



An introduction to meta-analysis in R

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About me



Background:

- PhD student in Department of Community Medicine, USM
- MSc (Medical Statistics) from USM, 2019
- MBBCh from Al-Azhar University, 2015

Interest:

- Medical statistics; survival analysis, poisson regression, meta-analysis
- Machine learning application in medical sciences
- Text analysis, bibliometrics, scientometrics

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Download material: https://tny.im/eOXVV





Things to note

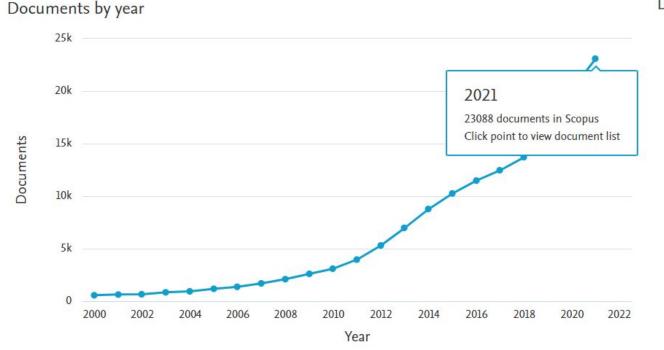
- I'm going to assume everyone has **some familiarity with R**, but feel free to ask anything
- use RStudio cloud
- We are not going to cover everything related to meta-analysis
- Hopefully, by the end of this workshop:
 - Able to understand meta-analysis paper
 - Able to grasp the flow and basic concept in meta-analysis
 - Gain basic knowledge to explore more



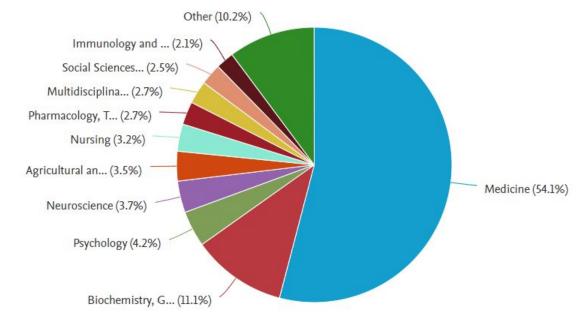


Background

- Meta-analysis:
 - Statistical methods used to combine the results of several scientific studies into a pooled result
- From Scopus database (01-11-2021): 152, 352 meta-analysis papers



Documents by subject area







Jargons

- Fixed vs random effect model
- Heterogeneity
- Publication bias
- Forest plot
- Funnel plot

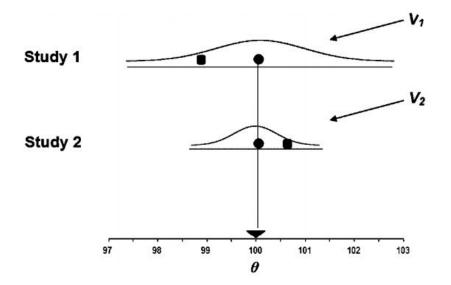






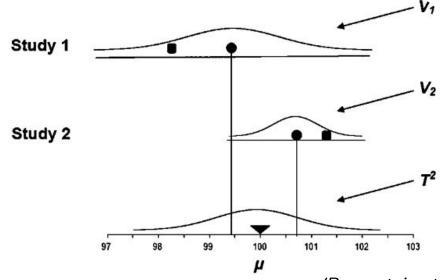
Fixed/common effect model:

- One true effect size
- Estimate one true effect size



Random effect model:

- True effects varies (ie; distribution of true effect sizes)
- Estimates mean of the distribution of true effects



(Borenstein et al., 2010)





- Heterogeneity (almost always refer to between study heterogeneity):
 - Variation in study outcomes between studies (statistical heterogeneity)
 - \circ Measurement: Q-statistics, T², I², H²
 - Other types of heterogeneity refer to Rucker at al., 2008
- Publication bias:
 - Studies being published depends on the its result
 - Consequences:
 - Overestimate the effect size
 - Overlook negative effect size





- Certain publication bias caused by small study effect and p-hacking can be statistically adjusted (most causes usually unknown)
- Publication bias tested using:
 - Visual: Funnel plot
 - Statistical (min k=10):
 - ✓ Classical: Begg, Egger (default), Thompson
 - ✓ Binary outcome: Peters, Harbord (default for OR), Schwarzer, Deeks, etc
 - ✓ SMD (for Hedges' g): Pustejovsky



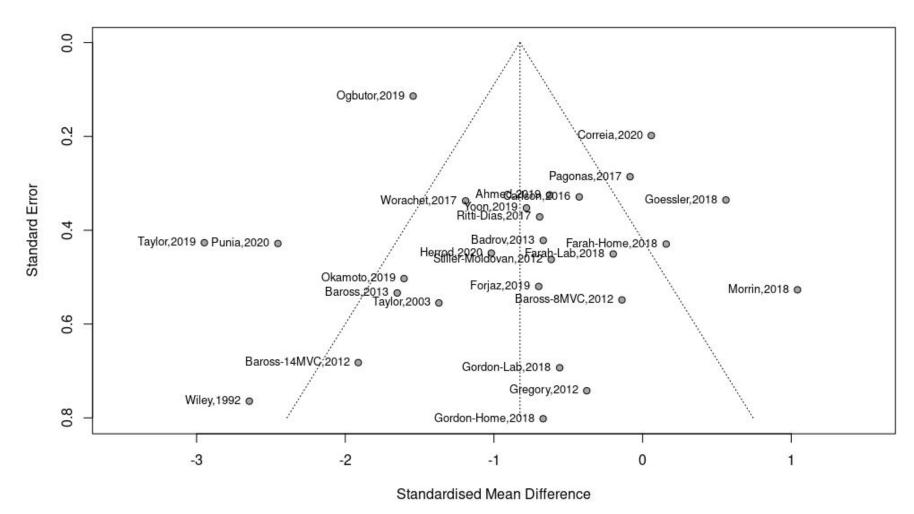
Forest plot

Study	Total	Expe Mean	rimental SD		Mean	Control SD	Standardised Mean Difference	SMD	95%-CI	Weight (common)		(-
Taylor,2019	24	-12.30	4.3800	24	0.30	4.0200	1	-2.95	[-3.78; -2.11]	2.4%	3.9%	
Wiley,1992		-12.70			2.60	7.4500	——- į		[-4.14; -1.15]	0.7%	2.6%	
Punia,2020	20	-5.75	3.9600	20	3.00	2.9600	É		[-3.29; -1.61]	2.3%	3.9%	
Baross-14MVC,2012	10	-10.80	5.8800	5	-0.20	3.2600			[-3.25; -0.58]	0.9%		
Baross,2013	10	-11.00	8.0000	10	-0.10	4.0000			[-2.70; -0.60]	1.5%	3.4%	
Okamoto,2019	11	-17.00	9.7300	11	-2.00	8.1900			[-2.59; -0.62]	1.7%	3.6%	
Ogbutor,2019	200	-7.47	1.6900	200	-4.07	2.6100	= 5	-1.54	[-1.77; -1.32]	32.9%	4.8%	1
Taylor,2003	9	-19.00	6.8200	8	-8.00	8.4400		-1.37	[-2.46; -0.28]	1.4%	3.4%	•
Worachet,2017	21	-4.23	4.6400	21	0.83	3.6400		-1.19	[-1.85; -0.53]	3.8%	4.2%	
Herrod,2020	11	-9.00	9.0000	12	-1.00	6.0000		-1.02	[-1.90; -0.14]	2.1%	3.8%	
Yoon,2019	17	-8.90	8.9000	18	-2.30	7.6000	-5-		[-1.47; -0.09]	3.4%		
Forjaz,2019	8	-3.00	8.1900	8	5.00	12.9300	- <u> </u>	-0.70	[-1.72; 0.32]	1.6%	3.5%	
Ritti-Dias,2017	15	-8.00	11.0900	16	0.00	11.4000	- 6-	-0.69	[-1.42; 0.04]	3.1%	4.1%	
Gordon-Home,2018	9	-9.70	10.2000	2	-2.30	9.3900			[-2.24; 0.90]	0.7%	2.5%	
Badrov,2013	12	-8.00	12.3900	12	1.00	13.5900	-6-		[-1.49; 0.16]	2.4%		
Ahmed,2019	20	-18.75	8.4500	20	-13.00	9.5400		-0.63	[-1.26; 0.01]	4.1%	4.3%	
Stiller-Moldovan,2012	11	-1.10	8.8200	9	5.20	10.9400	- [-	-0.61	[-1.52; 0.29]	2.0%	3.7%	
Gordon-Lab,2018	8	-9.10	11.6000	3	-2.30	9.3900		-0.56	[-1.92; 0.80]	0.9%	2.8%	
Carlson.2016	18	-7.00	10.8200	20	-2.00	12.0400	! • 		[-1.07: 0.22]	4.0%	4.2%	
Gregory,2012	5	-10.00	12.8700	3	-4.00	15.7200			[-1.83; 1.08]	0.8%	2.7%	1
Farah-Lab,2018	13	-9.00	13.5500	8	-6.00	16.1600	: + -	-0.20	[-1.08; 0.69]	2.1%		
Baross-8MVC,2012	10	-0.80	4.3700	5	-0.20	3.2600	<u> </u>	-0.14	[-1.21; 0.94]	1.4%	3.4%	
Pagonas,2017	24	0.01	14.6000	25	1.40	17.6000	£	-0.08	[-0.64; 0.48]	5.2%	4.4%	
Correia,2020	50	-2.00	16.7500	52	-3.00	17.3300	i +	0.06	[-0.33; 0.45]	10.9%	4.7%	
arah-Home,2018	17	-4.00	12.1300	8	-6.00	12.3900	€ 	0.16	[-0.68; 1.00]	2.3%	3.9%	
Goessler,2018	22	5.50	8.4600	16	1.00	6.9400	2		[-0.10; 1.22]	3.8%	4.2%	
Morrin,2018	9	6.10	9.0000	8	-2.40	6.0000			[0.01; 2.07]	1.5%	3.5%	
Common effect model	592			551			2 1	-0.92	[-1.04; -0.79]	100.0%	_	
Random effects model							S	-0.82	[-1.19; -0.46]	_	100.0%	
Prediction interval								4	[-2.53; 0.88]			





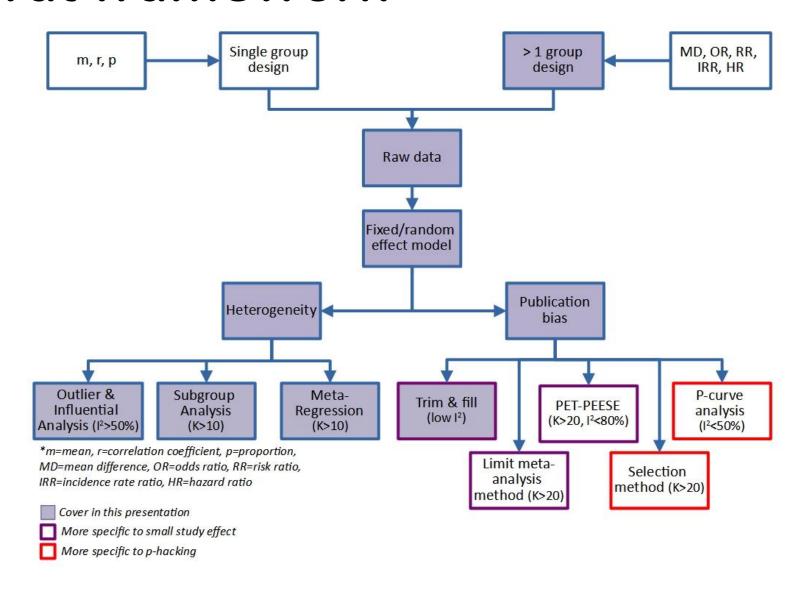
• Funnel plot







General framework







Type of meta-analysis

- "General" meta-analysis (Intervention/observational study)
 - Single group design: Pool mean, correlation coefficient, prevalence/proportion
 - >1 group design: Pool mean difference, OR, RR, IRR, HR
- "Multilevel" meta-analysis
 - There is 3rd level
- Network meta-analysis
 - Compare several treatment effect directly and indirectly
- Dose response meta-analysis
 - Quantify level of exposure effect to response





Type of meta-analysis (cont.)

- Diagnostic test accuracy meta-analysis
 - Pool sensitivity, specificity, AUC
- Multivariate/Anova/SEM meta-analysis
- Bayesian approach
- Genome meta-analysis





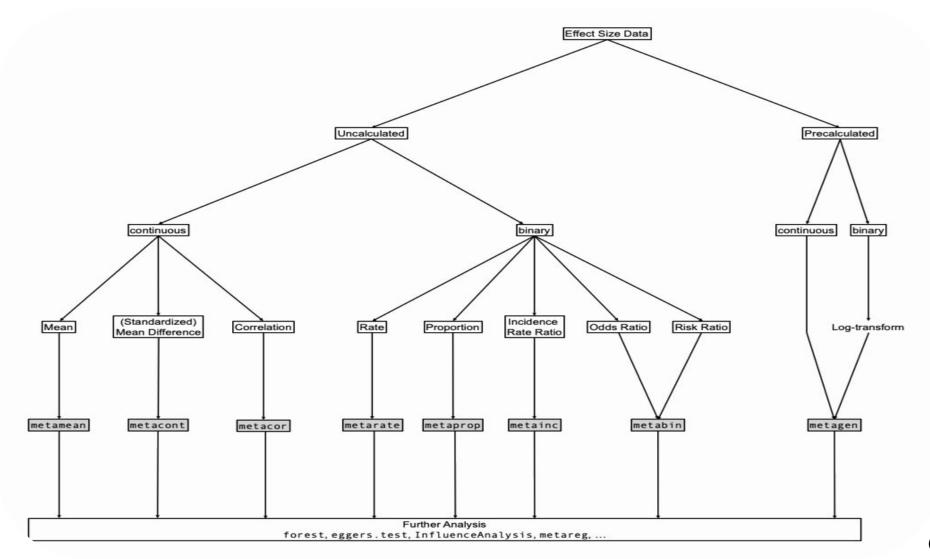
R packages for meta-analysis

- Main packages:
 - o meta
 - metafor
- Other packages on CRAN (a lot!)
- Unofficial packages (in GitHub, etc):
 - dmetar
 - dmetatools
 - o etc





Main functions in meta package







References

- Borenstein, M., Hedges, L. V., Higgins, J. P. T. & Rothstein, H. R. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res. Synth. Methods 1, 97–111 (2010).
- Harrer, M., Cuijpers, P., Furukawa, T.A., & Ebert, D.D. (2021). <u>Doing</u>
 <u>Meta-Analysis with R: A Hands-On Guide</u>. Boca Raton, FL and London:
 Chapman & Hall/CRC Press. ISBN 978-0-367-61007-4.
- Rücker, G., Schwarzer, G., Carpenter, J. R. & Schumacher, M. Undue reliance on 12 in assessing heterogeneity may mislead. BMC Med. Res. Methodol. 8, 1–9 (2008).





Question?







About data

- Our aim to assess the effectiveness of isometric resistance training (IRT) in reducing systolic blood pressure among hypertensive individuals
- Data:
 - Treatment IRT regiment
 - Control aerobic exercise, dynamic RT and non-exercise control (be physically active, etc)
- Study criterias:
 - Participants:
 - High-normal (SBP 130–139 mmHg or DBP 85–89 mmHg)
 - Grade 1 hypertension (SBP 140–159 mmHg or DBP 90–99 mmHg)
 - Grade 2 hypertension (SBP ≥160 mmHg or DBP ≥100 mmHg)
 - IRT must be 3 weeks duration





About data (cont.)

Resistance training - any exercise that causes muscle to contract against an external resistance



Isometric RT - involve muscle contraction without any movement of the surrounding joints



Dynamic RT - involves joint movement (imagine the pictures move)





Hands-on in R

