SESSION 11 – SOLUTIONS

Sample Size Determination Practical

a) On placebo expect

$p_{1C} = 0.05$
$p_{2C} = 0.20$
$p_{3C} = 0.40$
$p_{4C} = 0.25$
$p_{5C} = 0.10$

giving cumulative probabilities

$Q_{1C} = 0.05$
$Q_{2C} = 0.25$
$Q_{3C} = 0.65$
$Q_{4C} = 0.90$
$Q_{5C} = 1.00$

Wish to detect improvement of "Markedly or Slightly Improved" from 25% to 35%

$$\theta_R = \log\left\{\frac{0.35(1-0.25)}{0.25(1-0.35)}\right\}$$

$$= 0.480$$

Under the proportional odds model

$$Q_{kT} = \frac{e^{\theta_R} Q_{kC}}{(1-Q_{kC}) + e^{\theta_R} Q_{kC}} \qquad \text{for } k = 1,..., 4$$

$Q_{1T} = 0.08$
$Q_{2T} = 0.35$
$Q_{3T} = 0.75$
$Q_{4T} = 0.94$
$Q_{5T} = 1.00$

so that

$p_{1T} = 0.08$	$\bar{p}_1 = 0.064$
$p_{2T} = 0.27$	$\bar{p}_2 = 0.236$
$p_{3T} = 0.40$	$\bar{p}_3 = 0.400$
$p_{4T} = 0.19$	$\bar{p}_4 = 0.218$
$p_{5T} = 0.06$	$\bar{p}_5 = 0.082$

$$1-\left(\bar{p}_1^{\,3}+\bar{p}_2^{\,3}+\bar{p}_3^{\,3}+\bar{p}_4^{\,3}+\bar{p}_5^{\,3}\right)=1-0.088=0.912$$

$\alpha = 0.05$ $\quad U_{\alpha/2} = 1.96$

$1-\beta = 0.8$ $\quad U_{\beta} = 0.84$

Hence

$$n=\frac{12}{0.912}\left(\frac{1.96+0.842}{0.480}\right)^2=449$$

require 225 patients on each treatment

b) Create 4 categories by combining categories 1 and 2

$\bar{p}_1 + \bar{p}_2 = 0.300$

$\bar{p}_3 = 0.400$

$\bar{p}_4 = 0.218$

$\bar{p}_5 = 0.082$

$$1-\left\{\left(\bar{p}_1+\bar{p}_2\right)^3+\bar{p}_3^{\,3}+\bar{p}_4^{\,3}+\bar{p}_5^{\,3}\right\}=1-0.102=0.898$$

$$n=\frac{12}{0.898}\left(\frac{1.96+0.842}{0.480}\right)^2=457$$

require 229 patients on each treatment

c) Create 3 categories

$\bar{p}_1 + \bar{p}_2 = 0.300$

$\bar{p}_3 = 0.400$

$\bar{p}_4 + \bar{p}_5 = 0.300$

$$1-\left\{\left(\bar{p}_1+\bar{p}_2\right)^3+\bar{p}_3^{\,3}+\left(\bar{p}_4+\bar{p}_5\right)^3\right\}=1-0.118=0.882$$

$$n=\frac{12}{0.882}\left(\frac{1.96+0.842}{0.480}\right)^2=465$$

require 233 patients on each treatment

d) Create 2 categories

$\bar{p}_1 + \bar{p}_2 = 0.300$

$\bar{p}_3 + \bar{p}_4 + \bar{p}_5 = 0.700$

$$1-\left\{\left(\bar{p}_1+\bar{p}_2\right)^3+\left(\bar{p}_3+\bar{p}_4+\bar{p}_5\right)^3\right\}=1-0.37=0.63$$

$$n=\frac{12}{0.63}\left(\frac{1.96+0.842}{0.480}\right)^2=651$$

require 326 patients on each treatment

Notes on ordered categorical data

Construction of categories

$$n = \frac{12\left(U_{\alpha/2} + U_{\beta}\right)^2}{\theta_R^2\left(1 - \sum_{k=1}^{m} \overline{p}_k^{\;3}\right)}$$

When α, $1-\beta$ and θ_R are fixed

$$n \propto \left(1 - \sum_{k=1}^{m} \overline{p}_k^{\;3}\right)^{-1}$$

If investigators have control over the definition of categories, then m, and the likely values of $\overline{p}_1, \ldots, \overline{p}_m$ can be chosen to minimise n.

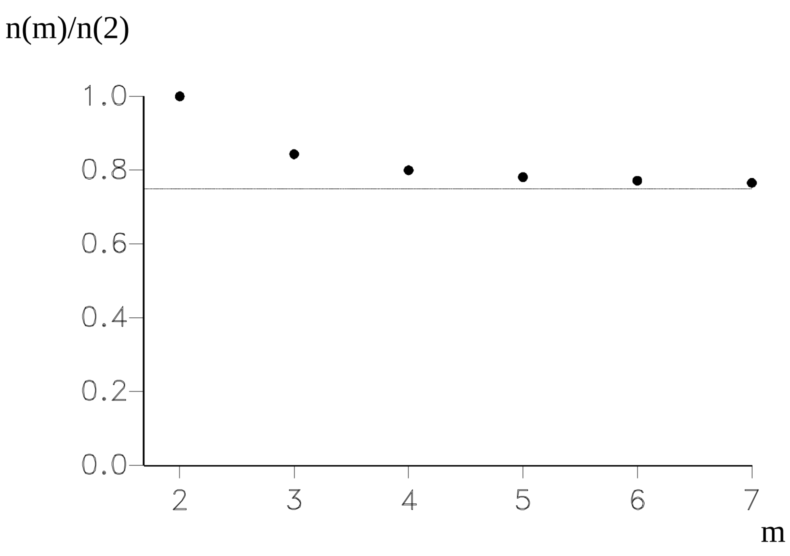
Choice of m

If categories are equally likely, $\overline{p}_1 = \ldots = \overline{p}_m = \frac{1}{m}$,

$$\left(1 - \sum_{k=1}^{m} \overline{p}_k^{\;3}\right) = \left(1 - \frac{1}{m^2}\right).$$

and the sample size as a function of m, n(m) is given by

$$n(m) = 0.75\, n(2)\left(1 - \frac{1}{m^2}\right)^{-1}$$



Choice of $\bar{p}_1, \ldots, \bar{p}_m$

For m = 4

$\bar{p}_1$	$\bar{p}_2$	$\bar{p}_3$	$\bar{p}_4$	n/n_0
0.25	0.25	0.25	0.25	1
0.10	0.20	0.30	0.40	1.04
0.10	0.30	0.30	0.30	1.14
0.05	0.05	0.45	0.45	1.15
0.10	0.10	0.10	0.70	1.43

where n_0 is sample size for equally likely categories

If possible, choose equally likely categories.

If possible, avoid dominant categories.