

Practicals - Logistic and Poisson regression

Epidemiological methods in medical research 2023

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Exercise 1: The BCG study revisited

We will revisit the BCG study (exercise 2 of the previous practical) where we are interested in comparing the risk of leprosy between the BCG vaccinated and non BCG vaccinated subjects:

- subjects were grouped into 7 age intervals: 0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34 (in years) and we would like to adjust for age since it may confound the association between vaccination and leprosy.
- the non-vaccinated group will be composed of the whole population survey of 80,622 persons (`conall` in the dataset).

The purpose of this exercise is to compare 3 different approaches to quantify the vaccine effect and discuss the underlying statistical models. To focus on these objectives the code and software output is provided.

Here is a summary of the dataset:

```
bcg <- read.table("https://bozenne.github.io/doc/Teaching/bcg.txt",
                  header = TRUE)
bcg$age <- as.character(bcg$age)
bcg$status <- as.character(bcg$status)
bcg.r <- bcg[bcg$status %in% c("case", "conall"),]

table227 <- xtabs(n~scar+status+age, data = bcg.r)
ftable(table227)
```

| | | age | 00_04 | 05_09 | 10_14 | 15_19 | 20_24 | 25_29 | 30_34 |
|------|--------|-----|-------|-------|-------|-------|-------|-------|-------|
| scar | status | | | | | | | | |
| 0 | case | | 1 | 11 | 28 | 16 | 20 | 36 | 47 |
| | conall | | 7593 | 7143 | 5611 | 2208 | 2438 | 4356 | 5245 |
| 1 | case | | 1 | 14 | 22 | 28 | 19 | 11 | 6 |
| | conall | | 11719 | 10184 | 7561 | 8117 | 5588 | 1625 | 1234 |

Part I

A simple approach consists in evaluating the probability of contracting leprosy in each age and vaccination subgroup, and comparing them between vaccination subgroups.


1. Can you make sense of the following software output?

Does it help to answer the research question?

```
table227.pc <- prop.table(table227, margin = c(1,3))
ftable(round(100*table227.pc,3))
```

```
      age  00_04  05_09  10_14  15_19  20_24  25_29  30_34
scar status
0  case      0.013  0.154  0.497  0.719  0.814  0.820  0.888
   conall    99.987 99.846 99.503 99.281 99.186 99.180 99.112
1  case      0.009  0.137  0.290  0.344  0.339  0.672  0.484
   conall    99.991 99.863 99.710 99.656 99.661 99.328 99.516
```

```
[1] "00_04" "05_09" "10_14" "15_19" "20_24" "25_29" "30_34"
```

2. Here is some more complicated  code.

Can you understand what it is doing? (appendix A should help)


Does it help to answer the research question?

```
age.groups <- dimnames(table227.pc)$age
age.groups
```

```
[1] "00_04" "05_09" "10_14" "15_19" "20_24" "25_29" "30_34"
```

```
library(exact2x2)
df.resI <- NULL
for(iAge in age.groups){
  iTab <- table227[, , iAge]
  iTest <- binomMeld.test(x1 = iTab["0", "case"], n1 = sum(iTab["0", ]),
                        x2 = iTab["1", "case"], n2 = sum(iTab["1", ]),
                        parmttype = "difference", conf.int = TRUE)
  df.resI <- rbind(df.resI,
                  data.frame(age = iAge,
                             estimate = unname(iTest$estimate),
                             lower = iTest$conf.int[1],
                             upper = iTest$conf.int[2],
                             p.value = iTest$p.value)
                )
}
df.resI
```

| | age | estimate | lower | upper | p.value |
|---|-------|---------------|--------------|---------------|------------|
| 1 | 00_04 | -4.635868e-05 | -0.000685681 | 0.0003805052 | 1.00000000 |
| 2 | 05_09 | -1.647831e-04 | -0.001577776 | 0.0010614538 | 0.92819700 |
| 3 | 10_14 | -2.064193e-03 | -0.004522346 | 0.0002342452 | 0.07826868 |
| 4 | 15_19 | -3.756553e-03 | -0.008367311 | -0.0002525178 | 0.03326422 |
| 5 | 20_24 | -4.748075e-03 | -0.009414869 | -0.0009798127 | 0.01037704 |
| 6 | 25_29 | -1.473005e-03 | -0.006202971 | 0.0044151797 | 0.69509953 |
| 7 | 30_34 | -4.042621e-03 | -0.008441027 | 0.0021433379 | 0.20074780 |

3. Here is the output from the same  code as before except that the argument `parmttype` has been changed to `"ratio"`.

Does it change your appreciation of the vaccine efficacy?

What property of the testing procedure do you notice?

| | age | estimate | lower | upper | p.value |
|---|-------|-----------|------------|------------|------------|
| 1 | 00_04 | 0.6479522 | 0.00827165 | 50.8580868 | 1.00000000 |
| 2 | 05_09 | 0.8928310 | 0.37676901 | 2.1720971 | 0.92819700 |
| 3 | 10_14 | 0.5842863 | 0.31889878 | 1.0578105 | 0.07826868 |
| 4 | 15_19 | 0.4778392 | 0.25028232 | 0.9440460 | 0.03326422 |
| 5 | 20_24 | 0.4164616 | 0.21071034 | 0.8206767 | 0.01037704 |
| 6 | 25_29 | 0.8202934 | 0.37734768 | 1.6425565 | 0.69509953 |
| 7 | 30_34 | 0.5448181 | 0.19061559 | 1.2730218 | 0.20074780 |

[Extra] Can you have perform a similar analysis with the `glm` function? (appendix A should help). What is the drawback of using `glm`?

Part II

A common analysis is to make a logistic model, using age as a covariate:

```
e.common <- glm(status=="case" ~ age + scar,
                 family = binomial(link="logit"),
                 weight = n,
                 data = bcg.r)
summary(e.common)
```

| | Estimate | Pr(> z) | | Estimate | Pr(> z) |
|-------------|-----------|--------------|------|------------|--------------|
| (Intercept) | -8.880038 | 7.238979e-36 | scar | -0.5470646 | 0.0001034434 |
| age05_09 | 2.623536 | 3.572990e-04 | | | |
| age10_14 | 3.583111 | 6.760471e-07 | | | |
| age15_19 | 3.824128 | 1.263355e-07 | | | |
| age20_24 | 3.900156 | 7.553260e-08 | | | |
| age25_29 | 4.155632 | 9.187360e-09 | | | |
| age30_34 | 4.157639 | 8.556965e-09 | | | |

4. What is the interpretation of each coefficient and corresponding p-values?
In particular how would you explicit the vaccine effect?
5. Same questions with the following logistic model

```
e.common2 <- glm(status=="case" ~ 0 + age + scar,
                  family = binomial(link="logit"),
                  weight = n,
                  data = bcg.r)
summary(e.common2)
```


| | Estimate | Pr(> z) | | Estimate | Pr(> z) |
|----------|-----------|---------------|------|------------|--------------|
| age00_04 | -8.880038 | 7.238979e-36 | scar | -0.5470646 | 0.0001034434 |
| age05_09 | -6.256502 | 6.277280e-195 | | | |
| age10_14 | -5.296927 | 2.940433e-257 | | | |
| age15_19 | -5.055910 | 1.366578e-175 | | | |
| age20_24 | -4.979882 | 2.502577e-169 | | | |
| age25_29 | -4.724406 | 8.390947e-222 | | | |
| age30_34 | -4.722399 | 4.365121e-253 | | | |

6. Have a look at the following predicted values. Can you guess what they are?
How would they look like for `e.common2`?
Can you compute those values yourself based on the estimated coefficients?

```
data.frame(age = bcg.r$age[1:14],
           scar = bcg.r$scar[1:14],
           pred1 = predict(e.common, type = "link")[1:14],
           pred2 = predict(e.common, type = "response")[1:14])
```

| | age | scar | pred1 | pred2 | | age | scar | pred1 | pred2 |
|----|-------|------|--------|---------|---|-------|------|--------|---------|
| 8 | 00_04 | 0 | -8.880 | 0.00014 | 1 | 00_04 | 1 | -9.427 | 0.00008 |
| 9 | 05_09 | 0 | -6.257 | 0.00191 | 2 | 05_09 | 1 | -6.804 | 0.00111 |
| 10 | 10_14 | 0 | -5.297 | 0.00498 | 3 | 10_14 | 1 | -5.844 | 0.00289 |
| 11 | 15_19 | 0 | -5.056 | 0.00633 | 4 | 15_19 | 1 | -5.603 | 0.00367 |
| 12 | 20_24 | 0 | -4.980 | 0.00683 | 5 | 20_24 | 1 | -5.527 | 0.00396 |
| 13 | 25_29 | 0 | -4.724 | 0.00880 | 6 | 25_29 | 1 | -5.271 | 0.00511 |
| 14 | 30_34 | 0 | -4.722 | 0.00882 | 7 | 30_34 | 1 | -5.269 | 0.00512 |

7. How would you assess the main modeling assumption based on the previous software outputs?

[Extra] The following  code fit a common effect model on the probability scale.
Why is this model less reasonable than the one using the odds scale?
Why is it challenging for the software to estimate the model parameters?
(this is why starting value are input to `glm`)

```
starting.values <- c(0.035,0.1,0.35,0.4,0.46,0.75,0.78,-0.03)/100
e.common3 <- glm(status=="case" ~ 0 + age + scar,
                 family = binomial(link="identity"),
                 weight = n,
                 data = bcg.r,
                 start = starting.values)
summary(e.common3)
```

| | Estimate | Pr(> z) | | Estimate | Pr(> z) |
|----------|--------------|--------------|------|---------------|-----------|
| age00_04 | 0.0003547222 | 7.061058e-02 | scar | -0.0002939937 | 0.1500859 |
| age05_09 | 0.0016196894 | 2.748984e-07 | | | |
| age10_14 | 0.0039166478 | 6.419051e-13 | | | |
| age15_19 | 0.0044351916 | 1.340900e-11 | | | |
| age20_24 | 0.0049835320 | 1.773590e-10 | | | |
| age25_29 | 0.0078678282 | 3.886355e-12 | | | |
| age30_34 | 0.0081484003 | 2.034830e-13 | | | |

Part III

Another possible analysis is to model an interaction between age and vaccine:

```
e.full <- glm(status=="case" ~ age * scar,
              family = binomial(link="logit"),
              weight = n,
              data = bcg.r)
summary(e.full)
```

| | Estimate | Pr(> z) | | Estimate | Pr(> z) |
|-------------|-----------|--------------|---------------|------------|-----------|
| (Intercept) | -8.934982 | 4.094169e-19 | scar | -0.4339847 | 0.7589523 |
| age05_09 | 2.458989 | 1.857212e-02 | age05_09:scar | 0.3204617 | 0.8275025 |
| age10_14 | 3.634702 | 3.556874e-04 | age10_14:scar | -0.1054519 | 0.9417362 |
| age15_19 | 4.007728 | 1.014914e-04 | age15_19:scar | -0.3082730 | 0.8314994 |
| age20_24 | 4.131781 | 5.550098e-05 | age20_24:scar | -0.4467520 | 0.7580548 |
| age25_29 | 4.139192 | 4.461984e-05 | age25_29:scar | 0.2344074 | 0.8720925 |
| age30_34 | 4.220099 | 2.976596e-05 | age30_34:scar | -0.1773891 | 0.9045692 |

8. What is the interpretation of each coefficient and corresponding p-values?
In particular how would you explicit the vaccine effect?

9. Same questions with the following logistic model:

```
e.full2 <- glm(status=="case" ~ 0 + age + age:scar,
               family = binomial(link="logit"),
               weight = n,
               data = bcg.r)
summary(e.full2)
```

| | Estimate | Pr(> z) | | Estimate | Pr(> z) |
|----------|-----------|---------------|---------------|------------|------------|
| age00_04 | -8.934982 | 4.094169e-19 | age00_04:scar | -0.4339847 | 0.75895232 |
| age05_09 | -6.475993 | 3.532959e-102 | age05_09:scar | -0.1135229 | 0.77828821 |
| age10_14 | -5.300280 | 3.119233e-172 | age10_14:scar | -0.5394366 | 0.05878419 |
| age15_19 | -4.927254 | 7.323866e-86 | age15_19:scar | -0.7422577 | 0.01819865 |
| age20_24 | -4.803201 | 1.552490e-101 | age20_24:scar | -0.8807367 | 0.00611894 |
| age25_29 | -4.795791 | 1.327620e-180 | age25_29:scar | -0.1995773 | 0.56376575 |
| age30_34 | -4.714883 | 3.389080e-227 | age30_34:scar | -0.6113738 | 0.15957550 |

10. Can you make sense of the following F-tests?

```
anova(e.full, test = "Chisq")
```

Analysis of Deviance Table

Model: binomial, link: logit

Response: status == "case"

Terms added sequentially (first to last)

| | Df | Deviance | Resid. Df | Resid. Dev | Pr(>Chi) |
|----------|----|----------|-----------|------------|---------------|
| NULL | | | 27 | 3504.0 | |
| age | 6 | 200.659 | 21 | 3303.3 | < 2.2e-16 *** |
| scar | 1 | 15.297 | 20 | 3288.0 | 9.187e-05 *** |
| age:scar | 6 | 3.600 | 14 | 3284.4 | 0.7306 |

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```
anova(e.full2, test = "Chisq")
```

Analysis of Deviance Table

Model: binomial, link: logit

Response: status == "case"

Terms added sequentially (first to last)

| | Df | Deviance | Resid. Df | Resid. Dev | Pr(>Chi) |
|----------|----|----------|-----------|------------|---------------|
| NULL | | | 28 | 112126 | |
| age | 7 | 108823 | 21 | 3303 | < 2.2e-16 *** |
| age:scar | 7 | 19 | 14 | 3284 | 0.008516 ** |

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

11. Discuss the pros and cons of each approach/parametrisation.
What would you report in a scientific article?

Exercise 2: The Bissau study revisited

In rural Guinea-Bissau, 5274 children under 7 months of age were visited two times at home, with an interval of approximately 6 months. Information about vaccination (BCG, DTP, measles vaccine) was collected at each visit and at second visit, death during follow-up was registered. Other children move away during follow-up or survive until the second visit ('censored'). The dataset `bissau.txt` contain the available information:

```
bissau <- read.table("https://bozenne.github.io/doc/Teaching/bissau.txt",
  header=TRUE)
str(bissau)
```

```
'data.frame':      5274 obs. of  8 variables:
 $ id      : int  1 2 3 4 5 6 7 8 9 10 ...
 $ fuptime : int  65 161 166 166 161 161 166 166 166 166 ...
 $ fupstatus: chr  "dead" "censored" "censored" "censored" ...
 $ bcg      : chr  "yes" "yes" "no" "yes" ...
 $ dtp      : int  1 2 0 0 0 0 2 1 2 2 ...
 $ age      : int  182 125 69 96 131 26 129 90 119 146 ...
 $ agem     : int   5 4 2 3 4 0 4 2 3 4 ...
 $ dtpany   : logi  TRUE TRUE FALSE FALSE FALSE FALSE ...
```

We already analyzed this dataset in Practical 1: we looked at the marginal risk, odds, and rate of death in each vaccination group and compare them between groups. We would now like account for age in the analysis of the effects of DTP and BCG on the mortality. To this end we will use a Poisson regression model, under the strong assumption that the mortality is constant over the follow-up time.

1. Fit a Poisson regression model for survival with follow-up time as the time variable (i.e., using `log(fuptime)` as offset), including `bcg` and `agem` as categorical covariates. How is BCG vaccination associated with the mortality rate?
2. Estimate the effect of any dose of DTP, using the created variable `dtpany`, adjusted only for `agem` as a categorical variable.
3. Now, also adjust for `bcg`. What happened? Can you explain?
4. Is there an interaction between DTP and `bcg`?

Appendix A: Comparing proportions of events between two groups

Consider only the first age group:

```
table227.age2 <- table227[,,"05_09"]
table227.age2
```

```
      status
scar  case conall
  0     11   7143
  1     14  10184
```

Difference

We can test the difference in proportion of infection between the groups using

```
library(exact2x2)
test.age2 <- binomMeld.test(x1 = table227.age2["0","case"],
                           n1 = sum(table227.age2["0",]),
                           x2 = table227.age2["1","case"],
                           n2 = sum(table227.age2["1",]),
                           parmtype = "difference", conf.int = TRUE)
test.age2
```

```
      melded binomial test for difference

data:  sample 1:(11/7154), sample 2:(14/10198)
proportion 1 = 0.0015376, proportion 2 = 0.0013728, p-value = 0.9282
alternative hypothesis: true difference is not equal to 0
95 percent confidence interval:
 -0.001577776  0.001061454
sample estimates:
difference (p2-p1)
 -0.0001647831
```

The results can be extract from the object `test.age2` doing:

```
data.frame(estimate = unname(test.age2$estimate),
            lower = test.age2$conf.int[1],
            upper = test.age2$conf.int[2],
            p.value = test.age2$p.value)
```

| | estimate | lower | upper | p.value |
|---|---------------|--------------|-------------|----------|
| 1 | -0.0001647831 | -0.001577776 | 0.001061454 | 0.928197 |

An alternative implementation uses a binomial model with an identity link:

```
e.glm_diff <- glm(status=="case" ~ scar,
                  family = binomial(link="identity"),
                  weight = n,
                  data = bcg.r[bcg.r$age=="05_09",])
summary(e.glm_diff)$coef
```

| | Estimate | Std. Error | z value | Pr(> z) |
|-------------|---------------|--------------|------------|------------|
| (Intercept) | 0.0015376013 | 0.0004632477 | 3.3191776 | 0.00090283 |
| scar | -0.0001647831 | 0.0005907876 | -0.2789211 | 0.78030537 |

Estimates are identical but p-value and confidence intervals will differ in small samples as the `glm` function rely on more crude approximation for quantifying the uncertainty compared to `binomMeld.test`.

Ratio

We can test the ratio between the proportion of infection in the two groups using

```
binomMeld.test(x1 = table227.age2["0","case"],
               n1 = sum(table227.age2["0",]),
               x2 = table227.age2["1","case"],
               n2 = sum(table227.age2["1",]),
               parmtype = "ratio", conf.int = TRUE)
```

melded binomial test for ratio

```
data: sample 1:(11/7154), sample 2:(14/10198)
proportion 1 = 0.0015376, proportion 2 = 0.0013728, p-value = 0.9282
alternative hypothesis: true ratio is not equal to 1
95 percent confidence interval:
 0.376769 2.172097
sample estimates:
ratio (p2/p1)
 0.892831
```

An alternative implementation uses a binomial model with a log link:

```
e.glm_ratio <- glm(status=="case" ~ scar,
                    family = binomial(link="log"),
                    weight = n,
                    data = bcg.r[bcg.r$age=="05_09",])
cbind(RR = exp(coef(e.glm_ratio)),summary(e.glm_ratio)$coef)
```

| | RR | Estimate | Std. Error | z value | Pr(> z) |
|-------------|-------------|------------|------------|-------------|--------------|
| (Intercept) | 0.001537601 | -6.4775316 | 0.3012794 | -21.5000784 | 1.55425e-102 |
| scar | 0.892831036 | -0.1133579 | 0.4026162 | -0.2815533 | 7.78286e-01 |

Note that the p-values for `binomMeld.test` do not depend on how the groups are compared (difference, ratio, odds ratio). This is not true for `glm`.

Appendix B: Parametrisation

All greek letters denote estimates (usually they are denoted with hat, e.g. $\hat{\theta}$ but it is omitted here for lisibility).

| Part I | model (probability scale) | | testing procedure | | |
|--------|---------------------------|---------------------|---------------------------------|------------------------------------|---------|
| strata | non-exposed | exposed | risk difference | risk ratio | p-value |
| 0-4 | $\alpha_1 = 0.013\%$ | $\beta_1 = 0.009\%$ | $\beta_1 - \alpha_1 = -0.005\%$ | $\frac{\beta_1}{\alpha_1} = 0.648$ | 1 |
| 5-9 | $\alpha_2 = 0.154\%$ | $\beta_2 = 0.137\%$ | $\beta_2 - \alpha_2 = -0.016\%$ | $\frac{\beta_2}{\alpha_2} = 0.893$ | 0.928 |
| 10-14 | $\alpha_3 = 0.497\%$ | $\beta_3 = 0.290\%$ | $\beta_3 - \alpha_3 = -0.206\%$ | $\frac{\beta_3}{\alpha_3} = 0.584$ | 0.078 |
| 15-19 | $\alpha_4 = 0.719\%$ | $\beta_4 = 0.344\%$ | $\beta_4 - \alpha_4 = -0.376\%$ | $\frac{\beta_4}{\alpha_4} = 0.478$ | 0.033 |
| 20-24 | $\alpha_5 = 0.814\%$ | $\beta_5 = 0.339\%$ | $\beta_5 - \alpha_5 = -0.745\%$ | $\frac{\beta_5}{\alpha_5} = 0.416$ | 0.010 |
| 25-29 | $\alpha_6 = 0.820\%$ | $\beta_6 = 0.672\%$ | $\beta_6 - \alpha_6 = -0.147\%$ | $\frac{\beta_6}{\alpha_6} = 0.820$ | 0.695 |
| 30-34 | $\alpha_7 = 0.888\%$ | $\beta_7 = 0.484\%$ | $\beta_7 - \alpha_7 = -0.404\%$ | $\frac{\beta_7}{\alpha_7} = 0.545$ | 0.201 |

| Part II 4 | model (odds scale) | | model (probability scale) | | risk |
|-----------|-----------------------------------|---|--|--|---------|
| | strata | non-exposed | exposed | non-exposed | exposed |
| 0-4 | $e^\alpha = 0.014\%$ | $e^\alpha e^\beta = 0.008\%$ | $\frac{1}{1+e^{-\alpha}} = 0.014\%$ | $\frac{1}{1+e^{-\alpha-\beta}} = 0.008\%$ | 0.571 |
| 5-9 | $e^\alpha e^{\gamma_1} = 0.192\%$ | $e^\alpha e^{\gamma_1} e^\beta = 0.111\%$ | $\frac{1}{1+e^{-\alpha-\gamma_1}} = 0.191\%$ | $\frac{1}{1+e^{-\alpha-\gamma_1-\beta}} = 0.111\%$ | 0.581 |
| 10-14 | $e^\alpha e^{\gamma_2} = 0.501\%$ | $e^\alpha e^{\gamma_2} e^\beta = 0.290\%$ | $\frac{1}{1+e^{-\alpha-\gamma_2}} = 0.498\%$ | $\frac{1}{1+e^{-\alpha-\gamma_2-\beta}} = 0.289\%$ | 0.580 |
| 15-19 | $e^\alpha e^{\gamma_3} = 0.637\%$ | $e^\alpha e^{\gamma_3} e^\beta = 0.269\%$ | $\frac{1}{1+e^{-\alpha-\gamma_3}} = 0.633\%$ | $\frac{1}{1+e^{-\alpha-\gamma_3-\beta}} = 0.367\%$ | 0.580 |
| 20-24 | $e^\alpha e^{\gamma_4} = 0.687\%$ | $e^\alpha e^{\gamma_4} e^\beta = 0.398\%$ | $\frac{1}{1+e^{-\alpha-\gamma_4}} = 0.683\%$ | $\frac{1}{1+e^{-\alpha-\gamma_4-\beta}} = 0.396\%$ | 0.580 |
| 25-29 | $e^\alpha e^{\gamma_5} = 0.888\%$ | $e^\alpha e^{\gamma_5} e^\beta = 0.514\%$ | $\frac{1}{1+e^{-\alpha-\gamma_5}} = 0.880\%$ | $\frac{1}{1+e^{-\alpha-\gamma_5-\beta}} = 0.511\%$ | 0.581 |
| 30-34 | $e^\alpha e^{\gamma_6} = 0.889\%$ | $e^\alpha e^{\gamma_6} e^\beta = 0.515\%$ | $\frac{1}{1+e^{-\alpha-\gamma_6}} = 0.882\%$ | $\frac{1}{1+e^{-\alpha-\gamma_6-\beta}} = 0.512\%$ | 0.580 |

Testing procedure: $\beta = -0.547$, p.value= 0.0001

| Part II 5 | model (odds scale) | | model (probability scale) | | risk | |
|-----------|--------------------------|------------------------------------|---------------------------------------|--|---------|-------|
| | strata | non-exposed | exposed | non-exposed | exposed | ratio |
| 0-4 | $e^{\alpha_1} = 0.014\%$ | $e^{\alpha_1} e^{\beta} = 0.008\%$ | $\frac{1}{1+e^{-\alpha_1}} = 0.014\%$ | $\frac{1}{1+e^{-\alpha_1} e^{-\beta}} = 0.008\%$ | | 0.571 |
| 5-9 | $e^{\alpha_2} = 0.192\%$ | $e^{\alpha_2} e^{\beta} = 0.111\%$ | $\frac{1}{1+e^{-\alpha_2}} = 0.191\%$ | $\frac{1}{1+e^{-\alpha_2} e^{-\beta}} = 0.111\%$ | | 0.581 |
| 10-14 | $e^{\alpha_3} = 0.501\%$ | $e^{\alpha_3} e^{\beta} = 0.290\%$ | $\frac{1}{1+e^{-\alpha_3}} = 0.498\%$ | $\frac{1}{1+e^{-\alpha_3} e^{-\beta}} = 0.289\%$ | | 0.580 |
| 15-19 | $e^{\alpha_4} = 0.637\%$ | $e^{\alpha_4} e^{\beta} = 0.269\%$ | $\frac{1}{1+e^{-\alpha_4}} = 0.633\%$ | $\frac{1}{1+e^{-\alpha_4} e^{-\beta}} = 0.367\%$ | | 0.580 |
| 20-24 | $e^{\alpha_5} = 0.687\%$ | $e^{\alpha_5} e^{\beta} = 0.398\%$ | $\frac{1}{1+e^{-\alpha_5}} = 0.683\%$ | $\frac{1}{1+e^{-\alpha_5} e^{-\beta}} = 0.396\%$ | | 0.580 |
| 25-29 | $e^{\alpha_6} = 0.888\%$ | $e^{\alpha_6} e^{\beta} = 0.514\%$ | $\frac{1}{1+e^{-\alpha_6}} = 0.880\%$ | $\frac{1}{1+e^{-\alpha_6} e^{-\beta}} = 0.511\%$ | | 0.581 |
| 30-34 | $e^{\alpha_7} = 0.889\%$ | $e^{\alpha_7} e^{\beta} = 0.515\%$ | $\frac{1}{1+e^{-\alpha_7}} = 0.882\%$ | $\frac{1}{1+e^{-\alpha_7} e^{-\beta}} = 0.512\%$ | | 0.580 |

Testing procedure: $\beta = -0.547$, p.value= 0.0001

Part III 8

| strata | model (odds scale) | | model (probability scale) | | p-value |
|--------|----------------------------------|--|---|---|---------|
| | non-exposed | exposed | non-exposed | exposed | |
| 0-4 | $e^\alpha = 0.013\%$ | $e^\alpha e^\gamma = 0.009\%$ | $\frac{1}{1+e^{-\alpha}} = 0.013\%$ | $\frac{1}{1+e^{-\alpha}e^{-\gamma}} = 0.009\%$ | 0.759 |
| 5-9 | $e^\alpha e^{\beta_1} = 0.154\%$ | $e^\alpha e^{\beta_1} e^\gamma e^{\delta_1} = 0.137\%$ | $\frac{1}{1+e^{-\alpha-\beta_1}} = 0.154\%$ | $\frac{1}{1+e^{-\alpha-\beta_1-\gamma-\delta_1}} = 0.137\%$ | 0.778 |
| 10-14 | $e^\alpha e^{\beta_2} = 0.499\%$ | $e^\alpha e^{\beta_2} e^\gamma e^{\delta_2} = 0.291\%$ | $\frac{1}{1+e^{-\alpha-\beta_2}} = 0.497\%$ | $\frac{1}{1+e^{-\alpha-\beta_2-\gamma-\delta_2}} = 0.290\%$ | 0.059 |
| 15-19 | $e^\alpha e^{\beta_3} = 0.725\%$ | $e^\alpha e^{\beta_3} e^\gamma e^{\delta_3} = 0.345\%$ | $\frac{1}{1+e^{-\alpha-\beta_3}} = 0.719\%$ | $\frac{1}{1+e^{-\alpha-\beta_3-\gamma-\delta_3}} = 0.344\%$ | 0.018 |
| 20-24 | $e^\alpha e^{\beta_4} = 0.820\%$ | $e^\alpha e^{\beta_4} e^\gamma e^{\delta_4} = 0.340\%$ | $\frac{1}{1+e^{-\alpha-\beta_4}} = 0.814\%$ | $\frac{1}{1+e^{-\alpha-\beta_4-\gamma-\delta_4}} = 0.339\%$ | 0.006 |
| 25-29 | $e^\alpha e^{\beta_5} = 0.826\%$ | $e^\alpha e^{\beta_5} e^\gamma e^{\delta_5} = 0.677\%$ | $\frac{1}{1+e^{-\alpha-\beta_5}} = 0.820\%$ | $\frac{1}{1+e^{-\alpha-\beta_5-\gamma-\delta_5}} = 0.672\%$ | 0.564 |
| 30-34 | $e^\alpha e^{\beta_6} = 0.886\%$ | $e^\alpha e^{\beta_6} e^\gamma e^{\delta_6} = 0.486\%$ | $\frac{1}{1+e^{-\alpha-\beta_6}} = 0.888\%$ | $\frac{1}{1+e^{-\alpha-\beta_6-\gamma-\delta_6}} = 0.484\%$ | 0.160 |

Testing procedure: $(\gamma, \gamma + \delta_1, \gamma + \delta_2, \gamma + \delta_3, \gamma + \delta_4, \gamma + \delta_5, \gamma + \delta_6)$ vs. 0

Part III 9

| strata | model (odds scale) | | model (probability scale) | | p-value |
|--------|--------------------------|--------------------------------------|---------------------------------------|---|---------|
| | non-exposed | exposed | non-exposed | exposed | |
| 0-4 | $e^{\alpha_1} = 0.013\%$ | $e^{\alpha_1} e^{\beta_1} = 0.009\%$ | $\frac{1}{1+e^{-\alpha_1}} = 0.013\%$ | $\frac{1}{1+e^{-\alpha_1}e^{-\beta_1}} = 0.009\%$ | 0.759 |
| 5-9 | $e^{\alpha_2} = 0.154\%$ | $e^{\alpha_2} e^{\beta_2} = 0.137\%$ | $\frac{1}{1+e^{-\alpha_2}} = 0.154\%$ | $\frac{1}{1+e^{-\alpha_2}e^{-\beta_2}} = 0.137\%$ | 0.778 |
| 10-14 | $e^{\alpha_3} = 0.499\%$ | $e^{\alpha_3} e^{\beta_3} = 0.291\%$ | $\frac{1}{1+e^{-\alpha_3}} = 0.497\%$ | $\frac{1}{1+e^{-\alpha_3}e^{-\beta_3}} = 0.290\%$ | 0.059 |
| 15-19 | $e^{\alpha_4} = 0.725\%$ | $e^{\alpha_4} e^{\beta_4} = 0.345\%$ | $\frac{1}{1+e^{-\alpha_4}} = 0.719\%$ | $\frac{1}{1+e^{-\alpha_4}e^{-\beta_4}} = 0.344\%$ | 0.018 |
| 20-24 | $e^{\alpha_5} = 0.820\%$ | $e^{\alpha_5} e^{\beta_5} = 0.340\%$ | $\frac{1}{1+e^{-\alpha_5}} = 0.814\%$ | $\frac{1}{1+e^{-\alpha_5}e^{-\beta_5}} = 0.339\%$ | 0.006 |
| 25-29 | $e^{\alpha_6} = 0.826\%$ | $e^{\alpha_6} e^{\beta_6} = 0.677\%$ | $\frac{1}{1+e^{-\alpha_6}} = 0.820\%$ | $\frac{1}{1+e^{-\alpha_6}e^{-\beta_6}} = 0.672\%$ | 0.564 |
| 30-34 | $e^{\alpha_7} = 0.886\%$ | $e^{\alpha_7} e^{\beta_7} = 0.486\%$ | $\frac{1}{1+e^{-\alpha_7}} = 0.888\%$ | $\frac{1}{1+e^{-\alpha_7}e^{-\beta_7}} = 0.484\%$ | 0.160 |

Testing procedure: $(\beta_1, \beta_2, \beta_3, \beta_4, \beta_5, \beta_6, \beta_7)$ vs. 0