

Wednesday, Mar 6

## 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.

```
fleas <- trtools::ceriodaphniastrain
fleas$strain <- factor(fleas$strain, levels = c(1,2), labels = c("a","b"))
m <- glm(count ~ concentration * strain, family = poisson, data = fleas)
summary(m)$coefficients
```

	Estimate	Std. Error	z value	Pr(> z )
(Intercept)	4.4811	0.04350	103.008	0.000e+00
concentration	-1.5979	0.06244	-25.592	1.862e-144
strainb	-0.3367	0.06704	-5.022	5.114e-07
concentration:strainb	0.1253	0.09385	1.336	1.817e-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"), concentration = 2))
```

estimate	lower	upper
3.616	2.970	4.402
3.318	2.671	4.122

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(concentration = 2))
```

strain	rate	SE	df	asyp.LCL	asyp.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|concentration, type = "response", at = list(concentration = c(1,2,3)))
```

```
concentration = 1:
strain rate SE df asyp.LCL asyp.UCL
a 17.872 0.815 Inf 16.343 19.54
b 14.467 0.725 Inf 13.113 15.96
```

```
concentration = 2:
strain rate SE df asyp.LCL asyp.UCL
a 3.616 0.363 Inf 2.970 4.40
b 3.318 0.367 Inf 2.671 4.12
```

```
concentration = 3:
  strain   rate    SE df asymp.LCL asymp.UCL
a         0.732 0.118 Inf    0.534    1.00
b         0.761 0.136 Inf    0.537    1.08
```

Confidence level used: 0.95

Intervals are back-transformed from the log scale

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

```
strain = a:
  concentration   rate    SE df asymp.LCL asymp.UCL
1 17.872 0.815 Inf 16.343 19.54
2 3.616 0.363 Inf 2.970 4.40
3 0.732 0.118 Inf 0.534 1.00
```

```
strain = b:
  concentration   rate    SE df asymp.LCL asymp.UCL
1 14.467 0.725 Inf 13.113 15.96
2 3.318 0.367 Inf 2.671 4.12
3 0.761 0.136 Inf 0.537 1.08
```

Confidence level used: 0.95

Intervals are back-transformed from the log scale

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

```
concentration strain   rate    SE df asymp.LCL asymp.UCL
1 a         17.872 0.815 Inf 16.343 19.54
2 a          3.616 0.363 Inf 2.970 4.40
3 a          0.732 0.118 Inf 0.534 1.00
1 b         14.467 0.725 Inf 13.113 15.96
2 b          3.318 0.367 Inf 2.671 4.12
3 b          0.761 0.136 Inf 0.537 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", concentration = 2),
  b = list(strain = "b", concentration = 2))
```

```
estimate lower upper
1.09 0.8132 1.46
```

```
pairs(emmeans(m, ~ strain, type = "response",
  at = list(concentration = 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 0.5648
```

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

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

```
concentration = 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  0.0018
```

```
concentration = 2:
  contrast ratio      SE df asymp.LCL asymp.UCL null z.ratio p.value
a / b      1.090 0.1628 Inf      0.813      1.46    1   0.576  0.5648
```

```
concentration = 3:
  contrast ratio      SE df asymp.LCL asymp.UCL null z.ratio p.value
a / b      0.961 0.2308 Inf      0.601      1.54    1  -0.164  0.8698
```

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*concentration, type = "response",
  at = list(concentration = c(1,2,3))), infer = TRUE)
```

contrast	ratio	SE	df	asymp.LCL	asymp.UCL	null	z.ratio	p.value
a concentration1 / b concentration1	1.235	0.084	Inf	1.018	1.50	1	3.118	0.0225
a concentration1 / a concentration2	4.942	0.309	Inf	4.137	5.90	1	25.592	<.0001
a concentration1 / b concentration2	5.386	0.645	Inf	3.830	7.58	1	14.068	<.0001
a concentration1 / a concentration3	24.428	3.050	Inf	17.114	34.87	1	25.592	<.0001
a concentration1 / b concentration3	23.486	4.323	Inf	13.900	39.68	1	17.149	<.0001
b concentration1 / a concentration2	4.001	0.449	Inf	2.906	5.51	1	12.362	<.0001
b concentration1 / b concentration2	4.360	0.306	Inf	3.571	5.32	1	21.015	<.0001
b concentration1 / a concentration3	19.775	3.330	Inf	12.237	31.96	1	17.721	<.0001
b concentration1 / b concentration3	19.012	2.664	Inf	12.752	28.34	1	21.015	<.0001
a concentration2 / b concentration2	1.090	0.163	Inf	0.712	1.67	1	0.576	0.9926
a concentration2 / a concentration3	4.942	0.309	Inf	4.137	5.90	1	25.592	<.0001
a concentration2 / b concentration3	4.752	0.972	Inf	2.652	8.51	1	7.617	<.0001
b concentration2 / a concentration3	4.535	0.885	Inf	2.600	7.91	1	7.746	<.0001
b concentration2 / b concentration3	4.360	0.306	Inf	3.571	5.32	1	21.015	<.0001
a concentration3 / b concentration3	0.961	0.231	Inf	0.485	1.91	1	-0.164	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".

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

```
concentration = 1:
```

contrast	ratio	SE	df	asympt.LCL	asympt.UCL	null	z.ratio	p.value
a / b	1.235	0.0837	Inf	1.082	1.41	1	3.118	0.0018

concentration = 2:

contrast	ratio	SE	df	asympt.LCL	asympt.UCL	null	z.ratio	p.value
a / b	1.090	0.1628	Inf	0.813	1.46	1	0.576	0.5648

concentration = 3:

contrast	ratio	SE	df	asympt.LCL	asympt.UCL	null	z.ratio	p.value
a / b	0.961	0.2308	Inf	0.601	1.54	1	-0.164	0.8698

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?

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

estimate	lower	upper
0.2023	0.1790	0.2287
0.2293	0.1999	0.2631

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

strain = a:

concentration	rate	SE	df	asympt.LCL	asympt.UCL
2	3.62	0.363	Inf	2.97	4.40
1	17.87	0.815	Inf	16.34	19.54

strain = b:

concentration	rate	SE	df	asympt.LCL	asympt.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, ~concentration|strain,
  at = list(concentration = c(2,1)), type = "response"))
```

strain = a:

contrast	ratio	SE	df	null	z.ratio	p.value
concentration2 / concentration1	0.202	0.0126	Inf	1	-25.592	<.0001

strain = b:

contrast	ratio	SE	df	null	z.ratio	p.value
concentration2 / concentration1	0.229	0.0161	Inf	1	-21.015	<.0001

Tests are performed on the log scale

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

```
strain = a:
  contrast              ratio      SE  df null z.ratio p.value
concentration2 / concentration1 0.202 0.0126 Inf    1 -25.592 <.0001
```

```
strain = b:
  contrast              ratio      SE  df null z.ratio p.value
concentration2 / concentration1 0.229 0.0161 Inf    1 -21.015 <.0001
```

Tests are performed on the log scale

What if we want to know if the rate ratios are significantly different?

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

```
strain concentration.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    -1.34
```

Confidence level used: 0.95

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

```
contrast estimate      SE  df z.ratio p.value
a - b      -0.125 0.0939 Inf   -1.335  0.1817
```

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

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

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

```
              Estimate Std. Error  z value Pr(>|z|)
(Intercept)   -2.81091    0.35845  -7.84177 4.442e-15
insecticideboth    1.22575    0.67176   1.82468 6.805e-02
insecticideDDT   -0.03893    0.50722  -0.07676 9.388e-01
deposit         0.62207    0.07786   7.98986 1.351e-15
insecticideboth:deposit 0.37010    0.20897   1.77109 7.655e-02
insecticideDDT:deposit -0.14143    0.10376  -1.36301 1.729e-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.

```
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    0.5743 0.5027 0.6429
both     0.9669 0.9212 0.9865
DDT      0.3902 0.3289 0.4550
```

```
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	0.0149	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	asympt.LCL	asympt.UCL	null	z.ratio	p.value
(g-BHC) / both	0.05	0.023	Inf	0.018	0.12	1	-6.275	<.0001
(g-BHC) / DDT	2.11	0.423	Inf	1.424	3.12	1	3.724	0.0002
both / DDT	45.71	22.260	Inf	17.600	118.72	1	7.849	<.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	0.04613	0.01765	0.1206
g-BHC / DDT	2.10871	1.42385	3.1230
both / DDT	45.71097	17.59954	118.7243

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	asympt.LCL	asympt.UCL	null	z.ratio	p.value
both / (g-BHC)	21.677	10.628	Inf	8.293	56.67	1	6.275	<.0001
DDT / (g-BHC)	0.474	0.095	Inf	0.320	0.70	1	-3.724	0.0002
DDT / both	0.022	0.011	Inf	0.008	0.06	1	-7.849	<.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	21.67723	8.292521	56.66581
DDT / g-BHC	0.47422	0.320208	0.70232
DDT / both	0.02188	0.008423	0.05682

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    0.07  0.02 Inf    0.035    0.13    1  -8.239 <.0001
(g-BHC) / DDT     1.83  0.37 Inf    1.234    2.72    1   3.004 0.0027
both / DDT       27.41  9.12 Inf   14.274   52.62    1   9.947 <.0001
```

```
deposit = 5:
contrast      odds.ratio    SE df asymp.LCL asymp.UCL null z.ratio p.value
(g-BHC) / both    0.05  0.02 Inf    0.018    0.12    1  -6.275 <.0001
(g-BHC) / DDT     2.11  0.42 Inf    1.424    3.12    1   3.724 0.0002
both / DDT       45.71 22.26 Inf   17.600  118.72    1   7.849 <.0001
```

```
deposit = 6:
contrast      odds.ratio    SE df asymp.LCL asymp.UCL null z.ratio p.value
(g-BHC) / both    0.03  0.02 Inf    0.008    0.12    1  -5.080 <.0001
(g-BHC) / DDT     2.43  0.60 Inf    1.495    3.95    1   3.584 0.0003
both / DDT       76.24 51.04 Inf   20.529  283.13    1   6.474 <.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

```
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    0.07  0.02 Inf    0.035    0.13    1  -8.239 <.0001
(g-BHC) / DDT     1.83  0.37 Inf    1.234    2.72    1   3.004 0.0027
both / DDT       27.41  9.12 Inf   14.274   52.62    1   9.947 <.0001
```

```
deposit = 5:
contrast      odds.ratio    SE df asymp.LCL asymp.UCL null z.ratio p.value
(g-BHC) / both    0.05  0.02 Inf    0.018    0.12    1  -6.275 <.0001
(g-BHC) / DDT     2.11  0.42 Inf    1.424    3.12    1   3.724 0.0002
both / DDT       45.71 22.26 Inf   17.600  118.72    1   7.849 <.0001
```

```
deposit = 6:
contrast      odds.ratio    SE df asymp.LCL asymp.UCL null z.ratio p.value
(g-BHC) / both    0.03  0.02 Inf    0.008    0.12    1  -5.080 <.0001
(g-BHC) / DDT     2.43  0.60 Inf    1.495    3.95    1   3.584 0.0003
both / DDT       76.24 51.04 Inf   20.529  283.13    1   6.474 <.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.

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

```
insecticide = g-BHC:
```

deposit	prob	SE	df	asympt.LCL	asympt.UCL
2	0.1727	0.0318	Inf	0.1190	0.244
1	0.1008	0.0261	Inf	0.0599	0.165

insecticide = both:

deposit	prob	SE	df	asympt.LCL	asympt.UCL
2	0.5985	0.0566	Inf	0.4844	0.703
1	0.3560	0.0892	Inf	0.2049	0.542

insecticide = DDT:

deposit	prob	SE	df	asympt.LCL	asympt.UCL
2	0.1314	0.0271	Inf	0.0867	0.194
1	0.0856	0.0232	Inf	0.0497	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	asympt.LCL	asympt.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	asympt.LCL	asympt.UCL	null	z.ratio	p.value
deposit2 / deposit1	2.70	0.523	Inf	1.84	3.94	1	5.116	<.0001

insecticide = DDT:

contrast	odds.ratio	SE	df	asympt.LCL	asympt.UCL	null	z.ratio	p.value
deposit2 / deposit1	1.62	0.111	Inf	1.41	1.85	1	7.007	<.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	0.1794
(deposit2 - deposit1 g-BHC) - (deposit2 - deposit1 DDT)	0.141	0.104	Inf	1.363	0.3605
(deposit2 - deposit1 both) - (deposit2 - deposit1 DDT)	0.511	0.206	Inf	2.487	0.0344

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	0.1794
(g-BHC) - DDT	0.141	0.104	Inf	1.363	0.3605
both - DDT	0.511	0.206	Inf	2.487	0.0344



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

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

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

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

Then it can be shown that

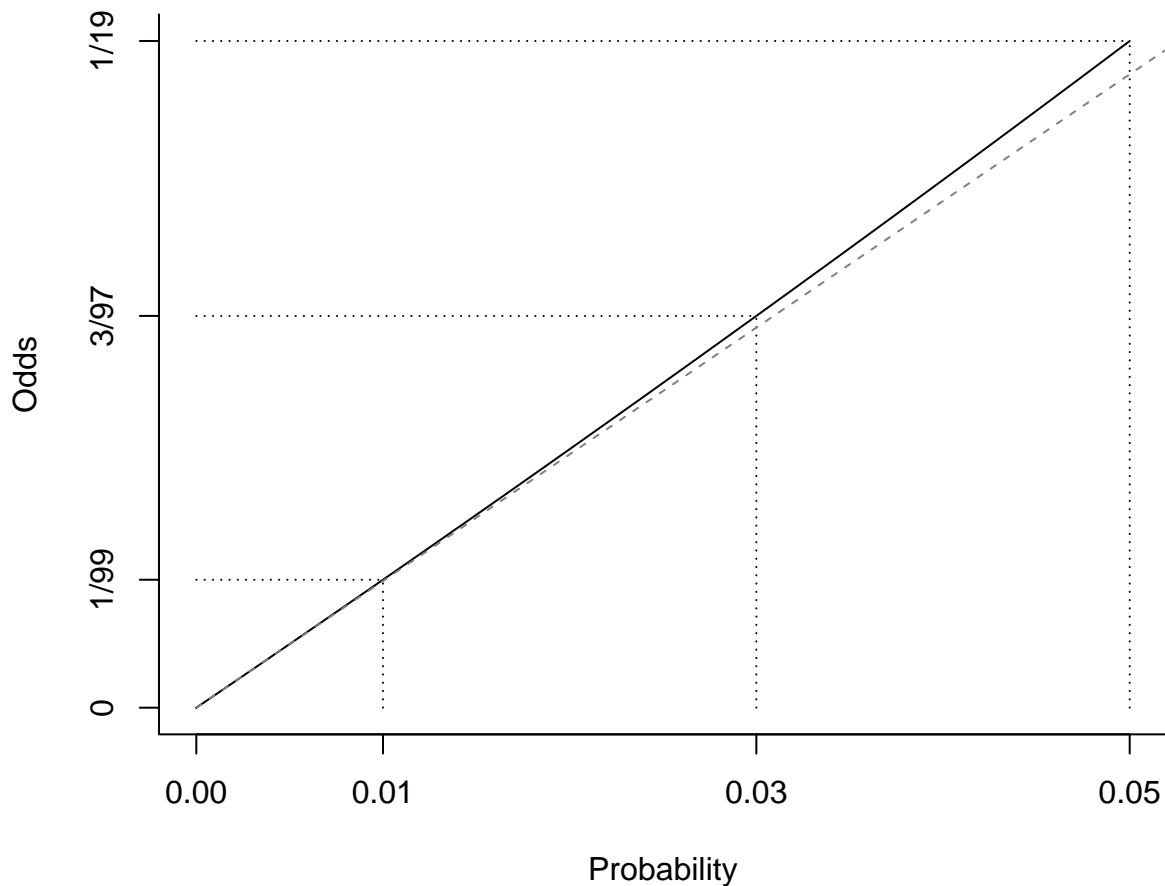
$$\lim_{m_i \rightarrow \infty} \binom{m_i}{c} \left( \frac{\lambda_i}{m_i} \right)^c \left( 1 - \frac{\lambda_i}{m_i} \right)^{m_i - c} = \frac{e^{-\lambda_i} \lambda_i^c}{c!},$$

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.

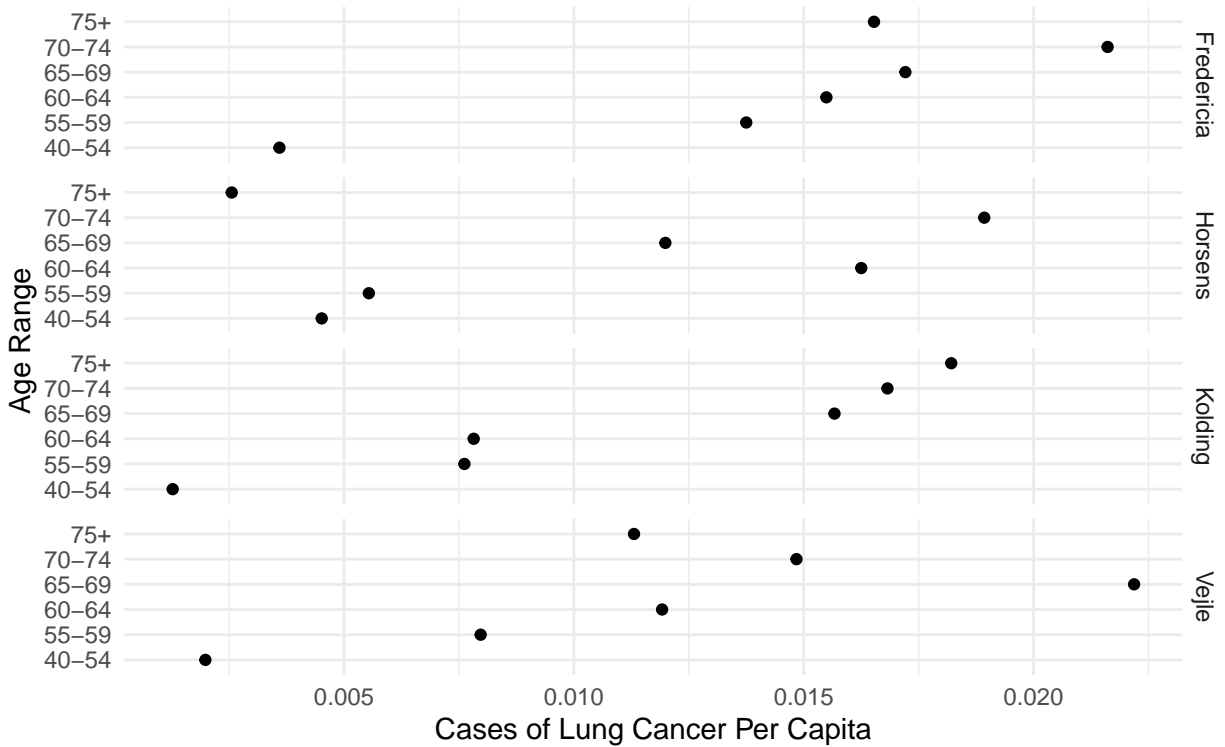
**Example:** Consider the following data on the incidence of lung cancer in four Danish cities.

```
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

```
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)	-5.6262	0.2008	-28.021	9.132e-173	-6.0385	-5.249799
cityHorsens	-0.3345	0.1827	-1.830	6.719e-02	-0.6946	0.023561
cityKolding	-0.3764	0.1890	-1.991	4.646e-02	-0.7504	-0.007412
cityVejle	-0.2760	0.1891	-1.459	1.444e-01	-0.6503	0.093162
age55-59	1.1070	0.2490	4.445	8.771e-06	0.6159	1.596828
age60-64	1.5291	0.2325	6.577	4.812e-11	1.0760	1.991225
age65-69	1.7819	0.2305	7.732	1.061e-14	1.3335	2.240675
age70-74	1.8727	0.2365	7.918	2.415e-15	1.4105	2.341695
age75+	1.4289	0.2512	5.688	1.289e-08	0.9328	1.922467

```
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)	-5.6321	0.2003	-28.125	4.911e-174	-6.0433	-5.256725
cityHorsens	-0.3301	0.1815	-1.818	6.899e-02	-0.6878	0.025582
cityKolding	-0.3715	0.1878	-1.978	4.789e-02	-0.7432	-0.004967
cityVejle	-0.2723	0.1879	-1.450	1.472e-01	-0.6441	0.094356
age55-59	1.1010	0.2483	4.434	9.230e-06	0.6114	1.589441
age60-64	1.5186	0.2316	6.556	5.528e-11	1.0672	1.979110
age65-69	1.7677	0.2294	7.704	1.314e-14	1.3213	2.224503
age70-74	1.8569	0.2353	7.891	3.005e-15	1.3970	2.323556

```
age75+      1.4197      0.2503      5.672  1.408e-08  0.9254  1.911381
```

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    1.397 0.9766 1.999
vs Kolding    1.457 1.0059 2.110
vs Vejle      1.318 0.9097 1.909
```

```
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    1.391 0.9746 1.985
vs Kolding    1.450 1.0035 2.095
vs Vejle      1.313 0.9086 1.897
```

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
0.003589 0.002424 0.005311
0.002571 0.001701 0.003885
0.002466 0.001625 0.003741
0.002726 0.001787 0.004155
```

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

```
      estimate lower upper
0.003581 0.002419 0.005303
0.002574 0.001704 0.003890
0.002470 0.001628 0.003747
0.002727 0.001789 0.004158
```

```
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 0.003589 0.002424 0.005311
2 Horsens 40-54 0.002571 0.001701 0.003885
3 Kolding 40-54 0.002466 0.001625 0.003741
4 Vejle 40-54 0.002726 0.001787 0.004155
5 Fredericia 55-59 0.010780 0.007192 0.016129
6 Horsens 55-59 0.007739 0.005135 0.011648
7 Kolding 55-59 0.007424 0.004884 0.011270
8 Vejle 55-59 0.008201 0.005378 0.012487
9 Fredericia 60-64 0.016348 0.011360 0.023473
10 Horsens 60-64 0.011755 0.008104 0.017024
11 Kolding 60-64 0.011278 0.007702 0.016489
```

```

12      Vejle 60-64 0.012454 0.008520 0.018170
13 Fredericia 65-69 0.020952 0.014654 0.029876
14      Horsens 65-69 0.015086 0.010513 0.021604
15      Kolding 65-69 0.014476 0.009925 0.021069
16      Vejle 65-69 0.015979 0.010956 0.023252
17 Fredericia 70-74 0.022898 0.015845 0.032986
18      Horsens 70-74 0.016496 0.011299 0.024025
19      Kolding 70-74 0.015830 0.010679 0.023407
20      Vejle 70-74 0.017471 0.011844 0.025703
21 Fredericia 75+ 0.014812 0.009872 0.022169
22      Horsens 75+ 0.010646 0.007042 0.016065
23      Kolding 75+ 0.010214 0.006661 0.015633
24      Vejle 75+ 0.011280 0.007368 0.017232

```

```

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 0.003581 0.002419 0.005303
2      Horsens 40-54 1 0.002574 0.001704 0.003890
3      Kolding 40-54 1 0.002470 0.001628 0.003747
4      Vejle 40-54 1 0.002727 0.001789 0.004158
5 Fredericia 55-59 1 0.010769 0.007174 0.016167
6      Horsens 55-59 1 0.007742 0.005133 0.011676
7      Kolding 55-59 1 0.007427 0.004883 0.011297
8      Vejle 55-59 1 0.008202 0.005375 0.012517
9 Fredericia 60-64 1 0.016351 0.011335 0.023587
10      Horsens 60-64 1 0.011755 0.008092 0.017075
11      Kolding 60-64 1 0.011277 0.007690 0.016536
12      Vejle 60-64 1 0.012453 0.008506 0.018231
13 Fredericia 65-69 1 0.020976 0.014623 0.030090
14      Horsens 65-69 1 0.015080 0.010488 0.021681
15      Kolding 65-69 1 0.014467 0.009899 0.021141
16      Vejle 65-69 1 0.015976 0.010929 0.023354
17 Fredericia 70-74 1 0.022932 0.015810 0.033263
18      Horsens 70-74 1 0.016486 0.011266 0.024123
19      Kolding 70-74 1 0.015816 0.010646 0.023497
20      Vejle 70-74 1 0.017466 0.011810 0.025830
21 Fredericia 75+ 1 0.014811 0.009848 0.022273
22      Horsens 75+ 1 0.010647 0.007034 0.016116
23      Kolding 75+ 1 0.010214 0.006654 0.015681
24      Vejle 75+ 1 0.011280 0.007358 0.017292

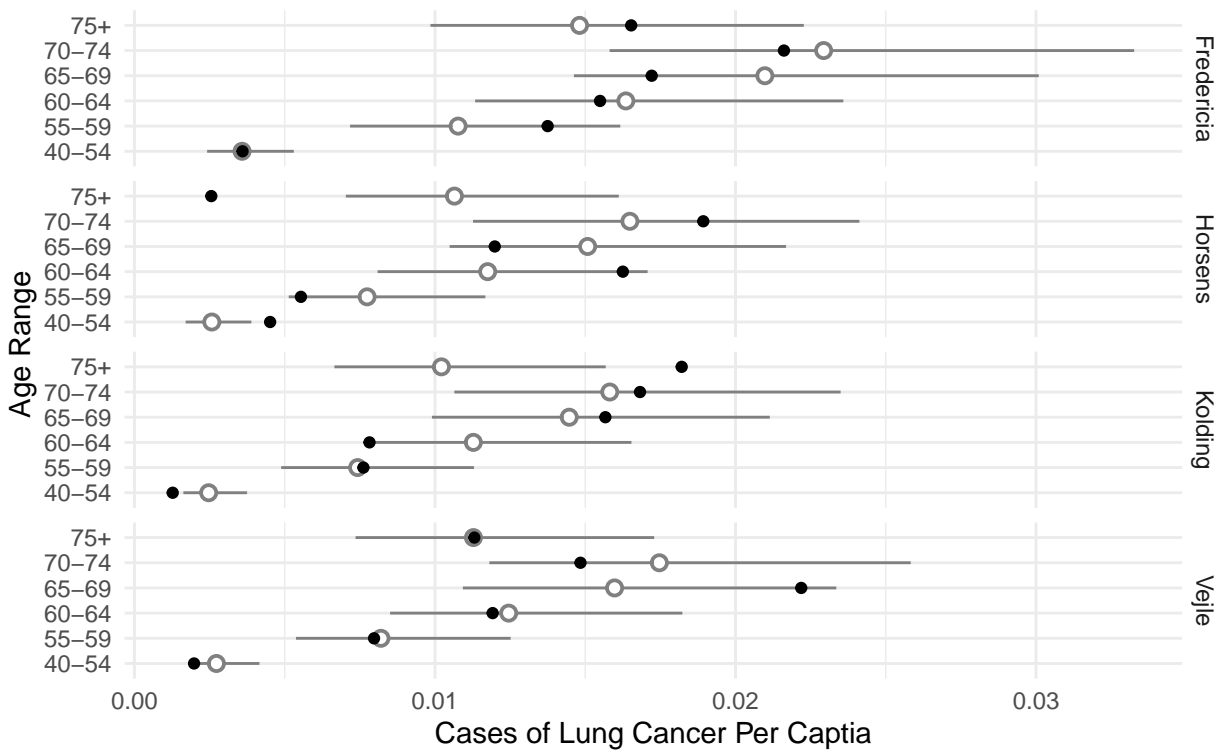
```

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

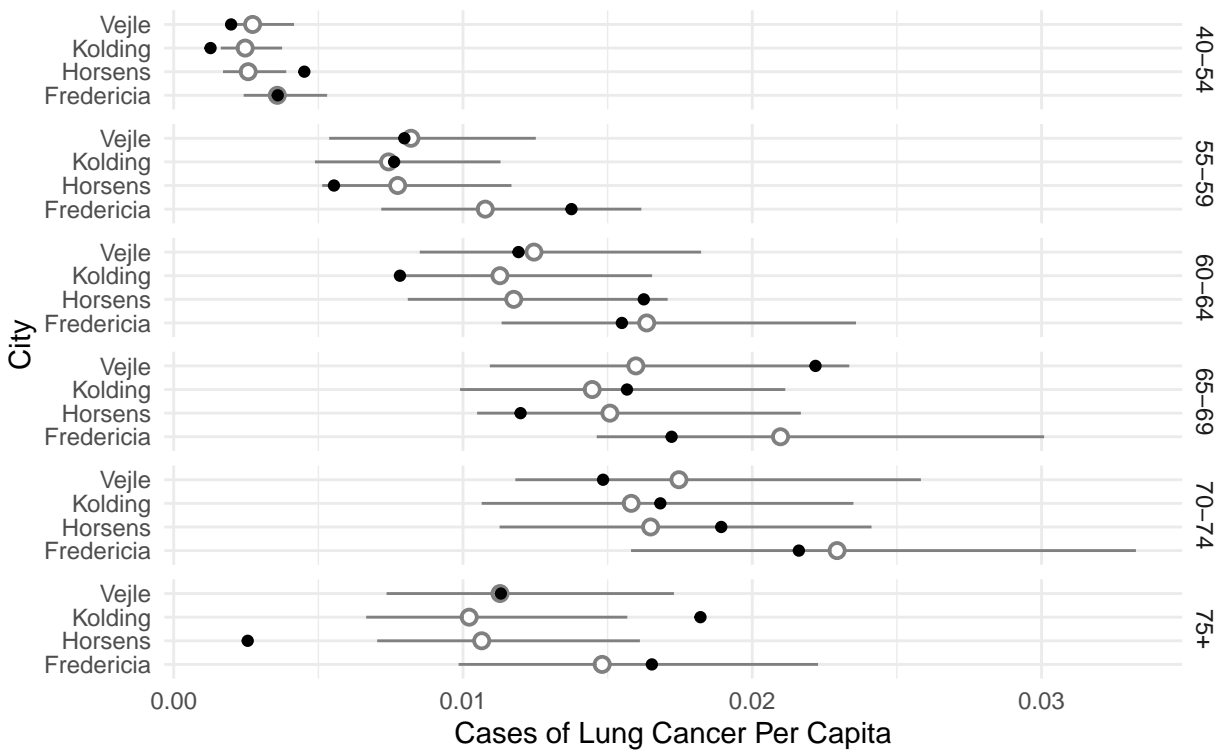
```

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)

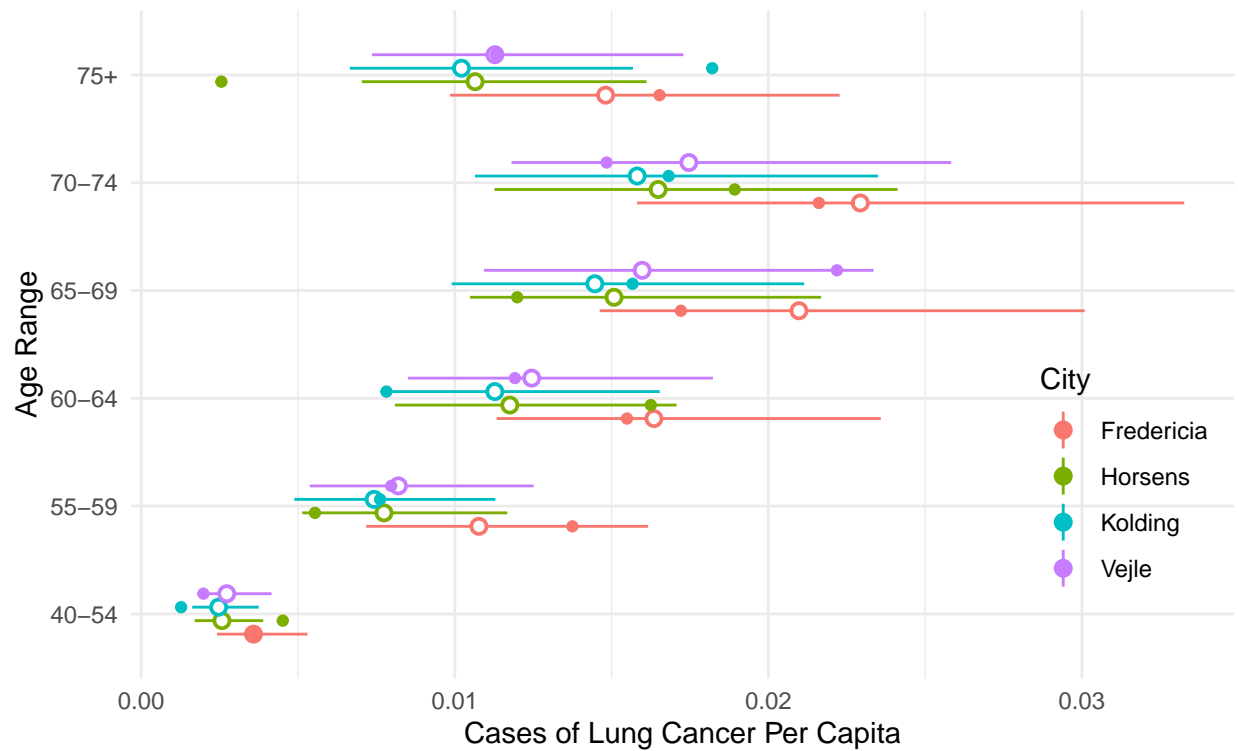
```



```
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 = 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.

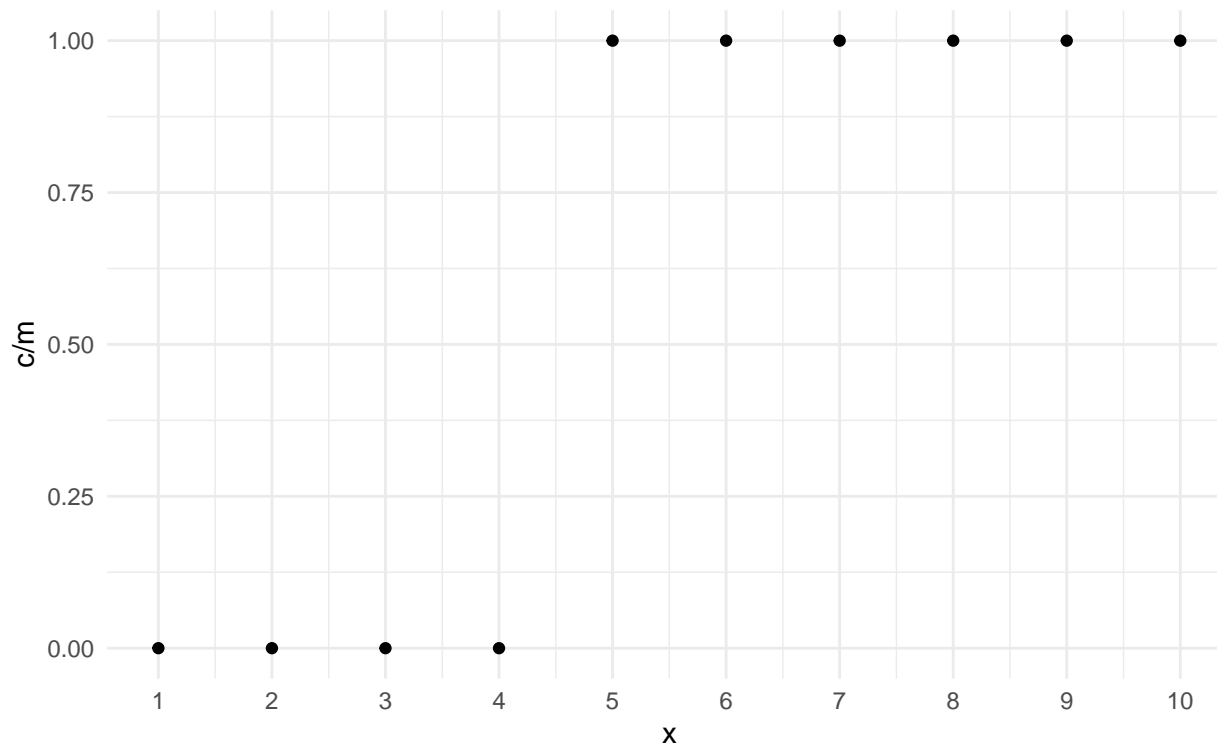
**Example:** Consider the following data.

```
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

```
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)	-212.11	114489	-0.001853	0.9985
x	47.12	25082	0.001879	0.9985

```
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

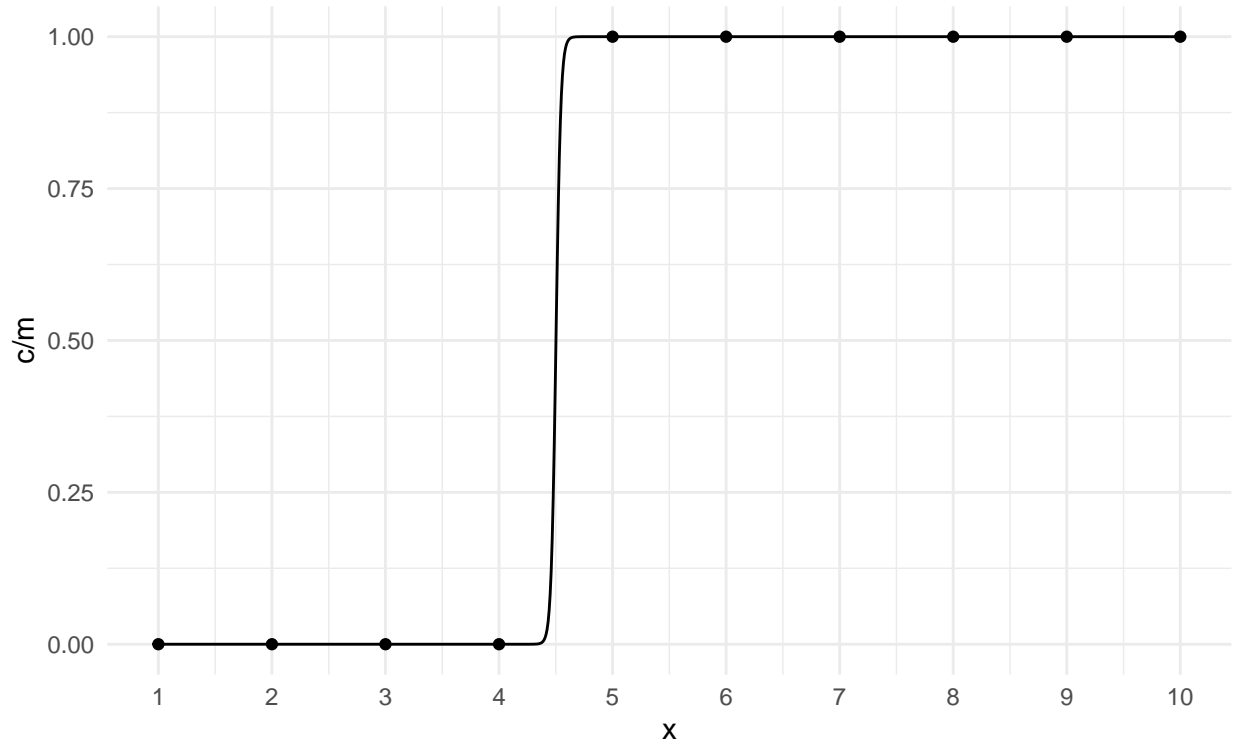
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred

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  $\beta_1 \rightarrow \infty$ , 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  $\beta_0$  to be  $-\beta_1 5.5 = -\infty$ . 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)	-39.231	5.542	-7.079	1.448e-12
x	7.133	1.006	7.087	1.371e-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

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

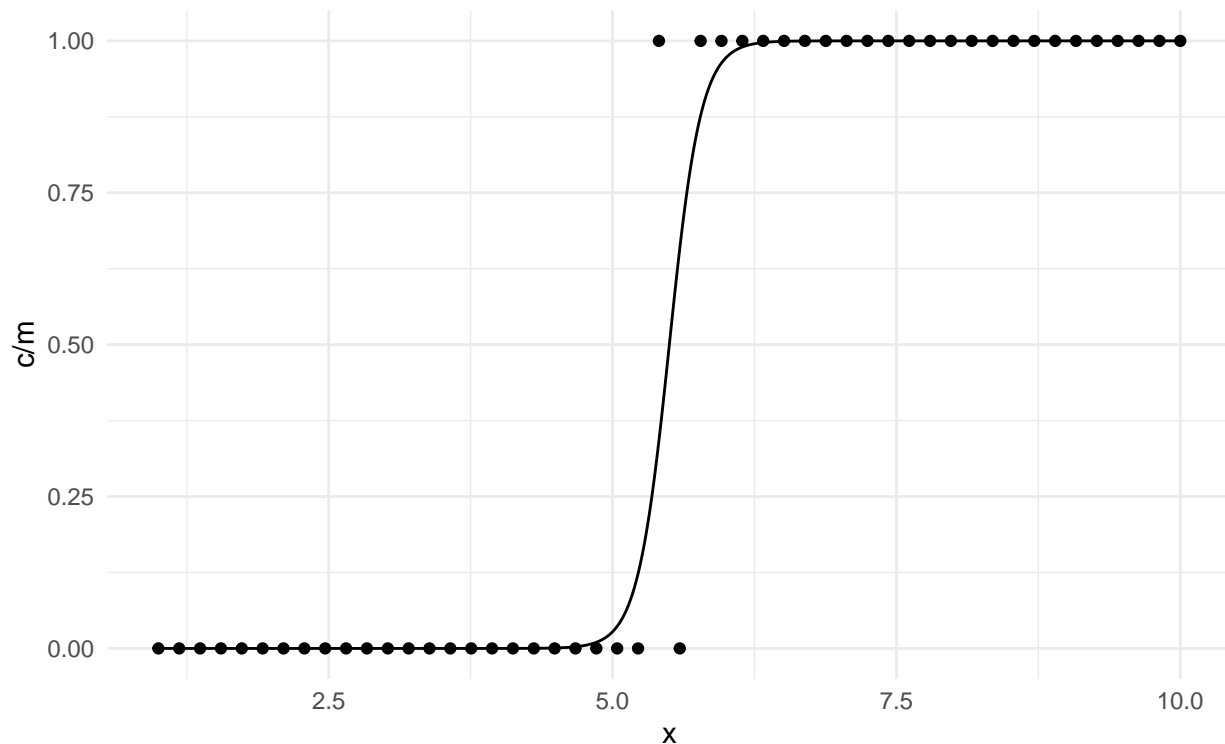
Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred

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

	2.5 %	97.5 %
(Intercept)	-51.696	-29.767
x	5.414	9.397

```
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.

```
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)	-1.099	2.309e-01	-4.7571308	1.964e-06
grouptreatment	28.410	5.169e+04	0.0005496	9.996e-01

```
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

2.5 %      97.5 %

```
(Intercept)      -1.571      -0.6611
group.treatment -1849.427 18872.0265
```

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)	2.9957	2.236e-01	13.3973220	6.268e-41
xb	-0.6931	3.873e-01	-1.7896983	7.350e-02
xc	0.9163	2.646e-01	3.4632534	5.337e-04
xd	-0.2877	3.416e-01	-0.8422469	3.996e-01
xe	-25.2983	4.225e+04	-0.0005988	9.995e-01

```
confint(m)
```

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

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Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

Warning: glm.fit: fitted rates numerically 0 occurred

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).