Medical Statistics (MATH38071) Exercise Sheet 10

(Meta-analysis)

1. The table below summarizes the outcome of three trials comparing dietary advice given by a dietician with that given by a nurse for patients for with high blood cholesterol. The treatment effect for each trial ($\hat{\theta}_i$, i = 1,2,3) is the difference in mean cholesterol between the dietician group and the nurse group. $Var\left[\hat{\theta}_i\right]$ is the sample variance estimate of the ith study.

Study	Reduction in blood cholesterol, $\hat{\theta}_i$	$Var\left[\hat{\theta}_i\right]$
O'Donoghue(1993)	0.34	0.0289
Ahmed (2001)	0.18	0.0729
Cohen (2003)	0.27	0.0676

(i)   Compute the minimum variance estimate of the overall treatment effect, $\hat{\theta}_{MV}$, and determine its 95% confidence interval, stating any assumptions you make.

(ii)   By calculating the p-value, test the hypothesis $H_0 : \theta = 0$ vs $H_1 : \theta \neq 0$ using a 5% significance level.

(iii)   What do you conclude from the meta-analysis?

2.   The table below summarizes the outcome for three trials testing a new drug against the standard treatment for patients with heart failure giving the survival after two years follow-up.

Study	New Died	New Alive	New N	Standard Died	Standard Alive	Standard N
A	33	214	247	45	201	246
B	6	61	67	12	58	70
C	5	44	49	7	41	48

(i)   From the data in the table estimate the odds ratio of death (OR) and $\log_e\left[OR\right]$ for each trial for New compared to Standard drug treatment.

(ii)   From the data in the table estimate the variance and standard error of $\log_e\left[OR\right]$ for each trial.

(iii)   Calculate the 95% confidence interval of the odds ratio (OR) for each trial.

(iv)   Determine the minimum variance estimate of the pooled log odds ratio.

(v)   Determine the standard error of the estimate from (iv).

(vi)   From (iv) and (v) calculate the 95% confidence interval the estimate of the pooled odds ratio).

(vii)   Using the estimate from (iv) and the standard error obtained from (v) test the hypothesis

$H_0 : OR = 1$ vs $H_1 : OR \neq 1$ using a 5% significance level.

(viii) Using the results of (i), (iii), (v) and (vi) sketch a forest plot of the odds ratio for your meta-analysis.

(ix)   Briefly comment on the results of the meta-analysis as compared to the results for individual trials.

Hint: To reduce the burden of calculation you may wish to carry out the calculation in parts (i)- (vii) using a spreadsheet such as Excel by copying the data from the online version of the exercise sheet.

3. Briefly comment on the funnel plot showing the results of a meta-analysis of 49 published trials considering the effectiveness of acupuncture for the treatment of Stroke.

http://www.bmj.com/cgi/content/full/319/7203/160

Funnel Plot

4. The forest and funnel plots below illustrates a meta-analysis of trials evaluating the efficacy of probiotics in prevention of diarrhoea associated with taking antibiotics. The trials estimate the odds ratio of diarrhoea after taking a probiotics dietary supplement compared to placebo. By examining the two figures consider whether there is evidence of publication bias.

Forest Plot

Study	Odds ratio	Odds ratio (95% CI)	Weight (%)
Surawicz[33*]		0.37 (0.16 to 0.88)	15.1
McFarland[37*]		0.46 (0.18 to 1.18)	12.1
Lewis[38*]		1.67 (0.47 to 5.89)	3.5
Adam[31*]		0.22 (0.10 to 0.48)	29.9
Tankanow[35]		0.88 (0.22 to 3.52)	3.9
Vanderhoof[39]		0.23 (0.09 to 0.56)	21.2
Orrhage[36]		0.58 (0.07 to 4.56)	2.2
Wunderlich[34]		0.25 (0.05 to 1.43)	5.2
Gotz[32]		0.34 (0.09 to 1.38)	7.0
Overall		0.37 (0.26 to 0.52)	

Funnel Plot

[http://www.bmj.com/cgi/content/full/324/7350/1361].