Contents

Combination of trials

centre 1

	S	F	
trt	30	70	30%S
plac	120	180	40%S
	150	250	

centre 2

	S	F	
trt	210	90	70%
plac	80	20	80%
	290	110	

- **centre 1**
  - looks like **placebo** better?
  - (χ^2 = 3.2, n.s.)
- **centre 2**
  - looks like **placebo** better?
  - (χ^2 = 3.76, n.s.)

centre 1 & 2

	S	F	
trt	240	160	60%S
plac	200	200	50%S
	440	360	

It looks like the **treatment** is better; (χ^2 =8.08, highly significant)

- i.e. **Simpson's Paradox**
  - Difference in overall S rates in two centres
    - 30–40% in centre 1
    - 70–80% in centre 2
  - ***i.e. centre differences***
  - *i.e. 'hidden factor'*: – 'centre'

- Really need a more complex model with Centre as a factor
  - e.g. log-linear model (see PAS372) or
  - logistic regression (see later & PAS372)
- Treatment x Centre interaction

- Always need to check (at least informally) that centres / tables are comparable before combining them.
- i.e. 'response rates' comparable

- Is there a way of combining the tables which avoids this problem when response rates are different?
  - Yes – **Mantel-Haenszel Test**
    - takes information from each table separately
- First, M-H Test for a single table:-

- **Mantel-Haenszel Test**

	Successes	Failures	
Treatments	Y_1	$n_1 - Y_1$	n_1
Placebo	Y_2	$n_2 - Y_2$	n_2
	t	n–t	n

- Can shew that
  - $E(Y_1)=n_1t/n$
  - $V(Y_1)=n_1n_2t(n-t)/n^2(n-1)$
- So
  $T_{MH} = [Y_1-E(Y_1)]^2/V(Y_1) \sim\chi_1^2$ under H_0
  - If $T_{MH} > \chi_{1;1-\alpha}^2$ then $p < \alpha$ and there is a significant treatment difference.

- **Example**

	S	F	total
Trt	30	70	100
plac	120	180	300
total	150	250	400

  - $E[Y_1]=100\times150/400=37.5$
  - $V(Y_1)=100\times300\times150\times250/400^2\times399=17.6$
  - $T_{MH} = [Y_1-E(Y_1)]^2/V(Y_1)=(37.5-30)^2/17.6$
  - =3.19 (almost same as before)

- Asymptotically equivalent to usual χ^2 test
- ***Mantel-Haenszel*** or *Randomization* test
- Can use Y_1, Y_2, $n–Y_1$ or $n–Y_2$.
- Combining several tables simple.
  - We use $W=\Sigma Y_{1j}$ then
    - $E(W)= \Sigma E(Y_{1j})$
    - $V(W)=\Sigma V(Y_{1j})$
    - $[W-E(W)]^2/V(W) \sim\chi_1^2$ under H_0 again

- **Example**

	S	F	total
Trt	210	90	300
Plac	80	20	100
Total	290	110	400

  - $E[Y_1]=290\times300/400=217.5$
  - $V(Y_1)=300\times100\times110\times290/400^2\times399=14.99$
  - $T_{MH} = [Y_1-E(Y_1)]^2/V(Y_1)=(210-217.5)^2/14.99$
  - =3.75 (almost same as before)

- **Combined:-**
  - $Y_{11}+Y_{12}=30+210=240$
  - $E[Y_{11}+Y_{12}] = 37.5+217.5 = 255.0$
  - $V(Y_{11}+Y_{12}) =1\ 7.6+14.99 = 32.59$
  - $T_{MH} = [Y_1-E(Y_1)]^2/V(Y_1) = (240-255.0)^2/32.59$
  - $= 6.9 > \chi_1{}^2{}_{;0.95} = 3.84$
    - (***different*** from before)
  - & conclude good evidence that **placebo** is better

- **Summary and Conclusions**
  - Simpson's Paradox
    - if response rates and sample sizes are very different
  - Resolve Simpson's paradox by more sophisticated modelling with 'trial effect'
  - Mantel-Haenszel test
    - easier to combine results from different trials
  - M-H does not overcome Simpson's Paradox
    - but it *avoids* it