Load the data:

```
data <- read.table("Treatment of Lead Exposed Children Trial.txt", quote="\"", comment.char="")
```

Check the format whether it's wide or long format and also, determine what format is needed for your package.

```
head(data)
```

Since our data is in wide format, we convert it to long format as:

```
library(tidyr)
data_long <- gather(data, Week, measurement, V3:V6, factor_key=TRUE)
data_long <- data_long[order(data_long$V1), ]
```

In addition, I sorted the rows based on the subjects.

To convert long to wide, it is relatively easy, but data-specific. If you know what you need, you can write a code for conversion.

I will modify the data a little bit to reflect the characteristics of the dataset.

```
data_new = data_long
data_new$Week <- as.character(data_new$Week)
data_new$Week[grep("V3", data_long$Week)] = "0"
data_new$Week[grep("V4", data_long$Week)] = "1"
data_new$Week[grep("V5", data_long$Week)] = "4"
data_new$Week[grep("V6", data_long$Week)] = "6"
data_new$Week <- as.numeric(data_new$Week)
```

The week variable is converted into a numeric variable first and then it will converted into a factor as well. We run a linear regression and then check the design matrix ($\mathbf{X}$) matrix in matrix-vector representation for linear regression using `model.matrix`. If you are using the notational regressions, it is important to check whether the corresponding design matrix is the one you want it to be. `gtsummary` is a great package to produce nice regression output tables.

```
ls <- lm(measurement~Week, data=data_new)
model.matrix(ls)
X <- model.matrix(ls)
coef(summary(ls))
solve(crossprod(X))%*%crossprod(X,data_new$measurement)
gtsummary::tbl_regression(ls)
anova(ls)
```

Now, weeks as factors:

```
ls <- lm(measurement~as.factor(Week), data=data_new)
model.matrix(ls)
coef(summary(ls))
gtsummary::tbl_regression(ls)
anova(ls)
```

In the case of linear mixed models as well, it is important to check whether the notational model leads to the design matrices you want for your mixed model. The following is for Week as a numeric variable.

```
library(lme4)
out <- lFormula(measurement ~ Week + (1|V1), data=data_new)
X <- as.matrix(out$X)
Z <- t(as.matrix(out$reTrms$Zt))
res <- lme4::lmer(measurement ~ Week + (1|V1), data = data_new)
```

Now, week as a factor variable:

```
library(lme4)
out <- lFormula(measurement ~ as.factor(Week) + (1|V1), data=data_new)
X <- as.matrix(out$X)
Z <- t(as.matrix(out$reTrms$Zt))
res <- lme4::lmer(measurement ~ as.factor(Week) + (1|V1), data = data_new)
```

Let's try another notation:

```
library(lme4)
out <- lFormula(measurement ~ Week + (1+Week|V1), data=data_new)
X <- as.matrix(out$X)
Z <- t(as.matrix(out$reTrms$Zt))
```

Even before running the model, you should check this, especially while running a linear mixed model (LMM). Notations in LMM are a bit complicated.

Now we compare the estimates and inferences for the model `measurement   as.factor(Week)` under linear regression and linear mixed regression.

```
ls <- lm(measurement~as.factor(Week), data=data_new)
coef(summary(ls))
gtsummary::tbl_regression(ls)

res <- lme4::lmer(measurement ~ as.factor(Week) + (1|V1), data = data_new)
coef(summary(res))
gtsummary::tbl_regression(res)
```

You will see again that the estimates do not change, the confidence intervals will as the estimates of variance change from linear model to linear mixed model.

Following are the two great resources to learn different functionalities in the `lme4` package for the linear mixed model. We will come back to these.

- `https://cran.r-project.org/web/packages/lme4/vignettes/lmer.pdf`
- `https://people.math.ethz.ch/~maechler/MEMo-pages/lMMwR.pdf`

1 Generalized least square

In generalized least square, the objective function to minimize is $f(\boldsymbol{\beta}) = \sum_{i=1}^{N}(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta})^T\boldsymbol{\Sigma}^{-1}(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta})$.

The first derivate of $f(\boldsymbol{\beta})$ wrt $\boldsymbol{\beta}$ is $-2\sum_{i=1}^{N}[\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta})$.

Equating $f(\boldsymbol{\beta}) = 0$, we get $\sum_{i=1}^{N}\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}\mathbf{X}_i\boldsymbol{\beta} = \sum_{i=1}^{N}\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}\mathbf{y}_i$ which leads to the solution $\hat{\boldsymbol{\beta}} = (\sum_{i=1}^{N}\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}\mathbf{X}_i)^{-1}(\sum_{i=1}^{N}\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}\mathbf{y}_i)$. Again $\mathrm{Var}(\mathbf{y}_i|\mathbf{X}_i) = \boldsymbol{\Sigma}$ and thus $\mathrm{Var}(\hat{\boldsymbol{\beta}} \mid \mathbf{X}) = (\sum_{i=1}^{N}\mathbf{X}_i^T\boldsymbol{\Sigma}^{-1}\mathbf{X}_i)^{-1}$