Friday, March 7

Using the emmeans Package for Poisson and Logistic Regression

The **emmeans** package can be used to produce many of the same inferences that are obtained using `contrast` with respect to estimated expected rates/probabilities as well as rate/odds ratios.

Example: Consider the following Poisson regression model for the `ceriodaphniastrain` data. I have renamed `concentration` and the categories of `strain` to make the example clearer.

```
library(dplyr)
waterfleas <- trtools::ceriodaphniastrain |>
  mutate(strain = factor(strain, levels = c(1,2), labels = c("a","b"))) |>
  rename(conc = concentration)
m <- glm(count ~ conc * strain, family = poisson, data = waterfleas)
summary(m)$coefficients
```

```
             Estimate Std. Error z value  Pr(>|z|)
(Intercept)     4.481     0.0435  103.01  0.00e+00
conc           -1.598     0.0624  -25.59 1.86e-144
strainb        -0.337     0.0670   -5.02  5.11e-07
conc:strainb    0.125     0.0939    1.34  1.82e-01
```

We can compute the expected count for a concentration of two for each strain using `contrast`.

```
trtools::contrast(m, tf = exp,
  a = list(strain = c("a","b"), conc = 2))
```

```
 estimate lower upper
     3.62  2.97  4.40
     3.32  2.67  4.12
```

And we can do it using `emmeans` if we specify `type = "response"` and use the `at` argument to specify the value of any quantitative explanatory variables.

```
library(emmeans)
emmeans(m, ~ strain, type = "response", at = list(conc = 2))
```

```
 strain rate    SE  df asymp.LCL asymp.UCL
 a      3.62 0.363 Inf      2.97      4.40
 b      3.32 0.367 Inf      2.67      4.12

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

```
emmeans(m, ~ strain|conc, type = "response", at = list(conc = c(1,2,3)))
```

```
conc = 1:
 strain  rate    SE  df asymp.LCL asymp.UCL
 a      17.87 0.815 Inf     16.34     19.54
 b      14.47 0.725 Inf     13.11     15.96

conc = 2:
```

```
 strain  rate    SE  df asymp.LCL asymp.UCL
 a       3.62 0.363 Inf      2.97      4.40
 b       3.32 0.367 Inf      2.67      4.12

conc = 3:
 strain  rate    SE  df asymp.LCL asymp.UCL
 a       0.73 0.118 Inf      0.53      1.00
 b       0.76 0.136 Inf      0.54      1.08

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

```
emmeans(m, ~ conc|strain, type = "response", at = list(conc = c(1,2,3)))
```

```
strain = a:
 conc  rate    SE  df asymp.LCL asymp.UCL
    1 17.87 0.815 Inf     16.34     19.54
    2  3.62 0.363 Inf      2.97      4.40
    3  0.73 0.118 Inf      0.53      1.00

strain = b:
 conc  rate    SE  df asymp.LCL asymp.UCL
    1 14.47 0.725 Inf     13.11     15.96
    2  3.32 0.367 Inf      2.67      4.12
    3  0.76 0.136 Inf      0.54      1.08

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

```
emmeans(m, ~ conc*strain, type = "response", at = list(conc = c(1,2,3)))
```

```
 conc strain  rate    SE  df asymp.LCL asymp.UCL
    1 a      17.87 0.815 Inf     16.34     19.54
    2 a       3.62 0.363 Inf      2.97      4.40
    3 a       0.73 0.118 Inf      0.53      1.00
    1 b      14.47 0.725 Inf     13.11     15.96
    2 b       3.32 0.367 Inf      2.67      4.12
    3 b       0.76 0.136 Inf      0.54      1.08

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

Note that `emmeans` does produce a valid standard error on the scale of the expected count/rate which `trtools::contrast` does not (by default), and that `trtools::contrast` will show the test statistic and p-value on the log scale if we omit the `tf = exp` argument.

We can compute the rate ratio to compare the two strains at a given concentration.

```
trtools::contrast(m, tf = exp,
  a = list(strain = "a", conc = 2),
  b = list(strain = "b", conc = 2))
```

```
 estimate lower upper
     1.09 0.813  1.46
```

```
pairs(emmeans(m, ~ strain, type = "response",
  at = list(conc = 2)), infer = TRUE)
```

```
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b     1.09 0.163 Inf     0.813      1.46    1   0.576  0.5650

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

```
pairs(emmeans(m, ~ strain|conc, type = "response",
  at = list(conc = c(1,2,3))), infer = TRUE)
```

```
conc = 1:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    1.235 0.0837 Inf     1.082      1.41    1   3.118  0.0020

conc = 2:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    1.090 0.1630 Inf     0.813      1.46    1   0.576  0.5650

conc = 3:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    0.961 0.2310 Inf     0.601      1.54    1  -0.164  0.8700

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

Note that you can use `reverse = TRUE` to “flip” a rate (or odds) ratio.

```
pairs(emmeans(m, ~ strain|conc, type = "response",
  at = list(conc = c(1,2,3))), infer = TRUE, reverse = TRUE)
```

```
conc = 1:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 b / a    0.810 0.0549 Inf     0.709     0.925    1  -3.118  0.0020

conc = 2:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 b / a    0.918 0.1370 Inf     0.685     1.230    1  -0.576  0.5650

conc = 3:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 b / a    1.040 0.2500 Inf     0.650     1.665    1   0.164  0.8700

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

If we apply `pairs` when using `*` we will get all possible pairwise comparisons.

```
pairs(emmeans(m, ~ strain*conc, type = "response",
  at = list(conc = c(1,2,3))), infer = TRUE)
```

```
 contrast          ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a conc1 / b conc1  1.24 0.08 Inf      1.02       1.5    1   3.120  0.0220
 a conc1 / a conc2  4.94 0.31 Inf      4.14       5.9    1  25.590  <.0001
 a conc1 / b conc2  5.39 0.64 Inf      3.83       7.6    1  14.070  <.0001
 a conc1 / a conc3 24.43 3.05 Inf     17.11      34.9    1  25.590  <.0001
```

```
 a conc1 / b conc3 23.49 4.32 Inf     13.90      39.7    1  17.150  <.0001
 b conc1 / a conc2  4.00 0.45 Inf      2.91       5.5    1  12.360  <.0001
 b conc1 / b conc2  4.36 0.31 Inf      3.57       5.3    1  21.010  <.0001
 b conc1 / a conc3 19.77 3.33 Inf     12.24      32.0    1  17.720  <.0001
 b conc1 / b conc3 19.01 2.66 Inf     12.75      28.3    1  21.010  <.0001
 a conc2 / b conc2  1.09 0.16 Inf      0.71       1.7    1   0.580  0.9930
 a conc2 / a conc3  4.94 0.31 Inf      4.14       5.9    1  25.590  <.0001
 a conc2 / b conc3  4.75 0.97 Inf      2.65       8.5    1   7.620  <.0001
 b conc2 / a conc3  4.54 0.89 Inf      2.60       7.9    1   7.750  <.0001
 b conc2 / b conc3  4.36 0.31 Inf      3.57       5.3    1  21.010  <.0001
 a conc3 / b conc3  0.96 0.23 Inf      0.49       1.9    1  -0.160  1.0000

Confidence level used: 0.95 
Conf-level adjustment: tukey method for comparing a family of 6 estimates 
Intervals are back-transformed from the log scale 
P value adjustment: tukey method for comparing a family of 6 estimates 
Tests are performed on the log scale 
```

To force `pairs` to only do pairwise comparisons within each value of concentration use `by = "concentration"`.

```r
pairs(emmeans(m, ~ strain*conc, type = "response",
  at = list(conc = c(1,2,3))), by = "conc", infer = TRUE)
```

```
conc = 1:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    1.235 0.0837 Inf     1.082      1.41    1   3.118  0.0020

conc = 2:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    1.090 0.1630 Inf     0.813      1.46    1   0.576  0.5650

conc = 3:
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 a / b    0.961 0.2310 Inf     0.601      1.54    1  -0.164  0.8700

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

Or alternatively use `~ strain|concentration` in the `emmeans` function.

What about the rate ratio for the effect of concentration?

```r
trtools::contrast(m, tf = exp,
  a = list(strain = c("a","b"), conc = 2),
  b = list(strain = c("a","b"), conc = 1))
```

```
 estimate lower upper
    0.202 0.179 0.229
    0.229 0.200 0.263
```

```r
emmeans(m, ~conc|strain,
  at = list(conc = c(2,1)), type = "response")
```

```
strain = a:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.62 0.363 Inf      2.97      4.40
    1 17.87 0.815 Inf     16.34     19.54
```

```
strain = b:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.32 0.367 Inf      2.67      4.12
    1 14.47 0.725 Inf     13.11     15.96

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

```
pairs(emmeans(m, ~conc|strain,
  at = list(conc = c(2,1)), type = "response"), infer = TRUE)
```

```
strain = a:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.202 0.0126 Inf     0.179     0.229    1 -25.590  <.0001

strain = b:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.229 0.0161 Inf     0.200     0.263    1 -21.010  <.0001

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

```
pairs(emmeans(m, ~conc*strain,
  at = list(conc = c(2,1)), type = "response"), infer = TRUE, by = "strain")
```

```
strain = a:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.202 0.0126 Inf     0.179     0.229    1 -25.590  <.0001

strain = b:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.229 0.0161 Inf     0.200     0.263    1 -21.010  <.0001

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

What if we want to know if the rate ratios are significantly different? There are a couple of ways to do this. We can compare the odds ratios for the effect of concentration.

```
pairs(pairs(emmeans(m, ~conc|strain,
  at = list(conc = c(2,1)), type = "response")), by = NULL)
```

```
 contrast                              ratio     SE  df null z.ratio p.value
 (conc2 / conc1 a) / (conc2 / conc1 b) 0.882 0.0828 Inf    1  -1.336  0.1817

Tests are performed on the log scale
```

You can also use `emtrends`, which is simpler, but limited to a one-unit increase in the quantitative variable.

```
emtrends(m, ~strain, var = "conc")
```

```
 strain conc.trend     SE  df asymp.LCL asymp.UCL
 a           -1.60 0.0624 Inf     -1.72     -1.48
 b           -1.47 0.0701 Inf     -1.61     -1.33
```

```
Confidence level used: 0.95
```

```r
pairs(emtrends(m, ~strain, var = "conc"))
```

```
 contrast estimate     SE  df z.ratio p.value
 a - b      -0.125 0.0939 Inf  -1.336  0.1817
```

Note that these are essentially slopes but for the log of the expected response. But the tests are the same.

Suppose there was a third explanatory variable, say two types of chemicals (note that there are several possible models here depending on which interactions are specified).

```r
set.seed(123)
waterfleas <- waterfleas |>
  mutate(chemical = sample(c("chem1","chem2"), n(), replace = TRUE))
m <- glm(count ~ conc * strain * chemical, family = poisson, data = waterfleas)
summary(m)$coefficients
```

```
                           Estimate Std. Error  z value  Pr(>|z|)
(Intercept)                  4.4747     0.0510  87.7927  0.00e+00
conc                        -1.5860     0.0729 -21.7686 4.60e-105
strainb                     -0.2949     0.0900  -3.2778  1.05e-03
chemicalchem2                0.0269     0.0989   0.2720  7.86e-01
conc:strainb                 0.1182     0.1198   0.9862  3.24e-01
conc:chemicalchem2          -0.0464     0.1427  -0.3249  7.45e-01
strainb:chemicalchem2       -0.0919     0.1422  -0.6467  5.18e-01
conc:strainb:chemicalchem2   0.0118     0.2017   0.0584  9.53e-01
```

```r
emmeans(m, ~conc|strain*chemical,
  at = list(conc = c(2,1)), type = "response")
```

```
strain = a, chemical = chem1:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.68 0.440 Inf      2.91      4.65
    1 17.97 1.010 Inf     16.10     20.05

strain = b, chemical = chem1:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.47 0.500 Inf      2.62      4.60
    1 15.06 0.962 Inf     13.29     17.07

strain = a, chemical = chem2:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.44 0.651 Inf      2.38      4.99
    1 17.62 1.410 Inf     15.07     20.61

strain = b, chemical = chem2:
 conc  rate    SE  df asymp.LCL asymp.UCL
    2  3.03 0.532 Inf      2.15      4.28
    1 13.63 1.100 Inf     11.63     15.98

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

```r
pairs(emmeans(m, ~conc|strain*chemical,
  at = list(conc = c(2,1)), type = "response"), infer = TRUE)
```

```
strain = a, chemical = chem1:
```

```
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.205 0.0149 Inf     0.177     0.236    1 -21.770  <.0001

strain = b, chemical = chem1:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.230 0.0219 Inf     0.191     0.278    1 -15.420  <.0001

strain = a, chemical = chem2:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.196 0.0240 Inf     0.154     0.249    1 -13.300  <.0001

strain = b, chemical = chem2:
 contrast      ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 conc2 / conc1 0.223 0.0236 Inf     0.181     0.274    1 -14.160  <.0001

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

Example: Consider the following logistic regression model for the `insecticide data`.

```r
m <- glm(cbind(deaths, total-deaths) ~ insecticide * deposit,
  family = binomial, data = trtools::insecticide)
summary(m)$coefficients
```

```
                        Estimate Std. Error z value Pr(>|z|)
(Intercept)              -2.8109     0.3585 -7.8418 4.44e-15
insecticideboth           1.2258     0.6718  1.8247 6.80e-02
insecticideDDT           -0.0389     0.5072 -0.0768 9.39e-01
deposit                   0.6221     0.0779  7.9899 1.35e-15
insecticideboth:deposit   0.3701     0.2090  1.7711 7.65e-02
insecticideDDT:deposit   -0.1414     0.1038 -1.3630 1.73e-01
```

We can use `trtools::contrast` or `emmeans` to produce estimates of the probability of death for a given insecticide at a given deposit value.

```r
trtools::contrast(m, tf = plogis,
  a = list(insecticide = c("g-BHC","both","DDT"), deposit = 5),
  cnames = c("g-BHC","both","DDT"))
```

```
      estimate lower upper
g-BHC    0.574 0.503 0.643
both     0.967 0.921 0.987
DDT      0.390 0.329 0.455
```

```r
emmeans(m, ~ insecticide, type = "response", at = list(deposit = 5))
```

```
 insecticide  prob     SE  df asymp.LCL asymp.UCL
 g-BHC       0.574 0.0360 Inf     0.503     0.643
 both        0.967 0.0150 Inf     0.921     0.987
 DDT         0.390 0.0323 Inf     0.329     0.455

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

Again, `emmeans` produces a valid standard error on the probability scale while `trtools::contrast` does not, and `trtools::contrast` will produce test statistics and p-values on the logit scale when the `tf = plogis` argument is omitted.

We can compute odds ratios to compare the insecticides at a given deposit.

```
pairs(emmeans(m, ~ insecticide, type = "response",
  at = list(deposit = 5)), adjust = "none", infer = TRUE)
```

```
 contrast       odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.0  0.02 Inf      0.02       0.1    1  -6.270  <.0001
 (g-BHC) / DDT         2.1  0.42 Inf      1.42       3.1    1   3.720  0.0002
 both / DDT           45.7 22.30 Inf     17.60     118.7    1   7.850  <.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 
```

```
trtools::contrast(m, tf = exp,
  a = list(insecticide = c("g-BHC","g-BHC","both"), deposit = 5),
  b = list(insecticide = c("both","DDT","DDT"), deposit = 5),
  cnames = c("g-BHC / both", "g-BHC / DDT", "both / DDT"))
```

```
             estimate   lower   upper
g-BHC / both   0.0461  0.0176   0.121
g-BHC / DDT    2.1087  1.4239   3.123
both / DDT    45.7110 17.5995 118.724
```

We can flip/reverse the odds ratios if desired (which can also be done with rate ratios).

```
pairs(emmeans(m, ~ insecticide, type = "response",
  at = list(deposit = 5)), adjust = "none", reverse = TRUE, infer = TRUE)
```

```
 contrast       odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 both / (g-BHC)      21.68 10.60 Inf      8.29      56.7    1   6.270  <.0001
 DDT / (g-BHC)        0.47  0.10 Inf      0.32       0.7    1  -3.720  0.0002
 DDT / both           0.02  0.01 Inf      0.01       0.1    1  -7.850  <.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 
```

```
trtools::contrast(m, tf = exp,
  a = list(insecticide = c("both","DDT","DDT"), deposit = 5),
  b = list(insecticide = c("g-BHC","g-BHC","both"), deposit = 5),
  cnames = c("both / g-BHC", "DDT / g-BHC", "DDT / both"))
```

```
             estimate   lower   upper
both / g-BHC  21.6772 8.29252 56.6658
DDT / g-BHC    0.4742 0.32021  0.7023
DDT / both     0.0219 0.00842  0.0568
```

We can estimate the odds ratios at several values of deposit.

```
pairs(emmeans(m, ~ insecticide|deposit, type = "response",
  at = list(deposit = c(4,5,6))), adjust = "none", infer = TRUE)
```

```
deposit = 4:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.1  0.0 Inf      0.04       0.1    1  -8.240  <.0001
 (g-BHC) / DDT         1.8  0.4 Inf      1.23       2.7    1   3.000  0.0027
 both / DDT           27.4  9.1 Inf     14.27      52.6    1   9.950  <.0001
```

```
deposit = 5:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.0  0.0 Inf      0.02       0.1    1  -6.270  <.0001
 (g-BHC) / DDT         2.1  0.4 Inf      1.42       3.1    1   3.720  0.0002
 both / DDT           45.7 22.3 Inf     17.60     118.7    1   7.850  <.0001

deposit = 6:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.0  0.0 Inf      0.01       0.1    1  -5.080  <.0001
 (g-BHC) / DDT         2.4  0.6 Inf      1.50       3.9    1   3.580  0.0003
 both / DDT           76.2 51.0 Inf     20.53     283.1    1   6.470  <.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, ~ insecticide*deposit, type = "response",
  at = list(deposit = c(4,5,6))), by = "deposit", adjust = "none", infer = TRUE)
```

```
deposit = 4:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.1  0.0 Inf      0.04       0.1    1  -8.240  <.0001
 (g-BHC) / DDT         1.8  0.4 Inf      1.23       2.7    1   3.000  0.0027
 both / DDT           27.4  9.1 Inf     14.27      52.6    1   9.950  <.0001

deposit = 5:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.0  0.0 Inf      0.02       0.1    1  -6.270  <.0001
 (g-BHC) / DDT         2.1  0.4 Inf      1.42       3.1    1   3.720  0.0002
 both / DDT           45.7 22.3 Inf     17.60     118.7    1   7.850  <.0001

deposit = 6:
 contrast       odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 (g-BHC) / both        0.0  0.0 Inf      0.01       0.1    1  -5.080  <.0001
 (g-BHC) / DDT         2.4  0.6 Inf      1.50       3.9    1   3.580  0.0003
 both / DDT           76.2 51.0 Inf     20.53     283.1    1   6.470  <.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
```

Here is how we can estimate the odds ratios for the effect of deposit.

```r
emmeans(m, ~deposit|insecticide, at = list(deposit = c(2,1)), type = "response") # probability
```

```
insecticide = g-BHC:
 deposit  prob     SE  df asymp.LCL asymp.UCL
       2 0.173 0.0318 Inf     0.119     0.244
       1 0.101 0.0261 Inf     0.060     0.165

insecticide = both:
 deposit  prob     SE  df asymp.LCL asymp.UCL
       2 0.598 0.0566 Inf     0.484     0.703
       1 0.356 0.0892 Inf     0.205     0.542

insecticide = DDT:
```

```
 deposit  prob     SE  df asymp.LCL asymp.UCL
       2 0.131 0.0271 Inf     0.087     0.194
       1 0.086 0.0232 Inf     0.050     0.143

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

```
pairs(emmeans(m, ~deposit|insecticide, at = list(deposit = c(2,1)), 
  type = "response"), infer = TRUE) # odds ratios
```

```
insecticide = g-BHC:
 contrast            odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 deposit2 / deposit1       1.86 0.145 Inf      1.60      2.17    1   7.990  <.0001

insecticide = both:
 contrast            odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 deposit2 / deposit1       2.70 0.523 Inf      1.84      3.94    1   5.120  <.0001

insecticide = DDT:
 contrast            odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 deposit2 / deposit1       1.62 0.111 Inf      1.41      1.85    1   7.010  <.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 
```

We can also compare the odds ratios.

```
pairs(pairs(emmeans(m, ~deposit|insecticide, at = list(deposit = c(2,1)))), by = NULL)
```

```
 contrast                                                estimate    SE  df z.ratio p.value
 (deposit2 - deposit1 g-BHC) - (deposit2 - deposit1 both)  -0.370 0.209 Inf  -1.771  0.1790
 (deposit2 - deposit1 g-BHC) - (deposit2 - deposit1 DDT)    0.141 0.104 Inf   1.363  0.3600
 (deposit2 - deposit1 both) - (deposit2 - deposit1 DDT)     0.512 0.206 Inf   2.487  0.0340

Results are given on the log odds ratio (not the response) scale. 
P value adjustment: tukey method for comparing a family of 3 estimates 
```

For odds ratios for a quantitative variable you can also compare using `emtrends`.

```
pairs(emtrends(m, ~insecticide, var = "deposit"))
```

```
 contrast       estimate    SE  df z.ratio p.value
 (g-BHC) - both   -0.370 0.209 Inf  -1.771  0.1790
 (g-BHC) - DDT     0.141 0.104 Inf   1.363  0.3600
 both - DDT        0.512 0.206 Inf   2.487  0.0340

P value adjustment: tukey method for comparing a family of 3 estimates 
```

Here I have left off `type = "response"`. Including it will give ratios of odds ratios, which is a bit confusing, but if all we care about is whether the odds ratios are significantly different this is sufficient. Note that to avoid controlling for family-wise Type I error rate include the option `adjust = "none"` as an argument to `pairs`.

Relationship Between Poisson and Logistic Regression

Suppose C_i has a binomial distribution with parameters p_i and m_i so that

$$P(C_i = c) = \binom{m_i}{c} p_i^y (1 - p_i)^{m_i - c}.$$

Define the expected count as $E(C_i) = m_i p_i = \lambda_i$. Then $p_i = \lambda_i / m_i$ so we can write

$$P(C_i = c) = \binom{m_i}{c} \left(\frac{\lambda_i}{m_i}\right)^y \left(1 - \frac{\lambda_i}{m_i}\right)^{c-y}.$$

Then it can be shown that

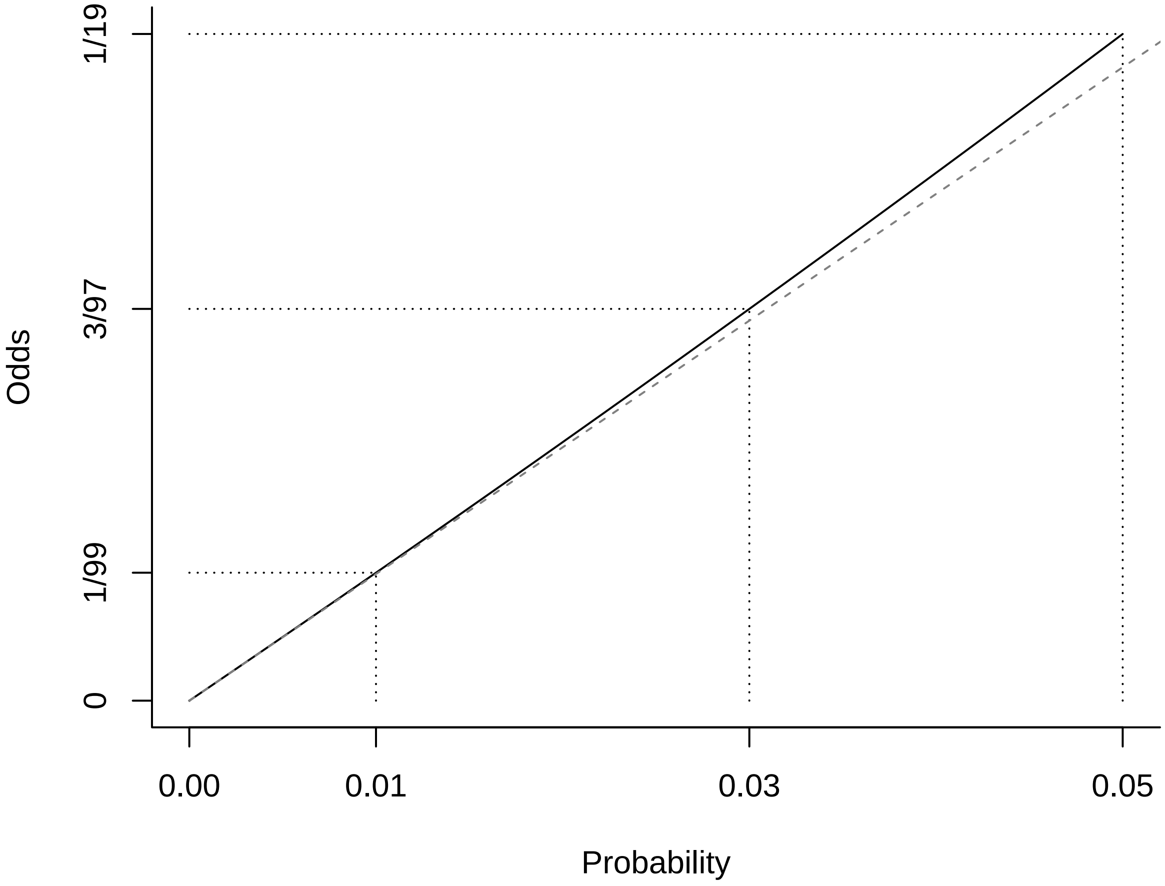
$$\lim_{m_i \to \infty} \binom{m_i}{c} \left(\frac{\lambda_i}{m_i}\right)^y \left(1 - \frac{\lambda_i}{m_i}\right)^{m_i - y} = \frac{e^{\lambda_i} \lambda_i^y}{y!},$$

which is the Poisson distribution.

Thus *in practice* if p_i is small relative to m_i we can *approximate a binomial distribution with a Poisson distribution*. Furthermore there is a close relationship between the model parameters. In logistic regression we have

$$O_i = \exp(\beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}),$$

where $O_i = p_i/(1 - p_i)$ is the odds of the event. But when p_i is very small then $O_i \approx p_i$.



So then

$$p_i \approx \exp(\beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}),$$

and because $E(C_i) = m_i p_i$,

$$E(C_i) \approx \exp(\log m_i + \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}),$$

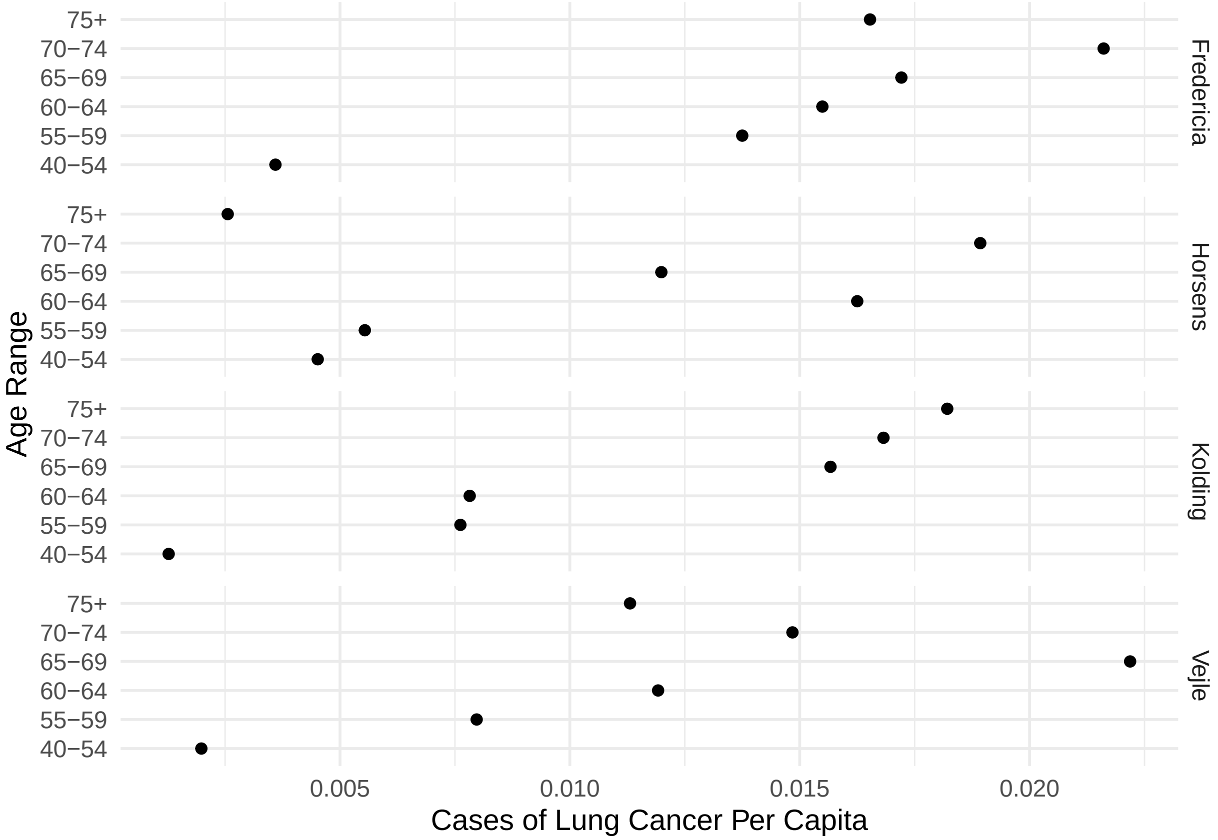
where $\log m_i$ is used as an offset in a Poisson regression model. That is, we can model a proportion (approximately) as a rate in a Poisson regression model for events that are rare and when m_i (i.e., the denominator of the proportion) is relatively large. This is relatively common in large-scale observational studies.

Example: Consider the following data on the incidence of lung cancer in four Danish cities.

```r
library(ISwR) # for eba1977 data
head(eba1977)
```

```
        city   age  pop cases
1 Fredericia 40-54 3059    11
2    Horsens 40-54 2879    13
3    Kolding 40-54 3142     4
4      Vejle 40-54 2520     5
5 Fredericia 55-59  800    11
6    Horsens 55-59 1083     6
```

```r
p <- ggplot(eba1977, aes(x = age, y = cases/pop)) +
  geom_point() + facet_grid(city ~ .) + coord_flip() +
  labs(x = "Age Range", y = "Cases of Lung Cancer Per Capita") +
  theme_minimal()
plot(p)
```



Consider both a logistic and Poisson regression models to compare the cities while controlling for age.

```
m.b <- glm(cbind(cases, pop-cases) ~ city + age, family = binomial, data = eba1977)
cbind(summary(m.b)$coefficients, confint(m.b))
```

```
            Estimate Std. Error z value  Pr(>|z|)  2.5 %   97.5 %
(Intercept)   -5.626      0.201  -28.02 9.13e-173 -6.039 -5.24980
cityHorsens   -0.334      0.183   -1.83  6.72e-02 -0.695  0.02356
cityKolding   -0.376      0.189   -1.99  4.65e-02 -0.750 -0.00741
cityVejle     -0.276      0.189   -1.46  1.44e-01 -0.650  0.09316
age55-59       1.107      0.249    4.45  8.77e-06  0.616  1.59683
age60-64       1.529      0.233    6.58  4.81e-11  1.076  1.99122
age65-69       1.782      0.230    7.73  1.06e-14  1.333  2.24067
age70-74       1.873      0.237    7.92  2.42e-15  1.411  2.34169
age75+         1.429      0.251    5.69  1.29e-08  0.933  1.92247
```

```
m.p <- glm(cases ~ offset(log(pop)) + city + age, family = poisson, data = eba1977)
cbind(summary(m.p)$coefficients, confint(m.p))
```

```
            Estimate Std. Error z value  Pr(>|z|)  2.5 %   97.5 %
(Intercept)   -5.632      0.200  -28.12 4.91e-174 -6.043 -5.25673
cityHorsens   -0.330      0.182   -1.82  6.90e-02 -0.688  0.02558
cityKolding   -0.372      0.188   -1.98  4.79e-02 -0.743 -0.00497
cityVejle     -0.272      0.188   -1.45  1.47e-01 -0.644  0.09436
age55-59       1.101      0.248    4.43  9.23e-06  0.611  1.58944
age60-64       1.519      0.232    6.56  5.53e-11  1.067  1.97911
age65-69       1.768      0.229    7.70  1.31e-14  1.321  2.22450
age70-74       1.857      0.235    7.89  3.00e-15  1.397  2.32356
age75+         1.420      0.250    5.67  1.41e-08  0.925  1.91138
```

The expected proportion/rate of cases in Fredericia appears to be the highest. Let's compare that city with the others while controlling for age.

```
trtools::contrast(m.b,
  a = list(city = "Fredericia", age = "40-54"),
  b = list(city = c("Horsens","Kolding","Vejle"), age = "40-54"),
  cnames = c("vs Horsens","vs Kolding","vs Vejle"), tf = exp)
```

```
           estimate lower upper
vs Horsens     1.40 0.977  2.00
vs Kolding     1.46 1.006  2.11
vs Vejle       1.32 0.910  1.91
```

```
trtools::contrast(m.p,
  a = list(city = "Fredericia", age = "40-54", pop = 1),
  b = list(city = c("Horsens","Kolding","Vejle"), age = "40-54", pop = 1),
  cnames = c("vs Horsens","vs Kolding","vs Vejle"), tf = exp)
```

```
           estimate lower upper
vs Horsens     1.39 0.975  1.99
vs Kolding     1.45 1.003  2.10
vs Vejle       1.31 0.909  1.90
```

Note that since there is no interaction in the model, contrasts for city will not depend on the age group. We can also compute the estimated expected proportion (i.e., probability) or expected rate for each model.

```
trtools::contrast(m.b, a = list(city = levels(eba1977$city), age = "40-54"), tf = plogis)
```

```
 estimate   lower   upper
  0.00359 0.00242 0.00531
```

```
  0.00257 0.00170 0.00389
  0.00247 0.00162 0.00374
  0.00273 0.00179 0.00415
```

```r
trtools::contrast(m.p, a = list(city = levels(eba1977$city), age = "40-54", pop = 1), tf = exp)
```

```
 estimate   lower   upper
  0.00358 0.00242 0.00530
  0.00257 0.00170 0.00389
  0.00247 0.00163 0.00375
  0.00273 0.00179 0.00416
```

```r
d <- expand.grid(city = unique(eba1977$city), age = unique(eba1977$age))
cbind(d, trtools::glmint(m.b, newdata = d))
```

```
         city   age     fit     low     upp
1  Fredericia 40-54 0.00359 0.00242 0.00531
2     Horsens 40-54 0.00257 0.00170 0.00389
3     Kolding 40-54 0.00247 0.00162 0.00374
4       Vejle 40-54 0.00273 0.00179 0.00415
5  Fredericia 55-59 0.01078 0.00719 0.01613
6     Horsens 55-59 0.00774 0.00513 0.01165
7     Kolding 55-59 0.00742 0.00488 0.01127
8       Vejle 55-59 0.00820 0.00538 0.01249
9  Fredericia 60-64 0.01635 0.01136 0.02347
10    Horsens 60-64 0.01176 0.00810 0.01702
11    Kolding 60-64 0.01128 0.00770 0.01649
12      Vejle 60-64 0.01245 0.00852 0.01817
13 Fredericia 65-69 0.02095 0.01465 0.02988
14    Horsens 65-69 0.01509 0.01051 0.02160
15    Kolding 65-69 0.01448 0.00993 0.02107
16      Vejle 65-69 0.01598 0.01096 0.02325
17 Fredericia 70-74 0.02290 0.01584 0.03299
18    Horsens 70-74 0.01650 0.01130 0.02403
19    Kolding 70-74 0.01583 0.01068 0.02341
20      Vejle 70-74 0.01747 0.01184 0.02570
21 Fredericia   75+ 0.01481 0.00987 0.02217
22    Horsens   75+ 0.01065 0.00704 0.01607
23    Kolding   75+ 0.01021 0.00666 0.01563
24      Vejle   75+ 0.01128 0.00737 0.01723
```

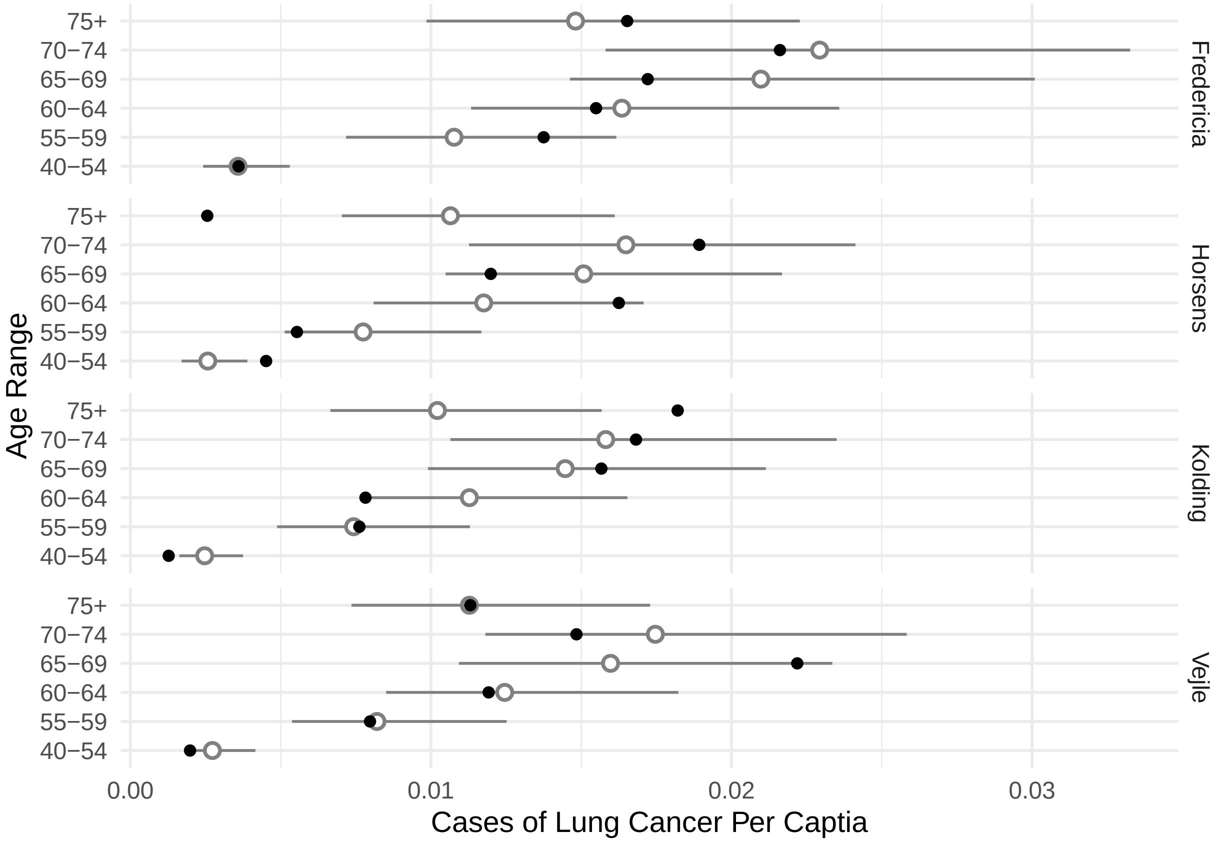
```r
d <- expand.grid(city = unique(eba1977$city), age = unique(eba1977$age), pop = 1)
cbind(d, trtools::glmint(m.p, newdata = d))
```

```
         city   age pop     fit     low     upp
1  Fredericia 40-54   1 0.00358 0.00242 0.00530
2     Horsens 40-54   1 0.00257 0.00170 0.00389
3     Kolding 40-54   1 0.00247 0.00163 0.00375
4       Vejle 40-54   1 0.00273 0.00179 0.00416
5  Fredericia 55-59   1 0.01077 0.00717 0.01617
6     Horsens 55-59   1 0.00774 0.00513 0.01168
7     Kolding 55-59   1 0.00743 0.00488 0.01130
8       Vejle 55-59   1 0.00820 0.00537 0.01252
9  Fredericia 60-64   1 0.01635 0.01134 0.02359
10    Horsens 60-64   1 0.01175 0.00809 0.01707
11    Kolding 60-64   1 0.01128 0.00769 0.01654
```

```
12       Vejle 60-64   1 0.01245 0.00851 0.01823
13 Fredericia 65-69   1 0.02098 0.01462 0.03009
14    Horsens 65-69   1 0.01508 0.01049 0.02168
15    Kolding 65-69   1 0.01447 0.00990 0.02114
16      Vejle 65-69   1 0.01598 0.01093 0.02335
17 Fredericia 70-74   1 0.02293 0.01581 0.03326
18    Horsens 70-74   1 0.01649 0.01127 0.02412
19    Kolding 70-74   1 0.01582 0.01065 0.02350
20      Vejle 70-74   1 0.01747 0.01181 0.02583
21 Fredericia   75+   1 0.01481 0.00985 0.02227
22    Horsens   75+   1 0.01065 0.00703 0.01612
23    Kolding   75+   1 0.01021 0.00665 0.01568
24      Vejle   75+   1 0.01128 0.00736 0.01729
```

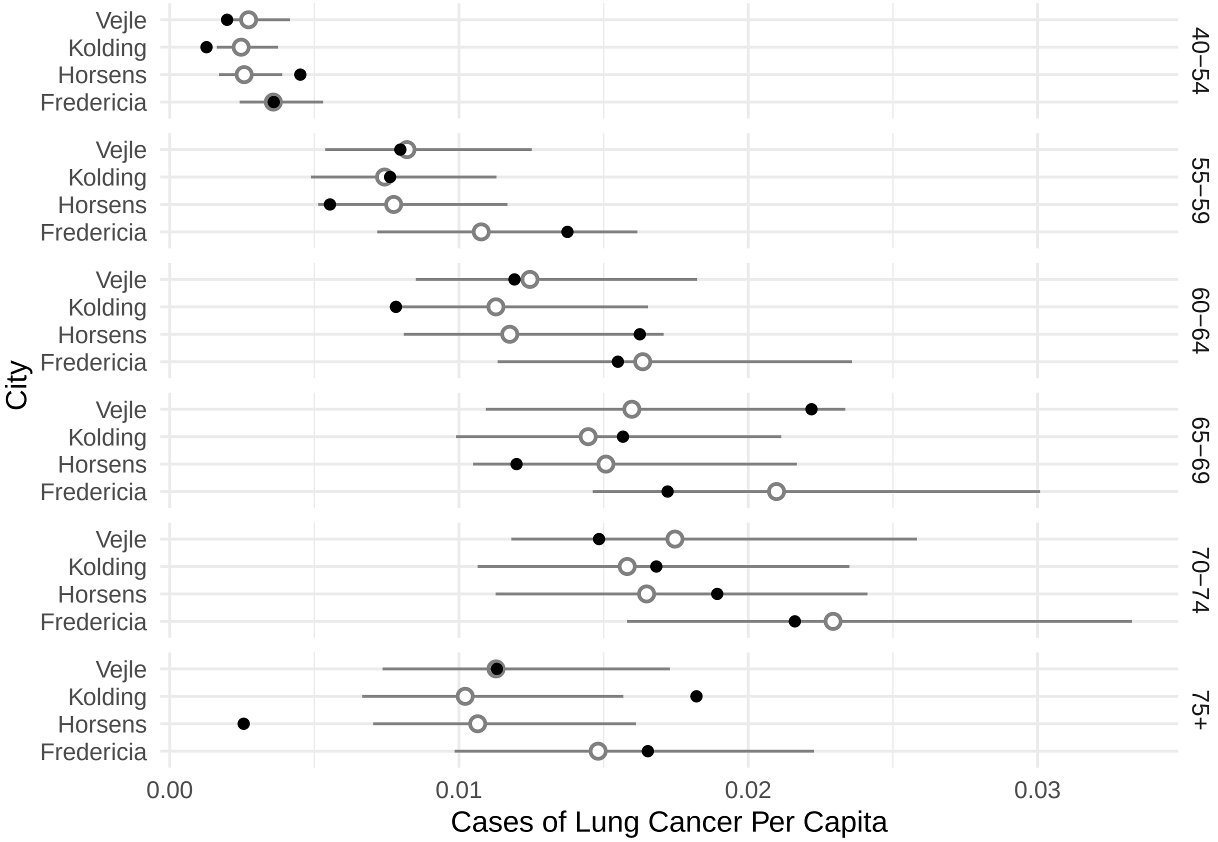
We can use this to make some helpful plots of the estimated rates (or probabilities) of lung cancer.

```
d <- expand.grid(age = unique(eba1977$age), city = unique(eba1977$city), pop = 1)
d <- cbind(d, trtools::glmint(m.p, newdata = d))
p <- ggplot(eba1977, aes(x = age, y = cases/pop)) +
  geom_pointrange(aes(y = fit, ymin = low, ymax = upp),
    shape = 21, fill = "white", data = d, color = grey(0.5)) +
  geom_point() + facet_grid(city ~ .) + coord_flip() +
  labs(x = "Age Range", y = "Cases of Lung Cancer Per Captia") +
  theme_minimal()
plot(p)
```

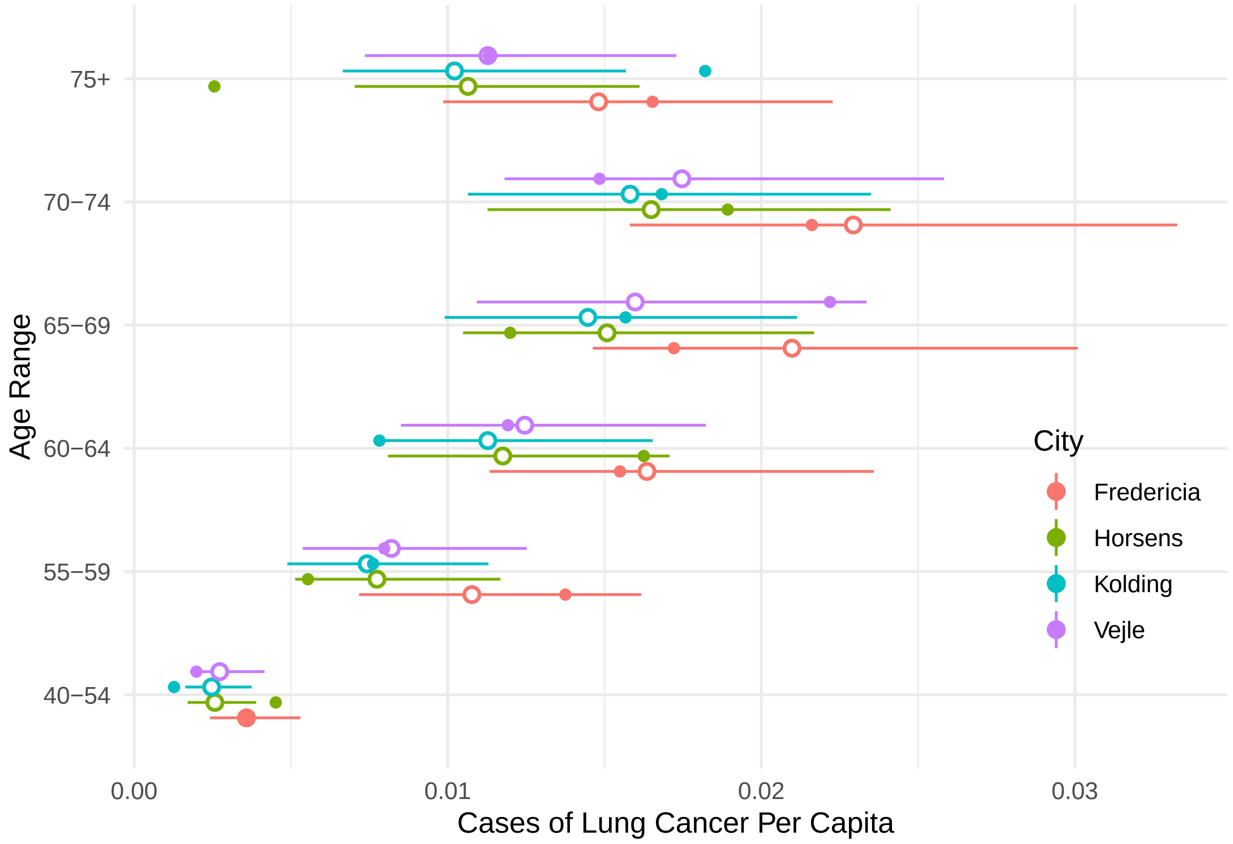


```
p <- ggplot(eba1977, aes(x = city, y = cases/pop)) +
  geom_pointrange(aes(y = fit, ymin = low, ymax = upp),
```

```
    shape = 21, fill = "white", data = d, color = grey(0.5)) +
  geom_point() + facet_grid(age ~ .) + coord_flip() +
  labs(x = "City", y = "Cases of Lung Cancer Per Capita") +
  theme_minimal()
plot(p)
```



```
p <- ggplot(eba1977, aes(x = age, y = cases/pop, color = city)) +
  geom_pointrange(aes(y = fit, ymin = low, ymax = upp),
    shape = 21, fill = "white", data = d,
      position = position_dodge(width = 0.5)) +
  geom_point(position = position_dodge(width = 0.5)) +
  coord_flip() +
  labs(x = "Age Range", y = "Cases of Lung Cancer Per Capita",
       color = "City") +
  theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.9,0.3))
plot(p)
```



Separation and Infinite Parameter Estimates

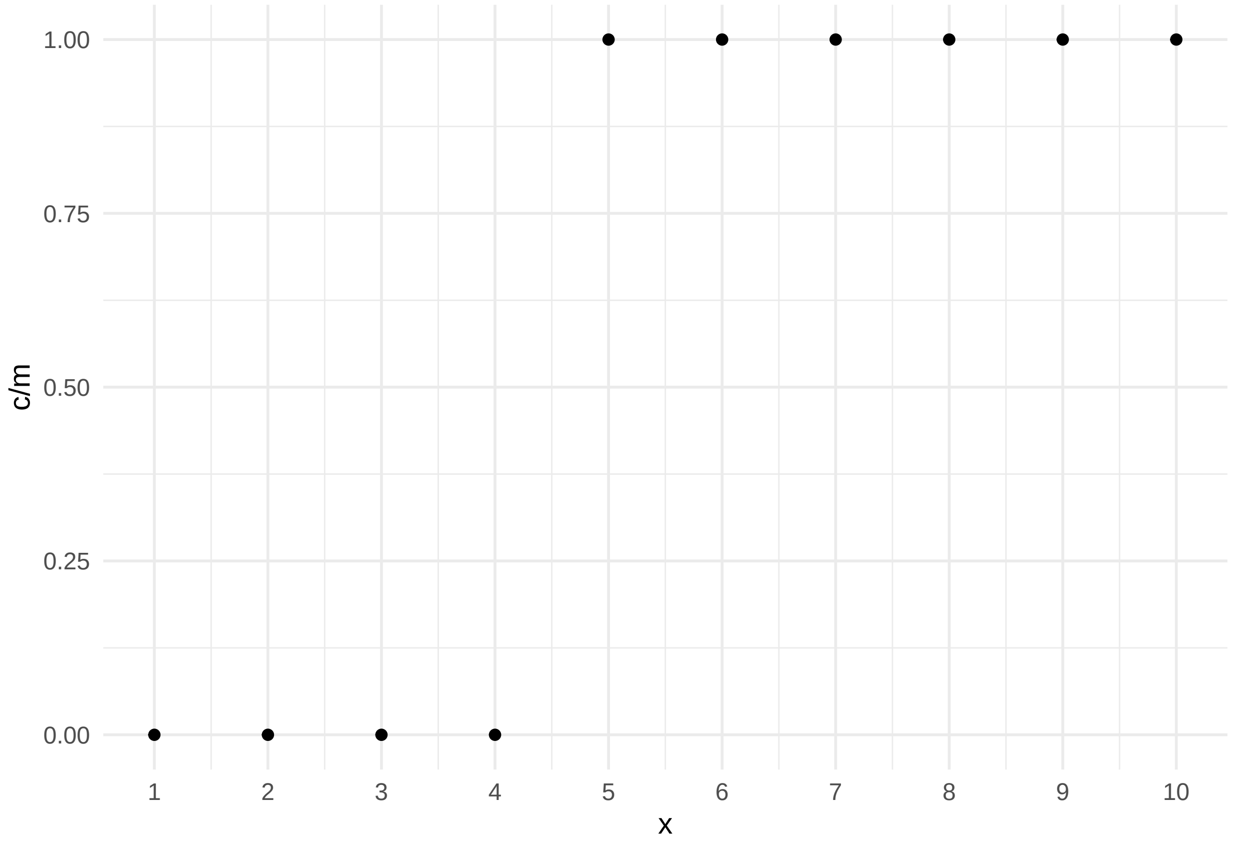
Some GLMs are prone to numerical problems due to (nearly) infinite parameter estimates.

Example: Consider the following data.

```r
mydata <- data.frame(m = rep(20, 10), c = rep(c(0,20), c(4,6)), x = 1:10)
mydata
```

```
    m  c  x
1  20  0  1
2  20  0  2
3  20  0  3
4  20  0  4
5  20 20  5
6  20 20  6
7  20 20  7
8  20 20  8
9  20 20  9
10 20 20 10
```

```r
p <- ggplot(mydata, aes(x = x, y = c/m)) + theme_minimal() +
  geom_point() + scale_x_continuous(breaks = 1:10)
plot(p)
```



If we try to estimate a logistic regression model we get errors and some extreme estimates, standard errors, and confidence intervals.

```
m <- glm(cbind(c,m-c) ~ x, family = binomial, data = mydata)
```

```
Warning: glm.fit: algorithm did not converge
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

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

```
            Estimate Std. Error  z value Pr(>|z|)
(Intercept)   -212.1     114489 -0.00185    0.999
x               47.1      25082  0.00188    0.999
```

```
confint(m)
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

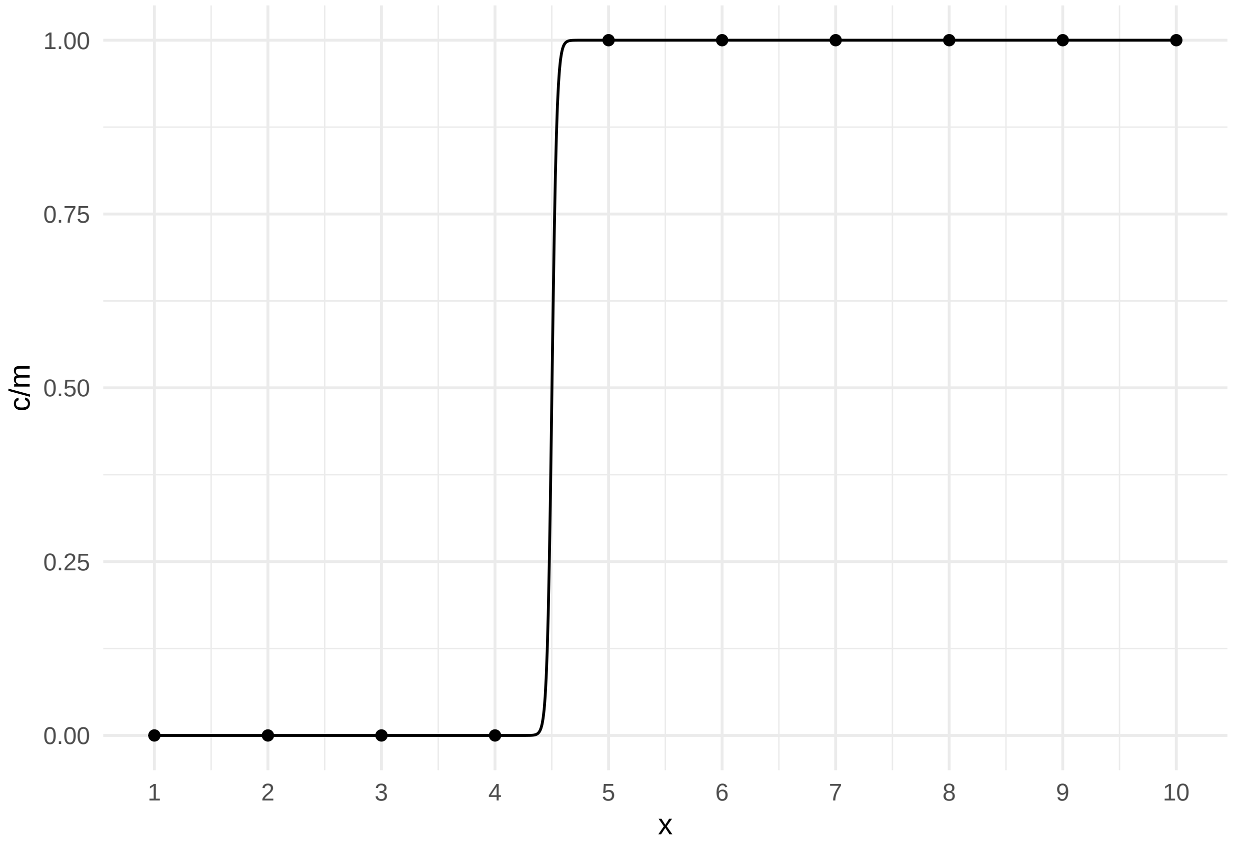
```
Warning: glm.fit: algorithm did not converge
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

```
             2.5 % 97.5 %
(Intercept) -29559 -28057
x             7969   1966
```

But we can still plot the model.

```
d <- data.frame(x = seq(1, 10, length = 1000))
d$yhat <- predict(m, newdata = d, type = "response")
p <- p + geom_line(aes(y = yhat), data = d)
plot(p)
```



The problem is that the estimation procedure “wants” the curve to be a step function, but that only occurs as $\beta_1 \to \infty$, and the value of x where the estimated expected response is 0.5 equals $-\beta_0/\beta_1$, and for the step function that would be 4.5, so the estimation procedure “wants” the estimate of β_0 to be $-\beta_1 4.5 = -\infty$. This is called *separation*. It is fairly obvious with a single explanatory variable, but much less so with multiple explanatory variables. The example above shows *complete separation* because we can separate the values of y based on the values of x. *Quasi-separation* occurs when this is almost true as in the following example.

```
mydata <- data.frame(m = rep(20, 50), x = seq(1, 10, length = 50),
  c = rep(c(0,20,0,20), c(24,1,1,24)))

m <- glm(cbind(c,m-c) ~ x, family = binomial, data = mydata)
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

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

```
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   -39.23       5.54   -7.08 1.45e-12
x               7.13       1.01    7.09 1.37e-12
```

```
confint(m)
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
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Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```
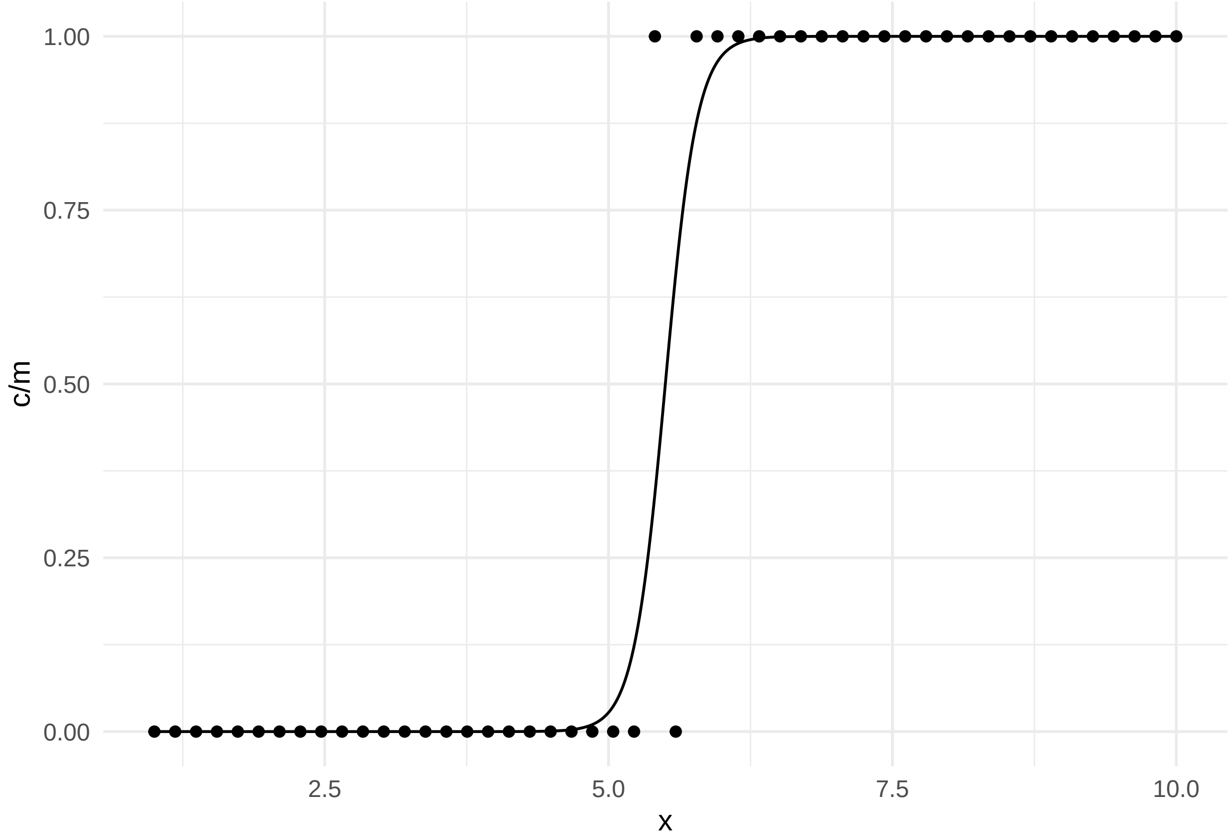

```
             2.5 % 97.5 %
(Intercept) -51.70  -29.8
x             5.41    9.4
```

```r
d <- data.frame(x = seq(1, 10, length = 10000))
d$yhat <- predict(m, newdata = d, type = "response")

p <- ggplot(mydata, aes(x = x, y = c/m)) + theme_minimal() +
  geom_point() + geom_line(aes(y = yhat), data = d)
plot(p)
```



Example: Consider the following data.

```r
mydata <- data.frame(m = c(100,100), c = c(25,100), group = c("control","treatment"))
mydata
```

```
    m   c     group
1 100  25   control
```

```
2 100 100 treatment
```

```
m <- glm(cbind(c,m-c) ~ group, family = binomial, data = mydata)
summary(m)$coefficients
```

```
               Estimate Std. Error  z value Pr(>|z|)
(Intercept)        -1.1   2.31e-01 -4.75713 1.96e-06
grouptreatment     28.4   5.17e+04  0.00055 1.00e+00
```

```
confint(m)
```

```
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
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Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

```
Warning in regularize.values(x, y, ties, missing(ties), na.rm = na.rm): collapsing to unique 'x'
values
```

```
                  2.5 %    97.5 %
(Intercept)       -1.57    -0.661
grouptreatment -1849.43 18872.026
```

A similar problem can happen in Poisson regression where the observed count or rate in a category is zero.

Example: Consider the following data and model.

```
mydata <- data.frame(y = c(20, 10, 50, 15, 0), x = letters[1:5])
mydata
```

```
   y x
1 20 a
2 10 b
3 50 c
4 15 d
5  0 e
```

```
m <- glm(y ~ x, family = poisson, data = mydata)
summary(m)$coefficients
```

```
            Estimate Std. Error   z value Pr(>|z|)
(Intercept)    2.996   2.24e-01 13.397322 6.27e-41
xb            -0.693   3.87e-01 -1.789698 7.35e-02
xc             0.916   2.65e-01  3.463253 5.34e-04
```

```
xd            -0.288   3.42e-01 -0.842247 4.00e-01
xe           -25.298   4.22e+04 -0.000599 1.00e+00
```

```r
confint(m)
```

```
Warning: glm.fit: fitted rates numerically 0 occurred
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```
Error: no valid set of coefficients has been found: please supply starting values
```

There are some solutions to this problem, depending on the circumstances.

1. In simple cases such as the logistic regression example with a control and treatment group, a nonparametric approach could be used for a significance test (e.g., Fisher's exact test).
2. In some cases with a categorical explanatory variable, we can omit the level(s) where the observed count is zero (in Poisson regression), or the observed proportion is 0 or 1 (in logistic regression). Clearly this precludes inferences concerning that level or its relationship with other levels.
3. For logistic regression (or similar models) a "penalized" or "bias-reduced" estimation method can be used for quasi-separation (see the **logistf** and **brglm** packages).