Introduction to Logistic Regression

EPI 204

Quantitative Epidemiology III

Statistical Models

Risk Estimation and Prediction

- Logistic regression is a method for estimating and predicting the risk of a binary event (such as disease/healthy) using one or more predictors.
- You have already seen methods for the case when there is one predictor that is also binary (such as exposure/non-exposure).
- We will first look at this again, with a special focus on risk ratios and odds ratios, which are important concepts for interpreting logistic regression.

Oral Contraceptive Use and Heart Attack (MI) over 3 years

	MI	No MI	
OC-Use	13	4,987	5,000
Non-OC-Use	7	9,993	10,000
Total	20	14,980	15,000

Estimated Risk for Oral Contraceptive Users

$$\hat{p}_{\text{OC}} = 13/5000 = 0.0026$$

Estimate Risk for Non-Users of Oral Contraceptives

$$\hat{p}_{\text{non-OC}} = 7/10000 = 0.0007$$

$$\widehat{RR} = 0.0026/0.0007 = 3.71$$

Oral Contraceptive Use and Heart Attack (MI) over 3 years

	MI	No MI	
OC-Use	13	4,987	5,000
Non-OC-Use	7	9,993	10,000
Total	20	14,980	15,000

Estimated Odds for Oral Contraceptive Users

$$\hat{O}_{\text{OC}} = \frac{13/5000}{4987/5000} = 13/4987 = 0.002607$$

Estimate Odds for Non-Users of Oral Contraceptives

$$\hat{O}_{\text{non-OC}} = 7/9993 = 0.000705$$

$$\widehat{OR} = 0.002607/0.000705 = 3.72$$

Effect of Study Design

- The table is from a follow-up study in which two populations were followed and the number of MI’s was observed.
- The risk is P(MI|OC) and P(MI|non-OC) and this is valid for this design.
- But suppose we had a case-control study in which we had 100 women with MI and selected a comparison group of 100 women without MI (matched on age, etc.).
- Then MI is not random, and we cannot compute P(MI|OC) and we cannot compute the risk ratio.

Effect of Study Design

- The odds ratio however can be computed.
- The disease odds ratio is the odds for the disease in the exposed group divided by the odds for the disease in the unexposed group, and we cannot validly compute and use these separate parts.
- But we can validly compute and use the exposure odds ratio, which is the odds for exposure in the disease group divided by the odds for exposure in the non-diseased group (because exposure can be treated as random).
- And these are numerically the same.

Effect of Study Design

- O1 = P(OC|MI)/(1 – P(OC|MI)
- O2 = P(OC|no MI)/(1 – P(OC|no MI)
- OR = O1/O2
- OR = (13×9993)/(7×4987) = 3.72
- And this is the formula for both odds ratios.
- Logistic regression validly estimates odds ratios but does not necessarily validly estimate risk ratios.

Cross-Sectional Studies

- If a cross-sectional study is a probability sample of a population (which it rarely is) then we can estimate risks.
- If it is a sample, but not an unbiased probability sample, then we need to treat it in the same way as a case-control study.
- We can validly estimate odds ratios in either case.
- But we can usually not validly estimate risks and risk ratios.

Risk Estimation and Prediction

- In this case, we are estimating the risk and the odds of MI for two discrete cases, as to whether of not the individual used oral contraceptives.
- If the predictor is quantitative (dose) or there is more than one predictor, the task becomes more difficult.
- In this case, we will use logistic regression, which is a generalization of the linear regression models you have been using that can account for a binary response instead of a continuous one.

Linear Regression

We have a response y and set of predictors which may be numeric or categorical

and a linear predictor of y

$\eta = \beta_0 + \beta_1 x_1 + \cdots \beta_p x_p$

We assume that y is normally distributed with mean η and variance σ^2

We estimate the parameters β_k by $\hat{\beta}_k$ minimizing the sum of the prediction errors $(y - \eta)^2$

This is characterized by

- The response y is normally distributed
- $E(y) = \eta$ the linear predictor
- The dispersion parameter $\sigma^2 = V(y \mid \eta)$

What do we do if y is binary and so cannot be normally distributed?

Generalized Linear Models

- The type of predictive model one uses depends on a number of issues; one is the type of response.
- Measured values such as quantity of a protein, age, weight usually can be handled in an ordinary linear regression model, possibly after a log transformation.
- Patient survival, which may be censored, calls for a different method (survival analysis, Cox regression).

- If the response is binary, then can we use logistic regression models
- If the response is a count, we can use Poisson regression
- If the count has a higher variance than is consistent with the Poisson, we can use a negative binomial or over-dispersed Poisson
- Other forms of response can generate other types of generalized linear models

Generalized Linear Models

- We need a *linear predictor* of the same form as in linear regression βx
- In theory, such a linear predictor can generate any type of number as a prediction, positive, negative, or zero
- We choose a suitable distribution for the type of data we are predicting (normal for any number, gamma for positive numbers, binomial for binary responses, Poisson for counts)
- We create a *link function* which maps the mean of the distribution onto the set of all possible linear prediction results, which is the whole real line (-∞, ∞).
- The inverse of the link function takes the linear predictor to the actual prediction

- Ordinary linear regression has identity link (no transformation by the link function) and uses the normal distribution
- If one is predicting an inherently positive quantity, one may want to use the log link since e^x is always positive.
- An alternative to using a generalized linear model with an log link, is to transform the data using the log. This is a device that works well with measurement data and may be usable in other cases

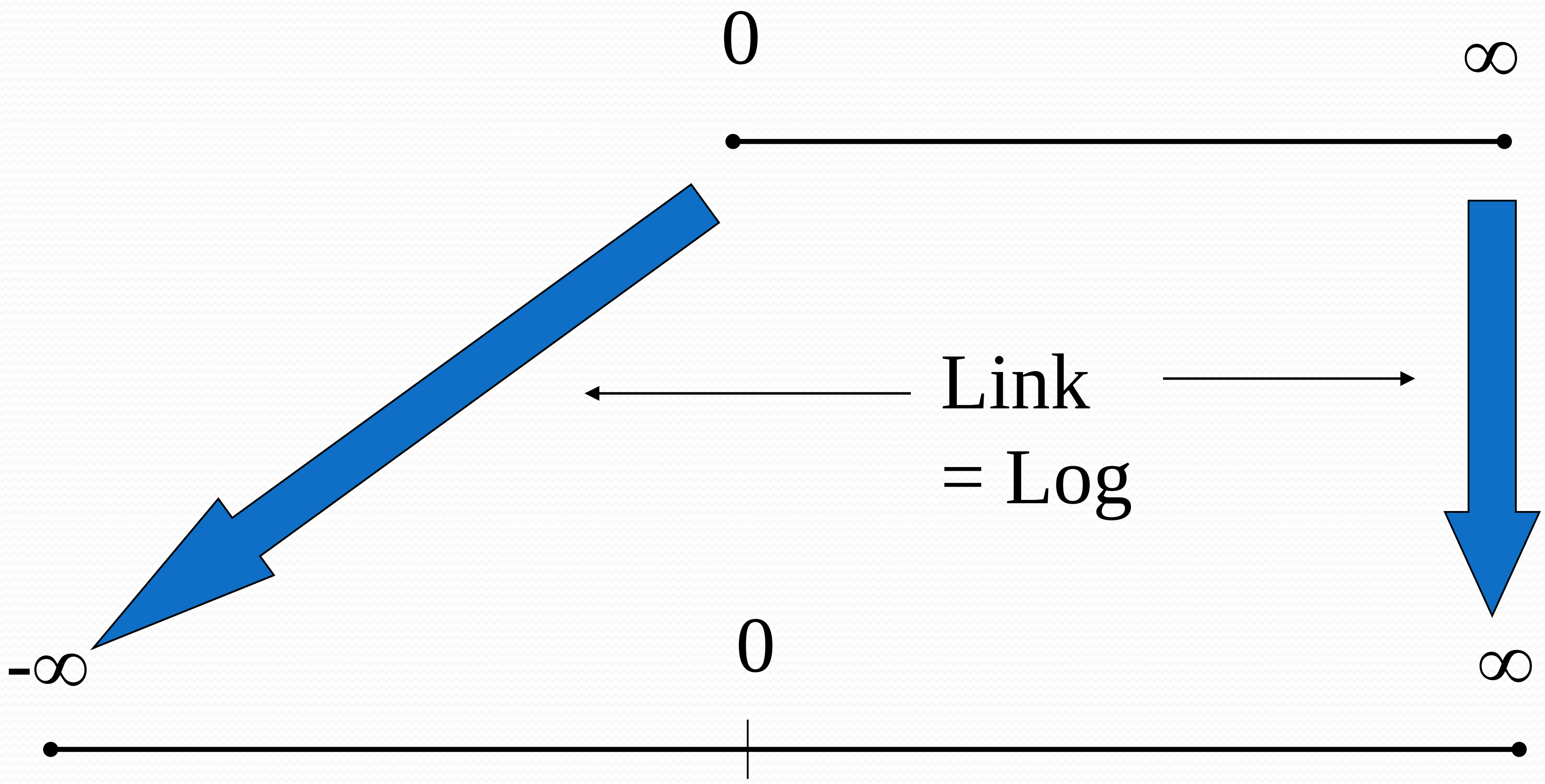
R glm() Families

Family	Links
gaussian	**identity**, log, inverse
binomial	**logit**, probit, cauchit, log, cloglog
Gamma	**inverse**, identity, log
inverse.gaussian	**1/mu^2**, inverse, identity, log
poisson	**log**, identity, sqrt
quasi	**identity**, logit, probit, cloglog, inverse, log, 1/mu^2 and sqrt
quasibinomial	**logit**, probit, identity, cloglog, inverse, log, 1/mu^2 and sqrt
quasipoisson	**log**, identity, logit, probit, cloglog, inverse, 1/mu^2 and sqrt

R glm() Link Functions

Links	Domain	Range	
identity	$(-\infty, \infty)$	$(-\infty, \infty)$	$\eta = X\beta = g(\mu) = \mu$
log	$(0, \infty)$	$(-\infty, \infty)$	$\eta = X\beta = g(\mu) = \log(\mu)$
inverse	$(0, \infty)$	$(0, \infty)$	$\eta = X\beta = g(\mu) = 1/\mu$
logit	$(0, 1)$	$(-\infty, \infty)$	$\eta = X\beta = g(\mu) = \log\left(p/(1-p)\right)$
probit	$(0, 1)$	$(-\infty, \infty)$	$\eta = X\beta = g(\mu) = \Phi^{-1}(p)$
cloglog	$(0, 1)$	$(-\infty, \infty)$	$\eta = X\beta = g(\mu) = \log(-\log(1-p))$
1/mu^2	$(0, \infty)$	$(0, \infty)$	$\eta = X\beta = g(\mu) = 1/\mu^2$
sqrt	$(0, \infty)$	$(0, \infty)$	$\eta = X\beta = g(\mu) = \sqrt{\mu}$

Possible Means



0

∞

Link
= Log

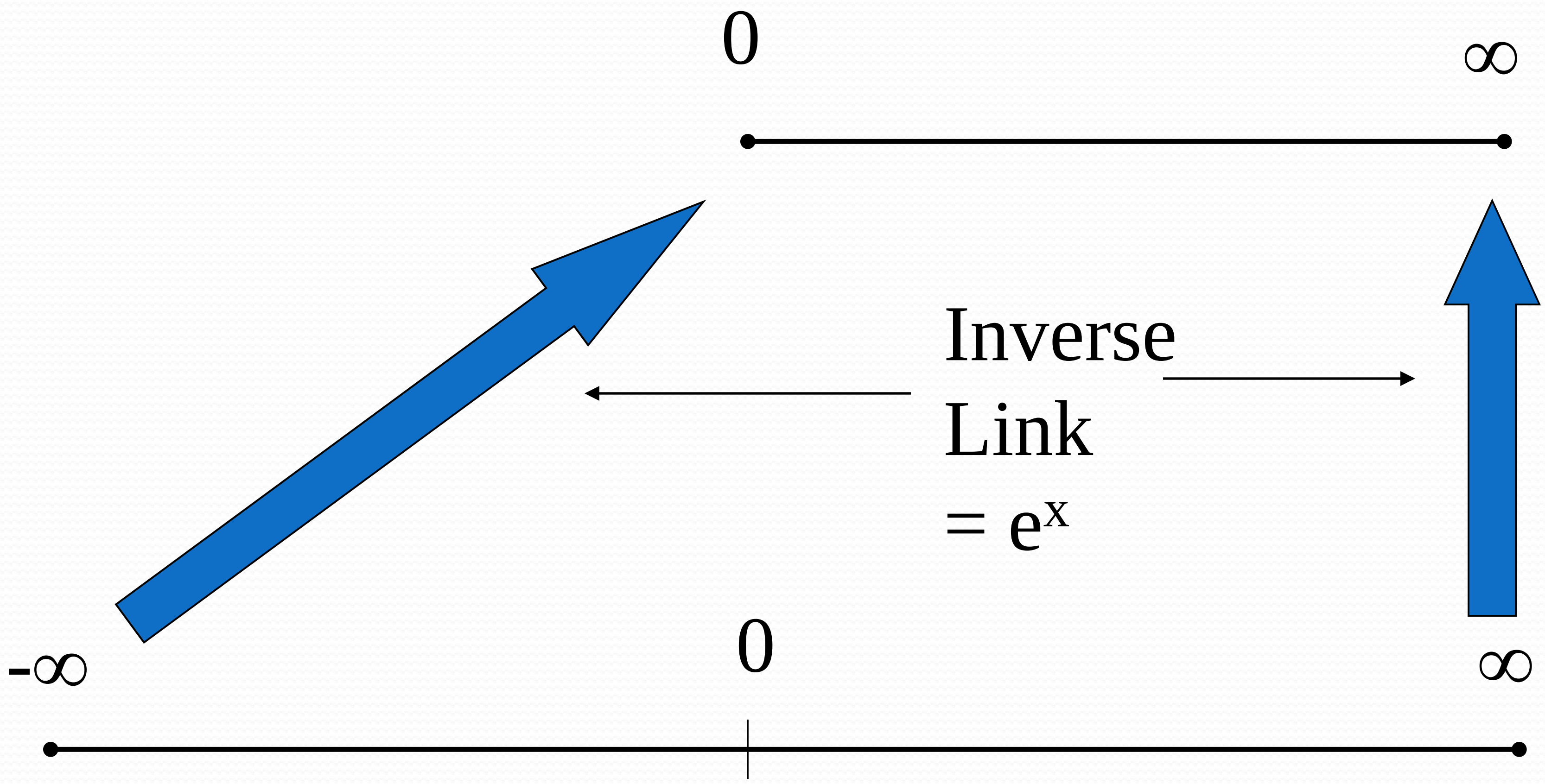
-∞

0

∞

Predictors

Possible Means



0

∞

Inverse
Link
= e^x

-∞

0

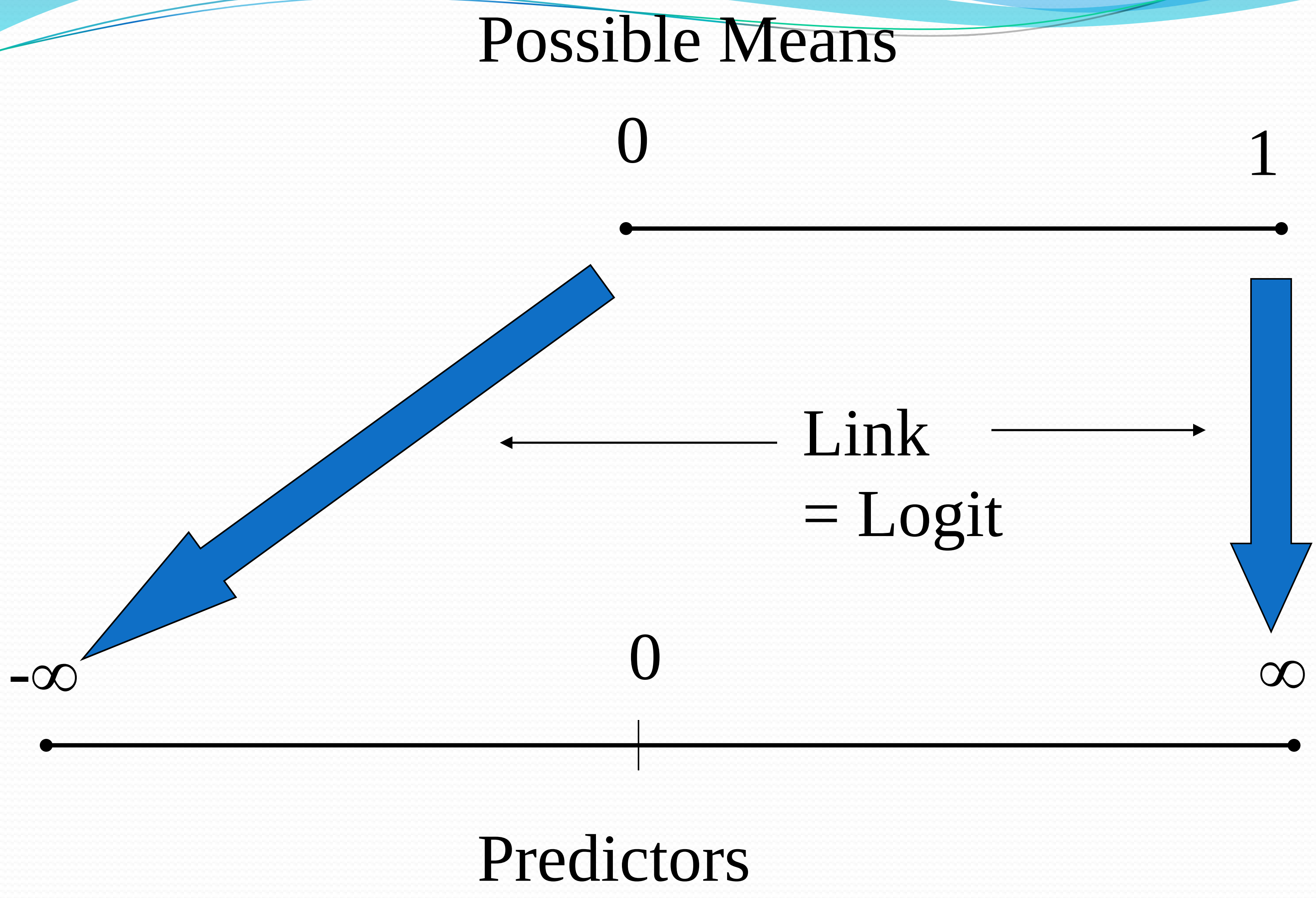
∞

Predictors

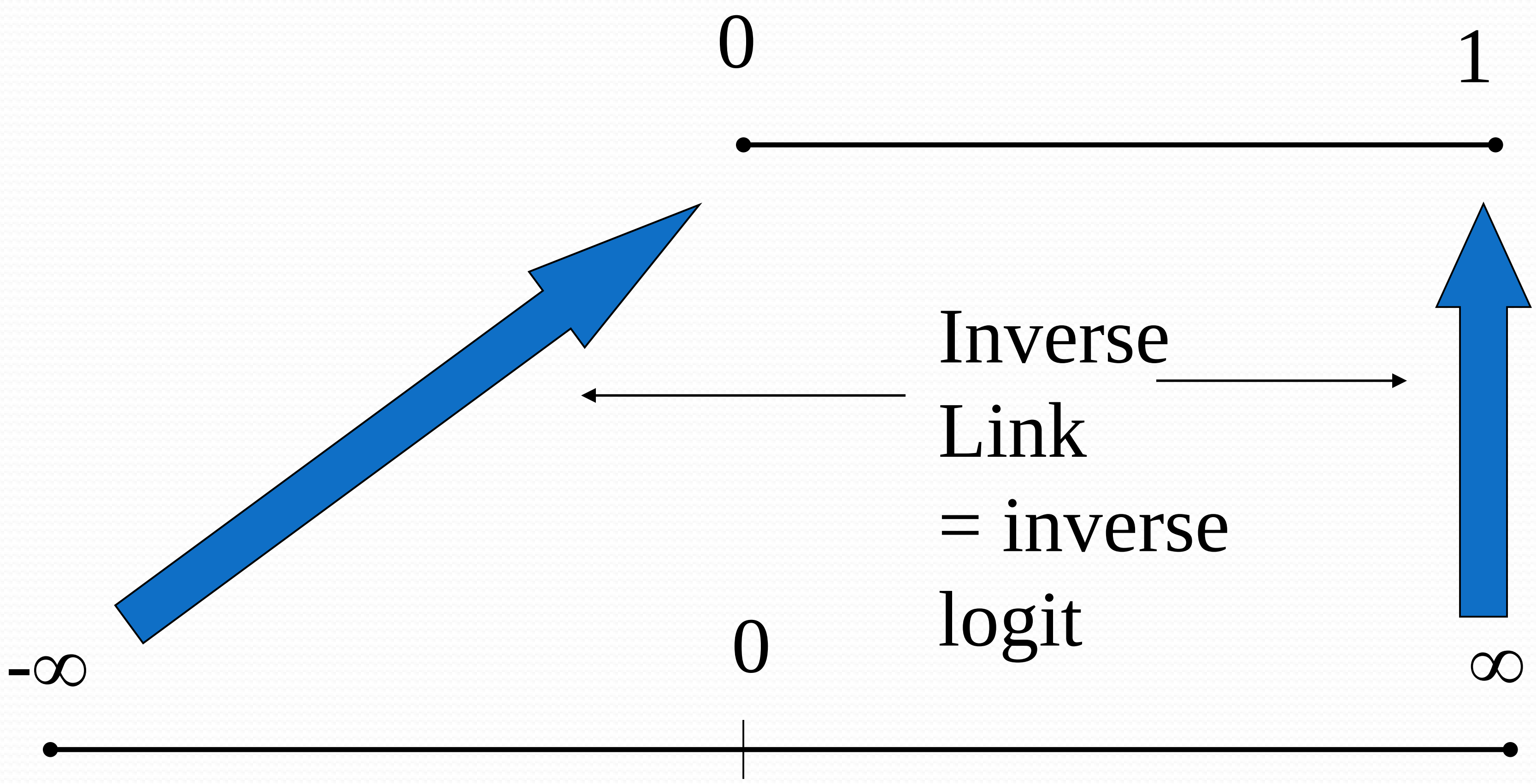
Logistic Regression

- Suppose we are trying to predict a binary variable (patient has ovarian cancer or not, patient is responding to therapy or not)
- We can describe this by a 0/1 variable in which the value 1 is used for one response (patient has ovarian cancer) and 0 for the other (patient does not have ovarian cancer
- We can then try to predict this response

- For a given patient, a prediction can be thought of as a kind of probability that the patient does have ovarian cancer. As such, the prediction should be between 0 and 1. Thus ordinary linear regression is not suitable
- The logit transform takes a number between 0 and 1, the scale of probabilities, and produces a number which can be anything, positive or negative, the scale of a linear predictor. Thus the logit link is useful for binary data


Possible Means
0
1
Link
= Logit
-∞
0
∞
Predictors

Possible Means



Predictors

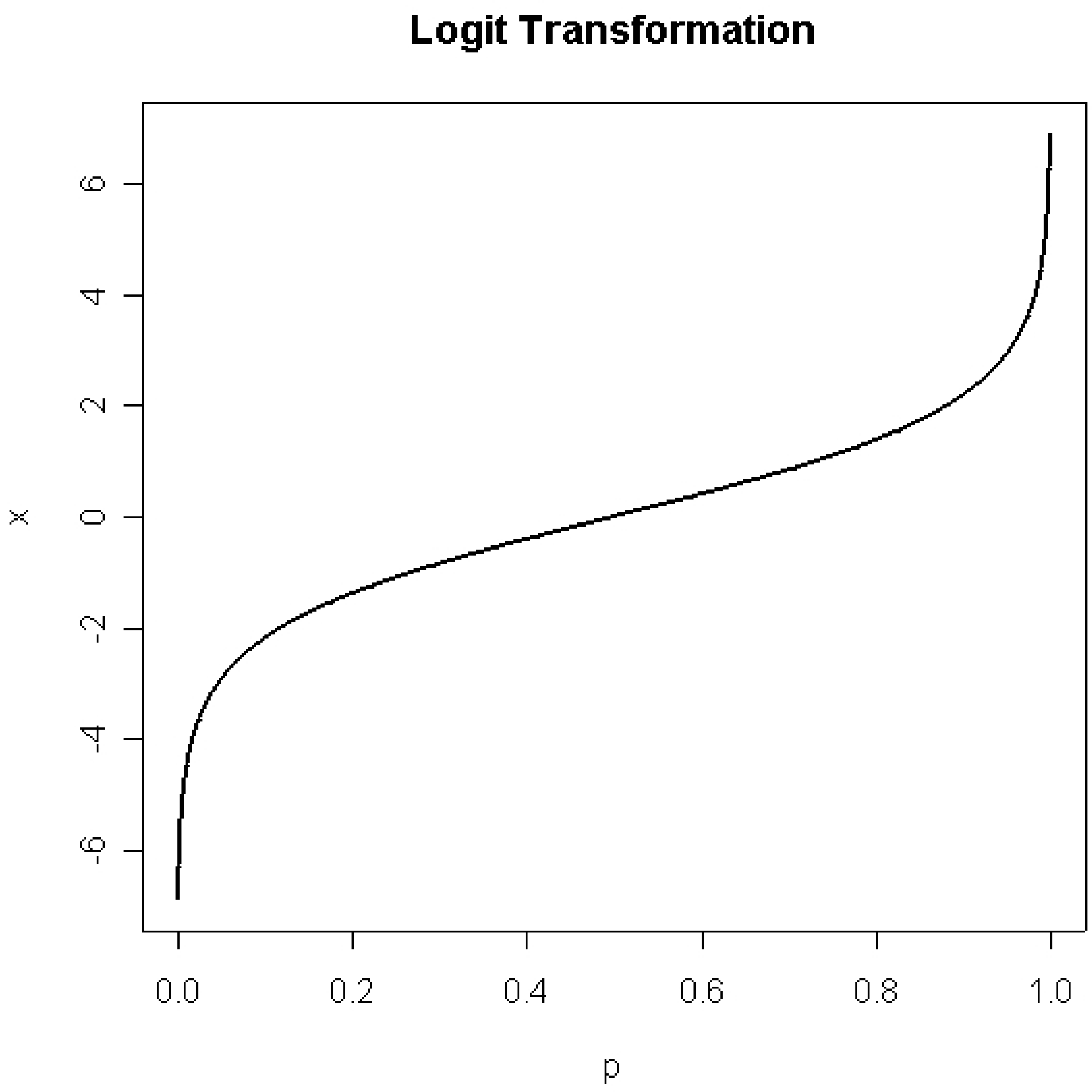
$$\operatorname{logit}(p) = \log\left(\frac{p}{1-p}\right) \quad \text{if } p \to 0 \text{ then } \operatorname{logit}(p) \to -\infty \quad \text{if } p \to 1 \text{ then } \operatorname{logit}(p) \to \infty$$

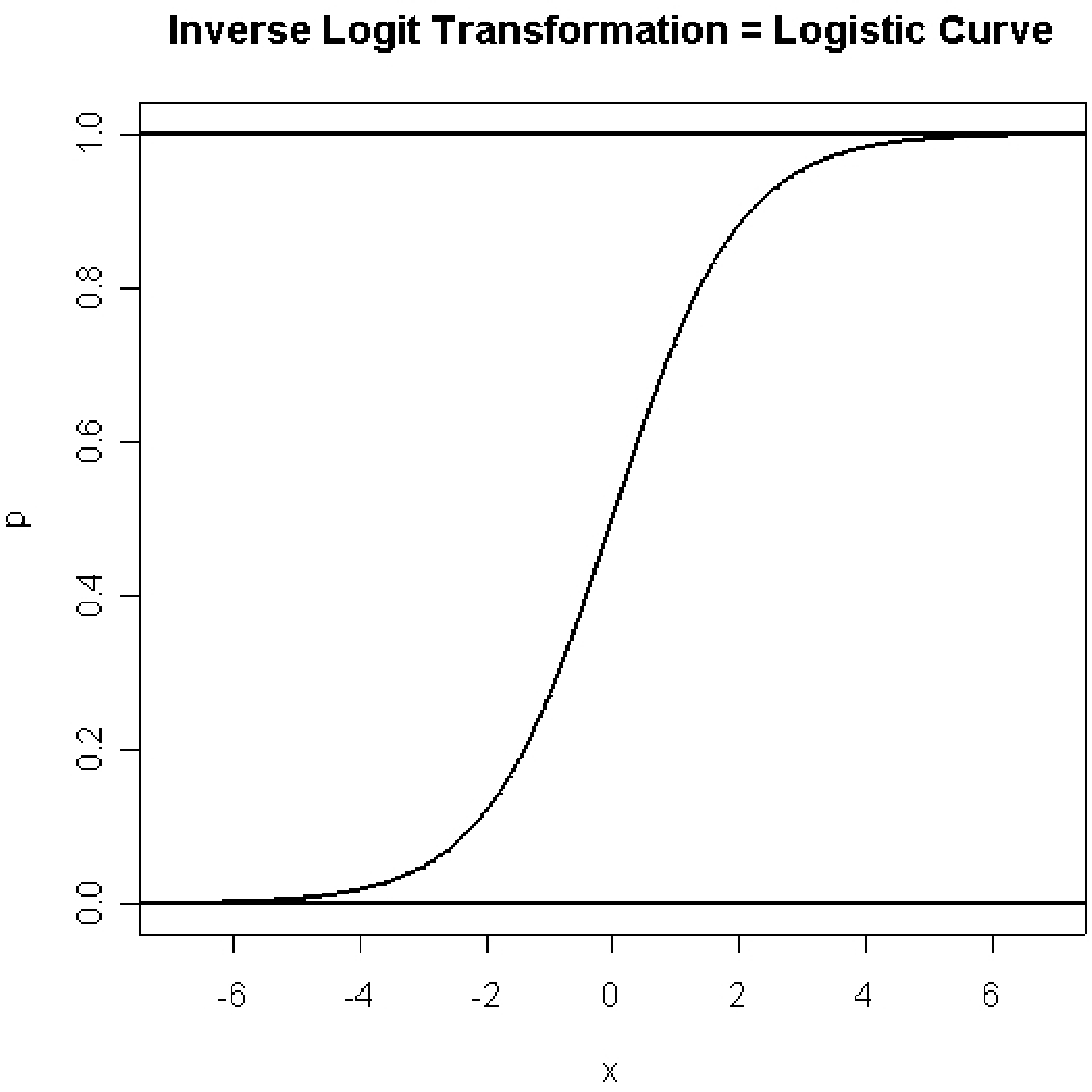
$$\operatorname{logit}^{-1}(x) = \frac{e^x}{1+e^x} \quad \text{if x} \to -\infty \text{ then } \operatorname{logit}^{-1}(x) \to 0 \quad \text{if x} \to \infty \text{ then } \operatorname{logit}^{-1}(x) \to 1$$

$$\log\left(\frac{\dfrac{e^x}{1+e^x}}{1-\dfrac{e^x}{1+e^x}}\right) = \log\left(\frac{\dfrac{e^x}{1+e^x}}{\dfrac{1+e^x-e^x}{1+e^x}}\right) = \log\left(\frac{\dfrac{e^x}{1+e^x}}{\dfrac{1}{1+e^x}}\right) = \log\left(e^x\right) = x$$

$\dfrac{p}{1-p}$ is the odds of the event when p is the probability of the event.

$\operatorname{logit}(p) = \log\left(\dfrac{p}{1-p}\right)$ is the log odds which is often a good scale to work on.


Logit Transformation
x
6
4
2
0
-2
-4
-6
0.0
0.2
0.4
0.6
0.8
1.0
p


Inverse Logit Transformation = Logistic Curve
p
0.0
0.2
0.4
0.6
0.8
1.0
-6
-4
-2
0
2
4
6
x

Analyzing Tabular Data with Logistic Regression

- Response is hypertensive y/n
- Predictors are smoking (y/n), obesity (y/n), snoring (y/n) [coded as 0/1 for Stata, R does not care]
- How well can these 3 factors explain/predict the presence of hypertension?
- Which are important?
- Since these are 8 discrete groups, each of which has an estimated odds, this is an easy generalization of the two-by-two case we examined above.

```
no.yes <- c("No","Yes")
smoking <- gl(2,1,8,no.yes)
obesity <- gl(2,2,8,no.yes)
snoring <- gl(2,4,8,no.yes)
n.tot <- c(60,17,8,2,187,85,51,23)
n.hyp <- c(5,2,1,0,35,13,15,8)
hyp <- data.frame(smoking,obesity,snoring,n.tot,n.hyp,n.hyp/n.tot)
print(hyp)
```

```
  smoking obesity snoring n.tot n.hyp n.hyp.n.tot
1      No      No      No    60     5  0.08333333
2     Yes      No      No    17     2  0.11764706
3      No     Yes      No     8     1  0.12500000
4     Yes     Yes      No     2     0  0.00000000
5      No      No     Yes   187    35  0.18716578
6     Yes      No     Yes    85    13  0.15294118
7      No     Yes     Yes    51    15  0.29411765
8     Yes     Yes     Yes    23     8  0.34782609
```

Specifying Logistic Regressions in R

- For each ‘cell’, we need to specify the diseased and normals, which will be what we try to fit.
- This can be specified either as a matrix with one column consisting of the number of diseased persons, and the other the number of normals (not the total).
- Or we can specify the proportions as a response, with weights equal to the sample size

```
hyp.tbl <- cbind(n.hyp, n.tot-n.hyp)
print(hyp.tbl)
glm.hyp1 <- glm(hyp.tbl ~ smoking+obesity+snoring,family=binomial("logit"))
glm.hyp2 <- glm(hyp.tbl ~ smoking+obesity+snoring,binomial)
prop.hyp <- n.hyp/n.tot
glm.hyp3 <- glm(prop.hyp ~ smoking+obesity+snoring,binomial,weights=n.tot)
```

```
 n.hyp
[1,]     5  55
[2,]     2  15
[3,]     1   7
[4,]     0   2
[5,]    35 152
[6,]    13  72
[7,]    15  36
[8,]     8  15
```

```
> summary(glm.hyp1)

Call:
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family = binomial("logit"))

Deviance Residuals: 
       1         2         3         4         5         6         7         8  
-0.04344   0.54145  -0.25476  -0.80051   0.19759  -0.46602  -0.21262   0.56231  

Coefficients:
            Estimate Std. Error z value Pr(>|z|)    
(Intercept) -2.37766    0.38018  -6.254    4e-10 ***
smokingYes  -0.06777    0.27812  -0.244   0.8075    
obesityYes   0.69531    0.28509   2.439   0.0147 *  
snoringYes   0.87194    0.39757   2.193   0.0283 *  
---
Signif. codes:  0 `***' 0.001 `**' 0.01 `*' 0.05 `.' 0.1 ` ' 1 

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 14.1259  on 7  degrees of freedom
Residual deviance:  1.6184  on 4  degrees of freedom
AIC: 34.537

Number of Fisher Scoring iterations: 4
```

```
             Estimate Std. Error z value Pr(>|z|)    
(Intercept) -2.37766    0.38018  -6.254    4e-10 ***
smokingYes  -0.06777    0.27812  -0.244   0.8075    
obesityYes   0.69531    0.28509   2.439   0.0147 *  
snoringYes   0.87194    0.39757   2.193   0.0283 *  
```

The coefficients of the linear predictor are on the log odds ratio scale. In this data set, only obesity and snoring are related to hypertension. For obesity, the coefficient is 0.69531. Since this is log odds ratio, we must exponentiate it to get the odds ratio of exp(0.6931) = 2.00, so obesity is estimated to double the odds of hypertension. Since this is a cross-sectional study, the actual probability cannot be determined. This depends on the intercept which is part of a measure of the average risk of the population, which we do not have access to.

A 95% CI for the coefficient is 0.69531 ± (1.960)(0.28509) or (0.13653,1.2541), which is on the log odds ratio scale, or (1.146, 3.505) on the odds ratio scale. So obesity raises the odds by 15% to a factor of 3.5.

```
> glm.hyp2 <- glm(hyp.tbl ~ smoking+obesity+snoring,binomial)

> coef(glm.hyp2)
(Intercept)  smokingYes  obesityYes  snoringYes
-2.37766146 -0.06777489  0.69530960  0.87193932

> exp(coef(glm.hyp2))
(Intercept)  smokingYes  obesityYes  snoringYes
 0.09276726  0.93447081  2.00432951  2.39154432     Estimated odds ratio

> confint.default(glm.hyp2)
                  2.5 %     97.5 %
(Intercept) -3.12280942 -1.6325135
smokingYes  -0.61288823  0.4773385
obesityYes   0.13655304  1.2540662
snoringYes   0.09270929  1.6511693

> exp(confint.default(glm.hyp2))
                 2.5 %    97.5 %
(Intercept) 0.04403329 0.1954377                    CI for odds ratios
smokingYes  0.54178381 1.6117789                    ignore intercept
obesityYes  1.14631567 3.5045641
snoringYes  1.09714274 5.2130721
```

```
> anova(glm.hyp1,test="Chisq")
Analysis of Deviance Table

Model: binomial, link: logit

Response: hyp.tbl

Terms added sequentially (first to last)


        Df Deviance Resid. Df Resid. Dev P(>|Chi|)
NULL                        7    14.1259
smoking  1   0.0022         6    14.1237    0.9627
obesity  1   6.8274         5     7.2963    0.0090
snoring  1   5.6779         4     1.6184    0.0172
```

```
> drop1(hyp.glm,test="Chisq")
Single term deletions

Model:
n.hyp.n.tot ~ smoking + obesity + snoring
        Df Deviance    AIC    LRT Pr(>Chi)
<none>       1.6184 34.537
smoking  1   1.6781 32.597 0.0597  0.80694
obesity  1   7.2750 38.194 5.6566  0.01739 *
snoring  1   7.2963 38.215 5.6779  0.01718 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
> predict(glm.hyp1)
         1          2          3          4          5          6          7
-2.3776615 -2.4454364 -1.6823519 -1.7501268 -1.5057221 -1.5734970 -0.8104126
         8
-0.8781874
> predict(glm.hyp1,type="response")
         1          2          3          4          5          6          7
0.08489206 0.07977292 0.15678429 0.14803121 0.18157364 0.17171843 0.30780259
         8
0.29355353
> rbind(predict(glm.hyp1,type="response"),prop.hyp)
                  1          2         3         4         5         6         7
         0.08489206 0.07977292 0.1567843 0.1480312 0.1815736 0.1717184 0.3078026
prop.hyp 0.08333333 0.11764706 0.1250000 0.0000000 0.1871658 0.1529412 0.2941176
                 8
         0.2935535
prop.hyp 0.3478261
> rbind(predict(glm.hyp1,type="response")*n.tot,n.hyp)
             1        2        3         4        5        6        7        8
      5.093524 1.356140 1.254274 0.2960624 33.95427 14.59607 15.69793 6.751731
n.hyp 5.000000 2.000000 1.000000 0.0000000 35.00000 13.00000 15.00000 8.000000
```

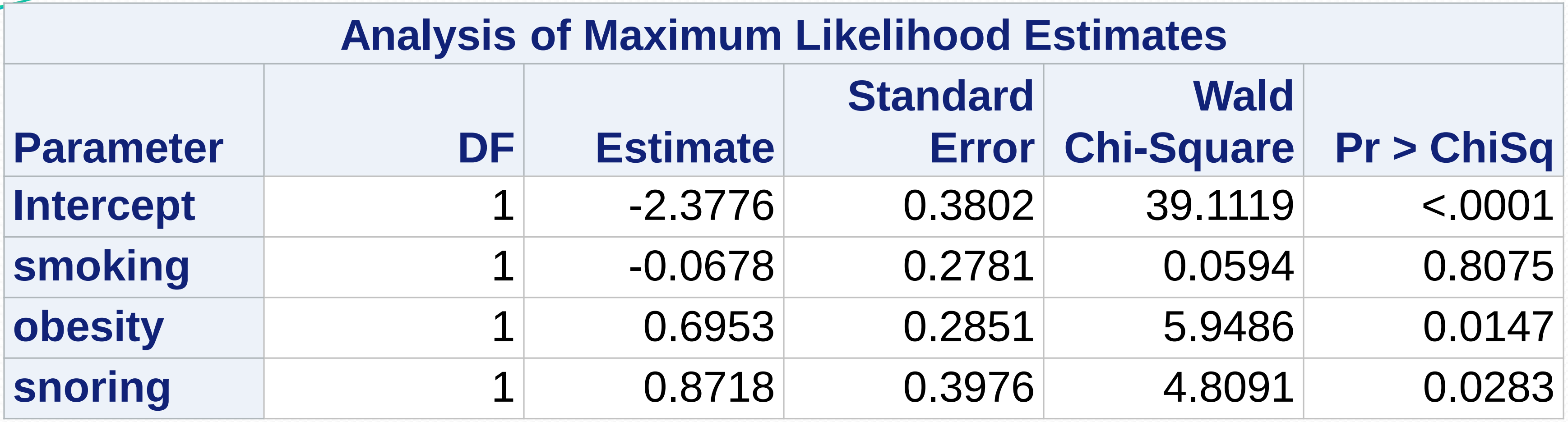
R and SAS Differences

- The only difference is caused by R using 0/1 coding for two-level class variables and SAS using -1/1 coding.
- So for the SAS code we used numeric 0/1 instead of strings.
- The hypothesis tests are essentially the same, as are the predicted values for each category, but the coefficients would differ if we used strings like “Yes” and “No” in SAS.
- You can try running the SAS version and compare the results.

```
data hyp;
   input smoking obesity snoring ntot nhyp ratio;
   datalines;
 0 0 0 60 5 0.0833333333333333
 1 0 0 17 2 0.117647058823529
 0 1 0 8 1 0.125
 1 1 0 2 0 0
 0 0 1 187 35 0.18716577540107
 1 0 1 85 13 0.152941176470588
 0 1 1 51 15 0.294117647058824
 1 1 1 23 8 0.347826086956522
;
run;

proc print data=hyp;
run;

proc logistic data=hyp;
model nhyp/ntot = smoking obesity snoring;
run;
```



Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-2.3776	0.3802	39.1119	<.0001
smoking	1	-0.0678	0.2781	0.0594	0.8075
obesity	1	0.6953	0.2851	5.9486	0.0147
snoring	1	0.8718	0.3976	4.8091	0.0283

```
            Estimate Std. Error z value   Pr(>|z|)
(Intercept) -2.37766    0.38018  -6.254    4e-10 ***
smokingYes  -0.06777    0.27812  -0.244   0.8075
obesityYes   0.69531    0.28509   2.439   0.0147 *
snoringYes   0.87194    0.39757   2.193   0.0283 *
```

Wald Chi-Square is the square of the “z-value”
The coefficient estimates may be different in SAS depending on the coding (0/1 vs. -1/1) but the p-values should be the same.

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
smoking	0.934	0.542	1.612
obesity	2.004	1.146	3.505
snoring	2.391	1.097	5.212

```
> exp(coef(glm.hyp2))
(Intercept)  smokingYes  obesityYes  snoringYes
 0.09276726  0.93447081  2.00432951  2.39154432

> exp(confint.default(glm.hyp2))
                 2.5 %    97.5 %
(Intercept) 0.04403329 0.1954377
smokingYes  0.54178381 1.6117789
obesityYes  1.14631567 3.5045641
snoringYes  1.09714274 5.2130721
```

Access to R and SAS

- You can download the main R binary at https://cran.r-project.org/
- R Studio (a integrated environment) is at https://www.rstudio.com/
- R packages can be installed from within R. In Windows, it is best to install packages after starting R as an administrator
- SAS University Edition is free if you have a .edu email address. Start at http://www.sas.com/en_us/software/university-edition.html or just search for SAS University Edition
- Be sure to read the QuickStart Guide because it installs from within Oracle VirtualBox.