ggPMX: an R package to easily generate an adequate set of diagnostics plots for population models

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Objectives

- At **Novartis**, we aimed at standardizing the set of diagnostic plots used for **PK** and **PKPD** modeling activities in order to reduce the overall effort required for generating such plots.

- An internal Novartis guidance has been developed describing an adequate set of diagnostics for modeling building assessement.

- **ggPMX** is a toolbox that can generate all diagnostic plots out of the guidance at a quality sufficient for publication and submissions using a few lines of R code.

Methods

ggPMX is an R package, i.e., a set of functions written in the R language, which is familiar to many pharmacometricians. The key components of the package are:

- **Reader** - Reader reads model outputs from different sources (i.e. text files containing population parameters, model predictions, individual random effects, simulations and data-related inputs like covariates) and restructures these outputs into standard formats

- **Generator** – Process outputs from Reader. It contains R language code to produce the plots and is factorized into a small set of flexible key functions. A set of default plots is defined in a configuration file. The configuration file can be adapted, e.g., to have different configurations for different types of modeling activities.

- **Controller** - The user will call Generator functions via wrapper functions in the Controller to produce either all the default plots or selected plots of interest. In addition to editing the configuration, the user has different options to adapt aspects of the plots to specific requirements. Plots may be adapted by setting parameters of the wrapper function that generate the plots; there exist additional wrapper functions to change aspects of the existing default plots; and the plots are, in general, returned as ggplot objects that can be further customized using ggplot functionality.

- **Reporter** - Generates sets of graphs and tables and integrates them into an output file (Word or PDF) with annotations.

Figure 1. intended use of ggPMX package
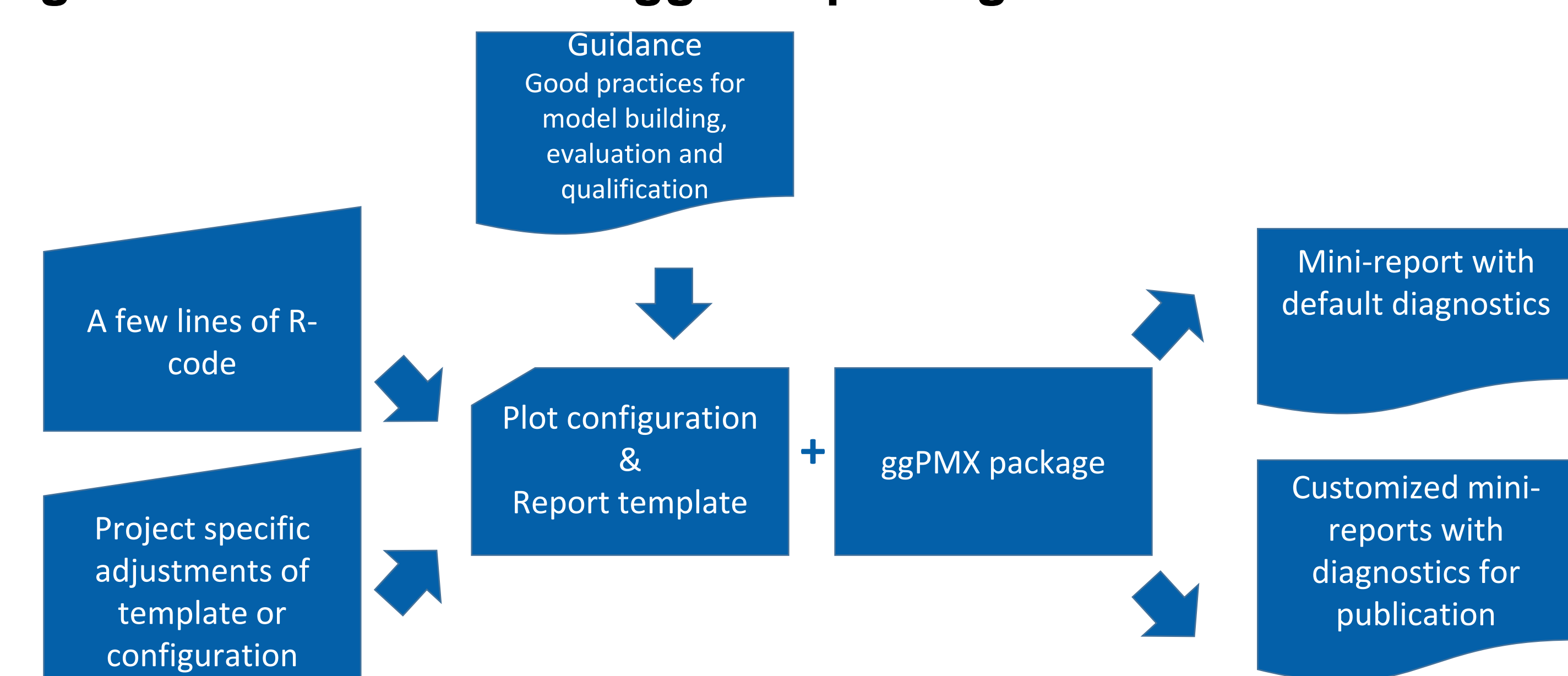
Results

- Using simple function calls, the toolbox can produce different model diagnostic plots (e.g. residual and EBE-based plots assessing possible trends and the shape of the distributions such as IWRES vs IPRED, VPCs, observations vs predictions, etc.).
- By default, the output file generated by the Reporter contains the diagnostics proposed in the Novartis internal guidance; however, these can be adapted to produce different sets of diagnostics as desired by the user, and any of the plots may be **customized individually**. The types of customizations include modifications of the graphical parameters and stratifications.
- ggPMX supports the generation of an output file (PDF or Word) containing diagnostic plots for any model with a few lines of code by the user.
- The package is planned to be made available to the user community on **CRAN**.

Conclusions

The first release of ggPMX will work with Monolix outputs and produce the necessary diagnostic plots mentioned in the Novartis internal guidance. Current plans are to enhance ggPMX to support NONMEM and nlmixr outputs as well.

Code

```
# initiate ggPMX controler

ctr <-
    pmx(sys = "mlx", config = "standing", directory = work_dir,
    input = input_data, dv = "Y", dvid = "DVID")

# generate report with model diagnostics

ctr %>%
    pmx_report(name = "my_report", output_type="report", save_dir
    = "some_location")
```
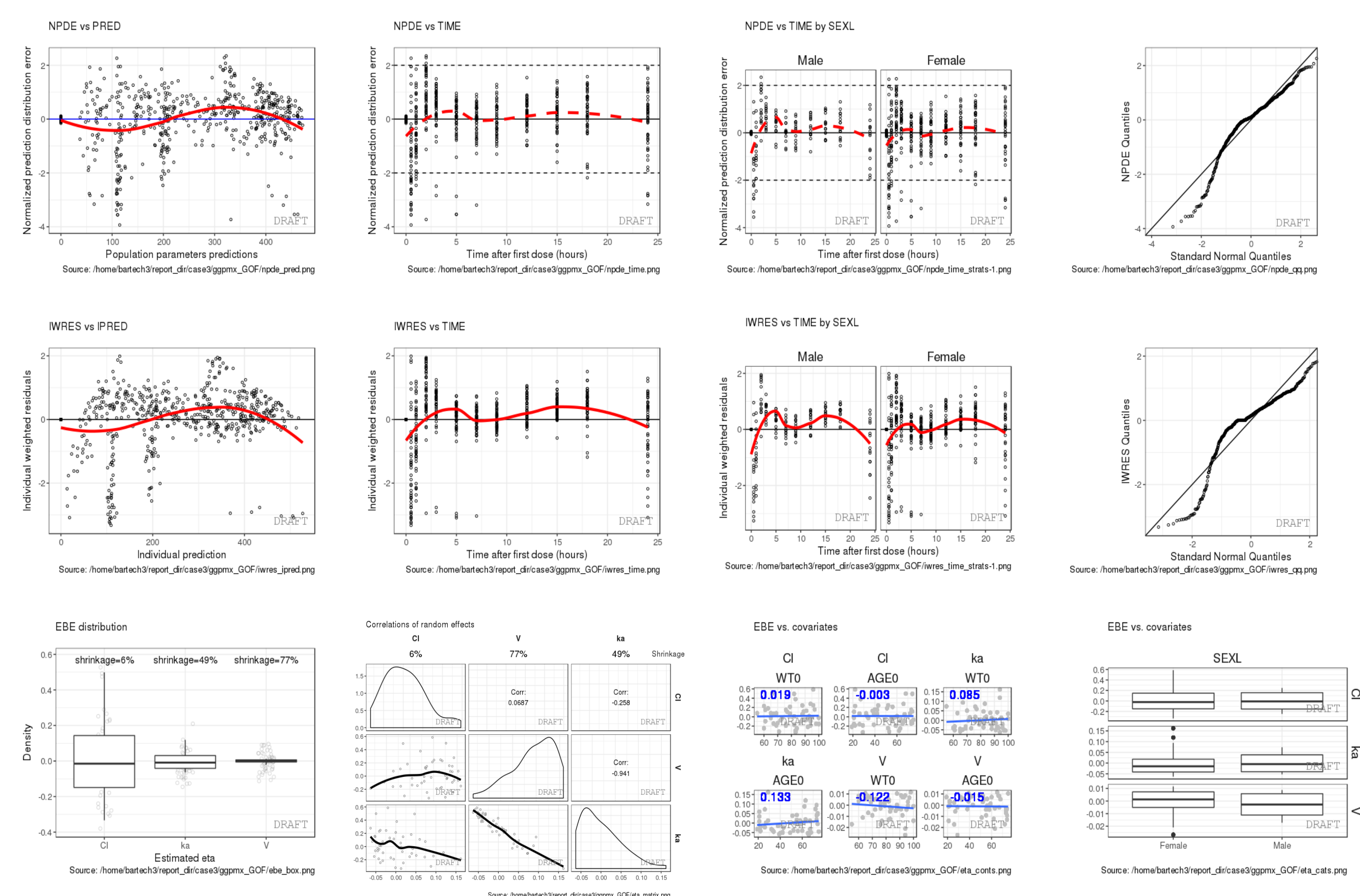
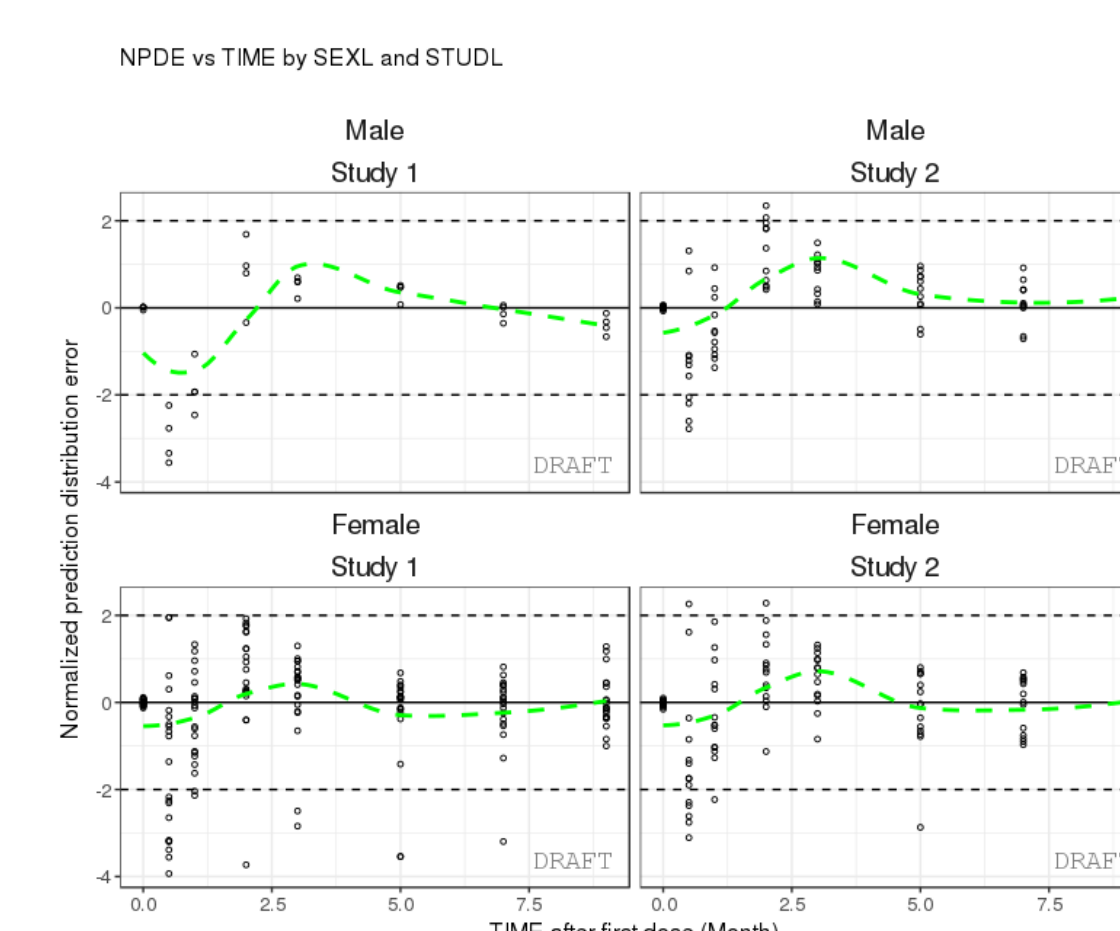**Generates PDF/word document**

Contents

Key diagnostics, annotated with file location

Customization

- Change time axis label in all plots
- Zoom into first six months
- Facetting by study and sex
- Change attributes of loess line
- ....

Disclosures