Absolute Epidemiology

Developing Software Skills for Estimation of Absolute Contrasts from Regression Models in Perinatal Epidemiology

Jay S. Kaufman, McGill University
Ashley H. Schempf, Maternal & Child Health Bureau

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Outline:

1) Motivation for absolute effect estimates (25 minutes)
(slides 3-32)

2) Simple models for generating absolute estimates in cohort and cross-sectional data (25 minutes)
(slides 33-66)

3) Extended examples for clustered and weighted data (25 minutes)
(slides 67-107)

4) Questions and discussion (15 minutes)

Epidemiology comes in two flavors:

ETIOLOGY SURVEILLANCE

Statistically:

Pr(Y|SET[X=x]) vs Pr(Y|X=x)

Which flavor of epidemiology are we having?

If our purpose is descriptive (i.e., what is the comparison of rates for different groups in the real world?), there should be <u>no adjustment</u>.

SURVEILLANCE

If our purpose is etiologic (causal), then we want to know:

ETIOLOGY

$Pr(Y=1|SET[X=x_1])$ versus $Pr(Y=1|SET[X=x_2])$

where x_1 and x_2 are two different levels of exposure

often, x_1 = exposed and
x_2 = unexposed

There are many ways to calculate the contrast

$Pr(Y=1|SET[X=x_1])$ versus $Pr(Y=1|SET[X=x_2])$

RISK DIFFERENCE (RD):

$$Pr(Y=1|SET[X=x_1]) - Pr(Y=1|SET[X=x_2])$$

RISK RATIO (RR):

$$Pr(Y=1|SET[X=x_1]) \,/\, Pr(Y=1|SET[X=x_2])$$

ODDS DIFFERENCE (OD):

$$\frac{Pr(Y=1|SET[X=x_1])}{Pr(Y=0|SET[X=x_1])} - \frac{Pr(Y=1|SET[X=x_2])}{Pr(Y=0|SET[X=x_2])}$$

ODDS RATIO (OR):

$$\frac{Pr(Y=1|SET[X=x_1])}{Pr(Y=0|SET[X=x_1])} \,/\, \frac{Pr(Y=1|SET[X=x_2])}{Pr(Y=0|SET[X=x_2])}$$

What are the advantages and disadvantages of these different choices?

Why are the OR and RR measures used so much more than the RD or OD measures?

How do these measures connect to different statistical regression models, like linear regression, logistic regression and Poisson regression?

Do these measures behave in similar ways with respect to confounding and effect measure modification?

Do the measures computed in observational data have similar causal implications?

1) Ratio Measures Hide Important Information

"People who take drug A are half as likely to die as people who take placebo (RR = 0.5)"

Without underlying absolute risks (the chance of death in each group) the information is useless.

RR = 0.5 is compatible with: **20% vs 10%**
1% vs 0.5%
0.0004% vs 0.0002%.

Effects presented in relative terms alone have been repeatedly shown to seem more impressive than the same effects presented in absolute terms in experimental studies of physicians, policy makers, and patients.

Schwartz LM, et al. BMJ. 2006 Dec 16;333(7581):1248.

RESEARCH AND PRACTICE

Black–White Health Disparities in the United States and Chicago: A 15-Year Progress Analysis

Jennifer M. Orsi, MPH, Helen Margellos-Anast, MPH, and Steven Whitman, PhD

Objectives. In an effort to examine national and Chicago, Illinois, progress in meeting the Healthy People 2010 goal of eliminating health disparities, we examined whether disparities between non-Hispanic Black and non-Hispanic White persons widened, narrowed, or stayed the same between 1990 and 2005.

Methods. We examined 15 health status indicators. We determined whether a disparity widened, narrowed, or remained unchanged between 1990 and 2005 by examining the percentage difference in rates between non-Hispanic Black and non-Hispanic White populations at both time points and at each location. We calculated *P* values to determine whether changes in percentage difference over time were statistically significant.

Results. Disparities between non-Hispanic Black and non-Hispanic White populations widened for 6 of 15 health status indicators examined for the United States (5 significantly), whereas in Chicago the majority of disparities widened (11 of 15, 5 significantly).

Conclusions. Overall, progress toward meeting the Healthy People 2010 goal of eliminating health disparities in the United States and in Chicago remains bleak. With more than 15 years of time and effort spent at the national and local level to reduce disparities, the impact remains negligible. (*Am J Public Health.* 2010;100:349–356. doi:10.2105/AJPH.2009.165407)

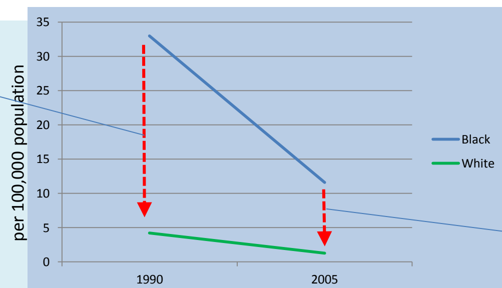
Racial disparities in health in the United States have been well documented, and federal initiatives have been undertaken to reduce these disparities. One of the first federal initiatives to bring awareness to racial disparities in health was the 1985 Report of the Secretary's Task Force on Black and Minority Health, which highlighted the need for programs and policies to address disparities in health within the United States.[1] Many initiatives have followed. The most recent federal initiative is Healthy People 2010, which consists of 2 main goals, 28 focus areas, and 467 objectives. One of the main goals is the elimination of health disparities within the United States.[2] This builds upon one of the goals from Healthy People 2000, which aimed at the reduction of health disparities.[3]

Interestingly, although the reduction and elimination of health disparities are declared

TABLE 2—Health Status Indicators and Rates, by Race, Year, and Associated Black–White Percentage Differences: United States, 1990 and 2005

Indicator	Non-Hispanic Black Rate	Non-Hispanic White Rate	Difference, %	*P*
All-cause mortality[a]				<.001
1990	1170.1	867.7	34.9	
2005	1147.7	892.1	28.7	
Tuberculosis case rate[f]				<.001
1990	33.0	4.2	685.7	
2005	11.6	1.3	792.3	

33.0 – 4.2 = 28.8



11.6 – 1.3 = 10.3

3) Ratio Measures Can Hide Important Changes

BMJ

RESEARCH

Faculty of Arts and Social Sciences, Furness College, Lancaster University, Lancaster LA1 4YG
Correspondence to: I.Gregory@lancaster.ac.uk

Cite this as: *BMJ* 2009;339:b3454
doi:10.1136/bmj.b3454

Comparisons between g... de... cer...

Ian N...

ABSTRACT

Objectives To examine the geog... mortality and deprivation in Eng... start of the 20th and 21st centu... evidence for a strengthening or w... over the century and test for rela... mortality and deprivation patter... modern mortality and causes of...

Design Census and mortality da... the 1900s directly compared wit... data from 2001.

Setting Census data and nation... and Wales in the 1900s and 20...

Population Entire population in both periods.

Main outcome measures Standardi... all districts for both periods with ad... ratios calculated for 2001. Depriva... for each district in 2001, with comp... created for the 1900s. Correlations... correlations between deprivation s... standardised mortality ratios in the... the 614 districts for which all data...

Results The was no evidence of a significant change in the strength of the relation between deprivation and mortality between the start and end of the 20th century. Modern patterns of mortality and deprivation remain closely related to the patterns of a century ago. Even after adjustment for modern deprivation, standardised mortality ratios from the 1900s show a significant correlation with modern mortality and most modern causes of death. Conversely, however, there was no significant relation between deprivation in the 1900s and modern mortality for most causes of death after adjustment for modern deprivation.

Conclusions Despite all the medical, public health, social, economic, and political changes over the 20th century, patterns of poverty and mortality and the relations between them remain firmly entrenched. There is a strong relation between the mortality levels of a century ago and those of today. This goes beyond what would have been expected from the continuing relation between deprivation and mortality and holds true for most major modern causes of death.

PUB MENU

EGGS	$3
MILK	$1
STEAK	$9
PICKLED HAM	$2
SHORT CAKES	$1
CHOP SUEY	$4
FOIE GRAS	$15

PUB MENU

EGGS	$6
MILK	$2
STEAK	$18
PICKLED HAM	$4
SHORT CAKES	$2
CHOP SUEY	$8
FOIE GRAS	$30

4) Ratio Measures Don't Have Direct Causal Interpretation

Once upon a time, a department chair was intrigued by the idea that teaching epidemiology might offer no benefit for a large number of students

He decided to save scarce funds by paying me for teaching <u>only those students</u> who would pass my course <u>because</u> they attended the class

Only 3 possible kinds of students:

type A would pass the exam with or without attending lectures
type B who would pass the exam if they attended but fail if they did not
type C were doomed to fail the exam regardless

The chair told me to figure out the number of type B's in the student population, because this is the only group worth teaching

Partition incoming class of 60 students at random: assures that expected proportions of each of the 3 latent types will be the same in the two groups of 30:

	Treatment Group (n=30)	Control Group (n=30)
Type A	p(A)	p(A)
Type B	p(B)	p(B)
Type C	p(C)	p(C)

p(A)+p(B)+p(C) = 100%

Teach one group of 30 students my usual course (treatment group)
Assign the other group to stay away (control group)

Everyone compliant with their assignments
No communication about epidemiology among the students

At the end of the term, the exam:

	Treatment Group (n=30)	Control Group (n=30)
Passed	18	6
Failed	12	24
Total	30	30

The number who passed in the group with instruction must be p(A+B), whereas the number who passed in the group without instruction was simply p(A)

The ratio of these numbers is the causal effect of teaching:
(18/30) / (6/30) = 18/6 = 3.0

My teaching tripled the pass rate!

The department chair was not satisfied

He wanted to pay me based on the number of people who were Type B, whereas my randomized controlled trial only identified the quantities A, A+B, and their ratio (A+B)/A

Solution:

Take the difference between the two numbers instead of their ratio

The difference of (A+B) in the treated group minus A in the untreated group yields B

A total of 18 − 6 = 12 students passed the examination because of the instruction, a number completely obscured by the relative contrast

(18/30) - (6/30) = 12/30 = 0.40

The following year, a worsening economy drove many highly qualified applicants back to graduate school, so the overall failure rate on exams decreased

There were again 60 students, with 30 assigned to each group:

	Treatment Group (n=30)	Control Group (n=30)
Passed	24	8
Failed	16	22
Total	30	30

The ratio (A+B)/A = (24/30) / (8/30) showed that once again my instruction had tripled the pass rate, since 24/8 = 3.0

Relying on the RR only, I would have claimed (incorrectly) to have had the same effect on my students as in the previous year

The truth was, however, that:

(24/30) – (8/30) = 16/30 = 0.533

Since 24–8 = 16, I could collect from the department chair an additional salary for having caused 4 more students to pass than in the previous year

My cohort size (n = 60) and my ratio measure of effect (RR = 3) were both identical, and yet I had affected 33% more students this year than the year before (16 versus 12)

You would never know that if you used on the RR

Kaufman JS. Toward a more disproportionate epidemiology. *Epidemiology* 2010 Jan;21(1):1-2.

5) The Odds Ratio is a Liar

Every individual *i* has risk under exposure (E=1) = r_{1i}
and another risk under non-exposure (E=0) = r_{0i}

Then the risk odds under the two exposure states are:

$$\omega_{1i} = \frac{r_{1i}}{(1-r_{1i})} \quad \text{and} \quad \omega_{0i} = \frac{r_{0i}}{(1-r_{0i})}$$

The INDIVIDUAL effect measures are then:

the risk difference $(r_{1i})-(r_{0i})$

the risk ratio $\dfrac{(r_{1i})}{(r_{0i})}$

and the risk odds ratio $\dfrac{(\omega_{1i})}{(\omega_{0i})}$

Over a population, you can construct RD in two ways:
Either take the average risk under exposure E=1 minus the average risk under non-exposure E=0:

$$\sum_i (r_{1i}) - \sum_i (r_{0i})$$

or take the average individual risk difference: $\sum_i (r_{1i} - r_{0i})$

That is, you can sum and then divide, or divide and then sum.

For the RD, **it doesn't matter in which order you do the operations.** The population incidence difference is interpretable as both **the absolute change in average risk of the exposed cohort that is due to exposure** (difference between the average individual risks) AND as **the average absolute change in risk produced by exposure among exposed** (average of the individual risk-differences).

For the RR, the incidence proportion ratio that you compute at the population level is interpretable as the **proportionate change in the average risk of the exposed group produced by exposure** (i.e. the ratio of the average individual risks).

But it is NOT interpretable as the **average proportionate change in risk produced by exposure among the exposed** (i.e. average of the individual RRs)

UNLESS the individual RRs $\frac{(r_{1i})}{(r_{0i})}$ are all constant.

That's a big assumption, but if you have some reason to believe that the individual RRs are not constant, maybe you should be trying to further stratify your analysis anyway.

For the OR, however, the situation is **hopeless**. The OR can be computed in THREE ways, since there are 3 algebraic operations involved (one summation and two divisions);

The usual (A/C) / (B/D) incidence-odds ratio corresponds to:

$$\frac{\left[\dfrac{\sum_{E=1}(r_{1i})}{\sum_{E=1}(1-r_{1i})}\right]}{\left[\dfrac{\sum_{E=0}(r_{0i})}{\sum_{E=0}(1-r_{0i})}\right]}$$

EXPOSED

UNEXPOSED

where $\Sigma_{E=1}$ and $\Sigma_{E=0}$ are summations over exposed (E=1) and unexposed (E=0), respectively.

If confounding is absent, this is equivalent to the counterfactual contrast of interest:

$$\frac{\left[\dfrac{\sum_{E=1}(r_{1i})}{\sum_{E=1}(1-r_{1i})}\right]}{\left[\dfrac{\sum_{E=1}(r_{0i})}{\sum_{E=1}(1-r_{0i})}\right]}$$

OBSERVED

COUNTERFACTUAL

(when the exposed group is the "target" population).

This is the **proportionate change in the incidence odds in the exposed that is due to exposure**.

It is NOT equivalent to the **proportionate change in the average odds in the exposed that is due to exposure**: $\left(\dfrac{mean\,\omega_{1i}}{mean\,\omega_{0i}}\right)$, nor is it equivalent to the average individual OR: $mean\left(\dfrac{\omega_{1i}}{\omega_{0i}}\right)$.

The three distinct constructions of the OR cannot be linked under any plausible assumption.

If the individual risk-odds ratios $\left(\frac{\omega_{1i}}{\omega_{0i}}\right)$ are constant (as assumed by a logistic model), then the second two formulations of the OR described above become equivalent, but still do not generally equal the incidence-odds ratio (A/C)/(B/D).

This is why Greenland (1987) concluded **"...the incidence-odds ratio lacks any simple interpretation in terms of exposure effect on average risk or odds, or average exposure effect on individual risk or odds."** and therefore that the OR is only useful to the extent that it approximates the RR.

Greenland S. Interpretation and choice of effect measures in epidemiologic analyses. *Am J Epidemiol* 1987;125(5):761-8.

Non-Collapsibility of the OR in an Analytic Setting

An Example:

Consider a study of 20 adult ischemic stroke victims in which the anticoagulation therapy rt-PA was administered within 2 hours of neurological symptoms for 10 subjects (X=1), and withheld for 10 subjects (X=0)

The outcome of death (Y=1) occurred for 10 subjects, and 10 survived (Y=0)

A potential covariate is pre-treatment blood pressure, which is dichotomized at

$\geq$ 185/110 mmHg (Z=1) vs $<$ 185/110 (Z=0)

The observed values are:

	Z = 1		Z = 0		TOTAL	
	X = 1	X = 0	X = 1	X = 0	X = 1	X = 0
Y = 1	4	3	2	1	6	4
Y = 0	1	2	3	4	4	6
TOTAL	5	5	5	5	10	10

The observed effect contrast measures are therefore:

	Z = 1		Z = 0		TOTAL	
	X = 1	X = 0	X = 1	X = 0	X = 1	X = 0
RISK	0.80	0.60	0.40	0.20	0.60	0.40
RISK DIFFERENCE	0.20		0.20		0.20	
RISK RATIO	1.33		2.00		1.50	
ODDS RATIO	2.67		2.67		2.25	

The OR and RR measures are not similar. Why not?

The outcome is common: P(Y=1) = 0.5

When P(Y=1) is large in any stratum of exposure (e.g., > 0.10), divergence between the OR and RR becomes substantial. When exposure affects average risk, the OR is farther from the null than the RR.

	Z = 1		Z = 0		TOTAL	
	X = 1	X = 0	X = 1	X = 0	X = 1	X = 0
RISK	0.80	0.60	0.40	0.20	0.60	0.40
RISK DIFFERENCE	0.20		0.20		0.20	
RISK RATIO	1.33		2.00		1.50	
ODDS RATIO	2.67		2.67		2.25	

Use the standardization formula for risk differences in RGL 2008 (Eq. 15-4, p. 266) to obtain the adjusted risk difference, standardized over covariate Z

If we use the total study population as the target:

$$RD_w = \frac{\sum_i w_i RD_i}{\sum_i w_i} = \frac{0.5(0.20)+0.5(0.20)}{0.5+0.5} = \frac{0.20}{1} = 0.20$$

Crude estimate = adjusted estimate, so causal effect estimated by the RD is not distorted by Z (blood pressure)

Using a collapsibility-based definition for detecting confounding (i.e., a change in estimate approach), we judge that no adjustment for pre-treatment blood pressure (Z) is necessary

Use the standardization formula for risk ratios in RGL 2008 (Eq. 15-5, p. 267) to obtain the adjusted risk ratio, standardized over covariate Z

If we use the total study population as the target:

$$RR_w = \frac{\sum_i w_i R_{0i} RR_i}{\sum_i w_i R_{0i}} = \frac{0.5(0.6)(1.33)+0.5(0.2)(2.00)}{0.5(0.6)+0.5(0.2)} = \frac{0.4+0.2}{0.4} = 1.50$$

Crude estimate = adjusted estimate, so causal effect estimated by the RR is not distorted by Z (blood pressure)

Using a collapsibility-based definition for detecting confounding (i.e., a change in estimate approach), we judge that no adjustment for pre-treatment blood pressure (Z) is necessary

Use the Mantel-Haenszel formula for uniform odds ratios in RGL 2008 (Eq. 15-23, p. 276) to obtain the adjusted odds ratio, pooled over covariate Z

$$OR_{MH} = \frac{\sum_i A_{1i}B_{0i}/N_i}{\sum_i A_{0i}B_{1i}/N_i} = \frac{[4(2)/10]+[2(4)/10]}{[1(3)/10]+[3(1)/10]} = \frac{1.6}{0.6} = 2.67$$

The crude and the adjusted estimates differ substantially (i.e., 2.25 $\neq$ 2.67). The change in estimate is roughly 17%

Using a collapsibility-based definition for detecting confounding (i.e., a change in estimate approach), we judge that **adjustment for pre-treatment blood pressure (Z) appears to be necessary**, since the covariate Z is not affected by exposure X

Based on the practical criteria traditionally employed for detecting confounding (i.e., a change-in-estimate approach), the decision in this example would be to adjust for covariate Z when using the OR as the effect measure

Note that in fact this covariate cannot be a causal confounder in the example because it is not associated with the exposure

The discrepancy arises because inequality between the crude and adjusted OR does not necessarily imply causal confounding if the OR does not approximate the RR

The odds ratio is the one of these three measures of effect that is **not collapsible**, meaning that the average of the stratum-specific values does not necessarily equal the crude value, even in the absence of confounding

Summary:

Absolute effect measures have advantages for comparison between groups, comparison across time, and causal inference

Absolute measures give the actual impact on individuals, and the inverse is the number needed to treat or harm

The OR overestimates the RR when the outcome is common, and because it is non-collapsible, it cannot be used to assess whether a covariate is a confounder

Ratio measures came to dominate because of statistical convenience, but modern software packages allow for estimation of absolute effect measures much more readily than in the past. There is often little justification now for ever reporting an OR

Some relevant citations:

Poole C. On the origin of risk relativism. *Epidemiology* 2010 Jan;21(1):3-9.

Langholz B. Case-control studies—odds ratio: Blame the retrospective model. *Epidemiology* 2010;21:10–12.

Hernán MA. The hazards of hazard ratios. *Epidemiology* 2010;21:13–15.

Greenland S. Interpretation and choice of effect measures in epidemiologic analyses. *American Journal of Epidemiology* 1987;125:761–8.

Schwartz LM, Woloshin S, Welch HG. Misunderstandings about the effects of race and sex on physicians' referrals for cardiac catheterization. *N Engl J Med* 1999;341:279–83.

Sackett DL, Deeks JJ, Altman DG. Down with odds ratios! *Evidence-Based Med* 1996; 1: 164–166.

Deeks JJ. When can odds ratios mislead? *BMJ* 1998; 317: 1155–1156.

Altman DG, Deeks JJ, Sackett DL. Odds ratios should be avoided when events are common *BMJ* 1998; 317: 1318.

Part II:

Simple models for generating absolute estimates in cohort and cross-sectional data (25 minutes)

Regression models for absolute effect estimates:

- linear probability model
- generalized linear model
- logistic regression or probit regression

Let's assume for now:

- simple random sampling from a target population
- binary outcome

Data Example:

Some Birth Certificate Data from 25 states in 2009
-Implemented the 2003 revision to the birth certificate
-Count dataset with frequency weights to run faster

```
table race [freq = count], c(n mager mean mager mean smoke mean parity mean ptb) f(%5.2f) row
---------------------------------------------------------------------------------------
race/ethnicity   |     N(mager)   mean(mager)   mean(smoke)  mean(parity)     mean(ptb)
-----------------+---------------------------------------------------------------------
        NH White |      1090800         28.10          0.15          0.58          0.10
        NH Black |      207,677         25.93          0.08          0.60          0.14
        Hispanic |      633,249         26.41          0.02          0.65          0.10
        NH AI/AN |       14,488         25.36          0.18          0.66          0.10
        NH Asian |      124,529         30.98          0.01          0.53          0.09
         NH NHPI |        4,706         27.39          0.07          0.66          0.11
NH Multiple Race |       29,904         26.29          0.16          0.54          0.10
-----------------+---------------------------------------------------------------------
           Total |      2105353         27.50          0.09          0.60          0.10
---------------------------------------------------------------------------------------

gen racex = race
replace racex = 4 if race > 3 & race < .
label define racex 1 "NH White"2 "NH Black" 3 "Hispanic" 4 "other"
label values racex racex
bysort racex: ci ptb  [freq = count]

  Race Group |        Obs       Mean       Std. Err.     [95% Conf. Interval]
-------------+-------------------------------------------------------------
    NH White |    1090800   0.095301    0.0002811     0.0947497, 0.0958517
    NH Black |     207677   0.142770    0.0007677     0.1412652, 0.1442744
    Hispanic |     633249   0.096483    0.0003710     0.0957562, 0.0972106
       Other |     173627   0.092728    0.0006961     0.0913632, 0.0940918
-------------+-------------------------------------------------------------
```

Tabular Risk Differences (easy):

```
. cs ptb smoke [freq =  count], by(racex) istandard rd

          racex |      RD      [95% Conf. Int]     Weight
-----------------+-------------------------------------
       NH White |   0.0235    0.0219, 0.0252     158579
       NH Black |   0.0337    0.0278, 0.0395      17478
       Hispanic |   0.0282    0.0225, 0.0340      12817
          other |   0.0318    0.0249, 0.0388       8866
-----------------+-------------------------------------
          Crude |   0.0235    0.0220, 0.0250
 I. Standardized |   0.0251    0.0236, 0.0266
```

But tabular approaches are limited:

- Can only adjust for 1-2 categorical confounders
- Difficult to handle continuous exposures/covariates
- Difficult to handle clustered data, other extensions

So we need to take a regression-based approach…

1) Linear Probability Model:

Advantages: very easy to fit
single uniform estimate
economists will love you

Disadvantages: possible to get impossible estimates
biostatisticians will hate you

Fit an OLS linear regression on the binary outcome variable:

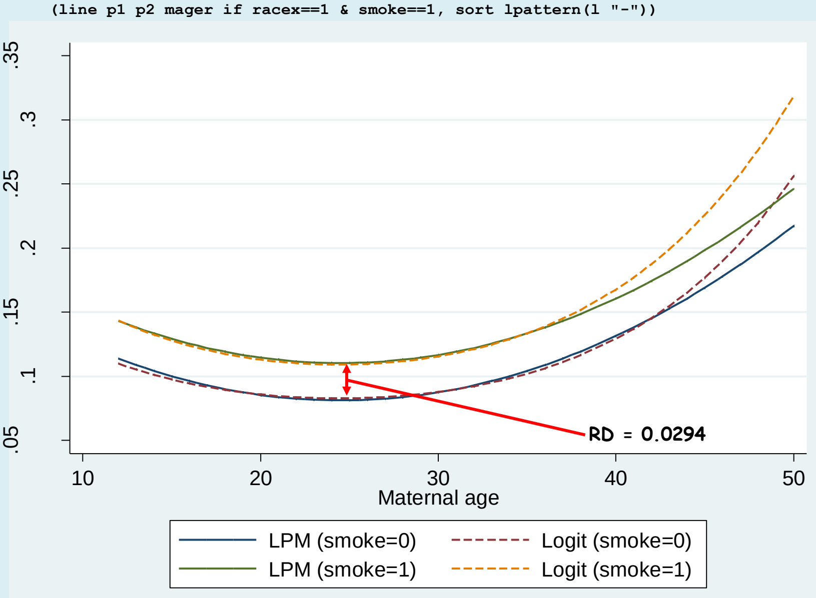
$$Pr(Y=1|X=x) = \beta_0 + \beta_1 X$$

Note: Homoskedasticity assumption cannot be met, since variance is a function of p. Therefore, use robust variance.

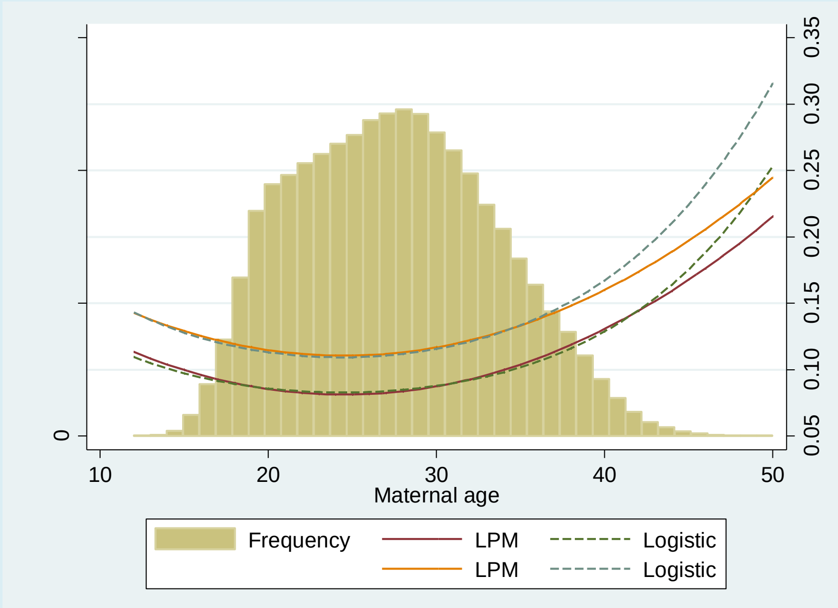
```
regress ptb smoke c.mager##c.mager i.racex [freq=count], vce(robust) cformat(%6.4f)

Linear regression                                      Number of obs = 2105353
                                                       F( 6,2105346) = 1290.18
                                                       Prob > F      =  0.0000
                                                       R-squared     =  0.0047
                                                       Root MSE      =  .29947

------------------------------------------------------------------------------
             |               Robust
         ptb |      Coef.   Std. Err.      t    P>|t|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
       smoke |     0.0294     0.0008    37.32   0.000      0.0278,   0.0309
       mager |    -0.0101     0.0003   -34.73   0.000     -0.0107,  -0.0095
             |
    c.mager#|
     c.mager |     0.0002     0.0000    39.92   0.000      0.0002,   0.0002
             |
       racex |
         2   |     0.0507     0.0008    61.47   0.000      0.0491,   0.0523
         3   |     0.0060     0.0005    12.43   0.000      0.0050,   0.0069
         4   |    -0.0025     0.0008    -3.37   0.001     -0.0040,  -0.0011
             |
       _cons |     0.2049     0.0040    51.03   0.000      0.1970,   0.2128
------------------------------------------------------------------------------
```

Adjusted RD for smoking =
0.0294 (95% CI: 0.0278, 0.0309)

```
predict p1
quietly logit ptb  smoke c.mager##c.mager i.racex [freq = count]
predict p2
twoway (line p1 p2 mager if racex==1 & smoke==0, sort lpattern(l "-") ylabel(0.05(0.05)0.35))
       (line p1 p2 mager if racex==1 & smoke==1, sort lpattern(l "-"))
```

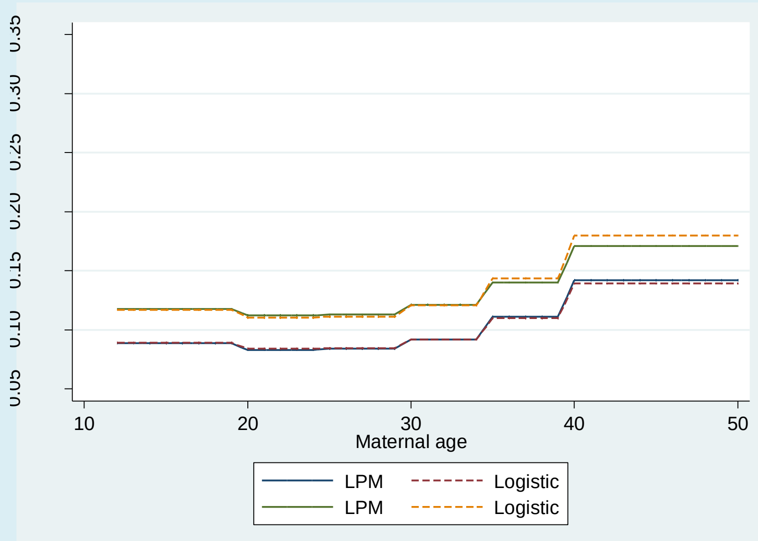


```
twoway (histogram mager [freq=count], bin(39) freq  yaxis(2))(line p1 p2 mager if racex==1 &
smoke==0, sort lpattern(l "-") ylabel(0.05(0.05)0.35) yaxis(1))(line p1 p2 mager if racex==1 &
smoke==1, sort lpattern(l "-") yaxis(1))
```




```
tab  magecat [freq=count]

age categories |      Freq.     Percent        Cum.
---------------+-----------------------------------
     <20 Years |    211,020       10.02       10.02
   20-24 Years |    512,234       24.33       34.35
   25-29 Years |    598,037       28.41       62.76
   30-34 Years |    486,153       23.09       85.85
   35-39 Years |    240,311       11.41       97.26
     40+ Years |     57,598        2.74      100.00
---------------+-----------------------------------
         Total |  2,105,353      100.00

regress ptb smoke i.magecat i.racex [freq=count], vce(robust) cformat(%6.4f)
----------------------------------------------------------------------------
         ptb |    Coef.   Robust SE    t     P>|t|      [95% Conf. Int]
-------------+--------------------------------------------------------------
       smoke |   0.0291     0.0008    36.95   0.000    0.0276,  0.0307
age cats  2  |  -0.0055     0.0008    -7.12   0.000   -0.0071, -0.0040
          3  |  -0.0046     0.0008    -5.97   0.000   -0.0061, -0.0031
          4  |   0.0033     0.0008     4.14   0.000    0.0018,  0.0049
          5  |   0.0225     0.0009    23.86   0.000    0.0207,  0.0244
          6  |   0.0534     0.0016    32.81   0.000    0.0503,  0.0566

regress ptb smoke c.mager##c.mager i.racex [freq=count], vce(robust) cformat(%6.4f)
----------------------------------------------------------------------------
       smoke |   0.0294     0.0008    37.32   0.000    0.0278,  0.0309
       mager |  -0.0101     0.0003   -34.73   0.000   -0.0107, -0.0095
  mager*mager|   0.0002     0.0000    39.92   0.000    0.0002,  0.0002
```

```
regress ptb smoke i.magecat i.racex [freq=count], vce(robust) cformat(%6.4f)
predict p1
quietly logit ptb smoke i.magecat i.racex [freq = count]
predict p2
twoway (line p1 p2 mager if racex==1 & smoke==0, sort lpattern(l "-")
   ylabel(0(0.002)0.012))(line p1 p2 mager if racex==1 & smoke==1, sort lpattern(l "-"))
```



2) Generalized Linear Model:

Advantages: single uniform estimate
biostatisticians will love you

Disadvantages: very difficult to fit
still possible to get impossible values

Fit a GLM with a binomial variance and an identity link

$$g[\Pr(Y=1|X=x)] = \beta_0 + \beta_1 X$$

Wacholder S.Binomial regression in GLIM: estimating risk ratios and risk differences. *Am J Epidemiol* 1986 Jan;123(1):174-84.

Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005 Aug 1;162(3):199-200.

```
glm ptb smoke c.mager##c.mager i.racex [freq=count], fam(b) lin(ident) cformat(%6.4f)
binreg ptb smoke c.mager##c.mager i.racex [freq=count], rd cformat(%6.4f)

Generalized linear models                          No. of obs      =   2105353
Optimization     : ML                              Residual df     =   2105346
                                                   Scale parameter =         1
Deviance         =  1361007.026                    (1/df) Deviance =  .6464529
Pearson          =  2105353.002                    (1/df) Pearson  =  1.000003

Variance function: V(u) = u*(1-u)                  [Bernoulli]
Link function    : g(u) = u                        [Identity]

Log likelihood   =  -680503.513
------------------------------------------------------------------------------
             |                 OIM
         ptb |     Coef.    Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       smoke |    0.0285      0.0008    36.77   0.000       0.0270,   0.0301
       mager |   -0.0101      0.0003   -36.23   0.000      -0.0107,  -0.0096
             |
     c.mager#|
     c.mager |    0.0002      0.0000    41.38   0.000       0.0002,   0.0002
             |
       racex |
         2   |    0.0502      0.0008    61.34   0.000       0.0486,   0.0518
         3   |    0.0055      0.0005    11.67   0.000       0.0046,   0.0065
         4   |   -0.0028      0.0007    -3.75   0.000      -0.0043,  -0.0013
             |
       _cons |    0.2065      0.0039    53.55   0.000       0.1989,   0.2140
------------------------------------------------------------------------------
Coefficients are the risk differences.
```

```
binreg neonatal unmar magecat##i.race, rd cformat(%6.4f)

Iteration 1:   deviance =  3001.645
Iteration 2:   deviance =  3001.386
Iteration 3:   deviance =  3001.381
Iteration 4:   deviance =  3001.381
Iteration 5:   deviance =  3001.381
Iteration 6:   deviance =  3001.381
Iteration 7:   deviance =  3001.381
Iteration 8:   deviance =  3001.381
Iteration 9:   deviance =  3001.381
Iteration 10:  deviance =  3001.381
Iteration 11:  deviance =  3001.381
Iteration 12:  deviance =  3001.381
Iteration 13:  deviance =  3001.381
Iteration 14:  deviance =  3001.381
Iteration 15:  deviance =  3001.381
Iteration 16:  deviance =  3001.381
Iteration 17:  deviance =  3001.381
Iteration 18:  deviance =  3001.381
Iteration 19:  deviance =  3001.381
Iteration 20:  deviance =  3001.381
Iteration 21:  deviance =  3001.381
Iteration 22:  deviance =  3001.381
Iteration 23:  deviance =  3001.381
Iteration 24:  deviance =   3001.38
Iteration 25:  deviance =   3001.38
Iteration 26:  deviance =   3001.38
Iteration 27:  deviance =   3001.38
Iteration 28:  deviance =   3001.38
Iteration 28:  deviance =   3001.38
Iteration 29:  deviance =   3001.38
Iteration 30:  deviance =   3001.38
Iteration 31:  deviance =   3001.38
Iteration 32:  deviance =   3001.38
Iteration 33:  deviance =   3001.38
Iteration 34:  deviance =   3001.38
Iteration 35:  deviance =   3001.38
Iteration 36:  deviance =   3001.38
Iteration 37:  deviance =   3001.38
Iteration 38:  deviance =   3001.38                      ad infinitum……
```

```
glm ptb smoke c.mager##c.mager i.racex [freq=count], fam(b) lin(log) cformat(%6.4f) eform
binreg ptb smoke c.mager##c.mager i.racex [freq=count], rr cformat(%6.4f)

Generalized linear models                          No. of obs      =   2105353
Optimization     : ML                              Residual df     =   2105346
                                                   Scale parameter =         1
Deviance         =  1360912.355                    (1/df) Deviance =  .6464079
Pearson          =  2105229.218                    (1/df) Pearson  =  .9999445

Variance function: V(u) = u*(1-u)                  [Bernoulli]
Link function    : g(u) = ln(u)                    [Log]

                                                   AIC             =  .6464124
Log likelihood   = -680456.1777                    BIC             = -2.93e+07
------------------------------------------------------------------------------
             |                 OIM
         ptb | Risk Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       smoke |    1.3130     0.0087    40.98   0.000       1.2960      1.3302
       mager |    0.9178     0.0022   -35.31   0.000       0.9135      0.9222
             |
    c.mager#|
     c.mager |    1.0018     0.0000    42.22   0.000       1.0017      1.0018
             |
       racex |
          2  |    1.5460     0.0096    70.28   0.000       1.5273      1.5649
          3  |    1.0630     0.0053    12.21   0.000       1.0526      1.0735
          4  |    0.9756     0.0079    -3.05   0.002       0.9602      0.9912
------------------------------------------------------------------------------
```

Adjusted RR for smoking =
1.31 (95% CI: 1.30, 1.33)

3) Logistic Regression or Probit Regression Model:

Advantages:
- always fits easily
- can never get impossible estimates
- epidemiologists will love you

Disadvantages:
- does not give a single uniform estimate
- choose between different formulations

Fit a standard logistic regression model:

$$\ln\left(\frac{\Pr(Y=1|X=x)}{(1\text{-}\Pr(Y=1|X=x))}\right)=\alpha+\beta_1 x$$

then just obtain and contrast the predicted probabilities:

$$\Pr(Y=1|X=x)=\left[\frac{e^{(\alpha+\beta_1 x)}}{1+e^{(\alpha+\beta_1 x)}}\right]$$

```
logit ptb smoke c.mager##c.mager i.racex [freq=count], cformat(%6.4f) nolog

Logistic regression                               Number of obs   =    2105353
                                                  LR chi2(6)      =    9089.04
                                                  Prob > chi2     =     0.0000
Log likelihood =  -680455.7                       Pseudo R2       =     0.0066
------------------------------------------------------------------------------
         ptb |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       smoke |     0.3065     0.0076    40.47   0.000       0.2916      0.3213
       mager |    -0.0984     0.0028   -35.35   0.000      -0.1039     -0.0930
             |
    c.mager#|
     c.mager |     0.0020     0.0000    41.91   0.000       0.0019      0.0021
             |
       racex |
          2  |     0.4954     0.0072    69.07   0.000       0.4814      0.5095
          3  |     0.0679     0.0056    12.23   0.000       0.0570      0.0788
          4  |    -0.0280     0.0090    -3.13   0.002      -0.0456     -0.0105
             |
       _cons |    -1.2047     0.0393   -30.63   0.000      -1.2818     -1.1276
------------------------------------------------------------------------------
```

Predicted probability of PTB for a 25 year old non-Hispanic white woman smoker:

$$\Pr(\text{PTB=1}|X=x)=\left[\frac{e^{-1.2047+0.3065-(25*0.0984)+(25^2*0.0020)}}{1+e^{-1.2047+0.3065-(25*0.0984)+(25^2*0.0020)}}\right]=0.1094$$

Many ways to generate these numbers in Stata:

1) use the postestimation –predict- command

```
predict p
tab p if mager == 25 & smoke ==1 & racex == 1

    Pr(ptb) |      Freq.     Percent
------------+-----------------------
   .1093692 |        515      100.00

tab p if mager == 25 & smoke == 0 & race == 1

    Pr(ptb) |      Freq.     Percent
------------+-----------------------
   .0828943 |        692      100.00
```

```
0.1093692 - 0.0828943 = 0.0264749
```

2) use the –display- command

```
disp invlogit(_b[_cons]+_b[smoke]+(25*_b[mager])+(25*25*_b[c.mager#c.mager]))

0.10936925

disp invlogit(_b[_cons]+_b[smoke]+(25*_b[mager])+(25*25*_b[c.mager#c.mager])) -
    invlogit(_b[_cons]+(25*_b[mager])+(25*25*_b[c.mager#c.mager]))

0.02647495
```

3) use the -nlcom- command

```
nlcom invlogit(_b[_cons]+_b[smoke]+(25*_b[mager])+(25*25*_b[c.mager#c.mager])) -
      invlogit(_b[_cons]+(25*_b[mager])+(25*25*_b[c.mager#c.mager]))
------------------------------------------------------------------------------
         ptb |      Coef.   Std. Err.      z     P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
   risk diff |   0.0265    0.00071     37.27    0.000      0.0251, 0.0279
------------------------------------------------------------------------------
```

The same command works just as easily for the RR:

```
nlcom invlogit(_b[_cons]+_b[smoke]+(25*_b[mager])+(25*25*_b[c.mager#c.mager])) /
      invlogit(_b[_cons]+(25*_b[mager])+(25*25*_b[c.mager#c.mager]))
------------------------------------------------------------------------------
         ptb |     Coef.    Std. Err.     z      P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
  risk ratio |  1.3194     0.00895    147.40    0.000     1.3018,    1.3369
------------------------------------------------------------------------------
```

But this is for a specific covariate pattern (in this case, NH-white women aged 25).

```
gen ind_rd =

invlogit(_b[_cons]+_b[smoke]+(mager*_b[mager])+(mager*mager*_b[c.mager#c.mager]))
- invlogit(_b[_cons]+(mager*_b[mager])+(mager*mager*_b[c.mager#c.mager]))

sum ind_rd [freq = count]

    Variable |       Obs      Mean     Std. Dev.    Min      Max
-------------+--------------------------------------------------
      ind_rd |   2105353    0.0287    0.00318    0.0265   0.0622
```

So the average individual RD = 0.0287

Compare to:

LPM: 0.0294

GLM: 0.0285

But we need confidence intervals...

Could bootstrap (somewhat slow with >2 million obs):

```
expand count
prog drop _all
program rd_code, rclass
version 11
quietly logit ptb smoke c.mager##c.mager i.racex
return scalar rd =
invlogit(_b[_cons]+_b[smoke]+(mager*_b[mager])+(mager*mager*_b[c.mager#c.mager])) -
 invlogit(_b[_cons]+(mager*_b[mager])+(mager*mager*_b[c.mager#c.mager]))
end

bootstrap effect=r(rd), reps(200) saving(ptb_rd, replace) nowarn: rd_code

----+--- 1 ---+--- 2 ---+--- 3 ---+--- 4 ---+--- 5
..................................................    50
..................................................   100
..................................................   150
..................................................   200

estat bootstrap, p
Bootstrap results                               Number of obs      =   2105353
                                                Replications       =       200
------------------------------------------------------------------------------
             |    Observed               Bootstrap
             |       Coef.       Bias    Std. Err.   [95% Conf. Interval]
-------------+----------------------------------------------------------------
      effect |    0.033667  -0.0049474   0.00326272    0.0259209  0.0383542 (P)
------------------------------------------------------------------------------
(P)    percentile confidence interval
```

But Stata has a handy utility that makes this easier:

```
quietly logit ptb smoke c.mager##c.mager i.racex [freq = count]
margins, dydx(smoke)
--------------------------------------------------------------------------
             |             Delta-method
             |     dy/dx   Std. Err.      z     P>|z|     [95% Conf. Int]
-------------+------------------------------------------------------------
       smoke |    0.0275   0.00068      40.43   0.000     0.0262, 0.0288
--------------------------------------------------------------------------
```

Average age-adjusted individual RD = 0.0275 (95% CI: 0.0262, 0.0288)

Comparison:

- average individual RD = 0.0287
- linear probability model = 0.0294
- generalized linear model = 0.0285
- logistic regression margins = 0.0275

Note that treating “smoke” as a factor variable gives a slightly different value:

```
quietly logit ptb i.smoke c.mager##c.mager i.racex [freq = count]
margins, dydx(smoke)
------------------------------------------------------------------------------
             |    dy/dx   Delta-method SE   z      P>|z|      [95% Conf. Int]
-------------+----------------------------------------------------------------
     1.smoke |    0.0303    0.00082      36.90    0.000      0.0287,  0.0319
------------------------------------------------------------------------------
```

Margins also works on sub-populations:

```
margins, dydx(smoke) over(racex)

Average marginal effects                          Number of obs  = 2105353
------------------------------------------------------------------------------
             |            Delta-method
             |      dy/dx   Std. Err.      z     P>|z|      [95% Conf. Int]
-------------+----------------------------------------------------------------
1.smoke      |
       racex |
          1  |     0.0287   0.00077    37.23    0.000     0.0272, 0.0302
          2  |     0.0409   0.00111    36.87    0.000     0.0387, 0.0430
          3  |     0.0300   0.00083    36.01    0.000     0.0284, 0.0316
          4  |     0.0287   0.00081    35.52    0.000     0.0271, 0.0303
------------------------------------------------------------------------------
Note: dy/dx for factor levels is the discrete change from the base level.
```

Average age-adjusted RD for NH Whites = 0.0287 (95% CI: 0.0272, 0.0302)

Average age-adjusted RD for NH Blacks = 0.0409 (95% CI: 0.0387, 0.0430)

Average age-adjusted RD for Hispanics = 0.0300 (95% CI: 0.0284, 0.0316)

Average age-adjusted RD for Others = 0.0287 (95% CI: 0.0271, 0.0303)

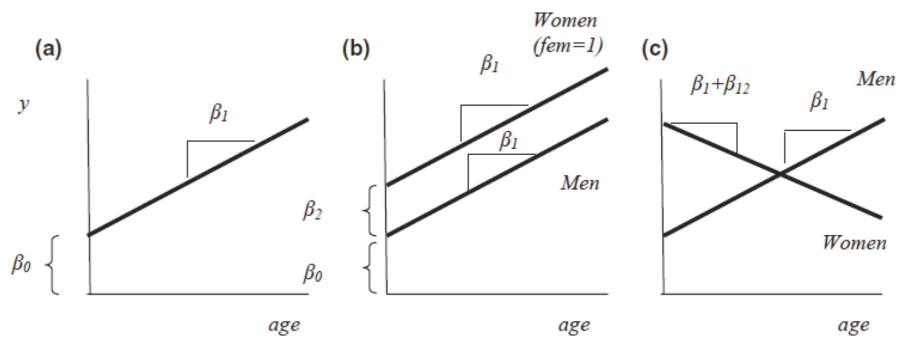
Test if NH Black RD is larger than the NH White RD:

```
margins smoke, at(race=(1 2)) post

Predictive margins                                Number of obs   =   2105353
Expression    : Pr(ptb), predict()
        1._at        : racex           =           1
        2._at        : racex           =           2
------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z     P>|z|   [95% Conf. Int]
-------------+----------------------------------------------------------------
   _at#smoke |
        1 0  |  0.0909954   0.000292   311.57   0.000    0.0904, 0.0916
        1 1  |  0.1196531   0.000740   161.74   0.000    0.1182, 0.1211
        2 0  |  0.1409752   0.000767   183.70   0.000    0.1395, 0.1425
        2 1  |  0.1821831   0.001390   131.04   0.000    0.1795, 0.1849
------------------------------------------------------------------------------

lincom (_b[2._at#1.smoke]-_b[2._at#0.smoke])-( _b[1._at#1.smoke]-_b[1._at#0.smoke])
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z     P>|z|      [95% Conf. Int]
-------------+----------------------------------------------------------------
         (1) |    0.01255    0.00039    32.16    0.000     0.0118, 0.0133
------------------------------------------------------------------------------

test (_b[2._at#1.smoke]-_b[2._at#0.smoke]) = ( _b[1._at#1.smoke]-_b[1._at#0.smoke])

          chi2(  1) = 1034.34       Prob > chi2 =     0.0000
```

This is a different model, however, than one which includes a race x treatment interaction explicitly:

```
logit ptb i.smoke##i.racex c.mager##c.mager [freq = count], cformat(%6.4f) nolog

Logistic regression                                 Number of obs    =    2105353
------------------------------------------------------------------------------
         ptb |      Coef.   Std. Err.       z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     1.smoke |     0.3040     0.0088    34.72    0.000       0.2869      0.3212
       racex |
          2  |     0.4980     0.0076    65.35    0.000       0.4830      0.5129
          3  |     0.0673     0.0057    11.83    0.000       0.0562      0.0785
          4  |    -0.0348     0.0093    -3.74    0.000      -0.0531     -0.0166
 smoke#racex |
        1 2  |    -0.0263     0.0228    -1.15    0.249      -0.0710      0.0184
        1 3  |     0.0131     0.0285     0.46    0.645      -0.0427      0.0690
        1 4  |     0.1021     0.0346     2.95    0.003       0.0343      0.1699
       mager |    -0.0982     0.0028   -35.26    0.000      -0.1037     -0.0928
     c.mager#|
     c.mager |     0.0020     0.0000    41.84    0.000       0.0019      0.0021
       _cons |    -1.2073     0.0394   -30.63    0.000      -1.2846     -1.1301
------------------------------------------------------------------------------

margins, dydx(smoke) at(race=(1 2))
------------------------------------------------------------------------------
             |          Delta-method
             |    dy/dx   Std. Err.       z     P>|z|      [95% Conf. Int]
-------------+----------------------------------------------------------------
smoke RD NHW |   0.0284   0.000887    32.03    0.000      0.02667, 0.03015
smoke RD NHB |   0.0371   0.003029    12.23    0.000      0.03111, 0.04299
------------------------------------------------------------------------------
```

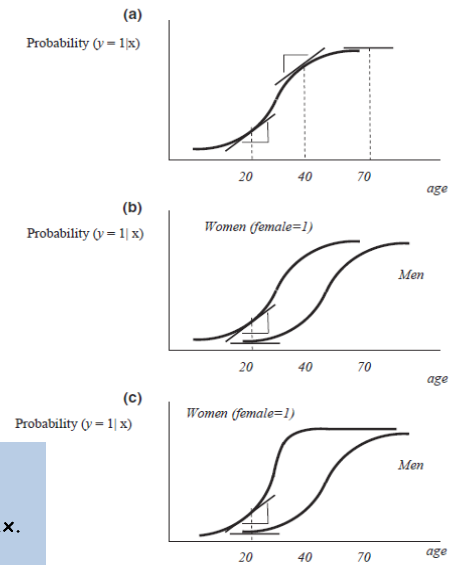
Figure 1: Interaction Terms in Linear Models



$$y = \beta_0 + \beta_1 age + \beta_2 female + u \quad (2)$$

Karaca-Mandic P, Norton EC, Dowd B. Interaction Terms in Nonlinear Models. Health Serv Res. 2011 Aug 30. doi: 10.1111/j.1475-6773.2011.01314.x. [Epub ahead of print]

Figure 2: (a) A Logit or Probit Model with a Single Continuous Explanatory Variable (*age*). (b) A Logit or Probit Model with Continuous (*age*) and Binary (*female*) Explanatory Variables. (c) A Logit or Probit Model with Continuous (*age*) and Binary (*female*) Explanatory Variables and Their Interaction



Karaca-Mandic P, Norton EC, Dowd B. Interaction Terms in Nonlinear Models. Health Serv Res. 2011 Aug 30. doi: 10.1111/j.1475-6773.2011.01314.x. [Epub ahead of print]

Use of the average marginal effect (AME) is most common in epidemiology:

Fleischer NL et al. Estimating the potential impacts of intervention from observational data: methods for estimating causal attributable risk in a cross-sectional analysis of depressive symptoms in Latin America. *J Epidemiol Community Health* 2010;64(1):16-21.

Ahern J et al. Estimating the effects of potential public health interventions on population disease burden: a step-by-step illustration of causal inference methods. *Am J Epidemiol* 2009;169(9):1140-7.

Snowden JM, et al. Implementation of G-computation on a simulated data set: demonstration of a causal inference technique. *Am J Epidemiol* 2011;173(7):731-8.

Localio AR et al. Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. *J Clin Epidemiol* 2007;60(9):874-82.

But a common approach in econometrics is to take the RD holding all covariates at their means:

```
quietly logit ptb i.smoke c.mager##c.mager i.racex [freq = count]
margins i.smoke, atmeans post

Adjusted predictions                              Number of obs    =    2105353
Model VCE     : OIM

Expression    : Pr(ptb), predict()
at            : 0.smoke          =    .9060775 (mean)
                1.smoke          =    .0939225 (mean)
                mager            =    27.50222 (mean)
                1.racex          =    .5181079 (mean)
                2.racex          =    .0986424 (mean)
                3.racex          =    .3007804 (mean)
                4.racex          =    .0824693 (mean)
------------------------------------------------------------------------
             |         Delta-method
             |   Margin   Std. Err.      z     P>|z|     [95% Conf. Int]
-------------+----------------------------------------------------------
       smoke |
           0 |  0.08966  0.0002572   348.59  0.000     0.08916, 0.09016
           1 |  0.11802  0.0007689   153.50  0.000     0.11651, 0.11952
-------------------------------------------------------------------------

. lincom _b[1.smoke] - _b[0.smoke]
-------------------------------------------------------------------------
             |    Coef.   Std. Err.      z    P>|z|      [95% Conf. Int]
-------------+-----------------------------------------------------------
         (1) |  0.02836  0.00077     36.72   0.000      0.02684, 0.02987
-------------------------------------------------------------------------
```

Adjusted RD for the average woman in the dataset = 0.0284 (95% CI: 0.0268, 0.0299)

Or the same thing in a single command line:

```
quietly logit ptb i.smoke c.mager##c.mager i.racex [freq = count]
margins, dydx(smoke) atmeans

Conditional marginal effects                  Number of obs    =    2105353
------------------------------------------------------------------------------
             |             Delta-method
             |     dy/dx    Std. Err.      z     P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
     1.smoke |   0.02836   0.0007724   36.72   0.000    0.02684, 0.02987
------------------------------------------------------------------------------

quietly logit ptb i.smoke##i.racex c.mager##c.mager [freq = count]
margins, dydx(smoke) atmeans over(racex)

Conditional marginal effects                      Number of obs = 2105353
-----------------------------------------------------------------------------
             |             Delta-method
             |     dy/dx    Std. Err.      z      P>|z|    [95% Conf. Int]
-------------+---------------------------------------------------------------
1.smoke      |
       racex |
           1 |    0.0268   0.0008417    31.87    0.000    0.0252, 0.0285
           2 |    0.0348   0.0028505    12.19    0.000    0.0292, 0.0403
           3 |    0.0292   0.0028129    10.39    0.000    0.0237, 0.0347
           4 |    0.0372   0.0035261    10.54    0.000    0.0302, 0.0441
-----------------------------------------------------------------------------
Note: dy/dx for factor levels is the discrete change from the base level.
```

And of course you can get the marginal RR at the mean values of the covariates, too:

```
quietly logit ptb i.smoke c.mager##c.mager i.racex [freq = count]
margins i.smoke, atmeans post

Adjusted predictions                              Number of obs    =    2105353
Expression    : Pr(ptb), predict()
at            : 0.smoke         =    .9060775 (mean)
                1.smoke         =    .0939225 (mean)
                mager           =    27.50222 (mean)
                1.racex         =    .5181079 (mean)
                2.racex         =    .0986424 (mean)
                3.racex         =    .3007804 (mean)
                4.racex         =    .0824693 (mean)

--------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Int]
-------------+------------------------------------------------------------
       smoke |
          0  |    0.08966   0.0002572   348.59   0.000     0.08916, 0.09016
          1  |    0.11802   0.0007689   153.50   0.000     0.11651, 0.11952
--------------------------------------------------------------------------

nlcom _b[1.smoke] / _b[0.smoke]
--------------------------------------------------------------------------
             |     Coef.    Std. Err.      z    P>|z|     [95% Conf. Int]
-------------+------------------------------------------------------------
       _nl_1 |    1.3163   0.0088229   149.19   0.000     1.2990, 1.3336
--------------------------------------------------------------------------
```

Adjusted RR for the average woman in the dataset = 1.32
(95% CI: 1.30,1.33)

Compare to other popular RR estimation approaches:

Modified Poisson regression:

```
poisson ptb i.smoke c.mager##c.mager i.racex [freq = count], nolog irr vce(robust)

Poisson regression                        Number of obs    =    2105353
----------------------------------------------------------------------
             |               Robust
         ptb |      IRR    Std. Err.     z    P>|z|    [95% Conf. Int]
-------------+--------------------------------------------------------
     1.smoke |    1.3127   0.0087566   40.78  0.000    1.2956, 1.3299
----------------------------------------------------------------------
```

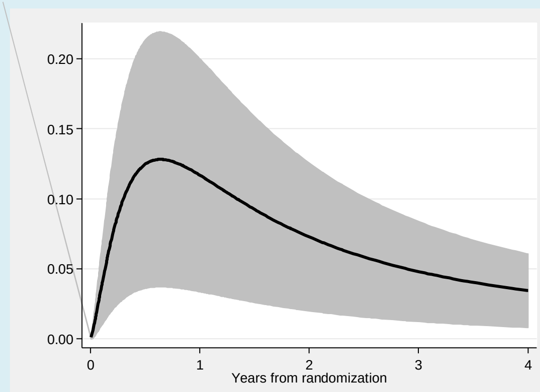
GLM (binomial regression)

```
binreg ptb i.smoke c.mager##c.mager i.racex [freq = count], nolog rr

Generalized linear models                       No. of obs  =  2105353
Variance function: V(u) = u*(1-u)                  [Bernoulli]
Link function    : g(u) = ln(u)                    [Log]
-----------------------------------------------------------------------
         ptb | Risk Ratio   EIM SE      z    P>|z|     [95% Conf. Int]
-------------+---------------------------------------------------------
     1.smoke |    1.3130   0.0087192   41.01  0.000     1.2960, 1.3302
-----------------------------------------------------------------------
```

Q: What about time to event data?
A: Plot differences between (adjusted) survival curves

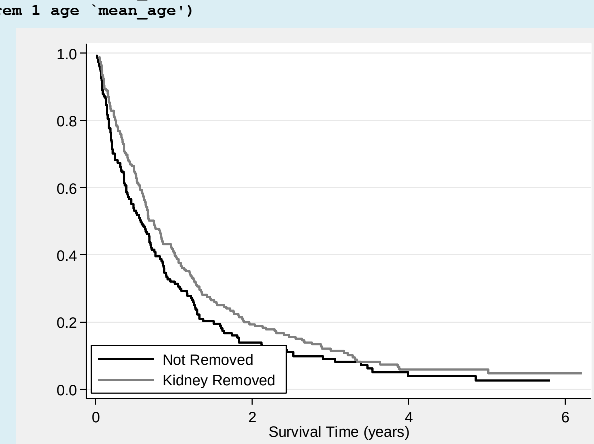
Quick demonstration (Royston & Lambert, pp. 274)

```
use kidney_ca
stset survtime, failure(cens) scale(365.24) exit(time 4 * 365.24)
quietly stpm2 trt, df(2) scale(odds)
predict sd, sdiff(trt 1) ci
twoway (rarea sd_lci sd_uci _t, sort pstyle(ci) yaxis(1)) ///
  (line sd _t, sort lpattern(solid) clwidth(thick) yaxis(1)), ///
   ylab(,angle(horizontal) format(%3.2f)) ///
   ytitle("Risk Difference", axis(1)) xtitle("Years from randomization") ///
   legend(off)
```

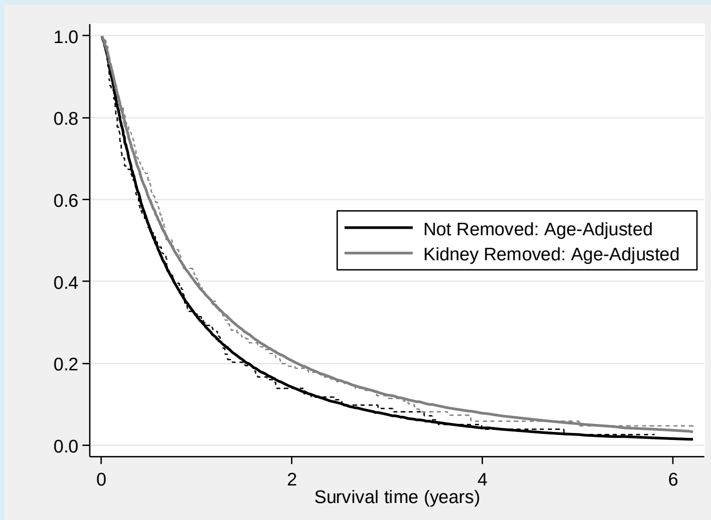


Royston P, Lambert PC. Flexible Parametric Survival Analysis Using Stata. Stata Press, 2011

```
sts gen s_km = s, by(rem)
twoway (line s_km _t if rem == 0, sort lpattern(solid) lwidth(medthick) lcolor(black) ///
connect(stairstep)) (line s_km _t if rem  == 1, sort lpattern(solid) lwidth(medthick) ///
lcolor(gs8) connect(stairstep)), legend(order(1 "Not Removed" 2 "Kidney Removed") ring(0) ///
pos(7) col(1) size(*1)) scheme(sj) xtitle("Survival Time (years)",) ///
ytitle("Survival function",) ylabel(0(0.2)1.0,angle(h) format(%3.1f)) name(km1, replace)
stpm2 rem, df(3) scale(hazard)  eform nolog
table rem, c(n age mean age sd age) format(%9.2f)
stpm2 rem age, df(3) scale(hazard)  eform nolog
summ age, meanonly
local mean_age = `r(mean)'
predict s0_meancov, survival at(rem 0 age `mean_age')
predict s1_meancov, survival at(rem 1 age `mean_age')
```



```
twoway (line s_km _t if rem==0, sort lpattern(shortdash) lwidth(thin) lcolor(black) ///
connect(stairstep))(line s_km _t if rem == 1, sort lpattern(shortdash) lwidth(thin) ///
lcolor(gs8) connect(stairstep))(line s0_meancov _t, sort lpattern(solid) lwidth(medthick) ///
lcolor(black))(line s1_meancov _t, sort lpattern(solid) lwidth(medthick) lcolor(gs8)), ///
legend(order(3 "Not Removed: Age-Adjusted" 4 "Kidney Removed: Age-Adjusted") ///
ring(0) pos(3) col(1) size(*1)) scheme(sj) xtitle("Survival time (years)",) ///
ytitle("Survival function",) ylabel(0(0.2)1.0,angle(h) format(%3.1f)) ///
name(km_meancov, replace)
```



Conclusions:

1) You don't ever have to report another OR again, (unless you have a cumulative case-control study with an unknown sampling fraction)

2) The popularity of the OR was based largely on statistical convenience, but modern software has largely overcome those early limitations.

3) Take a pledge, join a support group, and kick the habit.

Part 3: SAS Code for non-survey data
+
Complex Survey Example in SAS and STATA
+
Examples from the Literature

SAS Code – simple data example

Same Birth Certificate Data

- **linear probability model with robust SEs**
  - PROC SURVEYREG (easy way to get robust SEs even though it's non-survey)
  - PROC GENMOD (with repeated id statement)
  - Neither option works with count data
- **generalized linear model**
  - PROC GENMOD
- **logistic regression**
  - PROC RLOGIST (SUDAAN)

Linear Probability Model (OLS)

```
proc surveyreg order=formatted;
class racex;
model ptb = unmar mager mager*mager racex /clparm solution;
run;
```

N.B. Count data had to be expanded since analytic weights, not frequency, are allowed

Regression Analysis for Dependent Variable ptb

Estimated Regression Coefficients

Parameter	Estimate	Standard Error	t Value	Pr > |t|	95% Confidence Interval	
Intercept	0.2048949	0.00401532	51.03	<.0001	0.1970250	0.2127648
smoke	0.0293874	0.00078743	37.32	<.0001	0.0278441	0.0309308
mager	-0.0101005	0.00029081	-34.73	<.0001	-0.0106705	-0.0095306
mager*mager	0.0002061	0.00000516	39.92	<.0001	0.0001960	0.0002163
racex a Non-Hispanic Black	0.0507213	0.00082510	61.47	<.0001	0.0491042	0.0523385
racex b Hispanic	0.0059730	0.00048047	12.43	<.0001	0.0050313	0.0069147
racex c Other	-0.0025365	0.00075348	-3.37	0.0008	-0.0040133	-0.0010597
racex d Non-Hispanic White	0.0000000	0.00000000	.	.	0.0000000	0.0000000

Adjusted RD for marital status = 0.029 (95% CI 0.028 , 0.031)
Same results as in Stata

Generalized Linear Models (GLM)

Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005 Aug 1;162(3):199-200.

American Journal of EPIDEMIOLOGY
Vol. 162, No. 3
Printed in U.S.A.
DOI: 10.1093/aje/kwi188
August 1, 2005

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INVITED EDITORIAL NOTE

Easy SAS Calculations for Risk or Prevalence Ratios and Differences

We would like to make the readership aware that risk or prevalence ratios and differences, when they are the parameter of interest, can be directly calculated by using SAS software (SAS Institute, Inc., Cary, North Carolina). There is no longer any good justification for fitting logistic regression models and estimating odds ratios when the odds ratio is not a good approximation of the risk or prevalence ratio. Instead, SAS PROC GENMOD's log-binomial regression (1) capability can be used for estimation and inference about the parameter of interest. Here is an example of the code required to analyze the breast cancer survival data discussed by Greenland (2):

```
proc genmod descending;
model death=receptor stage2 stage3/dist=bin link=log;
estimate 'RR receptor low vs. high' receptor 1/exp;
estimate 'RR stage2 vs stage1' stage2 1/exp;
estimate 'RR stage 3 vs stage1' stage3 1/exp;
```

Binomial Model
Risk Difference, Identity Link

```
proc genmod descending;
class racex/order=formatted;
model ptb = smoke mager mager*mager racex / dist=bin
   link=identity;
weight count;
format racex racex.;
run;
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square
Intercept		1	0.2065	0.0039	0.1989	0.2140	2867.35
smoke		1	0.0285	0.0008	0.0270	0.0301	1352.38
mager		1	-0.0101	0.0003	-0.0107	-0.0096	1312.29
mager*mager		1	0.0002	0.0000	0.0002	0.0002	1712.02
racex	a Non-Hispanic Black	1	0.0502	0.0008	0.0486	0.0518	3762.13
racex	b Hispanic	1	0.0055	0.0005	0.0046	0.0065	136.25
racex	c Other	1	-0.0028	0.0007	-0.0043	-0.0013	14.07
racex	d Non-Hispanic White	0	0.0000	0.0000	0.0000	0.0000	.
Scale		0	1.0000	0.0000	1.0000	1.0000	

Adjusted RD for smoking =
0.0285 (95% CI 0.0270 , 0.0301)

Binomial Model
Risk Ratio, Log Link

```
proc genmod descending;
class racex/order=formatted;
model ptb = smoke mager mager*mager racex / dist=bin link=log;
estimate 'RR smoke' smoke 1;
weight count;
format racex racex.;
run;
```

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square
Intercept		1	-1.4446	0.0345	-1.5123	-1.3770	1751.13
smoke		1	0.2723	0.0066	0.2593	0.2853	1679.61
mager		1	-0.0858	0.0024	-0.0905	-0.0810	1246.74
mager*mager		1	0.0018	0.0000	0.0017	0.0018	1782.43
racex	a Non-Hispanic Black	1	0.4357	0.0062	0.4235	0.4478	4938.65
racex	b Hispanic	1	0.0611	0.0050	0.0513	0.0709	149.06
racex	c Other	1	-0.0247	0.0081	-0.0406	-0.0089	9.32
racex	d Non-Hispanic White	0	0.0000	0.0000	0.0000	0.0000	.
Scale		0	1.0000	0.0000	1.0000	1.0000	

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits	
RR smoke	1.3130	1.2960	1.3302	0.2723	0.0066	0.05	0.2593	0.2853

Adjusted RR for smoking =
1.31 (95% CI 1.30 , 1.33)

If Binomial fails to converge, try starting with a negative intercept

```
model ptb = smoke mager mager*mager racex / dist=bin link=log
   intercept=-4;
```

Otherwise, try Modified Poisson—less efficient but more likely to converge

generate a unique id number in data step
id=_n_;

N.B. does not work with frequency weights since every observation requires unique id

Out of memory with 2 million observations so select a random sample

```
proc surveyselect data=ahs.sper_example method=srs
   samprate=20 out=sample_20; run;
```

Modified Poisson
Risk Difference, Identity Link

```
proc genmod;
class id racex/order=formatted;
model ptb = smoke mager mager*mager racex / dist=poi link=id;
repeated subject=id / type=ind;
format racex racex.;
run;
```

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.2134	0.0088	0.1961	0.2307	24.19	<.0001
smoke		0.0280	0.0017	0.0246	0.0315	16.14	<.0001
mager		-0.0106	0.0006	-0.0119	-0.0094	-16.70	<.0001
mager*mager		0.0002	0.0000	0.0002	0.0002	19.00	<.0001
racex	a Non-Hispanic Black	0.0498	0.0018	0.0462	0.0534	27.07	<.0001
racex	b Hispanic	0.0057	0.0011	0.0036	0.0078	5.31	<.0001
racex	c Other	-0.0037	0.0017	-0.0069	-0.0005	-2.23	0.0256
racex	d Non-Hispanic White	0.0000	0.0000	0.0000	0.0000	.	.

SE for smoking doubled compared to Stata Poisson with full sample (0.0017 v. 0.0008)

Modified Poisson
Risk Ratio, Log Link

```
proc genmod;
class id racex/order=formatted;
model ptb = smoke mager mager*mager racex / dist=poi link=log;
estimate 'RR smoke' smoke 1 ;
repeated subject=id / type=ind;
format racex racex.;
run;
```

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		-1.3989	0.0778	-1.5513	-1.2465	-17.99	<.0001
smoke		0.2724	0.0149	0.2432	0.3017	18.25	<.0001
mager		-0.0893	0.0055	-0.1000	-0.0786	-16.38	<.0001
mager*mager		0.0018	0.0001	0.0016	0.0020	19.54	<.0001
racex	a Non-Hispanic Black	0.4357	0.0140	0.4083	0.4630	31.22	<.0001
racex	b Hispanic	0.0619	0.0112	0.0399	0.0839	5.52	<.0001
racex	c Other	-0.0342	0.0182	-0.0698	0.0014	-1.88	0.0600
racex	d Non-Hispanic White	0.0000	0.0000	0.0000	0.0000	.	.

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square
RR smoke	1.3132	1.2753	1.3522	0.2724	0.0149	0.05	0.2432	0.3017	332.93

SE for smoking doubled compared to Stata Poisson with full sample (0.015 v. 0.007)

Additive Interaction

```
proc genmod data=sample_20;
class id smoke racex/param=ref ref=first;
model ptb = smoke mager mager*mager racex smoke*racex/ dist=poi link=id;
estimate 'smoking among NH Black' smoke 1 smoke*racex 1 0 0;
repeated subject=id / type=ind;
format racex racex.;
run;
```

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.2144	0.0088	0.1971	0.2317	24.28	<.0001
smoke	1	0.0255	0.0019	0.0217	0.0292	13.31	<.0001
mager		-0.0107	0.0006	-0.0119	-0.0094	-16.77	<.0001
mager*mager		0.0002	0.0000	0.0002	0.0002	19.06	<.0001
racex	NH Black	0.0483	0.0019	0.0445	0.0520	25.27	<.0001
racex	Hispanic	0.0053	0.0011	0.0032	0.0074	4.87	<.0001
racex	Other	-0.0045	0.0017	-0.0078	-0.0012	-2.67	0.0075
smoke*racex	NH Black	0.0193	0.0071	0.0055	0.0332	2.73	0.0063
smoke*racex	Hispanic	0.0072	0.0068	-0.0062	0.0206	1.05	0.2926
smoke*racex	Other	0.0154	0.0082	-0.0005	0.0314	1.89	0.0583

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha
smoking among NH Black	0.0448	0.0315	0.0582	0.0448	0.0068	0.05

Effect of smoking greater among Black than White women

Multiplicative Interaction

```
proc genmod data=sample_20;
class id smoke racex/param=ref ref=first;
model ptb = smoke mager mager*mager racex smoke*racex/ dist=poi link=log;
estimate 'smoking among White' smoke 1;
estimate 'smoking among NH Black' smoke 1 smoke*racex 1 0 0;
repeated subject=id / type=ind;
format racex racex.;
Run;
```

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

Parameter			Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept			-1.3949	0.0780	-1.5477	-1.2421	-17.89	<.0001
smoke	1		0.2586	0.0175	0.2243	0.2929	14.78	<.0001
mager			-0.0894	0.0055	-0.1001	-0.0787	-16.38	<.0001
mager*mager			0.0018	0.0001	0.0016	0.0020	19.54	<.0001
racex	2		0.4314	0.0149	0.4021	0.4607	28.90	<.0001
racex	3		0.0587	0.0115	0.0361	0.0813	5.10	<.0001
racex	4		-0.0445	0.0189	-0.0816	-0.0074	-2.35	0.0188
smoke*racex	1	2	0.0313	0.0422	-0.0515	0.1140	0.74	0.4589
smoke*racex	1	3	0.0409	0.0552	-0.0672	0.1490	0.74	0.4580
smoke*racex	1	4	0.1329	0.0671	0.0014	0.2643	1.98	0.0476

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha
smoking among White	1.2951	1.2514	1.3403	0.2586	0.0175	0.05
smoking among NH Black	1.3362	1.2393	1.4408	0.2899	0.0384	0.05

Additive but not multiplicative interaction

Logistic Model

- May be possible to get CIs with NLMIXED but complicated, bootstrapping also an option
- SUDAAN may be better option -- simple random sample design without weights (frequency weights not allowed)

```
PROC RLOGIST design=srs data=ahs.sper_example;
class smoke racex /dir=descending;
model ptb = smoke mager mager_2 racex;
predmarg smoke /adjrr;
pred_eff smoke=(1 -1)/name="RD:smoke";
rformat racex racex.;
SETENV    decwidth=4;
run;
```

```
Variance Estimation Method: Taylor Series (SRS)
SE Method: Robust (Binder, 1983)
Working Correlations: Independent
Link Function: Logit
Response variable PTB: PTB
by: Independent Variables and Effects.
----------------------------------------------------------
Variables and                     Lower 95%    Upper 95%
  Effects              Odds Ratio   Limit OR     Limit OR
----------------------------------------------------------
SMOKE                  1.3586       1.3385       1.3790
  -------------------------------------------------------------------
-------------------------------------------------------------------------------------
Predicted Marginal     Predicted                 Lower 95%    Upper 95%
  #1                   Marginal            SE    Limit        Limit          T:Marg=0
-------------------------------------------------------------------------------------
SMOKE
  1                        0.1277       0.0008       0.1262       0.1293     161.2347
  0                        0.0974       0.0002       0.0970       0.0978     453.5252
-------------------------------------------------------------------------------------------
Contrasted Predicted   PREDMARG
  Marginal #1          Contrast            SE       T-Stat    P-value
----------------------------------------------------------------------
RD:smoke                   0.0303       0.0008      36.7540     0.0000
----------------------------------------------------------------------
Predicted Marginal     PREDMARG             Lower      Upper
  Risk Ratio #1        Risk                 95%        95%
                       Ratio           SE   Limit      Limit
----------------------------------------------------------------
SMOKE
  1 vs. 0                1.3111     0.0087     1.2942     1.3282
----------------------------------------------------------------
```

Same point estimates as in STATA but robust SEs

PTB is not very common so OR is not greatly inflated but RR is more interpretable

Complex Survey Example

- 2007 National Survey of Children's Health
  - Design: Children sampled within State-level strata, weights to account for unequal probability of selection, non-response, and population totals
  - Outcome: Breastfed to 6 months among subpopulation of children 6 months to 5 years
  - Covariates: poverty (multiply imputed), race/ethnicity
- Direct models, logistic margins
- Interpretation of OR, RR, and RD

Common Outcome

```
PROC CROSSTAB data = example design=wr;
nest State idnumr;
supopn FLG_06_MNTH=0 and ageyr_child<=5;
WEIGHT  NSCHWT;
class breastfed duration_6;
TABLE breastfed duration_6;
PRINT  nsum wsum rowper serow lowrow uprow /style=nchs nsumfmt=f10.0 wsumfmt=f10.0;
Run;
```

Variance Estimation Method: Taylor Series (WR)
For Subpopulation: FLG_06_MNTH = 0 AND AGEYR_CHILD <= 5
by: Breastfed for 6 months.

Breastfed for 6 months	Sample Size	Weighted Size	Row Percent	SE Row Percent	Lower 95% Limit ROWPER	Upper 95% Limit ROWPER
Total	25036	22306393	100.00	0.00	.	.
0	13374	12268495	55.00	0.80	53.43	56.56
1	11662	10037898	45.00	0.80	43.44	46.57

Prevalence of 45%, we will see inflated ORs

Linear Probability Model (OLS)

```
PROC REGRESS DATA=mimp1 design=wr mi_count=5;
nest State idnumr;
subpopn FLG_06_MNTH=0 and ageyr_child<=5;
WEIGHT  NSCHWT;
subgroup povl hisprace;
levels 4 5;
reflevel povl=1 hisprace=2;
rformat povl povl. ;
rformat hisprace hisprace.;
model duration_6 = povl hisprace;
run;
```

Variance Estimation Method: Taylor Series (WR) Using Multiply Imputed Data
SE Method: Robust (Binder, 1983)
Working Correlations: Independent
Link Function: Identity

Independent Variables and Effects	Beta Coeff.	SE Beta	Lower 95% Limit Beta	Upper 95% Limit Beta	T-Test B=0
Intercept	0.3547	0.0220	0.3115	0.3979	16.1069
HH Federal Poverty Level					
< 100%	0.0000	0.0000	.	.	.
100-199%	0.0455	0.0288	-0.0110	0.1021	1.5823
200-399%	0.1055	0.0246	0.0572	0.1537	4.2868
400+%	0.1773	0.0256	0.1271	0.2274	6.9386
Race/Ethnicity					
Hispanic	0.0823	0.0250	0.0333	0.1313	3.2918
NH white	0.0000	0.0000	.	.	.
NH black	-0.1136	0.0223	-0.1573	-0.0700	-5.1011
NH multi	0.0049	0.0403	-0.0741	0.0838	0.1208
nh other	0.0370	0.0417	-0.0447	0.1187	0.8877

Constant RD regardless of covariate pattern

- Adjusting for race/ethnicity, children at 200-299%FPL have a 10.6% point increased probability of having been breastfed and children at 400%+FPL have a 17.7% point increased probability of having been breastfed to 6 months compared to those <100%FPL
- Adjusting for income, Hispanic children have 8.2% point increased probability of having been breastfed and non-Hispanic Black children have 11.4% point decreased probability of having been breastfed to 6 months compared to non-Hispanic White children
- Could calculate RR by hand but no CIs
  - For income 400%+FPL v. <100%FPL among White children is (0.355+0.177)/.355= 1.50
  - OR is (0.532/0.468)/(0.355/0.645) = 2.07

Generalized Linear Model (GLM

Poisson with log link may be only SUDAAN option, so RRs only

```
PROC LOGLINK DATA=mimp1 design=wr
   mi_count=5;
nest State idnumr;
subpopn FLG_06_MNTH=0 and
   ageyr_child<=5;
WEIGHT  NSCHWT;
subgroup povl hisprace;
levels 4 5;
reflevel povl=1 hisprace=2;
rformat povl povl. ;
rformat hisprace hisprace.;
model duration_6 = povl hisprace;
run;
```

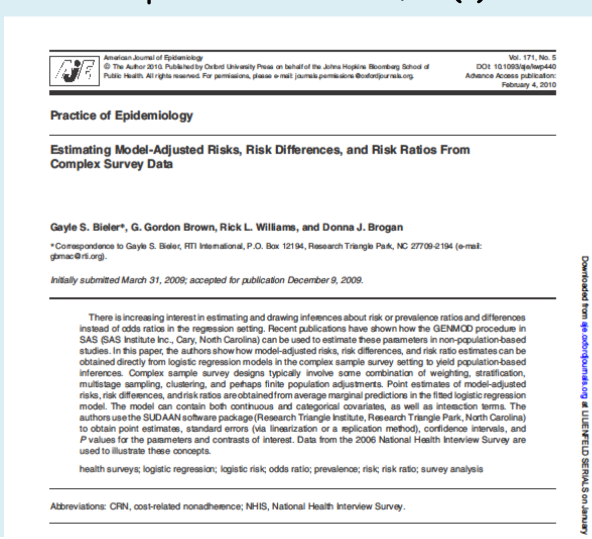
Independent Variables and Effects	Incidence Density Ratio	Lower 95% Limit IDR	Upper 95% Limit IDR
Intercept	0.36	0.32	0.40
HH Federal Poverty Level			
< 100%	1.00	.	.
100-199%	1.13	0.97	1.30
200-399%	1.29	1.14	1.46
400+%	1.49	1.32	1.69
Race/Ethnicity			
Hispanic	1.20	1.09	1.33
NH white	1.00	.	.
NH black	0.72	0.63	0.83
NH multi	1.01	0.85	1.21
nh other	1.08	0.92	1.27

Logistic Model

```
PROC RLOGIST DATA=mimp1 design=wr mi_count=5;
nest State idnumr;
subpopn FLG_06_MNTH=0 and ageyr_child<=5;
WEIGHT  NSCHWT;
subgroup povl hisprace;
levels 4 5;
reflevel povl=1 hisprace=2;
rformat povl povl. ;
rformat hisprace hisprace.;
model duration_6 = povl hisprace ;
predmarg povl(1)/adjrr;
predmarg hisprace(2)/adjrr;
pred_eff povl=(-1 1 0 0)/name="RD: 100-199%FPL v. <100% FPL";
pred_eff povl=(-1 0 1 0)/name="RD: 200-399%FPL v. <100% FPL";
pred_eff povl=(-1 0 0 1)/name="RD: 400%+ FPL v. <100% FPL";
pred_eff hisprace=(0 -1 1 0 0)/name="RD: NH Black v. NH White";
pred_eff hisprace=(1 -1 0 0 0)/name="RD: Hispanic v. NH White";
run;
```

SAS/SUDAAN

Bieler GS, Brown GG, Williams RL, Brogan DJ. Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. Am J Epidemiol. 2010 Mar 1;171(5):618-23.



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Practice of Epidemiology

Estimating Model-Adjusted Risks, Risk Differences, and Risk Ratios From Complex Survey Data

Gayle S. Bieler*, G. Gordon Brown, Rick L. Williams, and Donna J. Brogan

*Correspondence to Gayle S. Bieler, RTI International, P.O. Box 12194, Research Triangle Park, NC 27709-2194 (e-mail: gbmac@rti.org).

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There is increasing interest in estimating and drawing inferences about risk or prevalence ratios and differences instead of odds ratios in the regression setting. Recent publications have shown how the GENMOD procedure in SAS (SAS Institute Inc., Cary, North Carolina) can be used to estimate these parameters in non-population-based studies. In this paper, the authors show how model-adjusted risks, risk differences, and risk ratio estimates can be obtained directly from logistic regression models in the complex sample survey setting to yield population-based inferences. Complex sample survey designs typically involve some combination of weighting, stratification, multistage sampling, clustering, and perhaps finite population adjustments. Point estimates of model-adjusted risks, risk differences, and risk ratios are obtained from average marginal predictions in the fitted logistic regression model. The model can contain both continuous and categorical covariates, as well as interaction terms. The authors use the SUDAAN software package (Research Triangle Institute, Research Triangle Park, North Carolina) to obtain point estimates, standard errors (via linearization or a replication method), confidence intervals, and *P* values for the parameters and contrasts of interest. Data from the 2006 National Health Interview Survey are used to illustrate these concepts.

health surveys; logistic regression; logistic risk; odds ratio; prevalence; risk; risk ratio; survey analysis

Abbreviations: CRN, cost-related nonadherence; NHIS, National Health Interview Survey.

OR versus RR: Poverty

Independent Variables and Effects	Odds Ratio	Lower 95% Limit OR	Upper 95% Limit OR
Intercept	0.55	0.45	0.66
HH Federal Poverty Level			
< 100%	1.00	.	.
100-199%	1.22	0.96	1.55
200-399%	1.56	1.27	1.92
400+%	2.09	1.68	2.59

Predicted Marginal Risk Ratio #1	PREDMARG Risk Ratio	SE	Lower 95% Limit	Upper 95% Limit
HH Federal Poverty Level				
100-199% vs. <100%	1.13	0.09	0.97	1.31
200-399% vs. <100%	1.30	0.08	1.14	1.47
400+% vs. < 100%	1.49	0.09	1.32	1.69

Excess risk estimate is doubled for OR versus RR (~100% v. 50% for 400%+ Poverty)

OR versus RR: Race/Ethnicity

Independent Variables and Effects	Odds Ratio	Lower 95% Limit OR	Upper 95% Limit OR
Race/Ethnicity			
Hispanic	1.41	1.15	1.72
NH white	1.00	.	.
NH black	0.60	0.49	0.74
NH multi	1.02	0.74	1.41
nh other	1.16	0.83	1.62

Predicted Marginal Risk Ratio #2	PREDMARG Risk Ratio	SE	Lower 95% Limit	Upper 95% Limit
Race/Ethnicity				
Hispanic vs. NH white	1.19	0.06	1.08	1.31
NH black vs. NH white	0.74	0.05	0.65	0.84
NH multi vs. NH white	1.01	0.09	0.85	1.21
nh other vs. NH white	1.08	0.09	0.91	1.28

- SUDAAN 10 glitch: incorrect CIs for the RRs is when using multiply imputed data

- This will be corrected in SUDAAN 11 due out in August but you could use a single imputation for now; absolute risk differences are not affected

Risk Difference: Poverty

Predicted Marginal #1	Predicted Marginal	SE	Lower 95% Limit	Upper 95% Limit	T:Marg=0
HH Federal Poverty Level					
< 100%	0.36	0.02	0.32	0.40	17.99
100-199%	0.41	0.02	0.37	0.44	21.75
200-399%	0.47	0.01	0.44	0.49	33.78
400+%	0.54	0.01	0.51	0.57	36.10

Contrasted Predicted Marginal #2	PREDMARG Contrast	SE	T-Stat	P-value
RD: 200-399%FPL v. <100% FPL	0.11	0.02	4.31	0.0000
RD: 400%+ FPL v. <100% FPL	0.18	0.03	6.95	0.0000

Risk Difference: Race/Ethnicity

Predicted Marginal #2	Predicted Marginal	SE	Lower 95% Limit	Upper 95% Limit	T:Marg=0
Race/Ethnicity					
Hispanic	0.53	0.02	0.48	0.57	23.15
NH white	0.44	0.01	0.43	0.46	48.23
NH black	0.33	0.02	0.29	0.37	15.88
NH multi	0.45	0.04	0.37	0.53	11.48
nh other	0.48	0.04	0.40	0.56	11.84

Contrasted Predicted Marginal #5	PREDMARG Contrast	SE	T-Stat	P-value
RD: Hispanic v. NH White	0.08	0.02	3.34	0.0008
RD: NH Black v. NH White	-0.12	0.02	-5.11	0.0000

Advantage of Absolute Scale

- Can calculate actual numbers affected, excess cases attributable to a factor
  - Risk Difference x Number with factor = excess cases
  - Excess cases / Total cases = PAF
- Weighted N for children <100% FPL is 5.1 million
  - If children <100%FPL had same probability of being breastfed to 6 months as children 400%+, 0.18*5.1 = 0.9 million more children would have been breastfed to 6 months

STATA: Linear Probability Model

mi estimate: svy, subpop(subpop): regress duration_6 i.poverty ib2.hisprace

```
Multiple-imputation estimates                   Imputations       =          5
Survey: Linear regression                       Number of obs     =      90918

Number of strata   =        51                  Population size   =   73059497
Number of PSUs     =     90918                  Subpop. no. of obs =     24649
                                                Subpop. size      =   21867946
                                                Average RVI       =     0.0176
                                                Complete DF       =      90867
DF adjustment:   Small sample                   DF:     min       =     414.75
                                                        avg       =   40647.63
                                                        max       =   90855.21
Model F test:       Equal FMI                   F(   7,34040.5)   =      17.52
Within VCE type:   Linearized                   Prob > F          =     0.0000

------------------------------------------------------------------------------
  duration_6 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          2  |   .0455281   .0287728     1.58   0.114    -.0110306    .1020869
          3  |   .1054584   .0246006     4.29   0.000     .0571867    .1537301
          4  |   .1772861   .0255505     6.94   0.000     .1271252    .2274469
             |
    hisprace |
          1  |   .0822721   .0249932     3.29   0.001     .0332856    .1312586
          3  |  -.1136189   .0222733    -5.10   0.000    -.1572745   -.0699633
          4  |   .0048644   .0402772     0.12   0.904    -.0740784    .0838073
          5  |   .0369926   .0416748     0.89   0.375    -.0446896    .1186748
             |
       _cons |   .3547015   .0220216    16.11   0.000      .311463      .39794
------------------------------------------------------------------------------
```

STATA: Generalized Linear Model

mi estimate: svy, subpop(subpop): glm duration_6 i.poverty ib2.hisprace, family(bin) link(identity)

```
Multiple-imputation estimates                   Imputations       =          5
Survey: Generalized linear models               Number of obs     =      90918

Number of strata   =        51                  Population size   =   73059497
Number of PSUs     =     90918                  Subpop. no. of obs =     24649
                                                Subpop. size      =   21867946
                                                Average RVI       =     0.0164
                                                Complete DF       =      90867
DF adjustment:   Small sample                   DF:     min       =     460.63
                                                        avg       =   39901.41
Within VCE type:   Linearized                           max       =   90858.25

------------------------------------------------------------------------------
  duration_6 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          2  |   .0500759    .028643     1.75   0.081    -.0062113     .106363
          3  |   .1097926   .0247385     4.44   0.000     .0612576    .1583276
          4  |   .1813349   .0257437     7.04   0.000     .1308028    .2318669
             |
    hisprace |
          1  |   .0841305   .0244195     3.45   0.001     .0362684    .1319926
          3  |   -.113322   .0227859    -4.97   0.000    -.1579823   -.0686616
          4  |   .0029855   .0422457     0.07   0.944    -.0798157    .0857867
          5  |   .0388531    .040316     0.96   0.335     -.040166    .1178721
             |
       _cons |   .3499693   .0225387    15.53   0.000     .3057258    .3942128
------------------------------------------------------------------------------
```

STATA: Generalized Linear Model

mi estimate, saving (miest): svy, subpop(subpop): glm duration_6 i.poverty ib2.hisprace, family(bin) link(log)

mi estimate (rr: exp(_b[4.poverty])) using miest

```
------------------------------------------------------------------------------
  duration_6 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          2  |   .0983997   .0771079     1.28   0.203    -.0531998    .2499993
          3  |   .2241662   .0644546     3.48   0.001     .0976604     .350672
          4  |   .3660076   .0643298     5.69   0.000     .2396933    .4923219
             |
    hisprace |
          1  |   .1468517   .0474189     3.10   0.002     .0539109    .2397925
          3  |  -.3280586    .068963    -4.76   0.000    -.4632257   -.1928916
          4  |   .0280806   .0902574     0.31   0.756     -.148823    .2049842
          5  |   .0575744   .0814475     0.71   0.480    -.1020618    .2172107
             |
       _cons |  -.9995963   .0588938   -16.97   0.000    -1.115239    -.883954
------------------------------------------------------------------------------
Transformations
           rr: exp(_b[4.poverty])

------------------------------------------------------------------------------
  duration_6 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
          rr |    1.44212   .0927782    15.54   0.000     1.259949    1.624291
------------------------------------------------------------------------------
```

STATA: Logistic Model

Margins command can't be used with multiple imputation so select a single imputation

mi extract 1

svy, subpop(subpop): logistic duration_6 i.poverty ib2.hisprace

```
Survey: Logistic regression

Number of strata   =        51                  Number of obs      =     90918
Number of PSUs     =     90918                  Population size    =  73059497
                                                Subpop. no. of obs =     24649
                                                Subpop. size       =  21867946
                                                Design df          =     90867
                                                F(   7,  90861)    =     15.26
                                                Prob > F           =    0.0000

------------------------------------------------------------------------------
             |             Linearized
  duration_6 | Odds Ratio   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          2  |    1.19058   .1394594     1.49   0.136     .9463489    1.497842
          3  |   1.550998   .1584379     4.30   0.000     1.269574    1.894805
          4  |   2.056368   .2159416     6.87   0.000      1.67384    2.526316
             |
    hisprace |
          1  |   1.406887   .1442115     3.33   0.001     1.150818    1.719935
          3  |   .6032238   .0620274    -4.92   0.000     .4931184    .7379138
          4  |   1.022625   .1693499     0.14   0.893     .7391843    1.414751
          5  |   1.162023   .1975928     0.88   0.377     .8326699    1.621649
------------------------------------------------------------------------------
```

STATA Logistic: Risk Difference

- Use margins with the subpop since analyzing a subset of total sample (age<=5)
- Use vce(unconditional) to adjust SEs for survey design

svy, subpop(subpop): logistic duration_6 i.poverty ib2.hisprace
margins, subpop(subpop) dydx(*) vce(unconditional)

```
Average marginal effects                        Number of obs      =     90918
                                                Subpop. no. of obs =     24649

Expression   : Pr(duration_6), predict()
dy/dx w.r.t. : 2.poverty 3.poverty 4.poverty 1.hisprace 3.hisprace 4.hisprace
5.hisprace

------------------------------------------------------------------------------
             |            Linearized
             |      dy/dx   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          2  |   .0406776   .0272489     1.49   0.135      -.01273    .0940852
          3  |   .1047195   .0238716     4.39   0.000     .0579314    .1515076
          4  |   .1741176   .0245858     7.08   0.000     .1259297    .2223055
             |
    hisprace |
          1  |   .0835699   .0249702     3.35   0.001     .0346286    .1325113
          3  |  -.1171199   .0227721    -5.14   0.000    -.1617529   -.0724869
          4  |   .0054339    .040261     0.13   0.893    -.0734773    .0843452
          5  |   .0366576   .0416772     0.88   0.379    -.0450293    .1183445
------------------------------------------------------------------------------
Note: dy/dx for factor levels is the discrete change from the base level.
```

STATA Logistic: Relative Risk

svy, subpop(subpop): logistic duration_6 i.poverty ib2.hisprace
margins poverty, subpop(subpop) vce(unconditional) post

```
Predictive margins                              Number of obs      =     90918
                                                Subpop. no. of obs =     24649

Expression   : Pr(duration_6), predict()

------------------------------------------------------------------------------
             |            Linearized
             |     Margin   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     poverty |
          1  |   .3630598   .0191659    18.94   0.000     .3254949    .4006248
          2  |   .4037374   .0182501    22.12   0.000     .3679674    .4395075
          3  |   .4677794    .013761    33.99   0.000      .440808    .4947508
          4  |   .5371775   .0148679    36.13   0.000     .5080364    .5663185
------------------------------------------------------------------------------

 nlcom _b[4.poverty] / _b[1.poverty]

       _nl_1:  _b[4.poverty] / _b[1.poverty]

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _nl_1 |   1.479584   .0892086    16.59   0.000     1.304736    1.654432
------------------------------------------------------------------------------
```

Why both absolute and relative measures matter

- Absolute measures quantify actual risks and number affected
  - Necessary to evaluate/interpret the meaning of a given RR
- Relative measures allow standardized comparisons across groups, time periods, indicators (Jay disagrees)
- Lack of correspondence in some cases creates controversy of which is "better" but they provide complementary information
- If you only report one though, report the RD

Accurate Media Reporting

- Starts with researchers presenting appropriate statistics and understanding their own data
- Bad example – Schulman et al, NEJM 1999
- Good example – Chen et al, JAMA 2011

Disparities in Cardiac Catheterization

Table 1. Rate of Referral for Cardiac Catheterization, Odds of Referral, Odds Ratio, and Risk Ratio According to Sex and Race.*

Patients	Mean Referral Rate	Odds of Referral	Odds Ratio (95% CI)	Risk Ratio (95% CI)
	%			
Four strata				
White men†	90.6	9.6 to 1	1.0	
Black men	90.6	9.6 to 1	1.0 (0.5–2.1)	
White women	90.6	9.6 to 1	1.0 (0.5–2.1)	
Black women	78.8	3.7 to 1	0.4 (0.2–0.7)	0.87 (0.80–0.95)
Aggregate data				
White†	90.6	9.6 to 1	1.0	
Black	84.7	5.5 to 1	0.6 (0.4–0.9)	0.93 (0.89–0.99)
Men†	90.6	9.6 to 1	1.0	
Women	84.7	5.5 to 1	0.6 (0.4–0.9)	0.93 (0.89–0.99)
Overall	87.7	7.1 to 1		

- Odds Ratios were interpreted as Risk Ratios (large discrepancy due to common outcome)
- Focusing on absolute differences could have avoided this
- Universal effects of race and sex were purported when the only difference was for Black women
  - No effect of sex among Whites
  - No effect of race among Men
- Wide mischaracterization of results in the media

Alcohol Use and Breast Cancer

Table 2. Alcohol Consumption and Risk of Invasive Breast Cancer by Alcohol Intake

	Baseline Intake, 1980			Current Updated Intake[b]			Cumulative Intake[c]			
Alcohol Intake, g/d[a]	Cases, No.	Incidence Rate[d]	RR (95% CI)[e]	Cases, No.	Incidence Rate[d]	RR (95% CI)[e]	Cases, No.	Incidence Rate[d]	RR (95% CI)[e]	PAR
0	1776	312	1 [Reference]	2475	323	1 [Reference]	1669	281	1 [Reference]	
0.1-4.9	2016	331	1.07 (1.00-1.14)	1930	314	1.04 (0.98-1.11)	3143	309	1.06 (0.99-1.12)	2
5-9.9	723	363	1.15 (1.06-1.26)	692	334	1.11 (1.01-1.20)	1063	333	1.15 (1.06-1.24)	2
10-19.9	1020	370	1.15 (1.06-1.24)	863	340	1.11 (1.03-1.21)	1091	351	1.22 (1.13-1.32)	3
20-29.9	246	412	1.28 (1.12-1.47)	208	370	1.21 (1.05-1.40)	362	356	1.20 (1.07-1.35)	1
≥30	413	476	1.50 (1.34-1.67)	350	403	1.34 (1.19-1.50)	362	413	1.51 (1.35-1.70)	2
RR per 10-g increase			1.09 (1.07-1.11)			1.07 (1.05-1.10)			1.10 (1.07-1.12)	
P for trend	6194	344	<.001	6518	328	<.001	7690	316	<.001	10

Abbreviations: PAR, percent attributable risk; RR, relative risk.
[a] For example, a 4-ounce glass of wine contains 11 g of alcohol. The number of glasses of wine per week corresponding to the alcohol categories are 1-3 glasses/wk for 0.1-4.9 g/d, 3-6 glasses/wk for 5-9.9 g/d, 6-13 glasses/wk for 10-19.9 g/d, 13-19 glasses/wk for 20-29.9 g/d, and ≥19 glasses/wk for ≥30 g/d.
[b] For current intake, person-time for women missing alcohol intake during a specific questionnaire cycle was excluded, resulting in fewer cases for the analysis of current intake compared with that for cumulative use.
[c] Cumulative intake calculated from baseline (1980) forward.
[d] Per 100 000 person-years.
[e] Controlled for age, questionnaire year, ages at menarche and menopause, family history of breast cancer in first-degree relative, benign breast disease, body mass index, parity and age at first full-term birth, hormone therapy use, total duration of breastfeeding (months), and cigarette smoking.

- Appropriately interpreted as a 50% increase in breast cancer risk comparing 0 daily intake to 2+ drinks/day, translating to a 1.3% increase in the incidence of breast cancer over 10 years
- “while the increased risk found in this study is real, it is quite small. Women will need to weigh this slight increase in breast cancer risk with the beneficial effects alcohol is known to have on heart heath, said Dr. Wendy Chen, of Brigham and Women's Hospital in Boston. Any woman's decision will likely factor in her risk of either disease, Chen said.” MSNBC

Pediatric & Perinatal Examples

Maternity Leave & Breastfeeding

TABLE 5 Adjusted Analysis: The Effect of Total Maternity Leave Length, Paid Maternity Leave Length, and Time of Return to Work on Breastfeeding Initiation Among Women Who Worked in the 12 Months Before Delivery (N = 6150)

Characteristics	Model 1[a] (n = 6100)		Model 2[b] (n = 6100)		Model 3[c] (n = 5950)	
	OR (95% CI)	RR (95% CI)	OR (95% CI)	RR (95% CI)	OR (95% CI)	RR (95% CI)
Total maternity leave in weeks						
1–6 (reference)	1.00	1.00	1.00	1.00	1.00	1.00
7–12	1.50 (1.16–1.94)	1.13 (1.05–1.20)	1.20 (0.89–1.61)	1.06 (0.96–1.15)	1.16 (0.85–1.60)	1.05 (0.94–1.15)
≥13	1.58 (1.20–2.08)	1.15 (1.06–1.22)	1.31 (0.99–1.72)	1.09 (1.00–1.17)	1.28 (0.95–1.73)	1.08 (0.98–1.17)
Did not take maternity leave	1.11 (0.88–1.40)	1.04 (0.95–1.11)	1.39 (1.04–1.86)	1.11 (1.01–1.19)	1.26 (0.92–1.72)	1.08 (0.97–1.17)
Paid maternity leave in weeks						
0 (reference)	1.00	1.00	1.00	1.00	1.00	1.00
1–6	1.18 (0.91–1.55)	1.05 (0.97–1.13)	0.83 (0.62–1.11)	0.94 (0.83–1.03)	0.82 (0.61–1.11)	0.93 (0.83–1.03)
≥7	1.47 (1.11–1.94)	1.12 (1.03–1.19)	0.89 (0.65–1.21)	0.96 (0.85–1.06)	0.88 (0.64–1.21)	0.96 (0.84–1.06)
Did not take maternity leave	1.00 (0.80–1.26)	1.00 (0.92–1.07)	1.12 (0.86–1.47)	1.04 (0.95–1.12)	1.03 (0.77–1.38)	1.01 (0.91–1.10)
Time of return to work in weeks						
1–6 (reference)	1.00	1.00	1.00	1.00	1.00	1.00
7–12	1.38 (1.05–1.82)	1.11 (1.02–1.20)	1.18 (0.86–1.61)	1.05 (0.94–1.16)	1.15 (0.83–1.61)	1.05 (0.93–1.16)
≥13	1.37 (0.98–1.91)	1.11 (0.99–1.21)	1.32 (0.93–1.89)	1.10 (0.97–1.21)	1.33 (0.94–1.88)	1.10 (0.98–1.21)
Not yet returned to work[d]	1.48 (1.12–1.97)	1.14 (1.04–1.22)	1.67 (1.24–2.24)	1.17 (1.08–1.26)	1.46 (1.08–1.97)	1.13 (1.03–1.22)

Weight variable is W1R0. The corrected RR has been obtained using this formula: RR = OR/([1 − P_0)] + [P_0 * OR]), where P_0 is the incidence of the outcome (breastfeeding initiation) in the nonexposed group (reference group). Each main independent variable was assessed separately in each of the models without the other main independent variables.

[a] Unadjusted model.

[b] Adjusted for maternal characteristics only (race/ethnicity, age, marital status, education, 185% FPL, country of birth, and smoking status).

[c] Adjusted for all control variables (race/ethnicity, age, marital status, education, income status, country of birth, smoking status, birth weight, mode of delivery, birth order, health care professional advice about breastfeeding, separation from child for ≥1 week, child care arrangements, WIC participation within the last 12 months, region of residence, and urbanicity).

[d] Not yet returned to work by the 9-month interview.

SOURCE: US Department of Education, National Center for Education Statistics, ECLS-B Longitudinal 9 Month-Preschool Restricted Use data file.

Ogbuanu C, Glover S, Probst J, Liu J, Hussey J. The effect of maternity leave length and time of return to work on breastfeeding. Pediatrics. 2011 Jun;127(6):e1414-27.

Formula for Converting OR to RR

- $RR = \dfrac{OR}{1 - P_0 + P_0 * OR}$
- Popularized by an article in JAMA
- Confidence intervals are not correct
- Doesn't provide RDs
- Only proposed when software wasn't available to readily convert odds to marginal probabilities

Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998 Nov 18;280(19):1690-1.

Effect of age on decisions about the numbers of embryos to transfer in assisted conception: a prospective study

Debbie A Lawlor, Scott M Nelson

Summary

Background Elective single-embryo transfer has been proposed as a strategy to reduce the risk of multiple birth and adverse pregnancy outcomes after in-vitro fertilisation (IVF). Whether this approach should be restricted to young women is unclear.

Methods In a prospective study of UK Human Fertilisation and Embryology Authority data, we investigated whether perinatal livebirth outcomes varied by the number of embryos transferred in relation to maternal age. We compared rates of livebirth, multiple births, low birthweight (<2·5 kg), preterm birth (<37 weeks), and severe preterm birth (<33 weeks) in women younger than 40 years and those aged 40 years or older. We used logistic and binomial regression methods to assess, respectively, relative risk and absolute differences in risk.

Findings We assessed 124 148 IVF cycles overall, which yielded 33 514 livebirths. The odds ratios of livebirth were higher in women aged 40 years or older than in those younger than 40 years when two embryos were transferred compared with one embryo (3·12, 95% CI 2·56–3·77 *vs* 2·33, 2·20–2·46; p=0·0006 for interaction), but the absolute difference in risk of livebirth was smaller (0·090, 0·080–0·099 for women ≥40 years *vs* 0·156, 0·148–0·163 for those <40 years; p<0·0001). The odds ratios and absolute risk differences for multiple birth, preterm birth, and low birthweight were all smaller in older than in younger women (analyses were done in 32 732 cycles in which a livebirth had resulted and data on gestational age and birthweight were complete). Livebirth rates did not increase with transfer of three embryos, but the risk of adverse perinatal outcomes did increase.

Interpretation Transfer of three or more embryos at any age should be avoided. The decision to transfer one or two embryos should be based on prognostic indicators, such as age.

Lawlor DA, Nelson SM. Effect of age on decisions about the numbers of embryos to transfer in assisted conception: a prospective study. Lancet. 2012 Feb 11;379(9815):521-7.

	Transfer of two *vs* one embryo		Transfer of three *vs* one embryo	
	Adjusted* risk difference (95%CI)	Adjusted* NNT (95%CI)†	Adjusted* risk difference (95%CI)	Adjusted* NNT (95%CI)†
Livebirth (n=124 148)				
<40 years (n=104 873)	0·156 (0·148 to 0·163)	6 (6 to 7)	0·120 (0·100 to 0·140)	8 (7 to 10)
≥40 years (n=19 275)	0·090 (0·080 to 0·099)	11 (10 to 12)	0·091 (0·080 to 0·100)	11 (10 to 13)
p for interaction‡	..	..	..	<0·0001
Multiple birth (n=32 732)				
<40 years (n=30 551)	0·247 (0·239 to 0·255)	4 (4 to 4)	0·239 (0·201 to 0·277)	4 (4 to 5)
≥40 years (n=2181)	0·108 (0·083 to 0·133)	9 (8 to 13)	0·145 (0·113 to 0·177)	7 (6 to 9)
p for interaction‡	..	..	..	<0·0001
Preterm birth (n=32 732)				
<40 years (n=30 551)	0·099 (0·090 to 0·111)	10 (9 to 12)	0·089 (0·052 to 0·124)	11 (8 to 19)
≥40 years (n=2181)	0·031 (−0·028 to 0·091)	29 (11 to −38)	0·036 (−0·026 to 0·098)	28 (10 to −38)
p for interaction‡	..	..	..	0·03
Severe preterm birth (n=32 732)				
<40 years (n=30 551)	0·029 (0·021 to 0·037)	34 (27 to 48)	0·033 (0·012 to 0·054)	30 (19 to 83)
≥40 years (n=2181)	0·003 (−0·030 to 0·034)	333 (29 to 33)	0·020 (−0·014 to 0·055)	50 (18 to 71)
p for interaction‡	..	..	..	0·21
Low birthweight (n=32 732)				
<40 years (n=30 551)	0·151 (0·136 to 0·167)	7 (6 to 7)	0·142 (0·136 to 0·167)	7 (6 to 7)
≥40 years (n=2181)	0·060 (0·001 to 0·119)	17 (8 to 1000)	0·083 (0·021 to 0·145)	12 (7 to 48)
p for interaction‡	..	..	..	0·007

NNT=number needed to treat. *Adjusted for year of treatment and prediction score for successful livebirth. †NNT to result in one extra outcome; CI that include negative values suggest no strong statistical evidence that treating with more than one embryo transfer will increase the risk of the outcome. ‡Likelihood ratio test for the null hypothesis that the association of number of embryos transferred (three-category variable) with each outcome differs by maternal age (two-category variable).

Table 4: **Adjusted absolute association of number of embryos transferred with any livebirth and adverse perinatal outcomes stratified by women's age**

Perinatal Disparities

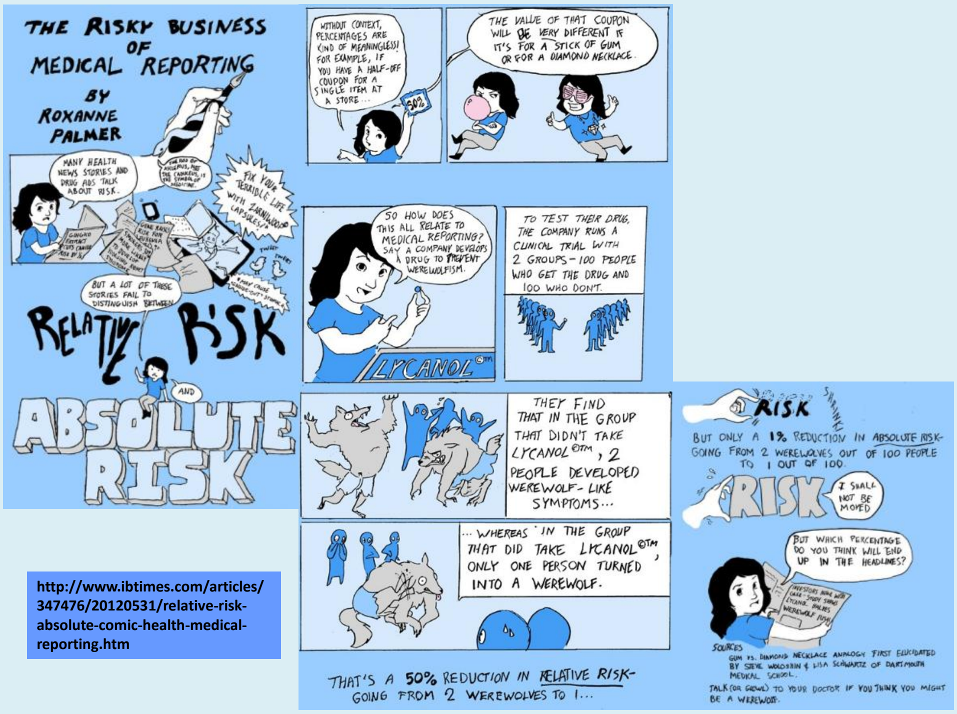
Table 3. Unadjusted and Adjusted Black-White Disparities in Preterm Birth, Wake and Durham Counties, North Carolina, 1999–2001

Birth Outcome and Race	Model 1 (Unadjusted)			Model 2[a] (Adjusted)					Model 3[b] (Adjusted Neighborhood Hybrid Fixed Effects)					Model 4[c] (Adjusted Random Effects With Control for Neighborhood SES)				
	%	RR	95% CI	%	RR	95% CI	% Change[d]	95% CI	%	RR	95% CI	% Change[d]	95% CI	%	RR	95% CI	% Change[d]	95% CI
Moderately preterm birth (32–36 weeks) ($n = 31{,}041$)																		
Black	10.5			8.8					8.2					8.5				
White	6.3			6.5					6.8					6.7				
Risk difference	4.2		3.5, 4.9	2.3		1.5, 3.0	−46	−58, −34	1.5		0.6, 2.3	−65	−82, −49	1.9		1.1, 2.7	−55	−70, −41
Relative risk		1.7	1.5, 1.8		1.3	1.2, 1.5	−48	−60, −36		1.2	1.1, 1.3	−68	−84, −51		1.3	1.1, 1.4	−58	−73, −43
Very preterm birth (<32 weeks) ($n = 31{,}489$)																		
Black	2.9			2.3					2.0[e]					2.0				
White	0.7			0.7					0.7					0.7				
Risk difference	2.2		1.9, 2.6	1.5		1.1, 1.9	−32	−44, −20	1.3		0.9, 1.7	−42	−53, −32	1.3		0.9, 1.7	−43	−53, −33
Relative risk		4.2	3.4, 5.1		3.0	2.3, 3.8	−37	−50, −24		2.8	2.1, 3.5	−44	−61, −28		2.8	2.1, 3.5	−45	−60, −30

Abbreviations: CI, confidence interval; RR, relative risk; SES, socioeconomic status.
[a] Adjusted for maternal age, education, marital status, and gravidity.
[b] Random-intercept model with adjustment for maternal age, education, marital status, gravidity, and neighborhood racial composition.
[c] Random-intercept model with adjustment for maternal age, education, marital status, gravidity, and neighborhood deprivation index.
[d] Percent change from unadjusted model (model 1); bootstrap confidence interval from 1,000 iterations.
[e] Random-intercept model with adjustment for maternal age, education, marital status, gravidity, neighborhood gravidity, and neighborhood racial composition.

- Used inverse logit for marginal effects at the mean
- Didn't have STATA 11 with margins command

Schempf AH, Kaufman JS, Messer LC, Mendola P. The neighborhood contribution to black-white perinatal disparities: an example from two north Carolina counties, 1999-2001. Am J Epidemiol. 2011 Sep 15;174(6):744-52.



http://www.ibtimes.com/articles/347476/20120531/relative-risk-absolute-comic-health-medical-reporting.htm