Sample size solutions for ${\cal N}=1$ intensive longitudinal designs

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Setup the environment

The code below chunk simply makes sure that all the libraries used here are installed. We should first check if the R packages are installed before we proceed.

```
## Do not run because we do not want to install packages (this should be your decision)
list.of.packages = c("data.table", "psych", "ggplot2", "tidyverse", "MASS")
new.packages = list.of.packages[!(list.of.packages %in% installed.packages()[, "Package"])]
```

```
if(length(new.packages)) install.packages(new.packages)
```

Now that we have all packages installed, we continue by loading them.

```
library(data.table) # to create lagged outcome
library(psych) # to compute descriptive statistics
library(ggplot2) # for making plots
library(tidyverse) # a useful package
library(MASS)
set.seed(1235) # Set a seed to reproduce analyses
```

The Leuven clinical study data set

We use data from Heininga et al. (2019); this study applies the ESM methodology to study emotion dynamics in people with Major Depressive Disorder. The study consist of an ESM testing period of 7 days in which participants had to fill out questions about mood and social context on their daily lives ten times a day (i.e., 70 measurement occasions). The data set contains 38 participants diagnosed with MDD and 40 control subjects. Participants filled out the ESM questionnaires in a stratified random interval scheme between 9:30 AM and 9:30 PM.

First, we are going to load the data set:

```
# Load data set
load(file="assets/data/clinical-dataset.RData")
```

Now, we are going to explore the data set to get a better understanding of the what's inside.

```
# Select the first participant diagnosed with major depressive
i.ID = unique(data$PID[data$MDD==1])[1]

# Select data from participant with person identification number PID=101
data = data[data$PID==101,]

# Find the dimensions
dim(data)
```

[1] 70 8

Find the structure str(data)

```
'data.frame': 70 obs. of 8 variables:
$ PID
           : num 101 101 101 101 101 101 101 101 101 ...
$ day
           : num 1 1 1 1 1 1 1 1 1 1 ...
$ daybeep : num 1 2 3 4 5 6 7 8 9 10 ...
$ PA
           : num NA 27.3 49.7 43 43 ...
$ NA.
           : num NA 30.4 23.8 24.2 32.8 19.6 18.4 21.2 23 21.8 ...
$ anhedonia: num NA 26 25 25 50 21 42 30 22 30 ...
$ MDD
         : num 1 1 1 1 1 1 1 1 1 1 ...
$ QIDS
           : num 12 12 12 12 12 12 12 12 12 12 ...
  # See the first 6 rows
  head(data)
 PID day daybeep
                      PA NA. anhedonia MDD QIDS
1 101
               1
                       NA
                            NΑ
                                     NA
                                          1
                                              12
2 101
               2 27.33333 30.4
                                     26
       1
                                              12
3 101
      1
               3 49.66667 23.8
                                     25
                                              12
4 101
              4 43.00000 24.2
       1
                                     25
                                              12
5 101
       1
              5 43.00000 32.8
                                              12
                                     50
                                          1
6 101
       1
               6 18.00000 19.6
                                              12
                                     21
                                          1
  # See the last 6 rows
  tail(data)
  PID day daybeep
                       PA NA. anhedonia MDD QIDS
65 101
        7
                5 24.33333 31.8
                                      52
                                           1
                                               12
        7
                6 28.66667 20.6
66 101
                                      53
                                           1
                                               12
67 101 7
               7 23.33333 23.8
                                      51
                                           1
                                              12
                8 33.66667 36.2
68 101
       7
                                      46 1
                                              12
69 101
        7
               9 41.66667 21.0
                                      29
                                           1 12
70 101
        7
               10 34.00000 18.4
                                      47
                                               12
```

Find the column names
names(data)

```
[1] "PID"
                 "day"
                               "daybeep"
                                            "PA"
                                                         "NA."
                                                                       "anhedonia"
[7] "MDD"
                 "QIDS"
  # Summary of the data
  summary(data)
      PID
                      day
                                 daybeep
                                                     PA
                                                                     NA.
Min.
        :101
                Min.
                                     : 1.0
                                              Min.
                                                      :14.67
                                                                Min.
                                                                        :14.40
                        :1
                             Min.
 1st Qu.:101
                             1st Qu.: 3.0
                                              1st Qu.:26.08
                                                                1st Qu.:21.40
                1st Qu.:2
Median:101
                             Median: 5.5
                                              Median :33.33
                                                                Median :25.90
                Median:4
Mean
        :101
                Mean
                        :4
                             Mean
                                     : 5.5
                                              Mean
                                                      :33.51
                                                                Mean
                                                                        :29.62
3rd Qu.:101
                             3rd Qu.: 8.0
                                              3rd Qu.:41.67
                                                                3rd Qu.:36.25
                3rd Qu.:6
Max.
         :101
                Max.
                        :7
                             Max.
                                     :10.0
                                              Max.
                                                      :57.33
                                                                Max.
                                                                        :65.60
                                              NA's
                                                      :6
                                                                NA's
                                                                        :6
   anhedonia
                        MDD
                                     QIDS
        :14.00
                                        :12
Min.
                  Min.
                          :1
                                Min.
 1st Qu.:24.75
                  1st Qu.:1
                                1st Qu.:12
Median :41.50
                  Median:1
                                Median:12
Mean
        :39.34
                                        :12
                  Mean
                          :1
                                Mean
3rd Qu.:52.00
                  3rd Qu.:1
                                3rd Qu.:12
Max.
        :83.00
                          :1
                                        :12
                  Max.
                                Max.
NA's
         :6
  # Number of participants
  length(unique(data$PID))
```

[1] 1

The data set contains the following variables: PID that denotes the individual identification number, day is a variable that ranges from 1 to 7 and identifies the day of ESM testing, daybeep is a variable that ranges from 1 to 10 and identifies the number of the prompt or beep within a day. PA is the Positive Affect computed as the mean of items: 'How happy do you feel at the moment?', 'How relaxed do you feel at the moment?' and 'How euphoric do you feel at the moment?'. NA. is the Negative Affect computed as the mean of items: 'How depressed do you feel at the moment?', 'How anxious do you feel at the moment?', 'How anxious do you feel at the moment?'. 'How angry do you feel at the moment?' and 'How restless do you feel at the moment?'. anhedonia corresponds to the ESM item 'To what degree do you find it difficult to experience pleasure in activities at the moment?'. MDD is a dummy variable equal to one when the individual has been diagnosed with MDD and 0 otherwise, finally QIDS denotes the sum of the items of the Quick Inventory of Depressive Symptomatology (i.e. QIDS) [@rush200316].

QIDS was measured before the ESM testing period. Time-varying variables (PA, NA, and anhedonia) have been lagged within days to account for the night breaks.

Visualizations and descriptive statistics

101

12

We first obtain some descriptive statistics including number of observations per day, and compliance.

```
# Get the number of assessment per day
  table(data$PID)
101
 70
  # Compute a binary variable indicating if a participant answered a beep. We take
  # the ESM item PA as reference because in this ESM design participants were not
  # allowed to skip items
  data$Compliance = ifelse(is.na(data$PA)==FALSE, 1, 0)
  # Mean, median of the compliance for the participant PID=101
  describe(data$Compliance)
                  sd median trimmed mad min max range skew kurtosis
   vars n mean
Х1
      1 70 0.91 0.28
                          1
                                       0
                                           0
                                               1
                                                     1 - 2.9
                                                                6.48 0.03
                                   1
```

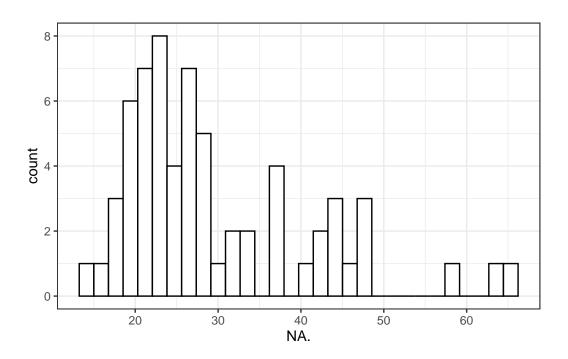
Next, we can obtain visualizations and statistics of the distribution of the person-level or time-invariant variables variables

```
# We create a data set that will aggregate the data from the time invariant
# variables: diagnosis (1 = MDD, 0 = control) and depression (QIDS)
dt.person = aggregate(cbind(data$MDD,data$QIDS), by = list(data$PID), mean, na.rm = TRUE)
colnames(dt.person) = c("Group.1","MDD","QIDS")
dt.person
Group.1 MDD QIDS
```

We now focus on time-varying variables NA, PA, and anhedonia and we obtain visualization and descriptive statistics

```
# Histogram for the time-varying variable negative affect (NA.)
ggplot(data, aes(NA.)) + geom_histogram(color="black", fill="white",bins=30) + theme_bw()
```

Warning: Removed 6 rows containing non-finite values (`stat_bin()`).



Descriptive statistics for NA.
describe(data\$NA.)

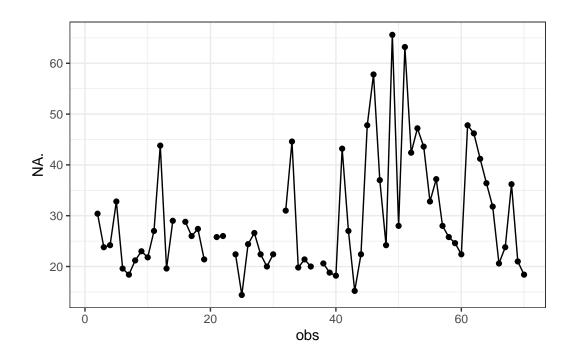
vars n mean sd median trimmed mad min max range skew kurtosis se X1 1.64.29.62.11.47 25.9 28.13.7.86.14.4.65.6 51.2.1.25 1.01.1.43

```
# Create obs order variable
data$obs = 1:nrow(data)

# Plot the trajectories of the time-varying variable NA by person
data %>%
    ggplot(aes(x = obs, y = NA.)) +
    geom_point() +
    geom_line() + theme_bw()
```

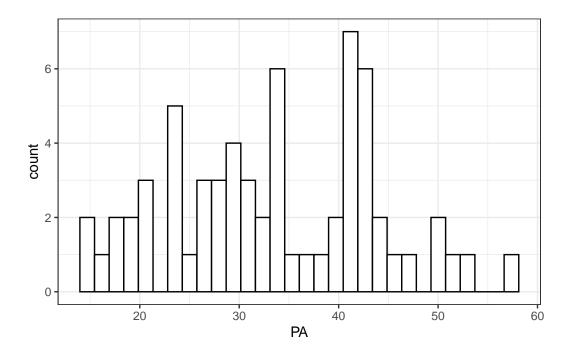
Warning: Removed 6 rows containing missing values (`geom_point()`).

Warning: Removed 1 row containing missing values (`geom_line()`).



```
# Histogram for the time-varying variable negative affect (PA)
ggplot(data, aes(PA)) + geom_histogram(color="black", fill="white",bins=30) + theme_bw()
```

Warning: Removed 6 rows containing non-finite values (`stat_bin()`).

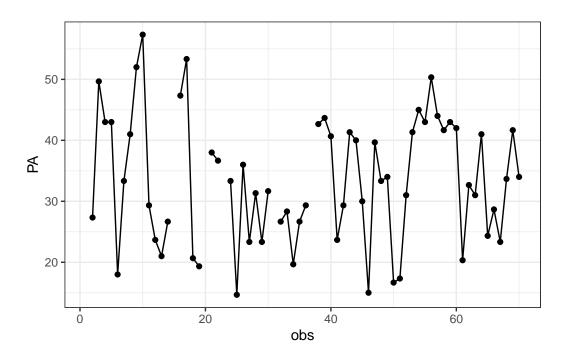


Descriptive statistics for PA
describe(data\$PA)

```
vars n mean sd median trimmed mad min max range skew kurtosis
X1     1 64 33.51 10.32     33.33     33.33 12.35 14.67 57.33 42.67 0.09     -0.84
     se
X1 1.29
```

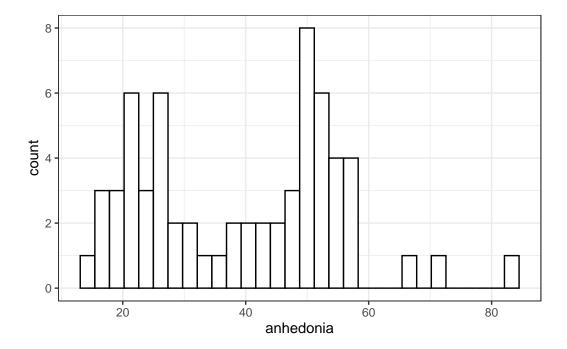
```
# Plot the trajectories of the time-varying variable PA by person
data %>%
    ggplot(aes(x = obs, y = PA)) +
    geom_point() +
    geom_line() + theme_bw()
```

Warning: Removed 6 rows containing missing values (`geom_point()`). Removed 1 row containing missing values (`geom_line()`).



```
# Histogram for the time-varying variable anhedonia
ggplot(data, aes(anhedonia)) + geom_histogram(color="black", fill="white",bins=30) + theme
```

Warning: Removed 6 rows containing non-finite values (`stat_bin()`).

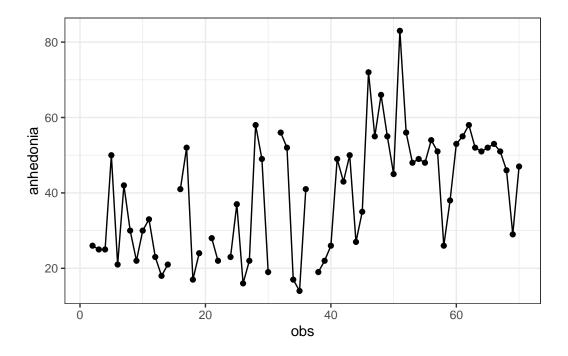


```
# Descriptive statistics for anhedonia
describe(data$anhedonia)
```

vars n mean sd median trimmed mad min max range skew kurtosis se X1 1 64 39.34 15.84 41.5 38.92 20.02 14 83 69 0.22 -0.77 1.98

```
# Plot the trajectories of the time-varying variable anhedonia by person
data %>%
    ggplot(aes(x = obs, y = anhedonia)) +
    geom_point() +
    geom_line() + theme_bw()
```

Warning: Removed 6 rows containing missing values (`geom_point()`). Removed 1 row containing missing values (`geom_line()`).



Finally, we create the lagged variables for PA and NA. They will be used on the following AR(1) and VAR(1) models.

Create lagged variables: lagged within days to take into account night breaks dataPA.lag = rep(NA, nrow(data))

```
data$NA.lag = rep(NA,nrow(data))
data$anhedonia.lag = rep(NA,nrow(data))
day.id = unique(data$day)
for (t in day.id) {
   data$PA.lag[which(data$day==t)] = shift(data$PA[which(data$day==t)],1)
   data$NA.lag[which(data$day==t)] = shift(data$NA.[which(data$day==t)],1)
   data$anhedonia.lag[which(data$day==t)] = shift(data$anhedonia[which(data$day==t)],1)
}
```

1. Estimate the AR(1) model for PA

We estimate an AR(1) model for PA using a linear regression model (ordinary least squares, OLS). You can extract the estimates with the 'summary()' function. Finally, you can compute the estimate of the standard deviation of the errors of the AR(1) model computing the standard deviation using the function 'sd()' on the residuals of the fitted model.

```
# AR(1) model for PA
  fit.AR.PA = lm(PA \sim 1 + PA.lag, data = data)
  summary(fit.AR.PA)
Call:
lm(formula = PA ~ 1 + PA.lag, data = data)
Residuals:
    Min
             1Q Median
                             3Q
                                    Max
-21.486 -5.866
                  2.070
                          5.820 18.155
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
                        4.5755 4.442 4.68e-05 ***
(Intercept) 20.3258
              0.4092
                         0.1308
                                  3.130 0.00287 **
PA.lag
___
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 9.658 on 52 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.1585,
                                Adjusted R-squared: 0.1423
F-statistic: 9.796 on 1 and 52 DF, p-value: 0.002866
```

```
\# Estimate the standard deviation of the errors sd(residuals(fit.AR.PA))
```

[1] 9.566865

2. Estimate the VAR(1) model for PA and NA

We estimate a VAR(1) model for PA and NA using two separate linear regression models. You can extract the estimates with the 'summary()' function. Finally, you can compute the estimate of the variance-covariance matrix of the errors of the VAR(1) model computing the covariance matrix using the function 'cov()' on the residuals of each of the fitted models.

```
# Linear regression model for PA
  fit.VAR.PA = lm(PA ~ 1 + PA.lag + NA.lag, data = data)
  summary(fit.VAR.PA)
Call:
lm(formula = PA ~ 1 + PA.lag + NA.lag, data = data)
Residuals:
   Min
            1Q Median
                           3Q
                                  Max
-21.551 -6.480 1.262
                        5.859 18.008
Coefficients:
           Estimate Std. Error t value Pr(>|t|)
(Intercept) 23.45530 6.27640 3.737 0.000471 ***
            0.39213
                      0.13341 2.939 0.004930 **
PA.lag
NA.lag
           0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Signif. codes:
Residual standard error: 9.702 on 51 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.1673,
                             Adjusted R-squared: 0.1346
F-statistic: 5.123 on 2 and 51 DF, p-value: 0.009391
  # Linear regression model for NA
  fit.VAR.NA = lm(NA. ~ 1 + PA.lag + NA.lag, data = data)
  summary(fit.VAR.NA)
```

```
Call:
lm(formula = NA. ~ 1 + PA.lag + NA.lag, data = data)
Residuals:
    Min
             1Q Median
                             3Q
                                   Max
-14.260 -5.933 -2.073
                         3.104 39.302
Coefficients:
           Estimate Std. Error t value Pr(>|t|)
                                 2.696 0.00949 **
(Intercept) 17.8818
                        6.6337
             -0.0202
                        0.1410 -0.143 0.88664
PA.lag
NA.lag
              0.3756
                        0.1194
                                 3.145 0.00277 **
               0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Signif. codes:
Residual standard error: 10.25 on 51 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.1692,
                               Adjusted R-squared: 0.1366
F-statistic: 5.194 on 2 and 51 DF, p-value: 0.008851
  # Estimate variance-covariance matrix of the errors
  res = cbind(residuals(fit.VAR.PA),residuals(fit.VAR.NA))
  cov(res)
          [,1]
                     [,2]
[1,] 90.572865
                4.295723
[2,] 4.295723 101.177796
```

3. Estimate the VAR(1) model for NA, PA and Anhedonia

We estimate a VAR(1) model for PA, NA and anhedonia using three separate linear regression models. You can extract the estimates with the 'summary()' function. Finally, you can compute the estimate of the variance-covariance matrix of the errors of the VAR(1) model by computing the covariance matrix using the function 'cov()' on the residuals of each of the fitted models.

```
# Linear regression model for PA
fit.VAR.PA = lm(PA ~ 1 + PA.lag + NA.lag + anhedonia.lag, data = data)
summary(fit.VAR.PA)
```

```
lm(formula = PA ~ 1 + PA.lag + NA.lag + anhedonia.lag, data = data)
Residuals:
   Min
            1Q Median
                           3Q
                                 Max
-22.374 -5.907 1.342 5.856 18.787
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
             22.60373 6.50921 3.473 0.00107 **
(Intercept)
             PA.lag
             -0.12662 0.13926 -0.909 0.36759
NA.lag
anhedonia.lag 0.05564
                        0.10179 0.547 0.58711
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 9.769 on 50 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.1722,
                            Adjusted R-squared: 0.1226
F-statistic: 3.468 on 3 and 50 DF, p-value: 0.02288
  # Linear regression model for NA
  fit.VAR.NA = lm(NA. ~ 1 + PA.lag + NA.lag + anhedonia.lag, data = data)
  summary(fit.VAR.NA)
Call:
lm(formula = NA. ~ 1 + PA.lag + NA.lag + anhedonia.lag, data = data)
Residuals:
   Min
            1Q Median
                                 Max
                           3Q
-14.413 -5.302 -2.096 3.864 33.201
Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept)
             14.84269
                       6.66252 2.228 0.0304 *
                       0.13752 -0.185
                                        0.8542
PA.lag
             -0.02541
NA.lag
             0.21894
                        0.14254 1.536
                                        0.1309
anhedonia.lag 0.19856
                        0.10419 1.906 0.0624 .
___
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

Call:

```
Residual standard error: 9.999 on 50 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.2255,
                              Adjusted R-squared: 0.179
F-statistic: 4.852 on 3 and 50 DF, p-value: 0.00486
  # Linear regression model for anhedonia
  fit.VAR.anhedonia = lm(anhedonia ~ 1 + PA.lag + NA.lag + anhedonia.lag, data = data)
  summary(fit.VAR.anhedonia)
Call:
lm(formula = anhedonia ~ 1 + PA.lag + NA.lag + anhedonia.lag,
   data = data)
Residuals:
            1Q Median
                            3Q
                                   Max
-29.750 -9.599 1.195 10.194 29.364
Coefficients:
             Estimate Std. Error t value Pr(>|t|)
                        8.92402 1.675 0.1002
(Intercept) 14.94851
             0.04386 0.18420 0.238 0.8128
PA.lag
              0.32640 0.19093 1.710 0.0936 .
NA.lag
anhedonia.lag 0.30771 0.13955 2.205 0.0321 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 13.39 on 50 degrees of freedom
  (16 observations deleted due to missingness)
Multiple R-squared: 0.268, Adjusted R-squared: 0.2241
F-statistic: 6.102 on 3 and 50 DF, p-value: 0.001276
  # Estimate variance-covariance matrix of the errors
  res = cbind(residuals(fit.VAR.PA),residuals(fit.VAR.NA),residuals(fit.VAR.anhedonia))
  cov(res)
                   [,2]
                             [,3]
          [,1]
[1,] 90.034929 2.375884 16.02124
[2,] 2.375884 94.326082 37.21901
```

[3,] 16.021244 37.219012 169.22933

How to run the shiny app?

The shiny application is associated to a package that is stored here: https://gitlab.kuleuven.be/ppw-okpiv/researchers/u0148925/shinyapp-paa_var_n1. To install the package and run the shiny app, please use the following R code in a new script or in a R terminal:

```
# Install the package
remotes::install_gitlab("ppw-okpiv/researchers/u0148925/shinyapp-paa_var_n1", host="https:
# Import the package in the R session
library(paavar1)

# Run the shiny app
run_paa_var1()
```

Exercise: Power analysis of VAR(1) with 3 variables

Power analysis result

Running the simulation with the application, you should end up with a similar plot:

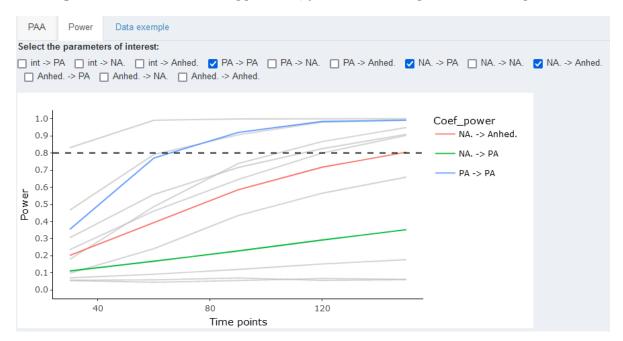


Figure 1: Power analysis VAR(1)

Sensitivity analysis for power: varying parameters

We slightly changed the values of three coefficients to investigate how they change either the sample size recommendation or the precision of estimates:

- $\beta_{11} = .39$ to $\beta_{11} = .8$
- $\sigma_{00} = 90$ to $\sigma_{00} = 180$ R = 1000 to R = 100

What conclusions can you draw based on the following power curves?

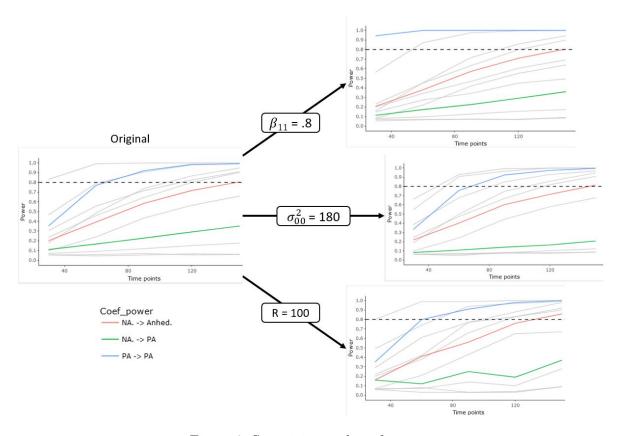


Figure 2: Sensitivity analysis for power

Sensitivity analysis for power: using CI

Following Lafit, Revol et al. (under review), we run a sensitivity analysis using the upper and lower boundaries of the estimated coefficients of interest. First, we extract the 95% confidence interval of the estimated values of each parameter.

```
# Linear regression model for PA
  confint(fit.VAR.PA, level=0.95)
                   2.5 %
                             97.5 %
(Intercept)
               9.5296021 35.6778667
PA.lag
               0.1208077
                          0.6605412
NA.lag
              -0.4063407
                          0.1530965
anhedonia.lag -0.1488169
                          0.2600881
  # Linear regression model for NA
  confint(fit.VAR.NA, level=0.95)
                    2.5 %
                              97.5 %
(Intercept)
               1.46062438 28.2247622
              -0.30162831 0.2508175
PA.lag
NA.lag
              -0.06736614 0.5052475
anhedonia.lag -0.01071022 0.4078257
  # Linear regression model for anhedonia
  confint(fit.VAR.anhedonia, level=0.95)
                    2.5 %
                              97.5 %
(Intercept)
              -2.97591249 32.8729333
PA.lag
              -0.32611856 0.4138472
NA.lag
              -0.05709339 0.7098859
anhedonia.lag 0.02741213 0.5880142
```

We only varied the parameter values for the auto-regressive effect of PA (β_{11}) following the confidence interval. We run two new power analyses. The results are displayed below. What conclusions can you draw based on the following power curves?

Exercise: PAA of VAR(1) with 3 variables

PAA result

Running the simulation with the application, you should end up with a similar plot:

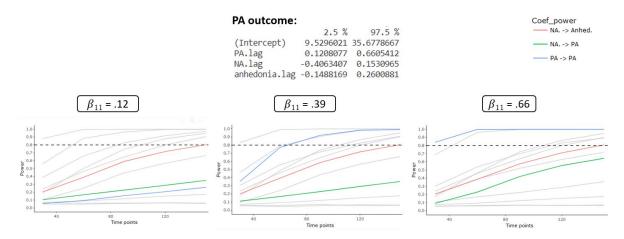


Figure 3: Sensitivity analysis for power

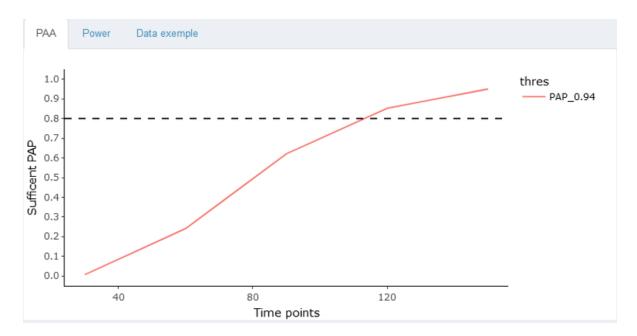


Figure 4: PAA for VAR(1)

Sensitivity analysis for power: varying parameters

We changed the values of the transition matrix to investigate how it changes the sample size recommendation. What conclusions can you draw based on the following power curves?

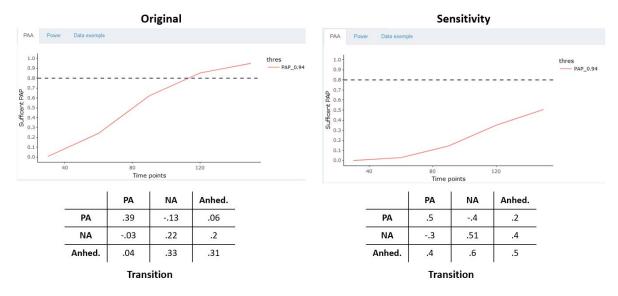


Figure 5: Sensitive PAA for VAR(1)

Note that, despites the raising of the coefficients, the new transition matrix still fulfills the stationary assumption. Higher coefficients could lead to a violation of this assumption.

Get the session info

Below we provide the **session** information (i.e., operating system, details about the R installation, and so on) for reproducibility purposes.

```
sessionInfo()
```

R version 4.3.0 (2023-04-21)

Platform: aarch64-apple-darwin20 (64-bit)

Running under: macOS Ventura 13.3.1

Matrix products: default

BLAS: /Library/Frameworks/R.framework/Versions/4.3-arm64/Resources/lib/libRblas.0.dylib LAPACK: /Library/Frameworks/R.framework/Versions/4.3-arm64/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

time zone: Europe/Amsterdam
tzcode source: internal

attached base packages:

[1] stats graphics grDevices utils datasets methods base

other attached packages:

[1] MASS_7.3-58.4	<pre>lubridate_1.9.2</pre>	forcats_1.0.0	stringr_1.5.0
[5] dplyr_1.1.2	purrr_1.0.1	readr_2.1.4	$tidyr_1.3.0$
[9] tibble_3.2.1	tidyverse_2.0.0	ggplot2_3.4.2	psych_2.3.3

[13] data.table_1.14.8

loaded via a namespace (and not attached):

[1]	gtable_0.3.3	jsonlite_1.8.4	compiler_4.3.0	tidyselect_1.2.0
[5]	parallel_4.3.0	scales_1.2.1	yam1_2.3.7	fastmap_1.1.1
[9]	lattice_0.21-8	R6_2.5.1	labeling_0.4.2	generics_0.1.3
[13]	knitr_1.43	munsell_0.5.0	pillar_1.9.0	tzdb_0.4.0
[17]	rlang_1.1.1	utf8_1.2.3	stringi_1.7.12	xfun_0.39
[21]	${\tt timechange_0.2.0}$	cli_3.6.1	withr_2.5.0	magrittr_2.0.3
[25]	digest_0.6.31	grid_4.3.0	rstudioapi_0.14	hms_1.1.3
[29]	lifecycle_1.0.3	nlme_3.1-162	vctrs_0.6.2	mnormt_2.1.1
[33]	evaluate_0.21	glue_1.6.2	farver_2.1.1	fansi_1.0.4
[37]	<pre>colorspace_2.1-0</pre>	rmarkdown_2.22	tools_4.3.0	pkgconfig_2.0.3

[41] htmltools_0.5.5