Analyzing RCTs: A Cookbook

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Dichotomous endpoints

4.1 Single follow-up

For a single follow-up assessment of a dichotomous endpoint, the main method I use is a standard logistic regression. Then we can adjust for stratification factors in the randomisation in addition to other pre-specified covariates, both categorical and continuous. In the simulated example, we define that the primary outcome is the dichotomous categorical outcome at time 3. Note that usually the baseline status of all patients are negative for the outcome, so adjusting for baseline is not necessary.

4.1.1 Stata code

```
use "stata/rct", clear
tabulate catout trt if time == 3, column
logistic catout i.trt i.site covar  if time==3, coef
```

```
(all strata combined)


+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+

Categorica |       Treatment
 l outcome |   Placebo     Active |     Total
-----------+----------------------+----------
```

```
  Negative |         9         22 |        31
           |     18.00      45.83 |     31.63
-----------+----------------------+----------
  Positive |        41         26 |        67
           |     82.00      54.17 |     68.37
-----------+----------------------+----------
     Total |        50         48 |        98
           |    100.00     100.00 |    100.00
```

```
Logistic regression                                     Number of obs =     98
                                                        LR chi2(5)    =  48.59
                                                        Prob > chi2   = 0.0000
Log likelihood = -36.862204                             Pseudo R2     = 0.3973

------------------------------------------------------------------------------
      catout | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
         trt |
      Active |  -2.890301   .7850252    -3.68   0.000    -4.428922   -1.351679
             |
        site |
           2 |   .7783404   .8580245     0.91   0.364    -.9033566    2.460037
           3 |   1.423791   .7786531     1.83   0.067    -.1023412    2.949923
           4 |   .0253234   .8082887     0.03   0.975    -1.558893     1.60954
             |
       covar |   1.001078   .2329461     4.30   0.000     .5445124    1.457644
       _cons |  -2.463577   .8925892    -2.76   0.006     -4.21302   -.7141344
------------------------------------------------------------------------------
```

Note that the use the `coef` option to get the log odds ratio estimates.

4.1.2 R code

```
rct <- read_dta("stata/rct.dta") %>%
  modify_at(c("trt","catout"), haven::as_factor, levels = "labels") %>%
  modify_at(c("site","time"), haven::as_factor)
rct %>%
  filter(time==3) %>%
  glm(catout ~ trt + site + covar , data=., family = binomial) %>%
  summary
```

```
Call:
glm(formula = catout ~ trt + site + covar, family = binomial,
    data = .)
```

```
Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -2.46358    0.89259  -2.760 0.005780 **
trtActive   -2.89030    0.78502  -3.682 0.000232 ***
site2        0.77834    0.85802   0.907 0.364337
site3        1.42379    0.77865   1.829 0.067470 .
site4        0.02532    0.80829   0.031 0.975007
covar        1.00108    0.23295   4.297 1.73e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 122.318  on 97  degrees of freedom
Residual deviance:  73.724  on 92  degrees of freedom
AIC: 85.724

Number of Fisher Scoring iterations: 6
```

Not surprisingly, the estimates are identical.

4.1.3 Reporting

Reporting for dichotomous endpoints is a bit tricky. The natural estimates from a logistic regression is odds and odds ratios, but these are less interpretable than risk differences or relative risk. As New England Journal of Medicine states in their Statistical Guidelines: "Odds ratios should be avoided, as they may overestimate the relative risks in many settings and be misinterpreted." Fortunately, both Stata and R can estimate adjusted risk differences and relative risks from logistic regressions.

4.1.3.1 Stata code

First we compute the average prediced marginal probabilities. Basically this is done by calculating the predicted probability of a positive outcome for each patient, under both treatments, and then averaging. The standard errors are computed by the delta method.

```
use "stata/rct", clear
quietly logistic catout i.trt i.site covar  if time==3, coef
margins trt
```

```
(all strata combined)
```

```
Predictive margins                                      Number of obs = 98
Model VCE: OIM

Expression: Pr(catout), predict()

------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
         trt |
    Placebo  |   .8499905   .0387218    21.95   0.000     .7740972    .9258839
     Active  |   .5111833   .0533918     9.57   0.000     .4065374    .6158293
------------------------------------------------------------------------------
```

The adjusted risk difference is calculated similarly.

```
use "stata/rct", clear
quietly logistic catout i.trt i.site covar  if time==3, coef
margins, dydx(trt)
```

```
(all strata combined)


Average marginal effects                                Number of obs = 98
Model VCE: OIM

Expression: Pr(catout), predict()
dy/dx wrt:  1.trt

------------------------------------------------------------------------------
             |            Delta-method
             |      dy/dx   std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
         trt |
     Active  |  -.3388072   .0661086    -5.13   0.000    -.4683777   -.2092367
------------------------------------------------------------------------------
Note: dy/dx for factor levels is the discrete change from the base level.
```

We see that the risk difference is the difference of the estimated marginal probabilities we computed previously.

The relative risk is a bit more difficult to calculate, but not much. It uses the `nlcom` method to compute non-linear combinations of estimates.

```
use "stata/rct", clear
quietly logistic catout i.trt i.site covar  if time==3, coef
quietly margins trt, post
```

```
margins, coeflegend
nlcom (ratio1: (_b[1.trt]/_b[0bn.trt]))
```

```
(all strata combined)



Predictive margins                                              Number of obs = 98
Model VCE: OIM

Expression: Pr(catout), predict()

------------------------------------------------------------------------------
             |     Margin   Legend
-------------+----------------------------------------------------------------
         trt |
     Placebo |   .8499905  _b[0bn.trt]
      Active |   .5111833  _b[1.trt]
------------------------------------------------------------------------------

      ratio1: (_b[1.trt]/_b[0bn.trt])

------------------------------------------------------------------------------
             | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
      ratio1 |   .6013989   .0686524     8.76   0.000     .4668426    .7359552
------------------------------------------------------------------------------
```

The trick is to know what goes into the _b[]-brackets, which will be revealed using the 'coeflegend´-option. Note that I do not know the properties of this estimator, and it might be clever to check the estimates using bootstrap.

Some journals require calculation of the number needed to treat (NNT), at least if the confidence interval of the adjusted risk difference does not include zero (for which the NNT is undefined). This is simply done by inverting the adjusted risk difference estimate (both point estimate and the confidence limits).

4.1.3.2 R code

The average predicted marginal probabilities was previously not easily computed in R, but with the emergence of the very nice `marginaleffects`-package, this is now much easier:

```
mod <- rct %>%
  filter(time == 3) %>%
  glm(catout ~ trt + site + covar , data=., family = binomial)
```

```
mod %>%
  avg_predictions(variables = list(trt = c("Active", "Placebo")), type = "response")
```

```
     trt Estimate Std. Error     z Pr(>|z|)     S 2.5 % 97.5 %
 Active     0.511     0.0534  9.57   <0.001  69.7 0.407  0.616
 Placebo    0.850     0.0387 21.95   <0.001 352.4 0.774  0.926

Columns: trt, estimate, std.error, statistic, p.value, s.value, conf.low, conf.high
Type:  response
```

We notice that the estimates are equal to the Stata output..

Another option is to bootstrap the predicted marginal predictions:

```
library(boot)

fpred <- function(formula, data, indices){
  d <- data[indices,]
  fit <- glm(formula, data = d, family = binomial)
  pred <- prediction(fit,data = d, at = list(trt = c("Active", "Placebo"))) %>%
    as_tibble %>%
    group_by(trt) %>%
    summarise(mean = mean(fitted)) %>%
    ungroup() %>%
    mutate(name = paste0(trt)) %>%
    select(name,mean) %>%
    spread(name,mean) %>%
    as_vector
  return(pred)
}

data <- filter(rct, time == 3)
result <- boot(data = data,
               statistic = fpred,
               R = 10000,
               formula = catout ~ trt + site + covar,
               parallel = "multicore",
               ncpus = 4) %>%
  tidy(conf.int = TRUE)
```

```
Error in prediction(fit, data = d, at = list(trt = c("Active", "Placebo"))): could not
```

```
result %>%
  select(-bias) %>%
  knitr::kable(digits = 3)
```

```
Error in eval(expr, envir, enclos): object 'result' not found
```

We see that the estimates are identical to the Stata estimates, although the standard errors and confidence limits are a bit different. But I actually think the bootstrap estimates are better.

The estimated marginal risk difference in R is computed using the `marginaleffects`-package again.

```
rlogistic <- rct %>%
 filter(time==3) %>%
 glm(catout ~ trt + site + covar , data=., family = binomial)


 rlogistic %>%
   avg_comparisons(variables = list(trt = c("Active", "Placebo")), type = "response")
```

```
 Term         Contrast Estimate Std. Error    z Pr(>|z|)    S 2.5 % 97.5 %
  trt Placebo - Active    0.339     0.0661 5.13   <0.001 21.7 0.209  0.468

Columns: term, contrast, estimate, std.error, statistic, p.value, s.value, conf.low, conf.high
Type:  response
```

We see that the estimates are identical to the Stata estimates.

The relative risk is very easily computed in R using the `marginaleffects`-package:

```
rlogistic <- rct %>%
 filter(time==3) %>%
 glm(catout ~ trt + site + covar , data=., family = binomial)


 rlogistic %>%
   avg_comparisons(variables = list(trt = c("Active", "Placebo")), type = "response", comparison
```

```
 Term                     Contrast Estimate Std. Error    z Pr(>|z|)    S 2.5 %
  trt mean(Placebo) / mean(Active)     1.66       0.19 8.76   <0.001 58.8  1.29
97.5 %
  2.03

Columns: term, contrast, estimate, std.error, statistic, p.value, s.value, conf.low, conf.high, p
Type:  response
```

The estimate is the inverse of the Stata estimate, and the confidence limits are very similar. There is probably a slight difference in how these are computed.

This is possible to do also by bootstrapping, but it is a bit more complicated:

```
library(boot)
library(prediction)


fpred <- function(formula, data, indices){
  d <- data[indices,]
  fit <- glm(formula, data = d, family = binomial)
  pred <- prediction(fit,data = d, at = list(trt = c("Active", "Placebo"))) %>%
    as_tibble %>%
    group_by(trt) %>%
    summarise(mean = mean(fitted)) %>%
    ungroup() %>%
    mutate(name = paste0(trt)) %>%
    select(name,mean) %>%
    spread(name,mean) %>%
    as_vector
  return(pred["Active"]/pred["Placebo"])
}

data <- filter(rct, time == 3)
result <- boot(data = data,
               statistic = fpred,
               R = 10000,
               formula = catout ~ trt + site + covar,
               parallel = "multicore",
               ncpus = 4) %>%
  tidy(conf.int = TRUE)

result %>%
  select(-bias) %>%
  knitr::kable(digits = 3)
```

term	statistic	std.error	conf.low	conf.high
Active	0.601	0.082	0.449	0.768

4.2 Repeated follow-up

When there are repeated dichotomous endpoints, there are usually two methods available, either the generalized estimating equations method or the generalized mixed model method. I prefer the mixed model approach because it has better missing data properties, and I like that the parameter estimates are interpretable conditional on the subject. In my mind it is more aligned to a causal interpretation. I will show how to do the mixed logistic regression model. We skip the simple model and go straight to a model with treatment-time interaction. Note that usually a dichotomous endpoint all have the same value at baseline (all

subjects are in the same state), thus we rarely include the baseline. The model is a simple random intercept model, but it could of course also be expanded to a random intercept and slope model.

4.3 Treatment-time interaction model

In Stata, the model is coded as:

```
use "stata/rct", clear
bysort time: tabulate catout trt, column
melogit catout i.trt i.site covar i.time i.trt#i.time if time != 0 || pid:
```

```
(all strata combined)


-------------------------------------------------------------------------------
-> time = 0

+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+

Categorica |       Treatment
 l outcome |   Placebo     Active |     Total
-----------+----------------------+----------
  Negative |        50         48 |        98
           |    100.00     100.00 |    100.00
-----------+----------------------+----------
     Total |        50         48 |        98
           |    100.00     100.00 |    100.00

-------------------------------------------------------------------------------
-> time = 1

+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+

Categorica |       Treatment
 l outcome |   Placebo     Active |     Total
```

```
-----------+----------------------+----------
  Negative |         24         32 |         56
           |      48.00      66.67 |      57.14
-----------+----------------------+----------
  Positive |         26         16 |         42
           |      52.00      33.33 |      42.86
-----------+----------------------+----------
     Total |         50         48 |         98
           |     100.00     100.00 |     100.00

-------------------------------------------------------------------------------
-> time = 2

+--------------------+
| Key                |
|--------------------|
|     frequency      |
| column percentage  |
+--------------------+

Categorica |       Treatment
 l outcome |   Placebo     Active |     Total
-----------+----------------------+----------
  Negative |         12         29 |         41
           |      24.00      60.42 |      41.84
-----------+----------------------+----------
  Positive |         38         19 |         57
           |      76.00      39.58 |      58.16
-----------+----------------------+----------
     Total |         50         48 |         98
           |     100.00     100.00 |     100.00

-------------------------------------------------------------------------------
-> time = 3

+--------------------+
| Key                |
|--------------------|
|     frequency      |
| column percentage  |
+--------------------+

Categorica |       Treatment
 l outcome |   Placebo     Active |     Total
-----------+----------------------+----------
  Negative |          9         22 |         31
```

```
           |     18.00      45.83 |     31.63
-----------+----------------------+----------
  Positive |        41         26 |        67
           |     82.00      54.17 |     68.37
-----------+----------------------+----------
     Total |        50         48 |        98
           |    100.00     100.00 |    100.00


Fitting fixed-effects model:

Iteration 0:  Log likelihood = -133.59899
Iteration 1:  Log likelihood = -129.32428
Iteration 2:  Log likelihood = -129.32244
Iteration 3:  Log likelihood = -129.32244

Refining starting values:

Grid node 0:  Log likelihood = -130.87679

Fitting full model:

Iteration 0:  Log likelihood = -130.87679
Iteration 1:  Log likelihood =  -129.7867
Iteration 2:  Log likelihood = -129.37214
Iteration 3:  Log likelihood = -129.31054
Iteration 4:  Log likelihood = -129.31042
Iteration 5:  Log likelihood = -129.31042

Mixed-effects logistic regression               Number of obs     =        294
Group variable: pid                             Number of groups  =         98

                                                Obs per group:
                                                              min =          3
                                                              avg =        3.0
                                                              max =          3

Integration method: mvaghermite                 Integration pts.  =          7

                                                Wald chi2(9)      =      57.65
Log likelihood = -129.31042                     Prob > chi2       =     0.0000
------------------------------------------------------------------------------
      catout | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
         trt |
```

```
      Active  |  -1.445692   .5336445    -2.71   0.007    -2.491616   -.3997679
              |
        site  |
          2   |  -.0293421   .4666747    -0.06   0.950    -.9440077    .8853234
          3   |     .72617   .4145006     1.75   0.080    -.0862363    1.538576
          4   |   .5185491   .4721013     1.10   0.272    -.4067524    1.443851
              |
       covar  |   .9174909   .1319527     6.95   0.000     .6588684    1.176113
              |
        time  |
          2   |   1.787348   .5856394     3.05   0.002     .6395156     2.93518
          3   |   2.365878   .6353582     3.72   0.000     1.120599    3.611157
              |
    trt#time  |
   Active#2   |  -1.406754   .7657322    -1.84   0.066    -2.907561    .0940536
   Active#3   |  -1.127376    .785537    -1.44   0.151       -2.667    .4122484
              |
        _cons |  -4.424402   .7595232    -5.83   0.000     -5.91304   -2.935764
--------------+------------------------------------------------------------------
pid           |
   var(_cons)|   .0684106   .4545936                      1.51e-07    31004.17
------------------------------------------------------------------------------
LR test vs. logistic model: chibar2(01) = 0.02        Prob >= chibar2 = 0.4384
```

In R, this model is coded as:

```
library(lme4)
rct %>%
  filter(time != 0) %>%
  glmer(catout ~ trt + time + trt*time + site + covar + (1|pid),
        data = .,
        family = binomial,
        nAGQ = 7) %>%
  summary()
```

```
Generalized linear mixed model fit by maximum likelihood (Adaptive
  Gauss-Hermite Quadrature, nAGQ = 7) [glmerMod]
 Family: binomial  ( logit )
Formula: catout ~ trt + time + trt * time + site + covar + (1 | pid)
   Data: .

     AIC      BIC   logLik deviance df.resid
   280.6    321.1   -129.3    258.6      283

Scaled residuals:
    Min      1Q  Median      3Q     Max
-2.8902 -0.5490  0.1407  0.5132  5.6565
```

```
Random effects:
 Groups Name        Variance Std.Dev.
 pid    (Intercept) 0.06842  0.2616
Number of obs: 294, groups:  pid, 98

Fixed effects:
               Estimate Std. Error z value Pr(>|z|)
(Intercept)    -4.42440    0.75952  -5.825 5.70e-09 ***
trtActive      -1.44556    0.53364  -2.709 0.006751 **
time2           1.78740    0.58564   3.052 0.002273 **
time3           2.36568    0.63534   3.724 0.000196 ***
site2          -0.02946    0.46667  -0.063 0.949661
site3           0.72598    0.41449   1.751 0.079861 .
site4           0.51846    0.47210   1.098 0.272110
covar           0.91750    0.13195   6.953 3.57e-12 ***
trtActive:time2 -1.40690    0.76574  -1.837 0.066163 .
trtActive:time3 -1.12718    0.78553  -1.435 0.151305
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr) trtAct time2  time3  site2  site3  site4  covar  trtA:2
trtActive   -0.117
time2       -0.555  0.349
time3       -0.604  0.295  0.475
site2       -0.188 -0.031  0.029  0.042
site3       -0.292 -0.115  0.059  0.077  0.477
site4       -0.306 -0.061  0.052  0.078  0.398  0.462
covar       -0.818 -0.226  0.293  0.373 -0.074  0.032  0.086
trtActv:tm2  0.385 -0.601 -0.750 -0.343 -0.020 -0.031 -0.037 -0.181
trtActv:tm3  0.363 -0.594 -0.336 -0.745 -0.029 -0.015 -0.048 -0.161  0.470
```

4.3.1 Reporting

Plotting i Stata

```
use stata/rct, clear
quietly melogit catout i.trt i.site covar i.time i.trt#i.time if time != 0 || pid:

*Compute the predictive margins by time and treatment

margins time#trt

*Plot the predictive margins. Note that the arguments after the comma is just to prettify the plo
```

```
marginsplot, graphregion(color(white)) graphregion(color(white)) plotregion(color(white
graph export stata/figures/cat_fig1.pdf, replace
```

```
(all strata combined)


Predictive margins                                              Number of obs = 294
Model VCE: OIM

Expression: Marginal predicted mean, predict()

------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
    time#trt |
  1#Placebo  |   .5476187   .0577701     9.48   0.000     .4343913     .660846
   1#Active  |   .3187847   .0540835     5.89   0.000     .2127831    .4247863
  2#Placebo  |   .7897137   .0463852    17.03   0.000     .6988004     .880627
   2#Active  |   .3770772   .0557815     6.76   0.000     .2677475    .4864068
  3#Placebo  |   .8467085   .0410465    20.63   0.000     .7662588    .9271581
   3#Active  |   .5147246   .0571038     9.01   0.000     .4028032     .626646
------------------------------------------------------------------------------


Variables that uniquely identify margins: time trt

file stata/figures/cat_fig1.pdf saved as PDF format
```

```
knitr::include_graphics("stata/figures/cat_fig1.pdf")
```


The same in R using the `marginaleffects`-package:

```
mod <- rct %>%
  filter(time != 0) %>%
  glmer(catout ~ trt + time + trt*time + site + covar + (1|pid),
        data = .,
        family = binomial,
        nAGQ = 7)

pred <- mod %>%
  avg_predictions(variables = list(trt = c( "Placebo", "Active"), time = c("1","2", "3
```

```
Warning: For this model type, `marginaleffects` only takes into account the
  uncertainty in fixed-effect parameters. You can use the `re.form=NA`
  argument to acknowledge this explicitly and silence this warning.
```

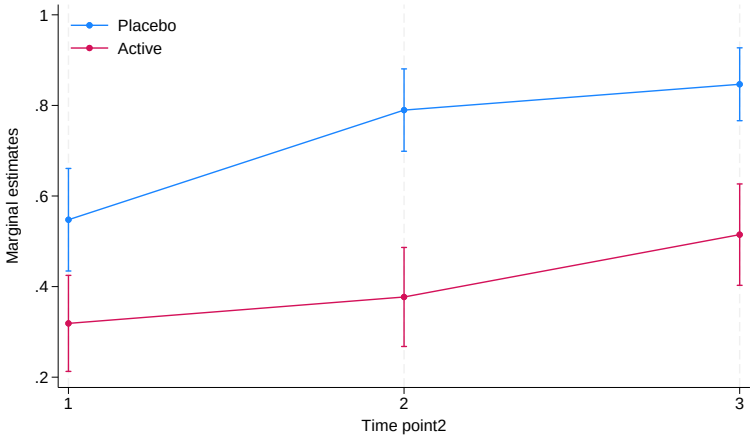


Figure 4.1: Margins plot by Stata

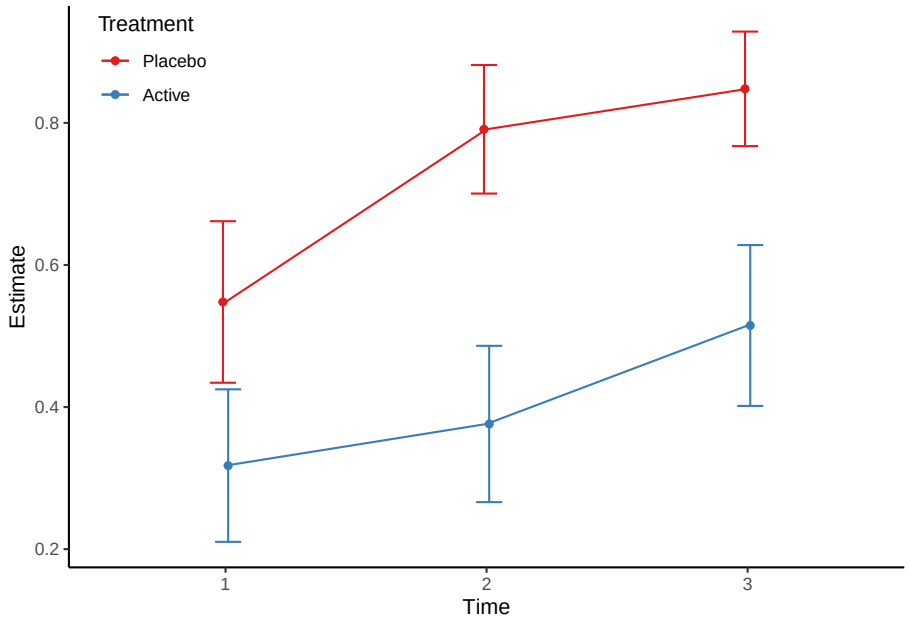
```
pred
```

```
 time     trt Estimate Std. Error     z Pr(>|z|)     S 2.5 % 97.5 %
    1 Placebo    0.548     0.0580  9.45   <0.001  67.9 0.434  0.662
    1 Active     0.318     0.0548  5.80   <0.001  27.2 0.210  0.425
    2 Placebo    0.791     0.0462 17.13   <0.001 216.1 0.701  0.882
    2 Active     0.376     0.0561  6.70   <0.001  35.5 0.266  0.486
    3 Placebo    0.848     0.0411 20.62   <0.001 311.3 0.767  0.929
    3 Active     0.515     0.0578  8.91   <0.001  60.8 0.402  0.628

Columns: trt, time, estimate, std.error, statistic, p.value, s.value, conf.low, conf.high
Type:  response
```

The estimated marginal plot is then given by:

```
pred %>%
  ggplot(aes(time, estimate, color=trt, group=trt)) +
  geom_point(position = position_dodge(0.04)) +
  geom_line() +
  geom_errorbar(aes(ymin = conf.low, ymax = conf.high),
                width=.2,
                position = position_dodge(0.04)) +
  ylab("Estimate") +
  xlab("Time") +
  theme_classic() +
  theme(legend.position=c(0.1,0.9)) +
  scale_colour_brewer(palette = "Set1", name = "Treatment")
```



The treatment differences at different timepoints are then calculated with:

```
use "stata/rct", clear
quietly melogit catout i.trt i.site covar i.time i.trt#i.time if time != 0 || pid:
margins time, dydx(trt)

(all strata combined)


Average marginal effects                                    Number of obs = 294
Model VCE: OIM

Expression: Marginal predicted mean, predict()
dy/dx wrt:  1.trt

------------------------------------------------------------------------------
             |            Delta-method
             |      dy/dx   std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
0.trt        |  (base outcome)
-------------+----------------------------------------------------------------
1.trt        |
        time |
          1  |   -.228834    .079152    -2.89   0.004     -.383969   -.0736989
          2  |  -.4126365   .0726801    -5.68   0.000    -.5550869   -.2701861
```

```
          3  |  -.3319839    .070613    -4.70   0.000    -.4703829   -.1935849
------------------------------------------------------------------------------
Note: dy/dx for factor levels is the discrete change from the base level.
```

In R this is done with the `marginaleffects`-package:

```
mod <- rct %>%
  filter(time != 0) %>%
  glmer(catout ~ trt + time + trt*time + site + covar + (1|pid),
        data = .,
        family = binomial,
        nAGQ = 7)

mod %>%
  avg_comparisons(variables = list(trt = c("Active", "Placebo")), by = "time", type = "response",
```

```
 Term                     Contrast time Estimate Std. Error    z Pr(>|z|)    S
  trt mean(Placebo) - mean(Active)    1    0.230     0.0797 2.89  0.00386  8.0
  trt mean(Placebo) - mean(Active)    2    0.414     0.0728 5.69  < 0.001 26.2
  trt mean(Placebo) - mean(Active)    3    0.333     0.0704 4.73  < 0.001 18.7
  2.5 % 97.5 %
 0.0741  0.387
 0.2717  0.557
 0.1947  0.471

Columns: term, contrast, time, estimate, std.error, statistic, p.value, s.value, conf.low, conf.h
Type:  response
```

We see the results are slightly different to the Stata results, but the differences are small.

Chapter 5

Time to event analyses

To be done

Chapter 6

Sample size calculations

To be done