## Lecture 5: Contingency Tables

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## Overview

- Over the next few lectures, we will examine the $2 \times 2$ contingency table
- Some authors refer to this as a "four fold table"
- We will consider various study designs and their impact on the summary measures of association


## Rows Fixed: Product Binomial Case - Generally Prospec-

## tive Studies

Question of interest: Does treatment affect outcome?
OUTCOME


## Columns Fixed: Also Product Binomial - Generally Retrospective Studies

Question of interest: Does alcohol exposure vary among cases and controls?


## $N$ Fixed: Multinomial Case - Generally Cross-Sectional

## Studies

Question of interest: Is there an association among cancer stage and smoking status?
CANCER STAGE


## Rows and Columns Fixed: Hypergeometric Case

Question of Interest: Is there gender bias in juror selection?


This distribution is will be used in Fisher's Exact testing.

## Prospective Studies

We are going to begin examining contingency tables first by looking at prospective studies.

- Number on each treatment (or experimental) arm fixed by design.
- Rows are independent binomials.
- Question of interest: Does treatment affect outcome?
- Usually the design for Experimental Studies, Clinical Trials.

In general, the $2 \times 2$ table is written as

|  |  | Outcome |  |  |
| :--- | :--- | :---: | :---: | :---: |
|  |  | 1 | 2 |  |
| Treatment | 1 | $Y_{1}$ | $n_{1}-Y_{1}$ | $n_{1}$ |
|  | 2 | $Y_{2}$ | $n_{2}-Y_{2}$ | $n_{2}$ |
|  |  |  |  |  |

## Facts about the distribution

- $n_{1}$ and $n_{2}$ are fixed by design
- $Y_{1}$ and $Y_{2}$ are independent with distributions:

$$
\begin{aligned}
& Y_{1} \sim \operatorname{Bin}\left(n_{1}, p_{1}\right) \\
& Y_{2} \sim \operatorname{Bin}\left(n_{2}, p_{2}\right)
\end{aligned}
$$

- The distribution is the product of 2 independent binomials; often called the 'product binomial':

$$
\begin{aligned}
P\left(y_{1}, y_{2} \mid p_{1}, p_{2}\right) & =P\left(Y_{1}=y_{1} \mid p_{1}\right) P\left(Y_{2}=y_{2} \mid p_{2}\right) \\
& =\binom{n_{1}}{y_{1}}\binom{n_{2}}{y_{2}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}} p_{2}^{y_{2}}\left(1-p_{2}\right)^{n_{2}-y_{2}}
\end{aligned}
$$

## Question of interest (all the same)

- Does treatment affect outcome?
- Are treatment and outcome associated ?
- Is the probability of success the same on both treatments?
- How do we quantify treatment differences?
- Also, what test statistics can we use for

$$
\mathrm{H}_{0}: p_{1}=p_{2}=p
$$

and the alternative is

$$
\mathrm{H}_{A}: p_{1} \neq p_{2}
$$

## MLE and estimated SEs of treatment differences

- To estimate these treatment differences, we must estimate the success probabilities $p_{1}$ and $p_{2}$.
- Intuitively, thinking of the two groups separately, the MLE's should be the proportion of successes in the two groups, i.e.,

$$
\widehat{p}_{1}=\frac{Y_{1}}{n_{1}}
$$

and

$$
\widehat{p}_{2}=\frac{Y_{2}}{n_{2}} .
$$

- However, we will derive these based on the likelihood of the product binomial.

The Likelihood for $\left(p_{1}, p_{2}\right)$ is the product binomial distribution of $\left(y_{1}, y_{2}, p_{1}, p_{2}\right)$.

$$
\begin{aligned}
L\left(p_{1}, p_{2}\right) & =P\left(Y_{1}=y_{1} \mid p_{1}\right) P\left(Y_{2}=y_{2} \mid p_{2}\right) \\
& =\binom{n_{1}}{y_{1}}\binom{n_{2}}{y_{2}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}} p_{2}^{y_{2}}\left(1-p_{2}\right)^{n_{2}-y_{2}}
\end{aligned}
$$

Then the log-likelihood is the sum of the two pieces,

$$
\begin{aligned}
& \log L\left(p_{1}, p_{2}\right)= \\
& \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]+\log \left[\binom{n_{2}}{y_{2}} p_{2}^{y_{2}}\left(1-p_{2}\right)^{n_{2}-y_{2}}\right]
\end{aligned}
$$

Similar to before, to find the MLE, we set the partial derivatives of $\log L\left(p_{1}, p_{2}\right)$ with respect to $p_{1}$ and $p_{2}$ to 0 , and solve for $\widehat{p}_{1}$ and $\widehat{p}_{2}$ :

Note: Agresti (and most statisticians) simply denote the natural logarithm as log instead of the $\ln$ as you would see in mathematics or physics. In this class, all references of log are consider the log to base $e$.

Now,

$$
\begin{aligned}
& \log L\left(p_{1}, p_{2}\right)= \\
& \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]+\log \left[\binom{n_{2}}{y_{2}} p_{2}^{y_{2}}\left(1-p_{2}\right)^{n_{2}-y_{2}}\right]
\end{aligned}
$$

The derivative of the log-likelihood with respect to $p_{1}$ is

$$
\begin{aligned}
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{1}}= & \frac{d}{d p_{1}} \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]+ \\
& \frac{d}{d p_{1}} \log \left[\binom{n_{2}}{y_{2}} p_{2}^{y_{2}}\left(1-p_{2}\right)^{n_{2}-y_{2}}\right] \\
= & \frac{d}{d p_{1}} \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]+0
\end{aligned}
$$

since the the second part is not a function of $p_{1}$.

Note, though,

$$
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{1}}=\frac{d}{d p_{1}} \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]
$$

is just the derivative of a binomial log-likelihood with respect to its parameter $p_{1}$. From before, we have

$$
\widehat{p}_{1}=\frac{y_{1}}{n_{1}}
$$

To explicitly show this, in the single binomial section, we showed that

$$
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{1}}=\frac{d}{d p_{1}} \log \left[\binom{n_{1}}{y_{1}} p_{1}^{y_{1}}\left(1-p_{1}\right)^{n_{1}-y_{1}}\right]=\frac{y_{1}-n_{1} p_{1}}{p_{1}\left(1-p_{1}\right)}
$$

Similarly,

$$
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{2}}=\frac{y_{2}-n_{2} p_{2}}{p_{2}\left(1-p_{2}\right)}
$$

Then, the MLE's are found by simultaneously solving

$$
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{1}}=\frac{y_{1}-n_{1} \widehat{p}_{1}}{\widehat{p}_{1}\left(1-\widehat{p}_{1}\right)}=0
$$

and

$$
\frac{d \log L\left(p_{1}, p_{2}\right)}{d p_{2}}=\frac{y_{2}-n_{2} \widehat{p}_{2}}{\widehat{p}_{2}\left(1-\widehat{p}_{2}\right)}=0
$$

which gives

$$
\widehat{p}_{1}=\frac{y_{1}}{n_{1}}
$$

and

$$
\widehat{p}_{2}=\frac{y_{2}}{n_{2}} .
$$

provided that $\widehat{p}_{1}, \widehat{p}_{2} \neq 0,1$

Since $Y_{1}$ and $Y_{2}$ are independent binomials we know that

$$
\operatorname{Var}\left(\widehat{p}_{1}\right)=\frac{p_{1}\left(1-p_{1}\right)}{n_{1}}
$$

and

$$
\operatorname{Var}\left(\widehat{p}_{2}\right)=\frac{p_{2}\left(1-p_{2}\right)}{n_{2}}
$$

## Estimating the treatment differences

To obtain the MLE of the log-odds ratio, we just plug $\widehat{p}_{1}$ and $\widehat{p}_{2}$ in to get

$$
\begin{aligned}
\log (\widehat{O R}) & =\log \left(\frac{\widehat{p}_{1} /\left(1-\widehat{p}_{1}\right)}{\widehat{p}_{2} /\left(1-\widehat{p}_{2}\right)}\right) \\
& =\operatorname{logit}\left(\widehat{p}_{1}\right)-\operatorname{logit}\left(\widehat{p}_{2}\right)
\end{aligned}
$$

Now, suppose we want to estimate the variance of $\log (\widehat{O R})$.
Since the treatment groups are independent, logit $\left(\widehat{p}_{1}\right)$ and logit $\left(\widehat{p}_{2}\right)$ are independent, so that

$$
\operatorname{Cov}\left[\operatorname{logit}\left(\widehat{p}_{1}\right), \operatorname{logit}\left(\widehat{p}_{2}\right)\right]=0,
$$

The variance of differences of independent random variables is

$$
\begin{aligned}
\operatorname{Var}[\log (\widehat{O R})] & =\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{1}\right)-\operatorname{logit}\left(\widehat{p}_{2}\right)\right] \\
& =\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{1}\right)\right]+\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{2}\right)\right]
\end{aligned}
$$

## Delta method approximation

- The $\operatorname{Var}[\log (\widehat{O R})]$ can be approximated by the delta method
- To do so we need to calculate

$$
\begin{aligned}
\frac{d}{d p}[\log (p)-\log (1-p)] & =\frac{1}{p}-\frac{-1}{1-p} \\
& =\frac{1}{p(1-p)}
\end{aligned}
$$

- Therefore,

$$
\begin{aligned}
\operatorname{Var}\left(\log \left(\frac{p}{1-p}\right)\right) & =\left(\frac{1}{p(1-p)}\right)^{2} \frac{p(1-p)}{n} \\
& =\frac{1}{n p(1-p)} \\
& =\frac{1}{n p}+\frac{1}{n(1-p)}
\end{aligned}
$$

- Using these results from the Delta Method, we have

$$
\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{1}\right)\right]=\frac{1}{n_{1} p_{1}}+\frac{1}{n_{1}\left(1-p_{1}\right)}
$$

and

$$
\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{2}\right)\right]=\frac{1}{n_{2} p_{2}}+\frac{1}{n_{2}\left(1-p_{2}\right)}
$$

Then,

$$
\begin{aligned}
\operatorname{Var}[\log (\widehat{O R})] & =\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{1}\right)\right]+\operatorname{Var}\left[\operatorname{logit}\left(\widehat{p}_{2}\right)\right] \\
& =\frac{1}{n_{1} p_{1}}+\frac{1}{n_{1}\left(1-p_{1}\right)}+\frac{1}{n_{2} p_{2}}+\frac{1}{n_{2}\left(1-p_{2}\right)}
\end{aligned}
$$

which we estimate by replacing $p_{1}$ and $p_{2}$ with $\widehat{p}_{1}$ and $\widehat{p}_{2}$,

$$
\begin{aligned}
\widehat{\operatorname{Var}}[\log (\widehat{O R})] & =\frac{1}{n_{1} \widehat{p}_{1}}+\frac{1}{n_{1}\left(1-\widehat{p}_{1}\right)}+\frac{1}{n_{2} \widehat{p}_{2}}+\frac{1}{n_{2}\left(1-\widehat{p}_{2}\right)} \\
& =\frac{1}{y_{1}}+\frac{1}{n_{1}-y_{1}}+\frac{1}{y_{2}}+\frac{1}{n_{2}-y_{2}}
\end{aligned}
$$

Note: This is the same result we obtained in the previous lecture; however, in this case we assumed two independent binomial distributions.

## General formula for variance of treatment difference

The MLE of a treatment difference

$$
\theta=g\left(p_{1}\right)-g\left(p_{2}\right)
$$

is

$$
\hat{\boldsymbol{\theta}}=g\left(\widehat{p}_{1}\right)-g\left(\widehat{p}_{2}\right)
$$

Also, since $\widehat{p}_{1}$ and $\widehat{p}_{2}$ are independent, so $g\left(\widehat{p}_{1}\right)$ and $g\left(\widehat{p}_{2}\right)$ are independent.
Recall, the variance of a difference of two independent random variables is

$$
\operatorname{Var}\left[g\left(\widehat{p}_{1}\right)-g\left(\widehat{p}_{2}\right)\right]=\operatorname{Var}\left[g\left(\widehat{p}_{1}\right)\right]+\operatorname{Var}\left[g\left(\widehat{p}_{2}\right)\right]
$$

Then, to obtain the large sample variance, we can apply the delta method to $g\left(\widehat{p}_{1}\right)$ to get $\operatorname{Var}\left[g\left(\widehat{p}_{1}\right)\right]$ and to $g\left(\widehat{p}_{2}\right)$ to get $\operatorname{Var}\left[g\left(\widehat{p}_{2}\right)\right]$ and then sum the two.

The results are summarized in the following table:

$\log (R R)$
RISK DIFF $\quad \hat{p}_{1}-\widehat{p}_{2} \quad \frac{p_{1}\left(1-p_{1}\right)}{n_{1}}+\frac{p_{2}\left(1-p_{2}\right)}{n_{2}}$

## ESTIMATE

$$
\widehat{p}_{1}-\widehat{p}_{2}
$$

$$
\log \left(\frac{\widehat{p}_{1}}{\widehat{p}_{2}}\right)
$$

$$
\log \left(\frac{\widehat{p}_{1} /\left(1-\widehat{p}_{1}\right)}{\widehat{p}_{2} /\left(1-\widehat{p}_{2}\right)}\right)
$$

$$
\left[\frac{1}{n_{1} p_{1}}+\frac{1}{n_{1}\left(1-p_{1}\right)}\right]+\left[\frac{1}{n_{2} p_{2}}+\frac{1}{n_{2}\left(1-p_{2}\right)}\right]
$$

## CONFIDENCE INTERVALS

To estimate the variances, we can replace $p_{1}$ and $p_{2}$ with $\widehat{p}_{1}$ and $\widehat{p}_{2}$.

$$
\begin{gathered}
\widehat{\operatorname{Var}}\left(\widehat{p}_{1}-\widehat{p}_{2}\right)=\frac{\widehat{p}_{1}\left(1-\widehat{p}_{1}\right)}{n_{1}}+\frac{\widehat{p}_{2}\left(1-\widehat{p}_{2}\right)}{n_{2}} \\
\widehat{\operatorname{Var}}[\log (\widehat{R R})]=\frac{1-\widehat{p}_{1}}{n_{1} \widehat{p}_{1}}+\frac{1-\widehat{p}_{2}}{n_{2} \widehat{p}_{2}} \\
\widehat{\operatorname{Var}}[\log (\widehat{O R})]=\frac{1}{n_{1} \widehat{p}_{1}}+\frac{1}{n_{1}\left(1-\widehat{p}_{1}\right)}+\frac{1}{n_{2} \widehat{p}_{2}}+\frac{1}{n_{2}\left(1-\widehat{p}_{2}\right)} \\
=\frac{1}{y_{1}}+\frac{1}{n_{1}-y_{1}}+\frac{1}{y_{2}}+\frac{1}{n_{2}-y_{2}}
\end{gathered}
$$

Then Large Sample 95\% confidence interval for treatment differences can be obtained via

$$
\begin{gathered}
\left(\widehat{p}_{1}-\widehat{p}_{2}\right) \pm 1.96 \sqrt{\frac{\widehat{p}_{1}\left(1-\widehat{p}_{1}\right)}{n_{1}}+\frac{\widehat{p}_{2}\left(1-\widehat{p}_{2}\right)}{n_{2}}} \\
\quad \log (\widehat{R R}) \pm 1.96 \sqrt{\frac{1-\widehat{p}_{1}}{n_{1} \widehat{p}_{1}}+\frac{1-\widehat{p}_{2}}{n_{2} \widehat{p}_{2}}}
\end{gathered}
$$

and

$$
\log (\widehat{O R}) \pm 1.96 \sqrt{\frac{1}{y_{1}}+\frac{1}{n_{1}-y_{1}}+\frac{1}{y_{2}}+\frac{1}{n_{2}-y_{2}}}
$$

## Confidence Interval for OR and RR

- You want a confidence interval for $R R$ or $O R$ that is assured to be in the interval $(0, \infty)$.
- Similar to what we did for a confidence interval for $p$, it is first better to get confidence intervals for $\log (R R)$ or $\log (O R)$, and to exponentiate the endpoints : i.e.,

$$
\exp \{\log (\widehat{O R}) \pm 1.96 \sqrt{\widehat{\operatorname{Var}}[\log (\widehat{O R})}]\}
$$

and

$$
\exp \{\log (\widehat{R R}) \pm 1.96 \sqrt{\widehat{\operatorname{Var}}[\log (\widehat{R R})}]\}
$$

## Example: MI example

- Suppose clinical trial participants are randomized to either Placebo or Aspirin
- The subjects are followed prospectively for 5 years to determine whether or not an MI (or heart attack) occurs
- The following table summarizes the results

|  | Myocardial Infarction <br> Heart or <br> Attack |  | No <br> Attack |
| :--- | :---: | :---: | :---: |
| Total per <br> Arm |  |  |  |
| Placebo | 189 | 10845 | 11,034 |
| Aspirin | 104 | 10933 | 11,037 |

- About 11000 randomized to each treatment
- Overall probability of heart attack is low

$$
\frac{293}{22071}=1.33 \%
$$

The disease is 'rare'.

## Estimates and Test Statistics

The test statistics for
$\mathrm{H}_{0}: p_{1}=p_{2}$
versus
$\mathrm{H}_{A}: p_{1} \neq p_{2}$

|  |  | Estimated <br> Standard Error | $Z-$ Statistic <br> (Est/SE) |
| :--- | :--- | :--- | :--- |
| RISK DIFF | .0077 | .00154 | 5.00 |
| log(RR) | .598 <br> $(R R=1.818)$ | .1212 | 4.934 |
|  |  |  |  |
| log(OR) | Estimate |  |  |
|  | $(\mathrm{OR}=1.832)$ | .1228 | 4.927 |
|  |  |  |  |

- In each case, we reject the null, and the $Z$-statistic is about 5 .


## Confidence Intervals Creation

- The following are the $95 \%$ confidence intervals

| Parameter | Estimate | $95 \%$ C.I. |
| :--- | :--- | :--- |
| RISK DIFF | .0077 | $[.0047, .0107]$ |
| RR | 1.818 | $[1.433,2.306]$ |
| OR | 1.832 | $[1.440,2.331]$ |

- For the $O R$ and $R R$, we exponentiated the $95 \%$ confidence intervals for the $\log (O R)$ and $\log (R R)$, respectively.
- None of the confidence intervals contain the null value for no association (0 for the RISK DIFFERENCE, 1 for the OR and RR).


## Interpretation

- The risk difference has the interpretation that the
'Excess Risk' of a heart attack on Placebo is .0077. This 'fraction' is not very meaningful for rare diseases, but stated in terms of subjects, we can say that we would expect 77 more heart attacks in 10000 placebo subjects than in 10000 aspirin users.
- The relative risk has the interpretation that

Individuals on Placebo have almost twice (1.8) the risk (or probability) of a heart attack than individuals on Aspirin

- The odds ratio has the interpretation that

Individuals on Placebo have almost twice (1.8) the odds of a heart attack versus no heart attack than individuals on Aspirin

## Relationship between OR and RR

- Recall,

$$
\begin{aligned}
O R & =\frac{p_{1} /\left(1-p_{1}\right)}{p_{2} /\left(1-p_{2}\right)} \\
O R & =\frac{p_{1} /\left(1-p_{1}\right)}{p_{2} /\left(1-p_{2}\right)} \\
& =\left(\frac{p_{1}}{p_{2}}\right)\left[\frac{1-p_{2}}{1-p_{1}}\right] \\
& =R R\left[\frac{1-p_{2}}{1-p_{1}}\right]
\end{aligned}
$$

- When the disease is rare (in the example, $\widehat{p}_{2}<\widehat{p}_{1}<2 \%$ ),

$$
\left[\frac{1-p_{2}}{1-p_{1}}\right] \approx \frac{1}{1}=1 ; \quad \text { and } \quad O R \approx R R .
$$

- In the example, $\widehat{O R}=1.832, \widehat{R R}=1.818$; i.e., they are almost identical.


## Likelihood Ratio Test

- Now, we want to test the null hypothesis

$$
\mathrm{H}_{0}: p_{1}=p_{2}=p
$$

versus the alternative

$$
\mathrm{H}_{A}: p_{1} \neq p_{2}
$$

with the likelihood ratio statistic (the likelihood ratio statistic generally has a two-sided alternative...i.e., it is $\chi^{2}$ based).

- The general likelihood ratio statistic involves the estimate of $p_{1}=p_{2}=p$ under the null and $\left(p_{1}, p_{2}\right)$ under the alternative.
- Thus, unlike the simple single binomial sample we discussed earlier, in which the null was

$$
\mathrm{H}_{0}: p=.5
$$

the parameters are not completely specified under the null. i.e., we must still estimate a common $p$ under the null for the likelihood ratio.

## General Likelihood Ratio Statistic

- The likelihood is a function of the parameter vector $\mathbf{p}=\left[p_{1}, p_{2}\right]^{\prime}$.
- In large samples, it can be shown that

$$
\begin{aligned}
& 2 \log \left\{\frac{L\left(\widehat{p}_{1}, \widehat{p}_{2} \mid \mathrm{H}_{A}\right)}{L\left(\tilde{p}_{1}, \tilde{p}_{2} \mid \mathrm{H}_{0}\right)}\right\}= \\
& \quad 2\left[\log L\left(\widehat{p}_{1}, \widehat{p}_{2} \mid \mathrm{H}_{A}\right)-\log L\left(\tilde{p}_{1}, \tilde{p}_{2} \mid \mathrm{H}_{0}\right)\right] \sim \chi_{d f}^{2}
\end{aligned}
$$

- where

$$
L\left(\widehat{p}_{1}, \widehat{p}_{2} \mid \mathrm{H}_{A}\right)
$$

is the likelihood after replacing $\left[p_{1}, p_{2}\right]$ by its estimate, $\left[\widehat{p}_{1}, \widehat{p}_{2}\right]$ under $\mathrm{H}_{A}$

- and

$$
L\left(\tilde{p}_{1}, \tilde{p}_{2} \mid \mathrm{H}_{0}\right)
$$

is the likelihood after replacing [ $p_{1}, p_{2}$ ] by its estimate, $\left[\tilde{p}_{1}, \tilde{p}_{2}\right]$, under $\mathrm{H}_{0}$ (In our case, $\left[\tilde{p}_{1}, \tilde{p}_{2}\right]=[\widehat{p}, \widehat{p}]^{\prime}$ since $p_{1}=p_{2}=p$ under the null $)$.

- and the degrees-of-freedom $d f$ is the difference in the number of parameters estimated under the alternative and null (In our example, $d f=2-1=1$ ).


## MLE under the Null

- Thus, to use the likelihood ratio statistic, we need to estimate the common $p$ under the null hypothesis.
- When $\mathrm{H}_{0}: p_{1}=p_{2}=p$,

$$
E\left(Y_{1}\right)=n_{1} p
$$

and

$$
E\left(Y_{2}\right)=n_{2} p
$$

- Then,

$$
E\left(Y_{1}+Y_{2}\right)=E\left(Y_{1}\right)+E\left(Y_{2}\right)=n_{1} p+n_{2} p=\left(n_{1}+n_{2}\right) p
$$

- The 'pooled' estimate of $p$ is

$$
\widehat{p}=\left(\frac{Y_{1}+Y_{2}}{n_{1}+n_{2}}\right)=\left(\frac{\text { total } \# \text { successes }}{\text { total sample size }}\right)
$$

which is unbiased and the MLE.

- Intuitively, when the probability of success is the same on both treatments, the best estimate (MLE) of $p$ is obtained by pooling over the treatments.


## Using the likelihood to obtain the MLE under the null

- Under the null $\mathrm{H}_{0}: p_{1}=p_{2}=p$, the MLE of $p$ is obtained from the likelihood

$$
\begin{aligned}
L(p) & =\binom{n_{1}}{y_{1}}\binom{n_{2}}{y_{2}} p^{y_{1}}(1-p)^{n_{1}-y_{1}} p^{y_{2}}(1-p)^{n_{2}-y_{2}} \\
& =\binom{n_{1}}{y_{1}}\binom{n_{2}}{y_{2}} p^{y_{1}+y_{2}}(1-p)^{\left(n_{1}+n_{2}\right)-\left(y_{1}+y_{2}\right)},
\end{aligned}
$$

- Then,

$$
\begin{aligned}
\frac{d \log L(p)}{d p}= & \frac{d}{d p_{1}} \log \left[\binom{n_{1}}{y_{1}}\binom{n_{2}}{y_{2}}\right] \\
& +\frac{d}{d p_{1}} \log \left[p^{y_{1}+y_{2}}(1-p)^{\left(n_{1}+n_{2}\right)-\left(y_{1}+y_{2}\right)}\right] \\
= & \frac{y_{1}+y_{2}-\left(n_{1}+n_{2}\right) p}{p(1-p)}
\end{aligned}
$$

- This is the same first derivative as a single binomial sample, in fact, under the null,

$$
Y_{1}+Y_{2} \sim \operatorname{Bin}\left(n_{1}+n_{2}, p\right)
$$

and it is easily shown that the solution is

$$
\widehat{p}=\frac{Y_{1}+Y_{2}}{n_{1}+n_{2}}
$$

## Using the Estimates to obtain the Likelihood Ratio Statistic

- Under the alternative,

$$
\widehat{p}_{1}=\frac{Y_{1}}{n_{1}} \quad \text { and } \quad \widehat{p}_{2}=\frac{Y_{2}}{n_{2}}
$$

and

$$
\begin{aligned}
& \log \left[L\left(\widehat{p}_{1}, \widehat{p}_{2} \mid \mathrm{H}_{A}\right)\right]= \\
& \log \binom{n_{1}}{y_{1}}+y_{1} \log \left(\widehat{p}_{1}\right)+\left(n_{1}-y_{1}\right) \log \left(1-\widehat{p}_{1}\right)+ \\
& \quad \log \binom{n_{2}}{y_{2}}+y_{2} \log \left(\widehat{p}_{2}\right)+\left(n_{2}-y_{2}\right) \log \left(1-\widehat{p}_{2}\right)
\end{aligned}
$$

Then,

$$
\begin{aligned}
& \log \left[L\left(\widehat{p}, \widehat{p} \mid H_{0}\right)\right]= \\
& \log \binom{n_{1}}{y_{1}}+y_{1} \log (\widehat{p})+\left(n_{1}-y_{1}\right) \log (1-\widehat{p})+ \\
& \quad \log \binom{n_{2}}{y_{2}}+y_{2} \log (\widehat{p})+\left(n_{2}-y_{2}\right) \log (1-\widehat{p})
\end{aligned}
$$

- Under the alternative, we estimate 2 parameters, under the null, we estimated 1, so $d f=2-1=1$.
- Then, we take 2 times the differences in the log-likelihoods and compare it to a chi-square with 1 df .


## Simplification of the Likelihood Ratio Statistic

- Then, the likelihood ratio statistic equals 2 times the difference in the log-likelihoods under the alternative and null, or

$$
\begin{aligned}
G^{2}= & 2\left[y_{1} \log \left(\frac{\widehat{p}_{1}}{\widehat{\widehat{p}}}\right)+\left(n_{1}-y_{1}\right) \log \left(\frac{\left(1-\widehat{p}_{1}\right)}{(1-\widehat{p})}\right)\right. \\
& \left.+y_{2} \log \left(\frac{\widehat{p}_{2}}{\widehat{p}}\right)+\left(n_{2}-y_{2}\right) \log \left(\frac{\left(1-\widehat{p}_{2}\right)}{(1-\widehat{p})}\right)\right] \\
= & 2\left[y_{1} \log \left(\frac{y_{1}}{n_{1} \widehat{p}}\right)+\left(n_{1}-y_{1}\right) \log \left(\frac{n_{1}-y_{1}}{n_{1}(1-\widehat{p})}\right)+\right. \\
& \left.+y_{2} \log \left(\frac{y_{2}}{n_{2} \widehat{p}}\right)+\left(n_{2}-y_{2}\right) \log \left(\frac{n_{2}-y_{2}}{n_{2}(1-\widehat{p})}\right)\right] \\
& \sim \chi_{1}^{2}
\end{aligned}
$$

under the null, in large samples.

## ‘OBSERVED’ and ‘EXPECTED’ Cell Counts

- First, let's look at the $(2 \times 2)$ table of ‘OBSERVED’ Cell Counts.

|  |  | OUTCOME |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  |  | 1 | 2 |  |
| TRT | 1 | $Y_{1}$ | $\left(n_{1}-Y_{1}\right)$ | $n_{1}$ |
|  | 2 | $Y_{2}$ | $\left(n_{2}-Y_{2}\right)$ | $n_{2}$ |
| total |  | $Y_{1}+Y_{2}$ | $\left[\left(n_{1}+n_{2}\right)\right.$ |  |
|  |  |  | $\left.\left(Y_{1}+Y_{1}\right)\right]$ |  |

- If we look at the likelihood ratio statistic,

$$
\begin{aligned}
G^{2}= & 2\left[y_{1} \log \left(\frac{y_{1}}{n_{1} \widehat{p}}\right)+\left(n_{1}-y_{1}\right) \log \left(\frac{n_{1}-y_{1}}{n_{1}(1-\widehat{p})}\right)+\right. \\
& \left.+y_{2} \log \left(\frac{y_{2}}{n_{2} \overparen{p}}\right)+\left(n_{2}-y_{2}\right) \log \left(\frac{n_{2}-y_{2}}{n_{2}(1-\widehat{p})}\right)\right]
\end{aligned}
$$

- In the numerator of the log's, we have the observed cell counts for the 4 cells in the table.
- Sometimes, statisticians let

$$
O_{i j}
$$

denote the observed count in row $i$, column $j$,

$$
O_{11}=Y_{1}, \quad O_{12}=n_{1}-Y_{1}, \quad O_{21}=Y_{2}, \quad O_{22}=n_{2}-Y_{2}
$$

- Then, we can rewrite the observed table as

|  |  | OUTCOME |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | $O_{11}$ | $O_{12}$ | $O_{11}+O_{12}$ |
| TRT | 1 |  |  |  |
|  | 2 | $O_{21}$ | $O_{22}$ | $O_{21}+O_{22}$ |
| total | $O_{11}+O_{21}$ | $O_{12}+O_{22}$ |  |  |

- We will show that the likelihood ratio statistic is often written as

$$
\begin{aligned}
G^{2}= & 2\left[y_{1} \log \left(\frac{y_{1}}{n_{1} \widehat{p}}\right)+\left(n_{1}-y_{1}\right) \log \left(\frac{n_{1}-y_{1}}{n_{1}(1-\widehat{p})}\right)+\right. \\
& \left.+y_{2} \log \left(\frac{y_{2}}{n_{2} \widehat{p}}\right)+\left(n_{2}-y_{2}\right) \log \left(\frac{n_{2}-y_{2}}{n_{2}(1-\widehat{p})}\right)\right] \\
= & 2 \sum_{i=1}^{2} \sum_{j=1}^{2} O_{i j} \log \left(\frac{O_{i j}}{E_{i j}}\right)
\end{aligned}
$$

## Simple Form of the Estimated Expected Counts

- First, suppose $p_{1} \neq p_{2}$,
- Then, the $(2 \times 2)$ table of expected cell counts is

|  |  | OUTCOME |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  |  | 1 | 2 |  |
| TRT | 1 | $n_{1} p_{1}$ | $n_{1}\left(1-p_{1}\right)$ | $n_{1}$ |
|  | 2 | $n_{2} p_{2}$ | $n_{2}\left(1-p_{2}\right)$ | $n_{2}$ |
| total | $n_{1} p_{1}+n_{2} p_{2}$ | $\left[\left(n_{1}+n_{2}\right)\right.$ | $\left(n_{1}+n_{2}\right)$ |  |
|  |  |  | $\left.-\left(n_{1} p_{1}+n_{2} p_{2}\right)\right]$ |  |

- If we look at the $n_{1}$ subjects in the first row, we expect $n_{1} p_{1}$ subjects to have outcome 1 , and $n_{1}\left(1-p_{1}\right)$ of them to have outcome 2 .
- Similarly, if we look at the $n_{2}$ subjects in the second row, we expect $n_{2} p_{2}$ subjects to have outcome 1, and $n_{2}\left(1-p_{2}\right)$ of them to have outcome 2.
- Under the null, when the probability of success is the same on both treatments, $p_{1}=p_{2}=p$, the table of expected counts looks like

|  |  | OUTCOME |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | 2 |  |  |
| TRT | 1 | $n_{1} p$ | $n_{1}(1-p)$ | $n_{1}$ |
|  | 2 | $n_{2} p$ | $n_{2}(1-p)$ | $n_{2}$ |
| total | $\left(n_{1}+n_{2}\right) p$ | $\left[\left(n_{1}+n_{2}\right)(1-p)\right]$ | $\left(n_{1}+n_{2}\right)$ |  |

- Here, if we look at the $n_{1}$ subjects in the first row, we expect $n_{1} p$ subjects to have outcome 1, and $n_{1}(1-p)$ of them to have outcome 2 .
- Similarly, if we look at the $n_{2}$ subjects in the second row, we expect $n_{2} p$ subjects to have outcome 1, and $n_{2}(1-p)$ of them to have outcome 2 .
- Under $H_{0}: p_{1}=p_{2}=p$, the table of estimated expected counts looks like

|  |  | OUTCOME |  |  |
| :--- | :---: | :---: | :---: | :---: |
|  |  | 1 | 2 |  |
| TRT | 1 | $n_{1} \widehat{p}$ | $n_{1}(1-\widehat{p})$ | $n_{1}$ |
|  | 2 | $n_{2} \widehat{p}$ | $n_{2}(1-\widehat{p})$ | $n_{2}$ |
| total |  | $\left(n_{1}+n_{2}\right) \widehat{p}$ | $\left[\left(n_{1}+n_{2}\right)(1-\widehat{p})\right]$ | $\left(n_{1}+n_{2}\right)$ |

- where, recall, $\widehat{p}$ is the 'pooled' estimate of $p$,

$$
\widehat{p}=\left(\frac{Y_{1}+Y_{2}}{n_{1}+n_{2}}\right)=\left(\frac{\text { total } \# \text { successes }}{\text { total sample size }}\right) .
$$

- These estimated expected counts are denoted $E_{i j}$, $\left(i^{t h}\right.$ row, $j^{\text {th }}$ column $)$, and are found in the denominator of the likelihood ratio statistic, with

$$
E_{11}=n_{1} \widehat{p}, \quad E_{12}=n_{1}(1-\widehat{p}), \quad E_{21}=n_{2} \widehat{p}, \quad E_{22}=n_{2}(1-\widehat{p})
$$

## Simplification of Expected Cell Counts

- Substituting

$$
\widehat{p}=\frac{Y_{1}+Y_{2}}{n_{1}+n_{2}}
$$

and

$$
1-\widehat{p}=1-\frac{Y_{1}+Y_{2}}{n_{1}+n_{2}}=\frac{\left(n_{1}+n_{2}\right)-\left(Y_{1}+Y_{2}\right)}{n_{1}+n_{2}}
$$

in the table, we get the $E_{i j}$ 's,

|  |  | OUTCOME |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  |  | 1 | 2 |  |
|  | 1 | $\frac{n_{1}\left(Y_{1}+Y_{2}\right)}{n_{1}+n_{2}}$ | $\frac{n_{1}\left[\left(n_{1}+n_{2}\right)-\left(Y_{1}+Y_{2}\right)\right]}{n_{1}+n_{2}}$ | $n_{1}$ |
| TRT |  | $\frac{n_{2}\left(Y_{1}+Y_{2}\right)}{n_{1}+n_{2}}$ | $\frac{n_{2}\left[\left(n_{1}+n_{2}\right)-\left(Y_{1}+Y_{2}\right)\right]}{n_{1}+n_{2}}$ | $n_{2}$ |
| total | 2 | $\left(Y_{1}+Y_{2}\right)$ | $\left[\left(n_{1}+n_{2}\right)\right.$ | $\left(n_{1}+n_{2}\right)$ |
|  |  | $\left.-\left(Y_{1}+Y_{2}\right)\right]$ |  |  |

- From this table, you can see that

$$
E_{i j}=\frac{\left[i^{t h} \text { row total }\right] \cdot\left[j^{t h} \text { column total }\right]}{\left[\text { total sample size }\left(n_{1}+n_{2}\right)\right]}
$$

## Summary

- We did all this to show that

$$
G^{2}=2 \sum_{i=1}^{2} \sum_{j=1}^{2} O_{i j} \log \left(\frac{O_{i j}}{E_{i j}}\right)
$$

- Note that, we can also write this as

$$
G^{2}=2 \sum_{i=1}^{2} \sum_{j=1}^{2} O_{i j}\left[\log \left(O_{i j}\right)-\log \left(E_{i j}\right)\right]
$$

- Writing it this way, we see that the likelihood ratio measures the discrepancy between the log of the observed counts, and the log of estimated expected counts under the null; if they are similar, you would expect the statistic to be small, and the null not to be rejected.

