

# Practicals

# Practical 1: Marginal Models Continuous

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- We will use the PBC dataset; this is available as the object `pb2` in the R workspace available on GitHub
- To load this workspace and make the data available execute the following steps:
  1. Open a new Rstudio session
  2. Create a new R script file (File → New File → R Script)
  3. Copy-paste and execute the following three lines

```
con <- url("https://raw.githubusercontent.com/drizopoulos/Repeated_Measurements/master/Data.RData")
load(con)
close(con)
```

# Practical 1: Marginal Models Continuous (cont'd)

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- The data are available in the data frame `pbc2` – we will need the following variables
  - \* `id`: patient id number
  - \* `prothrombin`: prothrombin time in sec (the response variable of interest)
  - \* `year`: follow-up times in years
  - \* `drug`: the randomized treatment
  - \* `sex`: the gender of the patients
  - \* `age`: the age of the patients

**Aim:** To build an appropriate marginal model to investigate the relationships between the prothrombin time and the aforementioned variables

# Practical 1: Marginal Models Continuous (cont'd)

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- **Q1:** We will start by producing some descriptive plots for the prothrombin time, similar to those we have seen in Chapter 1, i.e.,
  - ▷ spaghetti plot per treatment group including the loess curve
  - ▷ spaghetti plot per sex including the loess curve

(hint: see code for Section 1.1)

What observations can you make?

# Practical 1: Marginal Models Continuous (cont'd)

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- We will continue by starting our model building exercise

## Remember

- ▷ we start with a full specification of the mean structure, and investigate the covariance structure
  - ▷ based on our chosen covariance structure we can make inferences for the mean structure
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- Q2: Start by fitting a marginal model with independent error terms using `gls()` and the following specification of the mean structure (hint: see code for Section 2.4)
    - ▷ nonlinear time evolutions using natural cubic splines with 3 degrees of freedom
    - ▷ correct for `sex`, `drug` and `age`
    - ▷ interactions of the time effect with `sex` and `drug`

# Practical 1: Marginal Models Continuous (cont'd)

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- Q2:
  - ▷ interpret the results you obtained
  - ▷ should we simplify the model by excluding the non-significant terms?
- Q3: Continue with the same mean structure and try different covariance structures
  - ▷ first try different correlation structures, i.e., compound symmetry, continuous AR1, linear & Gaussian, and
  - ▷ then extend the above structures by assuming heteroscedastic errors, i.e., that the variance increases (or decreases) with time

(hint: see code for Section 2.9)

# Practical 1: Marginal Models Continuous (cont'd)

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- **Q4:** Using appropriate tools (hypothesis tests, information criteria) decide which structure is the best
  - ▷ which models are nested to which models?
- For the remainder we will use the covariance structure you have chosen in Q4
- **Q5:** Check if we can drop **all** the interaction terms
  - ▷ with an F-test
  - ▷ with a Likelihood Ratio Test

(hint: see code for Section 2.9)

# Practical 1: Marginal Models Continuous (cont'd)

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- **Q6:** Continue and check whether you can drop the nonlinear terms for the time effect
  - ▷ to do that fit a model that assumes a linear time trend, and
  - ▷ then do the likelihood ratio test to compare it to the model that includes the nonlinear terms
- **Q7:** Interpret the results of your final model
  - ▷ regression coefficients
  - ▷ covariance structure



# Practical 1: Marginal Models Continuous (cont'd)

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- Q8: Use an Effect Plot to depict the model with the following settings
  - ▷ **year**: in the range from 0 to 12 years of follow-up
  - ▷ **sex**: both males and females
  - ▷ **drug**: both treatment groups
  - ▷ **age**: fixed at 49 years old

(hint: see code for Section 2.4 – Effect Plot)

# Practical 2: Mixed Models Continuous

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## Practical 2: Mixed Models Continuous (cont'd)

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# Practical 3: Marginal Models Discrete

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## Practical 3: Marginal Models Discrete (cont'd)

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# Practical 4: Mixed Models Discrete

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## Practical 4: Mixed Models Discrete (cont'd)

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