

# Contingency Tables

## 2 x 2 tables

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Apply a treatment to 20 mice from strains A and B, and observe survival.

	N	Y	
A	18	2	20
B	11	9	20
	29	11	40

Question:

→ Are the survival rates in the two strains the same?

Gather 100 rats and determine whether they are infected with viruses A and B.

	I-B	NI-B	
I-A	9	9	18
NI-A	20	62	82
	29	71	100

Question:

→ Is infection with virus A independent of infection with virus B?

## Underlying probabilities

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→ Observed data

		B		
		0	1	
A	0	$n_{00}$	$n_{01}$	$n_{0+}$
	1	$n_{10}$	$n_{11}$	$n_{1+}$
		$n_{+0}$	$n_{+1}$	$n$

→ Underlying probabilities

		B		
		0	1	
A	0	$p_{00}$	$p_{01}$	$p_{0+}$
	1	$p_{10}$	$p_{11}$	$p_{1+}$
		$p_{+0}$	$p_{+1}$	$1$

Model:

$$(n_{00}, n_{01}, n_{10}, n_{11}) \sim \text{Multinomial}(n, \{p_{00}, p_{01}, p_{10}, p_{11}\})$$

or

$$n_{01} \sim \text{Binomial}(n_{0+}, p_{01}/p_{0+}) \quad \text{and} \quad n_{11} \sim \text{Binomial}(n_{1+}, p_{11}/p_{1+})$$

## Conditional probabilities

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Underlying probabilities

		B		
		0	1	
A	0	$p_{00}$	$p_{01}$	$p_{0+}$
	1	$p_{10}$	$p_{11}$	$p_{1+}$
		$p_{+0}$	$p_{+1}$	$1$

Conditional probabilities

$$\Pr(B = 1 \mid A = 0) = p_{01}/p_{0+}$$

$$\Pr(B = 1 \mid A = 1) = p_{11}/p_{1+}$$

$$\Pr(A = 1 \mid B = 0) = p_{10}/p_{+0}$$

$$\Pr(A = 1 \mid B = 1) = p_{11}/p_{+1}$$

→ The questions in the two examples are the same!

They both concern:  $p_{01}/p_{0+} = p_{11}/p_{1+}$

Equivalently:  $p_{ij} = p_{i+} \times p_{+j}$  for all  $i, j$  → think  $\Pr(A \text{ and } B) = \Pr(A) \times \Pr(B)$ .

## This is a composite hypothesis!

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2 x 2 table

		B		
		0	1	
A	0	$p_{00}$	$p_{01}$	$p_{0+}$
	1	$p_{10}$	$p_{11}$	$p_{1+}$
		$p_{+0}$	$p_{+1}$	1

A different view

$p_{00}$	$p_{01}$	$p_{10}$	$p_{11}$
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$$H_0: p_{ij} = p_{i+} \times p_{+j} \text{ for all } i, j$$

$$H_0: p_{ij} = p_{i+} \times p_{+j} \text{ for all } i, j$$

$$\text{Degrees of freedom} = 4 - 2 - 1 = 1$$

## Expected counts

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Observed data

		B		
		0	1	
A	0	$n_{00}$	$n_{01}$	$n_{0+}$
	1	$n_{10}$	$n_{11}$	$n_{1+}$
		$n_{+0}$	$n_{+1}$	$n$

Expected counts

		B		
		0	1	
A	0	$e_{00}$	$e_{01}$	$n_{0+}$
	1	$e_{10}$	$e_{11}$	$n_{1+}$
		$n_{+0}$	$n_{+1}$	$n$

To get the expected counts under the null hypothesis we:

- Estimate  $p_{1+}$  and  $p_{+1}$  by  $n_{1+}/n$  and  $n_{+1}/n$ , respectively.  
These are the MLEs under  $H_0$ !
- Turn these into estimates of the  $p_{ij}$ .
- Multiply these by the total sample size,  $n$ .

## The expected counts

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The expected count (assuming  $H_0$ ) for the “11” cell is the following:

$$\begin{aligned}e_{11} &= n \times \hat{p}_{11} \\ &= n \times \hat{p}_{1+} \times \hat{p}_{+1} \\ &= n \times (n_{1+}/n) \times (n_{+1}/n) \\ &= (n_{1+} \times n_{+1})/n\end{aligned}$$

The other cells are similar.

→ We can then calculate a  $\chi^2$  or LRT statistic as before!

## Example 1

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Observed data				Expected counts			
	N	Y		N	Y		
A	18	2	20	A	14.5	5.5	20
B	11	9	20	B	14.5	5.5	20
	29	11	40		29	11	40

$$\chi^2 = \frac{(18-14.5)^2}{14.5} + \frac{(11-14.5)^2}{14.5} + \frac{(2-5.5)^2}{5.5} + \frac{(9-5.5)^2}{5.5} = 6.14$$

$$\text{LRT} = 2 \times \left[ 18 \log\left(\frac{18}{14.5}\right) + \dots + 9 \log\left(\frac{9}{5.5}\right) \right] = 6.52$$

P-values (based on the asymptotic  $\chi^2$ (df = 1) approximation):

1.3% and 1.1%, respectively.

## Example 2

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Observed data				Expected counts			
	I-B	NI-B		I-B	NI-B		
I-A	9	9	18	I-A	5.2	12.8	18
NI-A	20	62	82	NI-A	23.8	58.2	82
	29	71	100		29	71	100

$$\chi^2 = \frac{(9-5.2)^2}{5.2} + \frac{(20-23.8)^2}{23.8} + \frac{(9-12.8)^2}{12.8} + \frac{(62-58.2)^2}{58.2} = 4.70$$

$$\text{LRT} = 2 \times \left[ 9 \log\left(\frac{9}{5.2}\right) + \dots + 62 \log\left(\frac{62}{58.2}\right) \right] = 4.37$$

P-values (based on the asymptotic  $\chi^2$ (df = 1) approximation):  
3.0% and 3.7%, respectively.

## Fisher's exact test

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Observed data			
	N	Y	
A	18	2	20
B	11	9	20
	29	11	40

- Assume the null hypothesis (independence) is true.
- Constrain the marginal counts to be as observed.
- What's the chance of getting this exact table?
- What's the chance of getting a table at least as "extreme"?

# Hypergeometric distribution

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- Imagine an urn with  $K$  white balls and  $N - K$  black balls.
- Draw  $n$  balls **without** replacement.
- Let  $x$  be the number of white balls in the sample.
- $x$  follows a hypergeometric distribution (w/ parameters  $K, N, n$ ).

	In urn		
	white	black	
sampled	x		n
not sampled			N - n
	K	N - K	N

# Hypergeometric probabilities

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Suppose  $X \sim \text{Hypergeometric}(N, K, n)$ .

No. of white balls in a sample of size  $n$ , drawn without replacement from an urn with  $K$  white and  $N - K$  black.

$$\Pr(X = x) = \frac{\binom{K}{x} \binom{N-K}{n-x}}{\binom{N}{n}}$$

Example:

	In urn		$N = 40, K = 29, n = 20$
	0	1	
sampled	18	2	20
not			20
	29	11	40

$$\Pr(X = 18) = \frac{\binom{29}{18} \binom{40-29}{20-18}}{\binom{40}{20}} \approx 1.4\%$$

## The hypergeometric in R

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```
dhyper(x, m, n, k)
phyper(q, m, n, k)
qhyper(p, m, n, k)
rhyper(nn, m, n, k)
```

In R, things are set up so that

m = no. white balls in urn

n = no. black balls in urn

k = no. balls sampled (without replacement)

x = no. white balls in sample

nn = no. of observations

## Back to Fisher's exact test

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Observed data

	N	Y	
A	18	2	20
B	11	9	20
	29	11	40

- Assume the null hypothesis (independence) is true.
- Constrain the marginal counts to be as observed.
- $\Pr(\text{observed table} \mid H_0) = \Pr(X=18)$   
 $X \sim \text{Hypergeometric}(N=40, K=29, n=20)$

## Fisher's exact test

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1. For all possible tables (with the observed marginal counts), calculate the relevant hypergeometric probability.
2. Use that probability as a statistic.
3. P-value (for Fisher's exact test of independence):
  - The sum of the probabilities for all tables having a probability equal to or smaller than that observed.

## An illustration

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The observed data

	N	Y	
A	18	2	20
B	11	9	20
	29	11	40

All possible tables (with these marginals):

20 0 9 11	→ 0.00007	14 6 15 5	→ 0.25994
19 1 10 10	→ 0.00160	13 7 16 4	→ 0.16246
18 2 11 9	→ 0.01380	12 8 17 3	→ 0.06212
17 3 12 8	→ 0.06212	11 9 18 2	→ 0.01380
16 4 13 7	→ 0.16246	10 10 19 1	→ 0.00160
15 5 14 6	→ 0.25994	9 11 20 0	→ 0.00007



## Fisher's exact test: example 1

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Observed data

	N	Y	
A	18	2	20
B	11	9	20
	29	11	40

P-value  $\approx$  3.1%

In R: `fisher.test()`

Recall:

→  $\chi^2$  test: P-value = 1.3%

→ LRT: P-value = 1.1%

## Fisher's exact test: example 2

---

Observed data

	I-B	NI-B	
I-A	9	9	18
NI-A	20	62	82
	29	71	100

P-value  $\approx$  4.4%

Recall:

→  $\chi^2$  test: P-value = 3.0%

→ LRT: P-value = 3.7%

## Summary

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Testing for independence in a 2 x 2 table:

- A special case of testing a composite hypothesis in a one-dimensional table.
- You can use either the LRT or  $\chi^2$  test, as before.
- You can also use Fisher's exact test.
- If Fisher's exact test is computationally feasible, do it!

## Paired data

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Gather 100 rats and determine whether they are infected with viruses A and B.

Underlying probabilities

	I-B	NI-B	
I-A	9	9	18
NI-A	20	62	82
	29	71	100

		B		
		0	1	
A	0	$p_{00}$	$p_{01}$	$p_{0+}$
	1	$p_{10}$	$p_{11}$	$p_{1+}$
		$p_{+0}$	$p_{+1}$	1

→ Is the rate of infection of virus A the same as that of virus B?

In other words: Is  $p_{1+} = p_{+1}$ ? Equivalently, is  $p_{10} = p_{01}$ ?

## McNemar's test

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$H_0: p_{01} = p_{10}$

Under  $H_0$ , e.g. if  $p_{01} = p_{10}$ , the expected counts for cells 01 and 10 are both equal to  $(n_{01} + n_{10})/2$ .

The  $\chi^2$  test statistic reduces to  $X^2 = \frac{(n_{01} - n_{10})^2}{n_{01} + n_{10}}$

For large sample sizes, this statistic has null distribution that is approximately a  $\chi^2(df = 1)$ .

For the example:  $X^2 = (20 - 9)^2 / 29 = 4.17 \rightarrow P = 4.1\%$ .

## An exact test

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Condition on  $n_{01} + n_{10}$ .

Under  $H_0$ ,  $n_{01} \mid n_{01} + n_{10} \sim \text{Binomial}(n_{01} + n_{10}, 1/2)$ .

In R, use the function `binom.test`.

→ For the example,  $P = 6.1\%$ .

## Paired data

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Paired data				Unpaired data			
	I-B	NI-B		I	NI		
I-A	9	9	18	A	18	82	100
NI-A	20	62	82	B	29	71	100
	29	71	100		47	153	200

→ P = 6.1%

→ P = 9.5%

→ Taking appropriate account of the “pairing” is important!

## r x k tables

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Population	Blood type				
	A	B	AB	O	
Florida	122	117	19	244	502
Iowa	1781	1351	289	3301	6721
Missouri	353	269	60	713	1395
	2256	1737	367	4258	8618

→ Same distribution of blood types in each population?

## Underlying probabilities

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Observed data

	1	2	...	k	
1	$n_{11}$	$n_{12}$	$\cdots$	$n_{1k}$	$n_{1+}$
2	$n_{21}$	$n_{22}$	$\cdots$	$n_{2k}$	$n_{2+}$
$\vdots$	$\vdots$	$\vdots$	$\cdots$	$\vdots$	$\vdots$
r	$n_{r1}$	$n_{r2}$	$\cdots$	$n_{rk}$	$n_{r+}$
	$n_{+1}$	$n_{+2}$	$\cdots$	$n_{+k}$	$n$

Underlying probabilities

	1	2	...	k	
1	$p_{11}$	$p_{12}$	$\cdots$	$p_{1k}$	$p_{1+}$
2	$p_{21}$	$p_{22}$	$\cdots$	$p_{2k}$	$p_{2+}$
$\vdots$	$\vdots$	$\vdots$	$\cdots$	$\vdots$	$\vdots$
r	$p_{r1}$	$p_{r2}$	$\cdots$	$p_{rk}$	$p_{r+}$
	$p_{+1}$	$p_{+2}$	$\cdots$	$p_{+k}$	1

$$H_0: p_{ij} = p_{i+} \times p_{+j} \quad \text{for all } i, j.$$

## Expected counts

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Observed data

	A	B	AB	O	
F	122	117	19	244	502
I	1781	1351	289	3301	6721
M	353	269	60	713	1395
	2256	1737	367	4258	8618

Expected counts

	A	B	AB	O	
F	131	101	21	248	502
I	1759	1355	286	3321	6721
M	365	281	59	689	1395
	2256	1737	367	4258	8618

$$\text{Expected counts under } H_0: e_{ij} = n_{i+} \times n_{+j} / n \quad \text{for all } i, j.$$

## $\chi^2$ and LRT statistics

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### Observed data

	A	B	AB	O	
F	122	117	19	244	502
I	1781	1351	289	3301	6721
M	353	269	60	713	1395
	2256	1737	367	4258	8618

### Expected counts

	A	B	AB	O	
F	131	101	21	248	502
I	1759	1355	286	3321	6721
M	365	281	59	689	1395
	2256	1737	367	4258	8618

$$X^2 \text{ statistic} = \sum \frac{(\text{obs} - \text{exp})^2}{\text{exp}} = \dots = 5.64$$

$$\text{LRT statistic} = 2 \times \sum \text{obs} \ln(\text{obs}/\text{exp}) = \dots = 5.55$$

## Asymptotic approximation

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If the sample size is large, the null distribution of the  $\chi^2$  and likelihood ratio test statistics will approximately follow a

$\chi^2$  distribution with  $(r - 1) \times (k - 1)$  d.f.

In the example,  $\text{df} = (3 - 1) \times (4 - 1) = 6$

$X^2 = 5.64 \rightarrow P = 0.46.$

$\text{LRT} = 5.55 \rightarrow P = 0.48.$

# Fisher's exact test

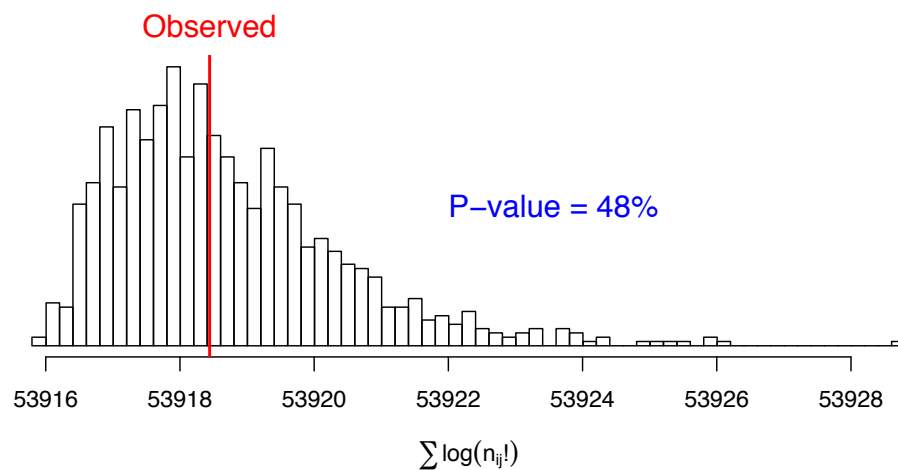
Observed data

	1	2	...	k	
1	$n_{11}$	$n_{12}$	...	$n_{1k}$	$n_{1+}$
2	$n_{21}$	$n_{22}$	...	$n_{2k}$	$n_{2+}$
...	...	...	...	...	...
r	$n_{r1}$	$n_{r2}$	...	$n_{rk}$	$n_{r+}$
	$n_{+1}$	$n_{+2}$	...	$n_{+k}$	$n$

- Assume  $H_0$  is true.
- Condition on the marginal counts
- Then  $\Pr(\text{table}) \propto 1 / \prod_{ij} n_{ij}!$

- Consider all possible tables with the observed marginal counts
- Calculate  $\Pr(\text{table})$  for each possible table.
- P-value = the sum of the probabilities for all tables having a probability equal to or smaller than that observed.

## Fisher's exact test: the example



- Since the number of possible tables can be very large, we often must resort to computer simulation.

## Another example

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Survival following treatment in five mouse strains:

Strain	Survive	
	No	Yes
A	15	5
B	17	3
C	10	10
D	17	3
E	16	4

→ Is the survival rate the same for all strains?

## Results

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Observed			Expected under $H_0$		
Strain	Survive		Strain	Survive	
	No	Yes		No	Yes
A	15	5	A	15	5
B	17	3	B	15	5
C	10	10	C	15	5
D	17	3	D	15	5
E	16	4	E	15	5

$X^2 = 9.07$  →  $P = 5.9\%$  (how many df?)

LRT = 8.41 →  $P = 7.8\%$

Fisher's exact test:  $P = 8.7\%$



## All pairwise comparisons

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	N	Y	
A	15	5	→ P=69%
B	17	3	

	N	Y	
B	17	3	→ P=4.1%
C	10	10	

	N	Y	
C	10	10	→ P=9.6%
E	16	4	

	N	Y	
A	15	5	→ P=19%
C	10	10	

	N	Y	
B	17	3	→ P=100%
D	17	3	

	N	Y	
D	17	3	→ P=100%
E	16	4	

	N	Y	
A	15	5	→ P=69%
D	17	3	

	N	Y	
B	17	3	→ P=100%
E	16	4	

	N	Y	
A	15	5	→ P=100%
E	16	4	

	N	Y	
C	10	10	→ P=4.1%
D	17	3	

Is this a good thing to do?

## Two-locus linkage in an intercross

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	BB	Bb	bb
AA	6	15	3
Aa	9	29	6
aa	3	16	13

Are these two loci linked?

## General test of independence

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Observed data

	BB	Bb	bb
AA	6	15	3
Aa	9	29	6
aa	3	16	13

Expected counts

	BB	Bb	bb
AA	4.3	14.4	5.3
Aa	7.9	26.4	9.7
aa	5.8	19.2	7.0

$\chi^2$  test:  $X^2 = 10.4 \rightarrow P = 3.5\%$  (df = 4)

LRT test:  $LRT = 9.98 \rightarrow P = 4.1\%$

Fisher's exact test:  $P = 4.6\%$

## A more specific test

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Observed data

	BB	Bb	bb
AA	6	15	3
Aa	9	29	6
aa	3	16	13

Underlying probabilities

	BB	Bb	bb
AA	$\frac{1}{4}(1 - \theta)^2$	$\frac{1}{2}\theta(1 - \theta)$	$\frac{1}{4}\theta^2$
Aa	$\frac{1}{2}\theta(1 - \theta)$	$\frac{1}{2}[\theta^2 + (1 - \theta)^2]$	$\frac{1}{2}\theta(1 - \theta)$
aa	$\frac{1}{4}\theta^2$	$\frac{1}{2}\theta(1 - \theta)$	$\frac{1}{4}(1 - \theta)^2$

$H_0: \theta = 1/2$  versus  $H_a: \theta < 1/2$

Use a likelihood ratio test!

- Obtain the general MLE of  $\theta$ .
- Calculate the LRT statistic =  $2 \ln \left\{ \frac{\Pr(\text{data} | \hat{\theta})}{\Pr(\text{data} | \theta=1/2)} \right\}$
- Compare this statistic to a  $\chi^2(\text{df} = 1)$ .

## Results

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	BB	Bb	bb
AA	6	15	3
Aa	9	29	6
aa	3	16	13

MLE:  $\hat{\theta} = 0.359$

LRT statistic:  $LRT = 7.74 \rightarrow P = 0.54\%$  (df = 1)

- Here we assume Mendelian segregation, and that deviation from  $H_0$  is “in a particular direction.”
- If these assumptions are correct, we’ll have greater power to detect linkage using this more specific approach.