Binary Outcomes – Logistic Regression (Chapter 6)

- 2 by 2 tables
- Odds ratio, relative risk, risk difference
- Binomial regression - the logistic, log and linear link functions
- Categorical predictors - Continuous predictors
- Estimation by maximum likelihood
- Predicted probabilities
- Separation (Quasi-separation)
- Assessing model fit

A binary outcome example: WCGS

The Western Collaborative Group Study (WCGS): a large epidemiological study of coronary heart disease (CHD).

Rosenman, R. H., Friedman, M., Straus, R., Wurm, M., Kositchek, R., Hahn, W. and Werthessen, N. T. (1964). A predictive study of coronary heart disease: the western collaborative group study. Journal of the American Medical Association, 189, 113–120.

Outcome - 0/1: an indicator of CHD status

Study question – Whether CHD rates are different between age groups (<50 vs. >=50)

2 by 2 tables (SAS)

```
proc freq;
          tables chd69 * bage_50/chisq cmh riskdiff;
run;
```

bage_50 Frequency / Percent / Row Pct / Col Pct	chd69 0	chd69 1	Total
0	2104	145	2249
	66.71	4.60	71.31
	93.55	6.45	
	72.63	56.42	
1	793	112	905
	25.14	3.55	28.69
	87.62	12.38	
	27.37	43.58	
Total	2897	257	3154
	91.85	8.15	100.00

Statistics for Table of chd69 by bage_50

Statistic	DF	Value	Prob
Chi-Square	1	30.3033	<.0001
Likelihood Ratio Chi-Square	1	28.2000	<.0001
Continuity Adj. Chi-Square	1	29.5164	<.0001
Mantel-Haenszel Chi-Square	1	30.2937	<.0001
Phi Coefficient		0.0980	
Contingency Coefficient		0.0976	
Cramer's V		0.0980	

Fisher's Exact Test

Cell (1,1) Frequency (F)	2104
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	7.622E-08
Table Probability (P)	3.993E-08
Two-sided Pr <= P	1.167E-07

2 by 2 tables (SAS): risk estimates

Column 1 Risk Estimates

	Risk	ASE	(Asymptotic) 95% Confidence Limits		(Exact) 95% Confidence Limits	
Row 1	0.9355	0.0052	0.9254	0.9457	0.9246	0.9453
Row 2	0.8762	0.0109	0.8548	0.8977	0.8530	0.8970
Total	0.9185	0.0049	0.9090	0.9281	0.9084	0.9278
Difference	0.0593	0.0121	0.0355	0.0830		

Difference is (Row 1 - Row 2)

Column 2 Risk Estimates

	Risk	ASE	(Asymptotic) 95% Confidence Limits		(Exact) 95% Confidence Limits	
Row 1	0.0645	0.0052	0.0543	0.0746	0.0547	0.0754
Row 2	0.1238	0.0109	0.1023	0.1452	0.1030	0.1470
Total	0.0815	0.0049	0.0719	0.0910	0.0722	0.0916
Difference	-0.0593	0.0121	-0.0830	-0.0355		

Difference is (Row 1 - Row 2)

- What is the rate of CHD in the younger group? What is the rate of CHD in the older group?
- What is the difference in the rates of CHD between the two age groups?

2 by 2 tables (SAS): odds ratio, risk ratio

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	30.2937	<.0001
2	Row Mean Scores Differ	1	30.2937	<.0001
3	General Association	1	30.2937	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control	Mantel-Haenszel	2.0494	1.5806	2.6572
(Odds Ratio)	Logit	2.0494	1.5806	2.6572
Cohort	Mantel-Haenszel	1.0677	1.0394	1.0966
(Col1 Risk)	Logit	1.0677	1.0394	1.0966
Cohort	Mantel-Haenszel	0.5210	0.4122	0.6584
(Col2 Risk)	Logit	0.5210	0.4122	0.6584

- How was 2.04945 calculated and what is it? How was 1.0677 calculated and what is it? How was 0.521 calculated and what is it?
- What is the relative rate of CHD if a person is <50 as compared to >50?
- Is there a significant effect of age<50 over age>50?

2 by 2 tables (Stata)

```
. tabulate bage_50 chd69, all exact row col
+--------------------+
| Key                |
|--------------------|
|     frequency      |
|  row percentage    |
| column percentage  |
+--------------------+

           |         chd69
   bage_50 |         0          1 |     Total
-----------+----------------------+----------
       <50 |     2,104        145 |     2,249
           |     93.55       6.45 |    100.00
           |     72.63      56.42 |     71.31
-----------+----------------------+----------
      >=50 |       793        112 |       905
           |     87.62      12.38 |    100.00
           |     27.37      43.58 |     28.69
-----------+----------------------+----------
     Total |     2,897        257 |     3,154
           |     91.85       8.15 |    100.00
           |    100.00     100.00 |    100.00

          Pearson chi2(1) =  30.3033   Pr = 0.000
 likelihood-ratio chi2(1) =  28.2000   Pr = 0.000
               Cramér's V =   0.0980
                    gamma =   0.3441  ASE = 0.058
          Kendall's tau-b =   0.0980  ASE = 0.020
           Fisher's exact =                 0.000
   1-sided Fisher's exact =                 0.000
```

Stata - Epitab “Tables for epidemiologists”

```
. cc chd69 bage_50      // for case-control study (to obtain estimated OR)
                                                      Proportion
                 |   Exposed   Unexposed  |      Total     Exposed
-----------------+------------------------+------------------------
           Cases |       112         145  |        257       0.4358
        Controls |       793        2104  |       2897       0.2737
-----------------+------------------------+------------------------
           Total |       905        2249  |       3154       0.2869
                 |      Point estimate    |    [95% Conf. Interval]
                 |------------------------+------------------------
      Odds ratio |          2.04938       |    1.565101    2.677467 (exact)
 Attr. frac. ex. |         .5120476       |    .3610636    .6265127 (exact)
 Attr. frac. pop |         .2231492       |
                 +-----------------------------------------------
                             chi2(1) =    30.30  Pr>chi2 = 0.0000
. cs chd69 bage_50      // for cohort study (to obtain estimated RD & RR)
                 | bage_50                |
                 |   Exposed   Unexposed  |      Total
-----------------+------------------------+------------
           Cases |       112         145  |        257
        Noncases |       793        2104  |       2897
-----------------+------------------------+------------
           Total |       905        2249  |       3154
            Risk |  .1237569    .0644731  |   .0814838
                 |      Point estimate    |    [95% Conf. Interval]
                 |------------------------+------------------------
 Risk difference |         .0592838       |    .0355493    .0830183
      Risk ratio |         1.919512       |     1.51876     2.42601
 Attr. frac. ex. |         .4790343       |    .3415682    .5878006
 Attr. frac. pop |          .208762       |
                 +-----------------------------------------------
                             chi2(1) =    30.30  Pr>chi2 = 0.0000
```

Examining Odds Ratio, Risk Ratio and Risk Difference

We are interested in comparing: P(Outcome|Exposure 1) to P(Outcome|Exposure 0). When the outcome is binary the probability is the same as the expected value, hence if we let X represent exposure(s) of interest (e.g. different treatments in a clinical trial, exposure to a carcinogen), we compare $E(Y|X = 1) = \pi_1$ to $E(Y|X = 0) = \pi_0$. So π_1 is probability of the event given that X = 1 has occurred and π_0 is the probability of the event given that X = 0 has occurred.

The relative risk (risk ratio) or relative rate (rate or prevalence ratio) is:

$$RR = \pi_1/\pi_0$$

The risk (or rate or prevalence) difference, or absolute risk reduction is:

$$RD = \pi_1 - \pi_0$$

The odds ratio is:

$$OR = \frac{\pi_1}{1-\pi_1} \Big/ \frac{\pi_0}{1-\pi_0}$$

Comparing OR, RR, and RD

This table considers scenarios when OR = 2

π_0	Odds	π_1	Odds	OR	RR	RD
.005	0.005025126	0.009950249	0.01005025	2	1.99	.00495
.03	0.03092784	0.05825243	0.06185567	2	1.94	.0282
.05	0.0526	0.0952381	0.1052	2	1.90	.045
.10	0.1111	0.1818182	0.2222	2	1.82	.0818
.2	0.25	0.33	0.5	2	1.65	.13
.5	1	0.67	2	2	1.34	.17
.8	4	0.89	8	2	1.11	.09
.9	9	0.95	18	2	1.06	.05
.98	49	0.99	98	2	1.01	.01

NOTE: odds = $\pi/(1-\pi)$, π = odds/(odds + 1)

- How does the RR differ from the OR across the different probabilities?
- How does the RD differ from the RR and OR?

Comparing OR, RR, and RD

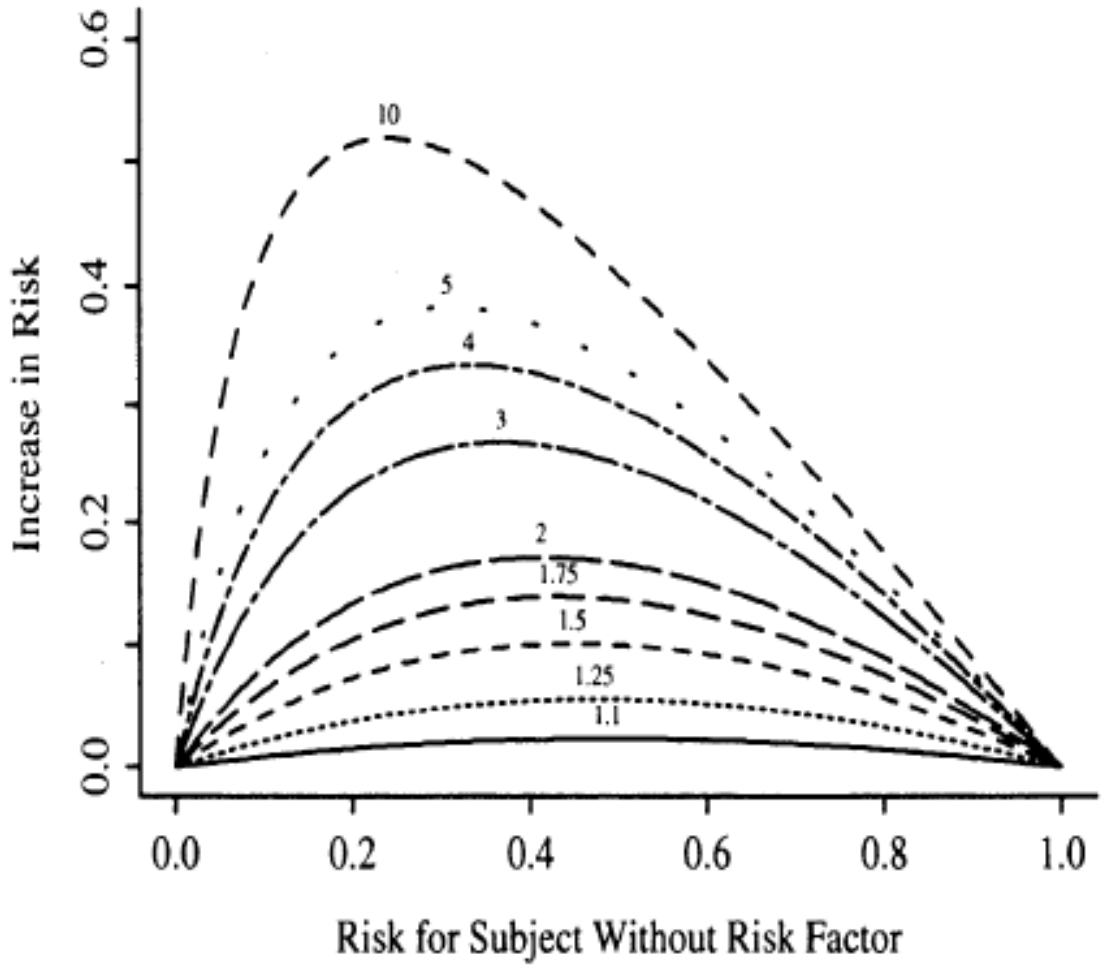


Figure 10.2: Absolute benefit as a function of risk of the event in a control subject and the relative effect (odds ratio) of the risk factor. The odds ratios are given for each curve.

From Chaprter 10 of Harrell F (2001) *Regression Modeling Strategies With applications to linear models, logistic regression and survival analysis*.

Notes on OR, RR, and RD

- Notice when the risk is small, the risk is well approximated by the odds and hence the relative risk is well approximated by the odds ratio. This is why you will hear the following: “The OR approximates the RR for rare diseases”.
- Notice that the risk difference becomes smaller as the rate is smaller, though the relative risk (and odds ratio) can remain large.
- As the risk becomes common (> 10%), the OR greatly overestimates the RR.
- RR and RD are arguably more interpretable than OR, nevertheless the odds ratio is ubiquitous in Public Health and Medicine despite the tendency for people to interpret ORs as if they are RRs
- Recent push in medical and public health literature to get researchers to estimate RR and RD (see more push for RD in medical literature with some Guidelines for reporting only allowing RD rather than relative measures) rather than OR. (e.g. Spiegelman, D. und Hertzmark, Easy SAS Calculations for Risk or Prevalence Ratios and Differences, *American Journal of Epidemiology*, 2005, 162, 199-205.)
- NOTE: If data were collected from a case control study, then we cannot estimate risk (or risk ratios) from the data without some auxiliary information about overall prevalence in the population. But we can still estimate odds and hence odds ratios.

2 by n tables

```
. tabulate agec chd69, all exact row col
           |         chd69
      agec |         0          1 |     Total
-----------+----------------------+----------
     35-40 |       512         31 |       543
           |     94.29       5.71 |    100.00
           |     17.67      12.06 |     17.22
-----------+----------------------+----------
     41-45 |     1,036         55 |     1,091
           |     94.96       5.04 |    100.00
           |     35.76      21.40 |     34.59
-----------+----------------------+----------
     46-50 |       680         70 |       750
           |     90.67       9.33 |    100.00
           |     23.47      27.24 |     23.78
-----------+----------------------+----------
     51-55 |       463         65 |       528
           |     87.69      12.31 |    100.00
           |     15.98      25.29 |     16.74
-----------+----------------------+----------
     56-60 |       206         36 |       242
           |     85.12      14.88 |    100.00
           |      7.11      14.01 |      7.67
-----------+----------------------+----------
     Total |     2,897        257 |     3,154
           |     91.85       8.15 |    100.00
           |    100.00     100.00 |    100.00

          Pearson chi2(4) =  46.6534   Pr = 0.000
 likelihood-ratio chi2(4) =  44.9464   Pr = 0.000
               Cramér's V =   0.1216
                    gamma =   0.2896  ASE = 0.045
          Kendall's tau-b =   0.1012  ASE = 0.016
           Fisher's exact =                 0.000
```

2 by n table: test for trend

```
. tabodds chd69 agec
-------------------------------------------------------------------------------
      agec  |      cases     controls       odds      [95% Conf. Interval]
------------+------------------------------------------------------------------
      35-40 |         31          512    0.06055        0.04214   0.08700
      41-45 |         55         1036    0.05309        0.04048   0.06963
      46-50 |         70          680    0.10294        0.08049   0.13165
      51-55 |         65          463    0.14039        0.10829   0.18200
      56-60 |         36          206    0.17476        0.12265   0.24900
-------------------------------------------------------------------------------
Test of homogeneity (equal odds): chi2(4)  =    46.64
                                  Pr>chi2  =   0.0000
Score test for trend of odds:     chi2(1)  =    40.76
                                  Pr>chi2  =   0.0000

. tabodds chd69 agec, or
-------------------------------------------------------------------------------
        agec |  Odds Ratio       chi2       P>chi2     [95% Conf. Interval]
-------------+-----------------------------------------------------------------
       35-40 |    1.000000          .          .              .          .
       41-45 |    0.876822       0.32       0.5692      0.557454   1.379156
       46-50 |    1.700190       5.74       0.0166      1.095789   2.637958
       51-55 |    2.318679      14.28       0.0002      1.479779   3.633160
       56-60 |    2.886314      18.00       0.0000      1.728069   4.820876
-------------------------------------------------------------------------------
```

Modeling binary outcomes

Since Y_i is 0-1 we can model it with a Binomial distribution with parameter π_i. So we have

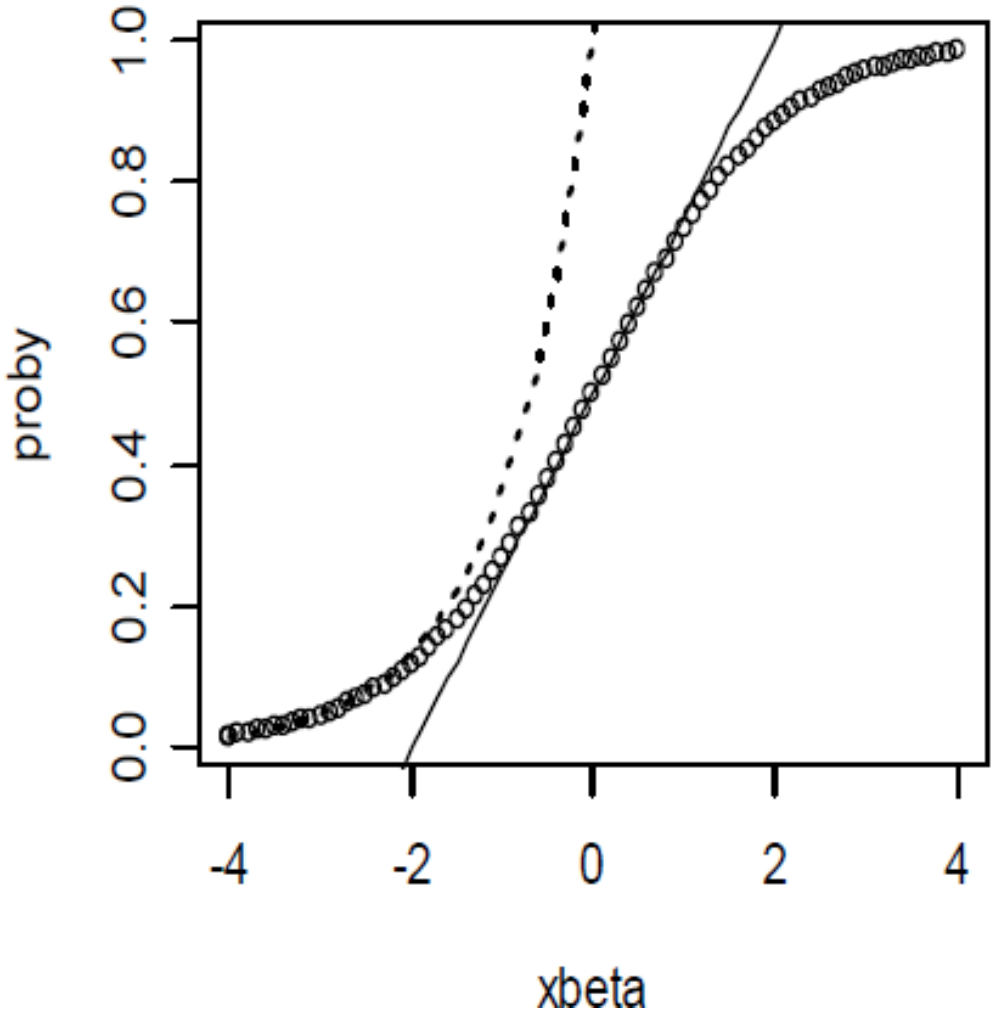
$$Y_i|X_i \sim Bin(1, \pi_i)$$

and we can model $E(Y_i|X_i) = \pi_i$ as a function of predictor variables X_i as

$$\begin{aligned} \pi_i &= \frac{exp(X_i\beta)}{1 + exp(X_i\beta)} \qquad \text{(logistic function)} \\ \pi_i &= exp(X_i\beta) \\ \pi_i &= X_i\beta \end{aligned}$$

Modeling binary outcomes

Since π_i is a probability, we require $0 \leq \pi_i \leq 1$. Hence, there are restrictions on the acceptable values of $X_i\beta$ (except for the logistic function)



Generalized linear modeling (GLM): Link functions

Given $Y_i|X_i \sim \text{Bin}(1, \pi_i)$ with $E(Y_i|X_i) = \pi_i = g(X\beta)$, we want to rewrite the relationship between π and $X\beta$ so that $X\beta$ is on a side by itself equal to a nonlinear function of π. This inverse function is called the link function in generalized linear modeling.

- The link function for the logistic is: $log\left(\frac{\pi}{1-\pi}\right) = X\beta$

  We call $log\left(\frac{\pi}{1-\pi}\right)$ the "logit link" and can write $\text{logit}(\pi) = X\beta$.

- The link function for the exponential is: $log(\pi) = X\beta$

  which we simply call the "log link".

- The link function for the $\pi = X\beta$ is: $I(\pi) = X\beta$

  which we call the "identity link" which means the relationship is already linear and we don't have to take any nonlinear function to make it linear.

Exponentiating coefficients in the Binomial-logistic model results in an Odds Ratio

Consider what happens when X is increased by 1 unit...

$$log\left(\frac{P(Y=1|X)}{P(Y=0|X)}\right) = X\beta$$

$$log\left(\frac{P(Y=1|X+1)}{P(Y=0|X+1)}\right) = (X+1)\beta$$

So taking the difference we have,

$$\beta = log\left(\frac{P(Y=1|X+1)}{P(Y=0|X+1)}\right) - log\left(\frac{P(Y=1|X)}{P(Y=0|X)}\right)$$

$$= log\left(\frac{\text{odds}(Y|X+1)}{\text{odds}(Y|X)}\right)$$

$$= log(\text{odds ratio of Y given one unit increase in X})$$

Hence, if we take exp(β) we have odds ratio of Y given one unit increase in X.

Exponentiating coefficients in the Binomial-log model results in a Relative Risk

Consider what happens when X is increased by 1 unit...

$$log(P(Y = 1|X)) = X\beta$$
$$log(P(Y = 1|X + 1)) = (X + 1)\beta$$

So taking the difference we have,

$$\begin{aligned}\beta &= log(P(Y = 1|X + 1)) - log(P(Y = 1|X)) \\ &= log\left(\frac{P(Y = 1|X + 1)}{P(Y = 1|X)}\right) \\ &= log(\text{relative risk of Y given one unit increase in X})\end{aligned}$$

Hence, if we take exp(β) we have relative risk of Y given one unit increase in X.

Coefficients in the Binomial-identity model result in Risk Differences

Consider what happens when X is increased by 1 unit...

$$P(Y = 1|X) = X\beta$$
$$P(Y = 1|X + 1) = (X + 1)\beta$$

So taking the difference we have,

$$\begin{aligned} \beta &= P(Y = 1|X + 1) - P(Y = 1|X) \\ &= \text{Difference in risk given a one unit increase in X} \end{aligned}$$

Binomial modeling in SAS

```
******* Logistic Binomial regression;
proc genmod data = wcgs descending;
          class bage_50 (ref = "0")/param = ref;
          model chd69 = bage_50/ dist = binomial link = logit type3;
          estimate "log(OR) age>=50 vs. <50" bage_50 1/exp;
run;
proc logistic data = wcgs descending;
          class bage_50 (ref = "0")/param = ref;
          model chd69 = bage_50;
run;

******* Log binomial regression;
proc genmod data = wcgs descending;
          class bage_50 (ref = "0")/param = ref;
          model chd69 = bage_50/ dist = binomial link = log type3;
          estimate "log(RR) age>=50 vs. <50" bage_50 1/exp;
run;

******** Linear Binomial regression;
proc genmod data = wcgs descending;
          class bage_50 (ref = "0")/param = ref;
          model chd69 = bage_50/ dist = binomial link = identity type3;
          estimate "RD age>=50 vs. <50" bage_50 1;
run;
```

Details about syntax for Binomial modeling in SAS

A common feature of GENMOD and LOGISTIC is the descending option on the PROC statement, which means for response data coded 0/1, SAS will analyze the probability of a response of ’1’ rather than the default level of ’0’. This option is an essential feature to recognize when interpreting the sign of estimated coefficients because interpretation would be completely opposite.

Potential confusion between the two procedures can arise from the CLASS statement. The defaults in the two procedures is different. To make them the same, we use the /param = ref option which allows us to specify whichever category we want to be the reference. By default Genmod would use the last category and fix to 0, by default Logistic would use a coding that makes the sum of the coefficients across categories = 0, which can lead to confusion when testing individual parameters.

Binomial modeling in Stata: logit link

```
. glm chd69 bage_50, family(binomial) link(logit)
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3152
                                                  Scale parameter =         1
Deviance         =  1753.043713                   (1/df) Deviance =  .5561687
Pearson          =         3154                   (1/df) Pearson  =  1.000635
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = ln(u/(1-u))             [Logit]
                                                  AIC             =  .5570842
Log likelihood   = -876.5218566                   BIC             = -23640.81
------------------------------------------------------------------------------
             |                 OIM
       chd69 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   .7175375   .1325196     5.41   0.000     .4578039    .9772711
       _cons |  -2.674862   .0858594   -31.15   0.000    -2.843143    -2.50658
------------------------------------------------------------------------------

. logistic chd69 bage_50
Logistic regression                               Number of obs   =      3154
                                                  LR chi2(1)      =     28.20
                                                  Prob > chi2     =    0.0000
Log likelihood = -876.52186                       Pseudo R2       =    0.0158
------------------------------------------------------------------------------
       chd69 | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   2.049379   .2715829     5.41   0.000     1.580598    2.657194
       _cons |   .0689163   .0059171   -31.15   0.000     .0582423    .0815466
------------------------------------------------------------------------------
```

Binomial modeling in Stata: log link

```
. glm chd69 bage_50, family(binomial) link(log)
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3152
                                                  Scale parameter =         1
Deviance         =  1753.043713                   (1/df) Deviance =  .5561687
Pearson          =         3154                   (1/df) Pearson  =  1.000635
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = ln(u)                   [Log]
                                                  AIC             =  .5570842
Log likelihood   = -876.5218566                   BIC             = -23640.81
------------------------------------------------------------------------------
             |                 OIM
       chd69 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   .6520711   .1194802     5.46   0.000     .4178943    .8862479
       _cons |  -2.741507   .0803238   -34.13   0.000    -2.898939   -2.584075
------------------------------------------------------------------------------

. di exp(_b[bage_50])            // estimated RR
1.9195123
```

Note: match the estimated RR with previous output of 2 by 2 table.

Binomial modeling in Stata: identity link

```
. glm chd69 bage_50, family(binomial) link(identity)
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3152
                                                  Scale parameter =         1
Deviance         =  1753.043713                   (1/df) Deviance =  .5561687
Pearson          =         3154                   (1/df) Pearson  =  1.000635
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = u                       [Identity]
                                                  AIC             =  .5570842
Log likelihood   = -876.5218566                   BIC             = -23640.81
------------------------------------------------------------------------------
             |                 OIM
       chd69 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   .0592838   .0121097     4.90   0.000     .0355493    .0830183
       _cons |   .0644731   .0051787    12.45   0.000      .054323    .0746232
------------------------------------------------------------------------------
Coefficients are the risk differences.
```

Note: match the estimated RD with previous output of 2 by 2 table.

Predicted probabilities

```
. glm chd69 i.bage_50, family(binomial) link(logit)
. margins bage_50
------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |
          0  |   .0644731   .0051787    12.45   0.000      .054323    .0746232
          1  |   .1237569   .0109464    11.31   0.000     .1023023    .1452115
------------------------------------------------------------------------------
. glm chd69 i.bage_50, family(binomial) link(log)
. margins bage_50
------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |
          0  |   .0644731   .0051787    12.45   0.000      .054323    .0746232
          1  |   .1237569   .0109464    11.31   0.000     .1023023    .1452115
------------------------------------------------------------------------------
. glm chd69 i.bage_50, family(binomial) link(identity)
. margins bage_50
------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |
          0  |   .0644731   .0051787    12.45   0.000      .054323    .0746232
          1  |   .1237569   .0109464    11.31   0.000     .1023023    .1452115
------------------------------------------------------------------------------
```

Categorical predictor with >2 groups

```
. glm chd69 i.agec, family(binomial) link(logit) eform
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3149
                                                  Scale parameter =         1
Deviance         =  1736.297321                   (1/df) Deviance =  .5513805
Pearson          =         3154                   (1/df) Pearson  =  1.001588
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = ln(u/(1-u))             [Logit]
                                                  AIC             =   .553677
Log likelihood   = -868.1486603                   BIC             = -23633.39
------------------------------------------------------------------------------
             |                 OIM
       chd69 | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        agec |
          1  |   .8768215   .2025406    -0.57   0.569     .5575563    1.378903
          2  |    1.70019   .3800504     2.37   0.018     1.097046    2.634935
          3  |   2.318679   .5274963     3.70   0.000     1.484545    3.621494
          4  |   2.886314   .7462298     4.10   0.000     1.738895    4.790864
             |
       _cons |   .0605469   .0111989   -15.16   0.000     .0421358    .0870026
------------------------------------------------------------------------------
```

Note: match the estimated OR with previous output of 2 by n table.

Note: Try to avoid choosing the smallest group as the reference group (inflate SE)

Aggregated binary outcomes: grouped data

With only categorical predictors it is possible to aggregate the data across all possible combination of categories and input and analyze the data in aggregated form - Bin(n_k, π_k).

Recall that the sum of n independent Bernoulli events from a trial with same probability π leads to the Binomial(n, π) distribution. That is, if $Y_i \sim \text{Bin}(1, \pi_i)$ where $\pi_i = \pi_k$ for all i in some group k of size n_k, then $\sum_{i=1}^{n_k} Y_i \sim Bin(n_k, \pi_i)$.

Data in aggregated Binomial form can be modeled in both Proc Logistic and Proc Genmod using the events/trials syntax in the model statement.

SAS:

```
data aggregate;
     input agegrp $ total totlechd;
     cards;
     <50 2249 145
     >=50 905 112
;
proc genmod data = aggregate;
     class agegrp(ref = "<50")/param = ref;;
     model totlechd / total = agegrp / dist = binomial link = logit type3;
     estimate "lnOR CG vs. SG" agegrp 1/exp;
run;
```

Stata:

```
blogit totalchd total agegrp, or
```

Categorical/Continuous predictors

With categorical predictors and without any adjustment for other variables, model fits (maximized log-likelihood & predicted probabilities) are the same across 3 different link functions since the form does not really come into the estimation (each category is its own dummy variable and hence can be perfectly fit by any of the 3 functions). Basically, with a categorical predictor and a dichotomous outcome, analysis mimic that for 2-way tables.

With a continuous predictor, the functional form matters and the different links will result in different fits to the data. A continuous predictor is assumed to be linearly related to the link function of the probability (for the identity link), but this means it is nonlinearly related to the probability by the logistic function (for the logit link) or the exponential function (for the log link).

Controlling for other variables: behavior pattern

The WCGS study measured a number of potential predictors of coronary heart disease, including total serum cholesterol, diastolic and systolic blood pressure, smoking, age, body size, and behavior pattern. Suppose we want to control for potential confounding effect of behavior pattern ("A" vs "B").

dibpat bage_50

Frequency Percent Row Pct Col Pct	0	1	Total
0	1182	383	1565
	37.48	12.14	49.62
	75.53	24.47	
	52.56	42.32	
1	1067	522	1589
	33.83	16.55	50.38
	67.15	32.85	
	47.44	57.68	
Total	2249	905	3154
	71.31	28.69	100.00

Statistics for Table of dibpat by bage_50

Statistic	DF	Value	Prob
Chi-Square	1	27.0485	<.0001
Likelihood Ratio Chi-Square	1	27.1342	<.0001
Continuity Adj. Chi-Square	1	26.6406	<.0001
Mantel-Haenszel Chi-Square	1	27.0399	<.0001
Phi Coefficient		0.0926	
Contingency Coefficient		0.0922	
Cramer's V		0.0926	

Behavior pattern vs. CHD

dibpat chd69

Frequency Percent Row Pct Col Pct	0	1	Total
0	1486	79	1565
	47.11	2.50	49.62
	94.95	5.05	
	51.29	30.74	
1	1411	178	1589
	44.74	5.64	50.38
	88.80	11.20	
	48.71	69.26	
Total	2897	257	3154
	91.85	8.15	100.00

Statistics for Table of dibpat by chd69

Statistic	DF	Value	Prob
Chi-Square	1	39.8975	<.0001
Likelihood Ratio Chi-Square	1	40.8995	<.0001
Continuity Adj. Chi-Square	1	39.0795	<.0001
Mantel-Haenszel Chi-Square	1	39.8849	<.0001
Phi Coefficient		0.1125	
Contingency Coefficient		0.1118	
Cramer's V		0.1125	

Stratification by behavior pattern

dibpat=0

bage_50 / Frequency / Percent / Row Pct / Col Pct	chd69 0	chd69 1	Total
0	1132 72.33 95.77 76.18	50 3.19 4.23 63.29	1182 75.53
1	354 22.62 92.43 23.82	29 1.85 7.57 36.71	383 24.47
Total	1486 94.95	79 5.05	1565 100.00

Chi-Square p-value = 0.0094

dibpat=1

bage_50 / Frequency / Percent / Row Pct / Col Pct	chd69 0	chd69 1	Total
0	972 61.17 91.10 68.89	95 5.98 8.90 53.37	1067 67.15
1	439 27.63 84.10 31.11	83 5.22 15.90 46.63	522 32.85
Total	1411 88.80	178 11.20	1589 100.00

Chi-Square p-value < 0.0001

Multiple predictors model: GLM

```
. glm chd69 bage_50 dibpat, family(binomial) link(logit) eform
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3151
                                                  Scale parameter =         1
Deviance         =  1717.723418                   (1/df) Deviance =   .545136
Pearson          =   3157.01249                   (1/df) Pearson  =  1.001908
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = ln(u/(1-u))             [Logit]
                                                  AIC             =  .5465198
Log likelihood   = -858.8617089                   BIC             = -23668.08
------------------------------------------------------------------------------
             |                 OIM
       chd69 | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   1.909471   .2553643     4.84   0.000     1.469187    2.481699
      dibpat |   2.249161   .3172902     5.75   0.000     1.705851    2.965513
       _cons |   .0437069   .0054894   -24.92   0.000     .0341698    .0559058
------------------------------------------------------------------------------
```

What is the interpretation of the estimated OR = 1.909?

How does the estimated OR change compared to the single predictor model?

Try to explain the direction of the change by the confounding/mediation effect.

Multiple predictors model: logistic regression

```
. logistic chd69 bage_50 dibpat
Logistic regression                               Number of obs   =       3154
                                                  LR chi2(2)      =      63.52
                                                  Prob > chi2     =     0.0000
Log likelihood = -858.86171                       Pseudo R2       =     0.0357
------------------------------------------------------------------------------
       chd69 | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   1.909472   .2553643     4.84   0.000     1.469188    2.481699
      dibpat |    2.24916   .3172901     5.75   0.000     1.705851    2.965513
       _cons |   .0437069   .0054894   -24.92   0.000     .0341698    .0559058
------------------------------------------------------------------------------
```

NOTE these results are identical to using the GLM function on the previous page. Similar to the difference in SAS between using PROC LOGISTIC versus PROC GENMOD.

Multiple predictors model: log link

```
. glm chd69 bage_50 dibpat, family(binomial) link(log) eform
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3151
                                                  Scale parameter =         1
Deviance         =  1717.702377                   (1/df) Deviance =  .5451293
Pearson          =  3153.822736                   (1/df) Pearson  =  1.000896
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = ln(u)                   [Log]
                                                  AIC             =  .5465131
Log likelihood   = -858.8511883                   BIC             =  -23668.1
------------------------------------------------------------------------------
             |                 OIM
       chd69 | Risk Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   1.787009   .2131373     4.87   0.000     1.414502    2.257615
      dibpat |   2.102816   .2747188     5.69   0.000     1.627786    2.716471
       _cons |   .0423275   .0050018   -26.76   0.000     .0335766    .0533592
------------------------------------------------------------------------------
```

What is the adjusted RR of having CHD for a person in the older age group?

How does the OR compare to the RR here?

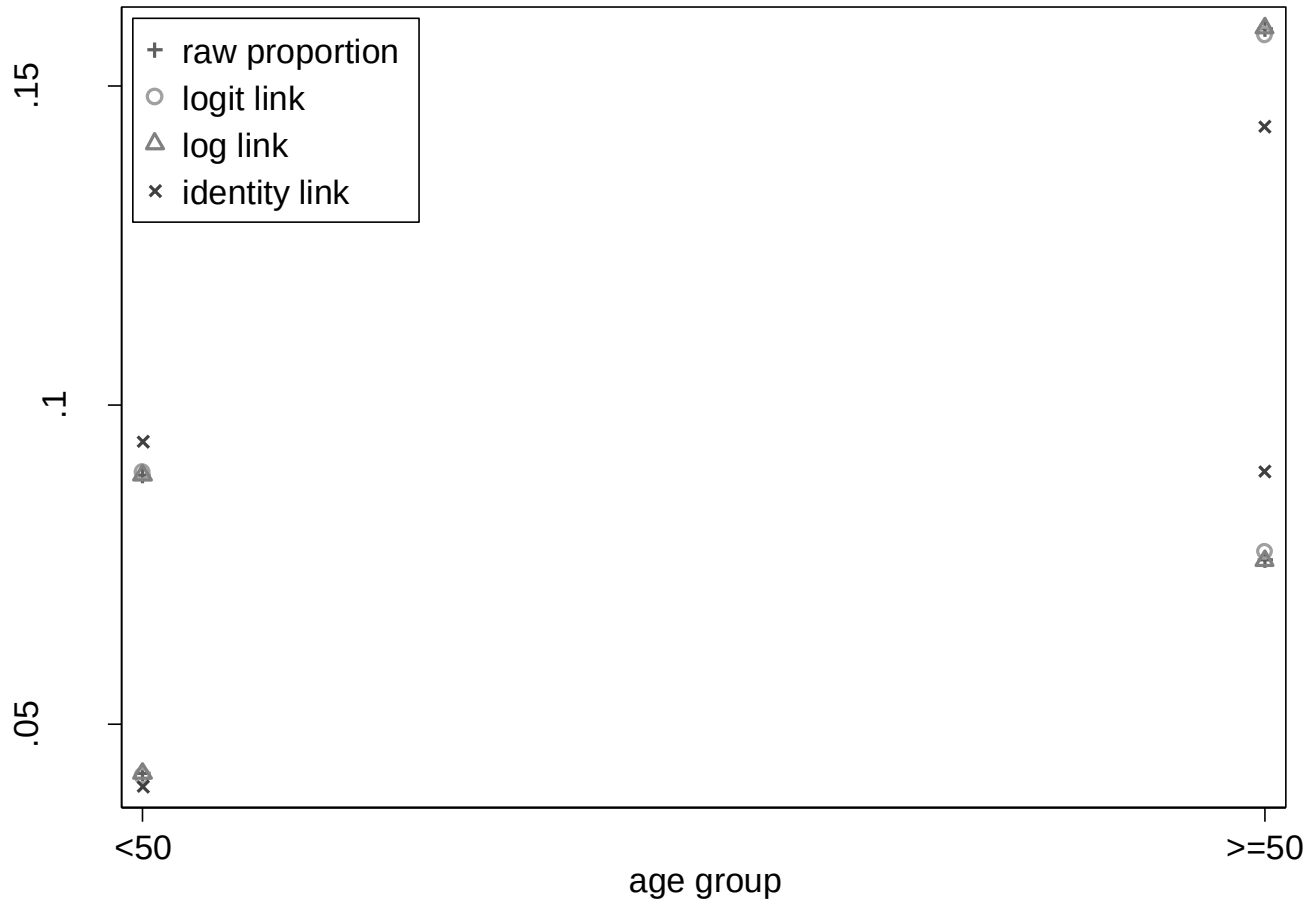
Multiple predictors model: identity link

```
. glm chd69 bage_50 dibpat, family(binomial) link(identity)
Generalized linear models                         No. of obs      =      3154
Optimization     : ML                             Residual df     =      3151
                                                  Scale parameter =         1
Deviance         =  1720.103889                   (1/df) Deviance =  .5458914
Pearson          =         3154                   (1/df) Pearson  =  1.000952
Variance function: V(u) = u*(1-u)                 [Bernoulli]
Link function    : g(u) = u                       [Identity]
                                                  AIC             =  .5472745
Log likelihood   = -860.0519445                   BIC             =  -23665.7
------------------------------------------------------------------------------
             |                 OIM
       chd69 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     bage_50 |   .0494105    .012024     4.11   0.000     .0258439    .0729771
      dibpat |   .0540685   .0096072     5.63   0.000     .0352387    .0728984
       _cons |   .0401764   .0054209     7.41   0.000     .0295516    .0508013
------------------------------------------------------------------------------
Coefficients are the risk differences.
```

What is the adjusted RD for having CHD?

NOTICE that the log-likelihoods are not exactly the same across link functions. Choice of link function can matter for model fit.

Predicted probabilities



After class: show how to calculate the predicted probability of CHD if a person was in the <50 age group and was with behavior patter “B” using the logit, log and identity models.

Predicted probabilities

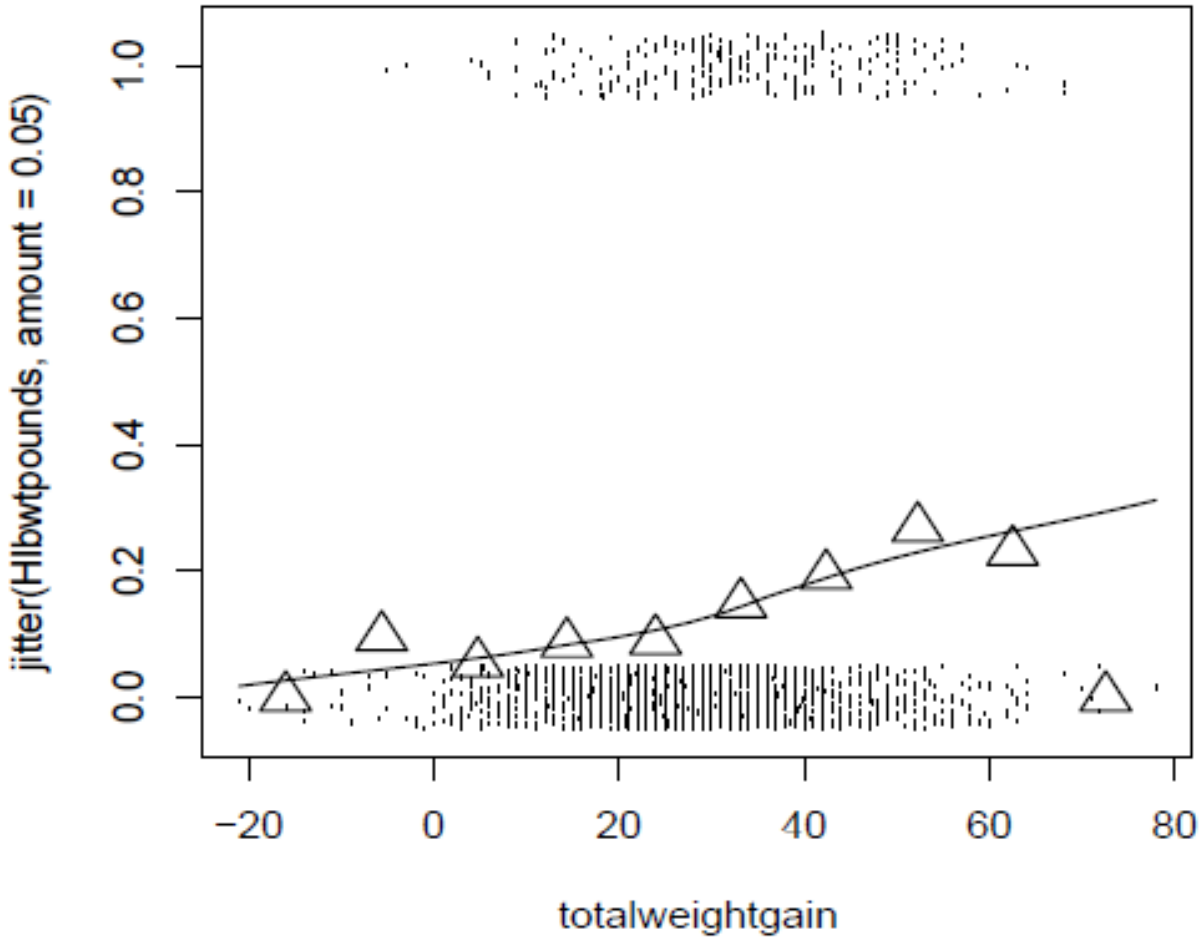
Here are the predicted probabilities of CHD based on the fit of the 3 different binomial regression models with main effects for age group and behavior pattern: (verify your calculations)

dibpat	bage_50	raw	logit	log	identity
0	<50	.042301	.0418766	.0423275	.0401764
1	<50	.089035	.0895051	.0890069	.094245
0	>=50	.075718	.0770284	.0756396	.089587
1	>=50	.159004	.1580424	.1590562	.1436555

Using the numbers above, show how you can get the estimated ORs, RRs, and RDs in the logit, log, and identity model results, respectively.

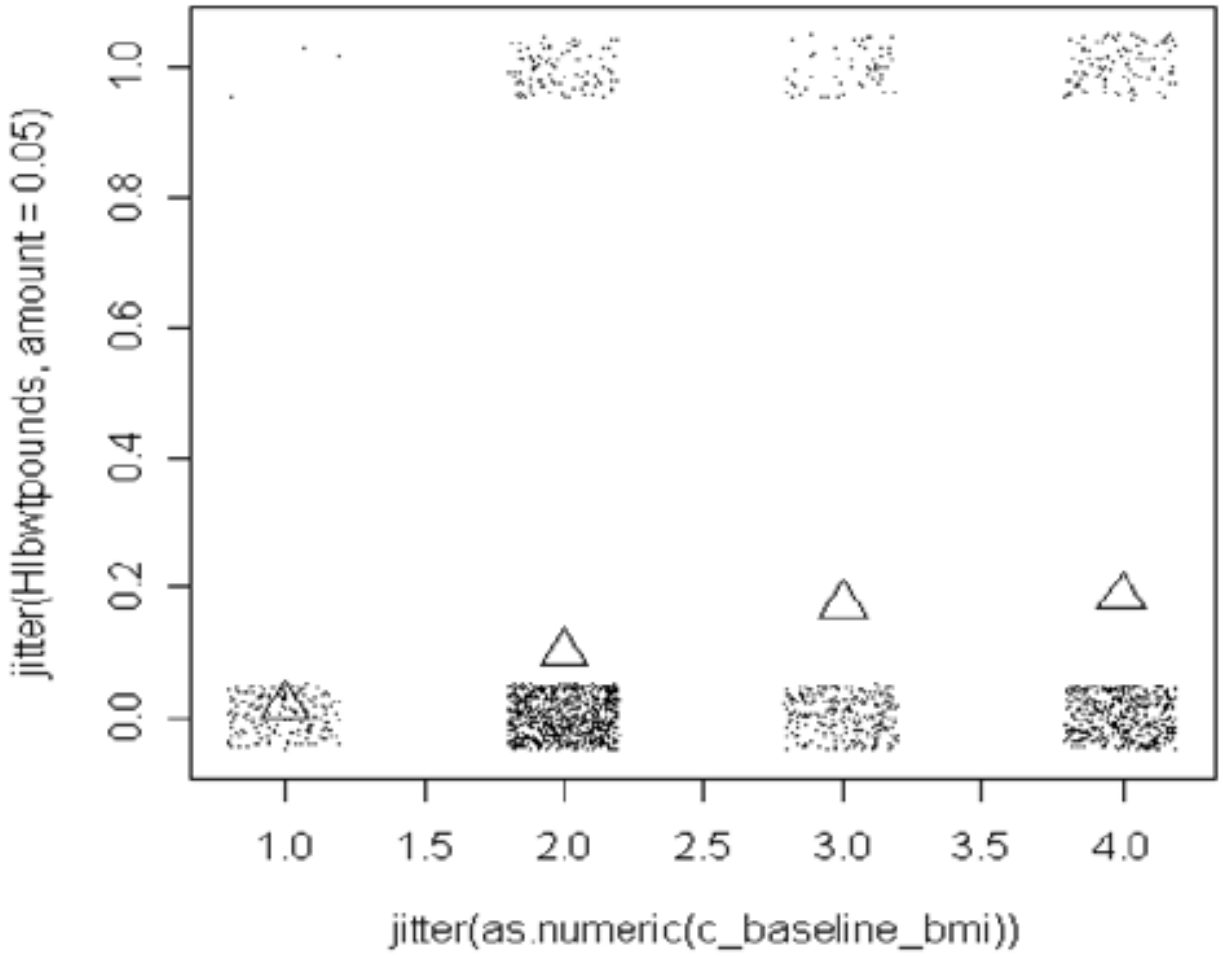
High birthweight example - a continuous predictor

How is a mother's gestational weight gain and baseline weight status related to the probability of the baby being born with a birthweight considered clinically in the High range (i.e. > 4000 grams or > 8.8 pounds).



High birthweight versus mother's baseline weight status

4 categories of baseline weight status: 1 underweight, 2 normal weight, 3 overweight, 4 obese.



Hight birthweight example: logistic regression (1)

```
proc logistic data = birthwgt2 descending;
      class c_baseline_bmi (ref = "2") /param = ref;
      model hibwt = totalweightgain c_baseline_bmi/expb;
run;

Response Profile
 Ordered                       Total
   Value        hibwt     Frequency
       1            1           260
       2            0          1740
Probability modeled is hibwt=1.

Model Fit Statistics
                              Intercept
              Intercept             and
Criterion          Only     Covariates
AIC            1547.547       1440.462
SC             1553.148       1468.467
-2 Log L       1545.547       1430.462

Testing Global Null Hypothesis: BETA=0
Test                 Chi-Square       DF     Pr > ChiSq
Likelihood Ratio       115.0847        4         <.0001
Score                  111.9801        4         <.0001
Wald                    97.3858        4         <.0001
```

Hight birthweight example: logistic regression (2)

Type 3 Analysis of Effects

Effect	DF	Wald Chi-Square	Pr > ChiSq
totalweightgain	1	59.3112	<.0001
c_baseline_bmi	3	61.4573	<.0001

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq	Exp(Est)
Intercept		1	-3.5707	0.2190	265.8230	<.0001	0.028
totalweightgain		1	0.0406	0.00527	59.3112	<.0001	1.041
c_baseline_bmi	1	1	-1.7757	0.5944	8.9254	0.0028	0.169
c_baseline_bmi	3	1	0.7550	0.1886	16.0255	<.0001	2.128
c_baseline_bmi	4	1	1.0724	0.1613	44.1827	<.0001	2.922

Odds Ratio Estimates

Effect		Point Estimate	95% Wald Confidence Limits	
totalweightgain		1.041	1.031	1.052
c_baseline_bmi	1 vs 2	0.169	0.053	0.543
c_baseline_bmi	3 vs 2	2.128	1.470	3.079
c_baseline_bmi	4 vs 2	2.922	2.130	4.009

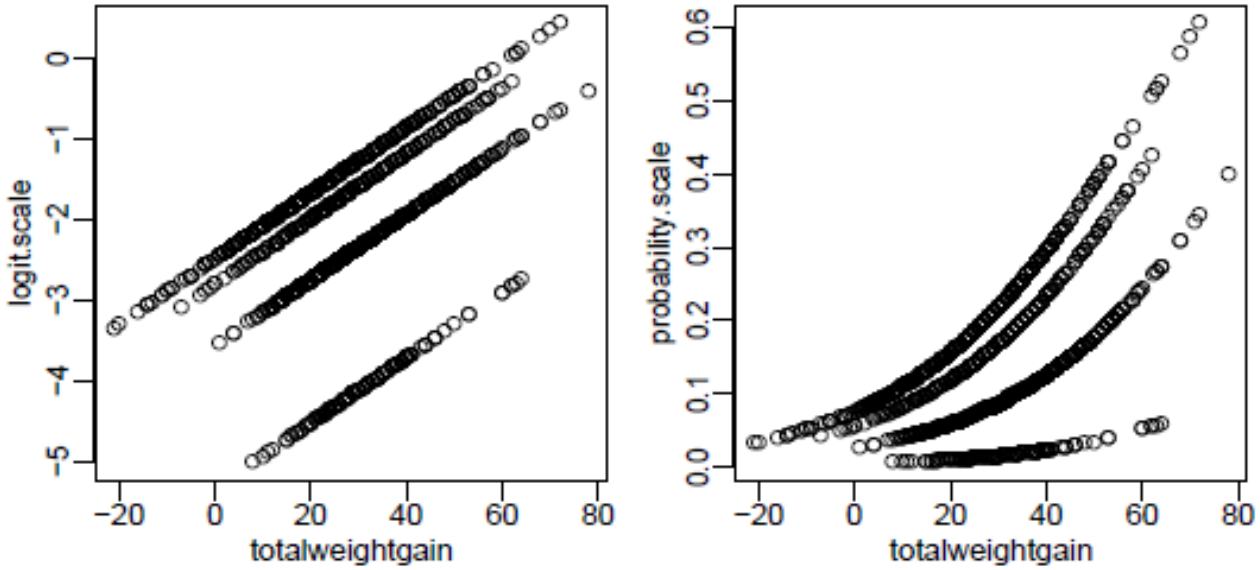
- How many women had Hi birthweight babies?
- What is the test statistic value associated with the Hypothesis that there are No differences across baseline bmi categories?
- What is the OR associated with a 10 pound higher gain in totalweightgain?
- How do we interpret the last OR estimate = 2.922? Is it stat sig?

Fitted values on the link scale and the probability scale

- $\widehat{logit(\pi)} = \widehat{log\frac{\pi_i}{1-\pi_i}} = \mathbf{X}_i\hat{\boldsymbol{\beta}} \leftarrow$ on the logit scale
- $\hat{\pi}_i = logit^{-1}(\mathbf{X}_i\hat{\boldsymbol{\beta}}) = \frac{exp(X_i\hat{\beta})}{1+exp(X_i\hat{\beta})} \leftarrow$ probability scale

Recall the high birthweight example. We regressed high birthweight on both mother's total weight gain AND mother's baseline BMI category.

$\text{logit}(\pi) = -3.57 + 0.0405 * \text{totwtgain} - 1.776 * \text{underwt} + 0.755 * \text{overwt} + 1.072 * \text{obese}$



Compare the differences between what a change in the predictors means on the two different scales.

Interpreting the intercept

$\text{logit}(\pi) = -3.57 + 0.0405 * \text{totwtgain} - 1.776 * \text{underwt} + 0.755 * \text{overwt} + 1.072 * \text{obese}$

What does the intercept represent? Back transform it.

Intercept Term in Case-Control Study

- Case-control studies collect a fixed number of cases and controls, whose ratio is typically different from population disease prevalence.
- Let Z indicate whether a subject is sampled or not. The probability of sampling a case $\rho_1 = P(Z=1|Y=1)$, and the probability of sampling a control $\rho_0 = P(Z=1|Y=0)$.

$$P\left(Y=1|\, z=1, x\right) = \frac{P\left(Z=1|\, y=1, x\right) P\left(Y=1|\, x\right)}{\sum_{j=0}^{1} P\left(Z=1|\, y=j, x\right) P\left(Y=j\,|\, x\right)} \quad \text{(Bayes' theorem)}$$

- Assume $P(Y = 1 \mid x)$ follows the logistic model, and the sampling probabilities does not depend on x. Then,

$$P\left(Y=1|\, z=1, x\right) = \frac{\rho_1 \exp\left(\alpha+\beta x\right)}{\rho_0 + \rho_1 \exp\left(\alpha+\beta x\right)}$$

and

$$\begin{aligned} \text{logit}\left[\, P\left(Y=1|\, z=1, x\right)\right] &= \left[\alpha + \log\left(\rho_1/\rho_0\right)\right] + \beta x \\ &= \alpha^{*} + \beta x \end{aligned}$$

Hight birthweight example: Stata output

```
. logistic hibwt totalweightgain ib2.c_baseline_bmi
/* "ib2." tells Stata that bmi==2 is the reference(base) level */

Logistic regression                                     Number of obs   =       2000
                                                        LR chi2(4)      =     115.08
                                                        Prob > chi2     =     0.0000
Log likelihood = -715.23104                             Pseudo R2       =     0.0745

------------------------------------------------------------------------------
       hibwt | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
totalweightgain |   1.041433   .0054899     7.70   0.000     1.030728    1.052248
             |
 c_baseline_bmi |
          1  |   .1693707   .1006664    -2.99   0.003      .052835    .5429432
          3  |   2.127668   .4012924     4.00   0.000      1.47015    3.079259
          4  |   2.922298   .4714581     6.65   0.000     2.130096    4.009128
             |
       _cons |   .0281374   .0061622   -16.30   0.000     .0183176    .0432215
------------------------------------------------------------------------------

old version:
. char c_baseline_bmi[omit] 2
. xi: logistic hibwt totalweightgain i.c_baseline_bmi
```

Estimation by Maximum Likelihood

- Given independent data $Y = Y_1, \ldots Y_n$ and $X = \mathbf{X}_1 \ldots \mathbf{X}_n$, where Y is the outcome of interest and $\mathbf{X}$ are predictors, and given a parametric model for $Y_i|X_i$, we can form the likelihood function.
- Generally we can write the model for $Y_i|X_i$ as $Y_i|X_i \sim Distr(\mathbf{\Theta}, X_i)$ where $\mathbf{\Theta}$ represents a set of unknown parameters and $Dist$ represents some specific distribution family, e.g. normal, binomial, Poisson, gamma.
- The likelihood is the joint distribution of the observations viewed as a function of the parameters,

$$\text{Likelihood} L(\mathbf{\Theta}|Y;X) = \prod_{i=1}^{n} f(Y_i|X_i;\mathbf{\Theta})$$

$$\text{Log Likelihood} \ell(\mathbf{\Theta}|Y;X) = \sum_{i=1}^{n} f(Y_i|X_i;\mathbf{\Theta})$$

- The goal is to find $\mathbf{\Theta}$ which maximizes this (log)likelihood function since intuitively that value would be the value of the parametric distribution most likely to have been the one that generated the data.

Maximizing the likelihood

- This goal of maximizing the likelihood is accomplished using calculus which provides tools for maximizing functions. The derivative of the log likelihood is taken with respect to the parameter vector Θ and set equal to 0. The derivative of the log likelihood is called the **score function**.
- The **maximum likelihood estimates** are found by solving the score function which will yield the values that maximize the likelihood assuming the likelihood is unimodal. In general this solution must be found numerically (no closed form).
- Problems can occur when likelihood function is multimodal (only find local maximum rather than global maximum) or when the maximum is found along the boundary of the parameter space.
- We use the hat notation, $\widehat{\Theta}$, to indicate the MLEs of Θ.
- The second derivative of the log likelihood is called the **information** and is used in creating standard errors.

The likelihood for logistic regression

Given the model

$$Y_i|X_i \sim Bin(1, \pi_i)$$
$$\pi_i = \frac{exp(X_i\boldsymbol{\beta})}{1 + exp(X_i\boldsymbol{\beta})}$$

and given n independent observations $(Y_i, \mathbf{X}_i)$

$$\begin{aligned} L(\boldsymbol{\beta}|Y, X) &= \prod_{i=1}^{n} \pi_i^{Y_i}(1-\pi_i)^{1-Y_i} \\ &= \prod_{i=1}^{n} \frac{exp(X_i\boldsymbol{\beta})}{1 + exp(X_i\boldsymbol{\beta})}^{Y_i} \frac{1}{1 + exp(X_i\boldsymbol{\beta})}^{1-Y_i} \\ \ell(\boldsymbol{\beta}|Y, X) &= \sum_{i=1}^{n} Y_i log\left(\frac{exp(X_i\boldsymbol{\beta})}{1 + exp(X_i\boldsymbol{\beta})}\right) + (1-Y_i) log\left(\frac{1}{1 + exp(X_i\boldsymbol{\beta})}\right) \end{aligned}$$

Take derivative of this function w.r.t $\boldsymbol{\beta}$ set equal to zero and solve in order to obtain MLE's for $\boldsymbol{\beta}$, ie $\hat{\boldsymbol{\beta}}$.

Hypothesis testing from maximum likelihood theory

Given some hypothesis: $H_0 : \boldsymbol{\Theta} = \boldsymbol{\Theta}_0$

- **Likelihood ratio test** - ratio of the likelihood at the hypothesized parameter value (under the null) to the likelihood of the data at the MLEs. Typically the likelihood ratio is defined as -2 time log likelihood ratio, i.e.

$$\begin{aligned} LR &= -2log\frac{L_{\boldsymbol{\Theta}_0}}{L_{\hat{\boldsymbol{\Theta}}}} \\ &= -2\ell_{\boldsymbol{\Theta}_0} + 2\ell_{\hat{\boldsymbol{\Theta}}} \end{aligned}$$

  Compare this value to a Chi-square distribution with d.f. equal to the number of parameters being constrained.

- **Wald Test** - generalization of the Z or t statistics. It is a function of the difference between the MLE and the $\boldsymbol{\Theta}_0$ divided by some estimate of the standard error of the MLE.

$$W = \frac{\hat{\boldsymbol{\Theta}} - \boldsymbol{\Theta}_0}{s.e.(\hat{\boldsymbol{\Theta}})}$$

- **Score Test** - measures how far away from zero the score function is when evaluated at the H_0. Typically it is standardized by the information.

High birthweight example - Overall Model tests

The value of the Model Fit Statistics are only meaningful when they are compared across models. By default SAS will compare the model with no predictors (Intercept only) to the full model you have specified (Intercept and Covariates). Here the model has totalwtgain (1 d.f.) and baseline BMI status (3 d.f).

Model Fit Statistics

Criterion	Intercept Only	Intercept and Covariates
AIC	1547.547	1440.462
SC	1553.148	1468.467
-2 Log L	1545.547	1430.462

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	115.0847	4	<.0001
Score	111.9801	4	<.0001
Wald	97.3858	4	<.0001

*. 1545.547-1430.462 = 115.085

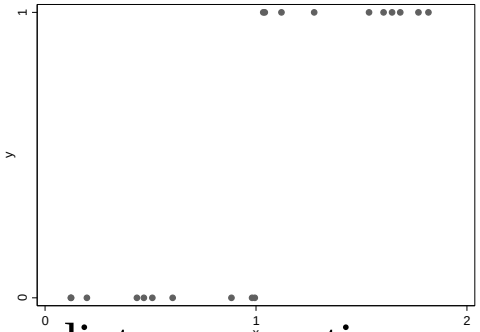
The tests of global null hypothesis are like the overall model F-test in ANOVA

Confidence intervals - Wald or likelihood ratio based

- Wald tests are computationally faster than likelihood ratio test
- SAS and Stata create Wald confidence intervals by default. Estimate +- 1.96 * S.E.
  - Adding the option CLodds = PL to the model statement in SAS will provide the “profile likelihood confidence intervals”. These confidence intervals based on the likelihood ratio test
- Hauck and Donner (1977) Wald’s test as applied to hypotheses in logit analysis. *Journal of the American Statistical Association*, 72:851-863 notice that the Wald CI can be too large especially when there are strong effects.
- LR confidence intervals considered better. With larger samples they will be very similarly (asymptotically the same).

Problem of Separation in Logistic Regression

- An identifiability problem that can arise in logistic regression, called separation, occurs when a predictor or a combination of predictors are perfectly aligned with the outcome such that y = 0 for ALL values of that predictor beyond some point and y = 1 for ALL values of that predictor less than some point.
- Often occurs in small or sparse samples with highly predictive covariates.
- Simples case is in the analysis of a 2 × 2 table with one zero cell count.
- For a continuous predictor, separation can be demonstrated by:



- For a categorical predictor separation means that in some category (or with multiple predictors, in some combination of categories) all individuals in that category either have a 1 or 0.
- Leads to non-convergence of the likelihood and/or infinite parameter estimates.

Solutions to the problem of Separation

Classical solution

Drop the predictor or somehow aggregate levels. Leave problematic predictors in but only report results for predictors without separation problem.

Modern solution

See the website http://www.meduniwien.ac.at/msi/biometrie/programme/fl/ "Logistic regression using Firth's bias reduction: a solution to the problem of separation in logistic regression". Heinze and Ploner, 2004 put together a SAS MACRO (%fl) and also an R package (logistf()) that uses a penalized maximum likelihood method to obtain estimates. In Stata, install user-written command -firthlogit-.

Summarizing predictive ability in logistic regression

- An intuitive measure is the error rate - the proportion of cases for which the prediction of $\hat{y}_i$ is the same as y_i. Depends on the cutoff value chosen to define "positive" prediction.
- A natural choice is to take

$$\begin{cases} \hat{y}_i = 1 \text{ if } \hat{\pi}_i \geq \hat{p} \\ \hat{y}_i = 0 \text{ if } \hat{\pi}_i < \hat{p} \end{cases} \tag{1}$$

  where $\hat{p}$ is the overall proportion of 1s in the sample. That is, $\hat{p} = \bar{Y}$.
- Comparing $\hat{y}_i$ to y_i yields a 2×2 table. The error rate is the proportion of observations on the off-diagonal
- To get this in SAS, use the ctable option after the model statement, can get error rate for any cutoff value
- To get this in STATA, can use the postestimation option - estat class, cut( ) and give the cutoff value you want inside the parentheses of the cut command.

Classification table: Stata output

```
. estat class, cutoff(.2)
Logistic model for hibwt
              -------- True --------
Classified |         D            ~D  |      Total
-----------+--------------------------+-----------
     +     |        89           239  |        328
     -     |       171          1501  |       1672
-----------+--------------------------+-----------
   Total   |       260          1740  |       2000

Classified + if predicted Pr(D) >= .2
True D defined as hibwt != 0
-------------------------------------------------
Sensitivity                     Pr( +| D)   34.23%
Specificity                     Pr( -|~D)   86.26%
Positive predictive value       Pr( D| +)   27.13%
Negative predictive value       Pr(~D| -)   89.77%
-------------------------------------------------
False + rate for true ~D        Pr( +|~D)   13.74%
False - rate for true D         Pr( -| D)   65.77%
False + rate for classified +   Pr(~D| +)   72.87%
False - rate for classified -   Pr( D| -)   10.23%
-------------------------------------------------
Correctly classified                        79.50%
-------------------------------------------------
```

Classification table: SAS output

The LOGISTIC Procedure

Classification Table

	Correct		Incorrect		Percentages				
Prob Level	Event	Non-Event	Event	Non-Event	Correct	Sensi-tivity	Speci-ficity	False POS	False NEG
0.000	260	0	1740	0	13.0	100.0	0.0	87.0	.
0.020	259	110	1630	1	18.5	99.6	6.3	86.3	0.9
0.040	258	163	1577	2	21.1	99.2	9.4	85.9	1.2
0.060	251	311	1429	9	28.1	96.5	17.9	85.1	2.8
0.080	239	534	1206	21	38.7	91.9	30.7	83.5	3.8
0.100	208	805	935	52	50.7	80.0	46.3	81.8	6.1
0.120	180	1020	720	80	60.0	69.2	58.6	80.0	7.3
0.140	157	1183	557	103	67.0	60.4	68.0	78.0	8.0
0.160	130	1327	413	130	72.9	50.0	76.3	76.1	8.9
0.180	101	1421	319	159	76.1	38.8	81.7	76.0	10.1
0.200	88	1501	239	172	79.5	33.8	86.3	73.1	10.3

...

Note: 1. can use pprob=(list) option to specify list of cutoff points, e.g.,

```
model hibwt = totalweightgain c_baseline_bmi/ ctable pprob = (.13);
```

2. SAS uses (approximate) leave-one-observation-out approach to calculate the classification table, which is expected to be a more valid assessment of prediction. Therefore the SAS output might be different from Stata output.

Classification table: using all samples

```
proc logistic ...; output out=z predicted=fitted_prob; run;
data check; set z;
     yhat = 0;
     if fitted_prob >= .20 then yhat = 1;
run;
proc freq data = check;
     tables yhat*hibwt;
run;
```

yhat Frequency Percent Row Pct Col Pct	hibwt 0	 1	 Total
0	1501 75.05 89.77 86.26	171 8.55 10.23 65.77	1672 83.60
1	239 11.95 72.87 13.74	89 4.45 27.13 34.23	328 16.40
Total	1740 87.00	260 13.00	2000 100.00

Classification Table

- Prediction: $\hat{y} = \begin{cases} 1, & if\ \hat{\pi}_i > \pi_0 \\ 0, & if\ \hat{\pi}_i \le \pi_0 \end{cases}$ for some cutoff π_0

- Classification Table:

		Observed 0	Observed 1
Prediction	0	True Negative	False Negative
	1	False Positive	True Positive

Sensitivity = TP/(TP+FN); Specificity = TN/(TN+FP).

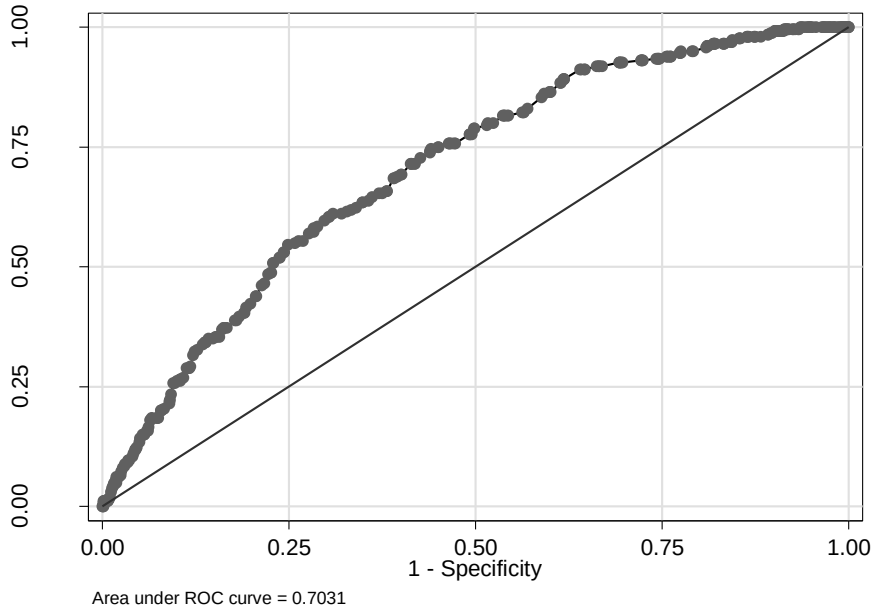
- Receiver Operating Characteristic (ROC) curve: plot of sensitivity against 1-specificity (i.e., false positive), for possible cutoff π_0.

Summarizing predictive ability in logistic regression

Better measures:

- R^2 or max-rescaled R^2 - function of the likelihood ratio test. Unlike linear regression it is not necessarily the case that more predictors lead to higher R^2 values. The maximum possible value of generalized R^2 is not 1.0 as it is for linear regression. Max-rescaled R^2 divides by this maximum value to fix this so its maximum is 1. Reference Nagelkerke (1991) Biometrika for this R^2 value.
- c index - rank correlation across pairs of observations between the predicted probability and the actual responses. Equivalent to the area under a receiver operating characteristic (ROC) curve. The larger the area under the curve (AUC), the better the predictions. Maximum is 1.0, and an area of 0.5 implies random predictions. Harrell (2001) (Regression Modeling strategies) gives a guideline of C exceeding 0.80 as implying useful predictability of the model. Output by default in Proc LOGISTIC, Output with logistic postestimation option: lroc in Stata.
- AIC is only useful as a comparative fit index and is a penalized function of the log-likelihood, penalized by the number of parameters in the model - when comparing two models, smaller values are better (in SAS).

Receiver Operating Characteristic (ROC) curve



Stata:

```
. lroc
area under ROC curve   =   0.7031
```

SAS:

```
Percent Concordant      69.9    Somers' D    0.406
Percent Discordant      29.3    Gamma        0.410
Percent Tied             0.9    Tau-a        0.092
Pairs                 452400    c            0.703  <-- area under ROC curve
```

An annotated explanation of the above values under “Association of Predicted Probabilities” can be found at https://www.ats.ucla.edu/stat/sas/output/SAS_logit_output.htm

More on ROC curve

1. If this curve was simply a diagonal straight line then the AUC would be .50 meaning the sensitivity and specificity were never larger than simply one minus the other, meaning the prediction was no better than a simple coin flip at fixed probabilities.

2. On the other hand, as the curve bends closer and closer to the upper left hand corner, the AUC goes to 1 indicating perfect prediction (100% sensitivity and 100% specificity).

Linear trends in 0-1 outcomes for categorical predictors

Cochran-Armitage Trend Test: test for LINEAR trend in categorical predictor for 0-1 outcome data. For simple unadjusted relationship, test is performed on 2 by K table where K is the number of categories and H_a is that $\pi_1 \leq \pi_2 \leq \ldots \leq \pi_K$ with at least one strict inequality (or visa versa $\geq$). In linear probability model:

$$\pi_j = \alpha + \beta s_j, \qquad j = 1, \ldots, K$$

This is to test for H_0: $\beta=0$.

The test is the same as treating categories as a continuous score with equal spaced increments in a simple logistic regression and using the overall Score test.

Can get this test in SAS Proc Freq using the /trend option or of course you can get it using logistic regression (but it won't be called the "Cochran-Armitage Trend Test" in the output).

Linear trends in 0-1 outcomes for categorical predictors

```
proc freq;
     tables c_baseline_bmi*hibwt / trend;
run;

Statistics for Table of c_baseline_bmi by hibwt
Cochran-Armitage Trend Test
_____________________________
Statistic (Z)       -6.5035
One-sided Pr <  Z    <.0001
Two-sided Pr > |Z|   <.0001
================================================================
proc logistic data = birthwgt2 descending;
     model hibwt = c_baseline_bmi;
run;

Testing Global Null Hypothesis: BETA=0
Test                 Chi-Square       DF     Pr > ChiSq
Likelihood Ratio        42.0261        1         <.0001
Score                   42.2960        1         <.0001     <--(-6.5035)^2 = 42.296
Wald                    40.9012        1         <.0001
```

*. In Stata, install –ptrend- command for trend test

```
. ptrendi 3 159 1 \ 95 850 2 \ 54 257 3 \ 108 474 4
Chi2(1) for trend =      42.296,  pr>chi2 = 0.0000
```

Goodness of Fit

The **Pearson** statistic is:

$$\sum_{i=1}^{n} \frac{(y_i - \hat{\mu}_i)^2}{v(\hat{\mu}_i)}$$

where $\hat{\mu}_i = \widehat{E(Y|X_i)}$ and $v() = Var(Y|X_i)$

The **Residual Deviance** statistic is:

2[*log*L(saturated model) − *log*L(the current model)]

These do not work properly for logistic regression except when there are only a few categorical predictors leading to aggregated data with large cell counts. Their validity relies on the assumption of large numbers of observations in binomial cells and both tests show unsatisfactory behaviour with sparse data. In fact with continuous predictors they can be shown to be completely meaningless (since continuous predictors lead to only one observation within every cell - sparse data). These statistics are NOT output by SAS when using Proc Logistic or Proc Genmod when the binomial distribution is specified (although they are output when Poisson distribution is specified). On the other hand, these statistics are output by Stata in the glm output even for binomial distribution.

Goodness of Fit - Hosmer Lemeshow test

A solution to the problems associated with the Pearson and Residual Deviance for binomial regression comes from the **Hosmer Lemeshow** test which groups the data before forming a chi-square type statistic.

The Hosmer-Lemeshow Statistic is a measure of lack of fit in a logistic regression model. Hosmer and Lemeshow recommend partitioning the observations into 10 equal sized groups according to their predicted probabilities. The test then computes a chi-square statistic from observed and expected frequencies in each of the 10 quantiles. The null is that the observed frequencies equal the expected frequencies, hence if we do NOT reject the null then we are saying the model is well-fitting, i.e. there is no significant difference between observed and model-predicted values.

In SAS: Get this statistics use the /lackfit option

In STATA: use the postestimation option: lfit, group(10) table

Goodness of Fit: SAS output

```
proc logistic data = birthwgt2 descending;
     class c_baseline_bmi (ref = "2") /param = ref;
     model hibwt = totalweightgain c_baseline_bmi/rsq ctable pprob = (.13) lackfit;
     output out=z predicted =fitted_prob;
run;
```

Partition for the Hosmer and Lemeshow Test

		hibwt = 1		hibwt = 0	
Group	Total	Observed	Expected	Observed	Expected
1	209	5	4.96	204	204.04
2	199	9	11.75	190	187.25
3	200	7	15.24	193	184.76
4	199	25	17.76	174	181.24
5	188	17	19.42	171	168.58
6	208	29	24.98	179	183.02
7	205	25	29.12	180	175.88
8	205	46	34.74	159	170.26
9	199	45	42.28	154	156.72
10	188	52	59.75	136	128.25

Hosmer and Lemeshow Goodness-of-Fit Test

Chi-Square	DF	Pr > ChiSq
16.5844	8	0.0347

Goodness of Fit: Stata output

```
. estat gof, group(10) table
Logistic model for hibwt, goodness-of-fit test
  (Table collapsed on quantiles of estimated probabilities)
  +--------------------------------------------------------+
  | Group |   Prob | Obs_1 | Exp_1 | Obs_0 | Exp_0 | Total |
  |-------+--------+-------+-------+-------+-------+-------|
  |     1 | 0.0473 |     5 |   5.0 |   204 | 204.0 |   209 |
  |     2 | 0.0668 |     8 |  11.5 |   187 | 183.5 |   195 |
  |     3 | 0.0819 |     8 |  15.0 |   190 | 183.0 |   198 |
  |     4 | 0.0949 |    25 |  17.9 |   176 | 183.1 |   201 |
  |     5 | 0.1122 |    19 |  22.7 |   199 | 195.3 |   218 |
  |-------+--------+-------+-------+-------+-------+-------|
  |     6 | 0.1294 |    27 |  22.1 |   155 | 159.9 |   182 |
  |     7 | 0.1541 |    25 |  29.1 |   180 | 175.9 |   205 |
  |     8 | 0.1849 |    46 |  34.7 |   159 | 170.3 |   205 |
  |     9 | 0.2389 |    44 |  40.1 |   146 | 149.9 |   190 |
  |    10 | 0.6046 |    53 |  61.9 |   144 | 135.1 |   197 |
  +--------------------------------------------------------+
       number of observations =      2000
             number of groups =        10
    Hosmer-Lemeshow chi2(8) =        17.15
                Prob > chi2 =         0.0286
```

Note: SAS and Stata outputs are different because they handle the ties differently.

Goodness of Fit: interpretation

The Null hypothesis being tested here is that the model matches the data. So finding a p-value <.05 means we would reject that the model is fitting well.

One thing this lack of fit could be indicating is missing covariates…if we add another covariate to the model, age_lmp, we find the following:

Hosmer and Lemeshow Goodness-of-Fit Test

Chi-Square	DF	Pr > ChiSq
10.8758	8	0.2088

Also, the AIC with age_lmp added is 1430.036 (smaller than the value previously, 1440.462) and, as expected, the c-index is larger 0.716.

Here are the estimated OR with age_lmp added to the model. Notice there is no qualitative differences in terms of the estimates for totalweightgain and c_baseline_bmi.

Odds Ratio Estimates

Effect		Point Estimate	95% Wald Confidence Limits	
totalweightgain		1.044	1.033	1.055
c_baseline_bmi	1 vs 2	0.186	0.058	0.598
c_baseline_bmi	3 vs 2	2.183	1.506	3.165
c_baseline_bmi	4 vs 2	2.939	2.139	4.038
age_lmp		1.047	1.021	1.075

Goodness of Fit - Hosmer Lemeshow test

NOTE: This test is known to be highly dependent on the actual groupings (the number of groups) and cutoff value used when conducting the test. It also tends to detect small differences when the sample size is large. VGSM reccommend using it cautiously.

NOTE: This test does not have anything to do with whether regression coefficients are significant or whether there is high predictability (e.g. high c-statistic) in the model.

From: “A comparison of goodness-of-fit tests for the logistic regression model” by DS Hosmer, T Hosmer, SL Cessie, and S Lemeshow *Statistics in Med*., VOL. 16, 965-980 (1997)

In the context of logistic regression the overall goodness of fit is assessing all of the following (not any one specifically)

- The logit transformation is the correct function linking covariates with the conditional mean $X\beta$
- The linear predictor is correct, i.e. we do not need to include additional variables, transformation of variables, or interactions of variables
- The variance is Bernoulli, i.e. $\text{var}(Y|X) = \pi(X)(1 - \pi(X))$

Interactions in models with 0-1 outcomes

SAS will not produce odds ratios when you include an interaction in a logistic regression. Stata will still produce odds ratios which are simply the exponential of the estimated coefficients.

-- We cannot interpret the coefficient of one predictor as a log odds ratio without specifying value of the other predictor.

-- Since the predictor X is involved in both main and interaction terms, OR(Y|X) = odds(Y|X+1)/odds(Y|X) needs to be computed using both the estimated coefficients for main and interaction terms.

Complete seminar about how to do this: Statistical Computing Seminars Visualizing Main Effects and Interactions for Binary Logit Models in Stata

http://www.ats.ucla.edu/stat/stata/seminars/stata_vibl/default.htm

Interactions: age group * presence of arcus senilis

```
proc logistic data = wcgs descending;
      class bage_50 (ref = "0") arcus (ref = "0") /param = ref;
      model chd69 = bage_50 arcus bage_50*arcus;
      contrast 'OR(arcus) in older group' arcus 1 bage_50*arcus 1 1 / estimate=exp;
run;
```

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-2.8828	0.1089	700.4573	<.0001
arcus 1	1	0.6480	0.1789	13.1236	0.0003
bage_50 1	1	0.8933	0.1721	26.9328	<.0001
bage_50*arcus 1 1	1	-0.5920	0.2722	4.7299	0.0296

Contrast	Type	Row	Estimate	Error	Alpha	Confidence Limits	
OR(arcus) in older group	EXP	1	1.0575	0.2170	0.05	0.7073	1.5811

Interpretation of the interaction term is similar to that in linear regression model. Instead of difference in the slope, it is now the difference in log(Odds Ratio). For example,

$$\log\left[\frac{P(1,0,0)}{1-P(1,0,0)}\right] - \log\left[\frac{P(0,0,0)}{1-P(0,0,0)}\right] = \beta_1 = 0.648$$

$$\log\left[\frac{P(1,1,1)}{1-P(1,1,1)}\right] - \log\left[\frac{P(0,1,0)}{1-P(0,1,0)}\right] = \beta_1 + \beta_3 = 0.056$$

Interactions: component odds ratios

Table 6.13. Component Odds Ratios for Arcus-Age Interaction Model

Odds ratio	Groups compared
$\exp(\beta_1) = 1.91$	arcus vs. no arcus, age 39-49
$\exp(\beta_1 + \beta_3) = 1.06$	arcus vs. no arcus, age 50-59
$\exp(\beta_2) = 2.44$	age 50-59 vs. age 39-49, no arcus
$\exp(\beta_2 + \beta_3) = 1.35$	age 50-59 vs. age 39-49, arcus
$\exp(\beta_1 + \beta_2 + \beta_3) = 2.58$	arcus *and* age 50-59 vs. no arcus and ages 39-49

Interactions: categorical and continuous predictors

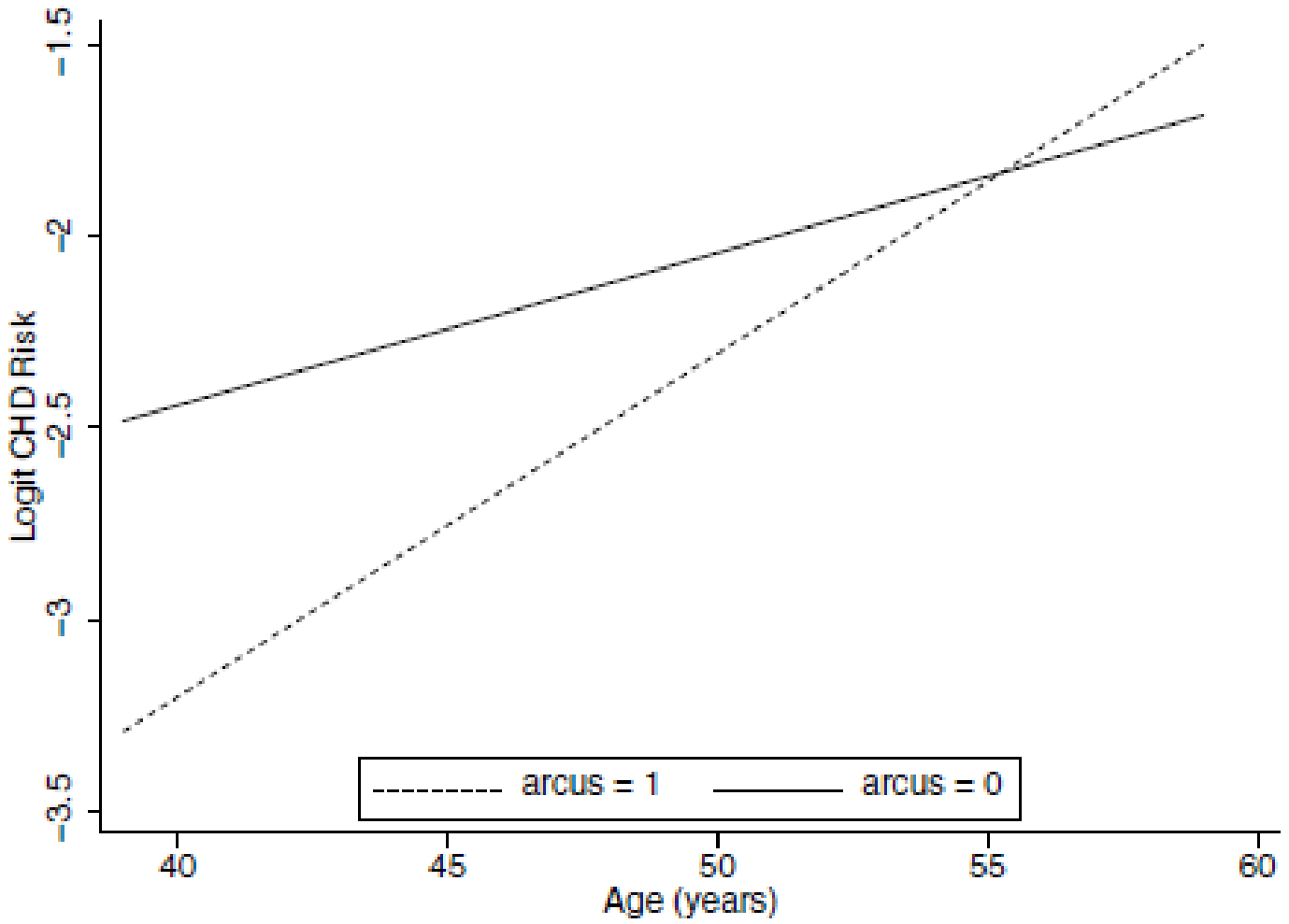


Fig. 6.2. Log Odds of CHD and Age for Individuals With and Without Arcus Senilis