Friday, Feb 2

Marginal Means

A *marginal mean* is effectively an average of expected responses. The **emmeans** package is particularly useful for making inferences about marginal means.

```
library(trtools)
library(emmeans)
```

Warning: The **emmeans** package contains a function called `contrast` which is not the same as the function of the same name in the **trtools** package, resulting in a namespace conflict if both packages are loaded. If you have both packages loaded in a given session, use `trtools::contrast` and `emmeans::contrast` to refer to a given function.

Example: Consider again the data from the platyfish study.

```
m <- lm(Percentage ~ Pair, data = Sleuth3::case0602)
summary(m)$coefficients
```

```
            Estimate Std. Error t value  Pr(>|t|)
(Intercept)   56.406      3.864 14.5965 5.208e-24
PairPair2      4.479      5.657  0.7919 4.308e-01
PairPair3      6.023      5.384  1.1187 2.667e-01
PairPair4     10.594      5.657  1.8727 6.485e-02
PairPair5      7.805      6.441  1.2118 2.292e-01
PairPair6      6.929      5.657  1.2250 2.243e-01
```

We see that there are indicator variables for male pairs 2-6. The model can be written as

$$E(Y_i) = \begin{cases} \beta_0, & \text{if the } i\text{-th observation was from the first male pair,} \\ \beta_0 + \beta_1, & \text{if the } i\text{-th observation was from the second male pair,} \\ \beta_0 + \beta_2, & \text{if the } i\text{-th observation was from the third male pair,} \\ \beta_0 + \beta_3, & \text{if the } i\text{-th observation was from the fourth male pair,} \\ \beta_0 + \beta_4, & \text{if the } i\text{-th observation was from the fifth male pair,} \\ \beta_0 + \beta_5, & \text{if the } i\text{-th observation was from the sixth male pair.} \end{cases}$$

We can use `contrast` to estimate the expected response for each pair.

```
contrast(m, a = list(Pair = paste("Pair", 1:6, sep = "")),
   cnames = paste("Pair", 1:6, sep = ""))
```

```
      estimate    se lower upper tvalue df    pvalue
Pair1    56.41 3.864 48.71 64.10  14.60 78 5.208e-24
Pair2    60.89 4.131 52.66 69.11  14.74 78 2.990e-24
Pair3    62.43 3.749 54.97 69.89  16.65 78 2.114e-27
Pair4    67.00 4.131 58.78 75.22  16.22 78 1.052e-26
Pair5    64.21 5.152 53.95 74.47  12.46 78 3.039e-20
Pair6    63.34 4.131 55.11 71.56  15.33 78 3.006e-25
```

Note how I used a shortcut to specify the pairs.

```r
paste("Pair", 1:6, sep = "")
```

```
[1] "Pair1" "Pair2" "Pair3" "Pair4" "Pair5" "Pair6"
```

This can also be done using the `emmeans` function from the package **emmeans**.

```r
library(emmeans)
emmeans(m, ~ Pair)
```

```
 Pair  emmean   SE df lower.CL upper.CL
 Pair1   56.4 3.86 78     48.7     64.1
 Pair2   60.9 4.13 78     52.7     69.1
 Pair3   62.4 3.75 78     55.0     69.9
 Pair4   67.0 4.13 78     58.8     75.2
 Pair5   64.2 5.15 78     54.0     74.5
 Pair6   63.3 4.13 78     55.1     71.6

Confidence level used: 0.95
```

Denote the six expected responses (one for each pair) as

$$
\begin{aligned}
\mu_1 &= \beta_0, \\
\mu_2 &= \beta_0 + \beta_1, \\
\mu_3 &= \beta_0 + \beta_2, \\
\mu_4 &= \beta_0 + \beta_3, \\
\mu_5 &= \beta_0 + \beta_4, \\
\mu_6 &= \beta_0 + \beta_5.
\end{aligned}
$$

One marginal mean would be the average expected response across the pairs. This could be written as

$$\mu = \frac{\mu_1 + \mu_2 + \mu_3 + \mu_4 + \mu_5 + \mu_6}{6} = \beta_0 + \tfrac{1}{6}\beta_1 + \tfrac{1}{6}\beta_2 + \tfrac{1}{6}\beta_3 + \tfrac{1}{6}\beta_4 + \tfrac{1}{6}\beta_5.$$

We can estimate this quantity with `lincon`.

```r
lincon(m, a = c(1,1/6,1/6,1/6,1/6,1/6))
```

```
                           estimate    se lower upper tvalue df    pvalue
(1,1/6,1/6,1/6,1/6,1/6),0     62.38 1.722 58.95 65.81  36.23 78 1.501e-50
```

We can also use `emmeans`.

```r
emmeans(m, ~ 1)
```

```
 1       emmean   SE df lower.CL upper.CL
 overall   62.4 1.72 78       59     65.8

Results are averaged over the levels of: Pair
Confidence level used: 0.95
```

Note that we can use the confidence interval to test the null hypothesis that $\mu = 50$. For a test statistic and p-value for this test we could write this as

$$\mu = 50 \Leftrightarrow \beta_0 + \tfrac{1}{6}\beta_1 + \tfrac{1}{6}\beta_2 + \tfrac{1}{6}\beta_3 + \tfrac{1}{6}\beta_4 + \tfrac{1}{6}\beta_5 = 50 \Leftrightarrow \beta_0 + \tfrac{1}{6}\beta_1 + \tfrac{1}{6}\beta_2 + \tfrac{1}{6}\beta_3 + \tfrac{1}{6}\beta_4 + \tfrac{1}{6}\beta_5 - 50 = 0.$$

Here is how we can do that with `lincon`.

```r
lincon(m, a = c(1,1/6,1/6,1/6,1/6,1/6), b = -50)
```

```
                              estimate    se lower upper tvalue df    pvalue
(1,1/6,1/6,1/6,1/6,1/6),-50     12.38 1.722  8.95 15.81  7.189 78 3.439e-10
```

Here is how we do it with `emmeans`.

```
emmeans(m, ~ 1, offset = -50, infer = TRUE)
```

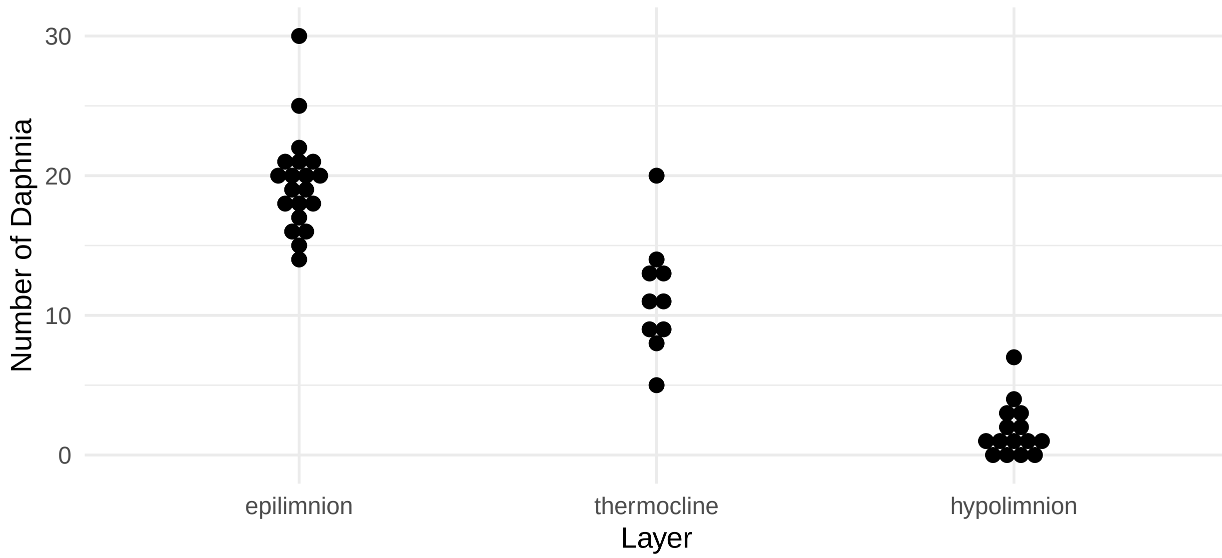
```
 1       emmean   SE df lower.CL upper.CL t.ratio p.value
 overall   12.4 1.72 78     8.95     15.8   7.189  <.0001

Results are averaged over the levels of: Pair
Confidence level used: 0.95
```

By *not* listing an explanatory variable on the right-hand side of `~`, we are asking that `emmeans` average over that explanatory variable. Also note that the argument `infer = TRUE` makes the `emmeans` function provide both confidence intervals as well as tests.

Note: If we just want to know whether or not we would reject the null hypothesis that $\mu = 50$ we can also just look at the confidence interval for μ.

Example: Consider the following data from a survey of water fleas.

```
library(ggplot2)
p <- ggplot(daphniastrat, aes(x = layer, y = count)) +
  geom_dotplot(binaxis = "y", stackdir = "center") +
  labs(x = "Layer", y = "Number of Daphnia") + theme_minimal()
plot(p)
```



We might model these data using the following linear model.

```
m <- lm(count ~ layer, data = daphniastrat)
summary(m)$coefficients
```

```
                 Estimate Std. Error t value  Pr(>|t|)
(Intercept)         19.50     0.7271  26.820 4.727e-28
layerthermocline    -8.20     1.2593  -6.512 7.293e-08
layerhypolimnion   -17.77     1.1106 -15.997 1.784e-19
```

So our model can be written as

$$E(Y_i) = \begin{cases} \beta_0, & \text{if the } i\text{-th observation is from the epilimnion layer,} \\ \beta_0 + \beta_1, & \text{if the } i\text{-th observation is from the thermocline layer,} \\ \beta_0 + \beta_2, & \text{if the } i\text{-th observation is from the hypolimnion layer.} \end{cases}$$

Let μ_e, μ_t, and μ_h denote the expected number of daphnia per liter for the epilimnion, thermocline, and hypolimnion layers, respectively (i.e., the density of daphnia in each layer). So

$$\mu_e = \beta_0, \ \mu_t = \beta_0 + \beta_1, \ \mu_h = \beta_0 + \beta_2.$$

It is known that the volumes of the epilimnion, thermocline, and hypolimnion layers are 100, 200, and 400 kL, respectively. The density for the entire lake is then

$$\mu = \tfrac{100}{700}\mu_e + \tfrac{200}{700}\mu_t + \tfrac{400}{700}\mu_h = \beta_0 + \frac{2}{7}\beta_1 + \frac{4}{7}\beta_2.$$

We can estimate this with `lincon` or `emmeans` using the `weights` option.

```
lincon(m, a = c(1, 2/7, 4/7))
```

```
              estimate    se lower upper tvalue df    pvalue
(1,2/7,4/7),0    7.005 0.572  5.85 8.159  12.25 42 1.907e-15
```

```
emmeans(m, ~ 1, weights = c(1/7, 2/7, 4/7))
```

```
 1       emmean    SE df lower.CL upper.CL
 overall      7 0.572 42     5.85     8.16

Results are averaged over the levels of: layer 
Confidence level used: 0.95 
```

Note that when using `emmeans` it is important to put the weights in the correct order. We can verify the order using `level` (if the variable is a factor) or by using `weights = "slow.levels"`.

```
levels(daphniastrat$layer)
```

```
[1] "epilimnion"  "thermocline" "hypolimnion"
```

```
emmeans(m, ~ 1, weights = "show.levels")
```

```
emmeans are obtained by averaging over these factor combinations

        layer
1  epilimnion
2 thermocline
3 hypolimnion
```

We can estimate the expected number of daphnia per liter for each layer.

```
emmeans(m, ~ layer)
```

```
 layer       emmean    SE df lower.CL upper.CL
 epilimnion   19.50 0.727 42   18.033    20.97
 thermocline  11.30 1.028 42    9.225    13.38
 hypolimnion   1.73 0.840 42    0.039     3.43

Confidence level used: 0.95 
```

```
trtools::contrast(m, a = list(layer = c("epilimnion","thermocline","hypolimnion")),
  cnames = c("epilimnion","thermocline","hypolimnion"))
```

```
             estimate     se    lower  upper tvalue df    pvalue
epilimnion     19.500 0.7271 18.03274 20.967 26.820 42 4.727e-28
thermocline    11.300 1.0282  9.22498 13.375 10.990 42 6.221e-14
hypolimnion     1.733 0.8395  0.03909  3.428  2.065 42 4.517e-02
```

We can also do inferences concerning the differences between pairs of layers.

```r
pairs(emmeans(m, ~ layer), adjust = "none")
```

```
 contrast                  estimate   SE df t.ratio p.value
 epilimnion - thermocline      8.20 1.26 42   6.512  <.0001
 epilimnion - hypolimnion     17.77 1.11 42  15.997  <.0001
 thermocline - hypolimnion     9.57 1.33 42   7.207  <.0001
```

```r
trtools::contrast(m,
  a = list(layer = c("epilimnion","epilimnion","thermocline")),
  b = list(layer = c("thermocline","hypolimnion","hypolimnion")),
  cnames = c("E-T","E-H", "T-H"))
```

```
    estimate    se  lower upper tvalue df    pvalue
E-T    8.200 1.259  5.659 10.74  6.512 42 7.293e-08
E-H   17.767 1.111 15.525 20.01 15.997 42 1.784e-19
T-H    9.567 1.327  6.888 12.25  7.207 42 7.363e-09
```

The `adjust = "none"` option for `pairs` specifies that no adjustment be made to confidence intervals or tests for the family-wise Type I error rate.[1]

Something to note when using the `weights` argument with the `emmeans` function is that the weights that are used must sum to one, and if they do not they will be normalized so that they do. For example, the following provide the same result.

```r
emmeans(m, ~ 1, weights = c(1/7, 2/7, 4/7))
```

```
 1       emmean    SE df lower.CL upper.CL
 overall      7 0.572 42     5.85     8.16

Results are averaged over the levels of: layer
Confidence level used: 0.95
```

```r
emmeans(m, ~ 1, weights = c(1, 2, 4)) # original weights multiplied by 7
```

```
 1       emmean    SE df lower.CL upper.CL
 overall      7 0.572 42     5.85     8.16

Results are averaged over the levels of: layer
Confidence level used: 0.95
```

If you want to use weights that do not sum to one, you can use the `contrast` function from the **emmeans** package (different from the function of the same name from **trtools**).

[1] The family-wise Type I error rate is the probability of making *at least one* Type I error. If it is desired that the family-wise Type I error rate be no greater than α (default is 0.05), then some adjustment can be made. This adjustment is seen in the p-values and confidence intervals. The most general method is to use `adjust = "mvt"`. Some special cases are more widely known such as Tukey (`adjust = "tukey"`) and Bonferroni (`adjust = "bonferroni"`), but the adjustment based on the multivariate t-distribution (`adjust = "mvt"`) is the most general and accurate. Note that an adjustment will produce "simultaneous" confidence intervals. A method of producing simultaneous confidence intervals has the property that the probability that *all* of the confidence intervals will contain the quantities being estimated is equal to the specified confidence level (95% by default). The multivariate t-distribution adjustment is perhaps not as well known, so a reference that you can cite is Edwards, D. & Berry, J. T. (1987). The efficiency of simulation-based multiple comparisons. *Biometrics*, *43(4)*, 913–928.

```r
emmeans(m, ~1, weights = c(1/7, 2/7, 4/7))
```

```
 1       emmean    SE df lower.CL upper.CL
 overall      7 0.572 42     5.85     8.16

Results are averaged over the levels of: layer
Confidence level used: 0.95
```

```r
emmeans::contrast(emmeans(m, ~layer), method = list(layer = c(1/7, 2/7, 4/7)), infer = TRUE)
```

```
 contrast estimate    SE df lower.CL upper.CL t.ratio p.value
 layer           7 0.572 42     5.85     8.16  12.245  <.0001

Confidence level used: 0.95
```

But suppose we wanted to estimate the *number* of daphnia in the lake (τ). It can be shown that this is

$$\tau = 700000\mu = 700000\left(\tfrac{1}{7}\mu_e + \tfrac{2}{7}\mu_t + \tfrac{4}{7}\mu_h\right) = 100000\mu_e + 200000\mu_t + 400000\mu_h.$$

Note that there are 700kL in the lake, which is 700000L (which is the scale used for the observations). This can be estimated as follows.

```r
emmeans::contrast(emmeans(m, ~layer),
  method = list(layer = 700000 *  c(1/7, 2/7, 4/7)), infer = TRUE)
```

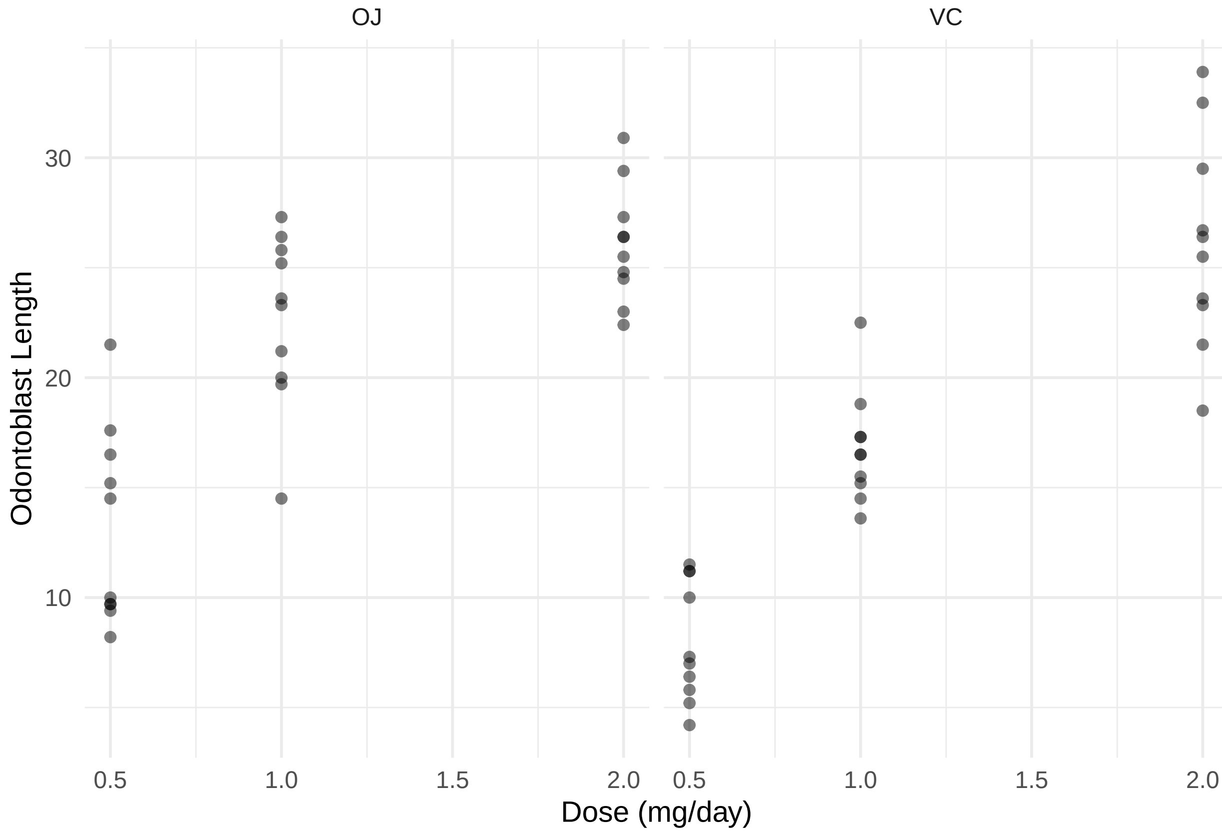
```
 contrast estimate    SE df lower.CL upper.CL t.ratio p.value
 layer     4903333 4e+05 42  4095230  5711437  12.245  <.0001

Confidence level used: 0.95
```

Another approach is to use `lincon` but your weights/coefficients will be different since they are applied to β_0, β_1, and β_2.

Marginal Means and "Main Effects"

Consider data from a randomized experiment with guinea pigs administered one of three doses of vitamin C (0.5, 1, or 2 mg/day) via one of two supplement methods: orange juice (OJ) or ascorbic acid (VC).

```r
p <- ggplot(ToothGrowth, aes(x = dose, y = len)) +
  geom_point(alpha = 0.5) + facet_wrap(~supp) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length") + theme_minimal()
plot(p)
```



Here we are going to model dose as a categorical variable so we need to coerce it to a factor. Perhaps the safest approach is to create a new variable.

```
ToothGrowth$dosef <- factor(ToothGrowth$dose)
```

Note: Whether a variable is a numeric, a factor, or something else can be seen use `str` (for "structure").

```
str(ToothGrowth)
```

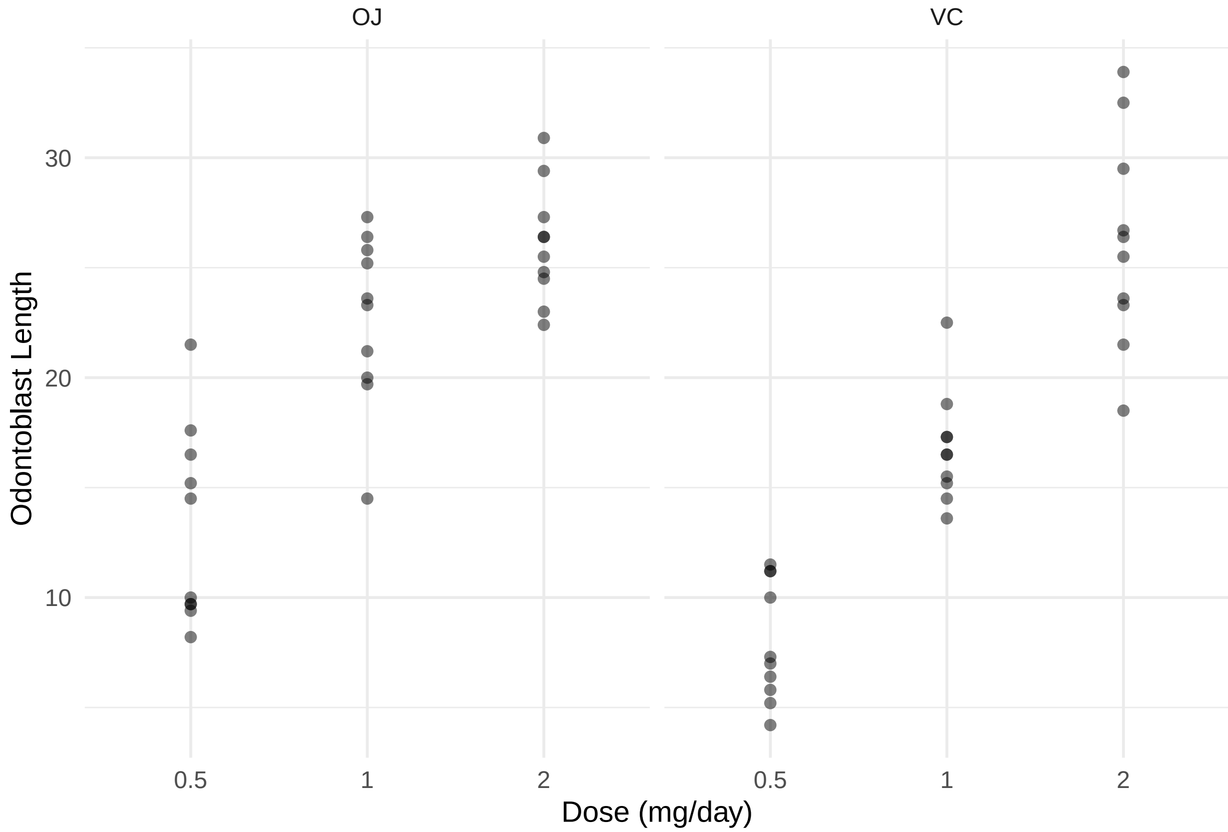
```
'data.frame':   60 obs. of  4 variables:
 $ len  : num  4.2 11.5 7.3 5.8 6.4 10 11.2 11.2 5.2 7 ...
 $ supp : Factor w/ 2 levels "OJ","VC": 2 2 2 2 2 2 2 2 2 2 ...
 $ dose : num  0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 ...
 $ dosef: Factor w/ 3 levels "0.5","1","2": 1 1 1 1 1 1 1 1 1 1 ...
```

Notice that `ggplot` responds differently.

```
summary(ToothGrowth)
```

```
      len        supp         dose       dosef 
 Min.   : 4.2   OJ:30   Min.   :0.50   0.5:20  
 1st Qu.:13.1   VC:30   1st Qu.:0.50   1  :20  
 Median :19.2           Median :1.00   2  :20  
 Mean   :18.8           Mean   :1.17           
 3rd Qu.:25.3           3rd Qu.:2.00           
 Max.   :33.9           Max.   :2.00           
```

```
p <- ggplot(ToothGrowth, aes(x = dosef, y = len)) +
  geom_point(alpha = 0.5) + facet_wrap(~supp) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length") + theme_minimal()
plot(p)
```



Now consider the following linear model.

```
m <- lm(len ~ dosef + supp + dosef:supp, data = ToothGrowth)
summary(m)$coefficients
```

```
               Estimate Std. Error t value  Pr(>|t|)
(Intercept)       13.23      1.148 11.5208 3.603e-16
dosef1             9.47      1.624  5.8312 3.176e-07
dosef2            12.83      1.624  7.9002 1.430e-10
suppVC            -5.25      1.624 -3.2327 2.092e-03
dosef1:suppVC     -0.68      2.297 -0.2961 7.683e-01
dosef2:suppVC      5.33      2.297  2.3207 2.411e-02
```

The model is

$$E(Y_i) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + \beta_4 x_{i4} + \beta_5 x_{i5},$$

where

$$x_{i1} = \begin{cases} 1, & \text{if dose is 1 mg/day,} \\ 0, & \text{otherwise,} \end{cases}$$

$$x_{i2} = \begin{cases} 1, & \text{if dose is 2 mg/day,} \\ 0, & \text{otherwise,} \end{cases}$$

$$x_{i3} = \begin{cases} 1, & \text{if supplement type is VC} \\ 0, & \text{otherwise,} \end{cases}$$

$$x_{i4} = x_{i1}x_{i3} = \begin{cases} 1, & \text{if dose is 1 mg/day and supplement type is VC,} \\ 0, & \text{otherwise,} \end{cases}$$

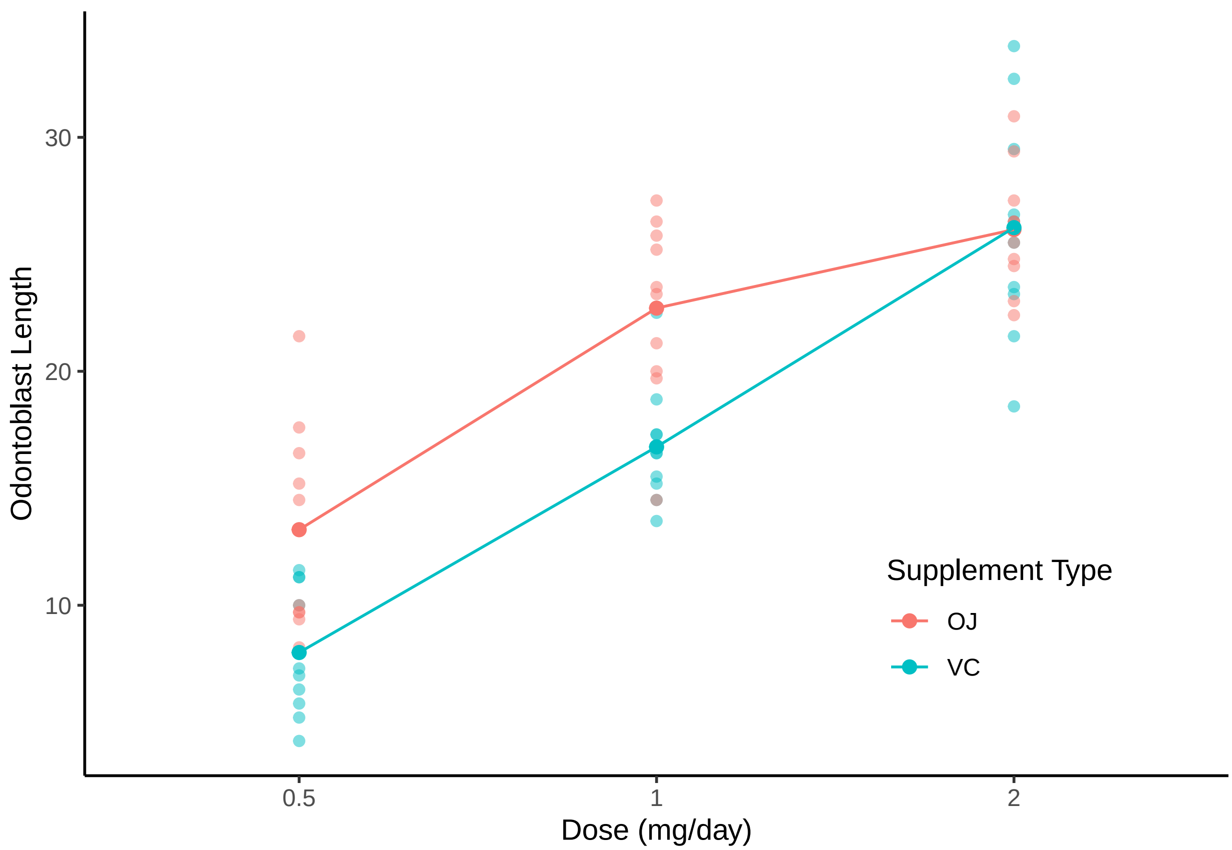
$$x_{i5} = x_{i2}x_{i3} = \begin{cases} 1, & \text{if dose is 2 mg/day and supplement type is VC,} \\ 0, & \text{otherwise.} \end{cases}$$

We can write this model case-wise.

$$E(Y_i) = \begin{cases} \beta_0, & \text{if dose is 0.5 mg/day and supplement type is OJ,} \\ \beta_0 + \beta_1, & \text{if dose is 1 mg/day and supplement type is OJ,} \\ \beta_0 + \beta_2, & \text{if dose is 2 mg/day and supplement type is OJ,} \\ \beta_0 + \beta_3, & \text{if dose is 0.5 mg/day and supplement type is VC,} \\ \beta_0 + \beta_1 + \beta_3 + \beta_4, & \text{if dose is 1 mg/day and supplement type is VC,} \\ \beta_0 + \beta_2 + \beta_3 + \beta_5, & \text{if dose is 2 mg/day and supplement type is VC.} \end{cases}$$

And we can visualize it.

```
d <- expand.grid(dosef = levels(ToothGrowth$dosef), supp = levels(ToothGrowth$supp))
d$yhat <- predict(m, newdata = d)

p <- ggplot(ToothGrowth, aes(x = dosef, y = len, color = supp)) +
  geom_point(alpha = 0.5) + theme_classic() +
  theme(legend.position = c(0.8,0.2)) +
  geom_point(aes(y = yhat), size = 2, data = d) +
  geom_line(aes(y = yhat, group = supp), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length", color = "Supplement Type")
plot(p)
```



We might want to compare the two supplement types at each dose level. These are sometimes called simple effects. We can do this using `contrast`.

```r
trtools::contrast(m,
    a = list(supp = "OJ", dosef = c("0.5","1","2")),
    b = list(supp = "VC", dosef = c("0.5","1","2")),
    cnames = c("OJ-VC @ 0.5 mg/day","OJ-VC @ 1.0 mg/day","OJ-VC @ 2.0 mg/day"))
```

```
                   estimate    se  lower upper   tvalue df    pvalue
OJ-VC @ 0.5 mg/day     5.25 1.624  1.994 8.506  3.23273 54 0.0020925
OJ-VC @ 1.0 mg/day     5.93 1.624  2.674 9.186  3.65144 54 0.0005897
OJ-VC @ 2.0 mg/day    -0.08 1.624 -3.336 3.176 -0.04926 54 0.9608934
```

We can also do this use `emmeans`. First note that we can use `emmeans` to also estimate the expected response for each level of `supp` within each level of `dosef`.

```r
emmeans(m, ~ supp | dosef)
```

```
dosef = 0.5:
 supp emmean   SE df lower.CL upper.CL
 OJ    13.23 1.15 54    10.93     15.5
 VC     7.98 1.15 54     5.68     10.3

dosef = 1:
 supp emmean   SE df lower.CL upper.CL
 OJ    22.70 1.15 54    20.40     25.0
 VC    16.77 1.15 54    14.47     19.1

dosef = 2:
 supp emmean   SE df lower.CL upper.CL
 OJ    26.06 1.15 54    23.76     28.4
 VC    26.14 1.15 54    23.84     28.4

Confidence level used: 0.95
```

We can use `pairs` to make inferences about the differences between levels of `supp` within each level of `dosef`.

```r
pairs(emmeans(m, ~ supp | dosef), adjust = "none", infer = TRUE)
```

```
dosef = 0.5:
 contrast estimate   SE df lower.CL upper.CL t.ratio p.value
 OJ - VC      5.25 1.62 54     1.99     8.51   3.233  0.0021

dosef = 1:
 contrast estimate   SE df lower.CL upper.CL t.ratio p.value
 OJ - VC      5.93 1.62 54     2.67     9.19   3.651  0.0006

dosef = 2:
 contrast estimate   SE df lower.CL upper.CL t.ratio p.value
 OJ - VC     -0.08 1.62 54    -3.34     3.18  -0.049  0.9609

Confidence level used: 0.95
```

The "main effect" of supplement method concerns μ_{OJ} and μ_{VC}, defined as

$$\mu_{\text{OJ}} = \frac{\mu_{\text{OJ},0.5} + \mu_{\text{OJ},1.0} + \mu_{\text{OJ},2.0}}{3}, \quad \mu_{\text{VC}} = \frac{\mu_{\text{VC},0.5} + \mu_{\text{VC},1.0} + \mu_{\text{OJ},2.0}}{3}.$$

So μ_{OJ} and μ_{VC} are the *marginal means* for `supp`, averaging over levels of `dose`.

```r
emmeans(m, ~ supp)
```

```
 supp emmean    SE df lower.CL upper.CL
 OJ     20.7 0.663 54     19.3     22.0
 VC     17.0 0.663 54     15.6     18.3

Results are averaged over the levels of: dosef 
Confidence level used: 0.95 
```

Inference for the main effect $\mu_{\text{OJ}} - \mu_{\text{VC}}$ can then be obtained as follows.

```r
pairs(emmeans(m, ~ supp), infer = TRUE)
```

```
 contrast estimate    SE df lower.CL upper.CL t.ratio p.value
 OJ - VC       3.7 0.938 54     1.82     5.58   3.946  0.0002

Results are averaged over the levels of: dosef 
Confidence level used: 0.95 
```

This main effect is simply a single linear function of $\beta_0, \beta_1, \dots, \beta_5$. From the case-wise representation of the model,

$$
E(Y_i) = \begin{cases}
\beta_0, & \text{if dose is 0.5 mg/day and supplement type is OJ,} \\
\beta_0 + \beta_1, & \text{if dose is 1 mg/day and supplement type is OJ,} \\
\beta_0 + \beta_2, & \text{if dose is 2 mg/day and supplement type is OJ,} \\
\beta_0 + \beta_3, & \text{if dose is 0.5 mg/day and supplement type is VC,} \\
\beta_0 + \beta_1 + \beta_3 + \beta_4, & \text{if dose is 1 mg/day and supplement type is VC,} \\
\beta_0 + \beta_2 + \beta_3 + \beta_5, & \text{if dose is 2 mg/day and supplement type is VC,}
\end{cases}
$$

we have that $\mu_{\text{OJ},0.5} = \beta_0$, $\mu_{\text{OJ},1.0} = \beta_0 + \beta_1$, $\mu_{\text{OJ},2.0} = \beta_0 + \beta_3$, $\mu_{\text{VC},0.5} = \beta_0 + \beta_3$, $\mu_{\text{VC},1.0} = \beta_0 + \beta_1 + \beta_3 + \beta_4$, $\mu_{\text{VC},2.0} = \beta_0 + \beta_1 + \beta_3 + \beta_5$. So, we can write this as

$$
\mu_{\text{OJ}} - \mu_{\text{VC}} = \frac{\mu_{\text{OJ},0.5} + \mu_{\text{OJ},1.0} + \mu_{\text{OJ},2.0}}{3} - \frac{\mu_{\text{VC},0.5} + \mu_{\text{VC},1.0} + \mu_{\text{OJ},2.0}}{3} = -\beta_3 - \frac{1}{3}\beta_4 - \frac{1}{3}\beta_5.
$$

```r
lincon(m, a = c(0,0,0,-1,-1/3,-1/3))
```

```
                           estimate     se lower upper tvalue df    pvalue
(0,0,0,-1,-1/3,-1/3),0          3.7 0.9376  1.82  5.58  3.946 54 0.0002312
```

Clearly using `emmeans` is much less tedious!

The "main effect" of dose concerns differences among the marginal means of dose defined as $\mu_{0.5}$, μ_1 and μ_2 where

$$
\mu_{0.5} = \frac{\mu_{\text{OJ},0.5} + \mu_{\text{VC},0.5}}{2}, \quad \mu_1 = \frac{\mu_{\text{OJ},1} + \mu_{\text{VC},1}}{2}, \quad \mu_2 = \frac{\mu_{\text{OJ},2} + \mu_{\text{VC},2}}{2}.
$$

```r
emmeans(m, ~ dosef)
```

```
 dosef emmean    SE df lower.CL upper.CL
 0.5     10.6 0.812 54     8.98     12.2
 1       19.7 0.812 54    18.11     21.4
 2       26.1 0.812 54    24.47     27.7

Results are averaged over the levels of: supp 
Confidence level used: 0.95 
```

```r
pairs(emmeans(m, ~ dosef), adjust = "none")
```

```
 contrast          estimate   SE df t.ratio p.value
 dosef0.5 - dosef1    -9.13 1.15 54  -7.951  <.0001
 dosef0.5 - dosef2   -15.49 1.15 54 -13.493  <.0001
 dosef1 - dosef2      -6.37 1.15 54  -5.543  <.0001

Results are averaged over the levels of: supp 
```

```
pairs(emmeans(m, ~ dosef), reverse = TRUE, adjust = "none")
```

```
 contrast          estimate   SE df t.ratio p.value
 dosef1 - dosef0.5     9.13 1.15 54   7.951  <.0001
 dosef2 - dosef0.5    15.49 1.15 54  13.493  <.0001
 dosef2 - dosef1       6.37 1.15 54   5.543  <.0001

Results are averaged over the levels of: supp 
```

In ANOVA tables the test of the "main effect" is the (joint) null hypothesis that all pairwise differences are zero. For the variable dose the null hypothesis is $\mu_{0.5} = \mu_1 = \mu_2$. This can be done using the `test` function.

```
test(pairs(emmeans(m, ~ dosef)), joint = TRUE)
```

```
 df1 df2 F.ratio p.value note
   2  54  92.000  <.0001  d  

d: df1 reduced due to linear dependence 
```

This is the traditional main effect that is sometimes reported in an "ANOVA table" such as that produced by `Anova` from the **car** package.

```
library(car)
m <- lm(len ~ dosef + supp + dosef:supp, data = ToothGrowth,
  contrast = list(dosef = contr.sum, supp = contr.sum))
Anova(m, type = 3)
```

```
Anova Table (Type III tests)

Response: len
            Sum Sq Df F value  Pr(>F)    
(Intercept)  21236  1 1610.39 < 2e-16 ***
dosef         2426  2   92.00 < 2e-16 ***
supp           205  1   15.57 0.00023 ***
dosef:supp     108  2    4.11 0.02186 *  
Residuals      712 54                    
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The option `contrast = list(dosef = contr.sum, supp = contr.sum)` is necessary here for the `Anova` function to do the correct calculations.[2]

The test of the main effect of supplement method was given by

```
pairs(emmeans(m, ~ supp), infer = TRUE)
```

```
 contrast estimate    SE df lower.CL upper.CL t.ratio p.value
 OJ - VC       3.7 0.938 54     1.82     5.58   3.946  0.0002
```

[2]I am demonstrating here what is sometimes called inferences based on Type III sums of squares. Another common approach is to use what is called Type II sums of squares. This can be done with the `Anova` function with `type = 2`. For inferences based on Type II sums of squares with the functions from the **emmeans** package an extra step is needed (email me for an example if you really want to know how to do it).

```
Results are averaged over the levels of: dosef
Confidence level used: 0.95
```

We do not need a joint test here since there are only two marginal means, but here it is anyway.

```
test(pairs(emmeans(m, ~ supp)), joint = TRUE)
```

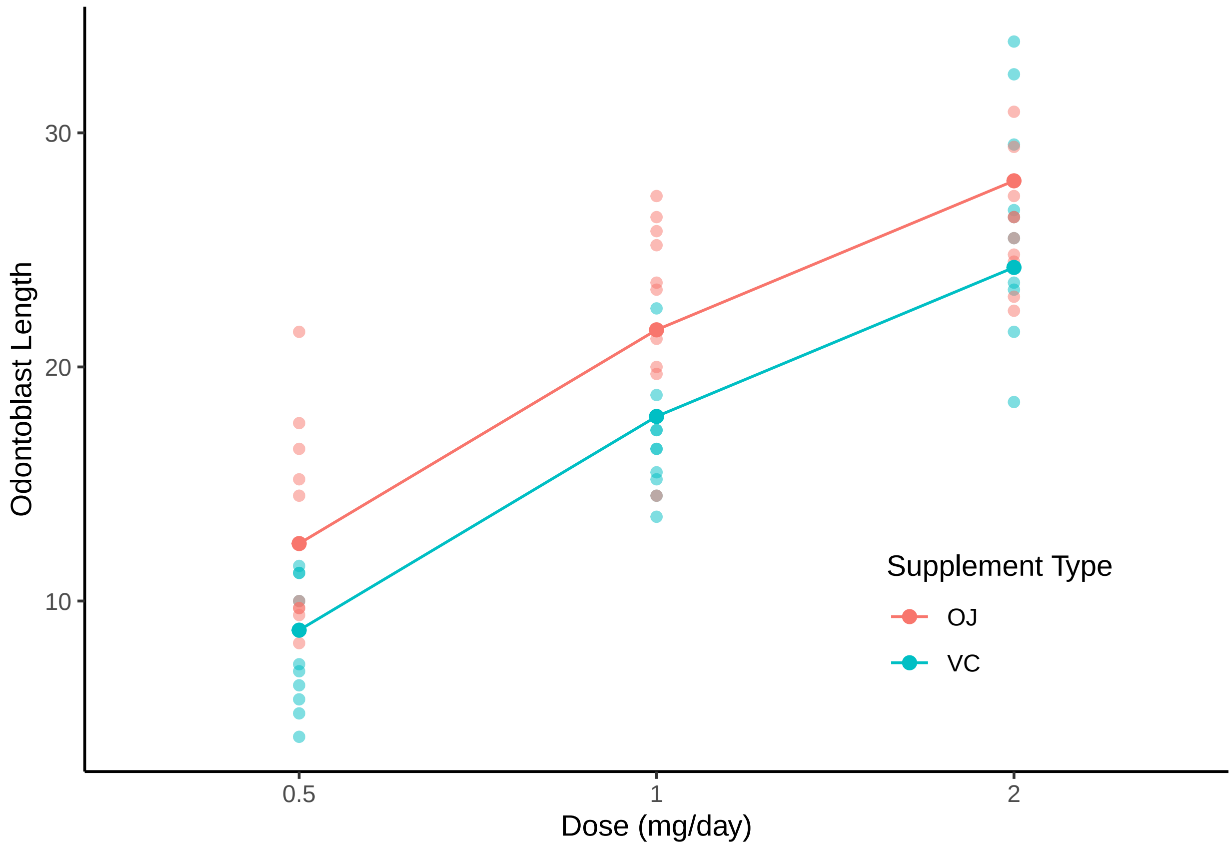
```
 df1 df2 F.ratio p.value
   1  54  15.572  0.0002
```

Now consider a model without the interaction.

```
m <- lm(len ~ dosef + supp, data = ToothGrowth)
summary(m)$coefficients
```

```
            Estimate Std. Error t value  Pr(>|t|)
(Intercept)    12.45     0.9883  12.603 5.490e-18
dosef1          9.13     1.2104   7.543 4.383e-10
dosef2         15.50     1.2104  12.802 2.852e-18
suppVC         -3.70     0.9883  -3.744 4.293e-04
```

```
d <- expand.grid(dosef = levels(ToothGrowth$dosef), supp = levels(ToothGrowth$supp))
d$yhat <- predict(m, newdata = d)

p <- ggplot(ToothGrowth, aes(x = dosef, y = len, color = supp)) +
  geom_point(alpha = 0.5) + theme_classic() +
  theme(legend.position = c(0.8,0.2)) +
  geom_point(aes(y = yhat), size = 2, data = d) +
  geom_line(aes(y = yhat, group = supp), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length", color = "Supplement Type")
plot(p)
```



Note that without the interaction the "simple effects" and "main effects" are equivalent. Here are the simple and main effects for supplement.

```
pairs(emmeans(m, ~ supp | dosef)) # simple
```

```
dosef = 0.5:
 contrast estimate    SE df t.ratio p.value
 OJ - VC       3.7 0.988 56   3.744  0.0004

dosef = 1:
 contrast estimate    SE df t.ratio p.value
 OJ - VC       3.7 0.988 56   3.744  0.0004

dosef = 2:
 contrast estimate    SE df t.ratio p.value
 OJ - VC       3.7 0.988 56   3.744  0.0004
```

```
pairs(emmeans(m, ~ supp))          # main
```

```
 contrast estimate    SE df t.ratio p.value
 OJ - VC       3.7 0.988 56   3.744  0.0004

Results are averaged over the levels of: dosef
```

And here are the simple and main effects for dose.

```
pairs(emmeans(m, ~ dosef | supp), adjust = "none") # simple
```

```
supp = OJ:
 contrast          estimate    SE df t.ratio p.value
```

```
 dosef0.5 - dosef1    -9.13 1.21 56  -7.543  <.0001
 dosef0.5 - dosef2   -15.49 1.21 56 -12.802  <.0001
 dosef1 - dosef2      -6.37 1.21 56  -5.259  <.0001

supp = VC:
 contrast          estimate   SE df t.ratio p.value
 dosef0.5 - dosef1    -9.13 1.21 56  -7.543  <.0001
 dosef0.5 - dosef2   -15.49 1.21 56 -12.802  <.0001
 dosef1 - dosef2      -6.37 1.21 56  -5.259  <.0001
```

```r
pairs(emmeans(m, ~ dosef), adjust = "none")        # main
```

```
 contrast          estimate   SE df t.ratio p.value
 dosef0.5 - dosef1    -9.13 1.21 56  -7.543  <.0001
 dosef0.5 - dosef2   -15.49 1.21 56 -12.802  <.0001
 dosef1 - dosef2      -6.37 1.21 56  -5.259  <.0001

Results are averaged over the levels of: supp
```

The joint test of the overall main effect for dose can be be obtained as follows.

```r
test(pairs(emmeans(m, ~ dosef)), joint = TRUE)
```

```
 df1 df2 F.ratio p.value note
   2  56  82.810  <.0001  d

d: df1 reduced due to linear dependence
```