this assumption does not hold.

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- When calculating the correlation coefficient $r=\frac{\hat{\sigma}_{XY}}{\sqrt{\hat{\sigma}_{X}.\hat{\sigma}_{Y}}}$, variable case analysis often might lead to implausible values of r, such as estimating correlations outside the range of -1.0 to 1.0. Errors in estimation occur because of the differeing number of observations used to estimate components of r.

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- ▶ These methods, known as single imputation techniques.



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- ► Multiple imputation uses a predicted value for a given subject and time point using statistical modeling of available data.
- ► The processes and results of data augmentation are quite similar to those of MI. But they are complex in nature.

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- ► The starting point for a maximum likelihood analysis is to specify a distribution for the population data.
- Suppose we have n independent observations (i = 1, ..., n) on k variables $(y_{i1}, y_{i2}, ..., y_{ik})$ and no missing data. Then the likelihood function is $L = \prod_{i=1}^{n} f_i(y_{i1}, y_{i2}, ..., y_{ik}; \theta)$

Now if there are m observations with complete data and n-m observations with data missing in y_1 and y_2 , the likelihood function for the full data set becomes

$$L = \prod_{i=1}^{m} f_i(y_{i1}, y_{i2}, ..., y_{ik}; \theta) \prod_{m+1}^{n} f_i^*(y_{i3}, ..., y_{ik}; \theta) \text{ where}$$

$$f_i^*(y_{i3}, ..., y_{ik}; \theta) = \sum_{y_1 \text{ and } y_2} \int f_i(y_{i1}, y_{i2}, ..., y_{ik}; \theta) dy_1 dy_2$$

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- ▶ This likelihood can then be maximized to get ML estimates of θ .
- Researchers in the social and the behavioral sciences routinely assume that their variables are normally distributed in the population.
- Maximum likelihood estimators is generally most powerful when the number of complete pairs of observations is moderately large (larger than 20) and the correlation is in the range of 0.3–0.9.

Statistical Analysis With Missing Data, Third Edition, Roderick J.A. Little, Donald B. Rubin.

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- Missing Values in Repeated Measurement Designs, Keumhee Cho Carriere, Rong Huang, Yuanyuan Liang, Xiaoming Sheng.

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► Applied Missing Data Analysis, Craig K. Enders



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