**Supplementary Material**

*Linear mixed-effects modelling for the effect of the circadian rhythm on cfDNA concentration and methylation levels of CDO1*, *SOX17,* and *TAC1*

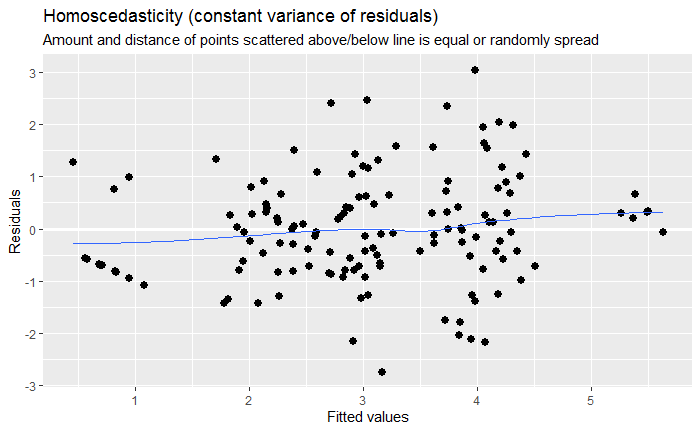
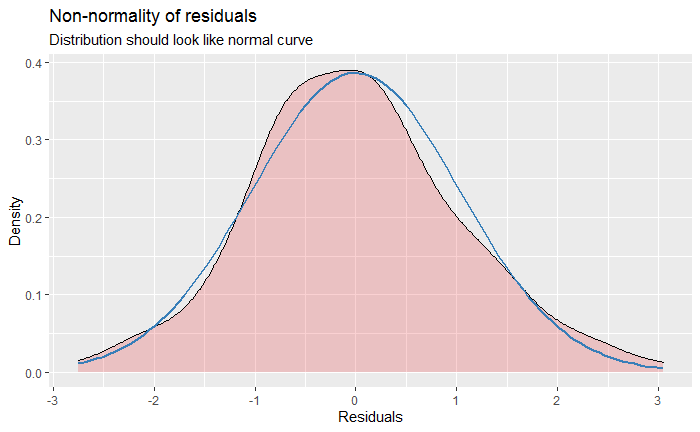
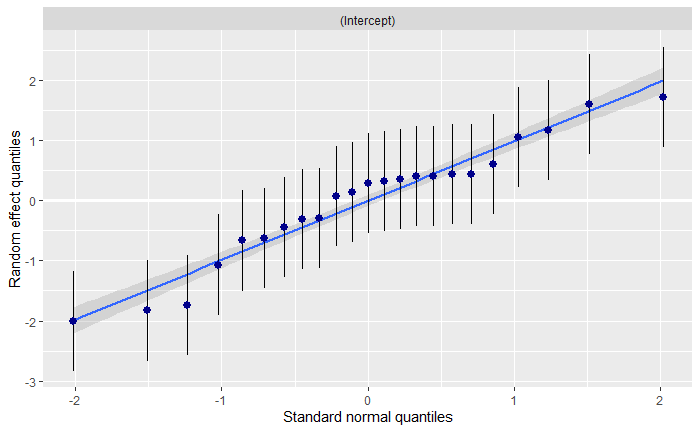
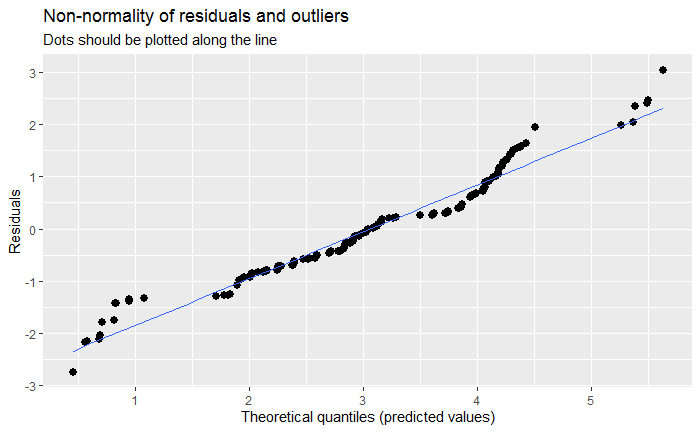
Models were fitted by backward stepwise elimination (*p* ≥ 0.05 for removal) to select fixed and random parts of the linear mixed model using the ‘lmerTest’ package in R. Final models are displayed below.



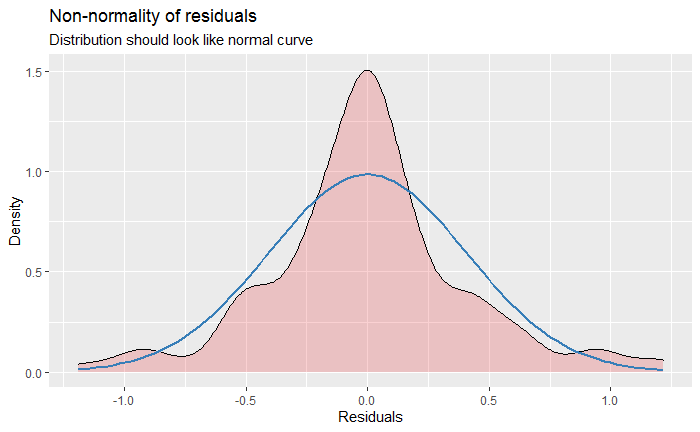
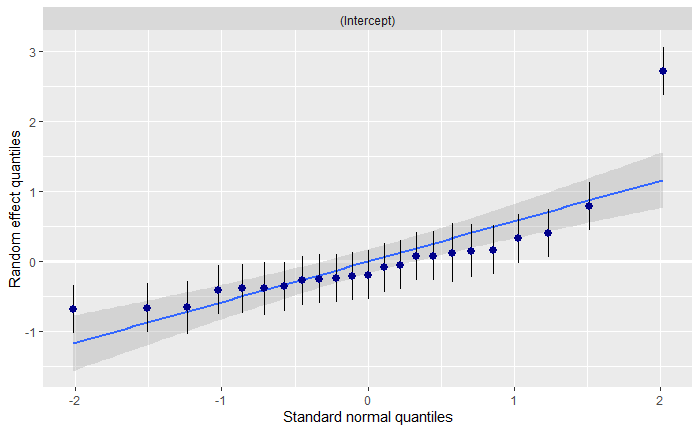
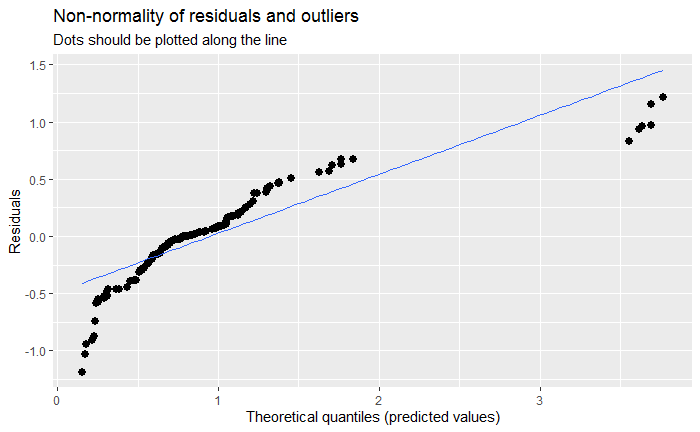
*Testing model assumptions*

The assumptions of linearity, normality of the residuals and random effects, and homoscedasticity (*i.e.* constant variance of the residuals) were checked visually. A series of diagnostic plots were computed using the ‘sjPlot’ package to check these assumptions.

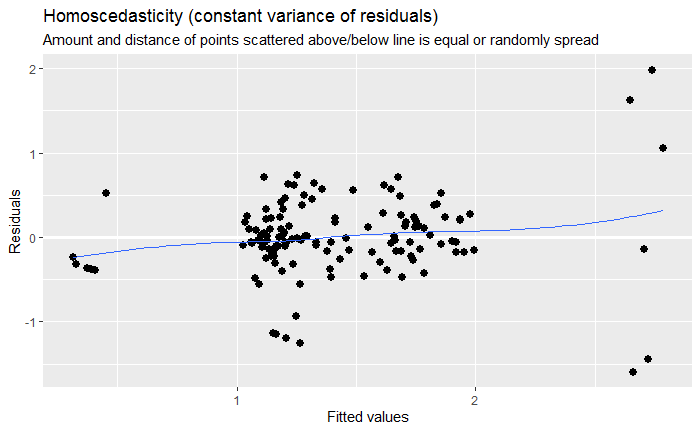
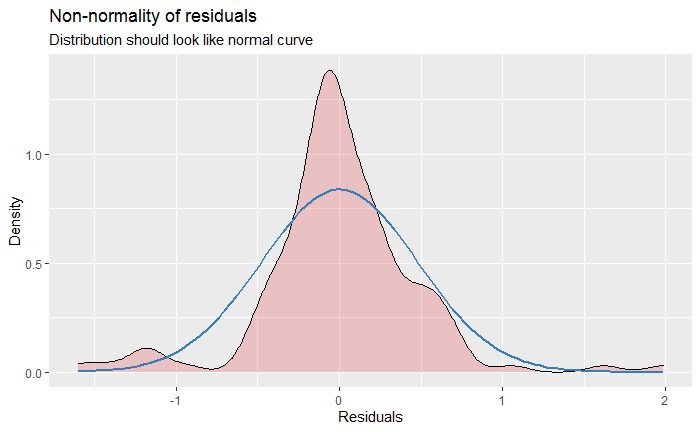
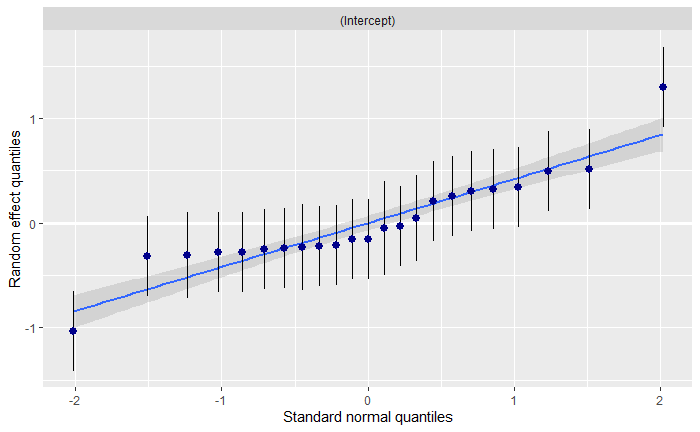
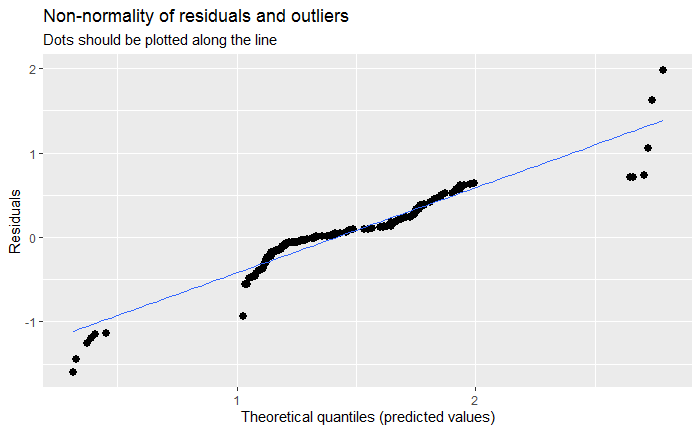
#1 – cfDNA concentration



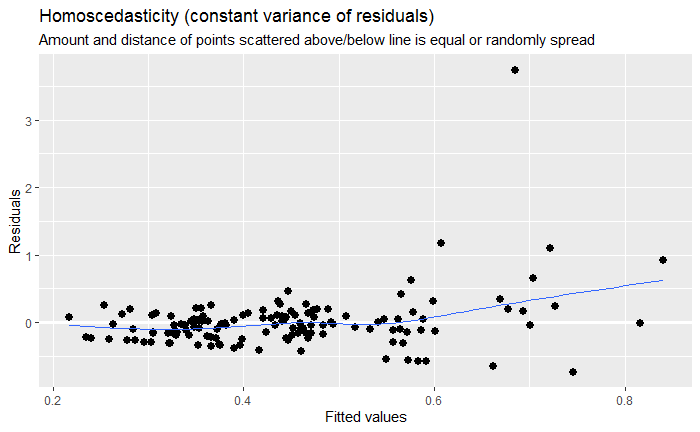
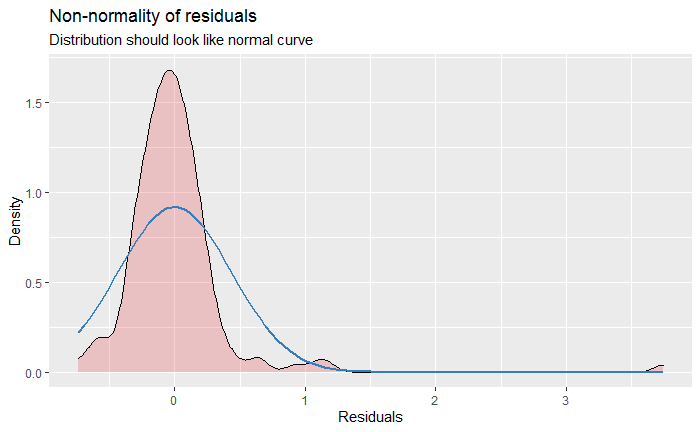
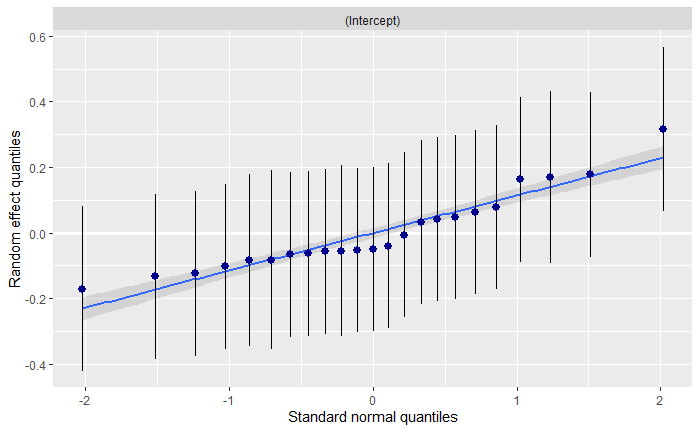
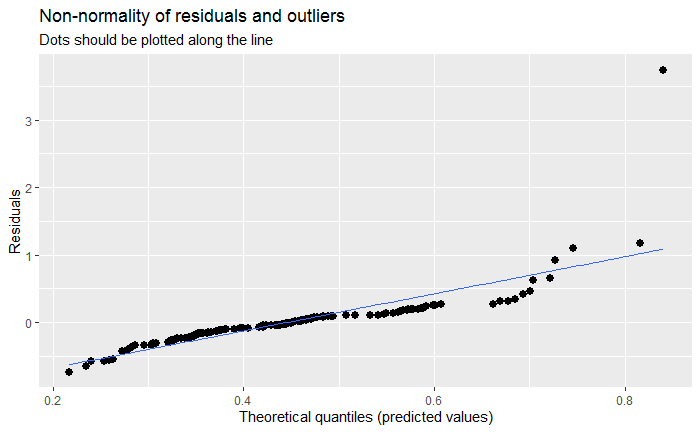
#2 – *CDO1* methylation level



#3 – *SOX17* methylation level



#4 – *TAC1* methylation level



*Linear mixed-effects modelling to compare the methylation levels of CDO1*, *SOX17,* and *TAC1* *in cases vs. controls and explore the additional value of collecting multiple urine samples*

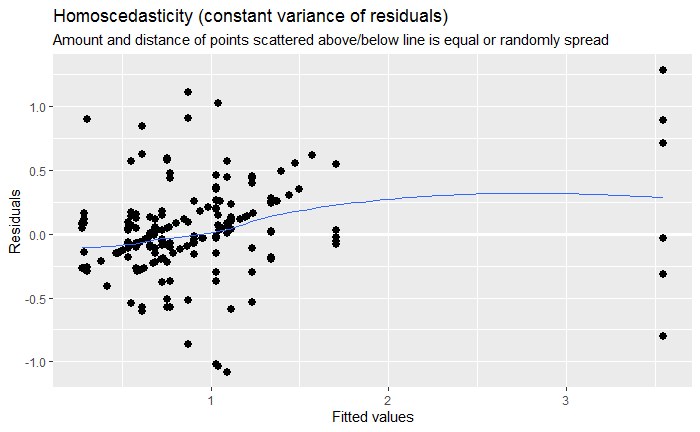
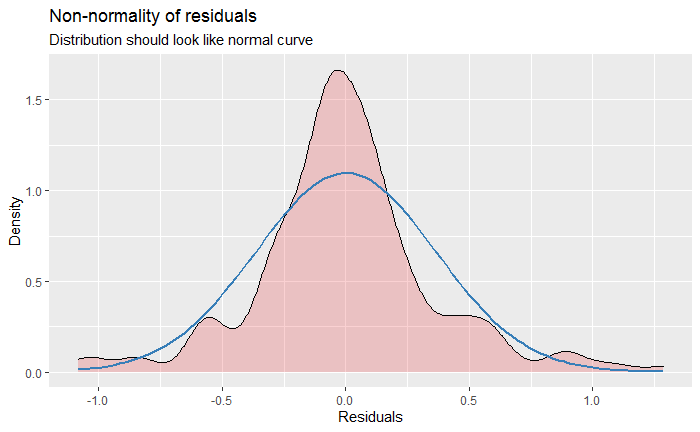
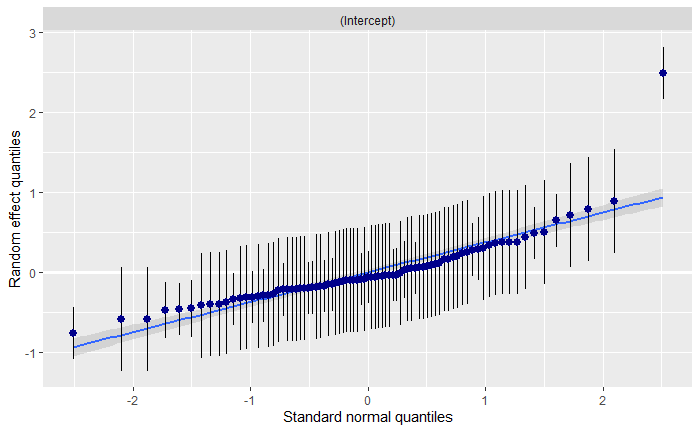
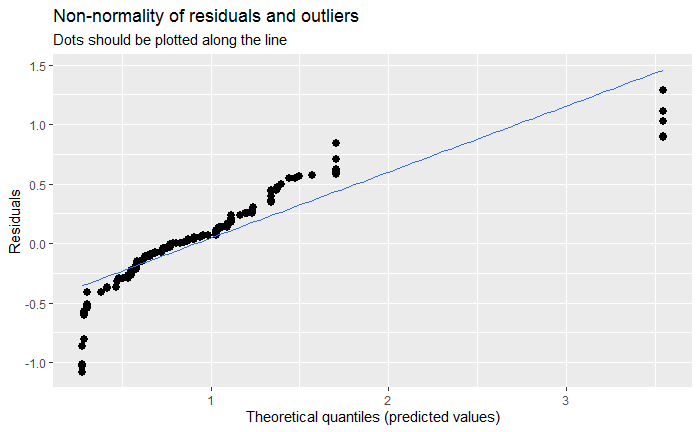
Models were fitted by backward stepwise elimination (*p* ≥ 0.05 for removal) to select fixed and random parts of the linear mixed model using the ‘lmerTest’ package in R. Final models are displayed below.



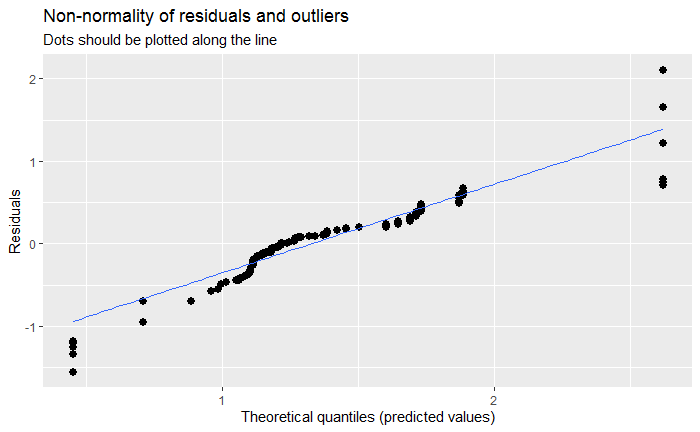
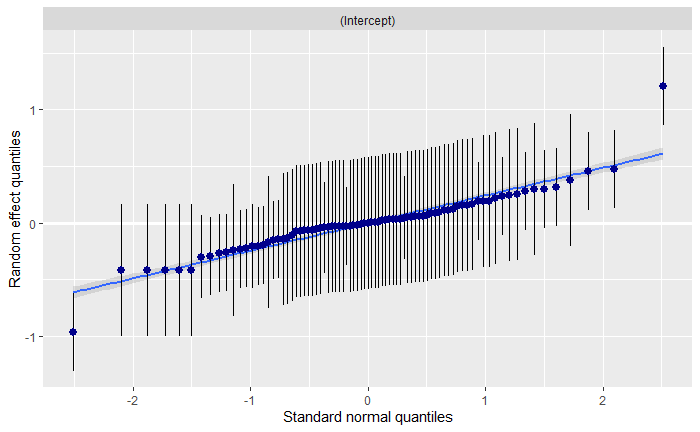
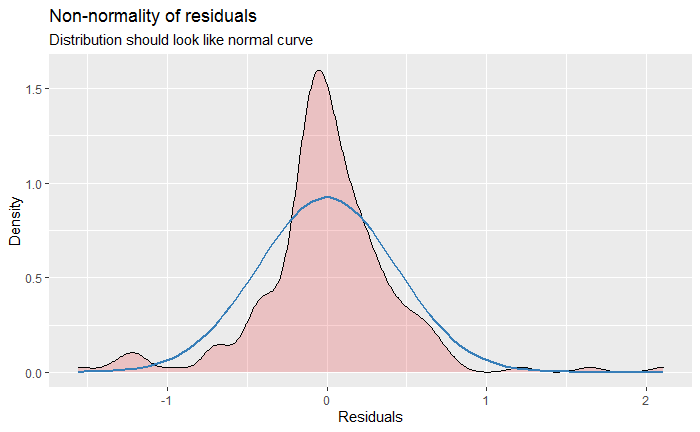
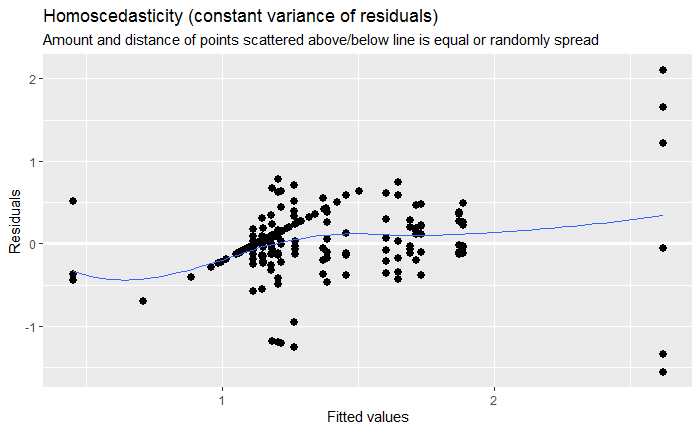
*Testing model assumptions*

The assumptions of linearity, normality of the residuals and random effects, and homoscedasticity (*i.e.* constant variance of the residuals) were checked visually. A series of diagnostic plots were computed using the ‘sjPlot’ package to check these assumptions.

#5 – *CDO1* methylation levels in cases vs. controls



#6 – *SOX17* methylation levels in cases vs. controls



#7 – *TAC1* methylation levels in cases vs. controls

