

S1 File: Appendix of statistical analyses

Neutrophil extracellular trap components associate with
myocardial recovery in post-ischemic acute heart failure

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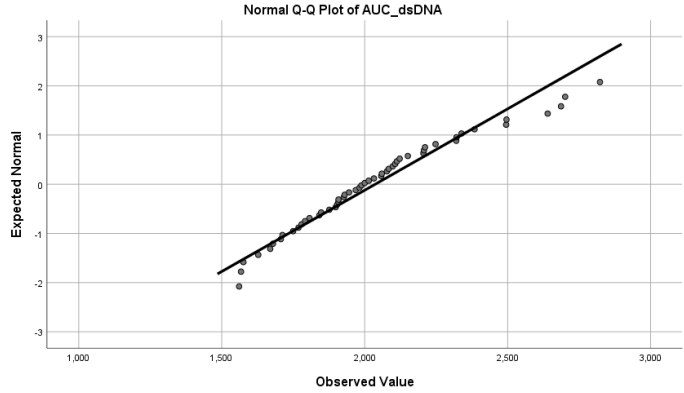
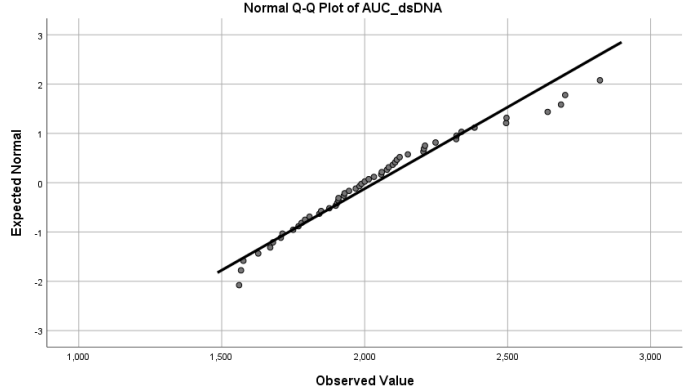
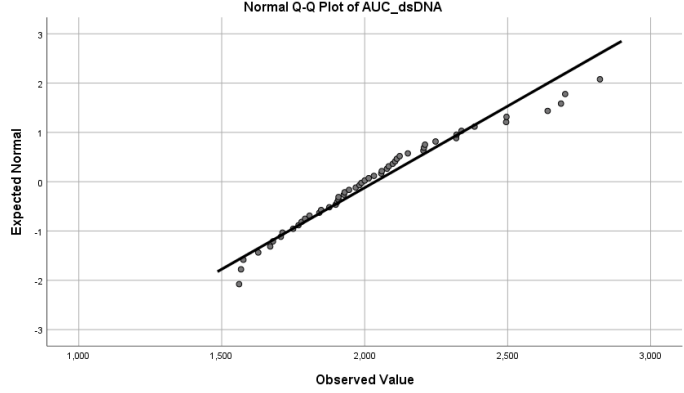
⁵ Oslo Centre for Biostatistics and Epidemiology, Institute for Basic Medical Sciences, University of Oslo, Oslo, Norway

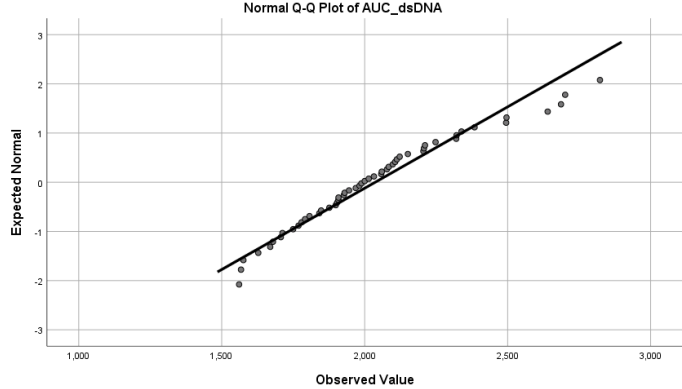
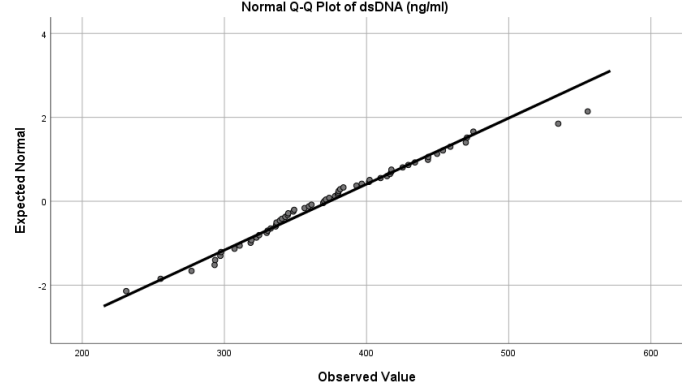
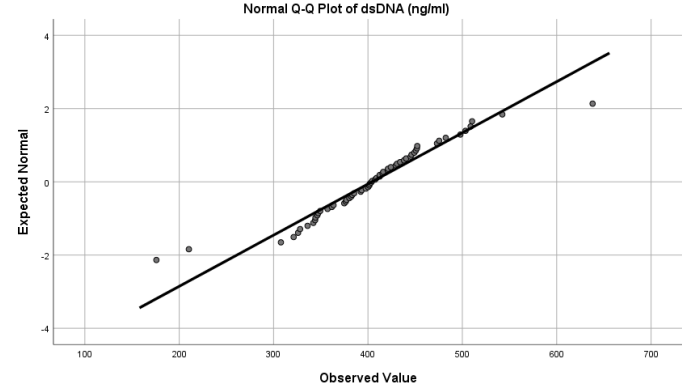
* Corresponding author

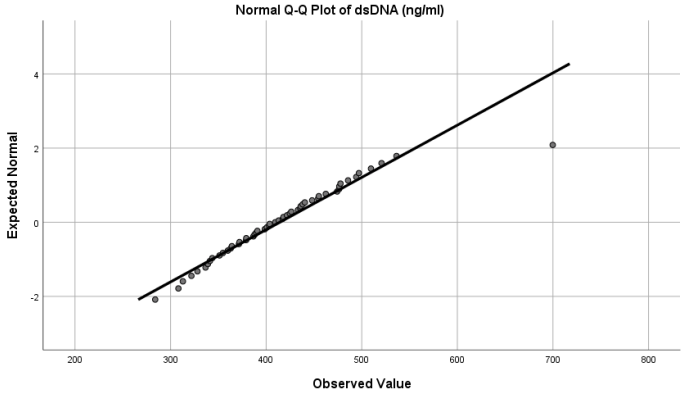
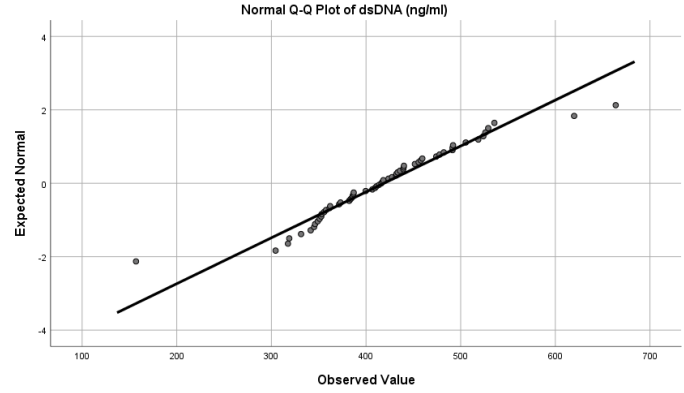
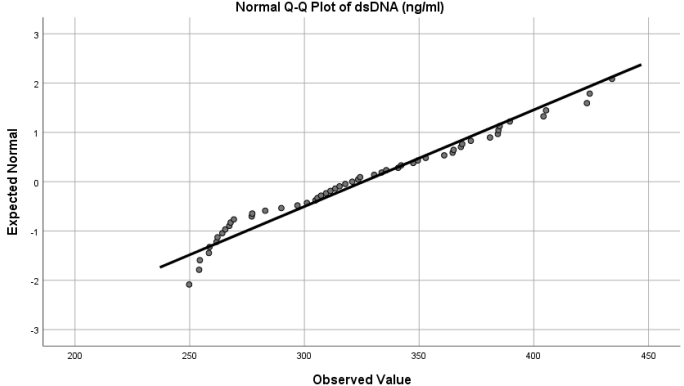
E-mail address: m.s.langseth@studmed.uio.no (MSL)

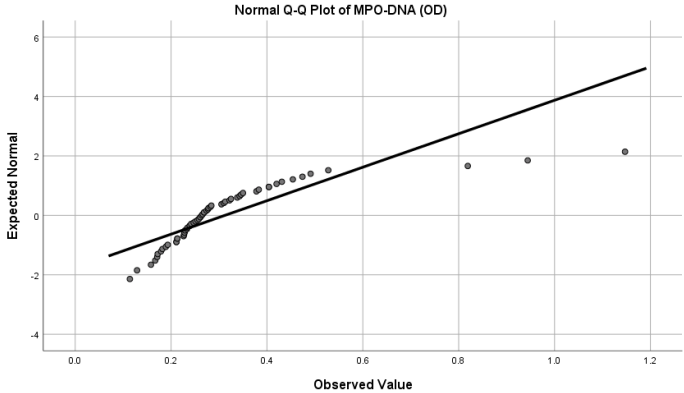
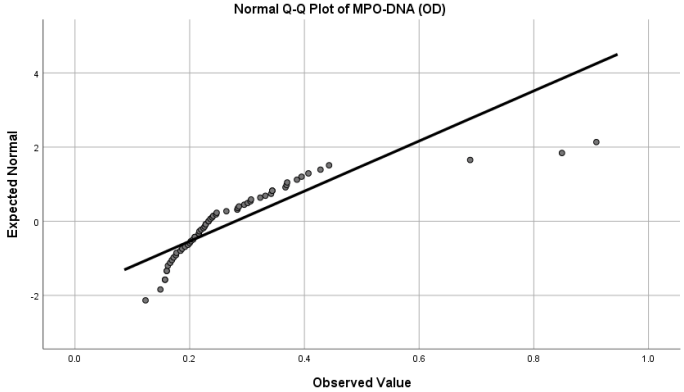
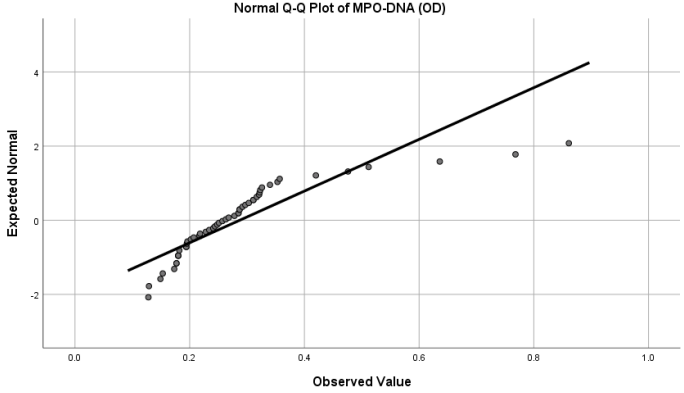
Assessing distributions of the variables

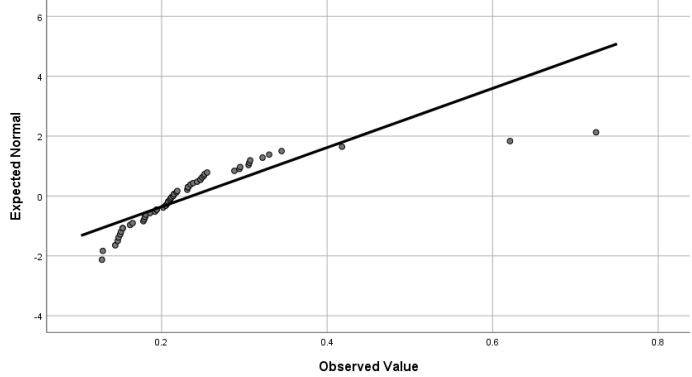
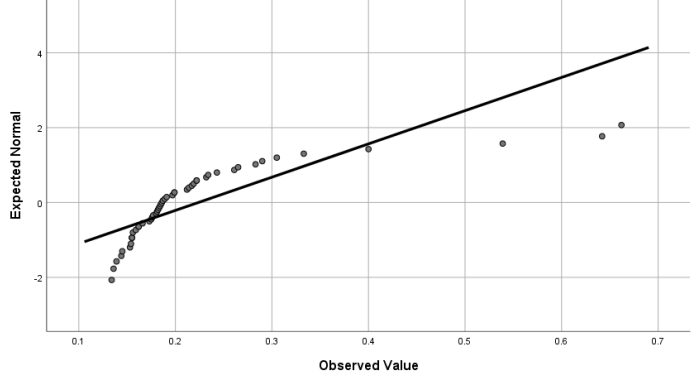
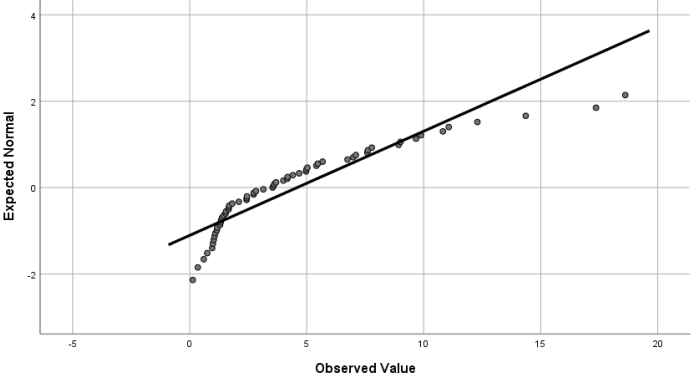
Variable	<i>n</i>	skewness	kurtosis	D*	<i>p</i> *	W**	<i>p</i> **	Normal Q-Q plot	Normal distribution?
dsDNA _{AUC}	53	0.66	0.12	0.09	0.20	0.96	0.08		YES
MPO-DNA _{AUC}	53	2.93	10.59	0.23	<0.001	0.70	<0.001		NO
CitH3 _{AUC}	53	0.81	0.36	0.15	0.003	0.92	0.002		NO

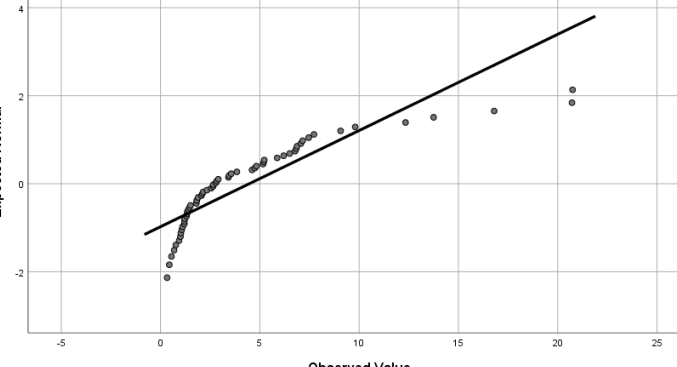
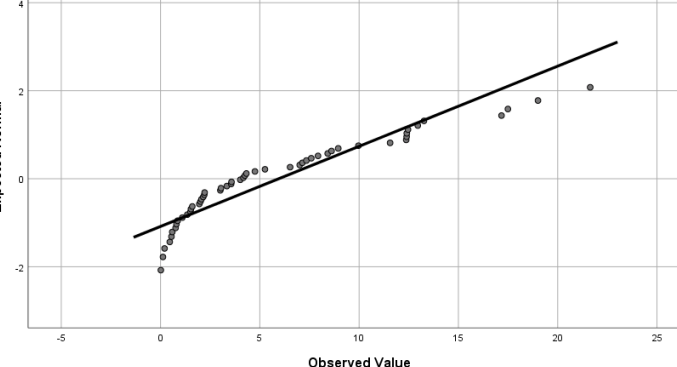
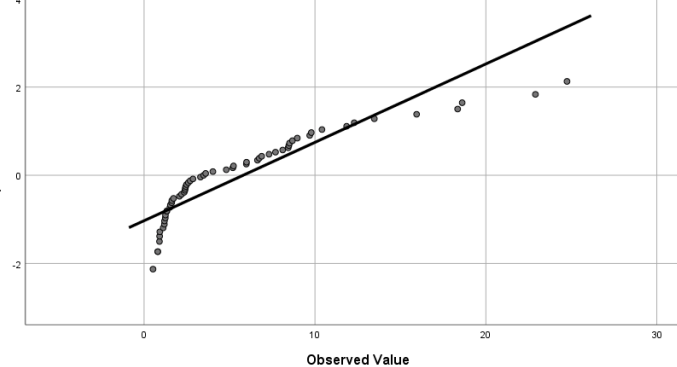
IL-8_{AUC}	53	1.71	3.96	0.15	0.006	0.84	<0.001		NO
ΔWMSI BL-day5	58	-0.02	0.64	0.09	0.20	0.98	0.49		YES
ΔGLS BL- day5	48	0.24	0.01	0.07	0.20	0.98	0.57		YES

ΔEF BL-day5	58	1.35	2.91	0.14	0.005	0.91	<0.001		NO
dsDNA BL	61	0.46	0.46	0.08	0.20	0.98	0.51		YES
dsDNA day 1	60	-0.10	2.80	0.10	0.20	0.95	0.02		NO

dsDNA day 2	53	1.19	3.72	0.07	0.20	0.93	0.006		NO
dsDNA day 5	59	0.21	2.20	0.09	0.20	0.96	0.04		YES
dsDNA day 42	53	0.29	-0.89	0.09	0.20	0.96	0.05		YES

MPO-DNA BL	61	2.91	10.20	0.20	<0.001	0.69	<0.001		NO
MPO-DNA day 1	60	2.65	8.39	0.19	<0.001	0.72	<0.001		NO
MPO-DNA day 2	52	2.33	6.43	0.22	<0.001	0.76	<0.001		NO

MPO-DNA day 5	59	3.01	11.66	0.22	<0.001	0.71	<0.001	<p data-bbox="1310 126 1528 149">Normal Q-Q Plot of MPO-DNA (OD)</p> 	NO
MPO-DNA day 42	51	2.76	7.90	0.25	<0.001	0.65	<0.001	<p data-bbox="1310 542 1528 565">Normal Q-Q Plot of MPO-DNA (OD)</p> 	NO
CitH3 BL	61	2.06	4.51	0.15	0.002	0.84	<0.001	<p data-bbox="1310 958 1528 980">Normal Q-Q Plot of CitH3 (ng/ml)</p> 	NO

CitH3 day 1	60	1.08	0.43	0.18	<0.001	0.76	<0.001	<p data-bbox="1310 133 1520 152">Normal Q-Q Plot of CitH3 (ng/ml)</p> 	NO
CitH3 day 2	52	1.61	2.45	0.17	<0.001	0.88	<0.001	<p data-bbox="1310 565 1520 584">Normal Q-Q Plot of CitH3 (ng/ml)</p> 	NO
CitH3 day 5	59	2.08	4.68	0.18	<0.001	0.81	<0.001	<p data-bbox="1310 997 1520 1016">Normal Q-Q Plot of CitH3 (ng/ml)</p> 	NO

CitH3 day 42	51	1.53	2.27	0.21	<0.001	0.77	<0.001		NO
IL-8 BL	60	3.99	19.06	0.24	<0.001	0.57	<0.001		NO
IL-8 day 1	59	1.38	1.94	0.17	<0.001	0.88	<0.001		NO

IL-8 day 2	52	2.33	7.60	0.15	0.007	0.80	<0.001		NO
IL-8 day 5	59	0.96	1.06	0.11	0.08	0.94	0.007		NO
IL-8 day 42	53	1.81	4.64	0.18	<0.001	0.84	<0.001		NO

* Kolmogorov-Smirnov test

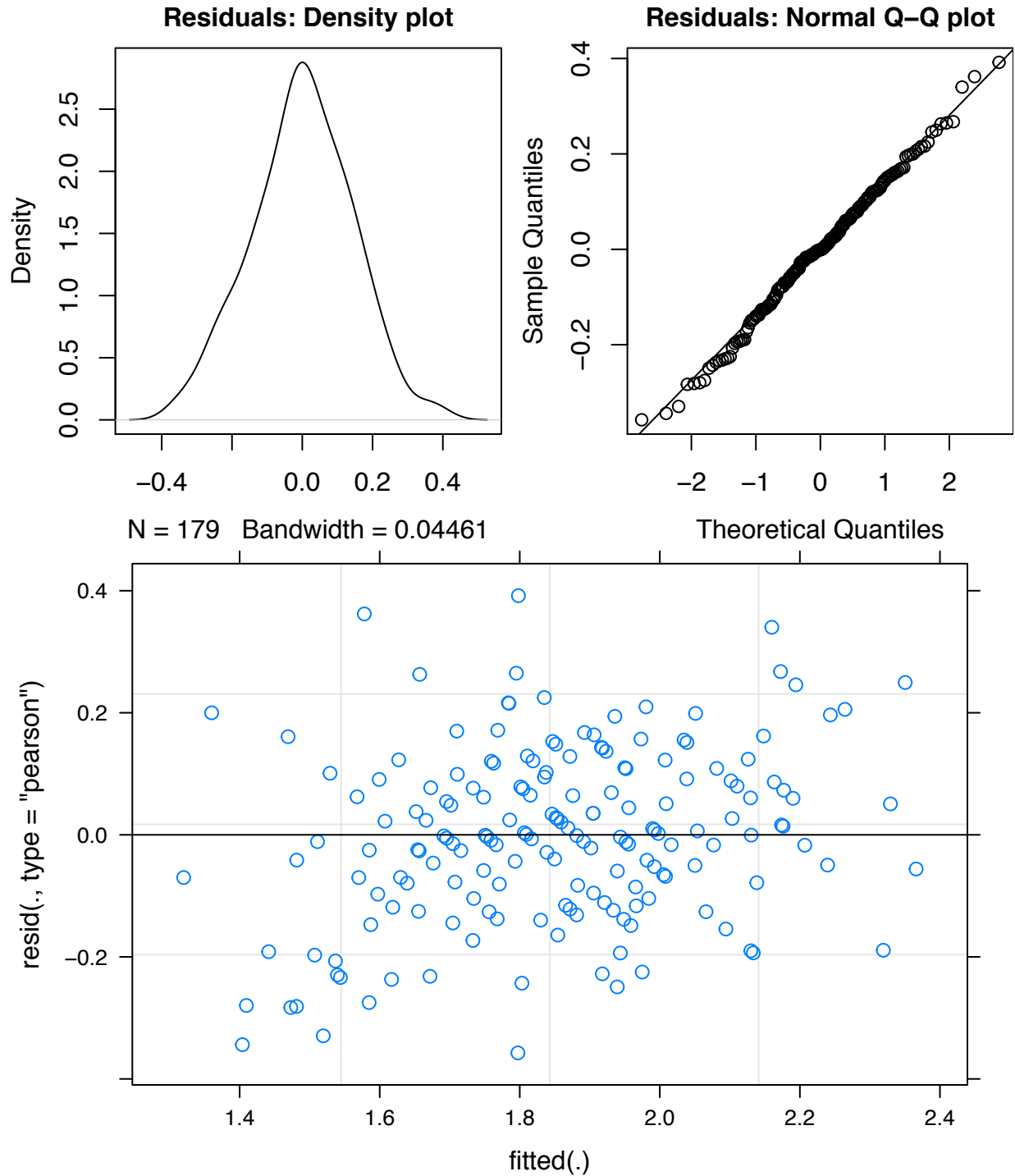
** Shapiro-Wilk test

2.1 WMSI

2.1.1 Check the model fit

For an example model (for $\text{WMSI} \sim \log.\text{dsDNA}$ without any of the potential confounders), check:

- Do the residuals follow a normal distribution?
- Are the residuals homoscedastic?



2.1.2 Check for confounders

```

## With NET variable log.dsDNA :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    2.341    0.774 160.334   3.024   0.003
## log.dsDNA     -0.065    0.129 148.651  -0.502   0.616
## day          -0.317    0.210 130.348  -1.512   0.133
## AGE           0.000    0.003  58.622   0.044   0.965
## SEX1         -0.041    0.070  56.809  -0.586   0.560
## KILLIPO      -0.007    0.043  56.199  -0.157   0.876
## log.dsDNA:day  0.047    0.035 130.587   1.329   0.186
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    2.401    0.792 150.178   3.032   0.003
## log.dsDNA     -0.065    0.134 140.667  -0.483   0.630
## day          -0.293    0.215 125.099  -1.360   0.176
## AGE          -0.001    0.003  57.266  -0.235   0.815
## SEX1         -0.038    0.072  53.887  -0.530   0.598
## RØYK_V01     -0.069    0.071  56.123  -0.967   0.338
## log.dsDNA:day  0.043    0.036 125.307   1.180   0.240
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    2.317    0.768 156.142   3.018   0.003
## log.dsDNA     -0.063    0.129 148.078  -0.483   0.630
## day          -0.316    0.210 130.561  -1.506   0.135
## AGE           0.001    0.003  56.907   0.193   0.848
## SEX1         -0.053    0.079  55.751  -0.671   0.505
## KREAT         0.000    0.001  56.172  -0.335   0.739
## log.dsDNA:day  0.046    0.035 130.789   1.322   0.188
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    2.749    0.847 158.821   3.246   0.001
## log.dsDNA     -0.129    0.139 149.268  -0.926   0.356
## day          -0.379    0.217 128.640  -1.748   0.083
## AGE          -0.001    0.003  56.782  -0.208   0.836
## SEX1         -0.036    0.070  56.389  -0.512   0.610
## LEUK_V0      -0.001    0.008  56.225  -0.106   0.916
## log.dsDNA:day  0.057    0.036 128.859   1.573   0.118
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    2.308    0.767 157.253   3.011   0.003
## log.dsDNA     -0.073    0.129 148.418  -0.565   0.573
## day          -0.315    0.210 130.820  -1.505   0.135
## AGE           0.000    0.003  58.551   0.081   0.935
## SEX1         -0.031    0.071  56.587  -0.436   0.664
## TnT           0.000    0.000  57.142   0.898   0.373
## log.dsDNA:day  0.046    0.035 131.050   1.322   0.188
##
## With NET variable log.CitH3 :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    1.929    0.208  56.095   9.261   0.000
## log.CitH3     -0.004    0.023 147.936  -0.172   0.864
## day          -0.034    0.010 121.775  -3.257   0.001
## AGE           0.000    0.003  55.201   0.140   0.889
## SEX1         -0.039    0.069  54.829  -0.563   0.576
## KILLIPO      -0.002    0.043  56.108  -0.039   0.969
## log.CitH3:day -0.003    0.007 125.661  -0.402   0.689
##      Estimate Std. Error      df t value Pr(>|t|)

```

```

## (Intercept)      2.003      0.190  56.044  10.530   0.000
## log.CitH3       -0.006      0.023 142.867  -0.277   0.782
## day            -0.035      0.010 116.146  -3.453   0.001
## AGE             0.000      0.003  53.956  -0.150   0.881
## SEX1           -0.036      0.071  52.855  -0.509   0.613
## RØYK_V01       -0.061      0.070  54.755  -0.873   0.386
## log.CitH3:day  -0.002      0.007 120.010  -0.287   0.775
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      1.933      0.169  57.541  11.414   0.000
## log.CitH3       -0.004      0.023 149.326  -0.163   0.871
## day            -0.034      0.010 121.646  -3.247   0.002
## AGE             0.001      0.003  55.206   0.257   0.798
## SEX1           -0.049      0.077  54.701  -0.637   0.527
## KREAT           0.000      0.001  55.161  -0.300   0.766
## log.CitH3:day  -0.003      0.007 125.465  -0.413   0.680
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      1.968      0.213  54.884   9.233   0.000
## log.CitH3       -0.001      0.023 146.728  -0.034   0.973
## day            -0.032      0.010 119.962  -3.109   0.002
## AGE             0.000      0.003  54.088  -0.145   0.885
## SEX1           -0.028      0.068  54.264  -0.409   0.684
## LEUK_V0        -0.001      0.008  55.489  -0.086   0.932
## log.CitH3:day  -0.004      0.007 124.268  -0.580   0.563
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      1.865      0.178  58.756  10.453   0.000
## log.CitH3       -0.003      0.023 149.652  -0.132   0.895
## day            -0.034      0.010 121.994  -3.278   0.001
## AGE             0.000      0.002  55.415   0.150   0.881
## SEX1           -0.028      0.069  55.002  -0.404   0.688
## TnT             0.000      0.000  56.568   0.905   0.369
## log.CitH3:day  -0.003      0.007 126.084  -0.386   0.700
##
## With NET variable log.MPODNA :
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      1.934      0.224  70.160   8.646   0.000
## log.MPODNA        0.002      0.056 156.407   0.042   0.967
## day            -0.027      0.028 125.466  -0.976   0.331
## AGE             0.000      0.003  56.253   0.147   0.884
## SEX1           -0.040      0.069  56.055  -0.577   0.567
## KILLIPO         -0.004      0.043  56.579  -0.101   0.920
## log.MPODNA:day   0.007      0.018 124.305   0.380   0.705
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      2.000      0.204  69.175   9.821   0.000
## log.MPODNA       -0.002      0.055 149.297  -0.040   0.968
## day            -0.021      0.027 118.182  -0.786   0.433
## AGE             0.000      0.003  54.515  -0.164   0.870
## SEX1           -0.038      0.071  53.526  -0.530   0.598
## RØYK_V01       -0.071      0.071  56.532  -1.004   0.320
## log.MPODNA:day   0.011      0.018 117.212   0.610   0.543
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      1.928      0.183  73.075  10.552   0.000
## log.MPODNA        0.001      0.056 156.784   0.024   0.981
## day            -0.027      0.028 125.439  -0.973   0.332
## AGE             0.001      0.003  56.299   0.267   0.791

```

## SEX1	-0.050	0.078	56.258	-0.644	0.522
## KREAT	0.000	0.001	56.084	-0.293	0.771
## log.MPODNA:day	0.007	0.018	124.242	0.385	0.701
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	1.967	0.229	68.131	8.590	0.000
## log.MPODNA	-0.001	0.056	155.885	-0.014	0.989
## day	-0.031	0.030	125.869	-1.050	0.296
## AGE	0.000	0.003	54.794	-0.148	0.883
## SEX1	-0.030	0.069	55.123	-0.443	0.660
## LEUK_VO	-0.001	0.008	56.635	-0.076	0.940
## log.MPODNA:day	0.004	0.020	123.576	0.206	0.837
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	1.857	0.192	74.121	9.656	0.000
## log.MPODNA	-0.001	0.056	156.876	-0.020	0.984
## day	-0.027	0.028	125.655	-0.996	0.321
## AGE	0.000	0.003	56.404	0.163	0.871
## SEX1	-0.029	0.069	56.058	-0.416	0.679
## TnT	0.000	0.000	57.370	0.929	0.357
## log.MPODNA:day	0.007	0.018	124.516	0.366	0.715

2.1.3 Summarise all final models (no confounders)

log.dsDNA:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: -0.8
##
## Scaled residuals:
## Min      1Q  Median      3Q      Max
## -2.0997 -0.5317 -0.0040  0.5696  2.3028
##
## Random effects:
## Groups   Name                Variance Std.Dev.
## ID      (Intercept)  0.04832  0.2198
## Residual                    0.02897  0.1702
## Number of obs: 179, groups: ID, 61
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   2.24355    0.75315 156.01538   2.979  0.00336 **
## log.dsDNA     -0.05225    0.12666 155.74092  -0.413  0.68049
## day           -0.30404    0.20911 131.77257  -1.454  0.14833
## log.dsDNA:day  0.04441    0.03498 132.02646   1.269  0.20650
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) lg.DNA day
## log.dsDNA    -0.999
## day          -0.680  0.680
## lg.dsDNA:dy  0.686 -0.686 -1.000
```

log.CitH3:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 7.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.22841 -0.52055 -0.01067  0.60425  2.45356
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID      (Intercept) 0.04624 0.2150
## Residual                0.02981 0.1727
## Number of obs: 179, groups: ID, 61
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   1.936718   0.041069 131.887588  47.158 < 2e-16 ***
## log.CitH3     -0.004523   0.023257 151.504920  -0.194  0.84605
## day           -0.033525   0.010340 122.391335  -3.242  0.00153 **
## log.CitH3:day -0.002917   0.006850 126.938271  -0.426  0.67091
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) lg.CH3 day
## log.CitH3    -0.606
## day          -0.436  0.423
## log.CtH3:dy  0.384 -0.611 -0.808
```


log.MPODNA:

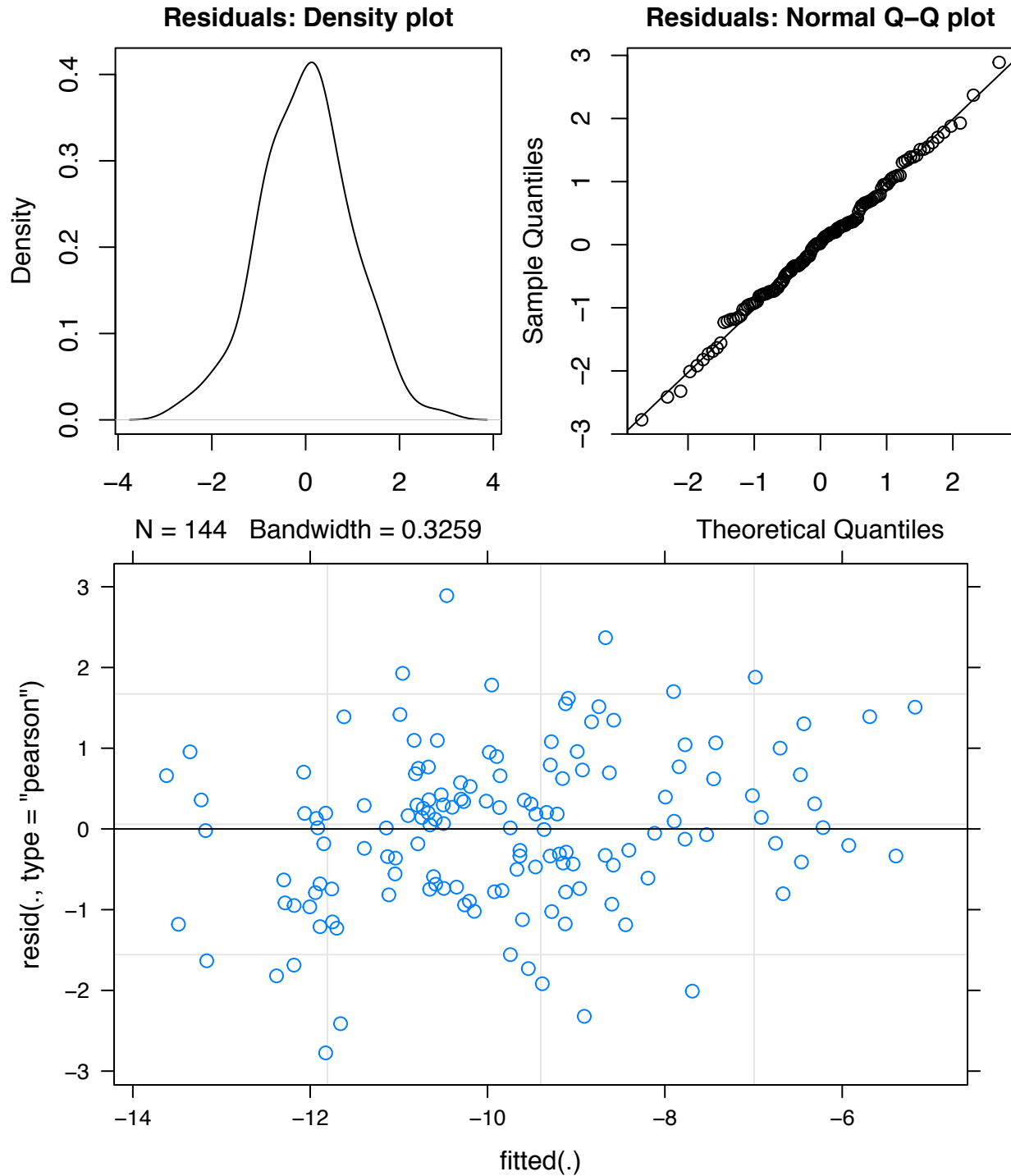
```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 3.5
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.22581 -0.48276 0.00195 0.61079 2.39270
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.04700 0.2168
## Residual 0.02969 0.1723
## Number of obs: 179, groups: ID, 61
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 1.938005 0.079411 174.203038 24.405 <2e-16 ***
## log.MPODNA 0.004663 0.055492 159.776526 0.084 0.933
## day -0.027170 0.027508 126.037352 -0.988 0.325
## log.MPODNA:day 0.006769 0.018379 124.858819 0.368 0.713
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) lg.MPODNA day
## log.MPODNA 0.910
## day -0.362 -0.349
## lg.MPODNA:d -0.405 -0.432 0.973
```

2.2 GLS

2.2.1 Check the model fit

For an example model (for $GLS \sim \log.dsDNA$ without any of the potential confounders), check:

- Do the residuals follow a normal distribution?
- Are the residuals homoscedastic?



2.2.2 Check for confounders

```

## With NET variable log.dsDNA :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -11.653    6.368 126.074  -1.830  0.070
## log.dsDNA     0.780    1.042 113.031   0.749  0.456
## day           0.477    1.757 104.014   0.271  0.787
## AGE          -0.026    0.025  44.949  -1.062  0.294
## SEX1         -1.226    0.623  44.677  -1.967  0.055
## KILLIPO      -0.026    0.382  44.876  -0.068  0.946
## log.dsDNA:day -0.132    0.295 104.087  -0.449  0.654
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -11.704    6.308 122.351  -1.855  0.066
## log.dsDNA     0.800    1.048 111.540   0.763  0.447
## day           0.472    1.758 103.888   0.269  0.789
## AGE          -0.028    0.026  46.208  -1.069  0.291
## SEX1         -1.224    0.622  44.614  -1.968  0.055
## RØYK_V01     -0.113    0.588  46.790  -0.192  0.849
## log.dsDNA:day -0.132    0.295 103.971  -0.447  0.656
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -12.126    6.274 123.390  -1.933  0.056
## log.dsDNA     0.678    1.039 114.106   0.652  0.515
## day           0.403    1.754 104.743   0.230  0.819
## AGE          -0.036    0.024  44.659  -1.492  0.143
## SEX1         -0.758    0.657  44.138  -1.154  0.255
## KREAT         0.018    0.010  44.379   1.767  0.084
## log.dsDNA:day -0.120    0.294 104.811  -0.407  0.685
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -14.988    7.215 125.243  -2.077  0.040
## log.dsDNA     1.151    1.143 115.455   1.007  0.316
## day           0.841    1.828 103.506   0.460  0.646
## AGE          -0.025    0.025  44.139  -1.021  0.313
## SEX1         -1.032    0.586  44.174  -1.761  0.085
## LEUK_V0       0.062    0.075  45.326   0.824  0.415
## log.dsDNA:day -0.193    0.307 103.570  -0.628  0.531
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -12.541    6.253 124.345  -2.005  0.047
## log.dsDNA     0.671    1.034 115.101   0.648  0.518
## day           0.470    1.747 105.781   0.269  0.788
## AGE          -0.021    0.023  45.874  -0.888  0.379
## SEX1         -1.038    0.600  45.056  -1.729  0.091
## TnT           0.000    0.000  45.542   2.204  0.033
## log.dsDNA:day -0.131    0.293 105.858  -0.447  0.656
##
## With NET variable log.CitH3 :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -7.058    1.899  43.841  -3.716  0.001
## log.CitH3     -0.045    0.189 111.927  -0.236  0.814
## day          -0.210    0.080  93.294  -2.635  0.010
## AGE          -0.027    0.024  43.884  -1.107  0.274
## SEX1         -1.174    0.613  44.157  -1.914  0.062
## KILLIPO       0.015    0.377  44.677   0.039  0.969
## log.CitH3:day -0.068    0.052  96.362  -1.312  0.193
##      Estimate Std. Error      df t value Pr(>|t|)

```

```

## (Intercept)      -7.071      1.702  46.019  -4.156    0.000
## log.CitH3        -0.044      0.189 113.084  -0.234    0.816
## day              -0.209      0.080  92.541  -2.623    0.010
## AGE              -0.026      0.025  44.369  -1.046    0.301
## SEX1             -1.175      0.612  44.104  -1.919    0.062
## RØYK_V01         0.045      0.574  44.861   0.078    0.938
## log.CitH3:day   -0.069      0.052  95.659  -1.316    0.191
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -7.981      1.583  45.114  -5.043    0.000
## log.CitH3     -0.076      0.188 113.588  -0.405    0.686
## day           -0.216      0.080  93.238  -2.706    0.008
## AGE           -0.038      0.024  43.613  -1.583    0.121
## SEX1          -0.694      0.645  43.574  -1.076    0.288
## KREAT         0.018      0.010  43.700   1.831    0.074
## log.CitH3:day -0.062      0.052  96.178  -1.193    0.236
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -7.934      1.956  43.531  -4.056    0.000
## log.CitH3     -0.036      0.188 113.119  -0.192    0.848
## day           -0.194      0.080  92.824  -2.416    0.018
## AGE           -0.027      0.024  43.191  -1.118    0.270
## SEX1          -0.979      0.571  43.689  -1.713    0.094
## LEUK_V0       0.054      0.072  43.813   0.738    0.464
## log.CitH3:day -0.076      0.053  96.505  -1.452    0.150
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -8.423      1.619  47.234  -5.202    0.000
## log.CitH3     -0.040      0.187 115.273  -0.212    0.832
## day           -0.215      0.079  94.439  -2.704    0.008
## AGE           -0.022      0.023  45.051  -0.957    0.343
## SEX1          -0.994      0.592  44.621  -1.679    0.100
## TnT           0.000      0.000  45.048   2.165    0.036
## log.CitH3:day -0.065      0.052  97.822  -1.264    0.209
##
## With NET variable log.MPODNA :
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -7.301      2.032  51.287  -3.593    0.001
## log.MPODNA    -0.120      0.420 118.940  -0.285    0.777
## day           -0.254      0.198  94.479  -1.288    0.201
## AGE           -0.025      0.025  43.966  -0.996    0.325
## SEX1          -1.272      0.626  43.916  -2.033    0.048
## KILLIPO      -0.009      0.384  44.437  -0.024    0.981
## log.MPODNA:day 0.038      0.135  93.780   0.280    0.780
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -7.251      1.822  53.767  -3.980    0.000
## log.MPODNA    -0.118      0.420 118.984  -0.280    0.780
## day           -0.253      0.198  93.071  -1.274    0.206
## AGE           -0.025      0.026  44.435  -0.986    0.330
## SEX1          -1.271      0.624  43.800  -2.036    0.048
## RØYK_V01     -0.059      0.588  45.457  -0.101    0.920
## log.MPODNA:day 0.039      0.135  92.413   0.288    0.774
##
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -8.279      1.693  52.380  -4.891    0.000
## log.MPODNA    -0.076      0.418 120.509  -0.181    0.857
## day           -0.260      0.197  94.703  -1.317    0.191
## AGE           -0.035      0.024  43.741  -1.449    0.154

```

## SEX1	-0.788	0.659	43.597	-1.195	0.239
## KREAT	0.018	0.010	43.570	1.794	0.080
## log.MPODNA:day	0.032	0.135	93.897	0.239	0.812
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	-8.195	2.150	53.537	-3.812	0.000
## log.MPODNA	-0.102	0.423	120.387	-0.241	0.810
## day	-0.234	0.215	96.672	-1.086	0.280
## AGE	-0.025	0.025	43.862	-1.003	0.321
## SEX1	-1.084	0.589	43.987	-1.841	0.072
## LEUK_V0	0.054	0.075	45.079	0.720	0.475
## log.MPODNA:day	0.046	0.144	94.942	0.319	0.750
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	-8.867	1.733	55.681	-5.118	0.000
## log.MPODNA	-0.165	0.416	121.148	-0.397	0.692
## day	-0.259	0.197	95.901	-1.319	0.190
## AGE	-0.020	0.024	45.103	-0.832	0.410
## SEX1	-1.077	0.602	44.558	-1.788	0.081
## TnT	0.000	0.000	45.374	2.250	0.029
## log.MPODNA:day	0.036	0.134	95.191	0.269	0.788

2.2.3 Summarise all final models (no confounders)

log.dsDNA:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [  
## lmerModLmerTest]  
## Formula: as.formula(fma)  
## Data: dat  
##  
## REML criterion at convergence: 563.9  
##  
## Scaled residuals:  
##      Min       1Q   Median       3Q      Max  
## -2.33264 -0.58340  0.02769  0.55400  2.42963  
##  
## Random effects:  
## Groups   Name                Variance Std.Dev.  
## ID       (Intercept)  3.481    1.866  
## Residual                    1.415    1.189  
## Number of obs: 144, groups: ID, 51  
##  
## Fixed effects:  
##              Estimate Std. Error      df t value Pr(>|t|)  
## (Intercept)  -14.1548    6.1920 113.6712  -2.286  0.0241 *  
## log.dsDNA     0.8544    1.0414 113.3206   0.820  0.4137  
## day           0.6208    1.7591 103.6545   0.353  0.7249  
## log.dsDNA:day -0.1566    0.2949 103.7294  -0.531  0.5967  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1  
##  
## Correlation of Fixed Effects:  
##              (Intr) lg.DNA day  
## log.dsDNA    -0.999  
## day          -0.678  0.678  
## lg.dsDNA:dy  0.682 -0.683 -1.000
```

log.CitH3:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 567.5
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.40081 -0.57233  0.07182  0.50516  2.36317
##
## Random effects:
## Groups   Name                Variance Std.Dev.
## ID      (Intercept)  3.360    1.833
## Residual                    1.392    1.180
## Number of obs: 144, groups: ID, 51
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -9.04320   0.35933 102.26670 -25.167  <2e-16 ***
## log.CitH3    -0.04431   0.18910 112.30498  -0.234   0.815
## day          -0.20659   0.07967  93.39517  -2.593   0.011 *
## log.CitH3:day -0.07076   0.05199  96.49800  -1.361   0.177
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) lg.CH3 day
## log.CitH3    -0.592
## day          -0.413  0.438
## log.CtH3:dy  0.386 -0.630 -0.815
```

log.MPODNA:

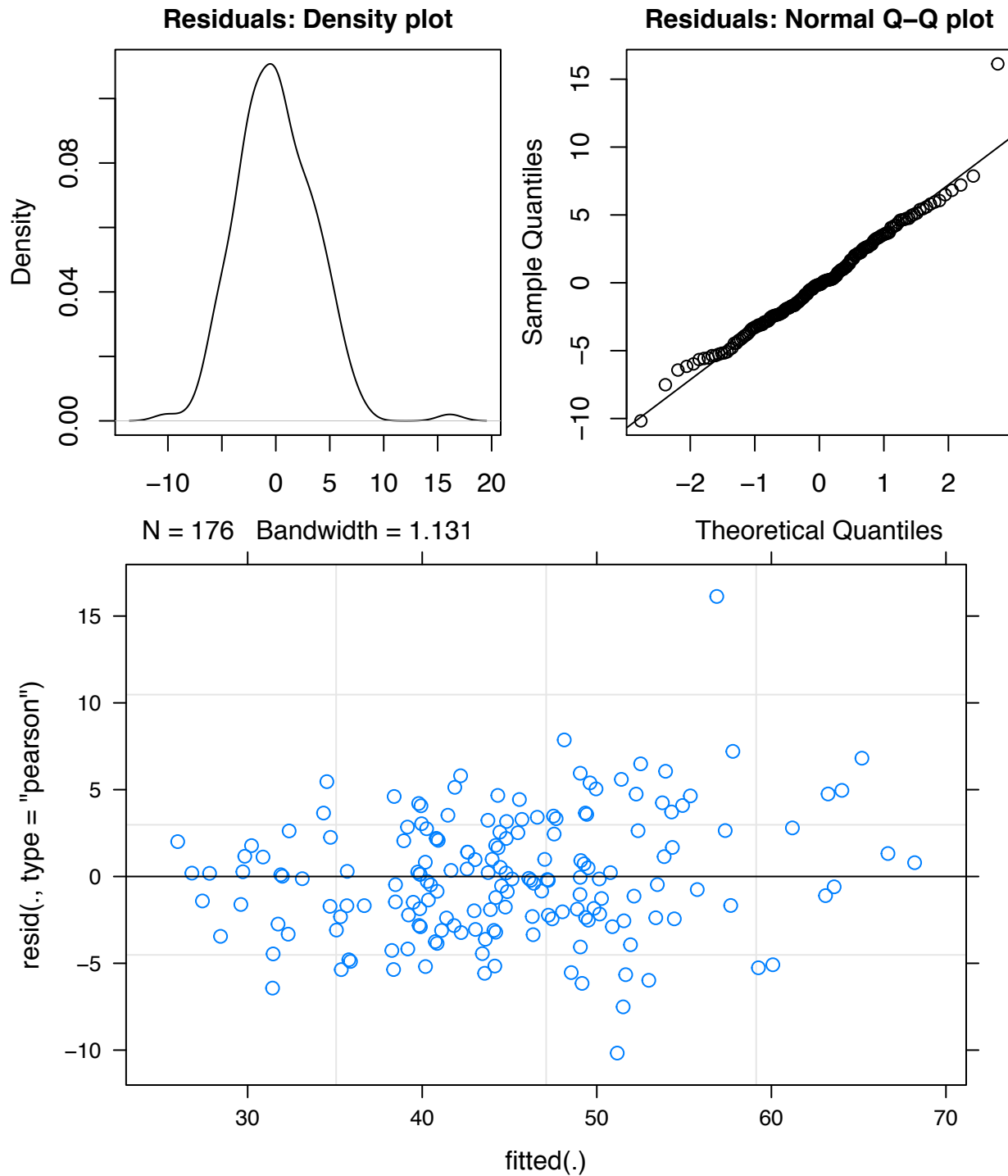
```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 567.4
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.32394 -0.55145 0.02868 0.52692 2.41617
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 3.530 1.879
## Residual 1.415 1.189
## Number of obs: 144, groups: ID, 51
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) -9.20708 0.61056 139.70924 -15.080 <2e-16 ***
## log.MPODNA -0.09901 0.42116 118.73502 -0.235 0.815
## day -0.25906 0.19748 94.61704 -1.312 0.193
## log.MPODNA:day 0.03421 0.13453 93.91229 0.254 0.800
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) lg.MPODNA day
## log.MPODNA 0.875
## day -0.331 -0.328
## lg.MPODNA:d -0.372 -0.414 0.969
```


2.3 EF

2.3.1 Check the model fit

For an example model (for $EF \sim \log.dsDNA$ without any of the potential confounders), check:

- Do the residuals follow a normal distribution?
- Are the residuals homoscedastic?



2.3.2 Check for confounders

```

## With NET variable log.dsDNA :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   65.871    21.160 157.647   3.113   0.002
## log.dsDNA     -3.613     3.413 131.490  -1.058   0.292
## day           4.655     5.495 122.656   0.847   0.399
## AGE          -0.005     0.096  56.903  -0.050   0.960
## SEX1          2.727     2.535  56.091   1.076   0.287
## KILLIPO      -0.912     1.577  55.717  -0.578   0.565
## log.dsDNA:day -0.609     0.919 122.731  -0.663   0.509
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   55.629    21.973 146.027   2.532   0.012
## log.dsDNA     -3.204     3.621 125.749  -0.885   0.378
## day           5.905     5.823 118.445   1.014   0.313
## AGE           0.063     0.104  55.411   0.608   0.546
## SEX1          2.296     2.603  53.412   0.882   0.382
## RØYK_V01      3.036     2.597  54.948   1.169   0.248
## log.dsDNA:day -0.819     0.974 118.513  -0.841   0.402
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   63.347    20.729 149.569   3.056   0.003
## log.dsDNA     -3.632     3.418 130.917  -1.063   0.290
## day           4.696     5.496 122.633   0.854   0.395
## AGE           0.009     0.104  55.997   0.086   0.931
## SEX1          2.596     2.862  55.488   0.907   0.368
## KREAT        -0.005     0.038  55.755  -0.143   0.887
## log.dsDNA:day -0.616     0.919 122.705  -0.670   0.504
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   63.509    23.135 152.480   2.745   0.007
## log.dsDNA     -2.961     3.699 131.688  -0.801   0.425
## day           5.800     5.684 120.579   1.020   0.310
## AGE           0.016     0.097  54.967   0.162   0.872
## SEX1          2.385     2.515  54.749   0.948   0.347
## LEUK_V0      -0.364     0.306  54.328  -1.189   0.239
## log.dsDNA:day -0.803     0.951 120.655  -0.844   0.400
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   65.056    20.737 151.524   3.137   0.002
## log.dsDNA     -3.499     3.413 131.495  -1.025   0.307
## day           4.692     5.491 122.978   0.855   0.394
## AGE           0.001     0.094  57.053   0.015   0.988
## SEX1          2.315     2.552  56.063   0.907   0.368
## TnT           0.000     0.000  56.347  -1.102   0.275
## log.dsDNA:day -0.616     0.918 123.050  -0.671   0.504
##
## With NET variable log.CitH3 :
##      Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   46.517     7.845  55.544   5.929   0.000
## log.CitH3      0.059     0.607 129.872   0.097   0.923
## day           0.483     0.261 116.547   1.851   0.067
## AGE          -0.029     0.095  55.273  -0.302   0.764
## SEX1          2.942     2.520  55.226   1.168   0.248
## KILLIPO      -1.155     1.578  56.100  -0.732   0.467
## log.CitH3:day  0.316     0.173 118.255   1.827   0.070
##      Estimate Std. Error      df t value Pr(>|t|)

```

```

## (Intercept)      38.987      7.202  54.715   5.414   0.000
## log.CitH3        0.078      0.613 126.242   0.128   0.899
## day              0.506      0.266 111.934   1.903   0.060
## AGE              0.031      0.103  53.691   0.302   0.763
## SEX1             2.432      2.606  53.193   0.933   0.355
## RØYK_V01         2.040      2.594  54.245   0.786   0.435
## log.CitH3:day    0.305      0.175 113.790   1.740   0.085
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      43.303      6.348  56.536   6.821   0.000
## log.CitH3        0.031      0.606 130.592   0.051   0.960
## day              0.483      0.261 116.527   1.847   0.067
## AGE             -0.008      0.103  55.422  -0.079   0.937
## SEX1             2.677      2.858  55.269   0.937   0.353
## KREAT           -0.010      0.038  55.482  -0.259   0.797
## log.CitH3:day    0.318      0.173 118.200   1.837   0.069
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      47.001      7.765  54.283   6.053   0.000
## log.CitH3       -0.001      0.608 128.628  -0.002   0.998
## day              0.465      0.262 114.714   1.771   0.079
## AGE             -0.007      0.096  53.794  -0.075   0.941
## SEX1             2.533      2.501  53.968   1.013   0.316
## LEUK_V0         -0.330      0.306  54.278  -1.080   0.285
## log.CitH3:day    0.338      0.175 116.668   1.927   0.056
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      45.699      6.652  57.347   6.870   0.000
## log.CitH3       -0.001      0.605 130.912  -0.002   0.998
## day              0.486      0.261 116.825   1.861   0.065
## AGE             -0.020      0.093  55.594  -0.215   0.831
## SEX1             2.533      2.544  55.458   0.996   0.324
## TnT              0.000      0.000  56.497  -1.112   0.271
## log.CitH3:day    0.317      0.173 118.661   1.835   0.069
##
## With NET variable log.MPODNA :
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      46.250      8.197  62.292   5.643   0.000
## log.MPODNA       -0.002      1.495 136.415  -0.001   0.999
## day              1.254      0.708 118.442   1.770   0.079
## AGE             -0.028      0.096  55.280  -0.296   0.768
## SEX1             3.136      2.551  55.360   1.229   0.224
## KILLIPO         -1.076      1.593  55.746  -0.675   0.502
## log.MPODNA:day    0.229      0.473 117.648   0.484   0.630
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      38.773      7.522  61.346   5.155   0.000
## log.MPODNA        0.059      1.514 131.238   0.039   0.969
## day              1.134      0.724 112.887   1.567   0.120
## AGE              0.034      0.104  53.430   0.323   0.748
## SEX1             2.634      2.632  53.004   1.001   0.322
## RØYK_V01         2.326      2.629  54.719   0.885   0.380
## log.MPODNA:day    0.141      0.485 112.227   0.292   0.771
##                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      43.219      6.642  63.935   6.506   0.000
## log.MPODNA       -0.053      1.494 136.474  -0.036   0.972
## day              1.254      0.708 118.347   1.770   0.079
## AGE             -0.007      0.104  55.318  -0.070   0.945

```

## SEX1	2.819	2.892	55.457	0.975	0.334
## KREAT	-0.011	0.038	55.292	-0.287	0.775
## log.MPODNA:day	0.230	0.473	117.538	0.487	0.627
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	47.150	8.159	61.447	5.779	0.000
## log.MPODNA	0.180	1.512	136.346	0.119	0.906
## day	1.360	0.772	118.409	1.761	0.081
## AGE	-0.007	0.097	53.622	-0.072	0.943
## SEX1	2.761	2.535	53.926	1.089	0.281
## LEUK_V0	-0.335	0.310	54.456	-1.080	0.285
## log.MPODNA:day	0.290	0.508	116.907	0.571	0.569
##	Estimate	Std. Error	df	t value	Pr(> t)
## (Intercept)	45.927	6.947	64.811	6.611	0.000
## log.MPODNA	0.027	1.493	136.857	0.018	0.986
## day	1.264	0.708	118.674	1.785	0.077
## AGE	-0.020	0.094	55.525	-0.217	0.829
## SEX1	2.670	2.566	55.445	1.041	0.302
## TnT	0.000	0.000	56.254	-1.223	0.226
## log.MPODNA:day	0.234	0.473	117.891	0.495	0.622

2.3.3 Summarise all final models (no confounders)

log.dsDNA:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 1153.8
##
## Scaled residuals:
## Min      1Q  Median      3Q      Max
## -2.3637 -0.5533 -0.0314  0.5724  3.7483
##
## Random effects:
## Groups   Name                Variance Std.Dev.
## ID      (Intercept)          71.38     8.449
## Residual                    18.51     4.303
## Number of obs: 176, groups: ID, 60
##
## Fixed effects:
##              Estimate Std. Error    df t value Pr(>|t|)
## (Intercept)   66.7472    20.1064 136.4426   3.320  0.00116 **
## log.dsDNA     -4.0577     3.3786 135.7707  -1.201  0.23185
## day           4.3888     5.4901 123.1275   0.799  0.42559
## log.dsDNA:day -0.5635     0.9180 123.2171  -0.614  0.54044
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) lg.DNA day
## log.dsDNA    -0.998
## day          -0.652  0.652
## lg.dsDNA:dy  0.659 -0.659 -1.000
```

log.CitH3:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 1159.7
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.2368 -0.5082 -0.0983 0.5560 3.6214
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 71.99 8.485
## Residual 18.33 4.282
## Number of obs: 176, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 42.71058 1.34621 100.61564 31.726 <2e-16 ***
## log.CitH3 0.01753 0.60508 131.34337 0.029 0.9769
## day 0.47309 0.26112 116.76459 1.812 0.0726 .
## log.CitH3:day 0.32679 0.17303 118.72834 1.889 0.0614 .
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) lg.CH3 day
## log.CitH3 -0.481
## day -0.332 0.408
## log.CitH3:dy 0.299 -0.597 -0.812
```

log.MPODNA:

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma)
## Data: dat
##
## REML criterion at convergence: 1161
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.3746 -0.5628 -0.0564 0.5784 3.8636
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 73.49 8.573
## Residual 18.99 4.358
## Number of obs: 176, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 42.4667 2.2766 171.9614 18.653 <2e-16 ***
## log.MPODNA -0.1589 1.4903 137.8116 -0.107 0.9152
## day 1.2610 0.7084 118.4098 1.780 0.0776 .
## log.MPODNA:day 0.2372 0.4734 117.6008 0.501 0.6173
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) lg.MPODNA day
## log.MPODNA 0.851
## day -0.293 -0.299
## lg.MPODNA:d -0.339 -0.387 0.973
```

3.1 WMSI

3.1.1 Fit models with IL-8 and with and without NETs variables

dsDNA:

```
iy <- 1

#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 19.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.27563 -0.50157 -0.02009  0.61078  2.41195
##
## Random effects:
## Groups Name          Variance Std.Dev.
## ID      (Intercept) 0.04763  0.2182
## Residual                0.02958  0.1720
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  1.944e+00  4.266e-02  1.333e+02  45.553 < 2e-16 ***
## IL8          -3.732e-04  8.748e-04  1.575e+02  -0.427  0.67019
## day          -3.871e-02  1.279e-02  1.319e+02  -3.026  0.00298 **
## IL8:day       2.028e-05  5.857e-04  1.450e+02   0.035  0.97243
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr) IL8      day
## IL8      -0.629
## day      -0.232  0.179
## IL8:day  -0.008 -0.014 -0.866

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[3], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
```



```

## Data: dat
##
## REML criterion at convergence: 29.3
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.26152 -0.48801 -0.00323  0.61658  2.39908
##
## Random effects:
##  Groups   Name      Variance Std.Dev.
##  ID       (Intercept) 0.04760  0.2182
##  Residual                0.03003  0.1733
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   1.951e+00  8.573e-02  1.675e+02  22.756  <2e-16 ***
## IL8           -3.331e-04  8.884e-04  1.573e+02  -0.375   0.708
## day           -2.928e-02  3.273e-02  1.251e+02  -0.895   0.373
## log.MPODNA    6.740e-03  5.624e-02  1.540e+02   0.120   0.905
## IL8:day       -1.994e-05  6.000e-04  1.410e+02  -0.033   0.974
## day:log.MPODNA 5.493e-03  1.908e-02  1.243e+02   0.288   0.774
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) IL8    day    1.MPOD IL8:dy
## IL8           -0.358
## day           -0.360  0.194
## log.MPODNA    0.865 -0.046 -0.316
## IL8:day       0.015 -0.039 -0.498  0.012
## dy:1.MPODNA  -0.421  0.134  0.914 -0.438 -0.171
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
##      npar    AIC    BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0     6 -7.6116 11.445  9.8058  -19.612
## fit1     8 -3.7731 21.636  9.8866  -19.773  0.1615  2    0.9224

```

CitH3:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 19.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.27563 -0.50157 -0.02009  0.61078  2.41195
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.04763 0.2182
## Residual 0.02958 0.1720
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 1.944e+00 4.266e-02 1.333e+02 45.553 < 2e-16 ***
## IL8 -3.732e-04 8.748e-04 1.575e+02 -0.427 0.67019
## day -3.871e-02 1.279e-02 1.319e+02 -3.026 0.00298 **
## IL8:day 2.028e-05 5.857e-04 1.450e+02 0.035 0.97243
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day
## IL8 -0.629
## day -0.232 0.179
## IL8:day -0.008 -0.014 -0.866

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[2], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 32.9
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.24833 -0.50432 -0.00947  0.57981  2.43362
```

```

##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.04691 0.2166
## Residual 0.03011 0.1735
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 1.944e+00 4.952e-02 1.544e+02 39.261 <2e-16 ***
## IL8 -3.457e-04 8.810e-04 1.554e+02 -0.392 0.6953
## day -3.557e-02 1.423e-02 1.253e+02 -2.500 0.0137 *
## log.CitH3 -2.222e-03 2.364e-02 1.476e+02 -0.094 0.9252
## IL8:day 1.229e-04 6.104e-04 1.439e+02 0.201 0.8407
## day:log.CitH3 -3.685e-03 7.160e-03 1.265e+02 -0.515 0.6077
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day lg.CH3 IL8:dy
## IL8 -0.533
## day -0.325 0.168
## log.CitH3 -0.505 -0.027 0.253
## IL8:day -0.062 -0.012 -0.653 0.094
## day:lg.CtH3 0.344 -0.008 -0.423 -0.618 -0.246
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0 6 -7.6116 11.445 9.8058 -19.612
## fit1 8 -4.1563 21.253 10.0782 -20.156 0.5447 2 0.7616

```

MPODNA:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 19.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.27563 -0.50157 -0.02009  0.61078  2.41195
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.04763 0.2182
## Residual 0.02958 0.1720
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 1.944e+00 4.266e-02 1.333e+02 45.553 < 2e-16 ***
## IL8 -3.732e-04 8.748e-04 1.575e+02 -0.427 0.67019
## day -3.871e-02 1.279e-02 1.319e+02 -3.026 0.00298 **
## IL8:day 2.028e-05 5.857e-04 1.450e+02 0.035 0.97243
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day
## IL8 -0.629
## day -0.232 0.179
## IL8:day -0.008 -0.014 -0.866

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[3], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 29.3
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.26152 -0.48801 -0.00323  0.61658  2.39908
```

```

##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.04760 0.2182
## Residual 0.03003 0.1733
## Number of obs: 177, groups: ID, 61
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 1.951e+00 8.573e-02 1.675e+02 22.756 <2e-16 ***
## IL8 -3.331e-04 8.884e-04 1.573e+02 -0.375 0.708
## day -2.928e-02 3.273e-02 1.251e+02 -0.895 0.373
## log.MPODNA 6.740e-03 5.624e-02 1.540e+02 0.120 0.905
## IL8:day -1.994e-05 6.000e-04 1.410e+02 -0.033 0.974
## day:log.MPODNA 5.493e-03 1.908e-02 1.243e+02 0.288 0.774
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day 1.MPOD IL8:dy
## IL8 -0.358
## day -0.360 0.194
## log.MPODNA 0.865 -0.046 -0.316
## IL8:day 0.015 -0.039 -0.498 0.012
## dy:1.MPODNA -0.421 0.134 0.914 -0.438 -0.171
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0 6 -7.6116 11.445 9.8058 -19.612
## fit1 8 -3.7731 21.636 9.8866 -19.773 0.1615 2 0.9224

```

3.2 GLS

3.2.1 Fit models with IL-8 and with and without NETs variables

dsDNA:

```
iy <- 2
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 573.2
##
## Scaled residuals:
##   Min       1Q   Median       3Q      Max
## -2.42878 -0.57319  0.07332  0.47303  2.45248
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID      (Intercept) 3.498  1.870
## Residual 1.400  1.183
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept) -9.353837   0.369160  99.958929 -25.338 <2e-16 ***
## IL8          0.008612   0.007291 114.985589  1.181  0.240
## day         -0.165389   0.107521 101.080157 -1.538  0.127
## IL8:day     -0.006230   0.005173 109.771837 -1.204  0.231
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr) IL8    day
## IL8   -0.598
## day   -0.166  0.127
## IL8:day -0.037  0.032 -0.890

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[1], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
```

```

##
## REML criterion at convergence: 569.9
##
## Scaled residuals:
##   Min       1Q   Median       3Q      Max
## -2.4019 -0.5430  0.0166  0.5060  2.4358
##
## Random effects:
##   Groups   Name            Variance Std.Dev.
##   ID       (Intercept)  3.472   1.863
##   Residual                1.400   1.183
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -18.197162   6.565691 115.664118  -2.772   0.0065 **
## IL8           0.011826   0.007630 118.986698   1.550   0.1238
## day           0.530841   1.817657  99.928838   0.292   0.7709
## log.dsDNA    1.473858   1.092774 114.639118   1.349   0.1801
## IL8:day      -0.008564   0.005695 107.737168  -1.504   0.1356
## day:log.dsDNA -0.111323   0.308062 100.319714  -0.361   0.7186
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) IL8    day    lg.DNA IL8:dy
## IL8          -0.326
## day          -0.656  0.178
## log.dsDNA    -0.998  0.294  0.656
## IL8:day      0.103 -0.016  0.188 -0.105
## dy:lg.dsDNA  0.645 -0.167 -0.998 -0.646 -0.242
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
##      npar   AIC   BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0    6 563.39 581.13 -275.70   551.39
## fit1    8 565.04 588.69 -274.52   549.04 2.3491  2    0.309

```

CitH3:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 573.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.42878 -0.57319  0.07332  0.47303  2.45248
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 3.498 1.870
## Residual 1.400 1.183
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) -9.353837 0.369160 99.958929 -25.338 <2e-16 ***
## IL8 0.008612 0.007291 114.985589 1.181 0.240
## day -0.165389 0.107521 101.080157 -1.538 0.127
## IL8:day -0.006230 0.005173 109.771837 -1.204 0.231
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day
## IL8 -0.598
## day -0.166 0.127
## IL8:day -0.037 0.032 -0.890

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[2], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 576
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.42421 -0.58664  0.09788  0.51099  2.37228
```



```

##
## Random effects:
## Groups   Name          Variance Std.Dev.
## ID       (Intercept) 3.335    1.826
## Residual                1.414    1.189
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -9.364441   0.442323 122.205513 -21.171  <2e-16 ***
## IL8          0.009089   0.007341 115.765246  1.238   0.218
## day         -0.114289   0.115008  93.910696 -0.994   0.323
## log.CitH3   -0.020984   0.195700 111.515220 -0.107   0.915
## IL8:day     -0.003587   0.005473 111.677900 -0.655   0.514
## day:log.CitH3 -0.071351   0.056043  96.890058 -1.273   0.206
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) IL8    day    lg.CH3 IL8:dy
## IL8          -0.557
## day          -0.265  0.151
## log.CitH3    -0.563  0.106  0.218
## IL8:day     -0.132  0.049 -0.678  0.169
## day:lg.CtH3  0.394 -0.085 -0.348 -0.651 -0.318
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
##      npar   AIC   BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0    6 563.39 581.13 -275.70  551.39
## fit1    8 564.18 587.83 -274.09  548.18 3.2079  2    0.2011

```

MPODNA:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 573.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.42878 -0.57319  0.07332  0.47303  2.45248
##
## Random effects:
## Groups   Name                Variance Std.Dev.
## ID       (Intercept)  3.498    1.870
## Residual                    1.400    1.183
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  -9.353837   0.369160  99.958929 -25.338  <2e-16 ***
## IL8           0.008612   0.007291 114.985589  1.181   0.240
## day          -0.165389   0.107521 101.080157 -1.538   0.127
## IL8:day      -0.006230   0.005173 109.771837 -1.204   0.231
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr) IL8    day
## IL8    -0.598
## day    -0.166  0.127
## IL8:day -0.037  0.032 -0.890

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[3], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 575
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.40737 -0.57721  0.02842  0.50315  2.42584
```

```

##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 3.461 1.860
## Residual 1.432 1.197
## Number of obs: 142, groups: ID, 51
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) -9.409813 0.645296 133.200007 -14.582 <2e-16 ***
## IL8 0.009463 0.007474 116.442080 1.266 0.208
## day -0.045881 0.245665 92.114696 -0.187 0.852
## log.MPODNA -0.022992 0.426381 113.588958 -0.054 0.957
## IL8:day -0.006753 0.005328 105.418516 -1.268 0.208
## day:log.MPODNA 0.074168 0.140455 91.172674 0.528 0.599
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day 1.MPOD IL8:dy
## IL8 -0.313
## day -0.306 0.191
## log.MPODNA 0.817 0.045 -0.256
## IL8:day -0.025 -0.007 -0.549 -0.021
## dy:1.MPODNA -0.389 0.137 0.890 -0.406 -0.171
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0 6 563.39 581.13 -275.70 551.39
## fit1 8 567.08 590.73 -275.54 551.08 0.3128 2 0.8552

```

3.3 EF

3.3.1 Fit models with IL-8 and with and without NETs variables

dsDNA:

```
iy <- 3
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 1164.1
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.3679 -0.5495 -0.0311 0.5294 3.8537
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 73.26 8.559
## Residual 19.13 4.374
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 42.27168 1.40252 106.80399 30.140 < 2e-16 ***
## IL8 0.01346 0.02362 136.77577 0.570 0.569654
## day 1.26096 0.33909 122.11709 3.719 0.000304 ***
## IL8:day -0.01652 0.01570 129.71692 -1.052 0.294720
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day
## IL8 -0.522
## day -0.151 0.117
## IL8:day -0.044 0.060 -0.874

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[1], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
```

```

##
## REML criterion at convergence: 1154.9
##
## Scaled residuals:
##   Min       1Q   Median       3Q      Max
## -2.3247 -0.5486 -0.0249  0.5762  3.6977
##
## Random effects:
##   Groups   Name      Variance Std.Dev.
##   ID       (Intercept) 71.59   8.461
##   Residual                19.11   4.372
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)  66.052564  21.682104 140.554995   3.046  0.00277 **
## IL8          0.004001   0.024758 141.926948   0.162  0.87186
## day          4.069929   6.035342 122.579214   0.674  0.50136
## log.dsDNA   -3.963336   3.603892 139.246779  -1.100  0.27334
## IL8:day     -0.003230   0.018089 128.169961  -0.179  0.85857
## day:log.dsDNA -0.498548   1.028117 123.106259  -0.485  0.62860
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) IL8    day    lg.DNA IL8:dy
## IL8          -0.335
## day          -0.623  0.173
## log.dsDNA   -0.998  0.304  0.623
## IL8:day      0.000  0.033  0.344 -0.003
## dy:lg.dsDNA  0.615 -0.165 -0.998 -0.616 -0.391
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
##      npar   AIC   BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0    6 1164.1 1183.1 -576.07  1152.1
## fit1    8 1164.7 1190.0 -574.34  1148.7 3.4656  2    0.1768

```

CitH3:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 1164.1
##
## Scaled residuals:
##   Min       1Q   Median       3Q      Max
## -2.3679 -0.5495 -0.0311  0.5294  3.8537
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID      (Intercept) 73.26  8.559
## Residual          19.13  4.374
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
##              Estimate Std. Error    df t value Pr(>|t|)
## (Intercept)  42.27168    1.40252 106.80399  30.140 < 2e-16 ***
## IL8           0.01346    0.02362 136.77577   0.570 0.569654
## day           1.26096    0.33909 122.11709   3.719 0.000304 ***
## IL8:day      -0.01652    0.01570 129.71692  -1.052 0.294720
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr) IL8    day
## IL8    -0.522
## day    -0.151  0.117
## IL8:day -0.044  0.060 -0.874

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[2], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 1158.2
##
## Scaled residuals:
##   Min       1Q   Median       3Q      Max
## -2.1791 -0.5082 -0.1038  0.5547  3.4840
```

```

##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 71.44 8.452
## Residual 18.53 4.304
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 42.55399 1.53584 131.19796 27.707 <2e-16 ***
## IL8 0.01088 0.02327 134.36207 0.468 0.6408
## day 0.91025 0.36613 117.50170 2.486 0.0143 *
## log.CitH3 -0.10710 0.61499 127.76683 -0.174 0.8620
## IL8:day -0.02670 0.01599 128.06594 -1.670 0.0974 .
## day:log.CitH3 0.40410 0.18134 116.56776 2.228 0.0278 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day lg.CH3 IL8:dy
## IL8 -0.467
## day -0.235 0.119
## log.CitH3 -0.433 -0.008 0.226
## IL8:day -0.095 0.068 -0.665 0.110
## day:lg.CtH3 0.295 -0.029 -0.410 -0.607 -0.251
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0 6 1164.1 1183.1 -576.07 1152.1
## fit1 8 1160.9 1186.1 -572.43 1144.9 7.2797 2 0.02626 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

MPODNA:

```
#
# Model with IL-8 only:
fma0 <- paste(Y[iy], "~ IL8 * day + (1 | ID)")
fit0 <- lmer(as.formula(fma0), data=dat, REML = TRUE)
summary(fit0)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma0)
## Data: dat
##
## REML criterion at convergence: 1164.1
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.3679 -0.5495 -0.0311 0.5294 3.8537
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 73.26 8.559
## Residual 19.13 4.374
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 42.27168 1.40252 106.80399 30.140 < 2e-16 ***
## IL8 0.01346 0.02362 136.77577 0.570 0.569654
## day 1.26096 0.33909 122.11709 3.719 0.000304 ***
## IL8:day -0.01652 0.01570 129.71692 -1.052 0.294720
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day
## IL8 -0.522
## day -0.151 0.117
## IL8:day -0.044 0.060 -0.874

#
# Model with IL-8 and NETs variable:
fma1 <- paste(Y[iy], "~ IL8 * day + ", X[3], "* day + (1 | ID)")
fit1 <- lmer(as.formula(fma1), data=dat, REML = TRUE)
summary(fit1)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: as.formula(fma1)
## Data: dat
##
## REML criterion at convergence: 1160.6
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.3257 -0.5293 -0.0370 0.5308 3.7631
```



```

##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 73.62 8.580
## Residual 19.33 4.396
## Number of obs: 174, groups: ID, 60
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 41.91346 2.42972 166.16265 17.250 <2e-16 ***
## IL8 0.01623 0.02401 135.99073 0.676 0.5001
## day 1.84933 0.84503 115.51875 2.188 0.0306 *
## log.MPODNA -0.20446 1.51027 132.69138 -0.135 0.8925
## IL8:day -0.01841 0.01597 125.83384 -1.153 0.2512
## day:log.MPODNA 0.36886 0.49387 115.64223 0.747 0.4566
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) IL8 day 1.MPOD IL8:dy
## IL8 -0.330
## day -0.300 0.185
## log.MPODNA 0.814 -0.029 -0.272
## IL8:day -0.010 0.035 -0.485 0.008
## dy:1.MPODNA -0.365 0.149 0.910 -0.393 -0.145
#
# Compare both models (does including NETs improve model fit?):
anova(fit0, fit1)

## Data: dat
## Models:
## fit0: as.formula(fma0)
## fit1: as.formula(fma1)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## fit0 6 1164.1 1183.1 -576.07 1152.1
## fit1 8 1167.5 1192.8 -575.76 1151.5 0.6123 2 0.7363

```

Software

```
## R version 4.0.2 (2020-06-22)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS Catalina 10.15.6
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRblas.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
##
## other attached packages:
## [1] lmerTest_3.1-2 lme4_1.1-23 Matrix_1.2-18 Hmisc_4.4-0
## [5] ggplot2_3.3.2 Formula_1.2-3 survival_3.1-12 lattice_0.20-41
## [9] haven_2.3.1
##
## loaded via a namespace (and not attached):
## [1] statmod_1.4.34 tidyselect_1.1.0 xfun_0.16
## [4] purrr_0.3.4 splines_4.0.2 colorspace_1.4-1
## [7] vctrs_0.3.3 generics_0.0.2 htmltools_0.5.0
## [10] yaml_2.2.1 base64enc_0.1-3 rlang_0.4.7
## [13] nloptr_1.2.2.1 pillar_1.4.6 foreign_0.8-80
## [16] glue_1.4.2 withr_2.2.0 RColorBrewer_1.1-2
## [19] jpeg_0.1-8.1 lifecycle_0.2.0 stringr_1.4.0
## [22] munsell_0.5.0 gtable_0.3.0 htmlwidgets_1.5.1
## [25] evaluate_0.14 latticeExtra_0.6-29 knitr_1.29
## [28] forcats_0.5.0 htmlTable_1.13.3 Rcpp_1.0.5
## [31] acepack_1.4.1 readr_1.3.1 scales_1.1.1
## [34] backports_1.1.9 checkmate_2.0.0 gridExtra_2.3
## [37] hms_0.5.3 png_0.1-7 digest_0.6.25
## [40] stringi_1.4.6 dplyr_1.0.2 numDeriv_2016.8-1.1
## [43] grid_4.0.2 tools_4.0.2 magrittr_1.5
## [46] tibble_3.0.3 cluster_2.1.0 crayon_1.3.4
## [49] pkgconfig_2.0.3 MASS_7.3-51.6 ellipsis_0.3.1
## [52] data.table_1.13.0 minqa_1.2.4 rmarkdown_2.2
## [55] rstudioapi_0.11 boot_1.3-25 R6_2.4.1
## [58] rpart_4.1-15 nlme_3.1-148 nnet_7.3-14
## [61] compiler_4.0.2
```