Normally Distributed Outcomes

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Effect Sizes based on Means

Main reference: Chapter 2 and 8 from Hartung, J., Knapp, G., and Sinha, B.K. (2008): Statistical Meta-Analysis with Applications. Wiley, Hoboken, New Jersey.

- Denote the population means of the two groups (experimental and control) by μ_1 and μ_2, and their variances by σ_1^2 and σ_2^2, respectively.

- Standardized difference between μ_1 and μ_2

$$\theta = \frac{\mu_1 - \mu_2}{\sigma},$$

  where σ denotes either the standard deviation σ_2 of the population control group, or an average population standard deviation (namely, an average of σ_1 and σ_2).

Effect Sizes based on Means

- Suppose we have a random sample of size n_1 from the first population with the sample mean $\bar{X}_1$ and sample variance S_1^2, and also a random sample of size n_2 from the second population with the sample mean $\bar{X}_2$ and sample variance S_2^2.

- Cohen's d:

$$d = \frac{\bar{X}_1 - \bar{X}_2}{S},$$

where

$$S^2 = \frac{(n_1 - 1)\, S_1^2 + (n_2 - 1)\, S_2^2}{n_1 + n_2}.$$

Effect Sizes based on Means

- Hedges's g:

$$g = \frac{\bar{X}_1 - \bar{X}_2}{S^*},$$

where

$$S^{*2} = \frac{(n_1 - 1)\, S_1^2 + (n_2 - 1)\, S_2^2}{n_1 + n_2 - 2}.$$

- It can be shown that

$$\begin{aligned} \mathsf{E}(g) &\approx \theta + \frac{3\,\theta}{4(n_1 + n_2) - 9} \\ \mathsf{Var}(g) &\approx \frac{n_1 + n_2}{n_1\ n_2} + \frac{\theta^2}{2(n_1 + n_2 - 3.94)} \end{aligned}$$

Effect Sizes based on Means

- In case $\sigma_1^2 = \sigma_2^2$ and under the assumption of normality of the data, it holds that $\sqrt{\tilde{n}}\, g$ follows a non-central t-distribution with non-centrality parameter $\sqrt{\tilde{n}}\,\theta$ and $(n_1 + n_2 - 2)$ degrees of freedom, $\tilde{n} = n_1\, n_2/(n_1 + n_2)$.

- With $N = n_1 + n_2$, the mean and variance of Hedges's g are given by

$$
\begin{aligned}
\mathsf{E}(g) &= \sqrt{\frac{N-2}{2}}\,\frac{\Gamma\left(\frac{N-3}{2}\right)}{\Gamma\left(\frac{N-2}{2}\right)}\,\theta \\
\mathsf{Var}(g) &= \frac{N-2}{N-4}\left(\frac{1}{\tilde{n}} + \theta^2\right) - \theta^2\,\frac{N-2}{2}\,\frac{\left(\Gamma\left(\frac{N-3}{2}\right)\right)^2}{\left(\Gamma\left(\frac{N-2}{2}\right)\right)^2}
\end{aligned}
$$

and $\Gamma(\cdot)$ denotes the gamma function.

Effect Sizes based on Means

- Approximately *unbiased* estimator g^* of the standardized mean difference is given as

$$g^* = \left(1 - \frac{3}{4(n_1 + n_2) - 9}\right) \; g$$

- Estimate of the variance

$$\widehat{\mathsf{Var}}(g^*) = \frac{n_1 + n_2}{n_1 \, n_2} + \frac{g^2}{2\,(n_1 + n_2 - 2)}$$

- Large-sample confidence interval

$$g^* \pm \sqrt{\widehat{\mathsf{Var}}(g)} \; z_{1-\alpha/2}$$

Effect Sizes based on Means

Typical data situation for meta-analysis

Studies of two anaesthetic agents relating to recovery time

Study	Total sample size	Standardized mean difference (g)	Unbiased standardized mean difference (g^*)
1	76	0.72	0.71
2	6167	0.06	0.06
3	355	0.59	0.59
4	1050	0.43	0.43
5	136	0.27	0.27
6	2925	0.89	0.89
7	45222	0.35	0.35

Example

Results of eight randomized controlled trials comparing the effectiveness of amlodipine and a placebo on work capacity

Protocol	Amlodipine 10 mg (E)			Placebo (C)		
	n_{Ei}	$\bar{y}_{Ei}$	s^2_{Ei}	n_{Ci}	$\bar{y}_{Ci}$	s^2_{Ci}
154	46	0.2316	0.2254	48	-0.0027	0.0007
156	30	0.2811	0.1441	26	0.0270	0.1139
157	75	0.1894	0.1981	72	0.0443	0.4972
162A	12	0.0930	0.1389	12	0.2277	0.0488
163	32	0.1622	0.0961	34	0.0056	0.0955
166	31	0.1837	0.1246	31	0.0943	0.1734
303A	27	0.6612	0.7060	27	-0.0057	0.9891
306	46	0.1366	0.1211	47	-0.0057	0.1291

Example: R Code

```
# Data in the first group (sample size, mean, and variance)
n1   <- c(    46,     30,     75,     12,     32,     31,     27,     46)
x1   <- c(0.2316, 0.2811, 0.1894, 0.0930, 0.1622, 0.1837, 0.6612, 0.1366)
var1 <- c(0.2254, 0.1441, 0.1981, 0.1389, 0.0961, 0.1246, 0.7060, 0.1211)
#
# Data in the second group (sample size, mean, and variance)
n2   <- c(     48,     26,     72,     12,     34,     31,      27,      47)
x2   <- c(-0.0027, 0.0270, 0.0443, 0.2277, 0.0056, 0.0943, -0.0057, -0.0057)
var2 <- c( 0.0007, 0.1139, 0.4972, 0.0488, 0.0955, 0.1734,  0.9891,  0.1291)
#
# load package
library(meta)
# use of metacont function
meta.1 <- metacont(n1, x1, sqrt(var1), n2, x2, sqrt(var2), sm="SMD")
meta.2 <- metacont(n1, x1, sqrt(var1), n2, x2, sqrt(var2), sm="SMD", hakn=T)
```

Example: R Output (slightly modified)

```
> summary(meta.1)

                          SMD            95%-CI      z  p-value
Fixed effect model   0.4202 [0.2570; 0.5834] 5.0465 < 0.0001
Random effects model 0.4237 [0.2259; 0.6215] 4.1988 < 0.0001

Quantifying heterogeneity:
tau^2 = 0.0225; H = 1.18 [1; 1.76]; I^2 = 28.1% [0%; 67.8%]

Test of heterogeneity:
    Q d.f.  p-value
 9.74    7   0.2037

Details on meta-analytical method:
- Inverse variance method
- DerSimonian-Laird estimator for tau^2
- Hedges' g (bias corrected standardised mean difference)
```

Example: R Output (slightly modified)

```
> summary(meta.2)

                        SMD            95%-CI    z|t  p-value
Fixed effect model   0.4202 [0.2570; 0.5834] 5.0465 < 0.0001
Random effects model 0.4237 [0.1759; 0.6716] 4.0428   0.0049

*** Heterogeneity statistics erased ***

Details on meta-analytical method:
- Inverse variance method
- DerSimonian-Laird estimator for tau^2
- Hartung-Knapp adjustment for random effects model
- Hedges' g (bias corrected standardised mean difference)
```

Effect Size based on Correlations

- An effect size based on correlation is directly taken as the value of the correlation ρ itself.

- Or its well known ζ-value, based on Fisher's variance-stabilizing transformation (of r), given by

$$\zeta = \frac{1}{2}\left[\ln\frac{1+\rho}{1-\rho}\right].$$

- These measures are readily estimated by the sample correlation r (for ρ), or its transformed version z (for ζ) given by

$$z = \frac{1}{2}\left[\ln\frac{1+r}{1-r}\right]$$

Effect Size based on Correlations

- Approximate variances of r and z

$$\begin{aligned} \mathsf{Var}(r) &\approx (1-\rho^2)^2/(n-1) \\ \mathsf{Var}(z) &\approx 1/(n-3). \end{aligned}$$

- Large sample tests for $H_0 : \rho = 0$ versus $H_1 : \rho \neq 0$ are typically based on the standardized normal statistics

$$Z_1 = \frac{r\sqrt{n-1}}{(1-r^2)}$$

$$Z_2 = z\sqrt{n-3}$$

Example for Correlation

Validity studies correlating student ratings of the instructor with student achievement

Study	n	r	Study	n	r
1	10	0.68	11	36	-0.11
2	20	0.56	12	75	0.27
3	13	0.23	13	33	0.26
4	22	0.64	14	121	0.40
5	28	0.49	15	37	0.49
6	12	-0.04	16	14	0.51
7	12	0.49	17	40	0.40
8	36	0.33	18	16	0.34
9	19	0.58	19	14	0.42
10	12	0.18	20	20	0.16

Example for Correlation: R Code

```
library(meta)
# sample sizes
n <- c(  10,   20,   13,  22, ... ,  40,   16,   14,   20)
# correlations
r <- c(0.68, 0.56, 0.23,0.64, ... ,0.40, 0.34, 0.42, 0.16)
# approximate standard error
se.r <-sqrt( (1- r^2)/(n-1))
# Fisher's z-transformation
z <- 0.5 * log((1+r)/(1-r))
# Two meta-analyses
meta.r.1 <- metagen(r, se.r, method.tau="PM")
meta.r.2 <- metagen(z, sqrt(1/(n-3)), method.tau="PM")
```

Example for Correlation: R Output (slightly modified)

```
> summary(meta.r.1)
                                         95%-CI      z  p-value
Fixed effect model   0.3743 [0.2996; 0.4491] 9.8149 < 0.0001
Random effects model 0.3743 [0.2996; 0.4491] 9.8149 < 0.0001

Quantifying heterogeneity:
tau^2 = 0; H = 1.06 [1; 1.35]; I^2 = 10.2% [0%; 45.5%]

Test of heterogeneity:
     Q d.f.  p-value
 21.17   19   0.3277

Details on meta-analytical method:
- Inverse variance method
- Paule-Mandel estimator for tau^2
```

Example for Correlation: R Output (slightly modified)

```
> summary(meta.r.2)

                                         95%-CI      z  p-value
Fixed effect model   0.3799 [0.2948; 0.465] 8.7461 < 0.0001
Random effects model 0.3799 [0.2948; 0.465] 8.7461 < 0.0001

Quantifying heterogeneity:
tau^2 = 0; H = 1.05 [1; 1.34]; I^2 = 9.4% [0%; 44.6%]

Test of heterogeneity:
     Q d.f.  p-value
 20.97   19   0.3382

Details on meta-analytical method:
- Inverse variance method
- Paule-Mandel estimator for tau^2
```

Example for Correlation

```
> summary(meta.r.1)
                                      95%-CI      z  p-value
Fixed effect model   0.3743 [0.2996; 0.4491] 9.8149 < 0.0001
Random effects model 0.3743 [0.2996; 0.4491] 9.8149 < 0.0001
```

Ergebnisse aus der zweiten Meta-Analyse auf die Originalskala zurcktransformiert:

$$r = \frac{exp(2\ z) - 1}{exp(2\ z) + 1}$$

$$r = 0.3626 \quad 95\%\text{CI} : [0.2865, 0.4342]$$

Example for Correlation

Study	TE	seTE		95%−CI	W(random)
1	0.68	0.2444	0.68	[0.20; 1.16]	2.4%
2	0.56	0.1901	0.56	[0.19; 0.93]	4.0%
3	0.23	0.2809	0.23	[−0.32; 0.78]	1.8%
4	0.64	0.1677	0.64	[0.31; 0.97]	5.2%
5	0.49	0.1678	0.49	[0.16; 0.82]	5.2%
6	−0.04	0.3013	−0.04	[−0.63; 0.55]	1.6%
7	0.49	0.2628	0.49	[−0.03; 1.01]	2.1%
8	0.33	0.1596	0.33	[0.02; 0.64]	5.7%
9	0.58	0.1920	0.58	[0.20; 0.96]	3.9%
10	0.18	0.2966	0.18	[−0.40; 0.76]	1.7%
11	−0.11	0.1680	−0.11	[−0.44; 0.22]	5.2%
12	0.27	0.1119	0.27	[0.05; 0.49]	11.6%
13	0.26	0.1707	0.26	[−0.07; 0.59]	5.0%
14	0.40	0.0837	0.40	[0.24; 0.56]	20.8%
15	0.49	0.1453	0.49	[0.21; 0.77]	6.9%
16	0.51	0.2386	0.51	[0.04; 0.98]	2.6%
17	0.40	0.1468	0.40	[0.11; 0.69]	6.8%
18	0.34	0.2428	0.34	[−0.14; 0.82]	2.5%
19	0.42	0.2517	0.42	[−0.07; 0.91]	2.3%
20	0.16	0.2265	0.16	[−0.28; 0.60]	2.8%
Random effects model			**0.37**	**[0.30; 0.45]**	**100%**

Heterogeneity: I−squared=10.2%, tau−squared=0, p=0.3277