

3 Primary Scientific Question

How do we assess pooled results of multiple studies, how do we assess heterogeneity between the studies.

4 Data Example, Pooling

A meta-analysis of the difference in systolic blood pressures (mm Hg) between patients treated with potassium and those with placebo. Diff = difference in systolic blood pressure between patients on potassium and placebo, var = variance = (standard error)²

	N	diff (systolic)	standard error	1/var	diff/var	diff ² /var
1. McGregor 1982	23	-7.0	3.1	0.104	-0.728	5.096
2. Siani 1987	37	-14.0	4.0	0.063	-0.875	12.348
3. Svetkey 1987	101	-6.4	1.9	0.272	-1.773	11.346
4. Krishna 1989	10	-5.5	3.8	0.069	-0.380	2.087
5. Obel 1989	48	-41.0	2.6	0.148	-6.065	248.788
6. Patki 1990	37	-12.1	2.6	0.148	-1.791	21.669
7. Fotherby 1992	18	-10.0	3.8	0.069	-0.693	6.900
8. Brancati 1996	87	-6.9	1.2	0.694	-4.792	33.041
9. Gu 2001	150	-5.0	1.4	0.510	-2.551	12.750
10. Sarkkinen 2011	45	-11.3	4.8	0.043	-0.490	5.091
						+
				2.125	-20.138	359.516

Pooled difference = $-20.138/2.125$ = -9.48 mm Hg

Chi-square value for pooled data = $(-20.138)^2 / 2.125$ = 206.91

According to the chi-square table the p-value for 1 degree of freedom = <0.001

The underneath chi-square table has an upper row with areas under the curve, a left-end column with degrees of freedom, and a whole lot of chi-square values.

Chi-squared distribution

<i>df</i>	Two-tailed <i>P</i> -value			
	0.10	0.05	0.01	0.001
1	2.706	3.841	6.635	10.827
2	4.605	5.991	9.210	13.815
3	6.251	7.851	11.345	16.266

(continued)

<i>df</i>	Two-tailed <i>P</i> -value			
	0.10	0.05	0.01	0.001
4	7.779	9.488	13.277	18.466
5	9.236	11.070	15.086	20.515
6	10.645	12.592	16.812	22.457
7	12.017	14.067	18.475	24.321
8	13.362	15.507	20.090	26.124
9	14.684	16.919	21.666	27.877
10	15.987	18.307	23.209	29.588
11	17.275	19.675	24.725	31.264
12	18.549	21.026	26.217	32.909
13	19.812	22.362	27.688	34.527
14	21.064	23.685	29.141	36.124
15	22.307	24.996	30.578	37.698
16	23.542	26.296	32.000	39.252
17	24.769	27.587	33.409	40.791
18	25.989	28.869	34.805	42.312
19	27.204	30.144	36.191	43.819
20	28.412	31.410	37.566	45.314
21	29.615	32.671	38.932	46.796
22	30.813	33.924	40.289	48.268
23	32.007	35.172	41.638	49.728
24	33.196	36.415	42.980	51.179
25	34.382	37.652	44.314	52.619
26	35.536	38.885	45.642	54.051
27	36.741	40.113	46.963	55.475
28	37.916	41.337	48.278	56.892
29	39.087	42.557	49.588	58.301
30	40.256	43.773	50.892	59.702
40	51.805	55.758	63.691	73.403
50	63.167	67.505	76.154	86.660
60	74.397	79.082	88.379	99.608
70	85.527	90.531	100.43	112.32
80	96.578	101.88	112.33	124.84
90	107.57	113.15	124.12	137.21
100	118.50	124.34	135.81	149.45

5 Data Example, Assessing Heterogeneity

The above example will now be assessed for heterogeneity.

Heterogeneity of this meta-analysis is tested by the fixed effect model.

Heterogeneity chi-square value = 359.516-206.91
= 152.6,
With 9 degrees of freedom the p -value
= <0.001.

Although the meta-analysis shows a significantly lower systolic blood pressure in patients with potassium treatment than those with placebo, this result has a limited meaning, since the studies are significantly heterogeneous. For heterogeneity testing it is tested whether there is a greater inequalities between the results of the separate trials than is compatible with the play of chance. Additional tests for heterogeneity testing are available (Cleophas and Zwinderman, *Meta-analysis. In: Statistics Applied to Clinical Studies*, Springer New York, 2012, 5th edition, pp 365–388). However, when there is heterogeneity, a careful investigation of its potential cause is often more important than a lot of additional statistical tests.

6 Conclusion

Meta-analyses are systematic reviews of multiple published studies with pooled data. Because the separate studies have different sample sizes a weighted average has to be calculated. Heterogeneity in a meta-analysis means that the differences in the results between the studies are larger than could happen by chance. With a significant heterogeneity the meaning of the pooled data is generally little.

Additional tests for heterogeneity testing are available in *Statistics Applied to Clinical Studies* 5th edition, Chaps 32–34, Springer New York, 2012). However, with significant heterogeneity in a meta-analysis, a careful investigation of its potential cause is more important than lots of statistical tests.

7 Note

More background, theoretical and mathematical information of meta-analysis given in *Statistics applied to clinical studies* 5th edition, Chaps. 32–34, Springer Heidelberg Germany, 2012, from the same authors.