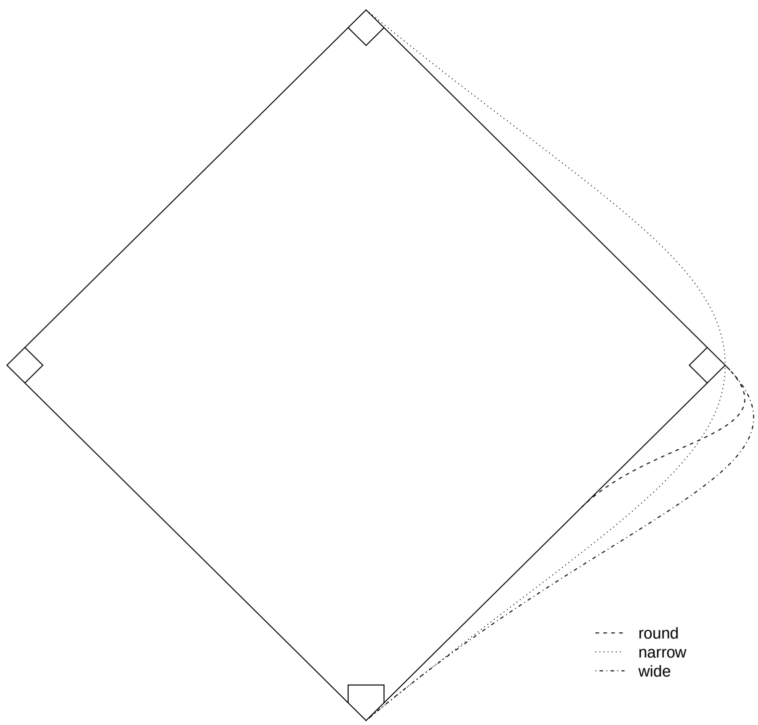
Friday, Apr 22

The Incidental Parameter Problem

Some kinds of designs result in a "factor" with a relatively large number of levels, where each level corresponds to an experimental/observational unit. This can arise for a variety of reasons. Such designs include *repeated measures*, *longitudinal data*, *panel data*, *multilevel data*, *pseudo-replication*, *within-subjects factors*, *dependent samples*, and *clustered data* to name a few (these are not mutually exclusive). Having a factor with a large number of levels can cause complications. This is known in econometrics as the "incidental parameter problem."

Example: Consider a study of the running times of three routes from home to second base on a baseball diamond.




```r
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
```

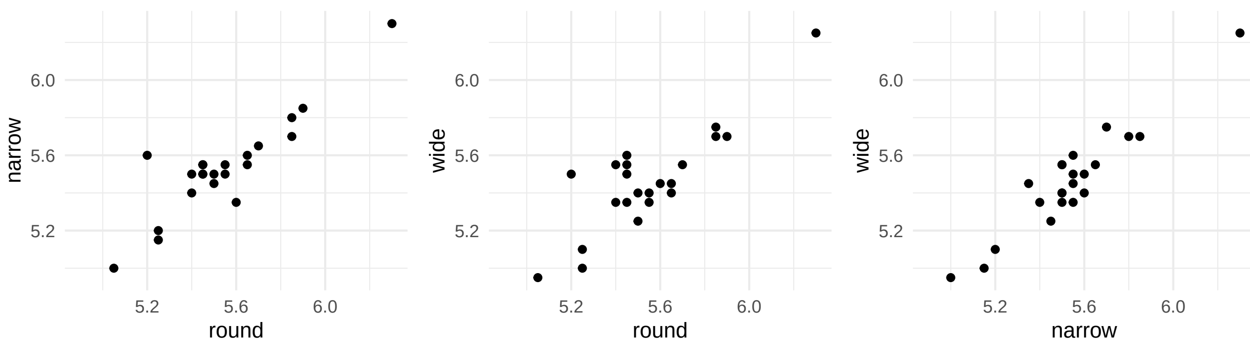
There is a considerable "effect" for the player. Players who are relatively fast/slow on one route tend to also be relatively fast/slow on the other routes.

```
p <- ggplot(baserun, aes(x = round, y = narrow)) + theme_minimal()
p <- p + geom_point() + xlim(4.9,6.3) + ylim(4.95,6.3)
p1 <- p

p <- ggplot(baserun, aes(x = round, y = wide)) + theme_minimal()
p <- p + geom_point() + xlim(4.9,6.3) + ylim(4.95,6.3)
p2 <- p

p <- ggplot(baserun, aes(x = narrow, y = wide)) + theme_minimal()
p <- p + geom_point() + xlim(4.9,6.3) + ylim(4.95,6.3)
p3 <- p

cowplot::plot_grid(p1, p2, p3, align = "h", ncol = 3)
```

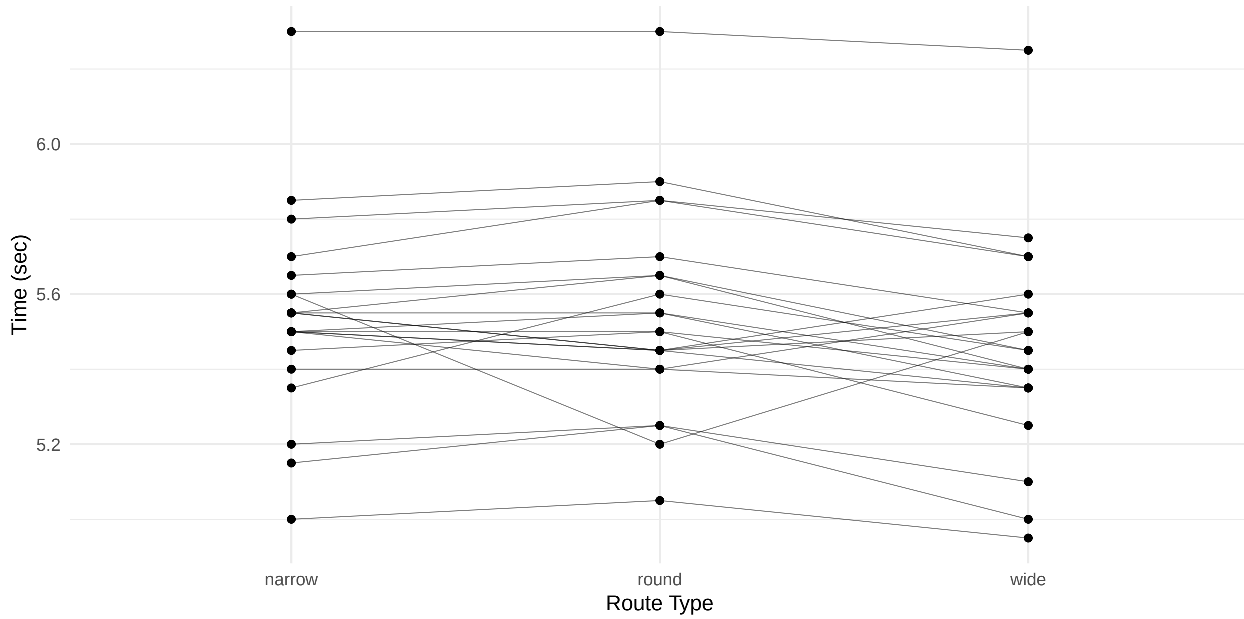


These data are in what is sometimes called "wide form" where there are multiple observations per unit (player) in a single row. For plotting and modeling it is often useful to "reshape" the data into "long form" with one observation of the response variable (running time) per row.

```
library(dplyr)
library(tidyr)
baselong <- 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
```

```
p <- ggplot(baselong, aes(x = route, y = time)) +
  geom_line(aes(group = player), size = 0.25, alpha = 0.5) +
  geom_point() + theme_minimal() +
  labs(x = "Route Type", y = "Time (sec)")
plot(p)
```



Again note that there appears to be a "player effect" in that the players show similar results over the routes.

What *could* we do (but not necessarily what we *should* do) in modeling these data.

We could ignore the effect of player.

```
m <- lm(time ~ route, data = baselong)
summary(m)$coefficients
```

```
             Estimate Std. Error t value  Pr(>|t|)
(Intercept)  5.534091    0.05718 96.7838 3.047e-70
routeround   0.009091    0.08086  0.1124 9.108e-01
routewide   -0.075000    0.08086 -0.9275 3.572e-01
```

Or we could model the effect of player as a factor.

```
m <- lm(time ~ route + player, data = baselong)
summary(m)$coefficients
```

```
              Estimate Std. Error    t value  Pr(>|t|)
(Intercept)  5.505e+00    0.05205  1.058e+02 1.320e-52
routeround   9.091e-03    0.02603  3.493e-01 7.286e-01
routewide   -7.500e-02    0.02603 -2.882e+00 6.208e-03
playerb      2.833e-01    0.07048  4.020e+00 2.366e-04
playerc     -5.000e-02    0.07048 -7.094e-01 4.820e-01
playerd      1.139e-15    0.07048  1.615e-14 1.000e+00
playere      3.333e-01    0.07048  4.729e+00 2.550e-05
playerf      5.000e-02    0.07048  7.094e-01 4.820e-01
playerg     -1.000e-01    0.07048 -1.419e+00 1.633e-01
playerh     -5.000e-02    0.07048 -7.094e-01 4.820e-01
playeri     -3.500e-01    0.07048 -4.966e+00 1.189e-05
playerj      3.000e-01    0.07048  4.256e+00 1.140e-04
playerk     -3.000e-01    0.07048 -4.256e+00 1.140e-04
playerl      6.667e-02    0.07048  9.459e-01 3.496e-01
playerm     -1.667e-02    0.07048 -2.365e-01 8.142e-01
playern     -4.833e-01    0.07048 -6.858e+00 2.323e-08
playero     -1.667e-02    0.07048 -2.365e-01 8.142e-01
```

```
playerp      1.667e-02    0.07048  2.365e-01 8.142e-01
playerq      8.406e-16    0.07048  1.193e-14 1.000e+00
playerr      1.667e-02    0.07048  2.365e-01 8.142e-01
players     -8.333e-02    0.07048 -1.182e+00 2.437e-01
playert      6.667e-02    0.07048  9.459e-01 3.496e-01
playeru      1.500e-01    0.07048  2.128e+00 3.923e-02
playerv      8.000e-01    0.07048  1.135e+01 2.238e-14
```

Or maybe we could do something else?

Example: Consider the following data from a meta-analysis of 26 studies of the effect of nicotine gum on smoking cessation.

```r
library(HSAUR3) # for the data
head(smoking)
```

```
             qt  tt qc  tc
Blondal89    37  92 24  90
Campbell91   21 107 21 105
Fagerstrom82 30  50 23  50
Fee82        23 180 15 172
Garcia89     21  68  5  38
Garvey00     75 405 17 203
```

Here `qt` and `tc` are the total number of subjects in the treatment and control groups, respectively, and `tt` and `tc` are the total number of subjects in the treatment and control groups, respectively.

These data require some rearranging prior to plotting and analysis. (Note: I'm using `dplyr::select` rather than just `select` because of a conflict with a function of the same name with another package I have loaded.)

```r
library(dplyr)
library(tidyr)
quitsmoke <- smoking
quitsmoke$study <- rownames(quitsmoke)
quitsmoke.quits <- quitsmoke %>% dplyr::select(study, qt, qc) %>%
  rename(gum = qt, control = qc) %>%
  pivot_longer(cols = c(gum,control),
    names_to = "treatment", values_to = "quit")
head(quitsmoke.quits)
```

```
# A tibble: 6 x 3
  study        treatment  quit
  <chr>        <chr>     <int>
1 Blondal89    gum          37
2 Blondal89    control      24
3 Campbell91   gum          21
4 Campbell91   control      21
5 Fagerstrom82 gum          30
6 Fagerstrom82 control      23
```

```r
quitsmoke.total <- quitsmoke %>% dplyr::select(study, tt, tc) %>%
  rename(gum = tt, control = tc) %>%
  pivot_longer(cols = c(gum,control), names_to = "treatment", values_to = "total")
head(quitsmoke.total)
```

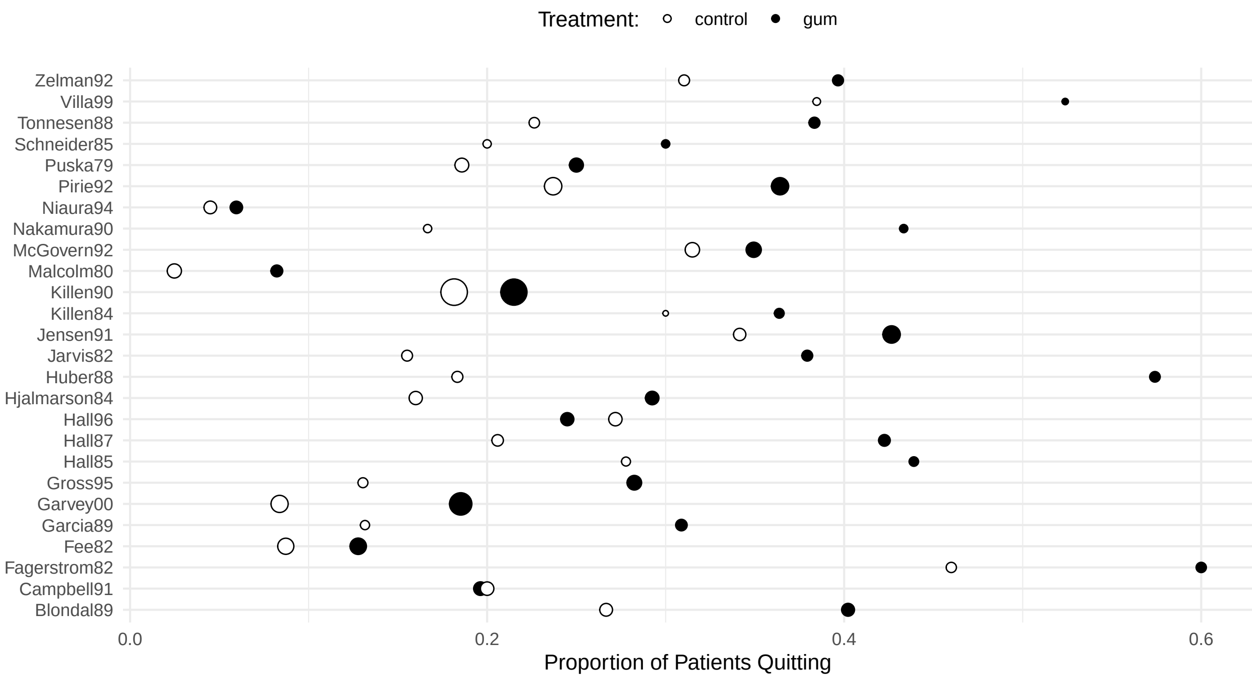
```
# A tibble: 6 x 3
  study        treatment total
  <chr>        <chr>     <int>
```

```
1 Blondal89    gum           92
2 Blondal89    control       90
3 Campbell91   gum          107
4 Campbell91   control      105
5 Fagerstrom82 gum           50
6 Fagerstrom82 control       50
```

```
quitsmoke <- full_join(quitsmoke.quits, quitsmoke.total) %>% mutate(study = factor(study)) %>% arrange(s
head(quitsmoke)
```

```
# A tibble: 6 x 4
  study        treatment  quit total
  <fct>        <chr>     <int> <int>
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
```

```
p <- ggplot(quitsmoke, aes(x = study, y = quit/total,
  size = total, fill = treatment)) + geom_point(pch = 21) +
  coord_flip() + guides(size = "none") +
  scale_fill_manual(values = c("White","Black")) + theme_minimal() +
  labs(x = NULL, y = "Proportion of Patients Quitting",
    fill = "Treatment:") + theme(legend.position = "top")
plot(p)
```



The studies may vary considerably in terms of (a) the proportion of subjects that quit overall and (b) the effectiveness of the gum treatment relative to the control condition.

What *could* we do (but not necessarily what we *should* do) in modeling these data.

We could ignore the effect of study.

```r
m <- glm(cbind(quit, total - quit) ~ treatment,
  family = binomial, data = quitsmoke)
summary(m)$coefficients
```

```
             Estimate Std. Error z value   Pr(>|z|)
(Intercept)   -1.4503    0.04901 -29.594 1.762e-192
treatmentgum   0.5071    0.06309   8.038  9.112e-16
```

Or we could model the main effect of study.

```r
m <- glm(cbind(quit, total - quit) ~ treatment + study,
  family = binomial, data = quitsmoke)
summary(m)$coefficients
```

```
                  Estimate Std. Error z value  Pr(>|z|)
(Intercept)       -0.95611    0.16223 -5.8935 3.782e-09
treatmentgum       0.51478    0.06571  7.8337 4.738e-15
studyCampbell91   -0.72182    0.23458 -3.0771 2.090e-03
studyFagerstrom82  0.82087    0.25660  3.1990 1.379e-03
studyFee82        -1.44471    0.23392 -6.1760 6.575e-10
studyGarcia89     -0.51371    0.27679 -1.8560 6.346e-02
studyGarvey00     -1.13119    0.19513 -5.7970 6.750e-09
studyGross95      -0.57476    0.23716 -2.4235 1.537e-02
studyHall85        0.11322    0.28635  0.3954 6.926e-01
studyHall87       -0.08874    0.24238 -0.3661 7.143e-01
studyHall96       -0.36356    0.22648 -1.6052 1.084e-01
studyHjalmarson84 -0.54554    0.23002 -2.3717 1.771e-02
studyHuber88       0.16466    0.25162  0.6544 5.128e-01
studyJarvis82     -0.32539    0.26384 -1.2333 2.175e-01
studyJensen91      0.18524    0.19887  0.9314 3.516e-01
studyKillen84     -0.05394    0.30863 -0.1748 8.613e-01
studyKillen90     -0.71634    0.17393 -4.1186 3.812e-05
studyMalcolm80    -2.28969    0.37670 -6.0784 1.214e-09
studyMcGovern92   -0.02349    0.20432 -0.1150 9.085e-01
studyNakamura90   -0.16186    0.32479 -0.4984 6.182e-01
studyNiaura94     -2.22602    0.37765 -5.8945 3.759e-09
studyPirie92      -0.15991    0.19132 -0.8358 4.033e-01
studyPuska79      -0.59867    0.22560 -2.6536 7.963e-03
studySchneider85  -0.41647    0.33913 -1.2281 2.194e-01
studyTonnesen88   -0.13127    0.25883 -0.5072 6.120e-01
studyVilla99       0.50932    0.33548  1.5182 1.290e-01
studyZelman92      0.08506    0.25163  0.3380 7.353e-01
```

We could also model an interaction of the treatment with the study.

```r
m <- glm(cbind(quit, total - quit) ~ treatment * study,
  family = binomial, data = quitsmoke)
summary(m)$coefficients
```

```
                                Estimate Std. Error   z value  Pr(>|z|)
(Intercept)                    -1.011601     0.2384 -4.243904 2.197e-05
treatmentgum                    0.615186     0.3194  1.925966 5.411e-02
studyCampbell91                -0.374693     0.3411 -1.098520 2.720e-01
studyFagerstrom82               0.851258     0.3706  2.297064 2.162e-02
studyFee82                     -1.336595     0.3604 -3.709126 2.080e-04
studyGarcia89                  -0.875469     0.5358 -1.633834 1.023e-01
```

```
studyGarvey00                 -1.380932     0.3479 -3.969605 7.199e-05
studyGross95                  -0.885519     0.4985 -1.776429 7.566e-02
studyHall85                    0.056089     0.4419  0.126927 8.990e-01
studyHall87                   -0.338326     0.3831 -0.883128 3.772e-01
studyHall96                    0.026317     0.3254  0.080884 9.355e-01
studyHjalmarson84             -0.646627     0.3622 -1.785045 7.425e-02
studyHuber88                  -0.482324     0.4100 -1.176276 2.395e-01
studyJarvis82                 -0.682995     0.4340 -1.573798 1.155e-01
studyJensen91                  0.354821     0.3332  1.064752 2.870e-01
studyKillen84                  0.164303     0.5431  0.302551 7.622e-01
studyKillen90                 -0.494459     0.2602 -1.899981 5.744e-02
studyMalcolm80                -2.660471     0.6314 -4.213818 2.511e-05
studyMcGovern92                0.234572     0.3055  0.767904 4.425e-01
studyNakamura90               -0.597837     0.5448 -1.097331 2.725e-01
studyNiaura94                 -2.044756     0.5644 -3.622682 2.916e-04
studyPirie92                  -0.157780     0.2881 -0.547567 5.840e-01
studyPuska79                  -0.465665     0.3396 -1.371344 1.703e-01
studySchneider85              -0.374693     0.5149 -0.727661 4.668e-01
studyTonnesen88               -0.217065     0.4056 -0.535119 5.926e-01
studyVilla99                   0.541597     0.4683  1.156483 2.475e-01
studyZelman92                  0.213093     0.3706  0.574934 5.653e-01
treatmentgum:studyCampbell91  -0.638716     0.4699 -1.359285 1.741e-01
treatmentgum:studyFagerstrom82 -0.049378     0.5156 -0.095762 9.237e-01
treatmentgum:studyFee82       -0.187742     0.4742 -0.395873 6.922e-01
treatmentgum:studyGarcia89     0.466259     0.6334  0.736093 4.617e-01
treatmentgum:studyGarvey00     0.295743     0.4273  0.692111 4.889e-01
treatmentgum:studyGross95      0.349557     0.5756  0.607252 5.437e-01
treatmentgum:studyHall85       0.095203     0.5827  0.163387 8.702e-01
treatmentgum:studyHall87       0.422366     0.4997  0.845244 3.980e-01
treatmentgum:studyHall96      -0.755913     0.4542 -1.664447 9.602e-02
treatmentgum:studyHjalmarson84  0.159542     0.4712  0.338590 7.349e-01
treatmentgum:studyHuber88      1.177232     0.5377  2.189539 2.856e-02
treatmentgum:studyJarvis82     0.586934     0.5539  1.059684 2.893e-01
treatmentgum:studyJensen91    -0.254387     0.4191 -0.607000 5.439e-01
treatmentgum:studyKillen84    -0.327504     0.6621 -0.494666 6.208e-01
treatmentgum:studyKillen90    -0.404172     0.3504 -1.153314 2.488e-01
treatmentgum:studyMalcolm80    0.643954     0.7908  0.814266 4.155e-01
treatmentgum:studyMcGovern92  -0.460208     0.4107 -1.120609 2.625e-01
treatmentgum:studyNakamura90   0.725988     0.6912  1.050312 2.936e-01
treatmentgum:studyNiaura94    -0.318839     0.7592 -0.419943 6.745e-01
treatmentgum:studyPirie92     -0.003513     0.3863 -0.009096 9.927e-01
treatmentgum:studyPuska79     -0.236532     0.4544 -0.520520 6.027e-01
treatmentgum:studySchneider85 -0.076189     0.6849 -0.111241 9.114e-01
treatmentgum:studyTonnesen88   0.138056     0.5294  0.260782 7.943e-01
treatmentgum:studyVilla99     -0.049872     0.6749 -0.073900 9.411e-01
treatmentgum:studyZelman92    -0.236532     0.5046 -0.468741 6.393e-01
```

Or maybe we could do something else?

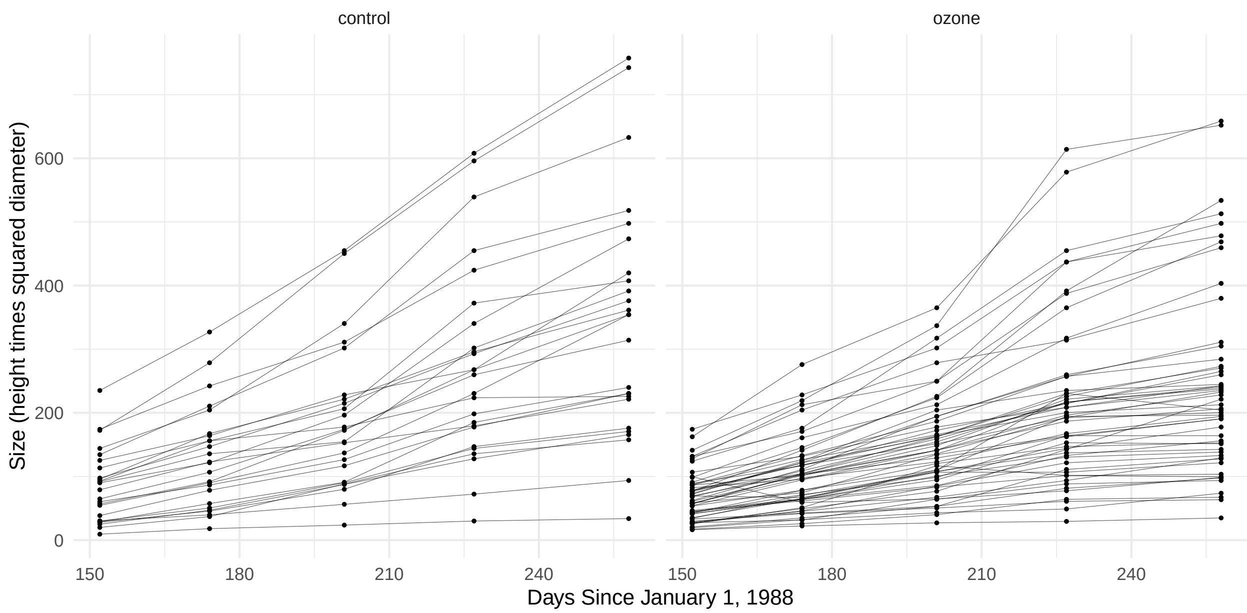
Example: Consider the following data from a study of the growth of Sitka spruce trees under two experimental conditions.

```r
library(MASS)
head(Sitka, 10) # note that size is on log scale
```

```
   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
```

```r
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)
```



Note that trees vary considerably in terms of their growth trajectories.

What *could* we do (but not necessarily what we *should* do) in modeling these data.

We could ignore the effect of tree.

```r
m <- lm(exp(size) ~ Time * treat, data = Sitka)
summary(m)$coefficients
```

```
                 Estimate Std. Error t value  Pr(>|t|)
(Intercept)     -305.1231    52.7109  -5.789 1.458e-08
Time               2.5093     0.2561   9.799 2.029e-20
treatozone       110.6754    63.7554   1.736 8.336e-02
Time:treatozone   -0.7881     0.3097  -2.544 1.133e-02
```

Or we could model the effect of tree.

```r
Sitka$tree <- factor(Sitka$tree)
m <- lm(exp(size) ~ Time * treat + Time * tree, data = Sitka)
```

```
summary(m)$coefficients
```

```
                 Estimate Std. Error   t value  Pr(>|t|)
(Intercept)     -1.974e+02    48.0069  -4.11226 5.405e-05
Time             1.408e+00     0.2332   6.03958 5.931e-09
treatozone      -2.912e+02    67.8920  -4.28865 2.618e-05
tree2            4.279e+02    67.8920   6.30301 1.412e-09
tree3            3.970e+02    67.8920   5.84783 1.642e-08
tree4            3.780e+02    67.8920   5.56735 6.985e-08
tree5           -1.316e+02    67.8920  -1.93822 5.378e-02
tree6            1.408e+02    67.8920   2.07383 3.918e-02
tree7            3.721e+02    67.8920   5.48016 1.084e-07
tree8            2.970e+02    67.8920   4.37387 1.829e-05
tree9            6.928e-01    67.8920   0.01020 9.919e-01
tree10           4.328e+02    67.8920   6.37442 9.499e-10
tree11           3.807e+02    67.8920   5.60680 5.715e-08
tree12           2.502e+02    67.8920   3.68495 2.835e-04
tree13           2.475e+02    67.8920   3.64509 3.285e-04
tree14           3.652e+02    67.8920   5.37941 1.791e-07
tree15           5.513e+02    67.8920   8.11978 2.555e-14
tree16           3.864e+02    67.8920   5.69212 3.691e-08
tree17           3.966e+02    67.8920   5.84235 1.690e-08
tree18           4.356e+02    67.8920   6.41580 7.540e-10
tree19           4.143e+02    67.8920   6.10243 4.227e-09
tree20           3.509e+02    67.8920   5.16904 4.998e-07
tree21           3.698e+02    67.8920   5.44752 1.277e-07
tree22           3.207e+02    67.8920   4.72312 3.979e-06
tree23           2.703e+02    67.8920   3.98059 9.144e-05
tree24           4.809e+02    67.8920   7.08401 1.587e-11
tree25           2.202e+02    67.8920   3.24404 1.348e-03
tree26           3.694e+02    67.8920   5.44055 1.322e-07
tree27           2.629e+02    67.8920   3.87247 1.394e-04
tree28           3.235e+02    67.8920   4.76549 3.287e-06
tree29           4.926e+01    67.8920   0.72562 4.688e-01
tree30           2.900e+02    67.8920   4.27110 2.817e-05
tree31           3.625e+02    67.8920   5.33967 2.179e-07
tree32           3.192e+02    67.8920   4.70104 4.393e-06
tree33           3.228e+02    67.8920   4.75483 3.449e-06
tree34           3.562e+02    67.8920   5.24674 3.433e-07
tree35           1.630e+02    67.8920   2.40061 1.714e-02
tree36           4.550e+02    67.8920   6.70248 1.483e-10
tree37          -8.903e+01    67.8920  -1.31131 1.910e-01
tree38           1.929e+02    67.8920   2.84066 4.894e-03
tree39           1.368e+02    67.8920   2.01454 4.508e-02
tree40           3.077e+02    67.8920   4.53271 9.242e-06
tree41          -1.973e+02    67.8920  -2.90579 4.010e-03
tree42           3.191e+02    67.8920   4.70040 4.406e-06
tree43           2.338e+02    67.8920   3.44344 6.790e-04
tree44           3.063e+02    67.8920   4.51129 1.014e-05
tree45           4.260e+02    67.8920   6.27499 1.648e-09
tree46           2.801e+02    67.8920   4.12501 5.133e-05
tree47           3.289e+02    67.8920   4.84461 2.293e-06
tree48           3.643e+02    67.8920   5.36604 1.914e-07
tree49           4.055e+02    67.8920   5.97237 8.497e-09
```

tree50	3.933e+02	67.8920	5.79232	2.196e-08
tree51	3.517e+02	67.8920	5.18101	4.719e-07
tree52	2.664e+02	67.8920	3.92443	1.140e-04
tree53	4.724e+02	67.8920	6.95807	3.347e-11
tree54	3.553e+02	67.8920	5.23390	3.654e-07
tree55	1.225e+02	67.8920	1.80458	7.241e-02
tree56	-4.331e+02	67.8920	-6.37975	9.221e-10
tree57	8.878e+01	67.8920	1.30764	1.923e-01
tree58	-1.151e+02	67.8920	-1.69465	9.146e-02
tree59	-2.000e+02	67.8920	-2.94616	3.538e-03
tree60	-1.659e+02	67.8920	-2.44333	1.528e-02
tree61	-4.666e+02	67.8920	-6.87237	5.534e-11
tree62	-2.055e+01	67.8920	-0.30272	7.624e-01
tree63	1.116e+01	67.8920	0.16441	8.695e-01
tree64	1.743e+02	67.8920	2.56720	1.087e-02
tree65	-4.367e+01	67.8920	-0.64325	5.207e-01
tree66	8.094e+00	67.8920	0.11922	9.052e-01
tree67	-1.051e+02	67.8920	-1.54801	1.230e-01
tree68	-2.049e+02	67.8920	-3.01786	2.824e-03
tree69	-1.764e+02	67.8920	-2.59776	9.971e-03
tree70	-7.682e+01	67.8920	-1.13154	2.590e-01
tree71	-2.491e+02	67.8920	-3.66955	3.001e-04
tree72	-9.720e+01	67.8920	-1.43172	1.535e-01
tree73	-3.402e+02	67.8920	-5.01033	1.063e-06
tree74	-1.164e+02	67.8920	-1.71433	8.778e-02
tree75	-9.117e+01	67.8920	-1.34293	1.806e-01
tree76	-1.130e+01	67.8920	-0.16645	8.679e-01
tree77	1.336e+02	67.8920	1.96726	5.032e-02
tree78	-3.176e+02	67.8920	-4.67841	4.861e-06
Time:treatozone	2.284e+00	0.3298	6.92483	4.069e-11
Time:tree2	-2.875e+00	0.3298	-8.71844	5.009e-16
Time:tree3	-2.695e+00	0.3298	-8.17016	1.846e-14
Time:tree4	-2.382e+00	0.3298	-7.22182	6.948e-12
Time:tree5	7.245e-01	0.3298	2.19679	2.900e-02
Time:tree6	-7.954e-01	0.3298	-2.41183	1.663e-02
Time:tree7	-2.413e+00	0.3298	-7.31591	3.932e-12
Time:tree8	-1.984e+00	0.3298	-6.01477	6.775e-09
Time:tree9	2.843e-01	0.3298	0.86199	3.896e-01
Time:tree10	-2.976e+00	0.3298	-9.02271	6.442e-17
Time:tree11	-2.571e+00	0.3298	-7.79504	2.025e-13
Time:tree12	-1.596e+00	0.3298	-4.83862	2.356e-06
Time:tree13	-1.537e+00	0.3298	-4.66113	5.250e-06
Time:tree14	-2.270e+00	0.3298	-6.88393	5.172e-11
Time:tree15	-3.608e+00	0.3298	-10.93813	8.237e-23
Time:tree16	-2.719e+00	0.3298	-8.24443	1.140e-14
Time:tree17	-2.382e+00	0.3298	-7.22131	6.970e-12
Time:tree18	-3.216e+00	0.3298	-9.75136	4.171e-19
Time:tree19	-2.932e+00	0.3298	-8.88966	1.586e-16
Time:tree20	-2.249e+00	0.3298	-6.81802	7.598e-11
Time:tree21	-2.471e+00	0.3298	-7.49216	1.337e-12
Time:tree22	-2.335e+00	0.3298	-7.08091	1.616e-11
Time:tree23	-1.807e+00	0.3298	-5.47996	1.085e-07
Time:tree24	-3.526e+00	0.3298	-10.69227	4.959e-22
Time:tree25	-1.856e+00	0.3298	-5.62600	5.182e-08

Time:tree26	-2.744e+00	0.3298	-8.32071	6.939e-15
Time:tree27	-1.919e+00	0.3298	-5.81946	1.905e-08
Time:tree28	-2.034e+00	0.3298	-6.16742	2.971e-09
Time:tree29	-7.204e-02	0.3298	-0.21842	8.273e-01
Time:tree30	-1.418e+00	0.3298	-4.29893	2.508e-05
Time:tree31	-2.592e+00	0.3298	-7.85878	1.354e-13
Time:tree32	-2.065e+00	0.3298	-6.26045	1.785e-09
Time:tree33	-2.003e+00	0.3298	-6.07233	4.973e-09
Time:tree34	-2.406e+00	0.3298	-7.29509	4.461e-12
Time:tree35	-4.642e-01	0.3298	-1.40749	1.606e-01
Time:tree36	-3.141e+00	0.3298	-9.52223	2.072e-18
Time:tree37	1.177e+00	0.3298	3.56966	4.326e-04
Time:tree38	-1.310e+00	0.3298	-3.97191	9.462e-05
Time:tree39	-5.341e-01	0.3298	-1.61936	1.067e-01
Time:tree40	-2.079e+00	0.3298	-6.30474	1.398e-09
Time:tree41	1.636e+00	0.3298	4.96135	1.337e-06
Time:tree42	-2.073e+00	0.3298	-6.28455	1.563e-09
Time:tree43	-1.618e+00	0.3298	-4.90595	1.729e-06
Time:tree44	-2.231e+00	0.3298	-6.76407	1.039e-10
Time:tree45	-3.171e+00	0.3298	-9.61599	1.078e-18
Time:tree46	-1.813e+00	0.3298	-5.49839	9.895e-08
Time:tree47	-2.234e+00	0.3298	-6.77472	9.769e-11
Time:tree48	-2.715e+00	0.3298	-8.23303	1.228e-14
Time:tree49	-2.981e+00	0.3298	-9.03704	5.844e-17
Time:tree50	-2.937e+00	0.3298	-8.90612	1.419e-16
Time:tree51	-2.610e+00	0.3298	-7.91242	9.634e-14
Time:tree52	-2.001e+00	0.3298	-6.06620	5.140e-09
Time:tree53	-3.369e+00	0.3298	-10.21559	1.548e-20
Time:tree54	-2.536e+00	0.3298	-7.68847	3.954e-13
Time:tree55	-1.729e-01	0.3298	-0.52409	6.007e-01
Time:tree56	3.545e+00	0.3298	10.74990	3.260e-22
Time:tree57	-1.251e-01	0.3298	-0.37938	7.047e-01
Time:tree58	1.250e+00	0.3298	3.79115	1.903e-04
Time:tree59	1.411e+00	0.3298	4.27870	2.729e-05
Time:tree60	1.627e+00	0.3298	4.93380	1.519e-06
Time:tree61	4.085e+00	0.3298	12.38687	1.672e-27
Time:tree62	3.715e-01	0.3298	1.12633	2.612e-01
Time:tree63	-4.085e-02	0.3298	-0.12386	9.015e-01
Time:tree64	-1.181e+00	0.3298	-3.58083	4.155e-04
Time:tree65	4.166e-01	0.3298	1.26329	2.077e-01
Time:tree66	6.261e-03	0.3298	0.01898	9.849e-01
Time:tree67	1.716e+00	0.3298	5.20262	4.252e-07
Time:tree68	1.511e+00	0.3298	4.58163	7.462e-06
Time:tree69	1.501e+00	0.3298	4.55058	8.549e-06
Time:tree70	1.075e+00	0.3298	3.25801	1.286e-03
Time:tree71	2.398e+00	0.3298	7.27149	5.147e-12
Time:tree72	1.238e+00	0.3298	3.75322	2.196e-04
Time:tree73	3.602e+00	0.3298	10.92026	9.389e-23
Time:tree74	1.051e+00	0.3298	3.18550	1.639e-03
Time:tree75	6.025e-01	0.3298	1.82687	6.898e-02
Time:tree76	9.330e-02	0.3298	0.28289	7.775e-01
Time:tree77	-8.044e-01	0.3298	-2.43887	1.547e-02
Time:tree78	2.343e+00	0.3298	7.10522	1.398e-11

Or maybe we could do something else?

Marginal Models and Generalized Estimating Equations

A marginal model *ignores* the many-leveled factor. One approach to estimating such models is to use what can be viewed as an extension of quasi-likelihood called *generalized estimating equations* (GEE). This approach actually involves two parts.

1. Estimate the model using generalized estimating equations. This uses an iterative generalized least squares that uses an estimated "working" correlation structure. This can be viewed as an extension of the iteratively weighted least squares algorithm we used earlier.

2. Compute *robust* estimates of standard errors to account for heteroscedasticity and correlations among observations. These are designed to deal with the fact that our observations are not independent.

Example: Consider two approaches to the `baserun` data: ignoring the player effect entirely and a marginal model with inferences based on GEE.

```
library(geepack)

# generalized linear model, but same as lm(time ~ route, data = baselong)
m.glm <- glm(time ~ route, family = gaussian(link = identity), data = baselong)

# generalized estimating equations
m.gee <- geeglm(time ~ route, family = gaussian(link = identity),
  id = player, corstr = "exchangeable", data = baselong)
```

Note: The data *must* be sorted by the `id` variable, and the `id` variable must be a *factor* or a *number* (not *character*).

Comparing inferences for the model parameters.

```
summary(m.glm)$coefficients
```

```
             Estimate Std. Error t value  Pr(>|t|)
(Intercept)  5.534091    0.05718 96.7838 3.047e-70
routeround   0.009091    0.08086  0.1124 9.108e-01
routewide   -0.075000    0.08086 -0.9275 3.572e-01
```

```
summary(m.gee)
```

```
Call:
geeglm(formula = time ~ route, family = gaussian(link = identity),
    data = baselong, id = player, corstr = "exchangeable")

 Coefficients:
            Estimate  Std.err     Wald Pr(>|W|)
(Intercept)  5.53409  0.05411 10461.38  < 2e-16 ***
routeround   0.00909  0.02564     0.13     0.72
routewide   -0.07500  0.01839    16.63  4.6e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)   0.0687  0.0278
```

```
  Link = identity

Estimated Correlation Parameters:
      Estimate Std.err
alpha    0.896  0.0585
Number of clusters:   22  Maximum cluster size: 3
```

Comparing inferences for the expected time for each route.

```
library(emmeans)

emmeans(m.glm, ~route)
```

```
 route  emmean     SE df lower.CL upper.CL
 narrow   5.53 0.0572 63     5.42     5.65
 round    5.54 0.0572 63     5.43     5.66
 wide     5.46 0.0572 63     5.34     5.57

Confidence level used: 0.95
```

```
emmeans(m.gee, ~route)
```

```
 route  emmean     SE  df asymp.LCL asymp.UCL
 narrow   5.53 0.0541 Inf      5.43      5.64
 round    5.54 0.0566 Inf      5.43      5.65
 wide     5.46 0.0568 Inf      5.35      5.57

Covariance estimate used: vbeta
Confidence level used: 0.95
```

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

```
 estimate     se lower upper tvalue df   pvalue
     5.53 0.0572  5.42  5.65   96.8 63 3.05e-70
     5.54 0.0572  5.43  5.66   96.9 63 2.75e-70
     5.46 0.0572  5.34  5.57   95.5 63 7.16e-70
```

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

```
 estimate     se lower upper tvalue df   pvalue
     5.53 0.0541  5.43  5.64  102.3 63 9.59e-72
     5.54 0.0566  5.43  5.66   97.9 63 1.48e-70
     5.46 0.0568  5.35  5.57   96.1 63 4.88e-70
```

Comparing inferences for the *differences* in expected time between routes.

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

```
 contrast       estimate     SE df lower.CL upper.CL t.ratio p.value
 narrow - round  -0.0091 0.0809 63  -0.1707    0.152  -0.112  0.9110
 narrow - wide    0.0750 0.0809 63  -0.0866    0.237   0.927  0.3570
 round - wide     0.0841 0.0809 63  -0.0775    0.246   1.040  0.3020

Confidence level used: 0.95
```

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

```
 contrast       estimate     SE  df asymp.LCL asymp.UCL z.ratio p.value
 narrow - round  -0.0091 0.0256 Inf   -0.0593    0.0412  -0.350  0.7230
```

```
 narrow - wide    0.0750 0.0184 Inf    0.0389    0.1111   4.080  <.0001
 round - wide     0.0841 0.0307 Inf    0.0239    0.1443   2.740  0.0060

Confidence level used: 0.95
```

```r
trtools::contrast(m.glm,
  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 -0.00909 0.0809 -0.1707 0.153 -0.112 63  0.911
narrow - wide   0.07500 0.0809 -0.0866 0.237  0.927 63  0.357
round - wide    0.08409 0.0809 -0.0775 0.246  1.040 63  0.302
```

```r
trtools::contrast(m.gee,
  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 -0.00909 0.0256 -0.0603 0.0421 -0.355 63 0.72410
narrow - wide   0.07500 0.0184  0.0382 0.1118  4.077 63 0.00013
round - wide    0.08409 0.0307  0.0227 0.1455  2.737 63 0.00805
```

Example: Consider two approaches to the `smoking` data: ignoring the study effect entirely and a marginal model with inferences based on GEE.

```r
head(quitsmoke)
```

```
# A tibble: 6 x 4
  study        treatment  quit total
  <fct>        <chr>     <int> <int>
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
```

```r
m.glm <- glm(cbind(quit, total - quit) ~ treatment,
  family = binomial, data = quitsmoke)
m.gee <- geeglm(cbind(quit, total - quit) ~ treatment,
  family = binomial, data = quitsmoke,
  id = study, corstr = "exchangeable")
```

Comparing inferences for the model parameters.

```r
summary(m.glm)$coefficients
```

```
             Estimate Std. Error z value  Pr(>|z|)
(Intercept)    -1.450     0.0490  -29.59 1.76e-192
treatmentgum    0.507     0.0631    8.04  9.11e-16
```

```r
summary(m.gee)
```

```
Call:
geeglm(formula = cbind(quit, total - quit) ~ treatment, family = binomial,
    data = quitsmoke, id = study, corstr = "exchangeable")
```

```
 Coefficients:
             Estimate Std.err  Wald Pr(>|W|)
(Intercept)    -1.444   0.116 155.5  < 2e-16 ***
treatmentgum    0.501   0.078  41.2  1.4e-10 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)   0.0601  0.0158
  Link = identity

Estimated Correlation Parameters:
      Estimate Std.err
alpha    0.445   0.229
Number of clusters:   26  Maximum cluster size: 2
```

Estimating the probability of quitting.

```
emmeans(m.glm, ~treatment, type = "response")
```

```
 treatment prob      SE  df asymp.LCL asymp.UCL
 control   0.19 0.00754 Inf     0.176     0.205
 gum       0.28 0.00801 Inf     0.265     0.296

Confidence level used: 0.95
Intervals are back-transformed from the logit scale
```

```
emmeans(m.gee, ~treatment, type = "response")
```

```
 treatment  prob     SE  df asymp.LCL asymp.UCL
 control   0.191 0.0179 Inf     0.158     0.229
 gum       0.280 0.0255 Inf     0.233     0.333

Covariance estimate used: vbeta
Confidence level used: 0.95
Intervals are back-transformed from the logit scale
```

```
trtools::contrast(m.glm, a = list(treatment = c("control","gum")),
  tf = plogis, cnames = c("control","gum"))
```

```
        estimate lower upper
control     0.19 0.176 0.205
gum         0.28 0.265 0.296
```

```
trtools::contrast(m.gee, a = list(treatment = c("control","gum")),
  tf = plogis, cnames = c("control","gum"))
```

```
        estimate lower upper
control    0.191 0.158 0.229
gum        0.280 0.233 0.333
```

Estimating the odds ratio for the effect of the gum treatment.

```r
pairs(emmeans(m.glm, ~treatment, type = "response"),
  reverse = TRUE, infer = TRUE)
```

```
 contrast       odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 gum / control        1.66 0.105 Inf      1.47      1.88    1   8.040  <.0001

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

```r
pairs(emmeans(m.gee, ~treatment, type = "response"),
  reverse = TRUE, infer = TRUE)
```

```
 contrast       odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 gum / control        1.65 0.129 Inf      1.42      1.92    1   6.420  <.0001

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

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

```
 estimate lower upper
     1.66  1.47  1.88
```

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

```
 estimate lower upper
     1.65  1.42  1.92
```

Example: Consider two approaches to the `Sitka` data.

```r
m.glm <- glm(exp(size) ~ Time * treat,
  family = gaussian(link = identity), data = Sitka)
m.gee <- geeglm(exp(size) ~ Time * treat,
  family = gaussian(link = identity), data = Sitka,
  id = tree, corstr = "exchangeable")
```

Comparing inferences for the model parameters.

```r
summary(m.glm)$coefficients
```

```
                Estimate Std. Error t value Pr(>|t|)
(Intercept)     -305.123     52.711   -5.79 1.46e-08
Time               2.509      0.256    9.80 2.03e-20
treatozone       110.675     63.755    1.74 8.34e-02
Time:treatozone   -0.788      0.310   -2.54 1.13e-02
```

```r
summary(m.gee)
```

```
Call:
geeglm(formula = exp(size) ~ Time * treat, family = gaussian(link = identity),
    data = Sitka, id = tree, corstr = "exchangeable")

 Coefficients:
```

```
                 Estimate  Std.err  Wald Pr(>|W|)
(Intercept)      -305.123   32.737 86.87   <2e-16 ***
Time                2.509    0.264 90.62   <2e-16 ***
treatozone        110.675   38.775  8.15   0.0043 **
Time:treatozone    -0.788    0.306  6.62   0.0101 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)    11432    2036
  Link = identity

Estimated Correlation Parameters:
      Estimate Std.err
alpha    0.752  0.0189
Number of clusters:   79  Maximum cluster size: 5
```

Estimating the growth rate in each treatment condition.

```
trtools::contrast(m.glm,
  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      251 25.6   201   301   9.80 391 2.03e-20
ozone        172 17.4   138   206   9.88 391 1.08e-20
```

```
trtools::contrast(m.gee,
  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      251 26.4   199   303   9.52 391 1.84e-19
ozone        172 15.6   141   203  11.03 391 8.23e-25
```

```
# Note: We can estimate the growth rates (per day)
# using emtrends from the emmeans package.
emtrends(m.glm, ~ treat, var = "Time")
```

```
 treat   Time.trend    SE  df lower.CL upper.CL
 control       2.51 0.256 391     2.01     3.01
 ozone         1.72 0.174 391     1.38     2.06

Confidence level used: 0.95
```

```
emtrends(m.gee, ~ treat, var = "Time")
```

```
 treat   Time.trend    SE  df asymp.LCL asymp.UCL
 control       2.51 0.264 Inf      1.99      3.03
 ozone         1.72 0.156 Inf      1.42      2.03

Covariance estimate used: vbeta
```

```
Confidence level used: 0.95
```

Comparing the growth rates between the treatment conditions.

```r
trtools::contrast(m.glm,
  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
     78.8 31  17.9   140   2.54 391 0.0113
```

```r
trtools::contrast(m.gee,
  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
     78.8 30.6  18.6   139   2.57 391 0.0105
```

```r
pairs(emtrends(m.glm, ~ treat, var = "Time"))
```

```
 contrast        estimate   SE  df t.ratio p.value
 control - ozone    0.788 0.31 391   2.544  0.0113
```

```r
pairs(emtrends(m.gee, ~ treat, var = "Time"))
```

```
 contrast        estimate    SE  df z.ratio p.value
 control - ozone    0.788 0.306 Inf   2.573  0.0101
```

Limitations of Marginal Models and GEE

1. Performs best when the data are relatively "shallow" meaning that there are many units (e.g., players, studies, or trees) but relatively few observations per unit (e.g., routes, treatment conditions, time points).

2. Difficult to use with "unbalanced" data where not every unit is observed at the same "points" (e.g., routes, treatments, time points).

3. Inefficient if the (working) correlation structure is a poor approximation.

4. Limited to "marginal inferences" in that it cannot tell us much about the variation among units (in contrast to models with "random effects" which we will discuss later).