

# EP16: Missing Values in Clinical Research: Multiple Imputation

## 1. What is Multiple Imputation?

Nicole Erler

Department of Biostatistics, Erasmus Medical Center

✉ [n.erler@erasmusmc.nl](mailto:n.erler@erasmusmc.nl)

# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s

## History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),

## History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and

# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and
- ▶ increased **availability of computers**.

# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and
- ▶ increased **availability of computers**.

# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and
- ▶ increased **availability of computers**.

**Goal:** data should be usable by (Rubin, 1996)

- ▶ a **large number of analysts**, who commonly have to rely on

# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and
- ▶ increased **availability of computers**.

**Goal:** data should be usable by (Rubin, 1996)

- ▶ a **large number of analysts**, who commonly have to rely on
- ▶ standard **software that can only handle complete data**, and usually



# History & Ideas

---

- ▶ Developed by **Donald B. Rubin** in the 1970s
- ▶ to handle missing values in **public use databases** (e.g., census data provided by the government),
- ▶ motivated by the **increase in missing values**, and
- ▶ increased **availability of computers**.

**Goal:** data should be usable by (Rubin, 1996)

- ▶ a **large number of analysts**, who commonly have to rely on
- ▶ standard **software that can only handle complete data**, and usually
- ▶ are **not experts in handling incomplete data**.

## History & Ideas (Rubin, 2004)

---

One imputed value cannot be correct in general.

➔ We need to represent missing values by a **number of imputations**.

To find **sensible values** to fill in, we need some kind of **model**.

## History & Ideas (Rubin, 2004)

---

One imputed value cannot be correct in general.

→ We need to represent missing values by a **number of imputations**.



**Missing data has a distribution.**



To find **sensible values** to fill in, we need some kind of **model**.



This **distribution depends on assumptions** that have been made about the model.

## History & Ideas (Rubin, 2004)

One imputed value cannot be correct in general.  
→ We need to represent missing values by a **number of imputations**.

To find **sensible values** to fill in, we need some kind of **model**.

**Missing data has a distribution.**

This **distribution depends on assumptions** that have been made about the model.

What we want is the **'predictive distribution'** of the missing values **given the observed values**.

## History & Ideas

---

**How to obtain that predictive distribution?**

# History & Ideas

---

## How to obtain that predictive distribution?

- ▶ fit a model to the observed data (“respondents”), and to
  - ▶ obtain for each “nonrespondent” the conditional distribution of the missing data (given the observed data) as if he/she was a respondent.
- ➔ We assume that **nonrespondents are just like respondents**, and obtain the predictive distribution from the model of the respondents’ data.

# History & Ideas

---

## How to obtain that predictive distribution?

- ▶ fit a model to the observed data (“respondents”), and to
  - ▶ obtain for each “nonrespondent” the conditional distribution of the missing data (given the observed data) as if he/she was a respondent.
- ➔ We assume that **nonrespondents are just like respondents**, and obtain the predictive distribution from the model of the respondents’ data.

### Example: survey including age, gender and height

10 – 12 year old boys answered (on average) that they are 1.45m tall.

- ➔ We assume that boys aged 10 to 12 who did not report their height are also around 1.45m tall.

## History & Ideas

---

### **How to represent the multiple imputed values?**

For each missing value, we now have multiple imputed values.



### **How to represent the multiple imputed values?**

For each missing value, we now have multiple imputed values.

- ▶ For each set of imputed values, create a dataset (datasets agree in the observed values but imputed values differ).
- ▶ Analyse each dataset.
- ▶ Combine the results from all analyses.

# History & Ideas

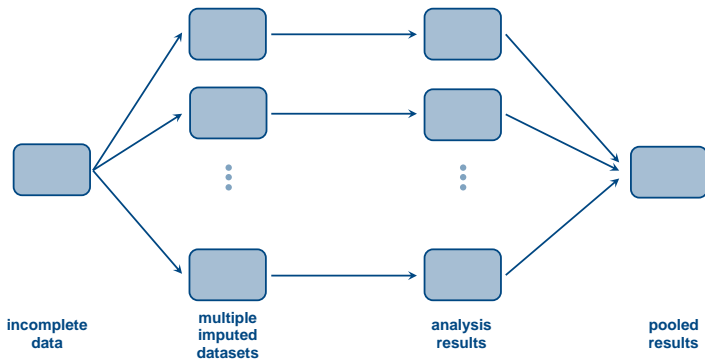
---

## How to represent the multiple imputed values?

For each missing value, we now have multiple imputed values.

- ▶ For each set of imputed values, create a dataset (datasets agree in the observed values but imputed values differ).
  - ▶ Analyse each dataset.
  - ▶ Combine the results from all analyses.
- ➔ We can describe how (much) the **results vary between the imputed datasets**, and calculate summary measures.

# Three Steps



## In summary:

- 1. Imputation:** impute multiple times → multiple completed datasets
- 2. Analysis:** analyse each of the datasets
- 3. Pooling:** combine results, taking into account additional uncertainty

## References

---

Rubin, D. B. (1996). Multiple imputation after 18+ years. *Journal of the American Statistical Association*, 91(434), 473–489.

<https://doi.org/10.2307/2291635>

Rubin, D. B. (2004). The design of a general and flexible system for handling nonresponse in sample surveys. *The American Statistician*, 58(4), 298–302. <https://doi.org/10.1198/000313004X6355>