431 Class 20 Extra Slides

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What is in these Extra Slides

Important supplemental examples related to Class 20

1. Working with a 2x2 table: Statin use in the `dm431` sample comparing Medicaid patients to the Uninsured
2. Working with a 5x2 table: Statin use by practice in the `dm431` sample
3. Three-Way Table: Auto Accidents in Alberta, Canada
4. Three-Way Table: Admissions to UC/Berkeley and Simpson's Paradox
5. Three-Way Table: A Meta-Analysis of Niacin and Heart Disease

Today's Setup and Data

```
knitr::opts_chunk$set(comment = NA)
options(dplyr.summarise.inform = FALSE)

library(Epi) # new today - for twoby2
library(vcd) # new today - for Woolf test
library(janitor)
library(knitr)
library(magrittr)
library(mosaic) # not usually something I load
library(broom)
library(tidyverse)

theme_set(theme_bw())

dm431 <- readRDS("data/dm431_2020.Rds")
source("data/Love-boost.R")
```

Extra Example 1: Statin use in Medicaid vs. Uninsured within the `dm431` study.

Statin use in Medicaid vs. Uninsured

In the dm431 data, suppose we want to know whether statin prescriptions are more common among Medicaid patients than Uninsured subjects. So, we want a two-way table with "Medicaid", "Statin" in the top left.

```
dm431 %>%
  filter(insurance %in% c("Medicaid", "Uninsured")) %>%
  tabyl(insurance, statin)
```

```
  insurance  0  1
 Commercial  0  0
   Medicaid 17 83
   Medicare  0  0
  Uninsured 15 29
```

But we want the tabyl just to show the levels of insurance we're studying. . .

Obtaining a 2x2 Table from a tibble

We want to know whether statin prescriptions are more common among Medicaid patients than Uninsured subjects.. So, we want a two-way table with "Medicaid", "Uninsured" in the top left.

```
dm431 %>%
  filter(insurance %in% c("Medicaid", "Uninsured")) %>%
  droplevels() %>%
  tabyl(insurance, statin)
```

```
 insurance  0  1
  Medicaid 17 83
 Uninsured 15 29
```

But we want Medicaid in the top row (ok) and "statin = yes" in the left column (must fix)...

Building and Releveling Factors in the tibble

```
exam1 <- dm431 %>%
  filter(insurance %in% c("Medicaid", "Uninsured")) %>%
  droplevels() %>%
  mutate(insur_f = fct_relevel(insurance, "Medicaid"),
         statin_f = fct_recode(factor(statin),
                               statin = "1", no_statin = "0"),
         statin_f = fct_relevel(statin_f, "statin"))

exam1 %>% tabyl(insur_f, statin_f)
```

```
   insur_f statin no_statin
  Medicaid     83         17
 Uninsured     29         15
```

Since Medicaid was already on top, we didn't *have to* set `insur_f`.

Adding percentages

```
exam1 %>% tabyl(insur_f, statin_f) %>%
  adorn_totals(where = c("row", "col")) %>%
  adorn_percentages(denom = "row") %>%
  adorn_pct_formatting(digits = 1) %>%
  adorn_ns(position = "front") %>%
  adorn_title(row = "Insurance", col = "Statin Status")
```

	Statin Status		
Insurance	statin	no_statin	Total
Medicaid	83 (83.0%)	17 (17.0%)	100 (100.0%)
Uninsured	29 (65.9%)	15 (34.1%)	44 (100.0%)
Total	112 (77.8%)	32 (22.2%)	144 (100.0%)

Running twoby2 against a data table

The twoby2 function from the Epi package can operate with tables (but not, alas, tabyls) generated from data.

Original Data

```
twoby2(exam1 %$% table(insur_f, statin_f))
```

(output on next slide)

With Bayesian Augmentation

```
twoby2(exam1 %$% table(insur_f, statin_f) + 2)
```

(output on the slide after that)

```
2 by 2 table analysis:
------------------------------------------------
Outcome    : statin
Comparing : Medicaid vs. Uninsured

           statin no_statin    P(statin) 95% conf. interval
Medicaid       83         17       0.8300    0.7434   0.8916
Uninsured      29         15       0.6591    0.5090   0.7829

                                      95% conf. interval
              Relative Risk: 1.2593    1.0003   1.5854
          Sample Odds Ratio: 2.5254    1.1202   5.6933
Conditional MLE Odds Ratio: 2.5074    1.0252   6.1298
    Probability difference: 0.1709    0.0218   0.3307

               Exact P-value: 0.0299
          Asymptotic P-value: 0.0255
------------------------------------------------
```

```
2 by 2 table analysis:
------------------------------------------------
Outcome    : statin
Comparing : Medicaid vs. Uninsured

           statin no_statin    P(statin) 95% conf. interval
Medicaid       85         19       0.8173    0.7312   0.8803
Uninsured      31         17       0.6458    0.5023   0.7671

                                      95% conf. interval
              Relative Risk: 1.2655    1.0071   1.5901
          Sample Odds Ratio: 2.4533    1.1327   5.3136
Conditional MLE Odds Ratio: 2.4375    1.0464   5.6838
    Probability difference: 0.1715    0.0245   0.3261

              Exact P-value: 0.0251
          Asymptotic P-value: 0.0228
------------------------------------------------
```

Extra Example 2. Statin Use by Practice in the `dm431` study

dm431: Statin Use by Practice

```
dm431 %>% tabyl(practice, statin)
```

practice	0	1
Arlington	20	101
Bristol	26	107
Chester	16	34
Dover	14	49
Franklin	10	54

Is there an association between rates of statin usage and practice?

Include the Percentages

```
dm431 %>% tabyl(practice, statin) %>%
  adorn_totals(where = "row") %>%
  adorn_percentages() %>% adorn_pct_formatting() %>%
  adorn_ns(position = "front") %>% adorn_title()
```

```
                statin
  practice           0           1
 Arlington 20 (16.5%) 101 (83.5%)
   Bristol 26 (19.5%) 107 (80.5%)
   Chester 16 (32.0%)  34 (68.0%)
     Dover 14 (22.2%)  49 (77.8%)
  Franklin 10 (15.6%)  54 (84.4%)
     Total 86 (20.0%) 345 (80.0%)
```

Does H_0 hold up well?

Chi-Square Test

```
dm431 %>% tabyl(practice, statin) %>% chisq.test()
```

```
    Pearson's Chi-squared test

data:  .
X-squared = 6.3987, df = 4, p-value = 0.1713
```

The association we see isn't strong enough to be detectable by this method. Is this because of the sample sizes?

Expected Counts for Practice - Statin Association

This is a 5×2 two-way table.

```
tab52 <- dm431 %>% tabyl(practice, statin) %>% chisq.test()
tab52$expected
```

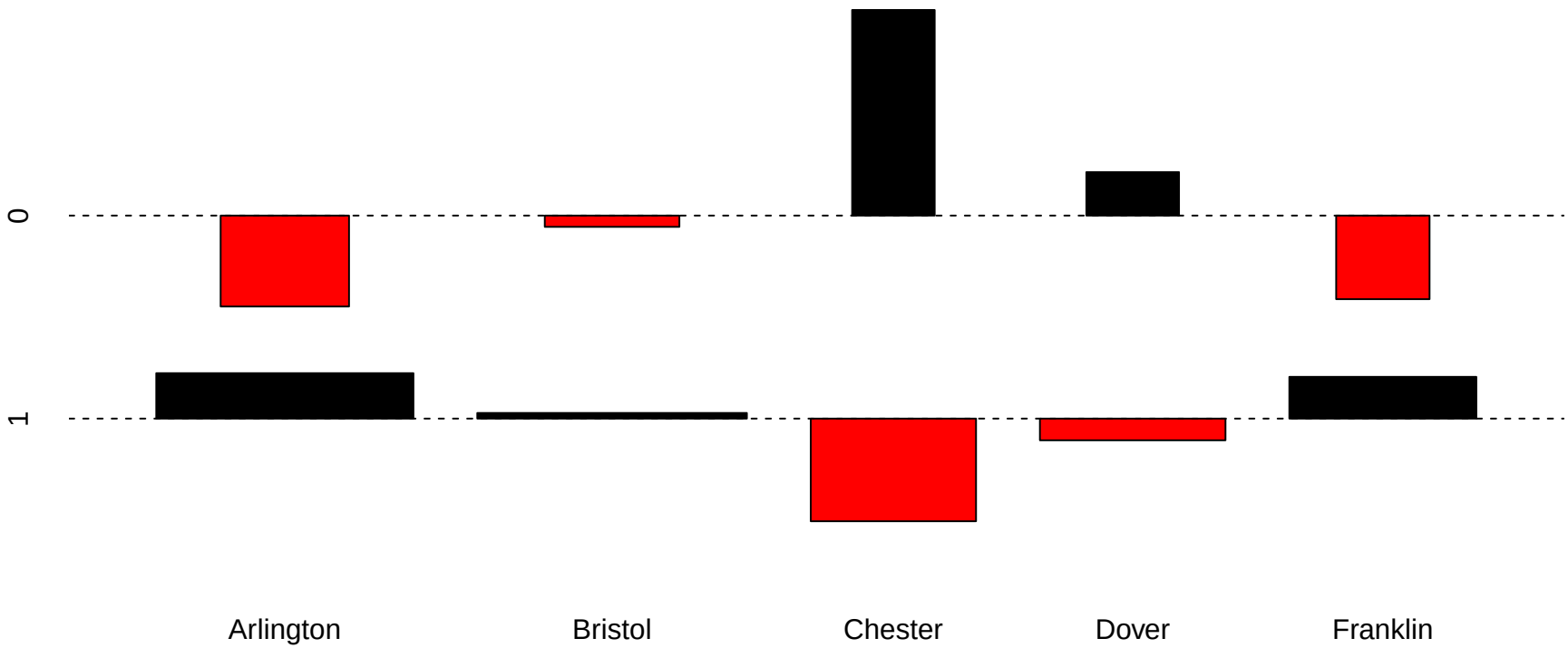
```
  practice         0          1
 Arlington 24.143852  96.85615
   Bristol 26.538283 106.46172
   Chester  9.976798  40.02320
     Dover 12.570766  50.42923
  Franklin 12.770302  51.22970
```

The expected frequencies look like they are 10 or more (with one slight exception.)

assocplot for practice × statin

Which practice might we look at most closely?

```
assocplot(table(dm431$practice, dm431$statin))
```



Extra Example 3: Auto Accidents in Alberta, Canada

Alberta Automobile Accidents

Prior to the enactment of seatbelt legislation in the province of Alberta, Canada, a sample of 86,769 auto accident reports were studied. For each report, we categorize:

- driver condition (normal, been drinking)
- was the driver wearing a seatbelt (yes, no)
- the injury level of the driver (none, minimal, minor, or major/fatal)

Source: Jobson JD, Table 6.23 *Applied Multivariate Data Analysis: Volume II: Categorical and Multivariate Methods*

So this is going to become a $2 \times 2 \times 4$ table.

A Two-Way Table

Ignoring the driver condition for a moment, here is the 2 × 4 table of seatbelt use and injury level.

–	None	Minimal	Minor	Major	Total
No Seatbelt	65963	4000	2642	303	72908
Seatbelt	12813	647	359	42	13861
Total	78776	4647	3001	345	86769

Calculating Probabilities using the Two-Way Table

We can calculate *marginal* probabilities from the table, like. . .

$$Pr(\text{Seatbelt}) = \frac{13861}{86769} = .160, \text{ and } Pr(\text{No injury}) = \frac{78776}{86769} = .908,$$

and we can calculate *conditional* probabilities, like . . .

$$Pr(\text{No injury}|\text{Seatbelt}) = \frac{12813}{13861} = 0.924$$

and

$$Pr(\text{No injury}|\text{No Seatbelt}) = \frac{65963}{72908} = 0.904$$

Three-Way Contingency Table (four 2 × 2)

We have **four** 2 × 2 tables,

- Injury = None (Odds Ratio = 2.57, 95% CI: 2.29, 2.89)

No Injury	Been Drinking	Normal
No Seatbelt	3992	61971
Seatbelt	313	12500

- Injury = Minimal (Odds Ratio = 1.92, 95% CI: 1.39, 2.65)

Minimal	Been Drinking	Normal
No Seatbelt	481	3519
Seatbelt	43	604

Three-Way Contingency Table (four 2 × 2)

and . . .

- Injury = Minor (Odds Ratio = 3.73, 95% CI: 2.20, 6.34)

Minor	Been Drinking	Normal
No Seatbelt	370	2272
Seatbelt	15	344

- Injury = Major (Odds Ratio = 2.65, 95% CI: 0.91, 7.68)

Major	Been Drinking	Normal
No Seatbelt	66	237
Seatbelt	4	38

Placing the Data in R

```
condition <- c(rep("Normal", 8), rep("Been_Drinking", 8))
seatbelt <- c(rep(c(rep("Yes", 4), rep("No", 4)), 2))
injury <- c(rep(c("None", "Minimal", "Minor", "Major"), 4))
counts <- c(12500, 604, 344, 38, 61971, 3519, 2272, 237,
            313, 43, 15, 4, 3992, 481, 370, 66)

aaa <- tibble(condition, seatbelt, injury, counts) %>%
  mutate(injury = fct_relevel(injury, "None", "Minimal",
                              "Minor", "Major"))
```

Viewing the Table

```
big_tab <- aaa %$% xtabs(counts ~ seatbelt + condition + injur
big_tab %>% ftable()
```

```
                          injury  None Minimal Minor Major
seatbelt condition
No       Been_Drinking            3992     481   370    66
         Normal                  61971    3519  2272   237
Yes      Been_Drinking             313      43    15     4
         Normal                  12500     604   344    38
```

We're trying to estimate the odds ratio for "been drinking" given that the driver is "not wearing a seatbelt" as compared to when the driver is wearing a seatbelt, assuming that it is the same across all four injury types. We have:

- row = condition (been drinking or normal)
- column = seatbelt (no or yes)
- strata = injury (four levels)

Can we assume that each injury level has a common odds ratio?

Recall that the sample odds ratios we saw were:

No Injury	Minimal	Minor	Major
2.57	1.92	3.73	2.65

The Woolf test assesses the null hypothesis of a common "condition and seatbelt" odds ratio across the four injury types. This (that a common odds ratio can be assumed to exist for each of the four injury types) is a key assumption of the Cochran-Mantel-Haenszel test.

Can we assume that each injury level has a common odds ratio?

```
woolf_test(big_tab)
```

```
    Woolf-test on Homogeneity of Odds Ratios (no
    3-Way assoc.)

data:  big_tab
X-squared = 4.9623, df = 3, p-value = 0.1746
```

Our conclusion from the Woolf test is that we are able to retain the null hypothesis of homogeneous odds ratios. So it's not crazy to fit a CMH test (that requires that all of the population odds ratios to be the same.)

Running the Cochran-Mantel-Haenszel test

So, we can use the Cochran-Mantel-Haenszel test to make inferences about the population odds ratio (for the driver having been drinking given no seatbelt rather than seatbelt) accounting for the four injury types. We'll use a 90% confidence interval, and the results appear on the next slide.

```
mantelhaen.test(big_tab, conf.level = .90)
```

Complete CMH output (Edited to fit on the screen)

```
mantelhaen.test(big_tab, conf.level = .90)
```

```
Mantel-Haenszel chi-squared test with continuity correction

data:  big_tab
Mantel-Haenszel X-squared = 314, df = 1, p-value < 2.2e-16

alt. hypothesis: true common odds ratio is not equal to 1

90 percent confidence interval: 2.327467 2.784538
sample estimates: common odds ratio 2.545765
```

What can we conclude in this case?

Alternate Specification of Three-Way Table

We also have **two** of these 2 × 4 tables:

- Driver had been drinking

Been Drinking	None	Minimal	Minor	Major	Total
No Seatbelt	3992	481	370	66	4909
Seatbelt	313	43	15	4	375
Total	4305	524	385	70	5284

- Driver had not been drinking (was "Normal")

Normal	None	Minimal	Minor	Major	Total
No Seatbelt	61971	3519	2272	237	67999
Seatbelt	12500	604	344	38	13486
Total	74471	4123	2616	275	81485

Could we have run the test changing the roles?

We ran this originally using four (strata) to identify four 2 (row) $\times$ 2 (column) tables.

If we did this with two strata (been drinking vs. normal), on a 2 (row - seatbelt or not) $\times$ 4 (column - injury type) table, we'd no longer get an odds ratio, but we would be able to obtain a p value for the null hypothesis of no relationship between seatbelt use and injury type, accounting for drinking status.

To get it, we'd just rearrange the big table (strata goes last):

```
big_tab2 <-
  aaa %$% xtabs(counts ~ seatbelt + injury + condition)
```

Results when Strata = drinking status

```
woolf_test(big_tab2)
```

```
    Woolf-test on Homogeneity of Odds Ratios (no
    3-Way assoc.)

data:  big_tab2
X-squared = 0.21445, df = 1, p-value = 0.6433
```

```
mantelhaen.test(big_tab2)
```

```
    Cochran-Mantel-Haenszel test

data:  big_tab2
Cochran-Mantel-Haenszel M^2 = 40.213, df = 3,
p-value = 9.601e-09
```

Extra Example 4: Admissions to Departments at the University of California at Berkeley and Simpson's Paradox

The UC Berkeley Student Admissions Example

The UCBAdmissions data set contains aggregate data on applicants to graduate school at Berkeley for the six largest departments in 1973, classified by whether the applicant was admitted, and their sex.

```
ftable(UCBAdmissions)
```

```
                 Dept   A   B   C   D   E   F
Admit    Gender
Admitted Male         512 353 120 138  53  22
         Female        89  17 202 131  94  24
Rejected Male         313 207 205 279 138 351
         Female        19   8 391 244 299 317
```

Do the data show evidence of sex bias in admission practices?

Summarizing Department D

In Department D, we have

Department D	Males	Females
Admitted	138	131
Not Admitted	279	244
Applicants	417	375

$$\text{Pr(Admitted if Male)} = \frac{138}{138+279} = 0.331$$

$$\text{Odds(Admitted if Male)} = \frac{138}{279} = 0.49$$

$$\text{Pr(Admitted if Female)} = \frac{131}{131+244} = 0.349$$

$$\text{Odds(Admitted if Female)} = \frac{131}{244} = 0.54$$

$$\text{Odds Ratio (Admit for Male vs Female)} = \frac{138*244}{131*279} = 0.92$$

Can we use the Cochran-Mantel-Haenszel test?

Are the odds ratios similar across departments?

Department	A	B	C	D	E	F
Admitted Males	512	353	120	138	53	22
Male Applicants	825	560	325	417	191	373
Admitted Females	89	17	202	131	94	24
Female Applicants	108	25	593	375	393	341
Pr(Admit if Male)	0.62	0.63	0.37	0.33	0.28	0.06
Pr(Admit if Female)	0.82	0.68	0.34	0.35	0.24	0.07
Odds(Admit if Male)	1.64	1.71	0.59	0.49	0.38	0.06
Odds(Admit if Female)	4.68	2.12	0.52	0.54	0.31	0.08
Odds Ratio	0.35	0.8	1.13	0.92	1.22	0.83

Can we use a Cochran-Mantel-Haenszel test?

A Cochran-Mantel-Haenszel test describes a single combined odds ratio accounting for department. This assumes that the population odds ratio for admission by sex is identical for each of the six strata (departments).

- Does that seem reasonable?
- Or is there a three-way interaction here, where the odds ratios for admission by sex differ significantly across departments?

Department	A	B	C	D	E	F
Odds Ratio	0.35	0.8	1.13	0.92	1.22	0.83

How can we test this?

Woolf Test for Interaction in UCB Admissions

- H_0: There is no three-way interaction.
  - Odds ratios are homogenous, and we may proceed with the CMH test.)
- H_A: There is a meaningful three-way interaction.
  - CMH test is inappropriate because there are significantly different odds ratios across the departments.

```
woolf_test(UCBAdmissions)
```

```
    Woolf-test on Homogeneity of Odds Ratios (no
    3-Way assoc.)

data:  UCBAdmissions
X-squared = 17.902, df = 5, p-value = 0.003072
```

What's Going On Here?

Department	A	B	C	D	E	F
Pr(Admit if Male)	0.62	0.63	0.37	0.33	0.28	0.06
Pr(Admit if Female)	0.82	0.68	0.34	0.35	0.24	0.07
Pr (Admitted, regardless of sex)	0.64	0.63	0.35	0.34	0.25	0.06
% of Applicants who are Female	11.6	4.3	64.6	47.3	67.3	47.8

- Females used to apply more to departments with lower admission rates.
- This is a famous example related to what is called Simpson's Paradox.

Simpson's Paradox

A trend appears in several different groups of data but disappears or reverses when these groups are combined.

- Wikipedia

  Simpson's paradox can also arise in correlations, in which two variables appear to have (say) a positive correlation towards one another, when in fact they have a negative correlation, the reversal having been brought about by a "lurking" confounder.

Example: Murder rates and ice cream sales

Extra Example 5: A Meta-Analysis of Niacin and Heart Disease

Niacin and Heart Disease Meta-Analysis

Duggal et al (2010) did a meta-analysis[1] of 5 placebo-controlled studies (AFREGS, ARBITER2, CLAS1, FATS and HATS) of niacin and heart disease, where the primary outcome was the need to do a coronary artery revascularization procedure.

For example, the FATS study had these results:

FATS	Revascularization	No Revasc.
Niacin	2	46
Placebo	11	41

FATS is just one of the five studies, and this table exists in each!

[1] Duggal JK et al. 2010. Effect of niacin therapy on cardiovascular outcomes in patients with coronary artery disease. J Cardiovasc Pharmacology & Therapeutics 15: 158-166. My Source: http://www.biostathandbook.com/cmh.html

Exploring the FATS study

FATS	Revascularization	No Revasc.
Niacin	2	46
Placebo	11	41

- Pr(revascularization | Niacin) $= \frac{2}{2+46} = 0.042$
- Odds(revascularization | Niacin) $= \frac{2}{46} = 0.043$
- Pr(revascularization | Placebo) $= \frac{11}{11+41} = 0.212$
- Odds(revascularization | Placebo) $= \frac{11}{41} = 0.268$

and so the Odds Ratio $= \frac{2*41}{11*46} = 0.16$.

But that is just the result for the FATS study.

Building the Meta-Analysis Table

```
study <- c(rep("FATS", 4), rep("AFREGS", 4),
           rep("ARBITER2", 4), rep("HATS", 4),
           rep("CLAS1", 4))
treat <- c(rep(c("Niacin", "Niacin",
                 "Placebo", "Placebo"),5))
outcome <- c(rep(c("Revasc.", "No Rev."), 10))
counts <- c(2, 46, 11, 41, 4, 67, 12, 60, 1, 86,
            4, 76, 1, 37, 6, 32, 2, 92, 1, 93)
meta <- tibble(study, treat, outcome, counts)
meta$treat <- fct_relevel(meta$treat, "Niacin")
meta$outcome <- fct_relevel(meta$outcome, "Revasc.")
meta.tab <- xtabs(counts ~ treat + outcome + study,
                  data = meta)
```

Five Studies in the Meta-Analysis

```
ftable(meta.tab)
```

```
                study AFREGS ARBITER2 CLAS1 FATS HATS
treat   outcome
Niacin  Revasc.           4        1     2    2    1
        No Rev.          67       86    92   46   37
Placebo Revasc.          12        4     1   11    6
        No Rev.          60       76    93   41   32
```

The three variables we are studying are:

- `treat` (2 levels: Niacin/Placebo),
- `outcome` (2 levels: Revascularization or No Revascularization) across
- `study` (5 levels: AFREGS, ARBITER2, CLAS1, FATS, HATS)

Cochran-Mantel-Haenszel Test

The Cochran-Mantel-Haenszel test is designed to test whether the rate of revascularization is the same across the two levels of the treatment (i.e. Niacin or Placebo).

- We *could* do this by simply adding up the results across the five studies, but that wouldn't be wise, because the studies used different populations and looked for revascularization after different lengths of time.
- But we can account for the differences between studies to some extent by adjusting for study as a stratifying variable in a CMH test.
- The big assumption we'll have to make, though, is that the odds ratio for revascularization given Niacin instead of Placebo does not change across the studies. Is this reasonable in our case?

Looking at the Study-Specific Odds Ratios

We'll calculate the odds ratios, comparing revascularization odds with niacin vs. placebo, within each separate study.

Study	Rev N	Rev P	NoRev N	NoRev P	Odds Ratio
AFREGS	4	67	12	60	$\frac{4*60}{67*12} = 0.3$
ARBITER2	1	86	4	76	0.22
CLAS1	2	92	1	93	2.02
FATS	2	46	11	41	0.16
HATS	1	37	6	32	0.14

The table shows patient counts for the categories in each of the respective two-by-two tables (Rev N = Revascularization and Niacin, NoRev P = No Revascularization and Placebo, etc.)

Can we assume a Common Odds Ratio?

The Woolf test checks a key assumption for the Cochran-Mantel-Haenszel test. The Woolf test assesses the null hypothesis of a common odds ratio across the five studies.

```
woolf_test(meta.tab)
```

```
    Woolf-test on Homogeneity of Odds Ratios (no
    3-Way assoc.)

data:  meta.tab
X-squared = 3.4512, df = 4, p-value = 0.4853
```

Our conclusion from the Woolf test is that we are able to retain the null hypothesis of homogeneous odds ratios. So it's not crazy to fit a test that requires that all of the odds ratios be the same in the population.

Running the Cochran-Mantel-Haenszel test

So, we can use the Cochran-Mantel-Haenszel test to make inferences about the population odds ratio (for revascularization given niacin rather than placebo) accounting for the five studies. We'll use a 90% confidence interval, and the results appear on the next slide.

```
mantelhaen.test(meta.tab, conf.level = .90)
```

Complete CMH output

```
mantelhaen.test(meta.tab, conf.level = .90)
```

```
Mantel-Haenszel chi-squared test with continuity correction

data:  meta.tab
Mantel-Haenszel
X-squared = 12.746, df = 1, p-value = 0.0003568

alt. hypothesis: true common odds ratio is not equal to 1

90 percent confidence interval: 0.1468942 0.4968686
sample estimates: common odds ratio 0.2701612
```

What can we conclude in this case?