Wednesday, Apr 27

Random Effects Approach

The random effects approach conceptualizes the parameters associated with the levels of the many-leveled factor as *random variables*. Another way to think of this is that the levels of that factor are a *sample* of levels from a real or conceptual population of levels.

Note: We sometimes use the term "mixed effects" model for a model where some parameters are modeled as random and some that are not modeled as random (i.e., fixed). Most (but not all) models with random effects also have some fixed effects, and are thus mixed effects models.

Example: Consider again the `baserun` data, but a system of subscripts that distinguishes between the *player* and the *observation within each player* so that Y_{ij} is the j-th observation of running time for the i-th player.

```
library(trtools)
head(baserun)
```

```
  round narrow wide
1  5.40   5.50 5.55
2  5.85   5.70 5.75
3  5.20   5.60 5.50
4  5.55   5.50 5.40
5  5.90   5.85 5.70
6  5.45   5.55 5.60
```

If we were to ignore the effect of player we could write a model for these data as

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2},$$

where x_{i1} and x_{i2} are indicator variables for two of the three routes.

In the *fixed effects* approach we include an indicator variable for each player, so the model would become

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \beta_3 x_{ij3} + \beta_4 x_{ij4} + \cdots + \beta_{23} x_{ij23},$$

where $x_{ij3}, x_{ij4}, \ldots, x_{ij23}$ are the 21 indicator variables for the 22 players.

In the *random effects* approach we would view $\beta_3, \beta_4, \ldots, \beta_{23}$ as *random variables*. To distinguish the random from the non-random (fixed) parameters I will change the symbols for the indicator variables and the parameters corresponding to the players and write the model as

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \delta_1 z_{ij1} + \delta_2 z_{ij2} + \cdots + \delta_{22} z_{ij22}.$$

Note also that here we have 22 rather than 21 indicator variables (each player has their own parameter). A more compact way to write this model is

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \underbrace{\delta_1 z_{ij1} + \delta_2 z_{ij2} + \cdots + \delta_{22} z_{ij22}}_{\delta_i} = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \delta_i,$$

so that δ_i represents the "random effect" of the i-th player.

Another way to write this model is

$$Y_{ij} = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \delta_i + \epsilon_{ij},$$

where ϵ_{ij} is the usual random error term, which is implicitly assumed to be normally-distributed. Thus on the right-hand side of the above expression we have *two* random variables on the right-hand side: δ_i and ϵ_{ij}.

To complete the model a distribution is needed to be assumed for each δ_i. Typically they are assumed to be normally distributed with zero mean and some variance σ_δ^2 so that we write $\delta_i \sim N(0, \sigma_\delta^2)$. Because the δ_i have a mean of zero they can be viewed as a "deviation" of the effect of the i-th player from a (conceptual) average player.

The presence of the random δ_i parameters fundamentally changes the likelihood function. Specialized inferential methods are (usually) necessary to arrive at correct inferences when random effects are specified. As with other approaches functions to implement these methods require that the data be in "long form" so we reshape the `baserun` data.

```
library(dplyr)
library(tidyr)
baselong <- trtools::baserun %>% mutate(player = factor(letters[1:n()])) %>%
  pivot_longer(cols = c(round, narrow, wide), names_to = "route", values_to = "time")
head(baselong)
```

```
# A tibble: 6 x 3
  player route   time
  <fct>  <chr>  <dbl>
1 a      round   5.4
2 a      narrow  5.5
3 a      wide    5.55
4 b      round   5.85
5 b      narrow  5.7
6 b      wide    5.75
```

The `lmer` function from the **lme4** package can estimate a *linear mixed effects regression* model with normally-distributed random effects. The model above can be estimated as follows.

```
library(lme4)
m <- lmer(time ~ route + (1 | player), data = baselong)
summary(m)
```

```
Linear mixed model fit by REML ['lmerMod']
Formula: time ~ route + (1 | player)
   Data: baselong

REML criterion at convergence: -51.4

Scaled residuals:
    Min      1Q  Median      3Q     Max
-3.0968 -0.3473  0.0031  0.5001  1.6424

Random effects:
 Groups   Name        Variance Std.Dev.
 player   (Intercept) 0.06448  0.2539
 Residual             0.00745  0.0863
Number of obs: 66, groups:  player, 22

Fixed effects:
            Estimate Std. Error t value
(Intercept)  5.53409    0.05718   96.78
routeround   0.00909    0.02603    0.35
routewide   -0.07500    0.02603   -2.88
```

```
Correlation of Fixed Effects:
           (Intr) rotrnd
routeround -0.228
routewide  -0.228  0.500
```

Profile likelihood confidence intervals for σ_δ^2 (the variance of the δ_i parameters), σ^2 (the variance of ϵ_{ij}), and β_0, β_1, and β_2 can be obtained using `confint`.

```
confint(m)
```

```
                2.5 %   97.5 %
.sig01        0.18688  0.34746
.sigma        0.06937  0.10557
(Intercept)   5.42025  5.64793
routeround   -0.04186  0.06004
routewide    -0.12595 -0.02405
```

Using `lincon` will produce Wald confidence intervals for β_0, β_1, and β_2.

```
trtools::lincon(m)
```

```
             estimate      se    lower    upper  tvalue  df   pvalue
(Intercept)  5.534091 0.05718  5.42202  5.64616 96.7838 Inf 0.000000
routeround   0.009091 0.02603 -0.04192  0.06010  0.3493 Inf 0.726871
routewide   -0.075000 0.02603 -0.12601 -0.02399 -2.8817 Inf 0.003956
```

Other inferences can be made using `trtools::contrast` and the **emmeans** package, but note that player is never specified when using these functions. These tools provide inferences only for the "fixed effects" of the model. We can estimate the expected running time for each route.

```
library(emmeans)

emmeans(m, ~route)
```

```
 route  emmean     SE   df lower.CL upper.CL
 narrow   5.53 0.0572 24.2     5.42     5.65
 round    5.54 0.0572 24.2     5.42     5.66
 wide     5.46 0.0572 24.2     5.34     5.58

Degrees-of-freedom method: kenward-roger
Confidence level used: 0.95
```

```
trtools::contrast(m, a = list(route = c("narrow","round","wide")),
  cnames = c("narrow","round","wide"))
```

```
       estimate      se lower upper tvalue  df pvalue
narrow    5.534 0.05718 5.422 5.646  96.78 Inf      0
round     5.543 0.05718 5.431 5.655  96.94 Inf      0
wide      5.459 0.05718 5.347 5.571  95.47 Inf      0
```

Notice that `emmeans` uses the "Kenward-Roger" method of computing approximate degrees of freedom. The issue of degrees of freedom is a difficult problem in models with random effects. Some statisticians suggest just using Wald methods which specify infinite degrees of freedom as an approximation (which is the default in my functions). This can be done using the `lmer.df = "asymptotic"` option.

```
emmeans(m, ~route, lmer.df = "asymptotic")
```

```
 route  emmean     SE  df asymp.LCL asymp.UCL
 narrow   5.53 0.0572 Inf      5.42      5.65
```

```
 round    5.54 0.0572 Inf      5.43      5.66
 wide     5.46 0.0572 Inf      5.35      5.57

Degrees-of-freedom method: asymptotic
Confidence level used: 0.95
```

We can also compare the routes as before.

```
pairs(emmeans(m, ~ route, lmer.df = "asymptotic"), adjust = "none", infer = TRUE)
```

```
 contrast       estimate    SE  df asymp.LCL asymp.UCL z.ratio p.value
 narrow - round -0.00909 0.026 Inf   -0.0601    0.0419  -0.349  0.7269
 narrow - wide   0.07500 0.026 Inf    0.0240    0.1260   2.882  0.0040
 round - wide    0.08409 0.026 Inf    0.0331    0.1351   3.231  0.0012

Degrees-of-freedom method: asymptotic
Confidence level used: 0.95
```

```
trtools::contrast(m, a = list(route = c("narrow","round","wide")),
  cnames = c("narrow","round","wide"))
```

```
       estimate      se lower upper tvalue  df pvalue
narrow    5.534 0.05718 5.422 5.646  96.78 Inf      0
round     5.543 0.05718 5.431 5.655  96.94 Inf      0
wide      5.459 0.05718 5.347 5.571  95.47 Inf      0
```

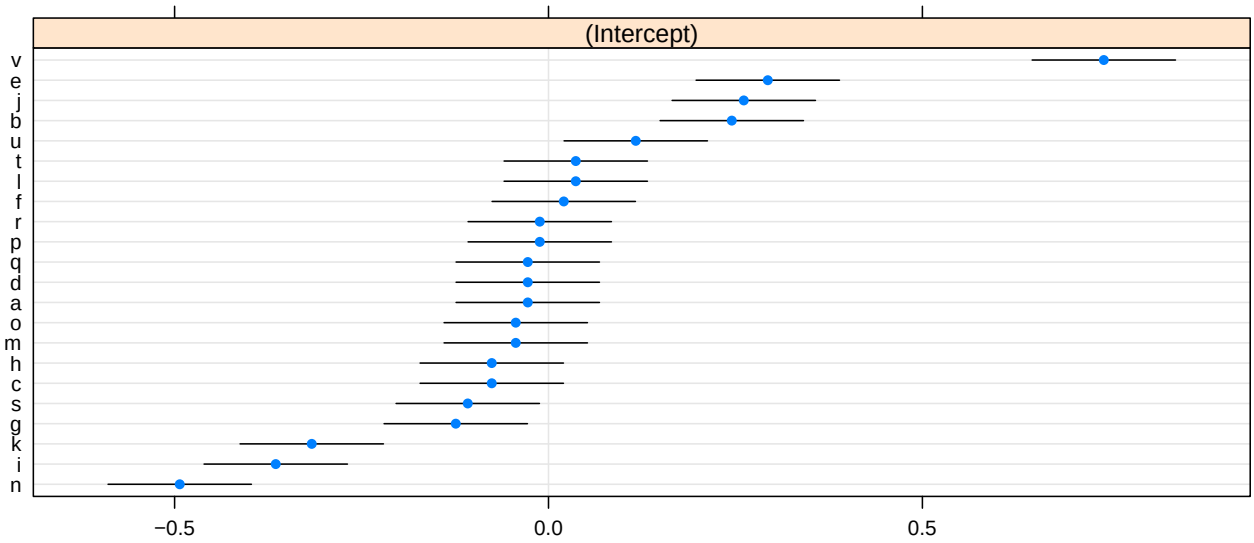
```
trtools::contrast(m,
  a = list(route = c("narrow","narrow","round")),
  b = list(route = c("round","wide","wide")),
  cnames = c("narrow - round","narrow - wide","round - wide"))
```

```
                estimate      se    lower   upper  tvalue  df   pvalue
narrow - round -0.009091 0.02603 -0.06010 0.04192 -0.3493 Inf 0.726871
narrow - wide   0.075000 0.02603  0.02399 0.12601  2.8817 Inf 0.003956
round - wide    0.084091 0.02603  0.03308 0.13510  3.2309 Inf 0.001234
```

Some built-in functions also allow us to plot estimates of the δ_i parameters.

```
lattice::dotplot(ranef(m, condVar = TRUE))
```

```
$player
```



Alternatively you can use the `ranef` function to return these estimates and plot them using `ggplot` or something else.

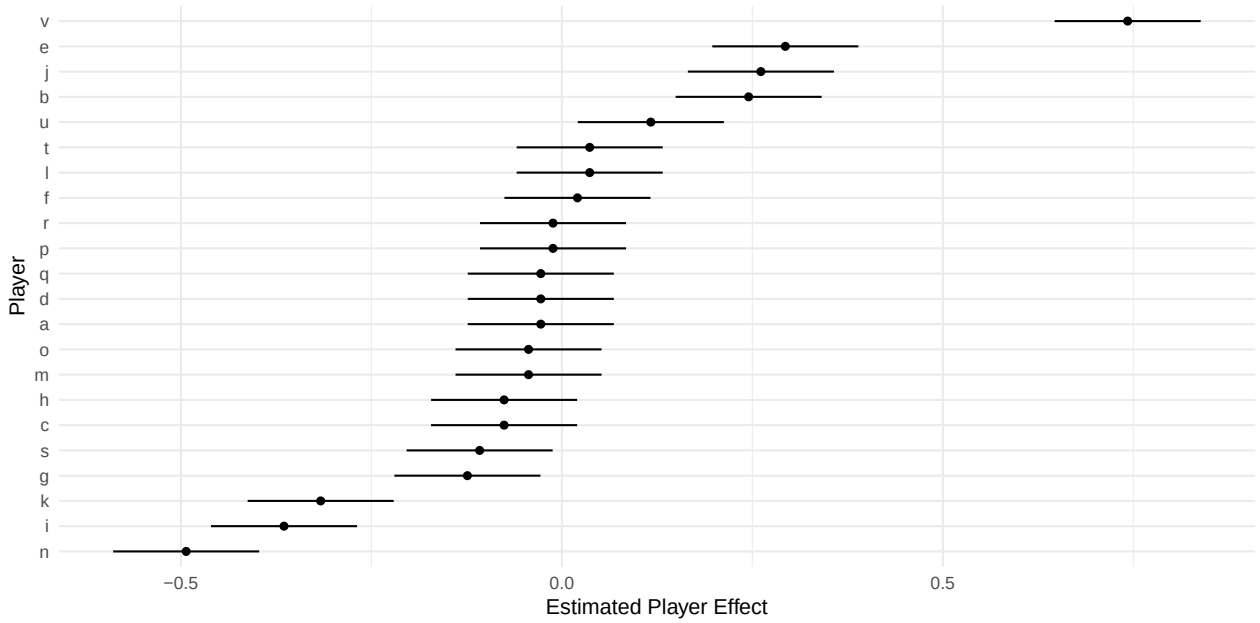
```
d <- as.data.frame(ranef(m))
head(d)
```

```
  grpvar        term grp  condval condsd
1 player (Intercept)   a -0.02772 0.0489
2 player (Intercept)   b  0.24510 0.0489
3 player (Intercept)   c -0.07587 0.0489
4 player (Intercept)   d -0.02772 0.0489
5 player (Intercept)   e  0.29325 0.0489
6 player (Intercept)   f  0.02043 0.0489
```

```
d <- d %>% mutate(lower = condval - 1.96 * condsd, upper = condval + 1.96 * condsd)
head(d)
```

```
  grpvar        term grp  condval condsd    lower   upper
1 player (Intercept)   a -0.02772 0.0489 -0.12357 0.06813
2 player (Intercept)   b  0.24510 0.0489  0.14925 0.34096
3 player (Intercept)   c -0.07587 0.0489 -0.17172 0.01999
4 player (Intercept)   d -0.02772 0.0489 -0.12357 0.06813
5 player (Intercept)   e  0.29325 0.0489  0.19740 0.38910
6 player (Intercept)   f  0.02043 0.0489 -0.07543 0.11628
```

```
p <- ggplot(d, aes(x = grp, y = condval)) +
  geom_linerange(aes(ymin = lower, ymax = upper)) +
  geom_point(size = 1.5) +
  theme_minimal() + coord_flip() +
  labs(x = "Player", y = "Estimated Player Effect")
plot(p)
```

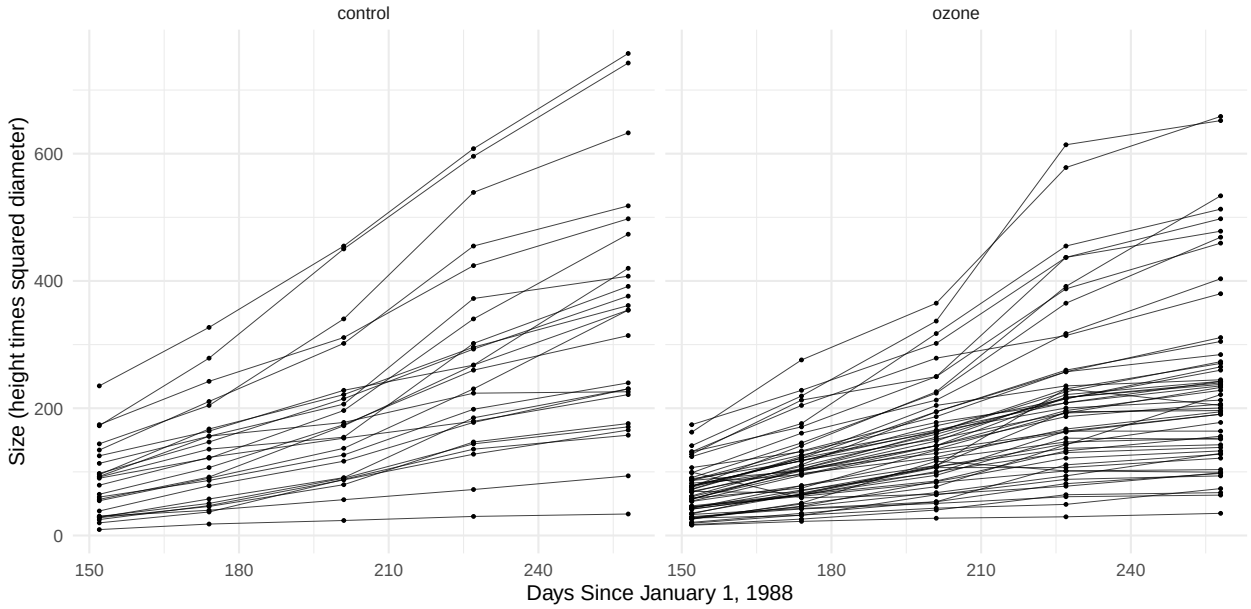


Example: Now consider again the `Sitka` data.

```
library(MASS)
head(Sitka, 10)
```

```
   size Time tree treat
1  4.51  152    1 ozone
2  4.98  174    1 ozone
3  5.41  201    1 ozone
4  5.90  227    1 ozone
5  6.15  258    1 ozone
6  4.24  152    2 ozone
7  4.20  174    2 ozone
8  4.68  201    2 ozone
9  4.92  227    2 ozone
10 4.96  258    2 ozone
```

```
p <- ggplot(Sitka, aes(x = Time, y = exp(size))) +
  geom_line(aes(group = tree), alpha = 0.75, size = 0.1) +
  facet_wrap(~ treat) + geom_point(size = 0.5) +
  labs(y = "Size (height times squared diameter)",
    x = "Days Since January 1, 1988") + theme_minimal()
plot(p)
```



First let's consider the model

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \beta_3 x_{ij3} + \delta_i,$$

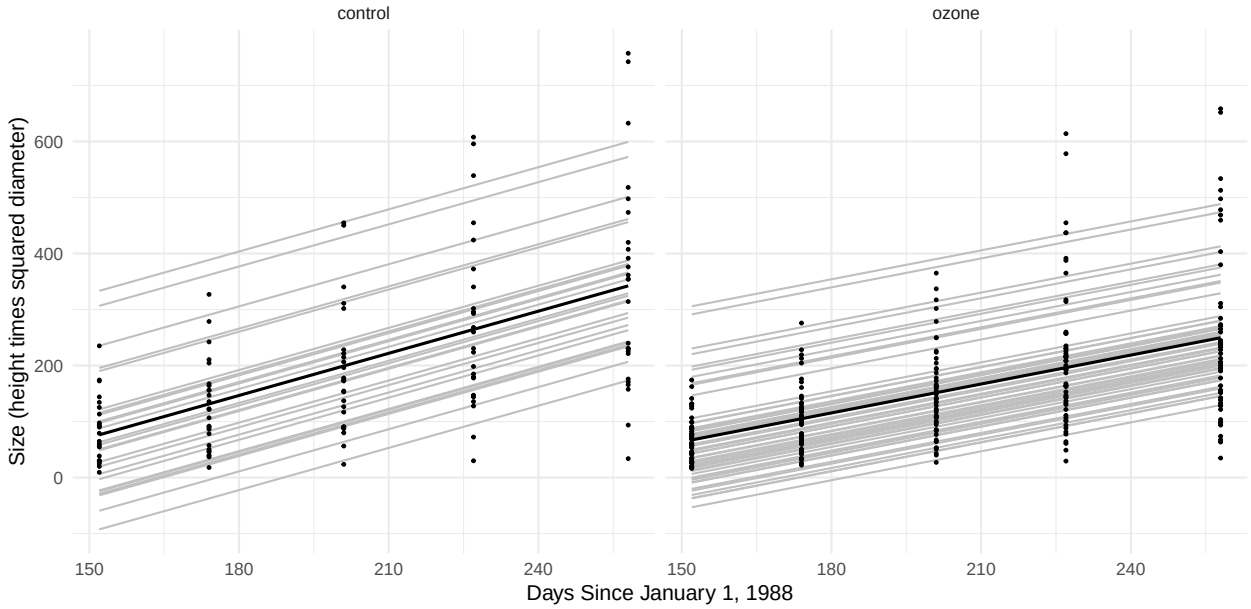
where Y_{ij} is the j-th observation of size for the i-th tree, x_{ij1} is an indicator for treatment (ozone), x_{ij2} is time, and $x_{ij3} = x_{ij1}x_{ij2}$.

```
m <- lmer(exp(size) ~ treat * Time + (1 | tree), data = Sitka)
summary(m)
```

```
Linear mixed model fit by REML ['lmerMod']
Formula: exp(size) ~ treat * Time + (1 | tree)
   Data: Sitka

REML criterion at convergence: 4472

Scaled residuals:
   Min     1Q Median     3Q    Max
-2.811 -0.436 -0.027  0.350  3.620

Random effects:
 Groups   Name        Variance Std.Dev.
 tree     (Intercept) 8827     94.0
 Residual             2857     53.5
Number of obs: 395, groups:  tree, 79

Fixed effects:
                Estimate Std. Error t value
(Intercept)     -305.123     32.256   -9.46
treatozone       110.675     39.014    2.84
Time               2.509      0.127   19.70
treatozone:Time   -0.788      0.154   -5.12

Correlation of Fixed Effects:
            (Intr) tretzn Time
```

```
treatozone  -0.827
Time        -0.799  0.661
treatozn:Tm  0.661 -0.799 -0.827
```

```
Sitka$yhat.sub <- predict(m)               # for each tree (with deltas)
Sitka$yhat.avg <- predict(m, re.form = NA) # for the "average" tree (deltas = 0)

p <- ggplot(Sitka, aes(x = Time, y = exp(size))) +
  labs(y = "Size (height times squared diameter)",
    x = "Days Since January 1, 1988") +
  theme_minimal() + facet_wrap(~treat) +
  geom_line(aes(y = yhat.sub, group = tree), color = grey(0.75)) +
  geom_line(aes(y = yhat.avg), size = 0.75) +
  geom_point(size = 0.5)
plot(p)
```



This doesn't really capture differences in the growth rates between trees (i.e., an *interaction* between tree and time). Such a model could be written as

$$E(Y_{ij}) = \beta_0 + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \beta_3 x_{ij3} + \delta_i + \gamma_i x_{ij2},$$

where now there are *two* random parameters for each tree: δ_i and γ_i. We can also write this model as

$$E(Y_{ij}) = \begin{cases} \beta_0 + \delta_i + (\beta_2 + \gamma_i) t_{ij}, & \text{if the treatment is control,} \\ \beta_0 + \beta_1 + \delta_i + (\beta_2 + \beta_3 + \gamma_i) t_{ij}, & \text{if the treatment is ozone,} \end{cases}$$

where t_{ij} is time. This means that the linear relationship between time and expected size varies over treatment conditions, but also trees — i.e., each tree has its own intercept and slope (rate).

```
m <- lmer(exp(size) ~ treat * Time + (1 + Time | tree), data = Sitka)
```

```
Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
failed to converge with max|grad| = 2.20761 (tol = 0.002, component 1)
```

```
Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model is nearly unidenti
 - Rescale variables?
```

Oh no! Models with random effects are cranky. But let's take the advice of the warning and re-scale time from days to weeks.

```
m <- lmer(exp(size) ~ treat * I(Time/7) + (1 + I(Time/7) | tree), data = Sitka)
```

```
Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
failed to converge with max|grad| = 0.0418627 (tol = 0.002, component 1)
```

That *probably* is not a problem. I suspect it is due to the very high correlation between the random intercept and slope parameters. But changing the optimizer seems to avoid the error.

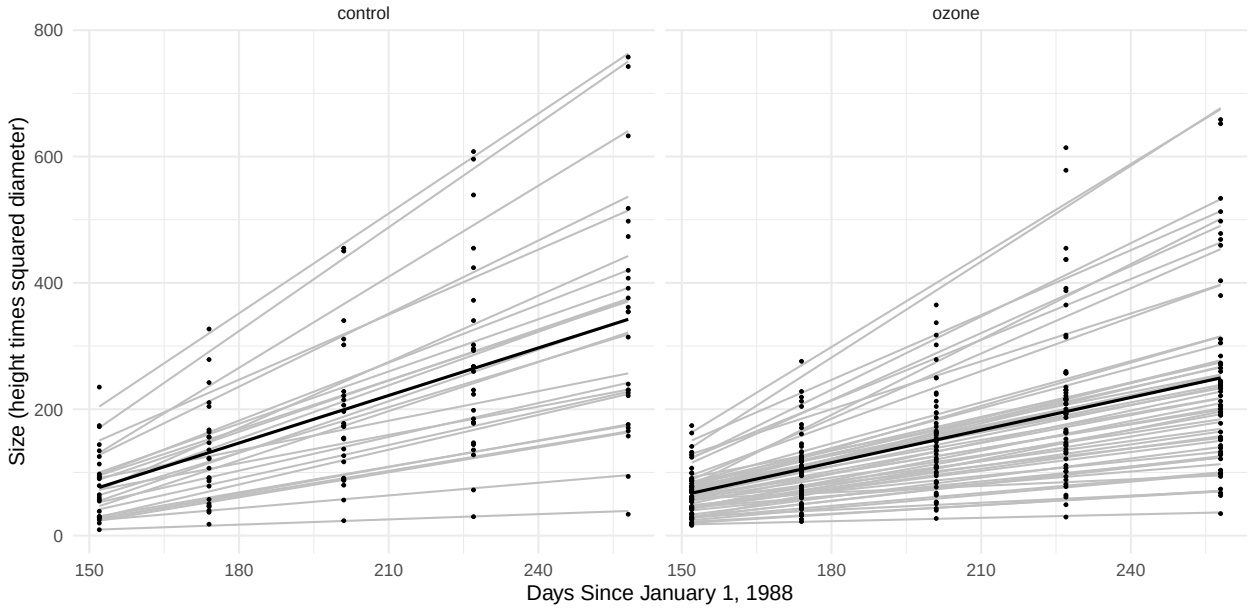
```
library(optimx)
m <- lmer(exp(size) ~ treat * I(Time/7) + (1 + I(Time/7) | tree), data = Sitka,
  control = lmerControl(optimizer = "optimx", optCtrl = list(method = "nlminb")))
summary(m)
```

```
Linear mixed model fit by REML ['lmerMod']
Formula: exp(size) ~ treat * I(Time/7) + (1 + I(Time/7) | tree)
   Data: Sitka
Control: lmerControl(optimizer = "optimx", optCtrl = list(method = "nlminb"))

REML criterion at convergence: 3915

Scaled residuals:
   Min     1Q Median     3Q    Max
-2.964 -0.395 -0.049  0.391  4.816

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 tree     (Intercept) 22745.6  150.82
          I(Time/7)      70.2    8.38   -0.99
 Residual               383.2   19.57
Number of obs: 395, groups:  tree, 79

Fixed effects:
                    Estimate Std. Error t value
(Intercept)          -305.12      31.65   -9.64
treatozone            110.68      38.29    2.89
I(Time/7)              17.56       1.71   10.29
treatozone:I(Time/7)   -5.52       2.06   -2.67

Correlation of Fixed Effects:
            (Intr) tretzn I(T/7)
treatozone  -0.827
I(Time/7)   -0.980  0.810
trtz:I(T/7)  0.810 -0.980 -0.827
```

I found that you get more or less the same result even without changing the optimizer. Here's a plot.

```
Sitka$yhat.sub <- predict(m)               # for each tree (with deltas)
Sitka$yhat.avg <- predict(m, re.form = NA) # for the "average" tree (deltas = 0)

p <- ggplot(Sitka, aes(x = Time, y = exp(size))) +
  labs(y = "Size (height times squared diameter)",
    x = "Days Since January 1, 1988") +
  theme_minimal() + facet_wrap(~treat) +
  geom_line(aes(y = yhat.sub, group = tree), color = grey(0.75)) +
```

```
  geom_line(aes(y = yhat.avg), size = 0.75) +
  geom_point(size = 0.5)
plot(p)
```



Now we can estimate and compare the (average) growth rates in the control and ozone conditions (per 100 days with `contrast` and per day with `emtrends`).

```
trtools::contrast(m,
  a = list(Time = 250, treat = c("control","ozone")),
  b = list(Time = 150, treat = c("control","ozone")),
  cnames = c("control","ozone"))
```

```
        estimate    se lower upper tvalue  df    pvalue
control    250.9 24.38 203.1 298.7  10.29 Inf 7.718e-25
ozone      172.1 16.59 139.6 204.6  10.37 Inf 3.227e-25
```

```
trtools::contrast(m,
  a = list(Time = 250, treat = "control"),
  b = list(Time = 150, treat = "control"),
  u = list(Time = 250, treat = "ozone"),
  v = list(Time = 150, treat = "ozone"))
```

```
 estimate    se lower upper tvalue  df   pvalue
    78.81 29.49    21 136.6  2.672 Inf 0.007537
```

```
emtrends(m, ~ treat, var = "Time", lmer.df = "asymptotic")
```

```
 treat   Time.trend    SE  df asymp.LCL asymp.UCL
 control       2.51 0.244 Inf      2.03      2.99
 ozone         1.72 0.166 Inf      1.40      2.05

Degrees-of-freedom method: asymptotic
Confidence level used: 0.95
```

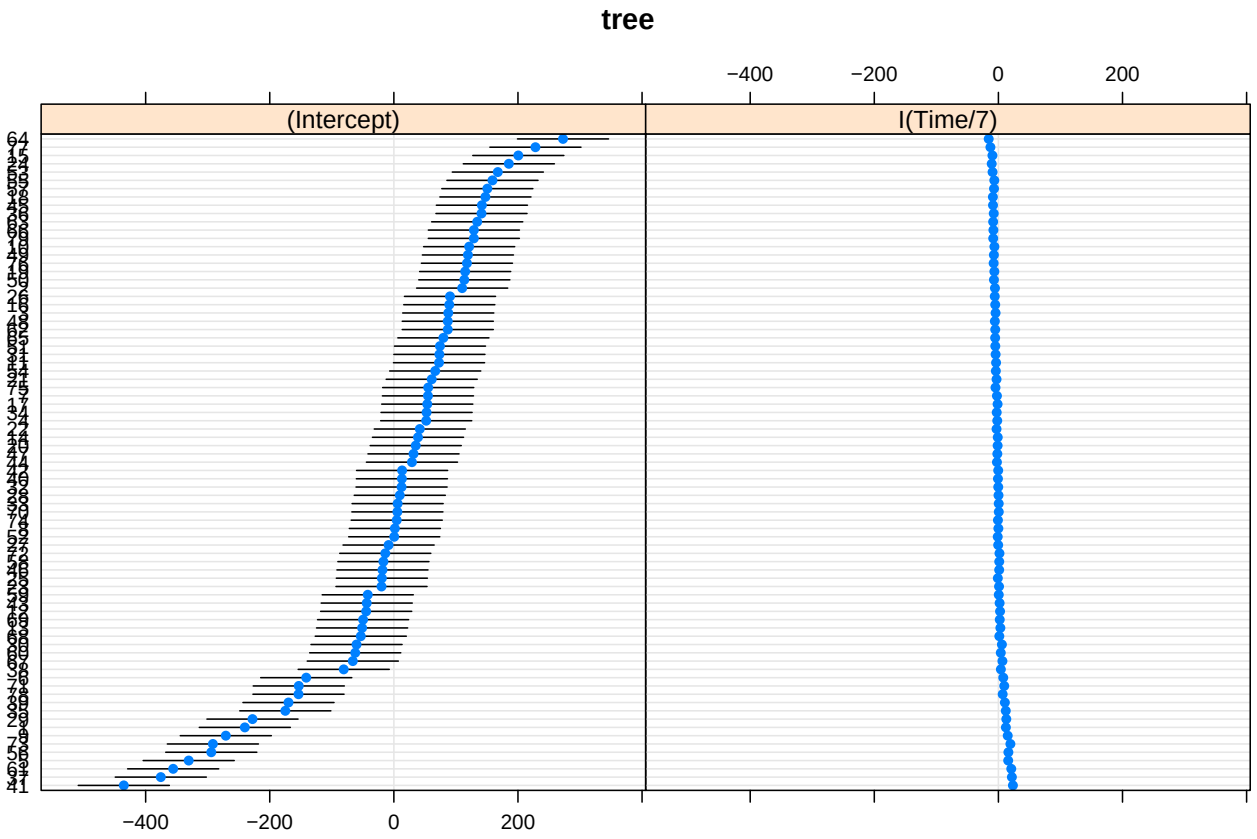
```
pairs(emtrends(m, ~ treat, var = "Time",
  lmer.df = "asymptotic"), infer = TRUE)
```

```
 contrast        estimate    SE  df asymp.LCL asymp.UCL z.ratio p.value
 control - ozone    0.788 0.295 Inf      0.21      1.37   2.672  0.0075

Degrees-of-freedom method: asymptotic
Confidence level used: 0.95
```

We can plot estimates of the δ_i and γ_i parameters for each tree.

```
lattice::dotplot(ranef(m, condVar = TRUE))
```

```
$tree
```




```
d <- as.data.frame(ranef(m))
head(d)
```

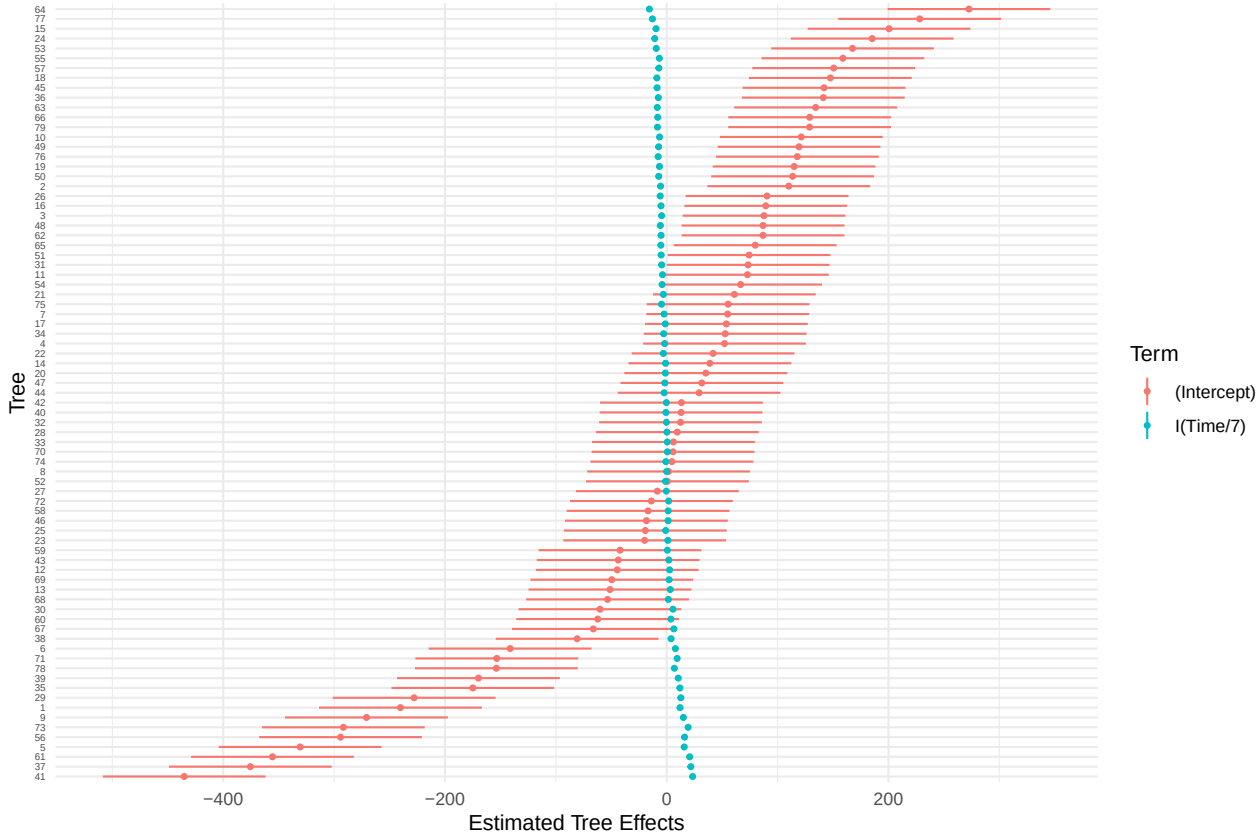
```
  grpvar        term grp condval condsd
1   tree (Intercept)   1 -240.18  37.45
2   tree (Intercept)   2  110.08  37.45
3   tree (Intercept)   3   87.68  37.45
4   tree (Intercept)   4   52.13  37.45
5   tree (Intercept)   5 -330.64  37.45
6   tree (Intercept)   6 -141.21  37.45
```

```
d <- d %>% mutate(lower = condval - 1.96 * condsd, upper = condval + 1.96 * condsd)
head(d)
```

```
  grpvar        term grp condval condsd   lower  upper
1   tree (Intercept)   1 -240.18  37.45 -313.59 -166.8
2   tree (Intercept)   2  110.08  37.45   36.67  183.5
```

```
3   tree (Intercept)   3   87.68  37.45   14.27  161.1
4   tree (Intercept)   4   52.13  37.45  -21.28  125.5
5   tree (Intercept)   5 -330.64  37.45 -404.05 -257.2
6   tree (Intercept)   6 -141.21  37.45 -214.62  -67.8
```

```
p <- ggplot(d, aes(x = grp, y = condval, color = term)) +
  geom_linerange(aes(ymin = lower, ymax = upper)) +
  geom_point(size = 1) +
  theme_minimal() + coord_flip() +
  labs(x = "Tree", y = "Estimated Tree Effects", color = "Term") +
  theme(axis.text.y = element_text(size = 5))
plot(p)
```



Example: Consider again the smoking cessation meta analysis data.

```
library(dplyr)
library(tidyr)
quitsmoke <- HSAUR3::smoking
quitsmoke$study <- rownames(quitsmoke)
quitsmoke.quits <- quitsmoke %>% dplyr::select(study, qt, qc) %>%
  rename(gum = qt, control = qc) %>%
  gather(gum, control, key = treatment, value = quit)
quitsmoke.total <- quitsmoke %>% dplyr::select(study, tt, tc) %>%
  rename(gum = tt, control = tc) %>%
  gather(gum, control, key = treatment, value = total)
quitsmoke <- full_join(quitsmoke.quits, quitsmoke.total) %>%
  mutate(study = factor(study)) %>% arrange(study)
```

```
head(quitsmoke)
```

```
         study treatment quit total
1    Blondal89       gum   37    92
2    Blondal89   control   24    90
3   Campbell91       gum   21   107
4   Campbell91   control   21   105
5 Fagerstrom82       gum   30    50
6 Fagerstrom82   control   23    50
```

We can introduce a random "study effect" into a logistic regression model to create a *generalized linear mixed effects regression* model. This would be written as

$$\log\left[\frac{E(Y_{ij})}{1-E(Y_{ij})}\right] = \beta_0 + \beta_1 x_{ij} + \delta_i,$$

where Y_{ij} is the j-th proportion of people quitting in the i-th study, and x_{ij} is an indicator variable for treatment (gum). This model can be estimated as follows.

```
m <- glmer(cbind(quit, total - quit) ~ treatment + (1 | study),
  family = binomial, data = quitsmoke)
summary(m)
```

```
Generalized linear mixed model fit by maximum likelihood (Laplace Approximation) [glmerMod
]
 Family: binomial  ( logit )
Formula: cbind(quit, total - quit) ~ treatment + (1 | study)
   Data: quitsmoke

     AIC      BIC   logLik deviance df.resid
   367.3    373.2   -180.6    361.3       49

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.9940 -0.6602 -0.0373  0.4633  2.3042

Random effects:
 Groups Name        Variance Std.Dev.
 study  (Intercept) 0.412    0.642
Number of obs: 52, groups:  study, 26

Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)   -1.3625     0.1376   -9.90  < 2e-16 ***
treatmentgum   0.5149     0.0655    7.87  3.6e-15 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr)
treatmentgm -0.281
```

We can estimate the odds ratio for the treatment, which is assumed to be the same for every study in this model.

```
trtools::contrast(m, tf = exp,
  a = list(treatment = "gum"),
  b = list(treatment = "control"))
```

```
 estimate lower upper
    1.673 1.472 1.902
```

```
pairs(emmeans(m, ~ treatment, type = "response"), reverse = TRUE)
```

```
 contrast      odds.ratio   SE  df null z.ratio p.value
 gum / control       1.67 0.11 Inf    1   7.867  <.0001

Tests are performed on the log odds ratio scale
```

We can extend the model so that the treatment effect varies over studies (i.e., an interaction between treatment and study).

```
m <- glmer(cbind(quit, total - quit) ~ treatment + (1 + treatment | study),
  family = binomial, data = quitsmoke)
summary(m)
```

```
Generalized linear mixed model fit by maximum likelihood (Laplace Approximation) [glmerMod
]
 Family: binomial  ( logit )
Formula: cbind(quit, total - quit) ~ treatment + (1 + treatment | study)
   Data: quitsmoke

     AIC      BIC   logLik deviance df.resid
   368.3    378.0   -179.1    358.3       47

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.4423 -0.4678  0.0217  0.3796  1.6638

Random effects:
 Groups Name         Variance Std.Dev. Corr
 study  (Intercept)  0.4211   0.649
        treatmentgum 0.0508   0.225    -0.12
Number of obs: 52, groups:  study, 26

Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)   -1.3991     0.1415   -9.89  < 2e-16 ***
treatmentgum   0.5723     0.0887    6.45  1.1e-10 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr)
treatmentgm -0.340
```

Now our odds ratios are for a "typical" study.

```
trtools::contrast(m, tf = exp,
  a = list(treatment = "gum"),
  b = list(treatment = "control"))
```

```
 estimate lower upper
    1.772 1.489 2.109
```

```
pairs(emmeans(m, ~ treatment, type = "response"), reverse = TRUE)
```

```
 contrast      odds.ratio    SE  df null z.ratio p.value
 gum / control       1.77 0.157 Inf    1   6.449  <.0001

Tests are performed on the log odds ratio scale
```

Note: In logistic regression, if your response variable is *binary* (i.e., not aggregated counts) use the option `nAGQ = x` where `x` is maybe 21+.

```
m <- glmer(cbind(quit, total - quit) ~ treatment + (1 | study),
  family = binomial, data = quitsmoke, nAGQ = 31)
summary(m)
```

```
Generalized linear mixed model fit by maximum likelihood (Adaptive Gauss-Hermite
  Quadrature, nAGQ = 31) [glmerMod]
 Family: binomial  ( logit )
Formula: cbind(quit, total - quit) ~ treatment + (1 | study)
   Data: quitsmoke

     AIC      BIC   logLik deviance df.resid
   136.2    142.0    -65.1    130.2       49

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.9943 -0.6602 -0.0374  0.4631  2.3039

Random effects:
 Groups Name        Variance Std.Dev.
 study  (Intercept) 0.413    0.642
Number of obs: 52, groups:  study, 26

Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)   -1.3625     0.1378   -9.89   <2e-16 ***
treatmentgum   0.5149     0.0655    7.86    4e-15 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr)
treatmentgm -0.281
```

It can also be used in other GLMERs. Because of the complexity of the likelihood function in these models, there are many different numerical approaches to estimation.

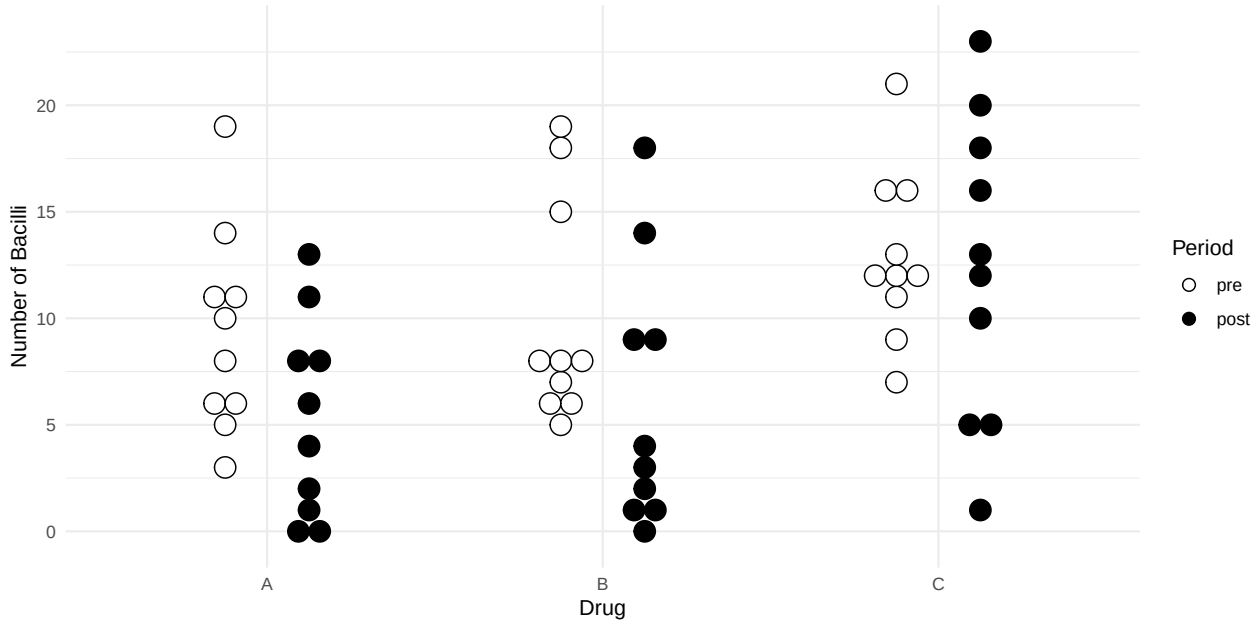
Example: Consider a random effects approach for the `leprosy` data.

```
library(ALA)
head(leprosy)
```

```
   id drug period nBacilli
1   1    A    pre       11
31  1    A   post        6
2   2    B    pre        6
```

```
32  2    B   post        0
3   3    C    pre       16
33  3    C   post       13
```

```
p <- ggplot(leprosy, aes(x = drug, y = nBacilli, fill = period)) +
  geom_dotplot(binaxis = "y", method = "histodot",
    stackdir = "center", binwidth = 1,
    position = position_dodge(width = 0.5)) +
  scale_fill_manual(values = c("white","black")) +
  labs(x = "Drug", y = "Number of Bacilli", fill = "Period") +
  theme_minimal()
plot(p)
```




```
m <- glmer(nBacilli ~ drug * period + (1 | id), family = poisson, data = leprosy)
summary(m)
```

```
Generalized linear mixed model fit by maximum likelihood (Laplace Approximation) [glmerMod
]
 Family: poisson  ( log )
Formula: nBacilli ~ drug * period + (1 | id)
   Data: leprosy

     AIC      BIC   logLik deviance df.resid
   363.9    378.6   -175.0    349.9       53

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.8757 -0.5729  0.0637  0.4264  1.9372

Random effects:
 Groups Name        Variance Std.Dev.
 id     (Intercept) 0.259    0.509
Number of obs: 60, groups:  id, 30
```

```
Fixed effects:
                 Estimate Std. Error z value Pr(>|z|)
(Intercept)        2.0936     0.1953   10.72  < 2e-16 ***
drugB              0.0506     0.2737    0.19  0.85320
drugC              0.3836     0.2682    1.43  0.15270
periodpost        -0.5623     0.1704   -3.30  0.00097 ***
drugB:periodpost   0.0680     0.2344    0.29  0.77164
drugC:periodpost   0.5147     0.2114    2.43  0.01490 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr) drugB  drugC  prdpst drgB:p
drugB       -0.707
drugC       -0.725  0.515
periodpost  -0.317  0.226  0.231
drgB:prdpst  0.230 -0.317 -0.168 -0.727
drgC:prdpst  0.255 -0.182 -0.321 -0.806  0.586
```

Estimated ratios for each drug.

```
pairs(emmeans(m, ~ period | drug, type = "response"),
  reverse = TRUE, infer = TRUE)
```

```
drug = A:
 contrast   ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 post / pre 0.570 0.0971 Inf     0.408     0.796    1  -3.300  0.0010

drug = B:
 contrast   ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 post / pre 0.610 0.0982 Inf     0.445     0.836    1  -3.071  0.0021

drug = C:
 contrast   ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 post / pre 0.954 0.1193 Inf     0.746     1.218    1  -0.381  0.7035

Confidence level used: 0.95
Intervals are back-transformed from the log scale
Tests are performed on the log scale
```

```
trtools::contrast(m, tf = exp,
  a = list(period = "post", drug = c("A","B","C")),
  b = list(period = "pre", drug = c("A","B","C")),
  cnames = c("A","B","C"))
```

```
  estimate  lower  upper
A   0.5699 0.4081 0.7958
B   0.6100 0.4450 0.8362
C   0.9535 0.7461 1.2185
```

We can also compare the rate ratios.

```
pairs(pairs(emmeans(m, ~ period | drug, type = "response"),
  reverse = TRUE), by = NULL, adjust = "none")
```

```
 contrast                       ratio    SE  df null z.ratio p.value
 (post / pre A) / (post / pre B) 0.934 0.219 Inf    1  -0.290  0.7716
```

```
 (post / pre A) / (post / pre C) 0.598 0.126 Inf    1  -2.435  0.0149
 (post / pre B) / (post / pre C) 0.640 0.130 Inf    1  -2.191  0.0284
```

Tests are performed on the log scale

```
trtools::contrast(m, tf = exp,
  a = list(period = "post", drug = "A"),
  b = list(period = "pre",  drug = "A"),
  u = list(period = "post", drug = "B"),
  v = list(period = "pre",  drug = "B"))
```

```
 estimate  lower upper
   0.9342 0.5901 1.479
```

```
trtools::contrast(m, tf = exp,
  a = list(period = "post", drug = "A"),
  b = list(period = "pre",  drug = "A"),
  u = list(period = "post", drug = "C"),
  v = list(period = "pre",  drug = "C"))
```

```
 estimate  lower  upper
   0.5977 0.3949 0.9045
```

```
trtools::contrast(m, tf = exp,
  a = list(period = "post", drug = "B"),
  b = list(period = "pre",  drug = "B"),
  u = list(period = "post", drug = "C"),
  v = list(period = "pre",  drug = "C"))
```

```
 estimate lower upper
   0.6397 0.429 0.954
```