FORMULAS FOR PRECISION BASED –INVERSE VARIANCE- METHODS (BINARY OUTCOMES AND CONTINUOUS OUTCOMES –MEANS-)

1. BINARY OUTCOMES

- FIXED EFFECT MODEL

Total (for trial *i*)	Exposed	Event	Non event		For person-time data
	Yes	a_i	b_i	n_{1i}	PT_{1i}
	No	c_i	d_i	n_{0i}	PT_{0i}
	Total$_i$	m_{1i}	m_{0i}	n_i	

Individual (by trial) statistics:

- $Risk\ Diff. = I_e - I_0 = \frac{a}{n_1} - \frac{c}{n_0}$; $se(RD) = \sqrt{\frac{I_e(1-I_e)}{n_1} + \frac{I_0(1-I_0)}{n_0}} = \sqrt{\frac{a \cdot b}{n_1^3} + \frac{c \cdot d}{n_0^3}}$

  $NNT = 1/Risk\ Diff.$ $\qquad IC100(1\text{-}a): RD \pm Z_{a/2}\ se(RD)$

- $RateDiff. = R_e - R_0 = \frac{a}{PT_1} - \frac{c}{PT_0}$; $se(RaD) = \sqrt{\frac{R_e}{PT_1} + \frac{R_o}{PT_0}} = \sqrt{\frac{a}{PT_1^2} + \frac{c}{PT_0^2}}$

  $IC100(1\text{-}a): RaD \pm Z_{a/2}\ se(RaD)$

- $RR = \frac{a/n_1}{c/n_0}$; $VAR[\ln(RR)] = \frac{1}{a} - \frac{1}{n_1} + \frac{1}{c} - \frac{1}{n_0}$; $\qquad IC100(1\text{-}a): e^{\ln(RR) \pm Z_{a/2}\sqrt{VAR[\ln(RR)]}}$

- $OR = \frac{a/b}{c/d} = \frac{ad}{bc}$; $VAR[\ln(OR)] = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$; $\qquad IC100(1\text{-}a): e^{\ln(OR) \pm Z_{a/2}\sqrt{VAR[\ln(OR)]}}$

- $RaR = \frac{a/PT_1}{c/PT_0}$; $\quad VAR[\ln(RaR)] = \frac{1}{a} + \frac{1}{c}$; $\qquad IC100(1\text{-}a): e^{\ln(RaR) \pm Z_{a/2}\sqrt{VAR[\ln(RaR)]}}$

Pooled statistics:

Notation:

- *k=Nr. of trials*
- $d_i = RD_i\ or\ RaD_i\ or \ln(RR_i)\ or \ln(OR_i)\ or \ln(RateR_i)$
- $w_i = \frac{1}{VAR(d_i)}$

$$Pooled\ Statistic: \quad d_P = \frac{\sum_{i=1}^{K} w_i d_i}{\sum_{i=1}^{K} w_i} \qquad se(d_P) = \sqrt{\frac{1}{\sum w_i}}$$

$d_P = RD_P\ or\ RaD_P\ or \ln(RR_P)\ or \ln(OR_P)\ or \ln(RateR_P)$

Relative weight: $w_i(\%) = 100\frac{w_i}{\sum w_i}$

Association & heterogeneity Chi-square:

Association Chi-square: $c_1^2 = d_P^2 \sum_{i=1}^{k} w_i$ $\qquad$ *Heterogeneity Chi-square:* $Q = c_{k-1}^2 = \sum_{i=1}^{k} w_i (d_i - d_P)^2$

Total Chi-square: $c_k^2 = \sum_{i=1}^{k} w_i d_i^2$ $\qquad$ *Higgins&Thompson H statistic:* $H = \sqrt{Q/(k-1)}$

- **RANDOM-EFFECTS MODEL**

Notation:

- *k=Nr. of trials*
- $d_i = RD_i \; or \; RaD_i \; or \ln(RR_i) \; or \ln(OR_i) \; or \ln(RateR_i)$
- $d_P = RD_P \; or \; RaD_P \; or \ln(RR_P) \; or \ln(OR_P) \; or \ln(RateR_P)$
- $w_i = \dfrac{1}{VAR(d_i)}$

The heterogeneity before taking τ^2 into consideration is the same as before:

$$Q = c^2_{k-1} = \sum_{i=1}^{k} w_i (d_i - d_P)^2$$

Tau-square:

$$T = \frac{\sum_{i=1}^{k} w_i d_i^2 - \left(\sum_{i=1}^{k} w_i d_i\right)^2 \Big/ \sum_{i=1}^{k} w_i - (K-1)}{\sum_{i=1}^{k} w_i - \sum_{i=1}^{k} w_i^2 \Big/ \sum_{i=1}^{k} w_i} = \frac{Q-(K-1)}{\sum_{i=1}^{k} w_i - \sum_{i=1}^{k} w_i^2 \Big/ \sum_{i=1}^{k} w_i}$$

$t^2 = T \quad if \; T > 0$

$t^2 = 0 \quad if \; T \le 0$

To calculate the pooled statistics (Dersimonian-Laird), the variance is first increased by τ^2:

var'=var+τ^2 $\qquad$ w_i'=1/var'

$$Pooled\,Statistic: \quad DL = \frac{\sum_{i=1}^{K} w'_i \, d_i}{\sum_{i=1}^{K} w'_i} \qquad se(DL) = \sqrt{\frac{1}{\sum w'_i}}$$

$DL = RD_P \; or \; RaD_P \; or \; \ln(RR_P) \; or \; \ln(OR_P) \; or \ln(RateR_P)$

Relative weight: $w'_i\,(\%) = 100\,\dfrac{w'_i}{\sum w'_i}$

Association Chi-square: $c^2_1 = d^2_P \sum_{i=1}^{k} w_i$

2. CONTINUOUS OUTCOMES

- **FIXED-EFFECT MODEL**

Individual (by trial) statistics:

Trial	Treated			Control			N_i	sd_i
i	$\bar{x}_{1i}$	sd_{1i}	n_{1i}	$\bar{x}_{2i}$	sd_{2i}	n_{2i}	$n_{1i}+n_{2i}$	$\sqrt{\dfrac{(n_{1i}-1)sd^2_{1i} + (n_{2i}-1)sd^2_{2i}}{N_i - 2}}$

WMD_i	$se(WMD)_i$	g_i	$se(g)_i$
$\bar{x}_{1i} - \bar{x}_{2i}$	$\sqrt{sd^2_{1i}/n_{1i} + sd^2_{2i}/n_{2i}}$	$(1 - 3/(4N_i - 9))(\bar{x}_{1i} - \bar{x}_{2i})/s_i$	$\sqrt{N_i/(n_{1i}n_{2j}) + g_i^2/(2(N_i - 3.94))}$

Pooled statistics:

$$Pooled\,WMD. = \frac{\sum w_i WMD_i}{\sum w_i} \qquad w_i = \frac{1}{VAR(WMD_i)} = \frac{1}{ee(WMD_i)^2} \qquad se(Pooled\,WMD) = \sqrt{\frac{1}{\sum w_i}}$$

$$Pooled\,g. = \frac{\sum w_i g_i}{\sum w_i} \qquad w_i = \frac{1}{VAR(g_i)} = \frac{1}{ee(g_i)^2} \qquad se(Pooled\,g) = \sqrt{\frac{1}{\sum w_i}}$$

Association & heterogeneity Chi-square:

Notation:

- *k=Nr. of trials*
- $d_i = WMD_i \text{ or } g_i$
- $d_P = WMD_P \text{ or } g_P$
- $w_i = \frac{1}{VAR(d_i)}$

Association Chi-square: $c_1^2 = d_P^2 \sum_{i=1}^{k} w_i$ Heterogeneity Chi-square: $Q = c_{k-1}^2 = \sum_{i=1}^{k} w_i (d_i - d_P)^2$

Higgins&Thompson H statistic: $H = \sqrt{Q/(k-1)}$

- **RANDOM-EFFECTS MODEL**

The heterogeneity before taking τ^2 into consideration is the same as before:

$$Q = c_{k-1}^2 = \sum_{i=1}^{k} w_i (d_i - d_P)^2$$

$$T = \frac{\sum_{i=1}^{k} w_i d_i^2 - \left(\sum_{i=1}^{k} w_i d_i\right)^2 \Big/ \sum_{i=1}^{k} w_i - (K-1)}{\sum_{i=1}^{k} w_i - \sum_{i=1}^{k} w_i^2 \Big/ \sum_{i=1}^{k} w_i} = \frac{Q-(K-1)}{\sum_{i=1}^{k} w_i - \sum_{i=1}^{k} w_i^2 \Big/ \sum_{i=1}^{k} w_i}$$

$t^2 = T \quad if\ T > 0$
$t^2 = 0 \quad if\ T \le 0$

To calculate the pooled statistics (Dersimonian-Laird), the variance is first increased by τ^2:

var'=var+τ^2 w_i'=1/var'

$$DL\,WMD. = \frac{\sum w'_i\, WMD_i}{\sum w'_i} \qquad se(Pooled\,WMD) = \sqrt{\frac{1}{\sum w'_i}}$$

$$DL\,g. = \frac{\sum w'_i\, g_i}{\sum w'_i} \qquad se(Pooled\,g) = \sqrt{\frac{1}{\sum w'_i}}$$

Relative weight: $w'_i\,(\%) = 100\,\frac{w'_i}{\sum w'_i}$

Association Chi-square: $c_1^2 = d_P^2 \sum_{i=1}^{k} w_i$

Good references to learn meta-analysis (from on-line journals):

http://www.bmj.com

- Sharp SJ, Thompson SG, Altman DG. The relation between treatment benefit and underlying risk in meta-analysis. BMJ 1996;313:735-738

- Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-634

- Tramèr MR, Reynolds DJM, Moore RA, McQuay HJ. Impact of covert duplicate publication on meta-analysis: a case study. BMJ 1997;315:635-640

- Egger M, Smith GD. Meta-analysis: Potentials and promise. BMJ 1997;315:1371-1374

- Egger M, Smith GD, Phillips AN. Meta-analysis: Principles and procedures. BMJ 1997;315:1533-1537

- Smith GD, Egger M, Phillips AN. Meta-analysis: Beyond the grand mean? BMJ 1997;315:1610-1614

- Egger M, Schneider M, Smith GD. Meta-analysis Spurious precision? Meta-analysis of observational Studies. BMJ 1998;316:140-144

- Egger M, Smith GD. Meta-analysis bias in location and selection of studies. BMJ 1998;316:61-66

- Smith GD, Egger M. Meta-analysis: Unresolved issues and future developments. BMJ 1998;316:221-225

http://www.acponline.org/journals/annals/01nov97/quantsyn.htm

- Lau J, Ioannidis JPA, Schmid CH. Quantitative synthesis in systematic reviews. Ann Inter Med 1997;127:820-6.