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 do

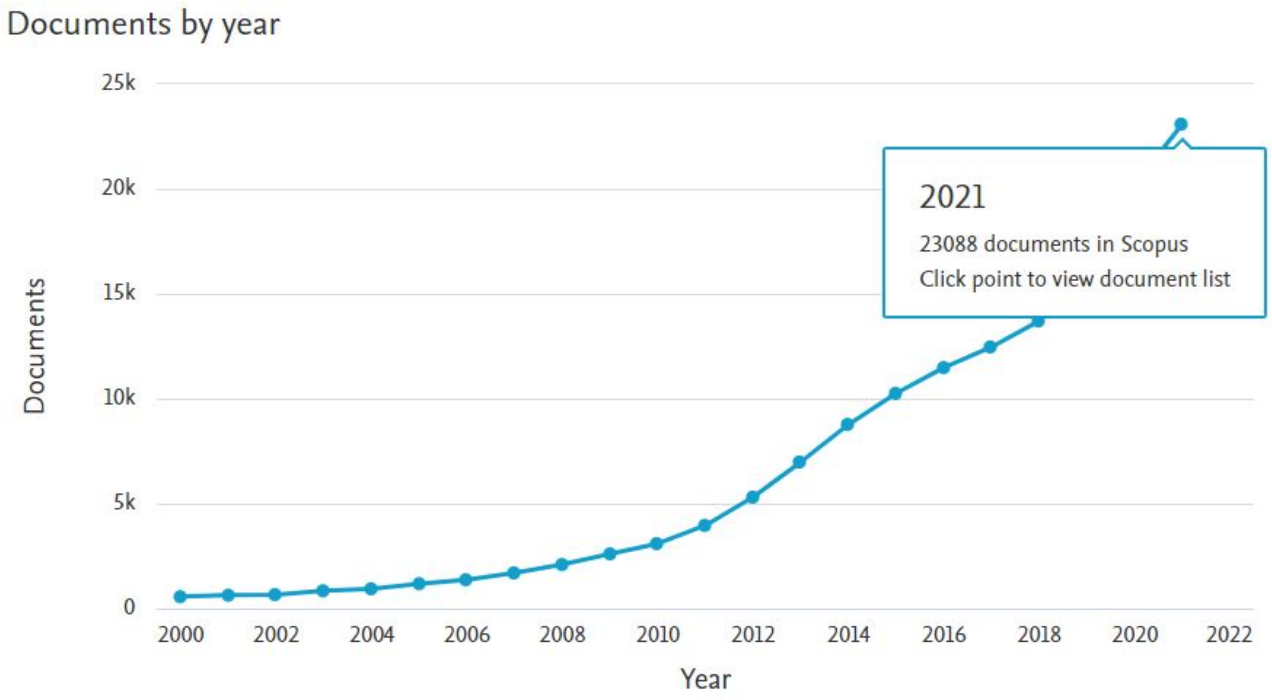
1. Set up RStudio cloud
2. Install required packages

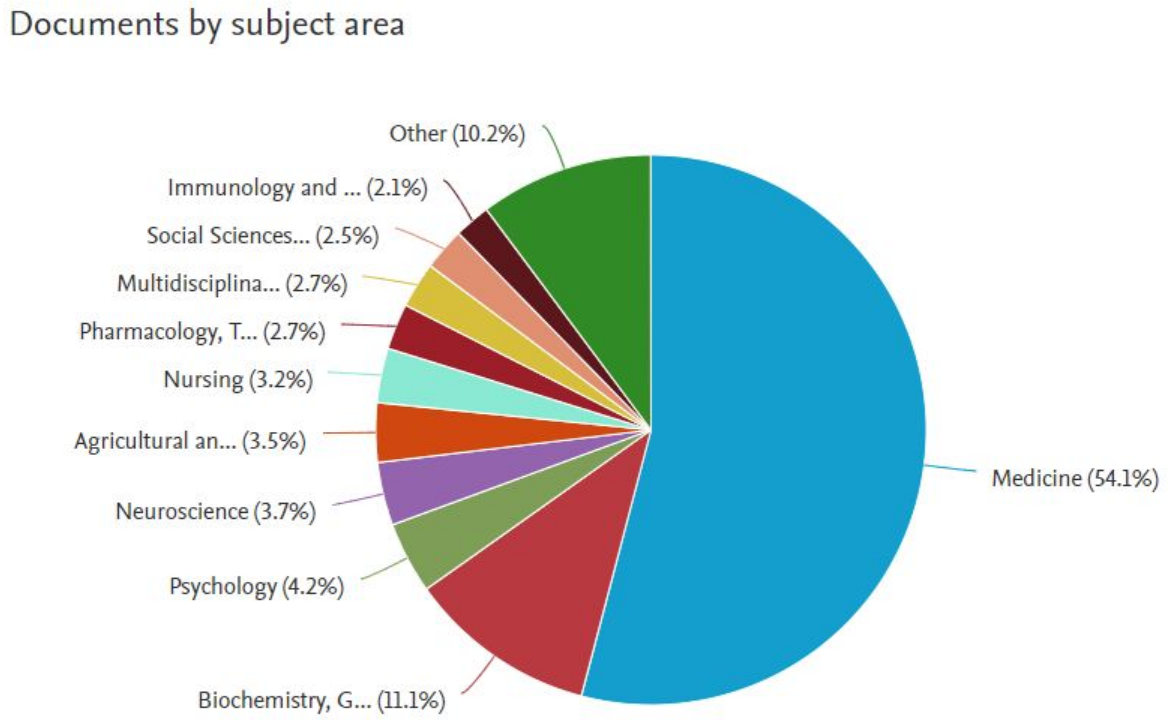
Things to note

- **Some familiarity with R is expected**, 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

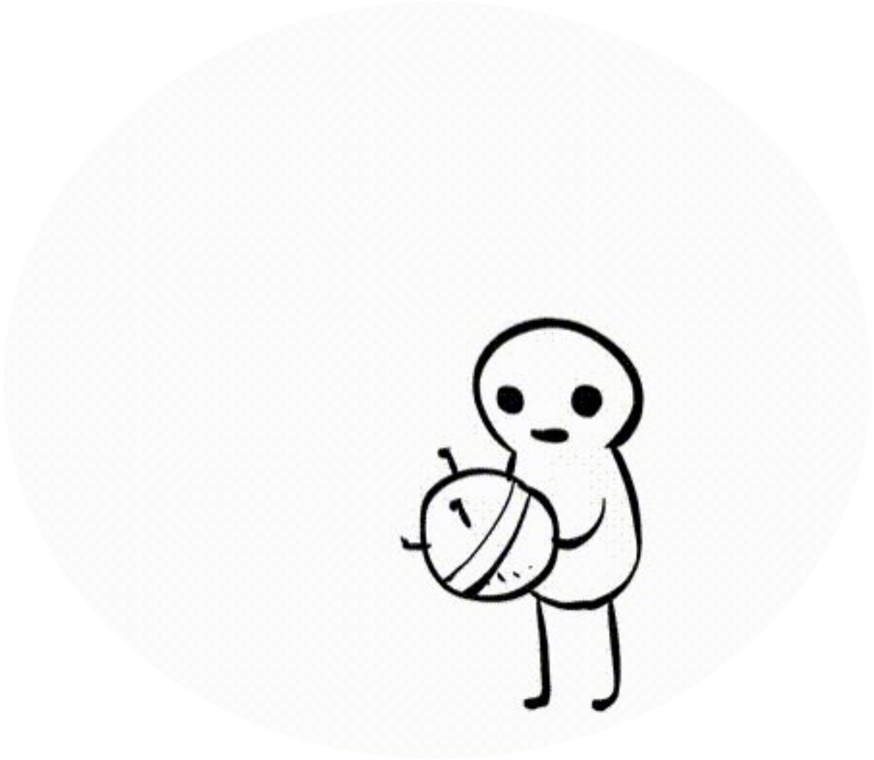
- Meta-analysis:
  - Statistical methods used to combine the results of several scientific studies into a pooled result
- From Scopus database (01-11-2021): 152, 352 meta-analysis papers





Jargons

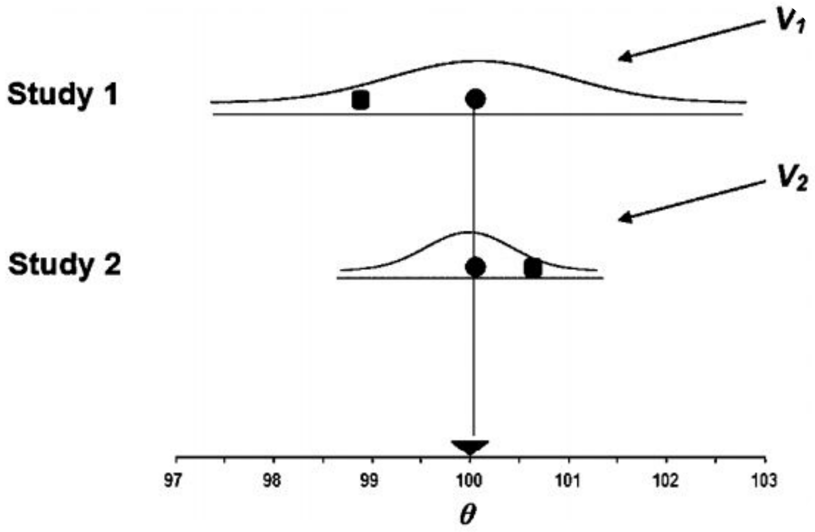
- Fixed vs random effect model
- Heterogeneity
- Publication bias
- Forest plot
- Funnel plot



Jargons (cont.)

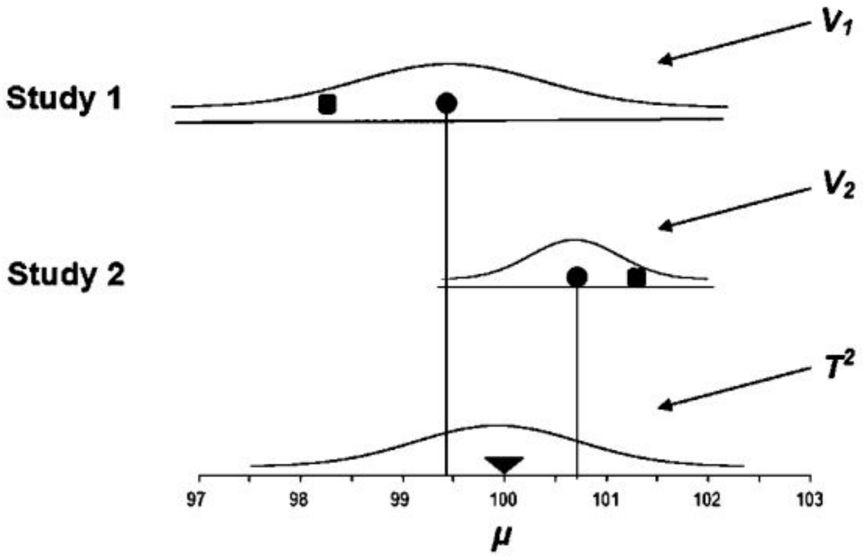
Fixed/common effect model:

- 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)

Jargons (cont.)

- Heterogeneity (almost always refer to between study heterogeneity):
  - Variation in study outcomes between studies (statistical heterogeneity)
  - Measurement: Q-statistics, T^2, I^2, H^2
  - 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

Jargons (cont.)

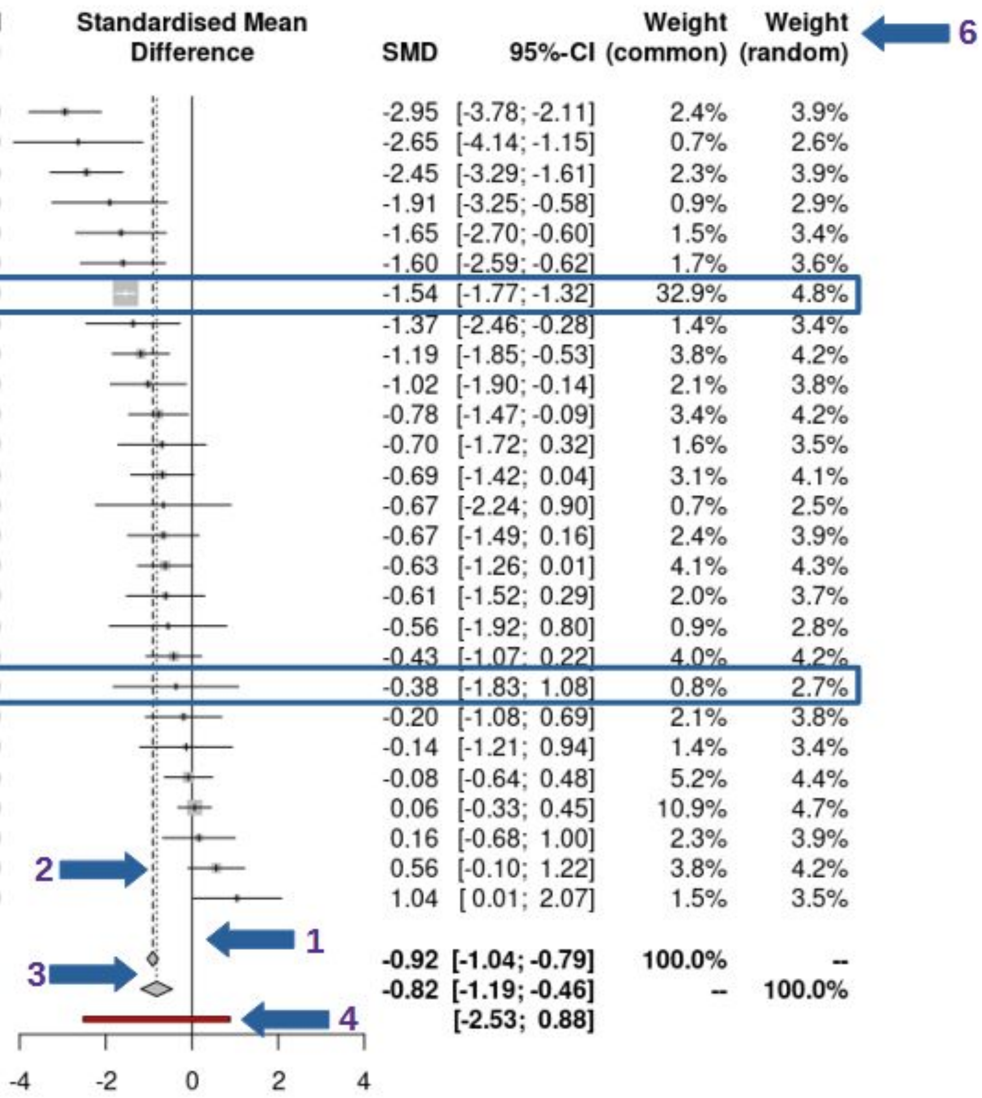
- Certain publication bias caused by small study effect and p-hacking can be statistically adjusted (most causes usually unknown)
- Publication bias tested using:
  - Visual: Funnel plot
  - Statistical (min k=10):
    - ✓ Classical: Begg, Egger (default), Thompson
    - ✓ Binary outcome: Peters, Harbord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

Jargons (cont.)

- Forest plot

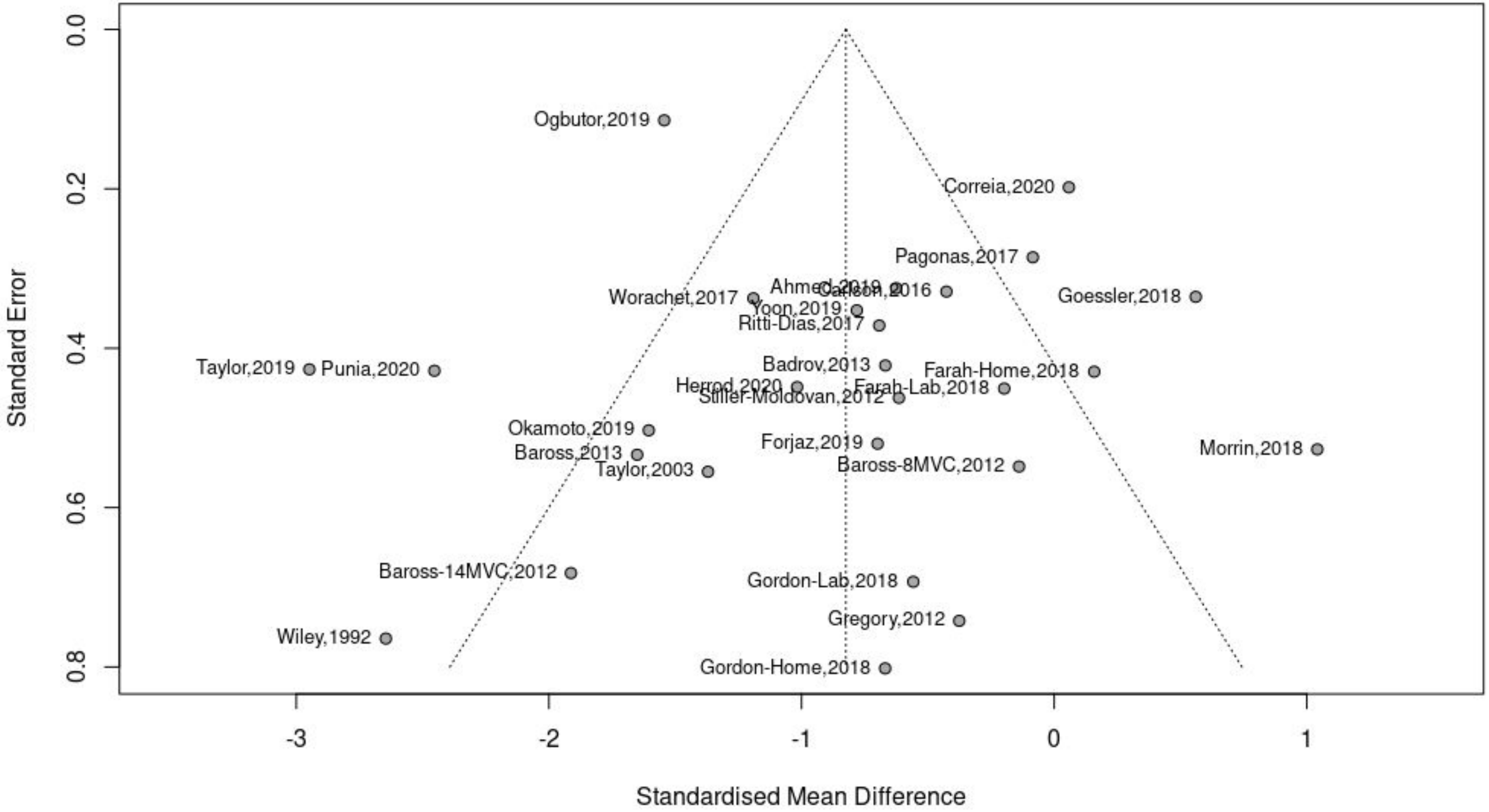
Study	Experimental Total	Experimental Mean	Experimental SD	Control Total	Control Mean	Control SD	SMD	95%-CI	Weight (common)	Weight (random)
Taylor,2019	24	-12.30	4.3800	24	0.30	4.0200	-2.95	[-3.78; -2.11]	2.4%	3.9%
Wiley,1992	8	-12.70	2.7300	7	2.60	7.4500	-2.65	[-4.14; -1.15]	0.7%	2.6%
Punia,2020	20	-5.75	3.9600	20	3.00	2.9600	-2.45	[-3.29; -1.61]	2.3%	3.9%
Baross-14MVC,2012	10	-10.80	5.8800	5	-0.20	3.2600	-1.91	[-3.25; -0.58]	0.9%	2.9%
Baross,2013	10	-11.00	8.0000	10	-0.10	4.0000	-1.65	[-2.70; -0.60]	1.5%	3.4%
Okamoto,2019	11	-17.00	9.7300	11	-2.00	8.1900	-1.60	[-2.59; -0.62]	1.7%	3.6%
Ogbutor,2019	200	-7.47	1.6900	200	-4.07	2.6100	-1.54	[-1.77; -1.32]	32.9%	4.8%
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	-0.78	[-1.47; -0.09]	3.4%	4.2%
Forjaz,2019	8	-3.00	8.1900	8	5.00	12.9300	-0.70	[-1.72; 0.32]	1.6%	3.5%
Ritti-Dias,2017	15	-8.00	11.0900	16	0.00	11.4000	-0.69	[-1.42; 0.04]	3.1%	4.1%
Gordon-Home,2018	9	-9.70	10.2000	2	-2.30	9.3900	-0.67	[-2.24; 0.90]	0.7%	2.5%
Badrov,2013	12	-8.00	12.3900	12	1.00	13.5900	-0.67	[-1.49; 0.16]	2.4%	3.9%
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	-0.43	[-1.07; 0.22]	4.0%	4.2%
Gregory,2012	5	-10.00	12.8700	3	-4.00	15.7200	-0.38	[-1.83; 1.08]	0.8%	2.7%
Farah-Lab,2018	13	-9.00	13.5500	8	-6.00	16.1600	-0.20	[-1.08; 0.69]	2.1%	3.8%
Baross-8MVC,2012	10	-0.80	4.3700	5	-0.20	3.2600	-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	0.06	[-0.33; 0.45]	10.9%	4.7%
Farah-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	0.56	[-0.10; 1.22]	3.8%	4.2%
Morrin,2018	9	6.10	9.0000	8	-2.40	6.0000	1.04	[0.01; 2.07]	1.5%	3.5%
Common effect model	**592**			**551**			**-0.92**	**[-1.04; -0.79]**	**100.0%**	**--**
Random effects model							**-0.82**	**[-1.19; -0.46]**	**--**	**100.0%**
Prediction interval								**[-2.53; 0.88]**		

Heterogeneity: $I^2 = 84\%$, $\tau^2 = 0.6503$, $p < 0.01$ 5

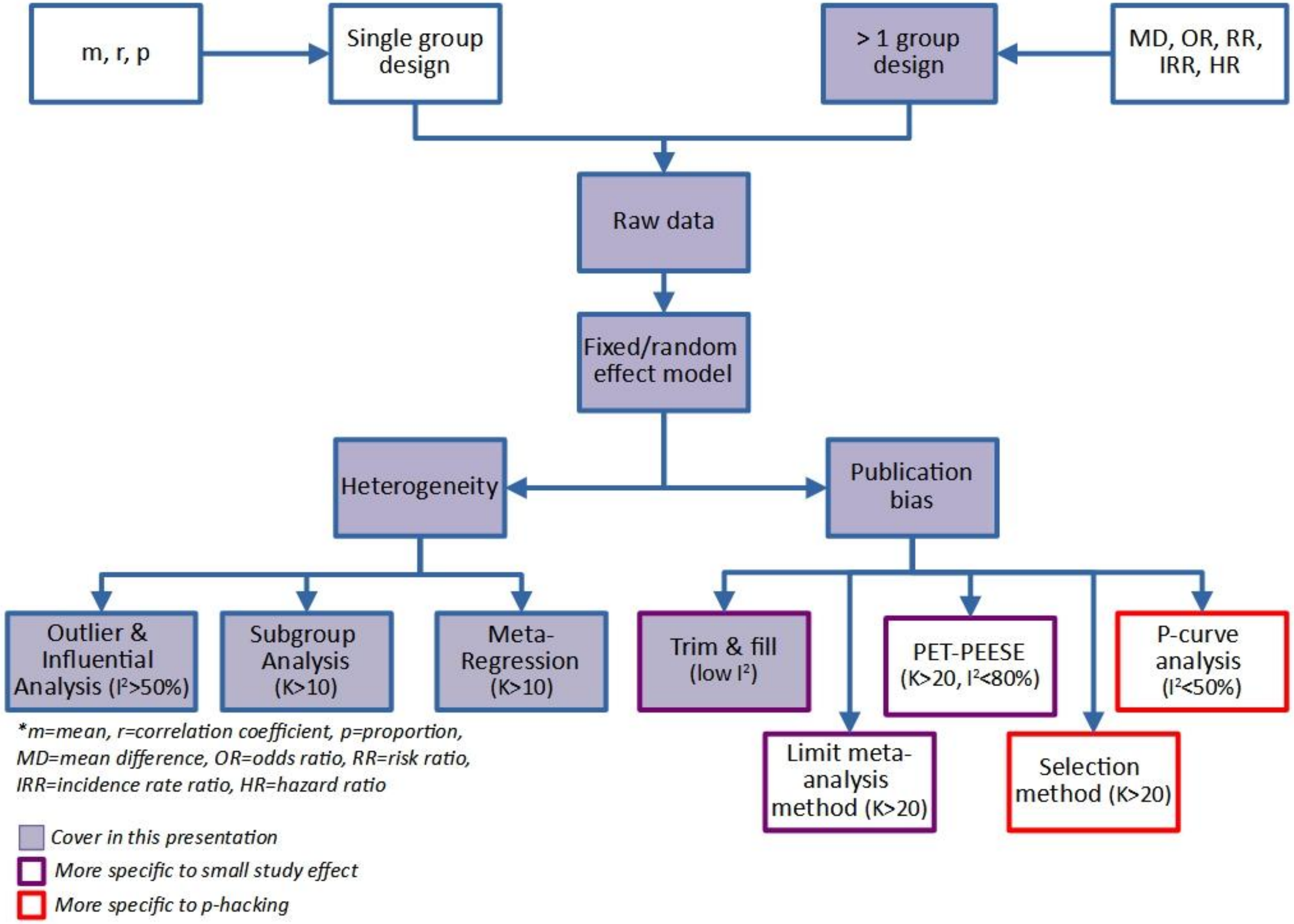


Jargons (cont.)

- 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

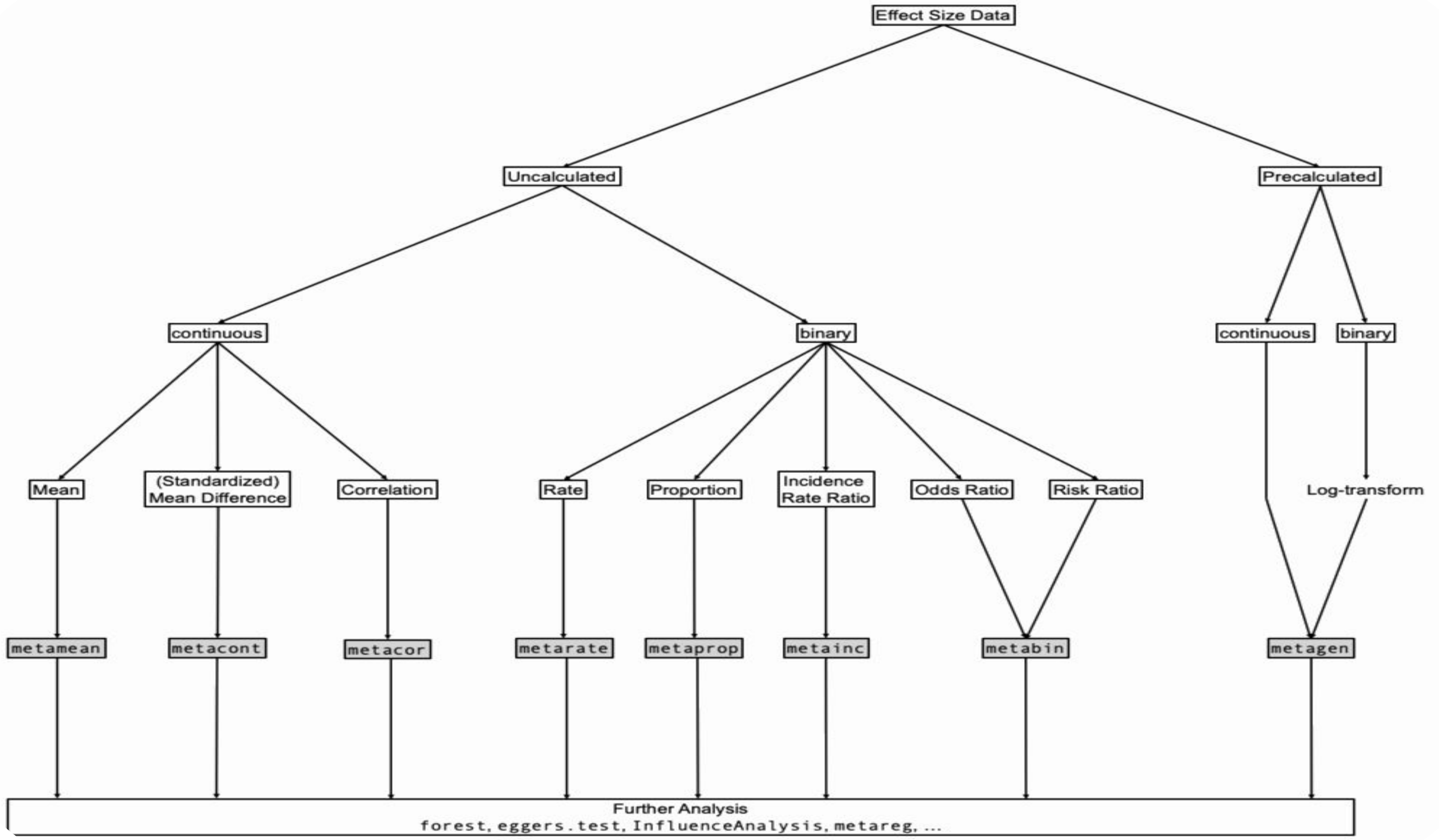
Type of meta-analysis (cont.)

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

Main functions in meta package



(Harrer et al., 2021)

References

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- Harrer, M., Cuijpers, P., Furukawa, T.A., & Ebert, D.D. (2021). Doing Meta-Analysis with R: A Hands-On Guide. 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 I2 in assessing heterogeneity may mislead. BMC Med. Res. Methodol. 8, 1–9 (2008).

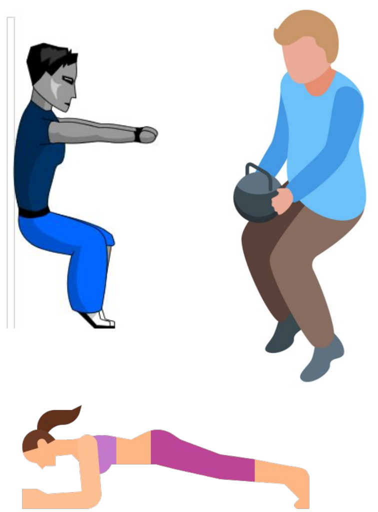
Question?

About data

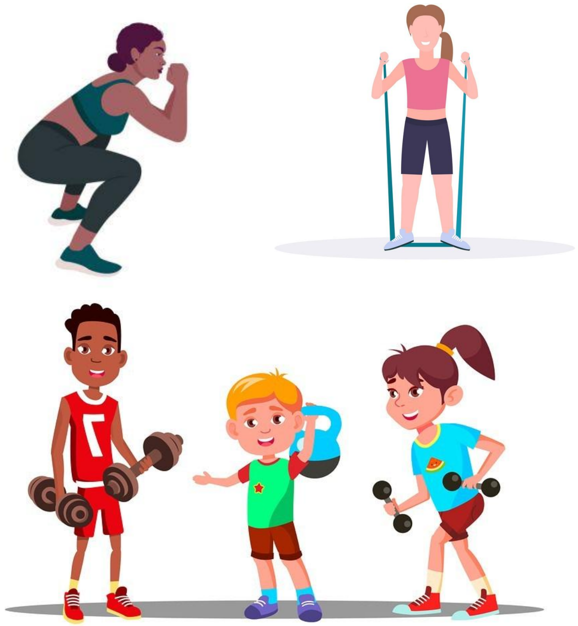
- Our aim - to assess the effectiveness of isometric resistance training (IRT) in reducing systolic blood pressure among hypertensive individuals
- Data:
  - Treatment - IRT regiment
  - Control - aerobic exercise, dynamic RT and non-exercise control (be physically active, etc)
- Study criterias:
  - 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