

nonmem2R: An R-package for Visual Predictive Checks and Goodness-of-fit Plots

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Introduction

- nonmem2R is an open-source R-package, freely available on CRAN[1].
- The previous versions had functionality for Visual Predictive Checks (VPC) plots and functions to extract parameter estimates from NONMEM[2] and PSN[3] generated output files
- The package have now been extended with functionality for Goodness-of-fit (GOF) plots.

Methods

- The plotting functionality in nonmem2R builds on the R-packages ggplot2[4] and as far as possible return ggplot-objects that can be further modified by adding ggplot formatting.
- The GOF functions use a default graphical setting to provide GOF's of similar appearance with a minimum input.
- Each GOF plot will have a red dashed reference line and blue solid lines are smoother's representing the actual data when applicable.
- The default setting can easily be modified to affect all GOF's within a script including captions text to indicate source script for each generated graph.
- The GOF function assume a data-frame as input as returned by e.g. read.table when reading a NONMEM \$TABLE output file.

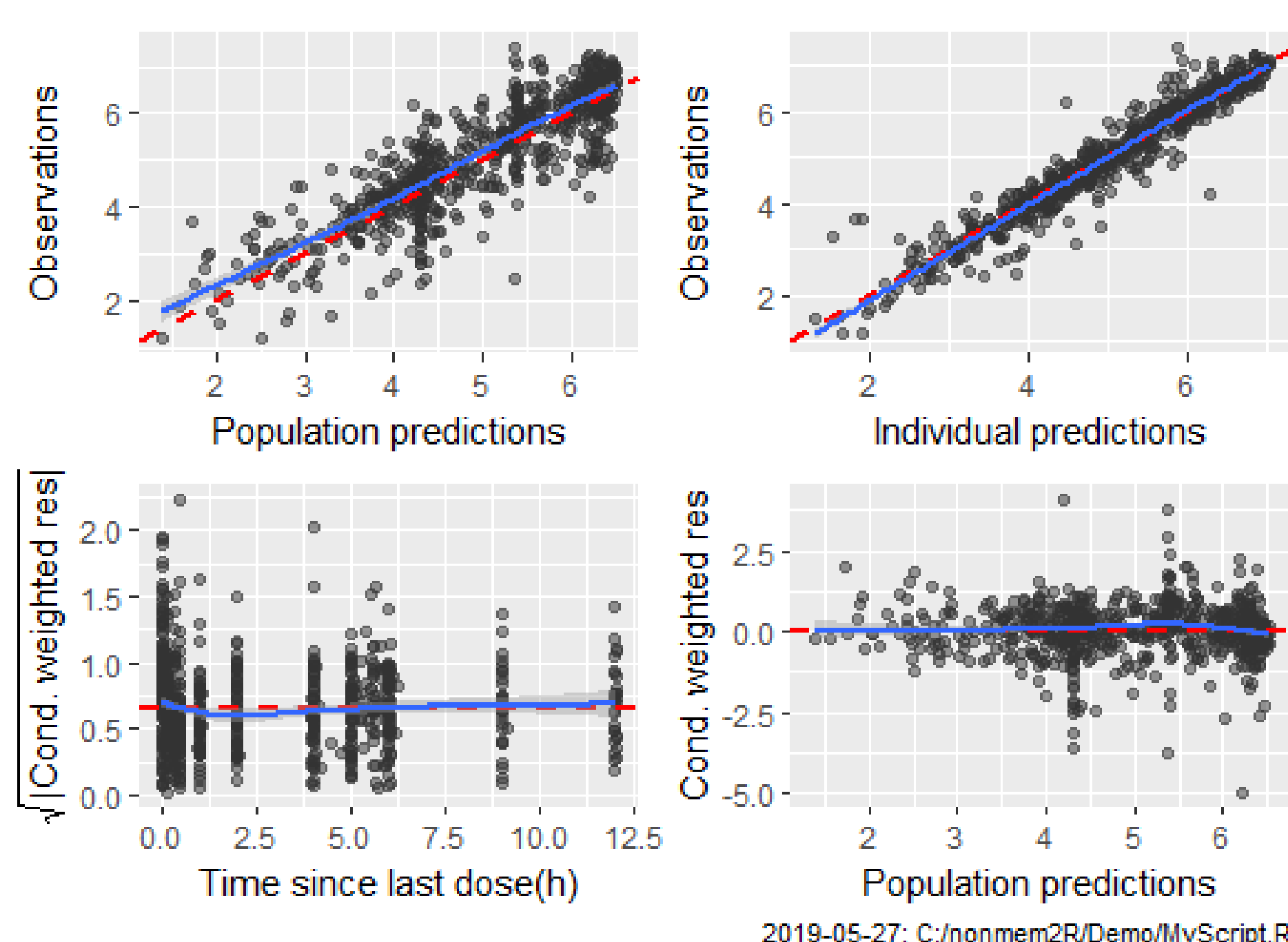
Results

The package has a set of tailored functions to provide basic GOF plots for NONMEM generated output files.

basic.GOF4 will provide a summary GOF of population and individual predictions vs observations together with conditional weighted residuals (CWRES) untransformed and transformed by square root of the absolute value, both plotted vs TIME by default.

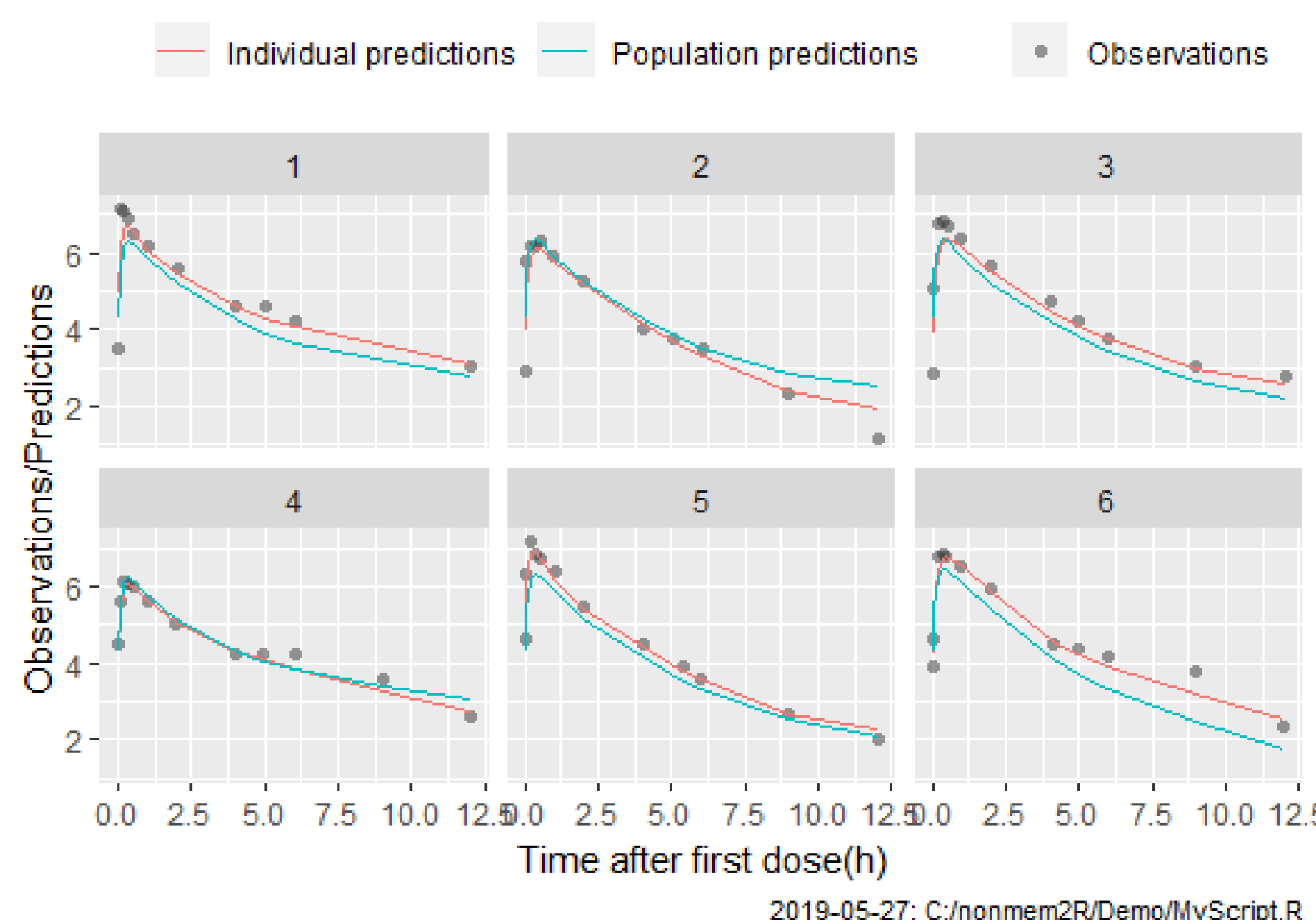
```
# Data prep for below examples
sdtab<-read.table(file="sdtab999",header=TRUE)
sdtab$gender<-c("Female","Male")[sdtab$SEX+1]
sdtab$weight<-cut(sdtab$BWT,breaks=c(25,80,150))
sdtab<-subset(sdtab,DV>0)
```

```
basic.GOF4(sdtab, idv1="TAPD",
idv2="PRED")
```



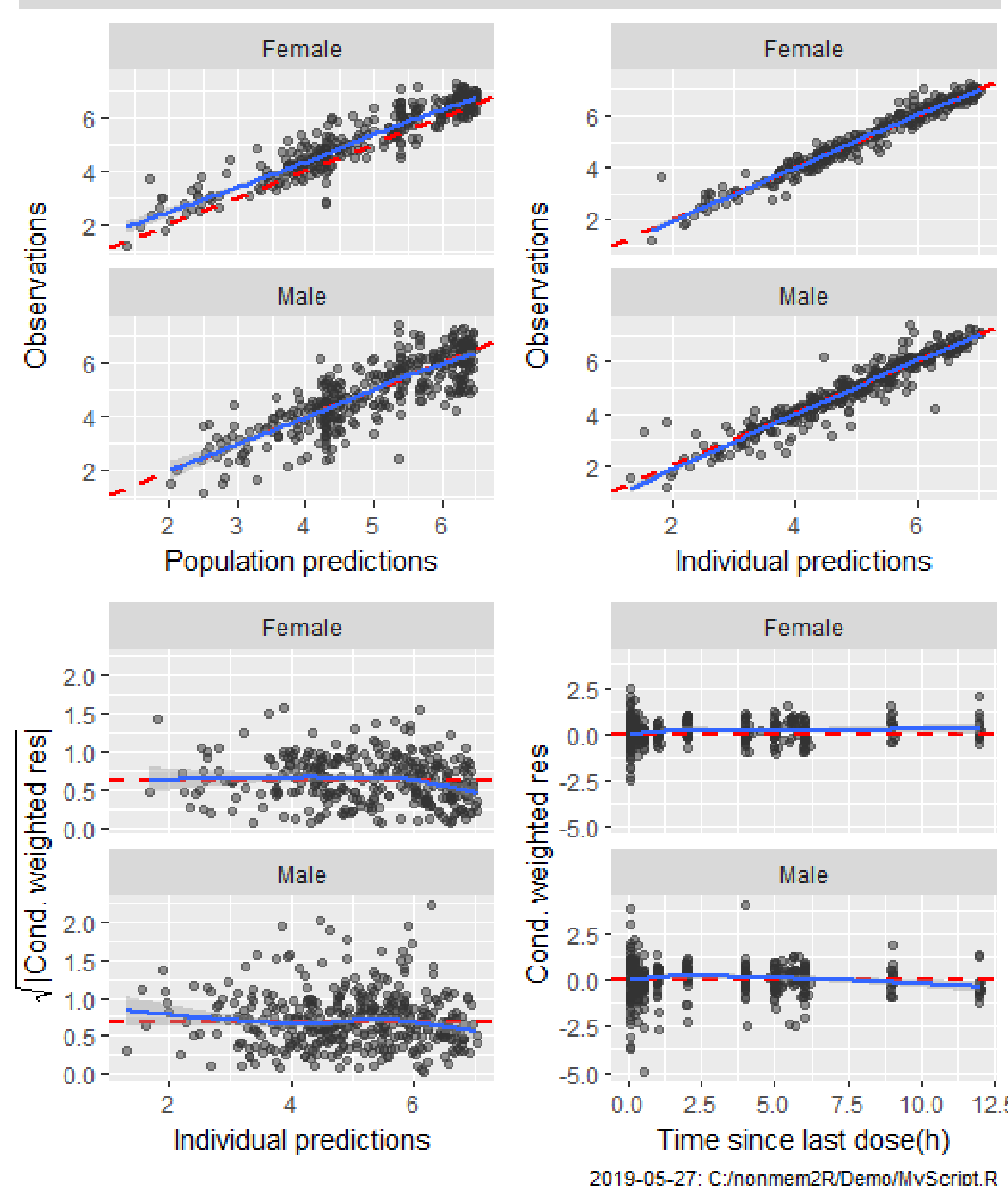
do.individual.GOF will provide GOF plots of PRED, IPRED and DV vs TIME with one panel per subject with default of 20 subjects/page.

```
do.individual.GOF(subset(sdtab,TIME<50),
per.page = 6)
```



It is also possible to add ggplot formatting to each sub GOF before combining into one single graph.

```
basic.GOF4(sdtab,global.ggplot.options=
facet_wrap(~gender,ncol=1))
```



All GOF's have arguments to change from the default setting e.g.

- time after last dose (TAD) on x-axis instead of TIME
- exclude the loess smoother
- drop the reference line.

With set.GOF.params formatting can be modified

- lines colors
- plot symbols
- histogram bars
- caption text.

and will then affect all subsections GOF's

Axis labels are set according to a dictionary, e.g.

- CWRES labelled "Cond. weighted res"
- TAD labelled "Time since last dose(hrs)".

The dictionary can be extended and or modified

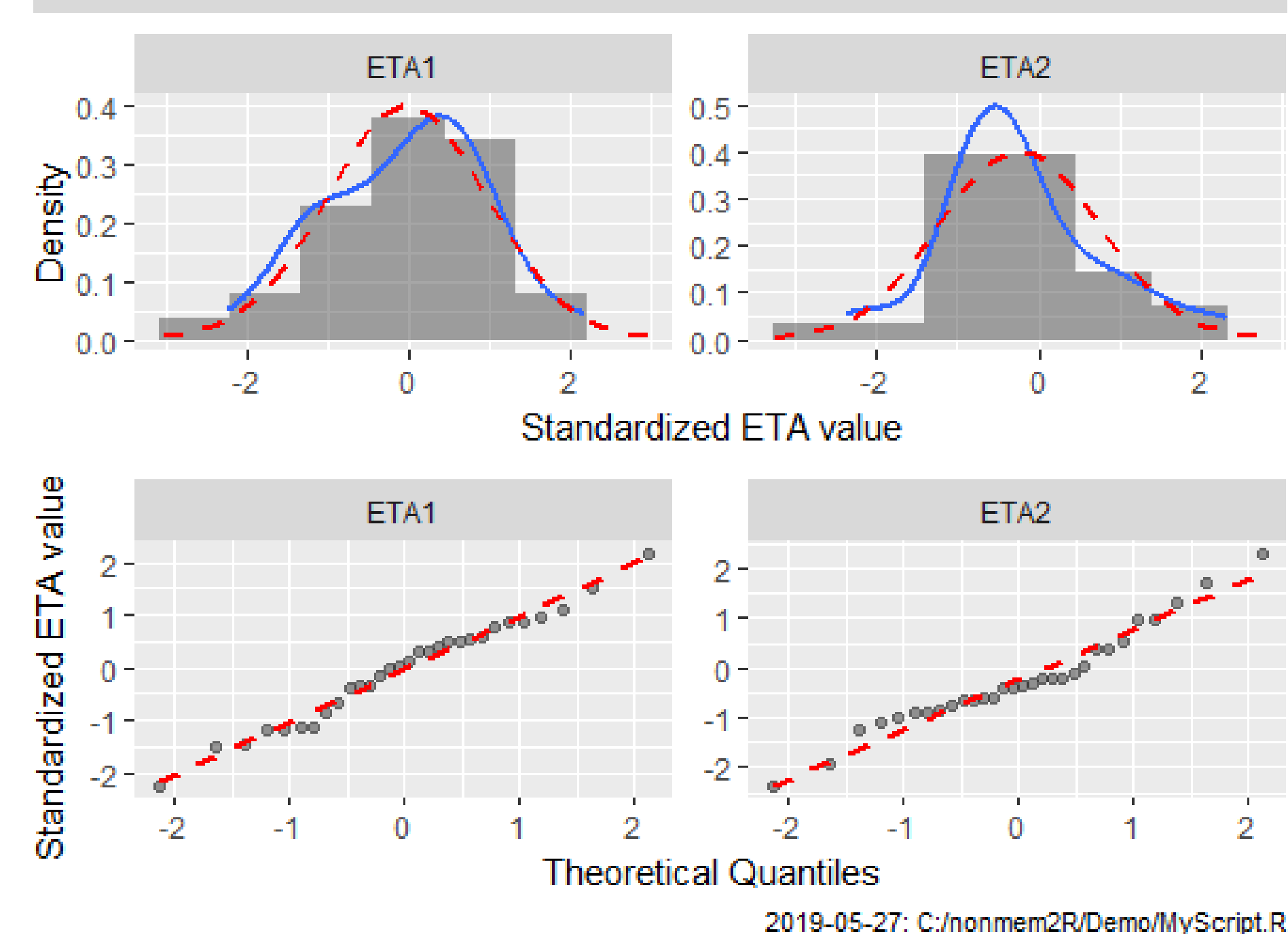
References

- <https://cran.r-project.org/web/packages/nonmem2R/index.html>
- NONlinear Mixed-Effect Modeling, <http://www.iconplc.com/innovation/solutions/nonmem/>
- Perl-speaks-NONMEM, <https://uupharmacometrics.github.io/PsN/>
- <https://cran.r-project.org/web/packages/ggplot2/index.html>

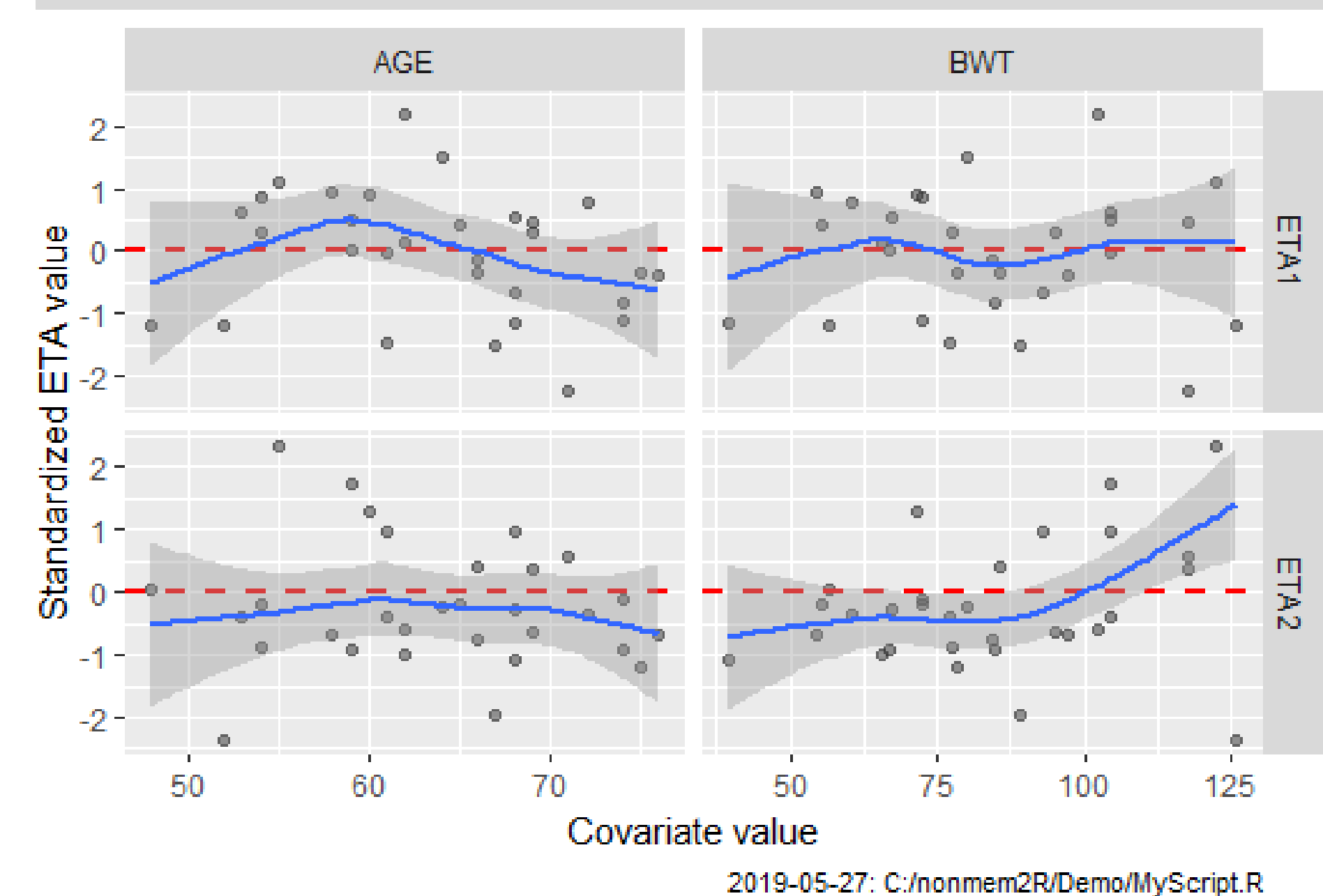
basic.eta.GOF, **eta.cov.GOF**, **eta.cat.GOF**, and **eta.pairs.GOF** are 4 tailored functions for doing GOF plots for ETA's.

These functions identify all ETA's in the input data-frame and provides different types of GOF plots for these columns. All 4 functions will by default exclude ETA's which are constant i.e. when set as FIX in your NONMEM model and each ETA is scaled to unit variance.

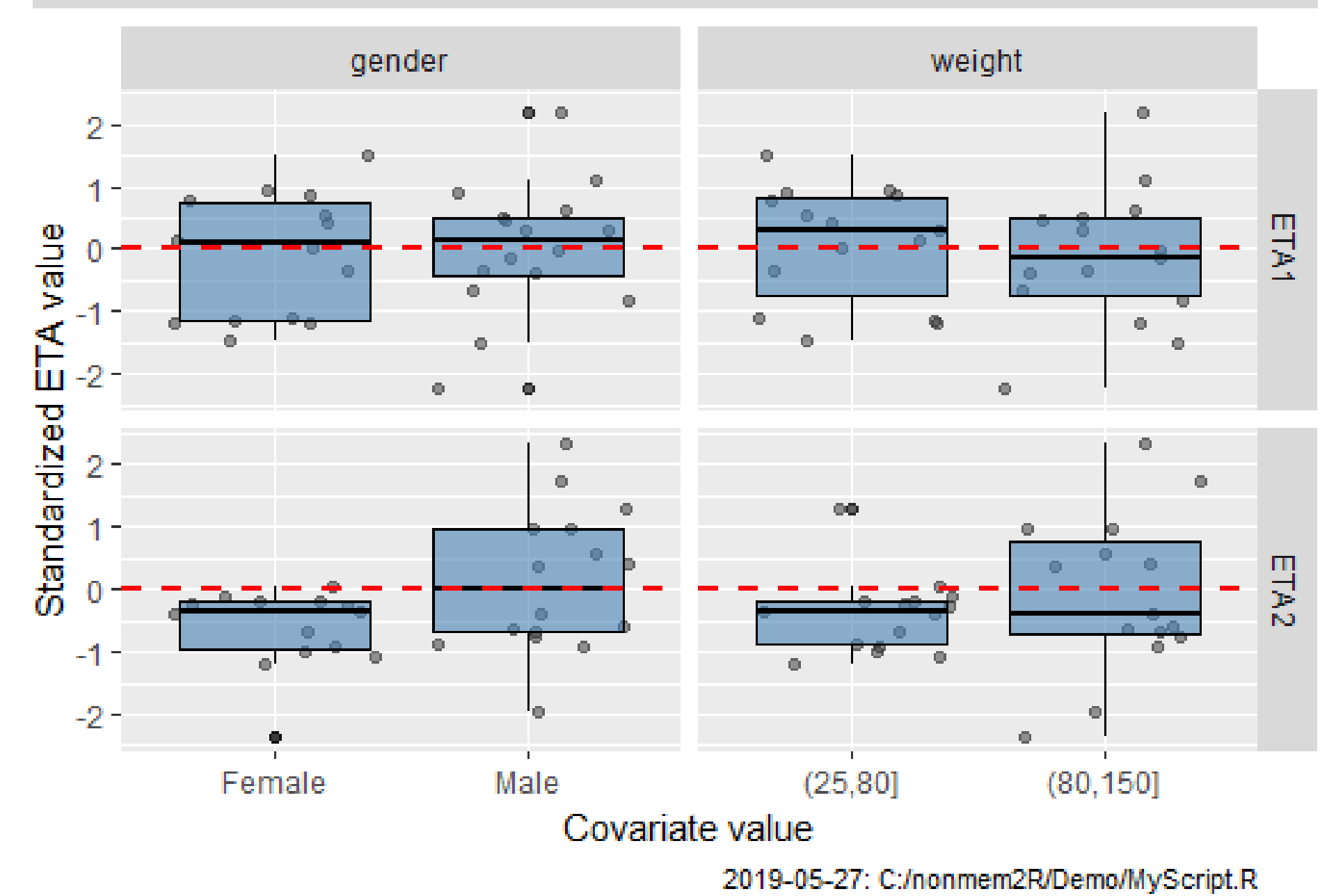
```
basic.eta.GOF(sdtab)
```



```
eta.cov.GOF(sdtab,
covariates=c("AGE","BWT"))
```



```
eta.cat.GOF(sdtab,
covariates=c("gender","weight"))
```



Conclusions

- With the addition of easy to use yet flexible functions for GOF plots nonmem2R now can produce the vast majority of graphics for model evaluation

