

cca_paper_example

7/6/2020

Load packages and Data set

```
## Loading required package: Matrix

## Loading 'metafor' package (version 2.1-0). For an overview
## and introduction to the package please type: help(metafor).

## Loading required package: OpenMx

## To take full advantage of multiple cores, use:
##   mxOption(key='Number of Threads', value=parallel::detectCores()) #now
##   Sys.setenv(OMP_NUM_THREADS=parallel::detectCores()) #before library(OpenMx)

##
## Attaching package: 'OpenMx'

## The following objects are masked from 'package:Matrix':
##
##   %&%, expm

## "SLSQP" is set as the default optimizer in OpenMx.

## mxOption(NULL, "Gradient algorithm") is set at "central".

## mxOption(NULL, "Optimality tolerance") is set at "6.3e-14".

## mxOption(NULL, "Gradient iterations") is set at "2".
```

Subset of the data

```
#Subset of variables needed for the analyses:
data_adt_cca<- data_adt[c("studyid", "es_g", "se_g", "g1permale", "g1perwhite", "g1age",
                          "g1hrsperweek", "g1txdays")]
```

```
#Visualize missingness
source("../code/wrappers.R")
```

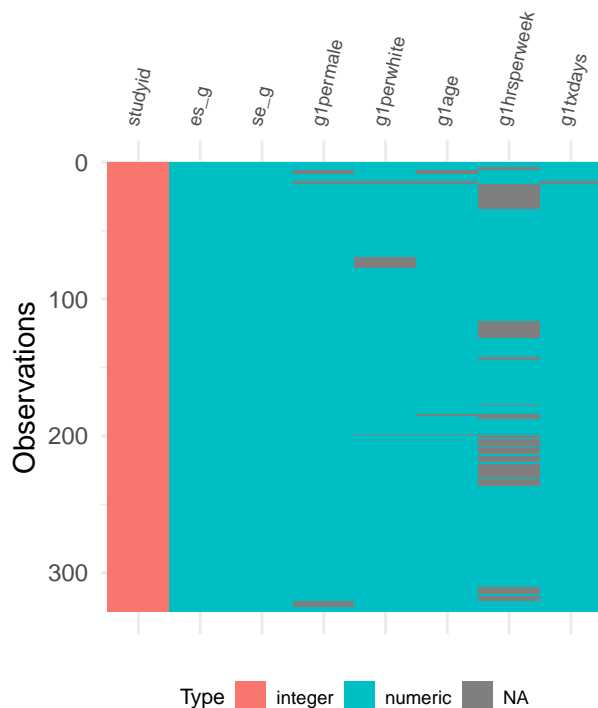
```
## -- Attaching packages -----
## v tibble  2.1.1      v purrr  0.3.3
## v tidyr   1.1.0      v dplyr  0.8.3
## v readr   1.3.1      v stringr 1.4.0
## v tibble  2.1.1      v forcats 0.4.0

## -- Conflicts -----
## x tidyr::expand() masks Matrix::expand()
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()
## x tidyr::pack()   masks Matrix::pack()
## x purrr::rerun()  masks metaSEM::rerun()
## x tidyr::unpack() masks Matrix::unpack()
```

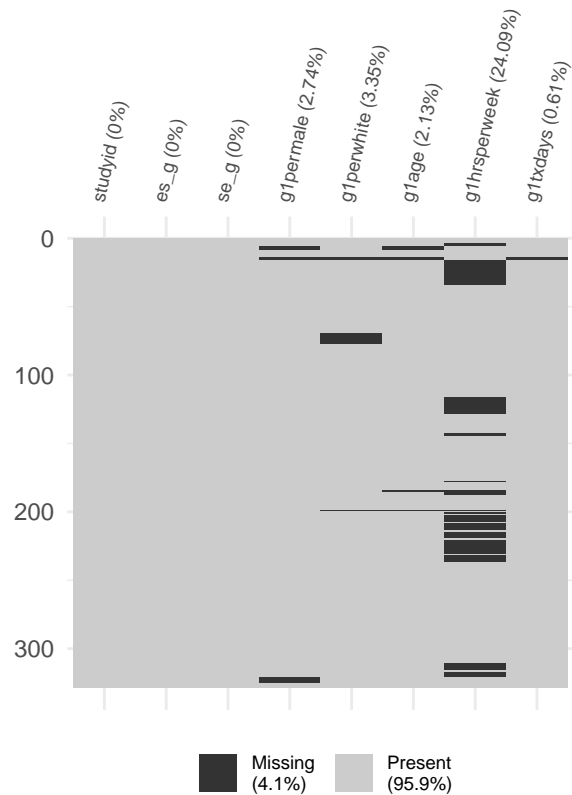
```
##
## *****
## Note: As of version 1.0.0, cowplot does not change the
## default ggplot2 theme anymore. To recover the previous
## behavior, execute:
## theme_set(theme_cowplot())
## *****
##
## Attaching package: 'gridExtra'
## The following object is masked from 'package:dplyr':
##
## combine
```

```
gg_summary_covariate_miss(data_adt_cca)
```

A



B



```
data.frame(k.NA=colSums(is.na(data_adt_cca)))
```

```
##          k.NA
## studyid      0
## es_g         0
## se_g         0
## g1permale     9
## g1perwhite    11
## g1age         7
## g1hrsperweek  79
```

```
## gltxdays      2
table(rowSums(is.na(data_adt_cca)))
```

```
##
##    0    1    2    3    4
## 232  89    4    1    2
```

```
#Percentage missing by variable
miss_var_summary(data_adt_cca)
```

```
## # A tibble: 8 x 3
##   variable      n_miss pct_miss
##   <chr>      <int>   <dbl>
## 1 glhrsperweek      79    24.1
## 2 glperwhite       11     3.35
## 3 glpermale         9     2.74
## 4 glage             7     2.13
## 5 gltxdays         2     0.610
## 6 studyid          0      0
## 7 es_g             0      0
## 8 se_g             0      0
```

```
#Percentage missing by Effect Size case
miss_case_summary(data_adt_cca)
```

```
## # A tibble: 328 x 3
##   case n_miss pct_miss
##   <int> <int>   <dbl>
## 1    15      4     50
## 2    16      4     50
## 3   199      3    37.5
## 4      7      2     25
## 5      8      2     25
## 6      9      2     25
## 7   185      2     25
## 8      5      1    12.5
## 9      6      1    12.5
## 10    17      1    12.5
## # ... with 318 more rows
```

Complete case analysis

While effect sizes and sampling variances are not missing for this dataset, there are a number of moderator (covariates) variables that are. A total of 328 ES available in the data.

```
#Meta-regression
#random-effects model
mr_cca<- rma(es_g, se_g^2, mods= ~ glpermale + glperwhite + glage +
  glhrsperweek + gltxdays , data= data_adt_cca)
```

```
## Warning in rma(es_g, se_g^2, mods = ~glpermale + glperwhite + glage +
## glhrsperweek + : Studies with NAs omitted from model fitting.
mr_cca
```

```
##
## Mixed-Effects Model (k = 232; tau^2 estimator: REML)
```

```
##
## tau^2 (estimated amount of residual heterogeneity):      0.0348 (SE = 0.0083)
## tau (square root of estimated tau^2 value):             0.1865
## I^2 (residual heterogeneity / unaccounted variability): 40.55%
## H^2 (unaccounted variability / sampling variability):    1.68
## R^2 (amount of heterogeneity accounted for):             6.78%
##
## Test for Residual Heterogeneity:
## QE(df = 226) = 388.2926, p-val < .0001
##
## Test of Moderators (coefficients 2:6):
## QM(df = 5) = 23.1900, p-val = 0.0003
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          0.5799  0.4128   1.4045  0.1602  -0.2293   1.3890
## g1permale        -0.3926  0.1377  -2.8514  0.0044  -0.6625  -0.1227  **
## g1perwhite         0.1728  0.0982   1.7595  0.0785  -0.0197   0.3653   .
## glage            -0.0117  0.0247  -0.4738  0.6356  -0.0602   0.0367
## g1hrsperweek      0.0570  0.0170   3.3475  0.0008   0.0236   0.0904  ***
## g1txdays        -0.0012  0.0006  -2.1821  0.0291  -0.0023  -0.0001   *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Only k=232 ES were included in the analysis. Thus, approximately 30% of the ES were excluded from the analysis, illustrating the loss of data that can occur when conducting a complete case analysis.

Complete case analysis - Nested models

```
##delete NA
data_adt_na<- na.omit(data_adt_cca)

##Meta-regression
##random-effects model

##Using rma.mv
rma_mv_cca<- rma.mv(es_g, se_g^2, mods= ~ 1 + g1permale + g1perwhite + glage +
                    g1hrsperweek + g1txdays,
                    random= ~ 1|studyid,
                    data= data_adt_na,
                    method="REML")
rma_mv_cca

##
## Multivariate Meta-Analysis Model (k = 232; method: REML)
##
## Variance Components:
##
##               estim      sqrt  nlvls  fixed  factor
## sigma^2        0.1055  0.3247    34     no  studyid
##
## Test for Residual Heterogeneity:
```

```

## QE(df = 226) = 388.2926, p-val < .0001
##
## Test of Moderators (coefficients 2:6):
## QM(df = 5) = 18.4383, p-val = 0.0024
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          2.0333  1.2352   1.6461  0.0997   -0.3877   4.4543   .
## g1permale        -0.5452  0.3742  -1.4571  0.1451   -1.2786   0.1882
## g1perwhite         0.6605  0.2064   3.2007  0.0014    0.2560   1.0649  **
## glage            -0.1072  0.0685  -1.5654  0.1175   -0.2414   0.0270
## glhrsperweek      0.0417  0.0425   0.9806  0.3268   -0.0416   0.1250
## g1txdays        -0.0013  0.0014  -0.9435  0.3454   -0.0041   0.0015
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

# Then use robust.rma.mv
robustrma_cca<- robust.rma.mv(rma_mv_cca, data_adt_na$studyid)
robustrma_cca

##
## Number of outcomes:  232
## Number of clusters:  34
## Outcomes per cluster: 1-36 (mean: 6.82, median: 4)
##
## Test of Moderators (coefficients 2:6):
## F(df1 = 5, df2 = 28) = 3.6155, p-val = 0.0120
##
## Model Results:
##
##           estimate      se      tval      pval      ci.lb      ci.ub
## intrcpt          2.0333  0.8744   2.3254  0.0275    0.2422   3.8244  *
## g1permale        -0.5452  0.3076  -1.7724  0.0872   -1.1753   0.0849   .
## g1perwhite         0.6605  0.2816   2.3453  0.0263    0.0836   1.2374  *
## glage            -0.1072  0.0534  -2.0079  0.0544   -0.2165   0.0022   .
## glhrsperweek      0.0417  0.0238   1.7492  0.0912   -0.0071   0.0905   .
## g1txdays        -0.0013  0.0017  -0.7858  0.4386   -0.0049   0.0022
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#Using mr3 with moderators
mr3<- meta3(es_g, se_g^2, cluster= studyid, data= data_adt_na,
            intercept.constraints = 0,
            x=model.matrix( ~ 1 + g1permale + g1perwhite + glage +
                             glhrsperweek + g1txdays))
summary(mr3)

##
## Call:
## meta3(y = es_g, v = se_g^2, cluster = studyid, x = model.matrix(~1 +
##   g1permale + g1perwhite + glage + glhrsperweek + g1txdays),
##   data = data_adt_na, intercept.constraints = 0)
##

```

```

## 95% confidence intervals: z statistic approximation (robust=FALSE)
## Coefficients:
##      Estimate   Std.Error   lbound   ubound z value Pr(>|z|)
## Slope_1  1.8417e+00  1.1390e+00 -3.9063e-01  4.0741e+00  1.6170 0.105877
## Slope_2 -5.4519e-01  3.4417e-01 -1.2198e+00  1.2937e-01 -1.5841 0.113176
## Slope_3  5.8655e-01  2.1655e-01  1.6213e-01  1.0110e+00  2.7087 0.006755
## Slope_4 -9.3703e-02  6.4010e-02 -2.1916e-01  3.1754e-02 -1.4639 0.143224
## Slope_5  4.4610e-02  3.9431e-02 -3.2673e-02  1.2189e-01  1.1314 0.257904
## Slope_6 -1.2636e-03  1.2864e-03 -3.7850e-03  1.2577e-03 -0.9823 0.325954
## Tau2_2   1.0000e-10  7.6231e-03 -1.4941e-02  1.4941e-02  0.0000 1.000000
## Tau2_3   8.0166e-02  2.8867e-02  2.3588e-02  1.3674e-01  2.7771 0.005485
##
## Slope_1
## Slope_2
## Slope_3 **
## Slope_4
## Slope_5
## Slope_6
## Tau2_2
## Tau2_3 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Q statistic on the homogeneity of effect sizes: 423.0366
## Degrees of freedom of the Q statistic: 231
## P value of the Q statistic: 1.946221e-13
##
## Explained variances (R2):
##                Level 2 Level 3
## Tau2 (no predictor)  1.0000e-10  0.0817
## Tau2 (with predictors) 1.0000e-10  0.0802
## R2                  1.1102e-16  0.0193
##
## Number of studies (or clusters): 34
## Number of observed statistics: 232
## Number of estimated parameters: 8
## Degrees of freedom: 224
## -2 log likelihood: 67.28976
## OpenMx status1: 6 ("0" or "1": The optimization is considered fine.
## Other values may indicate problems.)

## Warning in print.summary.meta(x): OpenMx status1 is neither 0 or 1. You are advised to 'rerun' it ag

#Using robu
#Intercept only model
#use .8 as correlation between ES
mr_robu<- robu( es_g ~ 1 , data=data_adt_na, studyid, se_g^2, rho=.8, small=TRUE)
print(mr_robu)

## RVE: Correlated Effects Model with Small-Sample Corrections
##
## Model: es_g ~ 1
##
## Number of studies = 34
## Number of outcomes = 232 (min = 1 , mean = 6.82 , median = 4 , max = 36 )

```

```
## Rho = 0.8
## I.sq = 59.67843
## Tau.sq = 0.06944127
##
##           Estimate StdErr t-value  dfs P(|t|>) 95% CI.L 95% CI.U Sig
## 1 X.Intercept.    0.193 0.0536     3.6 29.7 0.00113  0.0836   0.303 ***
## ---
## Signif. codes: < .01 *** < .05 ** < .10 *
## ---
## Note: If df < 4, do not trust the results

sensitivity(mr_robu)

## RVE: Correlated Effects Model with Small-Sample Corrections
## Model: es_g ~ 1
##
## Sensitivity Analysis
##
##           Rho = 0 Rho = 0.2 Rho = 0.4 Rho = 0.6 Rho = 0.8
## X.Intercept. Coefficient 0.1929 0.1930 0.1930 0.1931 0.1931
##           Std. Error 0.0535 0.0535 0.0536 0.0536 0.0536
## Tau.sq      Estimate 0.0687 0.0689 0.0691 0.0693 0.0694
## Rho = 1
## 0.1931
## 0.0536
## 0.0696

#with moderators
mr_robu2<- robu(es_g ~ g1permale + g1perwhite + glage +g1hrsperweek + g1txdays ,
               data=data_adt_na, modelweights="HIER", studyid, se_g^2, small=TRUE)
print(mr_robu2)

## RVE: Hierarchical Effects Model with Small-Sample Corrections
##
## Model: es_g ~ g1permale + g1perwhite + glage + g1hrsperweek + g1txdays
##
## Number of clusters = 34
## Number of outcomes = 232 (min = 1 , mean = 6.82 , median = 4 , max = 36 )
## Omega.sq = 0.002653204
## Tau.sq = 0.05106938
##
##           Estimate StdErr t-value  dfs P(|t|>) 95% CI.L 95% CI.U
## 1 X.Intercept.    0.64770 0.60010   1.08 3.87 0.343 -1.04080 2.33620
## 2   g1permale    -0.38983 0.23543  -1.66 3.59 0.181 -1.07424 0.29457
## 3   g1perwhite    0.20714 0.20480   1.01 10.45 0.335 -0.24654 0.66082
## 4       glage    -0.01605 0.03647  -0.44 3.53 0.686 -0.12290 0.09081
## 5 g1hrsperweek    0.05789 0.03184   1.82 4.13 0.141 -0.02940 0.14519
## 6   g1txdays   -0.00137 0.00121  -1.14 11.47 0.279 -0.00402 0.00127
## Sig
## 1
## 2
## 3
## 4
## 5
## 6
```

```
## ---
## Signif. codes: < .01 *** < .05 ** < .10 *
## ---
## Note: If df < 4, do not trust the results
```

Shifting units analysis

```
#g1permale
mr_shu_cov1<- rma(es_g, se_g^2, mods= ~ g1permale, data= data_adt_cca)

## Warning in rma(es_g, se_g^2, mods = ~g1permale, data = data_adt_cca):
## Studies with NAs omitted from model fitting.

mr_shu_cov1

##
## Mixed-Effects Model (k = 319; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity):      0.0229 (SE = 0.0052)
## tau (square root of estimated tau^2 value):             0.1515
## I^2 (residual heterogeneity / unaccounted variability): 35.42%
## H^2 (unaccounted variability / sampling variability):    1.55
## R^2 (amount of heterogeneity accounted for):             2.89%
##
## Test for Residual Heterogeneity:
## QE(df = 317) = 536.1762, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 4.3603, p-val = 0.0368
##
## Model Results:
##
##              estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          0.2518  0.0695   3.6201  0.0003   0.1155   0.3881   ***
## g1permale        -0.2018  0.0966  -2.0881  0.0368  -0.3912  -0.0124    *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

#319 EF out of 328

```
#g1perwhite
mr_shu_cov2<- rma(es_g, se_g^2, mods= ~ g1perwhite, data= data_adt_cca)

## Warning in rma(es_g, se_g^2, mods = ~g1perwhite, data = data_adt_cca):
## Studies with NAs omitted from model fitting.

mr_shu_cov2

##
## Mixed-Effects Model (k = 317; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity):      0.0295 (SE = 0.0059)
## tau (square root of estimated tau^2 value):             0.1719
## I^2 (residual heterogeneity / unaccounted variability): 41.12%
## H^2 (unaccounted variability / sampling variability):    1.70
```



```

## R^2 (amount of heterogeneity accounted for):          0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 315) = 570.7818, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 0.0412, p-val = 0.8391
##
## Model Results:
##
##           estimate      se    zval    pval    ci.lb    ci.ub
## intrcpt      0.1165  0.0391  2.9765  0.0029  0.0398  0.1931  **
## glperwhite    0.0130  0.0641  0.2031  0.8391 -0.1125  0.1386
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#317 EF out of 328

#glage
mr_shu_cov3<- rma(es_g, se_g^2, mods= ~ glage, data= data_adt_cca)

## Warning in rma(es_g, se_g^2, mods = ~glage, data = data_adt_cca): Studies
## with NAs omitted from model fitting.

mr_shu_cov3

##
## Mixed-Effects Model (k = 321; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity):      0.0260 (SE = 0.0055)
## tau (square root of estimated tau^2 value):             0.1611
## I^2 (residual heterogeneity / unaccounted variability): 38.07%
## H^2 (unaccounted variability / sampling variability):    1.61
## R^2 (amount of heterogeneity accounted for):             0.68%
##
## Test for Residual Heterogeneity:
## QE(df = 319) = 556.1142, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 1.1035, p-val = 0.2935
##
## Model Results:
##
##           estimate      se    zval    pval    ci.lb    ci.ub
## intrcpt    -0.1821  0.2881 -0.6321  0.5273 -0.7467  0.3825
## glage       0.0190  0.0181  1.0505  0.2935 -0.0164  0.0544
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#321 EF out of 328

#g1hrspersperweek
mr_shu_cov4<- rma(es_g, se_g^2, mods= ~ g1hrspersperweek, data= data_adt_cca)

```

```
## Warning in rma(es_g, se_g^2, mods = ~g1hrspersperweek, data = data_adt_cca):
## Studies with NAs omitted from model fitting.
mr_shu_cov4

##
## Mixed-Effects Model (k = 249; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity):      0.0398 (SE = 0.0085)
## tau (square root of estimated tau^2 value):             0.1995
## I^2 (residual heterogeneity / unaccounted variability): 43.86%
## H^2 (unaccounted variability / sampling variability):    1.78
## R^2 (amount of heterogeneity accounted for):             1.51%
##
## Test for Residual Heterogeneity:
## QE(df = 247) = 460.4483, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 6.7655, p-val = 0.0093
##
## Model Results:
##
##              estimate      se    zval    pval    ci.lb    ci.ub
## intrcpt          0.1203  0.0320  3.7575  0.0002  0.0576  0.1831 ***
## g1hrspersperweek  0.0379  0.0146  2.6011  0.0093  0.0093  0.0665 **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#249 EF out of 328

#g1txdays
mr_shu_cov5<- rma(es_g, se_g^2, mods= ~ g1txdays, data= data_adt_cca)

## Warning in rma(es_g, se_g^2, mods = ~g1txdays, data = data_adt_cca):
## Studies with NAs omitted from model fitting.
mr_shu_cov5

##
## Mixed-Effects Model (k = 326; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity):      0.0275 (SE = 0.0056)
## tau (square root of estimated tau^2 value):             0.1659
## I^2 (residual heterogeneity / unaccounted variability): 39.38%
## H^2 (unaccounted variability / sampling variability):    1.65
## R^2 (amount of heterogeneity accounted for):             0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 324) = 570.2498, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 6.7439, p-val = 0.0094
##
## Model Results:
##
```

```
##          estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      0.2144  0.0395   5.4299 <.0001   0.1370   0.2918 ***
## gltxdays   -0.0008  0.0003  -2.5969  0.0094  -0.0014  -0.0002  **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

#326 EF out of 328