Modelling

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Contents

Read in clean data

```
TSH_long  <- read_rds("../data/20191207-02_convert_long.rds")
```

Modelling

Three thyroid tests

We will use a mixed-effect model with the paper ID as a random intercept and thyroid method as a fixed effect. Need to convert `Sig` to factor. Also remove missing

```r
TSH_long  <-
  TSH_long %>%
  mutate(Sig = factor(Sig))
```

```r
TSH_long <-
  TSH_long %>% filter(!is.na(Sig))
```

Convert Thyroid test to factor

```r
TSH_long  <-
  TSH_long %>%
  mutate(
    Thyroid_test = factor(Thyroid_test)
  )
```

Load necessary packages

```r
pacman::p_load(lme4, lmerTest)
```

Random effects

Start with single fixed effect - thyroid test, and single random intercept (RI) for each paper.

```r
tsh_glmer  <- glmer(Sig ~ Thyroid_test + (1 | Paper), data = TSH_long, family = binomial)
```

Compare model to one without RI.

```r
tsh_glm  <- glm(Sig ~ Thyroid_test, data = TSH_long, family = binomial)
anova(tsh_glmer, tsh_glm)
```

```
## Data: TSH_long
## Models:
## tsh_glm: Sig ~ Thyroid_test
## tsh_glmer: Sig ~ Thyroid_test + (1 | Paper)
##           Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## tsh_glm    3 2351.5 2368.1 -1172.8   2345.5
## tsh_glmer  4 2062.8 2085.0 -1027.4   2054.8 290.67      1  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Looks like need RI.

Fixed effects

Test for significant differences between tests.

```r
tsh_glmer_null  <- glmer(Sig ~ 1 + (1 | Paper), data = TSH_long, family = binomial)
anova(tsh_glmer, tsh_glmer_null)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_null: Sig ~ 1 + (1 | Paper)
## tsh_glmer: Sig ~ Thyroid_test + (1 | Paper)
##                Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## tsh_glmer_null  2 2239.8 2250.9 -1117.9   2235.8
## tsh_glmer       4 2062.8 2085.0 -1027.4   2054.8 180.99      2  < 2.2e-16 ***
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Looks like significant effect of test.

Also check with BIC - smaller is better.

```
BIC(tsh_glmer_null, tsh_glm, tsh_glmer)
```

```
##                df      BIC
## tsh_glmer_null  2 2250.914
## tsh_glm         3 2368.130
## tsh_glmer       4 2084.998
```

So far best model is fixed effect of test with RI.

```
summary(tsh_glmer)
```

```
## Generalized linear mixed model fit by maximum likelihood (Laplace
##   Approximation) [glmerMod]
##  Family: binomial  ( logit )
## Formula: Sig ~ Thyroid_test + (1 | Paper)
##    Data: TSH_long
##
##      AIC      BIC   logLik deviance df.resid
##   2062.8   2085.0  -1027.4   2054.8     1876
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.3023 -0.6399 -0.3145  0.7176  4.3023
##
## Random effects:
##  Groups Name        Variance Std.Dev.
##  Paper  (Intercept) 1.31     1.145
## Number of obs: 1880, groups:  Paper, 58
##
## Fixed effects:
##                 Estimate Std. Error z value Pr(>|z|)
## (Intercept)      0.27599    0.17845   1.547    0.122
## Thyroid_testT3  -0.09313    0.17959  -0.519    0.604
## Thyroid_testTSH -1.55654    0.12655 -12.300   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Thy_T3
## Thyrd_tstT3 -0.204
## Thyrd_tsTSH -0.309  0.289
```

From this - look at fixed effect output. We have that TSH has a signicantly smaller probability of significance compared to T4. T3 and T4 are not significantly different.

Pairwise comparisons

```
summary(glht(tsh_glmer, linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
```

```
##   Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glmer(formula = Sig ~ Thyroid_test + (1 | Paper), data = TSH_long,
##     family = binomial)
##
## Linear Hypotheses:
##                 Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.09313    0.17959  -0.519     0.86
## TSH - FT4 == 0  -1.55654    0.12655 -12.300   <1e-04 ***
## TSH - T3 == 0   -1.46341    0.18745  -7.807   <1e-04 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

So significant difference between

- TSH and Free T4, and
- TSH and T3.

Notes

So we seem to have a lot of problems getting the RI to fit. May be able to tinker and improve. Looking at the various possible covariates we find that some of them increase the prediction of the probability of significance - system and number of subject. This is based on BIC. Number of covariates does not seem to improve the model.

Four thyroid tests

Will remove single T3

```
TSH_long %>% count(Thyroid_test_4)
```

```
## # A tibble: 4 x 2
##   Thyroid_test_4     n
##   <chr>          <int>
## 1 FT4              813
## 2 T3_Free          183
## 3 T3_Total          71
## 4 TSH              813
```

Random effects

```
tsh_glmer  <- glmer(Sig ~ Thyroid_test_4 + (1 | Paper),
                    data = TSH_long, family = binomial)
tsh_glm  <- glm(Sig ~ Thyroid_test_4,
                data = TSH_long, family = binomial)
anova(tsh_glmer, tsh_glm)
```

```
## Data: TSH_long
## Models:
```

```
## tsh_glm: Sig ~ Thyroid_test_4
## tsh_glmer: Sig ~ Thyroid_test_4 + (1 | Paper)
##           Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## tsh_glm    4 2333.8 2356.0 -1162.9   2325.8
## tsh_glmer  5 2062.2 2089.9 -1026.1   2052.2 273.61      1  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

So we need a random intercept.

Fixed effects

```
tsh_glmer_null  <- glmer(Sig ~ 1 + (1 | Paper),
                         data = TSH_long, family = binomial)
anova(tsh_glmer, tsh_glmer_null)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_null: Sig ~ 1 + (1 | Paper)
## tsh_glmer: Sig ~ Thyroid_test_4 + (1 | Paper)
##                Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## tsh_glmer_null  2 2239.8 2250.9 -1117.9   2235.8
## tsh_glmer       5 2062.2 2089.9 -1026.1   2052.2 183.61      3  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

So the treatments are significant.

```
summary(tsh_glmer)
```

```
## Generalized linear mixed model fit by maximum likelihood (Laplace
##   Approximation) [glmerMod]
##  Family: binomial  ( logit )
## Formula: Sig ~ Thyroid_test_4 + (1 | Paper)
##    Data: TSH_long
##
##      AIC      BIC   logLik deviance df.resid
##   2062.2   2089.9  -1026.1   2052.2     1875
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.3462 -0.6415 -0.3155  0.7191  4.2823
##
## Random effects:
##  Groups Name        Variance Std.Dev.
##  Paper  (Intercept) 1.289    1.135
## Number of obs: 1880, groups:  Paper, 58
##
## Fixed effects:
##                      Estimate Std. Error z value Pr(>|z|)
## (Intercept)            0.2783     0.1773   1.569    0.117
## Thyroid_test_4T3_Free -0.2561     0.2063  -1.241    0.214
## Thyroid_test_4T3_Total 0.3831     0.3521   1.088    0.277
## Thyroid_test_4TSH     -1.5473     0.1262 -12.265   <2e-16 ***
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##            (Intr) T__4T3_F T__4T3_T
## Thyr__4T3_F -0.182
## Thyr__4T3_T -0.096  0.046
## Thyrd__4TSH -0.310  0.232    0.177
```

Pairwise comparisons

```
summary(glht(tsh_glmer, linfct = mcp(Thyroid_test_4 = "Tukey")))
```

```
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glmer(formula = Sig ~ Thyroid_test_4 + (1 | Paper), data = TSH_long,
##     family = binomial)
##
## Linear Hypotheses:
##                      Estimate Std. Error z value Pr(>|z|)
## T3_Free - FT4 == 0     -0.2561    0.2063  -1.241    0.574
## T3_Total - FT4 == 0     0.3831    0.3521   1.088    0.674
## TSH - FT4 == 0         -1.5473    0.1262 -12.265   <0.001 ***
## T3_Total - T3_Free == 0  0.6392    0.3998   1.599    0.353
## TSH - T3_Free == 0     -1.2912    0.2154  -5.994   <0.001 ***
## TSH - T3_Total == 0    -1.9304    0.3524  -5.477   <0.001 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

So significant difference between

- TSH and Free T4,
- TSH and Free T3, and
- TSH and Total T3.

Try adding in other covariates.

For these, we keep thyroid test and try adding in the given covariate, also try upto two-way interaction.

System

```
system_models  <- get_cov("System")
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## unable to evaluate scaled gradient
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge: degenerate Hessian with 1 negative eigenvalues
```

```r
system_models %>% arrange(BIC) %>% knitr::kable()
```

sigma	logLik	AIC	BIC	deviance	df.residual	null.deviance	df.null	converge	models
1	-1027.4208	2062.842	2084.998	1902.484	1876	NA	NA	TRUE	test + RI
1	-1018.3724	2058.745	2119.674	1889.125	1869	NA	NA	TRUE	test + main + RI
1	-985.5945	2021.189	2159.665	1814.805	1855	NA	NA	FALSE	interaction + RI
NA	-1107.7225	2235.445	2290.835	2215.445	1870	2505.135	1879	TRUE	test + main
NA	-1079.9440	2207.888	2340.825	2159.888	1856	2505.135	1879	TRUE	interaction
NA	-1172.7563	2351.513	2368.130	2345.513	1877	2505.135	1879	TRUE	test

Best model (BIC) is thyroid test + random intercept.

N of subjects

```r
N_models  <- get_cov("N_bin")
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.00265913 (tol = 0.001, component 1)
```

```r
N_models %>% arrange(BIC) %>% knitr::kable()
```

sigma	logLik	AIC	BIC	deviance	df.residual	null.deviance	df.null	converge	models
1	-1027.421	2062.842	2084.998	1902.484	1876	NA	NA	TRUE	test + RI
1	-1018.546	2053.091	2097.404	1888.297	1872	NA	NA	TRUE	test + main + RI
1	-1009.499	2050.997	2139.622	1868.278	1864	NA	NA	FALSE	interaction + RI
NA	-1148.268	2310.536	2349.310	2296.536	1873	2505.135	1879	TRUE	test + main
NA	-1172.756	2351.513	2368.130	2345.513	1877	2505.135	1879	TRUE	test
NA	-1137.320	2304.640	2387.725	2274.640	1865	2505.135	1879	TRUE	interaction

Best model (BIC) is thyroid test + random intercept.

Number of covariates

```r
n_cov_models  <- get_cov("n_cov")
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.0025968 (tol = 0.001, component 1)
```

```r
n_cov_models %>% arrange(BIC) %>% knitr::kable()
```

sigma	logLik	AIC	BIC	deviance	df.residual	null.deviance	df.null	converge	models
1	-1027.421	2062.842	2084.998	1902.484	1876	NA	NA	TRUE	test + RI
1	-1024.718	2063.437	2102.210	1899.315	1873	NA	NA	TRUE	test + main + RI
1	-1017.073	2060.146	2132.154	1885.452	1867	NA	NA	FALSE	interaction + RI
NA	-1152.328	2316.655	2349.889	2304.655	1874	2505.135	1879	TRUE	test + main
NA	-1172.756	2351.513	2368.130	2345.513	1877	2505.135	1879	TRUE	test
NA	-1139.386	2302.771	2369.239	2278.771	1868	2505.135	1879	TRUE	interaction

Best model (BIC) is thyroid test + random intercept.

Model to take into account cohorts

Background

We have added a cohort based on sample size within paper

```
TSH_long %>%
  dplyr::select(
  Paper, N, cohort
)
```

```
## # A tibble: 1,880 x 3
##    Paper            N cohort
##    <chr>        <dbl> <chr>
##  1 Cappola et al  2673 C4
##  2 Cappola et al  2673 C4
##  3 Cappola et al  2673 C4
##  4 Cappola et al  2673 C4
##  5 Cappola et al  2673 C4
##  6 Cappola et al  2673 C4
##  7 Cappola et al  2215 C3
##  8 Cappola et al  2215 C3
##  9 Cappola et al  2215 C3
## 10 Cappola et al  2215 C3
## # ... with 1,870 more rows
```

So we have cohort nested within paper.

Looked at the lme4 paper

Fitting Linear Mixed-Effects Models Using lme4

Douglas Bates	Martin Mächler	Benjamin M. Bolker	Steven C. Walker
University of Wisconsin-Madison	ETH Zurich	McMaster University	McMaster University

The notation is given in Table 2 of the paper:

Formula	Alternative	Meaning
`(1 | g)`	`1 + (1 | g)`	Random intercept with fixed mean.
`0 + offset(o) + (1 | g)`	`-1 + offset(o) + (1 | g)`	Random intercept with *a priori* means.
`(1 | g1/g2)`	`(1 | g1)+(1 | g1:g2)`	Intercept varying among g1 and g2 within g1.
`(1 | g1) + (1 | g2)`	`1 + (1 | g1) + (1 | g2).`	Intercept varying among g1 and g2.
`x + (x | g)`	`1 + x + (1 + x | g)`	Correlated random intercept and slope.
`x + (x || g)`	`1 + x + (1 | g) + (0 + x | g)`	Uncorrelated random intercept and slope.

Table 2: Examples of the right-hand-sides of mixed-effects model formulas. The names of

Looks like we want

`(1 | paper/cohort)`

Fit models

```
tsh_glmer_M_paperRI  <- glmer(Sig ~ Thyroid_test + (1 | Paper),
                         data = TSH_long, family = binomial)
tsh_glmer_M_paper_cohort_RI  <- glmer(Sig ~ Thyroid_test + (1 | Paper / cohort),
                              data = TSH_long, family = binomial)
tsh_glmer_M_no_test  <- glmer(Sig ~ 1 + (1 | Paper / cohort),
                         data = TSH_long, family = binomial)
```

Random terms

First test for whether need cohort RI:

```
anova(tsh_glmer_M_paperRI, tsh_glmer_M_paper_cohort_RI)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_M_paperRI: Sig ~ Thyroid_test + (1 | Paper)
## tsh_glmer_M_paper_cohort_RI: Sig ~ Thyroid_test + (1 | Paper/cohort)
##                             Df    AIC    BIC  logLik deviance  Chisq Chi Df
## tsh_glmer_M_paperRI          4 2062.8 2085.0 -1027.4   2054.8
## tsh_glmer_M_paper_cohort_RI  5 2026.0 2053.7 -1008.0   2016.0 38.816      1
##                             Pr(>Chisq)
## tsh_glmer_M_paperRI
## tsh_glmer_M_paper_cohort_RI  4.656e-10 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Small p-value so looks like we need cohort and paper RI.

Fixed effects

Now test for significant effect of test

```
anova(tsh_glmer_M_paper_cohort_RI, tsh_glmer_M_no_test)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_M_no_test: Sig ~ 1 + (1 | Paper/cohort)
## tsh_glmer_M_paper_cohort_RI: Sig ~ Thyroid_test + (1 | Paper/cohort)
##                               Df    AIC    BIC  logLik deviance  Chisq Chi Df
## tsh_glmer_M_no_test            3 2212.6 2229.2 -1103.3   2206.6
## tsh_glmer_M_paper_cohort_RI    5 2026.0 2053.7 -1008.0   2016.0 190.58      2
##                               Pr(>Chisq)
## tsh_glmer_M_no_test
## tsh_glmer_M_paper_cohort_RI  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

So still significant effect of type of test.

Final model

Look at effect of test.

```
summary(tsh_glmer_M_paper_cohort_RI)
```

```
## Generalized linear mixed model fit by maximum likelihood (Laplace
##   Approximation) [glmerMod]
##  Family: binomial  ( logit )
## Formula: Sig ~ Thyroid_test + (1 | Paper/cohort)
##    Data: TSH_long
##
##      AIC      BIC   logLik deviance df.resid
##   2026.0   2053.7  -1008.0   2016.0     1875
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.5228 -0.6271 -0.3054  0.6843  6.1372
##
## Random effects:
##  Groups       Name        Variance Std.Dev.
##  cohort:Paper (Intercept) 0.794    0.891
##  Paper        (Intercept) 1.010    1.005
## Number of obs: 1880, groups:  cohort:Paper, 142; Paper, 58
##
## Fixed effects:
##                 Estimate Std. Error z value Pr(>|z|)
## (Intercept)       0.3364     0.1877   1.793    0.073 .
## Thyroid_testT3   -0.1295     0.1824  -0.710    0.478
## Thyroid_testTSH  -1.6593     0.1323 -12.546   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Thy_T3
## Thyrd_tstT3 -0.197
## Thyrd_tsTSH -0.311  0.293
```

As before probability of significance is significantly lower than FT4 and T3.

Pairwise comparisons

```
summary(glht(tsh_glmer_M_paper_cohort_RI, linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glmer(formula = Sig ~ Thyroid_test + (1 | Paper/cohort), data = TSH_long,
##     family = binomial)
##
## Linear Hypotheses:
##                Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.1295     0.1824  -0.710    0.754
## TSH - FT4 == 0  -1.6593     0.1323 -12.546   <1e-04 ***
## TSH - T3 == 0   -1.5299     0.1914  -7.992   <1e-04 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

Assumptions

```
plot(tsh_glmer_M_paper_cohort_RI)
```
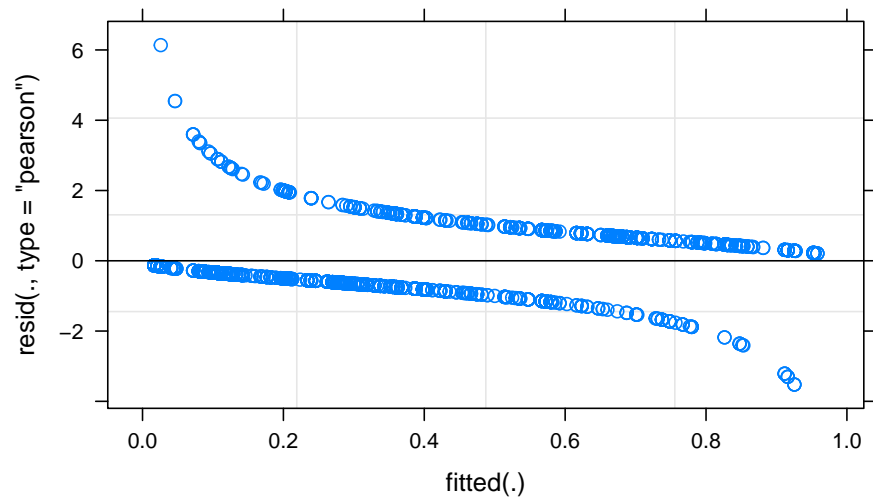

Model to take into account style

Will be similar to above. First examine possible styles

```r
TSH_long %>%
  count(CvQ) %>%
  knitr::kable()
```

CvQ	n
continuous	1313
dichotomous	42
performance	48
quartile	228
quintiles	192
tertiles	57

Fit all models

```r
tsh_glmer_M_paperRI  <- glmer(Sig ~ Thyroid_test + (1 | Paper),
                        data = TSH_long, family = binomial)
tsh_glmer_M_paper_style_RI  <- glmer(Sig ~ Thyroid_test + (1 | Paper / CvQ),
                            data = TSH_long, family = binomial)
tsh_glmer_M_no_test  <- glmer(Sig ~ 1 + (1 | Paper / CvQ),
                        data = TSH_long, family = binomial)
```

Random terms

```r
anova(tsh_glmer_M_paperRI, tsh_glmer_M_paper_style_RI)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_M_paperRI: Sig ~ Thyroid_test + (1 | Paper)
## tsh_glmer_M_paper_style_RI: Sig ~ Thyroid_test + (1 | Paper/CvQ)
##                            Df    AIC    BIC  logLik deviance  Chisq Chi Df
## tsh_glmer_M_paperRI         4 2062.8 2085.0 -1027.4   2054.8
## tsh_glmer_M_paper_style_RI  5 2061.5 2089.2 -1025.8   2051.5 3.3332      1
##                            Pr(>Chisq)
## tsh_glmer_M_paperRI
## tsh_glmer_M_paper_style_RI     0.0679 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

No significant effect of style.

Model to take into account sophistication

Check and clean

```r
TSH_long %>%
  count(Sophistication)
```

```
## # A tibble: 4 x 2
```

```
##   Sophistication     n
##   <chr>          <int>
## 1 Crude            515
## 2 High             301
## 3 Low              291
## 4 Medium           773
```

Fit all models

```
tsh_glmer_M_paperRI  <- glmer(Sig ~ Thyroid_test + (1 | Paper),
                              data = TSH_long, family = binomial)
tsh_glmer_M_paper_soph_RI  <- glmer(Sig ~ Thyroid_test + (1 | Paper / Sophistication),
                                    data = TSH_long, family = binomial)
tsh_glmer_M_no_test  <- glmer(Sig ~ 1 + (1 | Paper / cohort),
                              data = TSH_long, family = binomial)
```

Random effects

First test for whether need sophistication RI:

```
anova(tsh_glmer_M_paperRI, tsh_glmer_M_paper_soph_RI)
```

```
## Data: TSH_long
## Models:
## tsh_glmer_M_paperRI: Sig ~ Thyroid_test + (1 | Paper)
## tsh_glmer_M_paper_soph_RI: Sig ~ Thyroid_test + (1 | Paper/Sophistication)
##                           Df    AIC    BIC  logLik deviance Chisq Chi Df
## tsh_glmer_M_paperRI        4 2062.8 2085.0 -1027.4   2054.8
## tsh_glmer_M_paper_soph_RI  5 2064.1 2091.8 -1027.0   2054.1 0.744      1
##                           Pr(>Chisq)
## tsh_glmer_M_paperRI
## tsh_glmer_M_paper_soph_RI     0.3884
```

No sighnificant random intercept.

Apply Devil's Advocate

Small size, small model

```
TSH_DA  <- TSH_long %>% filter(min_size_min_method)
TSH_DA
```

```
## # A tibble: 133 x 35
##    `hyper/hypo` Paper CvQ   `Condition and ... `Condition Clas... System `Include?`
##    <chr>        <chr> <chr> <chr>              <chr>             <chr>        <dbl>
## 1 Hyper         Capp... quar... Dementia       dementia          Demen...         1
## 2 Hyper         Capp... quar... Dementia       dementia          Demen...         1
## 3 Hyper         Chak... cont... AF prevalent no... AF             Cardi...         0
## 4 Hyper         Chak... cont... AF prevalent no... AF             Cardi...         0
## 5 Hyper         Chak... cont... AF incident nor... AF             Cardi...         1
## 6 Hyper         Chak... cont... AF incident nor... AF             Cardi...         1
## 7 Hyper         Gamm... cont... prevalent AF, n... AF             Cardi...         0
## 8 Hyper         Gamm... cont... prevalent AF, n... AF             Cardi...         0
```

```
##  9 Hyper        Heer... cont... incident AF     AF              Cardi...          1
## 10 Hyper        Heer... cont... incident AF     AF              Cardi...          1
## # ... with 123 more rows, and 28 more variables: `NOS score` <dbl>, `TSH
## #   incong` <chr>, `cross-section` <chr>, `abstract score` <dbl>, ID <int>,
## #   condition <chr>, cohort <chr>, min_size_min_method <lgl>,
## #   min_size_max_method <lgl>, max_size_min_method <lgl>,
## #   max_size_max_method <lgl>, Thyroid_test <fct>, N <dbl>, method <chr>,
## #   Sig <fct>, Sophistication <chr>, cov <chr>, total <chr>, inferred <lgl>,
## #   pv <dbl>, bounded <lgl>, OR <dbl>, ORCI <chr>, count <chr>, countCI <chr>,
## #   Thyroid_test_4 <chr>, n_cov <chr>, N_bin <fct>
```

```r
thyroid_model  <- glm(Sig ~ Thyroid_test,
            data = TSH_DA, family = binomial)
null_model  <- glm(Sig ~ 1,
            data = TSH_DA, family = binomial)
anova(null_model, thyroid_model, test = "LRT")
```

```
## Analysis of Deviance Table
##
## Model 1: Sig ~ 1
## Model 2: Sig ~ Thyroid_test
##   Resid. Df Resid. Dev Df Deviance  Pr(>Chi)
## 1       132     184.19
## 2       130     167.04  2   17.147 0.0001891 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
summary(glht(thyroid_model,
            linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
##    Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glm(formula = Sig ~ Thyroid_test, family = binomial, data = TSH_DA)
##
## Linear Hypotheses:
##              Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.8369     0.5607  -1.493 0.289971
## TSH - FT4 == 0  -1.5995     0.4019  -3.980 0.000174 ***
## TSH - T3 == 0   -0.7626     0.5651  -1.349 0.363072
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

Small size, large model

```r
TSH_DA  <- TSH_long %>% filter(min_size_max_method)
TSH_DA
```

```
## # A tibble: 133 x 35
##    `hyper/hypo` Paper CvQ   `Condition and ... `Condition Clas... System `Include?`
```

```
##      <chr>       <chr> <chr> <chr>          <chr>           <chr>       <dbl>
## 1 Hyper       Capp... cont... Dementia      dementia        Demen...        1
## 2 Hyper       Capp... cont... Dementia      dementia        Demen...        1
## 3 Hyper       Capp... cont... Dementia      dementia        Demen...        1
## 4 Hyper       Chak... cont... AF prevalent no... AF         Cardi...        0
## 5 Hyper       Chak... cont... AF prevalent no... AF         Cardi...        0
## 6 Hyper       Chak... quar... AF incident, no... AF         Cardi...        1
## 7 Hyper       Chak... quar... AF incident, no... AF         Cardi...        1
## 8 Hyper       Gamm... cont... prevalent AF, n... AF         Cardi...        0
## 9 Hyper       Gamm... cont... prevalent AF, n... AF         Cardi...        0
## 10 Hyper      Heer... cont... incident AF    AF             Cardi...        1
## # ... with 123 more rows, and 28 more variables: `NOS score` <dbl>, `TSH
## #   incong` <chr>, `cross-section` <chr>, `abstract score` <dbl>, ID <int>,
## #   condition <chr>, cohort <chr>, min_size_min_method <lgl>,
## #   min_size_max_method <lgl>, max_size_min_method <lgl>,
## #   max_size_max_method <lgl>, Thyroid_test <fct>, N <dbl>, method <chr>,
## #   Sig <fct>, Sophistication <chr>, cov <chr>, total <chr>, inferred <lgl>,
## #   pv <dbl>, bounded <lgl>, OR <dbl>, ORCI <chr>, count <chr>, countCI <chr>,
## #   Thyroid_test_4 <chr>, n_cov <chr>, N_bin <fct>
```

```r
thyroid_model  <- glm(Sig ~ Thyroid_test,
             data = TSH_DA, family = binomial)
null_model  <- glm(Sig ~ 1,
             data = TSH_DA, family = binomial)
anova(null_model, thyroid_model, test = "LRT")
```

```
## Analysis of Deviance Table
##
## Model 1: Sig ~ 1
## Model 2: Sig ~ Thyroid_test
##   Resid. Df Resid. Dev Df Deviance Pr(>Chi)
## 1       132     182.68
## 2       130     168.35  2   14.331 0.000773 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
summary(glht(thyroid_model,
          linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glm(formula = Sig ~ Thyroid_test, family = binomial, data = TSH_DA)
##
## Linear Hypotheses:
##               Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.8492     0.5622  -1.510    0.281
## TSH - FT4 == 0  -1.4576     0.3994  -3.649   <0.001 ***
## TSH - T3 == 0   -0.6084     0.5737  -1.060    0.534
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

```
lm <- glht(thyroid_model,
           linfct = mcp(Thyroid_test = "Tukey"))
slm <- summary(lm)
slm
```

```
##
##    Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glm(formula = Sig ~ Thyroid_test, family = binomial, data = TSH_DA)
##
## Linear Hypotheses:
##               Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.8492     0.5622  -1.510    0.281
## TSH - FT4 == 0  -1.4576     0.3994  -3.649   <0.001 ***
## TSH - T3 == 0   -0.6084     0.5737  -1.060    0.534
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

Large size, small model

```
TSH_DA  <- TSH_long %>% filter(max_size_min_method)
TSH_DA
```

```
## # A tibble: 134 x 35
##     `hyper/hypo` Paper CvQ   `Condition and ... `Condition Clas... System `Include?`
##     <chr>        <chr> <chr> <chr>              <chr>              <chr>       <dbl>
##  1 Hyper        Capp... quar... Mortality       mortality          Morta...        1
##  2 Hyper        Capp... quar... Mortality       mortality          Morta...        1
##  3 Hyper        Chak... cont... AF prevalent    AF                 Cardi...        0
##  4 Hyper        Chak... cont... AF prevalent    AF                 Cardi...        0
##  5 Hyper        Chak... cont... AF incident     AF                 Cardi...        1
##  6 Hyper        Chak... cont... AF incident     AF                 Cardi...        1
##  7 Hyper        Gamm... cont... prevalent AF    AF                 Cardi...        0
##  8 Hyper        Gamm... cont... prevalent AF    AF                 Cardi...        0
##  9 Hyper        Heer... cont... incident AF     AF                 Cardi...        1
## 10 Hyper        Heer... cont... incident AF     AF                 Cardi...        1
## # ... with 124 more rows, and 28 more variables: `NOS score` <dbl>, `TSH
## #   incong` <chr>, `cross-section` <chr>, `abstract score` <dbl>, ID <int>,
## #   condition <chr>, cohort <chr>, min_size_min_method <lgl>,
## #   min_size_max_method <lgl>, max_size_min_method <lgl>,
## #   max_size_max_method <lgl>, Thyroid_test <fct>, N <dbl>, method <chr>,
## #   Sig <fct>, Sophistication <chr>, cov <chr>, total <chr>, inferred <lgl>,
## #   pv <dbl>, bounded <lgl>, OR <dbl>, ORCI <chr>, count <chr>, countCI <chr>,
## #   Thyroid_test_4 <chr>, n_cov <chr>, N_bin <fct>
```

```
thyroid_model  <- glm(Sig ~ Thyroid_test,
           data = TSH_DA, family = binomial)
null_model  <- glm(Sig ~ 1,
           data = TSH_DA, family = binomial)
```

```
anova(null_model, thyroid_model, test = "LRT")
```

```
## Analysis of Deviance Table
##
## Model 1: Sig ~ 1
## Model 2: Sig ~ Thyroid_test
##   Resid. Df Resid. Dev Df Deviance Pr(>Chi)
## 1       133     185.64
## 2       131     176.67  2    8.973  0.01126 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
summary(glht(thyroid_model,
             linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glm(formula = Sig ~ Thyroid_test, family = binomial, data = TSH_DA)
##
## Linear Hypotheses:
##               Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.4925     0.5436  -0.906  0.63226
## TSH - FT4 == 0  -1.1343     0.3867  -2.933  0.00933 **
## TSH - T3 == 0   -0.6419     0.5464  -1.175  0.46338
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

Large size, large model

```
TSH_DA  <- TSH_long %>% filter(max_size_max_method)
TSH_DA
```

```
## # A tibble: 135 x 35
##    `hyper/hypo` Paper CvQ  `Condition and ... `Condition Clas... System `Include?`
##    <chr>        <chr> <chr> <chr>               <chr>             <chr>        <dbl>
##  1 Hyper        Capp... cont... Total Mortality  mortality         Morta...         1
##  2 Hyper        Capp... cont... Total Mortality  mortality         Morta...         1
##  3 Hyper        Capp... cont... Total Mortality  mortality         Morta...         1
##  4 Hyper        Chak... cont... AF prevalent     AF                Cardi...         0
##  5 Hyper        Chak... cont... AF prevalent     AF                Cardi...         0
##  6 Hyper        Chak... cont... AF incident      AF                Cardi...         1
##  7 Hyper        Chak... cont... AF incident      AF                Cardi...         1
##  8 Hyper        Gamm... cont... prevalent AF     AF                Cardi...         0
##  9 Hyper        Gamm... cont... prevalent AF     AF                Cardi...         0
## 10 Hyper        Heer... cont... incident AF      AF                Cardi...         1
## # ... with 125 more rows, and 28 more variables: `NOS score` <dbl>, `TSH
## #   incong` <chr>, `cross-section` <chr>, `abstract score` <dbl>, ID <int>,
## #   condition <chr>, cohort <chr>, min_size_min_method <lgl>,
```

```
## #   min_size_max_method <lgl>, max_size_min_method <lgl>,
## #   max_size_max_method <lgl>, Thyroid_test <fct>, N <dbl>, method <chr>,
## #   Sig <fct>, Sophistication <chr>, cov <chr>, total <chr>, inferred <lgl>,
## #   pv <dbl>, bounded <lgl>, OR <dbl>, ORCI <chr>, count <chr>, countCI <chr>,
## #   Thyroid_test_4 <chr>, n_cov <chr>, N_bin <fct>
```

```r
thyroid_model  <- glm(Sig ~ Thyroid_test,
              data = TSH_DA, family = binomial)
null_model  <- glm(Sig ~ 1,
              data = TSH_DA, family = binomial)
anova(null_model, thyroid_model, test = "LRT")
```

```
## Analysis of Deviance Table
##
## Model 1: Sig ~ 1
## Model 2: Sig ~ Thyroid_test
##   Resid. Df Resid. Dev Df Deviance  Pr(>Chi)
## 1       134     183.87
## 2       132     169.22  2   14.651 0.0006587 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
summary(glht(thyroid_model,
          linfct = mcp(Thyroid_test = "Tukey")))
```

```
##
##    Simultaneous Tests for General Linear Hypotheses
##
## Multiple Comparisons of Means: Tukey Contrasts
##
##
## Fit: glm(formula = Sig ~ Thyroid_test, family = binomial, data = TSH_DA)
##
## Linear Hypotheses:
##                 Estimate Std. Error z value Pr(>|z|)
## T3 - FT4 == 0   -0.9589     0.5461  -1.756     0.181
## TSH - FT4 == 0  -1.4730     0.4025  -3.660    <0.001 ***
## TSH - T3 == 0   -0.5142     0.5622  -0.914     0.627
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```