7. Cross tabulation and logistic regression

(PROC FREQ and PROC LOGISTIC)

Use of SAS
March 2011

Table analyses: PROC FREQ

```
/* One-way table */
proc freq data=afrika.bissau;
  tables dead;
run;


/* Two-way table */
proc freq data=afrika.bissau;
  tables bcg*dead;
run;


/* Three-way table */
proc freq data=afrika.bissau;
  tables agemm*bcg*dead;
run;
```

etc.

Two-way table (2 x 2 table)

```
proc freq data=afrika.bissau;
  tables bcg*dead;
run;
```

```
                          Table of bcg by dead

           bcg        dead

           Frequency|
           Percent  |
           Row Pct  |
           Col Pct  |        1|        2|  Total
           ---------+--------+--------+
                1 |    124 |   3176 |   3300
                  |   2.35 |  60.23 |  62.58
                  |   3.76 |  96.24 |
                  |  56.11 |  62.87 |
           ---------+--------+--------+
                2 |     97 |   1876 |   1973
                  |   1.84 |  35.58 |  37.42
                  |   4.92 |  95.08 |
                  |  43.89 |  37.13 |
           ---------+--------+--------+
           Total         221     5052     5273
                        4.19    95.81   100.00
```

Two-way table (2 x 2 table)

	Outcome		
Exposure	Yes	No	Total
Yes	a	b	n_1
No	c	d	n_2
Total	$a + c$	$b + d$	n

Hypothesis H_0: The probability of having the outcome is the same in the two exposure groups.

The probability of having the outcome under H_0:

$$p = \frac{a + c}{n}$$

.

The EXPECTED numbers under H_0 in the four cells are calculated as:

Exposure	Outcome		Total
	Yes	No	
Yes	$E(a) = p \times n_1$	$E(b) = (1-p) \times n_1$	n_1
No	$E(c) = p \times n_2$	$E(d) = (1-p) \times n_2$	n_2
Total	$a + c$	$b + d$	n

Chi-square test for testing H_0 (observed - expected):

$$X^2 = \frac{(a - E(a))^2}{E(a)} + \frac{(b - E(b))^2}{E(b)} + \frac{(c - E(c))^2}{E(c)} + \frac{(d - E(d))^2}{E(d)}$$
$$\sim \chi^2(1)$$

H_0 is rejected if p-value < 0.05 which corresponds to $X^2 > 3.84$.

Risk of Dying and BCG

```
proc freq data=afrika.bissau;
  tables bcg*dead / expected chisq nocol nopercent;
run;
```

```
                 Table of bcg by dead

           bcg          dead

           Frequency|
           Expected |
           Row Pct  |        1|        2|  Total
           ---------+--------+--------+
                 1 |     124 |   3176 |   3300
                   | 138.31 | 3161.7 |
                   |    3.76 |  96.24 |
           ---------+--------+--------+
                 2 |      97 |   1876 |   1973
                   | 82.692 | 1890.3 |
                   |    4.92 |  95.08 |
           ---------+--------+--------+
           Total          221     5052     5273


                 Statistics for Table of bcg by dead


Statistic                        DF      Value      Prob
---------------------------------------------------------

Chi-Square                        1     4.1291     0.0422
Likelihood Ratio Chi-Square       1     4.0516     0.0441
Continuity Adj. Chi-Square        1     3.8456     0.0499
Mantel-Haenszel Chi-Square        1     4.1283     0.0422
Phi Coefficient                         -0.0280
Contingency Coefficient                  0.0280
Cramer's V                              -0.0280
```

Risk Ratio

| | Outcome | | |
Exposure	Yes	No	Total
Yes	a	b	n_1
No	c	d	n_2
Total	$a+c$	$b+d$	n

Risk ratio:

$$\text{RR} = \frac{\text{probability of outcome among exposed}}{\text{probability of outcome among not-exposed}} = \frac{a/n_1}{c/n_2}.$$

The H_0 corresponds to RR $= 1$.

Odds ratio

| | Outcome | | |
Exposure	Yes	No	Total
Yes	a	b	n_1
No	c	d	n_2
Total	$a + c$	$b + d$	n

Odds ratio:

$$\text{OR} = \frac{\text{odds of outcome among exposed}}{\text{odds of outcome among not-exposed}} = \frac{a/b}{c/d} = \frac{a \times d}{b \times c}$$

The H_0 corresponds to OR $= 1$.

RR and OR in `proc freq`

```
proc freq data=afrika.bissau;
  table bcg*dead / RELRISK nocol nopercent;
run;
```

```
                            Table of bcg by dead

              bcg          dead

              Frequency|
              Row Pct  |       1|       2|  Total
              ---------+--------+--------+
                     1 |    124 |   3176 |   3300
                       |   3.76 |  96.24 |
              ---------+--------+--------+
                     2 |     97 |   1876 |   1973
                       |   4.92 |  95.08 |
              ---------+--------+--------+
              Total         221     5052     5273


                       Statistics for Table of bcg by dead

                     Estimates of the Relative Risk (Row1/Row2)
```

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	0.7551	0.5754	0.9909
Cohort (Col1 Risk)	0.7643	0.5895	0.9910
Cohort (Col2 Risk)	1.0122	1.0000	1.0245

OR and RR in `proc freq`

It is important that the two variables in the `table` statement are coded properly when using the OR and RR:

```
data hope;
  set afrika.bissau;
  if dead=2 then deadny=0;
  if dead=1 then deadny=1;
proc freq data=hope;
  table bcg*deadny / relrisk nocol nopercent norow;
run;
```

```
              bcg        deadny

              Frequency|
              Row Pct  |      0|      1|  Total
              ---------+-------+-------+
                    1 |  3176 |   124 |   3300
              ---------+-------+-------+
                    2 |  1876 |    97 |   1973
              ---------+-------+-------+
              Total       5052     221    5273


           Statistics for Table of bcg by deadny
           Estimates of the Relative Risk (Row1/Row2)
       Type of Study                 Value       95% Confidence Limits
       ----------------------------------------------------------------
       Case-Control (Odds Ratio)     1.3243       1.0092       1.7378
       Cohort (Col1 Risk)            1.0122       1.0000       1.0245
       Cohort (Col2 Risk)            0.7643       0.5895       0.9910
```

R x C tables

```
proc freq data=afrika.bissau;
  table ethnic*dead / chisq;
run;
```

```
ethnic     dead

Frequency|
Percent  |
Row Pct  |
Col Pct  |       1|       2|  Total
---------+--------+--------+
Balanta  |     37 |    788 |    825
         |   0.70 |  14.94 |  15.65
         |   4.48 |  95.52 |
         |  16.74 |  15.60 |
---------+--------+--------+
Fula     |     52 |   1370 |   1422
         |   0.99 |  25.98 |  26.97
         |   3.66 |  96.34 |
         |  23.53 |  27.12 |
---------+--------+--------+
Mandinga |     49 |   1113 |   1162
         |   0.93 |  21.11 |  22.04
         |   4.22 |  95.78 |
         |  22.17 |  22.03 |
---------+--------+--------+
Other    |     23 |    724 |    747
         |   0.44 |  13.73 |  14.17
         |   3.08 |  96.92 |
         |  10.41 |  14.33 |
---------+--------+--------+
Pepel    |     60 |   1057 |   1117
         |   1.14 |  20.05 |  21.18
         |   5.37 |  94.63 |
         |  27.15 |  20.92 |
---------+--------+--------+
Total         221     5052     5273
             4.19    95.81   100.00
```

12

```
                 Statistics for Table of ethnic by dead

Statistic                         DF       Value       Prob
------------------------------------------------------------

Chi-Square                         4       7.3670     0.1177
Likelihood Ratio Chi-Square        4       7.3268     0.1196
Mantel-Haenszel Chi-Square         1       1.0857     0.2974
Phi Coefficient                            0.0374
Contingency Coefficient                    0.0374
Cramer's V                                 0.0374
```

Exercise: PROC FREQ

Using the bissau data:

1. Investigate whether DTP-vaccinated children (variable `dtp`) dies more often than DTP-unvaccinated children.

2. Calculate the odds ratio (OR) and corresponding 95% confidence interval.

3. The variable `region` indicates the rural region of the children. Is mortality associated with region?

Logistic regression: PROC LOGISTIC

Logistic regression is like a linear regression, but here the outcome
is DISCRETE with two levels (yes/no, died/survived, ill/well).
Look again at the 2 x 2 table

	Outcome		
Exposure	Yes	No	Total
Yes	a	b	n_1
No	c	d	n_2

Let $p = a/n_1$ be the probability of outcome among exposed. Odds
can then be defined as

$$\text{odds} = \frac{p}{1-p} = \frac{a/n_1}{1 - a/n_1} = \frac{a/n_1}{b/n_1} = \frac{a}{b}$$

Logistic regression for 2 x 2 table

What is modeled in a logistic regression is the NATURAL LOGARITHM of the ODDS of outcome:

$$\ln(\text{odds}) = \ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X,$$

where X is the exposure covariate. We call $\ln(\text{odds})$ for the LOG-ODDS. Now let us assume that the exposure is coded like

$$X = \begin{cases} 1 & \text{Exposed} \\ 0 & \text{Non-exposed} \end{cases}$$

The log-odds of outcome among exposed $(X = 1)$ is

$$\ln \left(\frac{p_1}{1 - p_1} \right) = \beta_0 + \beta_1 \times 1 = \beta_0 + \beta_1.$$

The log-odds of outcome among non-exposed $(X = 0)$ is

$$\ln \left(\frac{p_0}{1 - p_0} \right) = \beta_0 + \beta_1 \times 0 = \beta_0.$$

The β_0 is the log-odds of outcome in non-exposed.

Now, the difference in log-odds between exposed and non-exposed is

$$\ln \left(\frac{p_1}{1 - p_1} \right) - \ln \left(\frac{p_0}{1 - p_0} \right) = \beta_0 + \beta_1 - \beta_0 = \beta_1$$

Using the rule of logarithms

$$\ln(a) - \ln(b) = \ln(\frac{a}{b})$$

we get

$$\ln\left(\frac{p_1/(1-p_1)}{p_0/(1-p_0)}\right) = \beta_1$$

and

$$\frac{p_1/(1-p_1)}{p_0/(1-p_0)} = \exp(\beta_1)$$

This means that the odds ratio between exposed and non-exposed is

$$\mathrm{OR} = \exp(\beta_1).$$

Estimation of the regression coefficients is done using maximum likelihood.

PROC LOGISTIC

```
proc logistic data=afrika.bissau;
  class bcg / param=ref;
  model dead(event="1")=bcg;
run;
```

REMEMBER the option `param=ref`

Part of output:

```
                Analysis of Maximum Likelihood Estimates
                                    Standard           Wald
    Parameter      DF    Estimate      Error    Chi-Square    Pr > ChiSq

    Intercept       1     -2.9621     0.1041      809.3011       <.0001
    bcg       1     1     -0.2810     0.1386        4.1074       0.0427


                        Odds Ratio Estimates

                             Point          95% Wald
            Effect        Estimate      Confidence Limits

            bcg 1 vs 2       0.755      0.575       0.991
```

Multiple logistic regression

$$\ln(\text{odds}) = \ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \cdots,$$

The interpretation is still that $\exp(\beta_1)$ is an odds ratios, but now adjusted for the covariates $X_2, X_3, \cdots$. The same idea as in linear regression.

Remember that the response or outcome is discrete with two categories. However the covariates $(X_1, X_2, X_3, \cdots)$ do not need to be categorical, they can also be continuous.

In SAS one use the CLASS statement to indicate categorical variables, and variables in a MODEL statement that is not listed in the CLASS statement is assumed to be continuous.

Multiple logistic regression: PROC LOGISTIC

```
proc logistic data=afrika.bissau;
  class bcg / param=ref;
  model dead(event="1")=bcg agemm;
run;
```

```
                      Type 3 Analysis of Effects
                                    Wald
             Effect      DF     Chi-Square     Pr > ChiSq
             bcg          1        5.4366         0.0197
             agemm        1        1.5307         0.2160


              Analysis of Maximum Likelihood Estimates
                                 Standard        Wald
    Parameter      DF    Estimate      Error    Chi-Square    Pr > ChiSq
    Intercept       1     -3.0510     0.1281     567.4989       <.0001
    bcg        1    1     -0.3450     0.1480       5.4366        0.0197
    agemm           1      0.0486     0.0393       1.5307        0.2160


                       Odds Ratio Estimates
                           Point           95% Wald
             Effect       Estimate     Confidence Limits
             bcg   1 vs 2   0.708       0.530      0.946
             agemm          1.050       0.972      1.134
```

Interpretation: For each increase of 1 in `agemm` the odds increases with 1.050.

Multiple logistic regression: PROC LOGISTIC

The variable `agemm` is now used as a CLASS variable:

```
proc logistic data=afrika.bissau;
  class bcg agemm / param=ref;
  model dead(event="1")=bcg agemm;
run;
```

`agemm` has 7 classes: 0 to 6. SAS automatically generates 7 indicator functions for each class and include 6 of these in the regression model. The class not included (SAS uses per default the highest class) is the reference against which all other classes are listed in the output.

The test in TYPE 3 for `agemm` is a test for the hypothesis of equal risk of dying in the 7 classes. This test does not change when you change reference.

```
                          Type 3 Analysis of Effects
                                      Wald
              Effect        DF    Chi-Square    Pr > ChiSq
              bcg            1      5.2393         0.0221
              agemm          6      7.3938         0.2860


                  Analysis of Maximum Likelihood Estimates


                                  Standard         Wald
    Parameter         DF   Estimate    Error   Chi-Square   Pr > ChiSq
    Intercept         1    -3.0948    0.3281     88.9498      <.0001
    bcg         1     1    -0.3430    0.1499      5.2393       0.0221
    agemm       0     1     0.0588    0.3599      0.0267       0.8703
    agemm       1     1     0.1803    0.3513      0.2635       0.6077
    agemm       2     1    -0.1925    0.3650      0.2783       0.5978
    agemm       3     1     0.2700    0.3514      0.5904       0.4423
    agemm       4     1     0.4044    0.3492      1.3410       0.2469
    agemm       5     1     0.3618    0.3549      1.0392       0.3080


                          Odds Ratio Estimates
                              Point        95% Wald
              Effect        Estimate   Confidence Limits
              bcg    1 vs 2    0.710     0.529     0.952
              agemm 0 vs 6     1.061     0.524     2.147
              agemm 1 vs 6     1.198     0.602     2.384
              agemm 2 vs 6     0.825     0.403     1.687
              agemm 3 vs 6     1.310     0.658     2.608
              agemm 4 vs 6     1.498     0.756     2.971
              agemm 5 vs 6     1.436     0.716     2.879
```

Change of reference group: REF=""

The variable `agemm` is again used as a CLASS variable but now choosing agegroup 4 as reference:

```
proc logistic data=afrika.bissau;
  class bcg agemm(ref="4") / param=ref;
  model dead(event="1")=bcg agemm;
run;
```

```
                    Type 3 Analysis of Effects
                                    Wald
            Effect       DF    Chi-Square    Pr > ChiSq
            bcg           1       5.2393        0.0221
            agemm         6       7.3938        0.2860



                 Analysis of Maximum Likelihood Estimates
                                  Standard        Wald
    Parameter       DF    Estimate     Error    Chi-Square    Pr > ChiSq
    Intercept        1     -2.6904    0.1973     185.9085       <.0001
    bcg       1      1     -0.3430    0.1499       5.2393       0.0221
    agemm     0      1     -0.3456    0.2479       1.9444       0.1632
    agemm     1      1     -0.2241    0.2368       0.8953       0.3441
    agemm     2      1     -0.5969    0.2575       5.3731       0.0204
    agemm     3      1     -0.1344    0.2385       0.3175       0.5731
    agemm     5      1     -0.0426    0.2442       0.0304       0.8616
    agemm     6      1     -0.4044    0.3492       1.3410       0.2469



                      Odds Ratio Estimates
                           Point          95% Wald
            Effect         Estimate    Confidence Limits
            bcg    1 vs 2    0.710     0.529      0.952
            agemm 0 vs 4     0.708     0.435      1.150
            agemm 1 vs 4     0.799     0.502      1.271
            agemm 2 vs 4     0.551     0.332      0.912
            agemm 3 vs 4     0.874     0.548      1.395
            agemm 5 vs 4     0.958     0.594      1.546
            agemm 6 vs 4     0.667     0.337      1.323
```

Exercise: PROC LOGISTIC

Using the Bissau data:

1. Make a logistic regression where outcome is `dead` and exposure is `dtp`. Interpret the results and compare with the results from the exercise using `proc freq` on page 14.

2. Now control for `bcg` in the logistic regression from 1 above. What happend with the odds ratio for `dtp`?

3. Add variables `agemm` and `region` to the model as class variables. Let `region=7` be the reference group for variable `region`. Did inclusion of these variables change interpretation of effect `dtp`?

Logistic regression: PROC GENMOD

The procedure `proc genmod` (GENeralized linear MODels) can also perform logistic regression:

```
proc genmod data=afrika.bissau;
  class bcg;
  model dead=bcg / dist=binomial;
  estimate "BCG+ vs BCG-" bcg 1 -1 / exp;
run;
```

Getting the odds ratios and their confidence intervals out is however not as easy as in `proc logistic`, but done with `estimate` statements. `proc genmod` is however very flexible and can analyse other types of regression models like Poisson (event per person-years) and linear regression.