Lecture 25

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Outline

1. Hypothesis tests of marginal homgeneity
2. Estimating marginal risk differences
3. Estimating marginal odds ratios
4. A brief note on the distinction between conditional and marginal odds ratios

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Matched pairs binary data

First survey	Second Survey: Approve	Second Survey: Disapprove	Total
Approve	794	150	944
Disapprove	86	570	656
Total	880	720	1600

Controls	Cases: Exposed	Cases: Unexposed	Total
Exposed	27	29	56
Unexposed	3	4	7
Total	30	33	63

[1]

[1] Both data sets from Agresti, Categorical Data Analysis, second edition

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Dependence

- Matched binary can arise from
  - Measuring a response at two occasions
  - Matching on case status in a retrospective study
  - Matching on exposure status in a prospective or cross-sectional study
- The pairs on binary observations are dependent, so our existing methods do not apply
- We will discuss the process of making conclusions about the marginal probabilities and odds

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Notation

	time 2		
time 1	Yes	No	Total
Yes	n_{11}	n_{12}	n_{1+}
no	n_{21}	n_{22}	n_{2+}
Total	n_{+1}	n_{+2}	n

	time 2		
time 1	Yes	No	Total
Yes	π_{11}	π_{12}	π_{1+}
no	π_{21}	π_{22}	π_{2+}
Total	π_{+1}	π_{+2}	1

- We assume that the $(n_{11}, n_{12}, n_{21}, n_{22})$ are multinomial with n trials and probabilities $(\pi_{11}, \pi_{12}, \pi_{21}, \pi_{22})$
- π_{1+} and π_{+1} are the marginal probabilities of a yes response at the two occasions
- $\pi_{1+} = P(\text{Yes} \mid \text{Time 1})$
- $\pi_{+1} = P(\text{Yes} \mid \text{Time 2})$

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Marginal homogeneity

- Marginal homogeneity is the hypothesis $H_0 : \pi_{1+} = \pi_{+1}$
- Marginal homogeneity is equivalent to symmetry $H_0 : \pi_{12} = \pi_{21}$
- The obvious estimate of $\pi_{12} - \pi_{21}$ is $n_{12}/n - n_{21}/n$
- Under H_0 a consistent estimate of the variance is $(n_{12} + n_{21})/n^2$
- Therefore
$$\frac{(n_{12} - n_{21})^2}{n_{12} + n_{21}}$$
follows an asymptotic χ^2 distribution with 1 degree of freedom

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McNemar's test

- The test from the previous page is called McNemar's test
- Notice that only the discordant cells enter into the test
  - n_{12} and n_{21} carry the relevant information about whether or not π_{1+} and π_{+1} differ
  - n_{11} and n_{22} contribute information to estimating the magnitude of this difference

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Example

- Test statistic $\frac{(80-150)^2}{86+150} = 17.36$
- P-value $= 3 \times 10^{-5}$
- Hence we reject the null hypothesis and conclude that there is evidence to suggest a change in opinion between the two polls
- In R

```
mcnemar.test(matrix(c(794, 86, 150, 570), 2),
                  correct = FALSE)
```

The `correct` option applies a continuity correction

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Estimation

- Let $\hat{\pi}_{ij} = n_{ij}/n$ be the sample proportions
- $d = \hat{\pi}_{1+} - \hat{\pi}_{+1} = (n_{12} - n_{21})/n$ estimates the difference in the marginal proportions
- The variance of d is

$$\sigma_d^2 = \{\pi_{1+}(1-\pi_{1+})+\pi_{+1}(1-\pi_{+1})-2(\pi_{11}\pi_{22}-\pi_{12}\pi_{21})\}/n$$

- $\frac{d-(\pi_{1+}-\pi_{+1})}{\hat{\sigma}_d}$ follows an asymptotic normal distribution
- Compare σ_d^2 with what we would use if the proportions were independent

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Example

- $d = 944/1600 - 880/1600 = .59 - .55 = .04$
- $\hat{\pi}_{11} = .50$, $\hat{\pi}_{12} = .09$, $\hat{\pi}_{21} = .05$, $\hat{\pi}_{22} = .36$
- $\hat{\sigma}_d^2 = \{.59(1-.59) + .55(1-.55) - 2(.50 \times .36 - .09 \times .05)\}/1600$
- $\hat{\sigma}_d = .0095$
- 95% CI - $.04 \pm 1.96 \times .0095 = [.06, .02]$
- Note ignoring the dependence yields $\hat{\sigma}_d = .0175$

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Relationship with CMH test

- Each subject's (or matched pair's) responses can be represented as one of four tables.

	Response	
Time	Yes	No
First	1	0
Second	1	0

	Response	
Time	Yes	No
First	1	0
Second	0	1

	Response	
Time	Yes	No
First	0	1
Second	1	0

	Response	
Time	Yes	No
First	0	1
Second	0	1

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Result

- McNemar's test is equivalent to the CMH test where subject is the stratifying variable and each 2×2 table is the observed zero-one table for that subject
- This representation is only useful for conceptual purposes

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Exact version

- Consider the cells n_{12} and n_{21}
- Under H_0, $\pi_{12}/(\pi_{12} + \pi_{21}) = .5$
- Therefore, under H_0, $n_{21} \mid n_{21} + n_{12}$ is binomial with success probability .5 and $n_{21} + n_{12}$ trials
- We can use this result to come up with an exact P-value for matched pairs data

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- Consider the approval rating data
- $H_0 : \pi_{21} = \pi_{12}$ versus $H_a : \pi_{21} < \pi_{12}$ $(\pi_{+1} < \pi_{1+})$
- $P(X \leq 86 \mid 86 + 150) = .000$ where X is binomial with 236 trials and success probability $p = .5$
- For two sided tests, double the smaller of the two one-sided tests

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Estimating the marginal odds ratio

- The marginal odds ratio is

$$\frac{\pi_{1+}/\pi_{2+}}{\pi_{+1}/\pi_{+2}} = \frac{\pi_{1+}\pi_{+2}}{\pi_{+1}\pi_{2+}}$$

- The maximum likelihood estimate of the margina *log* odds ratio is

$$\hat{\theta} = \log\{\hat{\pi}_{1+}\hat{\pi}_{+2}/\hat{\pi}_{+1}\hat{\pi}_{2+}\}$$

- The asymptotic variance of this estimator is

$$\begin{aligned} &\{(\pi_{1+}\pi_{2+})^{-1} + (\pi_{+1}\pi_{+2})^{-1} \\ - \;& 2(\pi_{11}\pi_{22} - \pi_{12}\pi_{21})/(\pi_{1+}\pi_{2+}\pi_{+1}\pi_{+2})\}/n \end{aligned}$$

Example

- In the approval rating example the marginal OR compares the odds of approval at time 1 to that at time 2
- $\hat{\theta} = \log(944 \times 720/880 \times 656) = .16$
- Estimated standard error $= .039$
- CI for the log odds ratio $= .16 \pm 1.96 \times .039 = [.084, .236]$

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Conditional versus marginal odds

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Conditional versus marginal odds

- n_{ij} cell counts
- n total sample size
- π_{ij} the multinomial probabilities
- The ML estimate of the marginal *log* odds ratio is

$$\hat{\theta} = \log\{\hat{\pi}_{1+}\hat{\pi}_{+2}/\hat{\pi}_{+1}\hat{\pi}_{2+}\}$$

- The asymptotic variance of this estimator is

$$\begin{aligned} & \{(\pi_{1+}\pi_{2+})^{-1} + (\pi_{+1}\pi_{+2})^{-1} \\ - \quad & 2(\pi_{11}\pi_{22} - \pi_{12}\pi_{21})/(\pi_{1+}\pi_{2+}\pi_{+1}\pi_{+2})\}/n \end{aligned}$$

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- Consider the following model

$$\text{logit}\{P(\text{Person } i \text{ says Yes at Time 1})\} = \alpha + U_i$$
$$\text{logit}\{P(\text{Person } i \text{ says Yes at Time 2})\} = \alpha + \gamma + U_i$$

- Each U_i contains person-specific effects. A person with a large U_i is likely to answer Yes at both occasions.
- γ is the **log odds ratio** comparing a response of Yes at Time 1 to a response of Yes at Time 2.
- γ is **subject specific effect**. If you subtract the log odds of a yes response for two different people, the U_i terms would not cancel

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Conditional ML cont'd

- One way to eliminate the U_i and get a good estimate of γ is to condition on the total number of Yes responses for each person
  - If they answered Yes or No on both occasions then you know both responses
  - Therefore, only discordant pairs have any relevant information after conditioning
- The conditional ML estimate for γ and its SE turn out to be

$$\log\{n_{21}/n_{12}\} \qquad \sqrt{1/n_{21} + 1/n_{12}}$$

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Distinctions in interpretations

- The marginal ML has a marginal interpretation. The effect is averaged over all of the values of U_i.
- The conditional ML estimate has a subject specific interpretation.
- Marginal interpretations are more useful for policy type statements. Policy makers tend to be interested in how factors influence populations.
- Subject specific interpretations are more useful in clinical applications. Physicians are interested in how factors influence individuals.