Against all Odds

Michael P. LaValley
Boston University
http://people.bu.edu/mlava/

ACR/ARHP Annual Scientific Meeting
San Antonio Texas 10/20/2004

Outline

- Measures of Risk
  - Relative Risk (RR)
  - Odds Ratio (OR)
- Obtaining Adjusted RR
  - Logistic Regression with Transformation
  - Binomial Regression
  - Modified Poisson Regression
- Summary

Measures of Risk

- Measure relationship between two binary variables
  - Binary variables: 0/1 or No/Yes
- Usually expressed as
  - At how much greater risk of X is one group than another?
- Example
  - At how much greater risk of osteoarthritis (OA) are women than men?

Measures of Risk

- Often want to adjust for differences between groups in other factors
  - Remove the effects of the other factors from the group difference
- Example
  - At how much greater risk of OA are women than men after adjusting for age and body mass index?

Relative Risk

- Relative Risk (RR)
  - Ratio of the probabilities of the occurrence of the outcome of interest in group 1 to group 2

$$RR = \frac{\Pr_1}{\Pr_2}$$

  - $\Pr_1$ is the probability of the outcome in group 1
  - $\Pr_2$ is the probability of the outcome in group 2

Odds

- Odds (used in odds ratio)
  - Odds are the probability of occurrence divided by the probability of non-occurrence

$$Odds_1 = \frac{\Pr_1}{1 - \Pr_1}$$

  - $Odds_2$ defined using Pr_2

Odds

- Odds are used in gambling
  - ‘The odds are two to one for Seabiscuit to win’
  - 2:1 → odds = 2 → Pr = 0.67
- Translating odds to probabilities
  - Odds = 3.0 ↔ Pr = 0.75
  - Odds = 2.0 ↔ Pr = 0.67
  - Odds = 1.0 ↔ Pr = 0.50
  - Odds = 0.5 ↔ Pr = 0.33

Odds Ratio

- Odds Ratio (OR)
  - **Ratio** of the *odds* of the occurrence of the event of interest in group 1 to group 2

$$OR = \frac{Odds_1}{Odds_2} = \frac{\left(\Pr_1 / (1 - \Pr_1) \right)}{\left(\Pr_2 / (1 - \Pr_2) \right)}$$

RR and OR Comparison

- RR and OR are *ratio* measures
  - 1.0 is the point of no difference between groups (the null value)
  - Are greater than 1 if group 1 is at increased risk relative to group 2
  - Are less than 1 if group 1 is at decreased risk relative to group 2
  - Reciprocals are the same distance from the null value
    - E.g. 2 and ½ are equivalent group differences

RR and OR Comparison

- The RR is more understandable
  - When the RR=2 then the probability of the outcome in group 1 is twice that of group 2
  - This is not true for the odds ratio
- Most people are more comfortable with probabilities or percentages that with odds

RR and OR Comparison

- However, the OR has some advantages
  - In case-control studies the OR can be estimated but not the RR
  - The OR is symmetric to which outcome level is chosen as being of interest, the RR is not

RR and OR Comparison

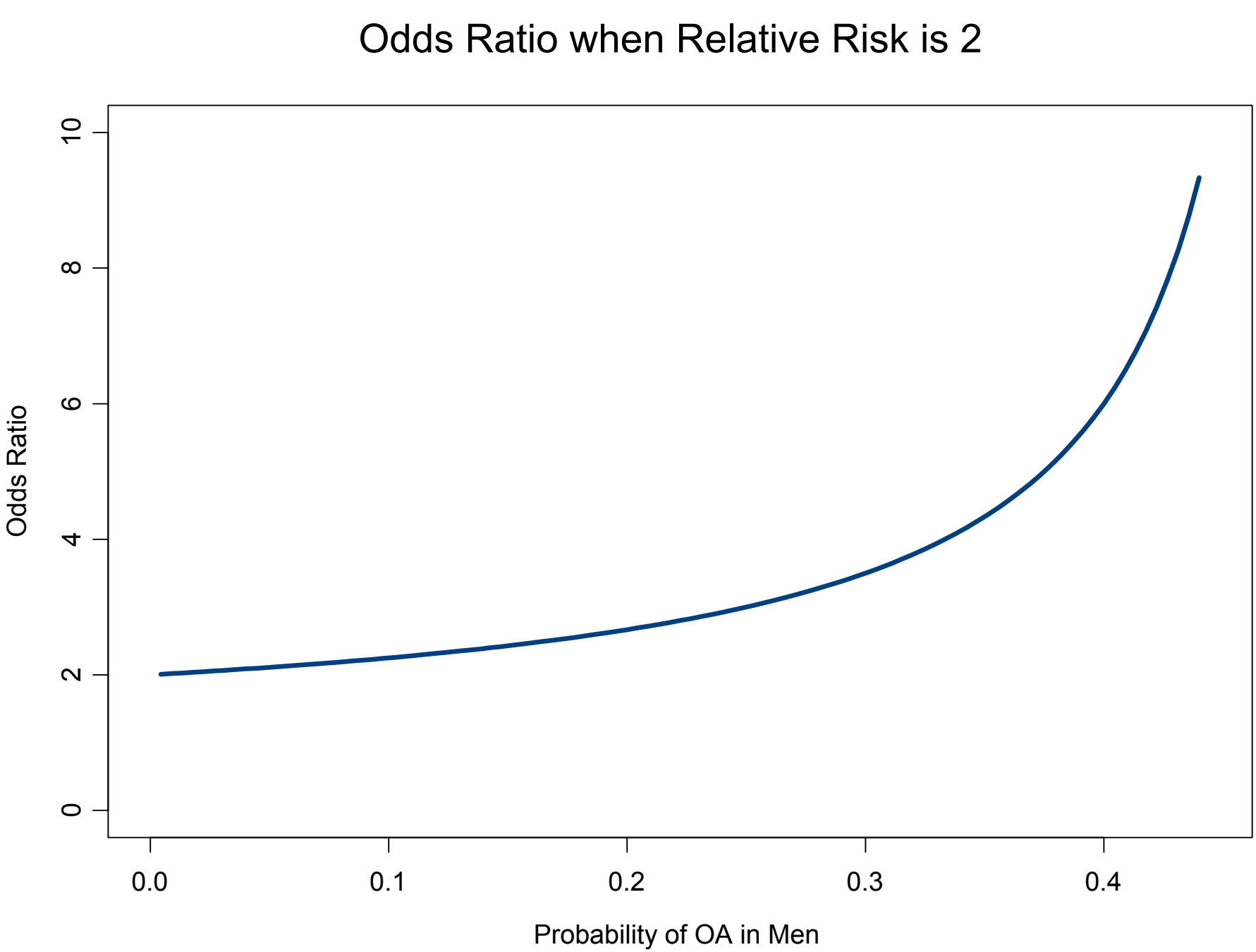
- When are the RR and OR Similar?
  - If the probability of the event is small, the odds and the probability are close

$$Odds_1 = \frac{\Pr_1}{1 - \Pr_1} \approx \Pr_1$$

  - When the probability of the event is small in both the OR is a good approximation to the RR
  - Rule of thumb for small: Pr < 0.1

RR and OR Comparison

- The OR is always more extreme (farther from 1) than the RR
- When the events of interest are common, the OR can be much larger than the RR


Odds Ratio when Relative Risk is 2
Odds Ratio
0
2
4
6
8
10
0.0
0.1
0.2
0.3
0.4
Probability of OA in Men

Which is Better?

- For case-control studies need to present the OR
- For cohort studies and clinical trials the RR is better to report
  - Reduces the chance of incorrect interpretation
  - Becoming preferred to report RR in medical journals

Osteoarthritis in Framingham

- In the Framingham Osteoarthritis study, prevalence of osteoarthritis (OA) was measured in 1992-93
- Female sex is an established risk factor for OA
- At how much greater risk of osteoarthritis are women than men in this study?

Osteoarthritis in Framingham

- Subset of 840 subjects to evaluate the prevalence of OA in women versus men
- 538 women
- 302 men
- 513 (61%) no OA
- 327 (39%) with OA

	No OA	OA	Total
Women	316	222	538
Men	197	105	302
Total	513	327	840

Osteoarthritis in Framingham

- In men
  - 197 (65%) no OA
  - 105 (35%) with OA
- In women
  - 316 (59%) no OA
  - 222 (41%) with OA
- RR = 0.41/0.35 = 1.19
- OR = 1.32

	No OA	OA	Total
Women	316	222	538
Men	197	105	302
Total	513	327	840

Osteoarthritis in Framingham

- Women have 1.19 times ***the risk*** of OA compared to men
- Women have 1.30 times ***the odds*** of OA compared to men
- If we interpret OR as an RR, we would mistakenly conclude women are at 1.3 times the risk of OA

Osteoarthritis in Framingham

- Suppose we look at No OA as the outcome
  - RR for No OA is 0.59/0.65 = 0.91
  - But RR for OA is 1.19 and 1/1.19 = 0.84
- The RR implies that sex plays a larger role for OA than for No OA!

	No OA	OA	Total
Women	316	222	538
Men	197	105	302
Total	513	327	840

Osteoarthritis in Framingham

- RR is not symmetric around the null value for both outcome levels
  - RR for No OA ≠ 1/RR for OA
- OR is symmetric
  - OR for No OA = 1/OR for OA
- Usually the outcome to choose is clear and this isn't a problem. But some situations aren't clear
  - E.g. use 'lived' or 'died'?

Adjusted RR

- Logistic regression provides adjusted OR
- But, until recently it has been difficult to obtain adjusted RR
- Three methods for getting adjusted RR
  - Logistic regression with transformation
  - Binomial regression
  - Modified Poisson regression

Logistic Regression

- Logistic regression is widely used regression method for binary outcomes
- Logistic regression coefficients are log(OR)
- Provides adjusted OR if adjustors are used as additional predictors

Logistic Regression

- If outcome probabilities are < 0.1 for all values of the predictors then the OR are good approximations to RR
- Otherwise Zhang and Yu proposed a formula to convert OR to RR

$$RR = \frac{OR}{\left(1 - \mathrm{Pr}_2\right) + \left(\mathrm{Pr}_2 \times OR\right)}$$

Logistic Regression

- However the conversion formula has been criticized*
  - Leads to confidence intervals for RR that are too small
  - Gives biased estimate if some regression predictors are confounders
  - Doesn't work if there are interactions in the regression model

*See McNutt et al.

Binomial Regression

- Binomial regression is a rarely used regression method for binary outcomes
- Binomial regression coefficients are log(RR)
- Provides adjusted RR if adjustors are used as additional predictors

Binomial Regression

- This model often fails due to numerical problems
- Especially failure prone if
  - Correlated predictors
  - One or more continuous predictors

Modified Poisson Regression

- Poisson regression is a method for count outcomes
  - Count outcomes: 0, 1, 2, 3, ….
- Poisson regression coefficients are log(RR)
- Provides adjusted RR if adjustors are used as additional predictors
- Poisson regression is conservative for binary outcomes
  - Less likely to be significant
  - Confidence intervals too wide

Modified Poisson Regression

- Modification due to Zou
  - Adjust variability with generalized estimating equations (GEE)
  - Uses variability in the data to adjust model
- This has been shown to work very well
- Software implementation
  - SAS in Lundquist
  - STATA in Barros and Hirakata

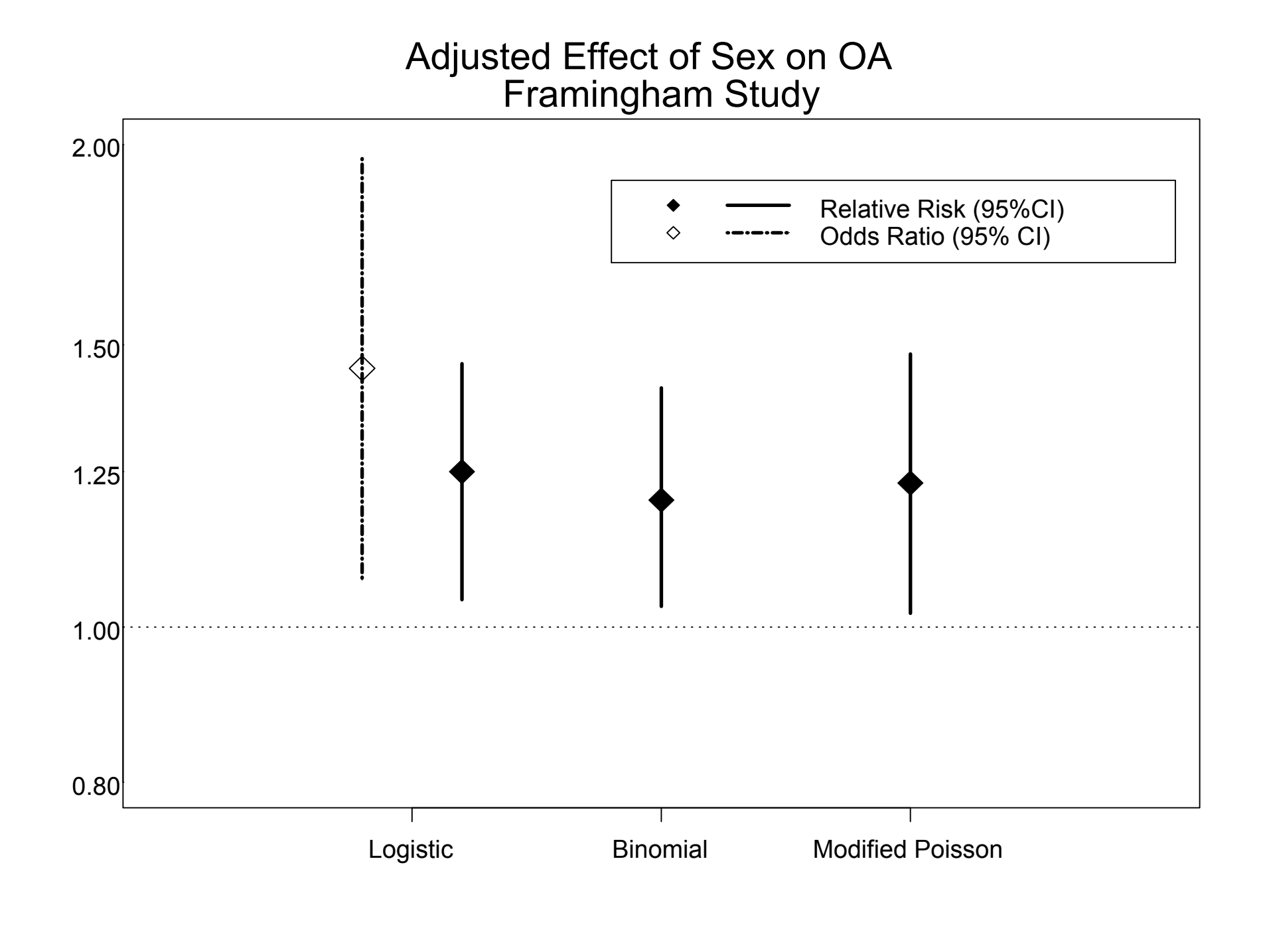
Osteoarthritis in Framingham

- We found greater risk of OA in women than men
  - Could this be due to age differences between women and men?
  - Could this be due to differences in body mass index between women and men?
- Use regression models with sex, age, and body mass index

Osteoarthritis in Framingham

- After adjustment for age and body mass index
  - Logistic OR = 1.45
  - Transformed Logistic RR = 1.25
  - Binomial RR = 1.20*
  - Modified Poisson RR = 1.23

*Failed to arrive at final estimate


Adjusted Effect of Sex on OA
Framingham Study
2.00
1.50
1.25
1.00
0.80
Relative Risk (95%CI)
Odds Ratio (95% CI)
Logistic
Binomial
Modified Poisson

Summary

- Medical literature is moving toward reporting RR instead of OR whenever possible
  - Need to keep in mind that the RR changes in non-intuitive ways when outcomes are switched
- When reporting OR make it clear that it is not the RR
- Modified Poisson regression will become standard method for obtaining adjusted RR

References

- Simon SD. Understanding the odds ratio and the relative risk. *Journal of Andrology* **22**:533-6, 2001
- Zhang J, Yu KF. What's the relative risk? *JAMA* **280**:1690-1, 1998
- McNutt L-A, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *American Journal of Epidemiology* **157**:940-3, 2003

References

- Zou G. A modified poisson regression approach to prospective studies with binary data. *American Journal of Epidemiology* **159**:702-6, 2004
- Lundquist K. SAS FAQ: How to estimate relative risk in SAS using PROC GENMOD for common outcomes in cohort studies. http://www.ats.ucla.edu/stat/sas/faq/relative_risk.htm
- Barros AJD, Hirakata VN. Alternatives for logistic regression in cross-sectional studies. *BMC Medical Research Methodology* **3**:21, 2003