ACRM 2018 Longitudinal Data Analysis Workshop

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Practical Session 3: The Effects of Missing Data

This handout is designed to accompany the script you will be working with in the practical session. A copy of the script file, the data, set, and this handout can be found at: https://github.com/keithlohse/LMER_Clinical_Science.

The R code is interspersed with explanations below. All R code is highlighted in grey and color coded to show different functions, arguments, and comments in the code.

First, you will need to open the five packages we will be using for this session using the library function:

```
# Loading the essential libraries.
library("ggplot2"); library("lme4"); library("car"); library("dplyr");
library("lmerTest");
```

If you haven't already installed these packages, you will need to use the install.packages() function first. This can take some time and will require an internet connect.

```
# If these packages are not installed already, run the following code:
install.packages("ggplot2"); install.packages("lme4");
install.packages("car"); install.packages("dplyr");
install.packages("lmerTest");
```

Next, as we have done in the past, we will need to set our working directory to on LMER project folder and import the dataset we saved at the end of Session 2.

```
## Setting the Directory -------------------------------------------------------
getwd()
# Note that you need to use forward slashes. R will give you an error if you
use forward slashes.
setwd("C:/Users/Folder/SubFolder/SubSubFolder/")
list.files()
# Make sure that the file data_session2.csv is saved in your working
directory.

# Import the .csv file into R.
# We will save this file in the R environment as an object called "DATA".
DATA<-read.csv("./data_session3.csv", header = TRUE, sep=",",
               na.strings=c("NA","NaN"," ",""))

# Use the head() function to check the structure of the data file.
head(DATA)

# Alternately you can also download the data file from the web here:
# DATA <-
read.csv("https://raw.githubusercontent.com/keithlohse/LMER_Clinical_Science/
master/data/data_session2.csv")
# head(DATA)
```

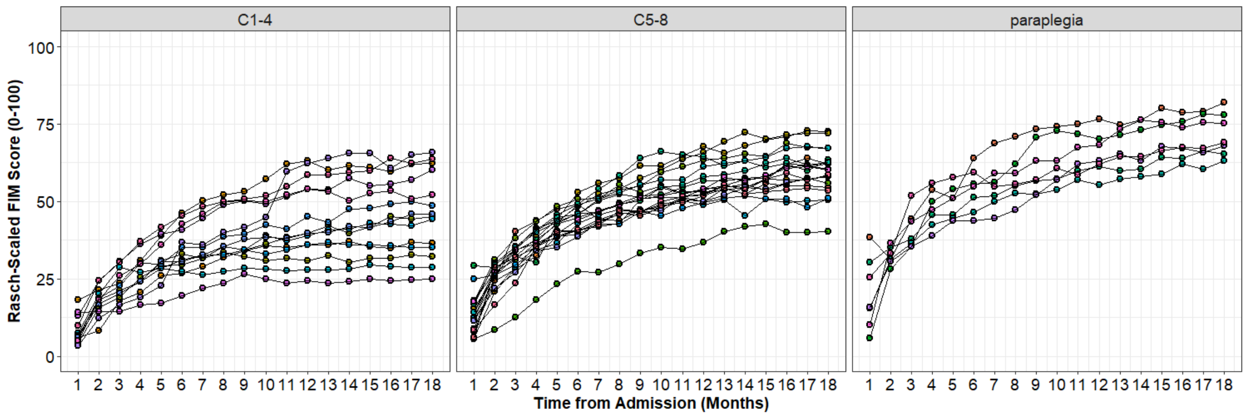
3.1 Visualizing Missing Data

Up to this point, we have been working with a much idealized dataset in which every participant has an equal and complete set of observations. When doing clinical science “in the wild” this is almost never going to happen. We will have participants observed for differing lengths of time (e.g., “inpatient stay” might be two weeks for some but four weeks for others). We are also likely to have participants with different amounts of missing data (e.g., participants may withdraw from a study, move away, or even die, all of which result in missing data).

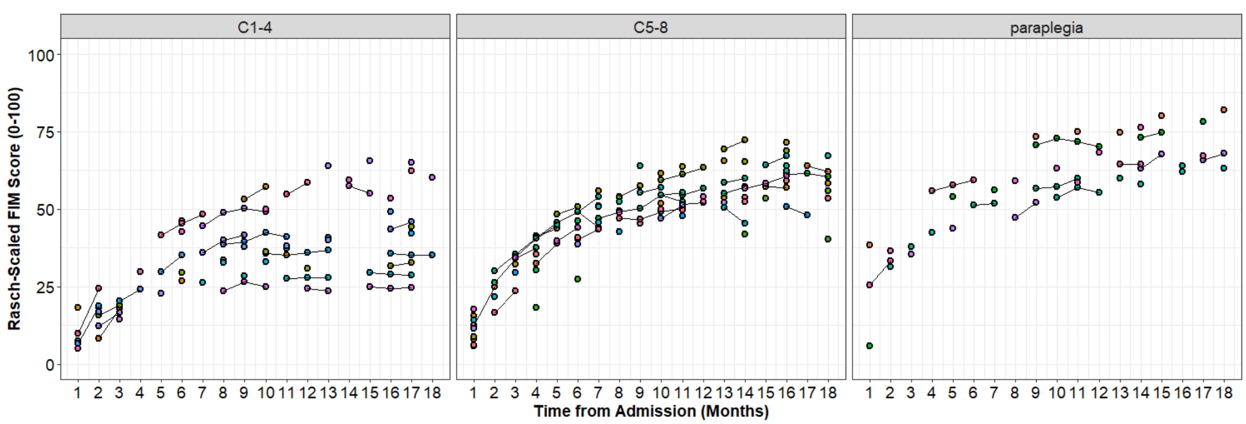
“Missingness” is an interesting phenomenon and the reasons for missing data interact with our design (e.g., the density and number of time-points) to ultimately shape our data. Many traditional methods of dealing with missingness are problematic. For instance, in a repeated measures ANOVA you need complete data for all participants. This means that participants with missing data either need to be excluded (which reduces or sample size) or the missing data needs to be imputed in some way (which biases the estimate of the variance).

One of the strengths of the LMER approach (compared to RM ANOVA) is that it can handle missing data very flexibly, estimating slopes and intercepts for individual participants that are weighted proportionally to the number of observations (i.e., the slope for participant with 18 observations has a smaller standard error than a participant with 8 observations). However, this does not mean that we can ignore the effects of missing data when using LMER. In the exercises below, we consider three different cases: ***Missing at Random*** (MAR) in which data from any time-point are equally likely to be missing; ***Missing Not at Random*** (MNAR) in which data from later time-points are more likely to be missing; and ***Last Observation Carried Forward*** (LOCF), which is a common method of imputation in which the last observation is used in place of missing values.

```
## ------------------- Visualizing Missing Data -----------------------------
## FIM scores with complete data -------------------------------------------
g1<-ggplot(DATA, aes(x = month, y = rasch_FIM)) +
  geom_point(aes(fill=as.factor(subID)), pch=21, size=2, stroke=1.25) +
  geom_line(aes(group=subID)) +
  facet_wrap(~AIS_grade)
g2<-g1+scale_x_continuous(name = "Time from Admission (Months)",
breaks=c(0:18)) +
  scale_y_continuous(name = "Rasch-Scaled FIM Score (0-100)",limits=c(0,100))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)
```

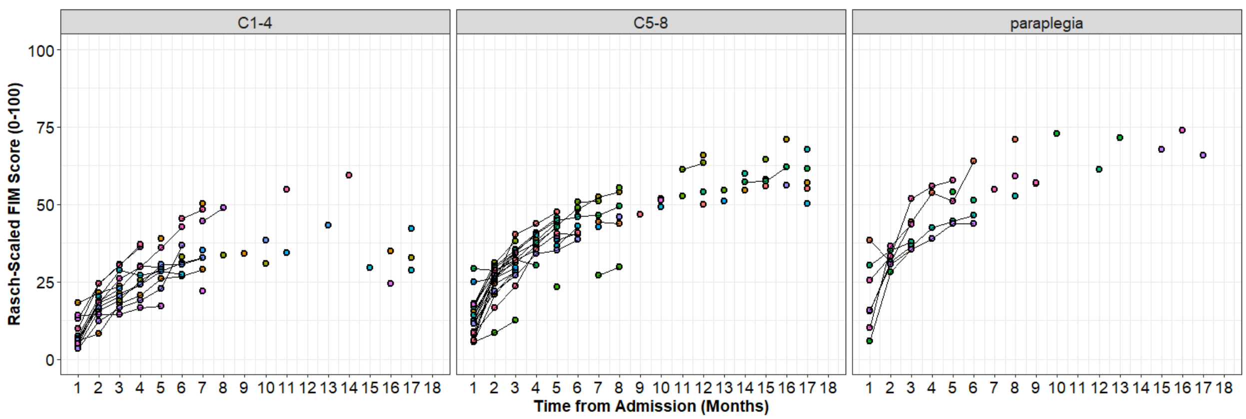



```
## FIM scores with data missing random ----------------------------------------
g1<-ggplot(DATA, aes(x = month, y = rasch_FIM_MAR)) +
  geom_point(aes(fill=as.factor(subID)), pch=21, size=2, stroke=1.25) +
  geom_line(aes(group=subID)) +
  facet_wrap(~AIS_grade)
g2<-g1+scale_x_continuous(name = "Time from Admission (Months)",
breaks=c(0:18)) +
  scale_y_continuous(name = "Rasch-Scaled FIM Score (0-100)",limits=c(0,100))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)

Warning messages:
1: Removed 437 rows containing missing values (geom_point).
2: Removed 126 rows containing missing values (geom_path).
# Note we get a warning message due to the missing values.
```

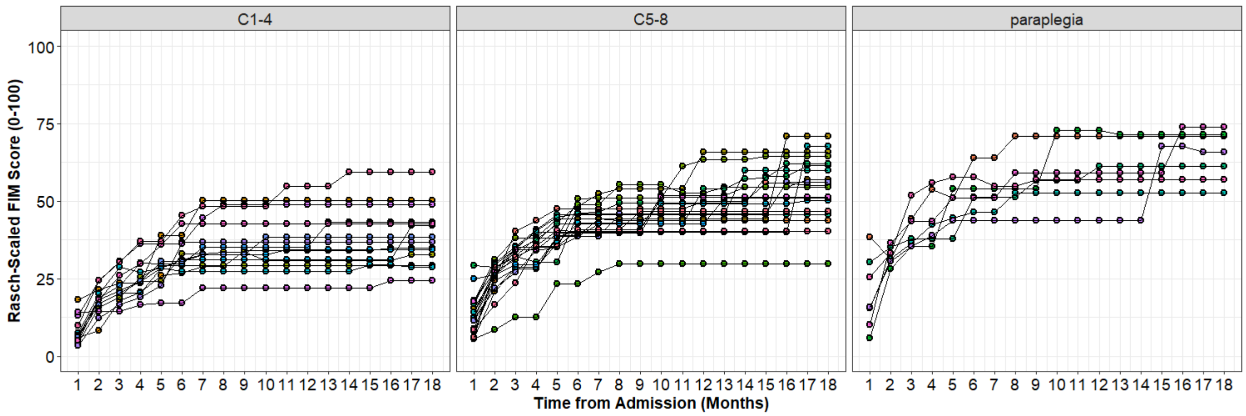



```
## FIM scores with data missing not at random ---------------------------------
g1<-ggplot(DATA, aes(x = month, y = rasch_FIM_MNAR)) +
  geom_point(aes(fill=as.factor(subID)), pch=21, size=2, stroke=1.25) +
  geom_line(aes(group=subID)) +
```

```
  facet_wrap(~AIS_grade)
g2<-g1+scale_x_continuous(name = "Time from Admission (Months)",
breaks=c(0:18)) +
  scale_y_continuous(name = "Rasch-Scaled FIM Score (0-100)",limits=c(0,100))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)

Warning messages:
1: Removed 445 rows containing missing values (geom_point).
2: Removed 228 rows containing missing values (geom_path).
```




```
## FIM scores with Last Observation Carried Forward -------------------------
g1<-ggplot(DATA, aes(x = month, y = rasch_FIM_LOCF)) +
  geom_point(aes(fill=as.factor(subID)), pch=21, size=2, stroke=1.25) +
  geom_line(aes(group=subID)) +
  facet_wrap(~AIS_grade)
g2<-g1+scale_x_continuous(name = "Time from Admission (Months)",
breaks=c(0:18)) +
  scale_y_continuous(name = "Rasch-Scaled FIM Score (0-100)",limits=c(0,100))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)
```

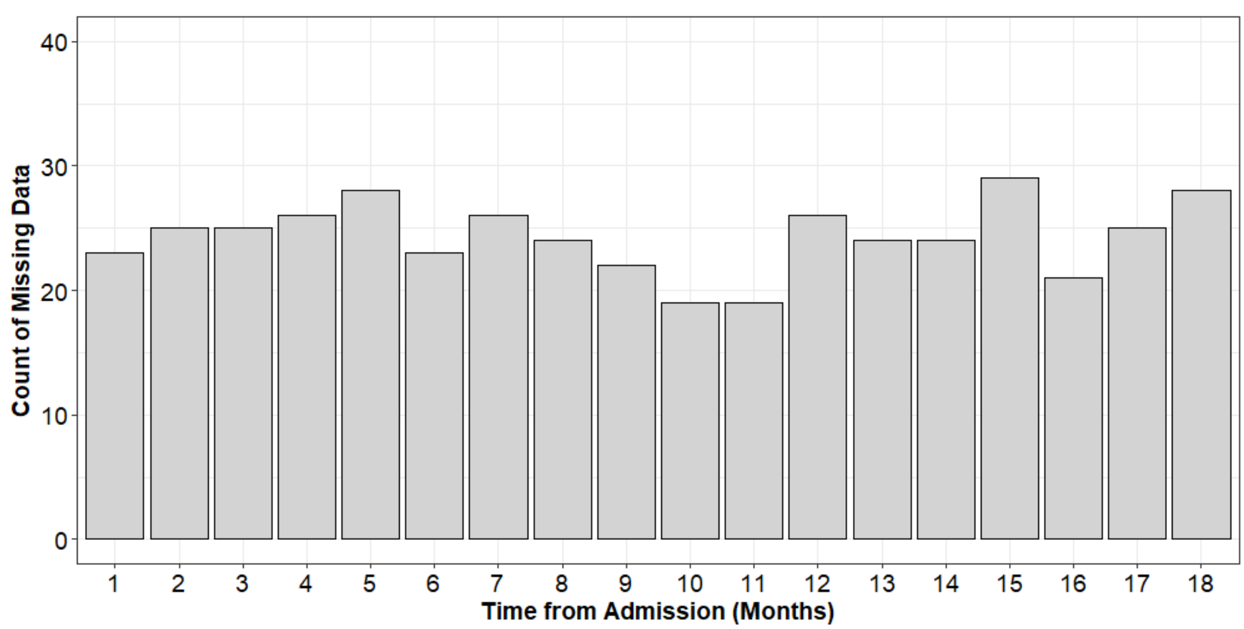


C1-4
C5-8
paraplegia
Rasch-Scaled FIM Score (0-100)
100
75
50
25
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Time from Admission (Months)

2.2 Identifying Missing Data

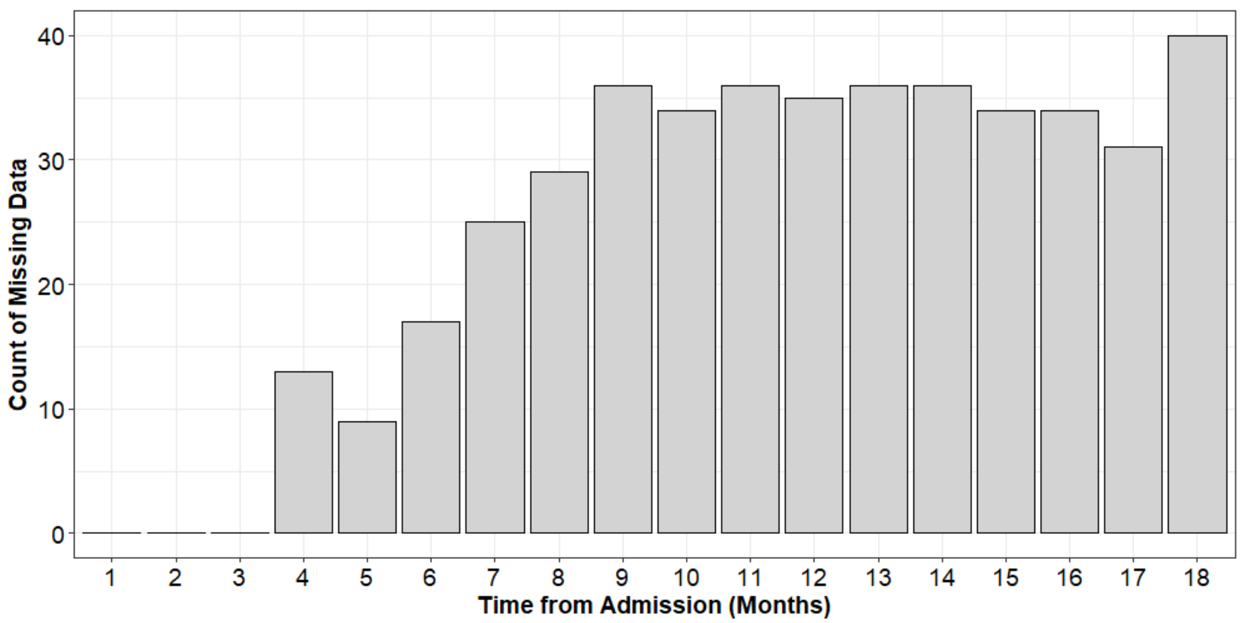
To really see the difference between the MAR and MNAR data, lets plot the proportion of missing values at each time-point. In order to plot these frequencies, we will use the is.na() function in R. This function returns the value of "TRUE" if the value is missing and "FALSE" and a value is present. We then use the as.numeric() function to convert these logical TRUE/FALSE statements into 1s and 0s respectively.

```
## -------------------- Identifying Missing Data ----------------------------
# Missing at Random
DATA$MAR_missing<-as.numeric(is.na(DATA$rasch_FIM_MAR))
summary(DATA$MAR_missing)

xtabs(MAR_missing ~ month, DATA)

x<-as.data.frame(xtabs(MAR_missing ~ month, DATA))
x


g1<-ggplot(x, aes(x = month, y=Freq)) +
  geom_col(fill= "light grey", color="black")
g2<-g1+scale_x_discrete(name = "Time from Admission (Months)") +
  scale_y_continuous(name = "Count of Missing Data", limits=c(0,40))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)
```




```
# Missing Not at Random
DATA$MNAR_missing<-as.numeric(is.na(DATA$rasch_FIM_MNAR))
```

```
summary(DATA$MNAR_missing)

xtabs(MNAR_missing ~ month, DATA)

y<-as.data.frame(xtabs(MNAR_missing ~ month, DATA))
y


g1<-ggplot(y, aes(x = month, y=Freq)) +
  geom_col(fill= "light grey", color="black")
g2<-g1+scale_x_discrete(name = "Time from Admission (Months)") +
  scale_y_continuous(name = "Count of Missing Data", limits=c(0,40))
g3 <- g2 + theme_bw() +
  theme(axis.text=element_text(size=14, colour="black"),
        axis.title=element_text(size=14,face="bold")) +
  theme(strip.text.x = element_text(size = 14))+
  theme(legend.position="none")

plot(g3)
```



2.3 Comparing Different Effects of Time

To understand the effects that different kinds of missingness (MAR or MNAR) or imputation (LOCF) have on our models, let's take our cubic model from the previous session and apply it to the three different types of dependent variable.

```
## -------------- The Effects of Missingness on Time ------------------------
# Cubic model with complete data
complete<-lmer(rasch_FIM~
                    # Fixed-effects
                    1+year.0+year.0_sq+year.0_cu+
                    # Random-effects
                    (1+year.0+year.0_sq+year.0_cu|subID), data=DATA,
REML=FALSE)



# Cubic model with data Missing at Random
MAR<-lmer(rasch_FIM_MAR~
                 # Fixed-effects
                 1+year.0+year.0_sq+year.0_cu+
                 # Random-effects
                 (1+year.0+year.0_sq+year.0_cu|subID), data=DATA, REML=FALSE)


# Cubic model with Missing Not at Random
MNAR<-lmer(rasch_FIM_MNAR~
                 # Fixed-effects
                 1+year.0+year.0_sq+year.0_cu+
                 # Random-effects
                 (1+year.0+year.0_sq+year.0_cu|subID), data=DATA, REML=FALSE)


# Cubic model with Last Observation Carried Forward
LOCF<-lmer(rasch_FIM_LOCF~
                 # Fixed-effects
                 1+year.0+year.0_sq+year.0_cu+
                 # Random-effects
                 (1+year.0+year.0_sq+year.0_cu|subID), data=DATA, REML=FALSE)



summary(complete)
```

```
Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
approximations to degrees of freedom [lmerMod]
Formula: rasch_FIM ~ 1 + year.0 + year.0_sq + year.0_cu + (1 + year.0 +
    year.0_sq + year.0_cu | subID)
   Data: DATA

     AIC       BIC    logLik deviance df.resid
  3741.4    3810.1   -1855.7   3711.4       705

Scaled residuals:
    Min       1Q   Median       3Q      Max
-4.1697 -0.5265 -0.0002  0.5186  3.5018
```

```
Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subID    (Intercept)   42.779  6.541
          year.0       635.959 25.218    0.06
          year.0_sq   1179.868 34.349   -0.07 -0.88
          year.0_cu    213.005 14.595    0.10  0.77 -0.98
 Residual                5.481  2.341
Number of obs: 720, groups:  subID, 40




Fixed effects:
            Estimate Std. Error      df t value Pr(>|t|)
(Intercept)   14.977      1.073  40.000  13.954  < 2e-16 ***
year.0        95.033      4.378  40.000  21.706  < 2e-16 ***
year.0_sq    -83.232      6.213  40.000 -13.397 2.22e-16 ***
year.0_cu     26.483      2.698  40.000   9.815 3.30e-12 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
          (Intr) year.0 yr.0_s
year.0    -0.041
year.0_sq  0.027 -0.891
year.0_cu  0.001  0.797 -0.981
```

```
summary(MAR)
```

```
Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
approximations to degrees of freedom [lmerMod]
Formula: rasch_FIM_MAR ~ 1 + year.0 + year.0_sq + year.0_cu + (1 + year.0 +
    year.0_sq + year.0_cu | subID)
   Data: DATA

     AIC      BIC   logLik deviance df.resid
  1578.7   1633.4   -774.4   1548.7      268

Scaled residuals:
    Min      1Q  Median      3Q     Max
-3.1629 -0.5279 -0.0332  0.4599  2.8911

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subID    (Intercept)   69.001  8.307
          year.0      1070.150 32.713   -0.21
          year.0_sq   2259.949 47.539    0.17 -0.94
          year.0_cu    387.773 19.692   -0.12  0.90 -0.99
 Residual                3.774  1.943
Number of obs: 283, groups:  subID, 40

Fixed effects:
            Estimate Std. Error      df t value Pr(>|t|)
(Intercept)   14.454      1.440  36.330  10.039 5.06e-12 ***
year.0        96.908      6.144  39.880  15.774  < 2e-16 ***
```

```
year.0_sq    -86.756      9.197  41.260  -9.433 7.43e-12 ***
year.0_cu     28.363      3.933  40.750   7.211 8.60e-09 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
          (Intr) year.0 yr.0_s
year.0    -0.350
year.0_sq  0.291 -0.945
year.0_cu -0.237  0.898 -0.990
```

```r
summary(MNAR)
```

```
Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
approximations to degrees of freedom [lmerMod]
Formula: rasch_FIM_MNAR ~ 1 + year.0 + year.0_sq + year.0_cu + (1 + year.0 +
    year.0_sq + year.0_cu | subID)
   Data: DATA

     AIC      BIC   logLik deviance df.resid
  1651.8   1706.0   -810.9   1621.8      260

Scaled residuals:
     Min       1Q   Median       3Q      Max
-2.51404 -0.49176 -0.03217  0.50924  2.64296

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subID    (Intercept)   42.712  6.535
          year.0      1216.743 34.882   -0.07
          year.0_sq   3433.180 58.593    0.08 -0.95
          year.0_cu    787.349 28.060   -0.01  0.93 -1.00
 Residual                8.101  2.846
Number of obs: 275, groups:  subID, 40

Fixed effects:
            Estimate Std. Error       df t value Pr(>|t|)
(Intercept)   13.998      1.102   39.890  12.705 1.33e-15 ***
year.0       109.302      6.540   36.790  16.713  < 2e-16 ***
year.0_sq   -114.288     12.300   32.430  -9.292 1.17e-10 ***
year.0_cu     42.066      6.339   32.420   6.636 1.64e-07 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
          (Intr) year.0 yr.0_s
year.0    -0.196
year.0_sq  0.188 -0.939
year.0_cu -0.130  0.886 -0.987
```

```r
summary(LOCF)
```

```
Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
approximations to degrees of freedom [lmerMod]
Formula: rasch_FIM_LOCF ~ 1 + year.0 + year.0_sq + year.0_cu + (1 + year.0 +
    year.0_sq + year.0_cu | subID)
```

```
   Data: DATA

     AIC      BIC   logLik deviance df.resid
  4107.0   4175.7  -2038.5   4077.0      705

Scaled residuals:
    Min      1Q  Median      3Q     Max
-3.2159 -0.4227  0.0041  0.4549  4.5406

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subID    (Intercept)   43.598  6.603
          year.0       586.840 24.225   -0.04
          year.0_sq   1739.954 41.713    0.06 -0.86
          year.0_cu    458.504 21.413   -0.02  0.73 -0.97
 Residual                9.326  3.054
Number of obs: 720, groups:  subID, 40

Fixed effects:
            Estimate Std. Error      df t value Pr(>|t|)
(Intercept)   14.892      1.109  40.000  13.426 2.22e-16 ***
year.0        96.284      4.498  40.020  21.405  < 2e-16 ***
year.0_sq   -101.753      7.680  40.030 -13.249 4.44e-16 ***
year.0_cu     37.040      3.846  40.020   9.632 5.60e-12 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
          (Intr) year.0 yr.0_s
year.0    -0.176
year.0_sq  0.166 -0.887
year.0_cu -0.107  0.770 -0.972
```

First, let's look at the amount of data available in each model. In the MAR data, about 61% of the data are missing, but recall these data are missing from all different times. In the MNAR data, 62% of the data are missing, but these data are missing largely from the later time-points. We also include the deviance and the AIC from these models so that you can see how these values depend on the number of observations. This should reinforce the idea that we can only compare the deviance and AIC from datasets of the same size!

Variable	Complete	MAR	MNAR	LOCF
# of Subjects	40	40	40	40
# of Observations	720	283	275	720
Deviance	3711.4	1548.7	1621.8	4077.0
AIC	3741.4	1478.7	1651.8	4107.0

Next, let's look at the effect that missing data has on the fixed-effects of our cubic time model. Each model contains a point-estimate for the effect (β) and a standard error (SE). Broadly speaking, we expect the SE to be inversely related to the amount of data (i.e., more missing data should mean bigger SE). Similarly, we expect the point estimates to change as a function of the "shape" of the data. The complete dataset is our archtypal shape. The MAR dataset will mimic this shape, albeit with fewer data points. The MNAR dataset departs from this shape because most of the data is only available early in time, when the rate of change is at its hightest. Similarly, the LOCF dataset departs from this shape because it looses the fine resolution of change in later time-points. (Look back at the LOCF data above to see this “stair-case” effect in the data.)

	Complete		MAR		MNAR		LOCF	
Effect	**β**	**SE**	**β**	**SE**	**β**	**SE**	**β**	**SE**
Time (linear)	95.03	4.38	96.91	6.14	109.30	6.54	96.28	4.50
Time (quadratic)	-83.23	6.21	-86.76	9.20	-114.28	12.30	-101.75	7.68
Time (cubic)	26.48	2.70	28.36	3.93	42.07	6.34	37.04	3.85

We can more easily show these effects by expressing each β and SE as a proportion of the β/SE from the complete data set.

	MAR		MNAR		LOCF	
Effect	**β**	**SE**	**β**	**SE**	**β**	**SE**
Time (linear)	1.02	1.40	1.15	1.49	1.01	1.03
Time (quadratic)	1.04	1.48	1.37	1.98	1.22	1.23
Time (cubic)	1.07	1.46	1.59	2.35	1.40	1.42

If the missingness or our imputation is not having an effect, these values should be close to one. You can see that MAR does well in terms of the estimate of β, but the SE’s are larger by a factor of 40 to 50%. This isn’t too bad; it means our estimates are less certain, but not biased. In contrast, look at the MNAR where the β’s are biased to overestimate. However, the SE’s are also biased upward, so at least as our estimate gets less precise our confidence is correspondingly going down. The LOCF estimates, in our opinion, pose the biggest threat to decision making. Note the β’s can overestimate the effect by as much as 40%, but the SE’s are somewhere between the MAR and the complete dataset. As such, by carrying the last observation forward, we might have a spurious confidence in our model’s estimates.

These general effects on the β’s and the SE’s will be true, on average, across different types on data sets. In the current dataset, however, the distortions might not seem too bad. Keep in mind, however, that we have an idealized dataset for two reasons. First, our simulated data were generated from mathematical functions with relatively little noise. Second, we have a lot of time-points, 18, in our study. In most studies, this level of resolution in time is probably not feasible.