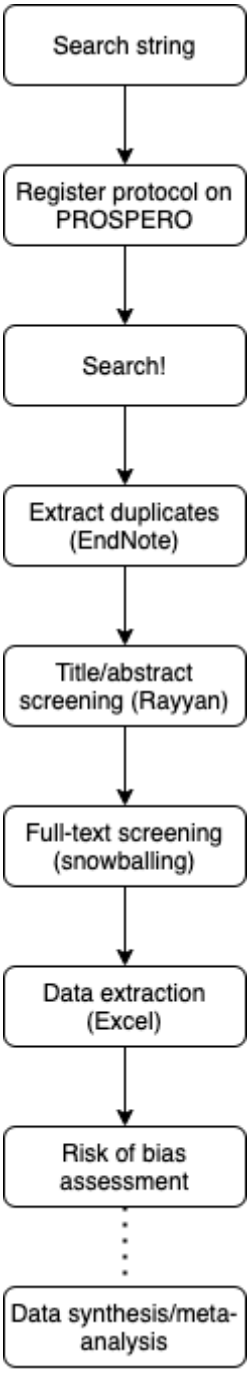
Writing a systematic review + meta-analysis



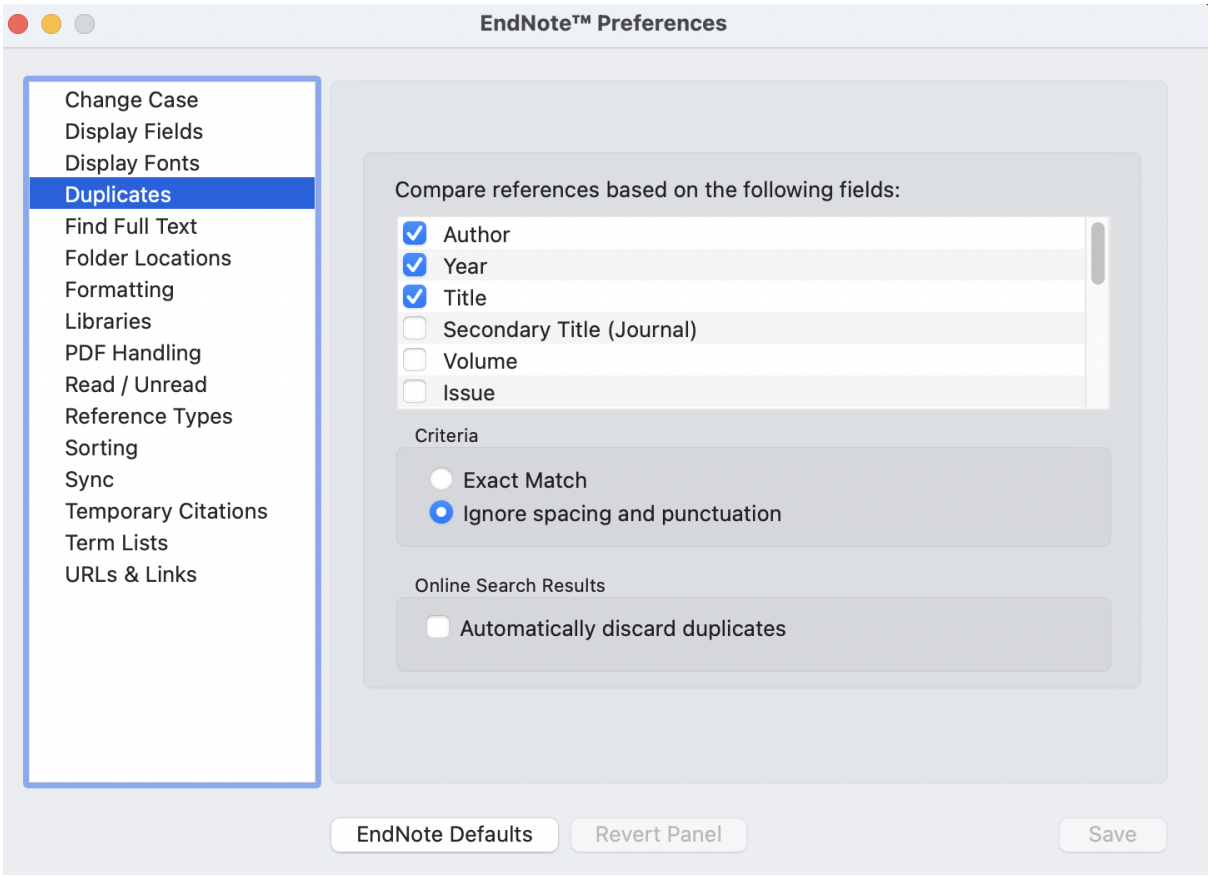
Search string

- In consultation with the UU librarian (Paulien Wiersma, p.h.wiersma@uu.nl)
- See '***Search Planning Form_UM***' in DropBox folder
- See '***Search Operators for Different Databases***' in DropBox folder
- See example at the end of the document
- Export search results from all databases into EndNote
    - For example from PubMed: https://libguides.library.cqu.edu.au/ld.php?content_id=37972647
    - For example from Cochrane: https://libguides.library.cqu.edu.au/ld.php?content_id=37972636

****It is imperative to mention that from the beginning of your search, throughout the duplicate deletion process, title/abstract screening, and full-text screening to track the amount of articles found and duplicates removed. Once they are deleted, you cannot go back and see the original number.****
Use the Prisma Work Flow, and most importantly, keep it up to date! (Prisma Work Flow can be found in the DropBox)

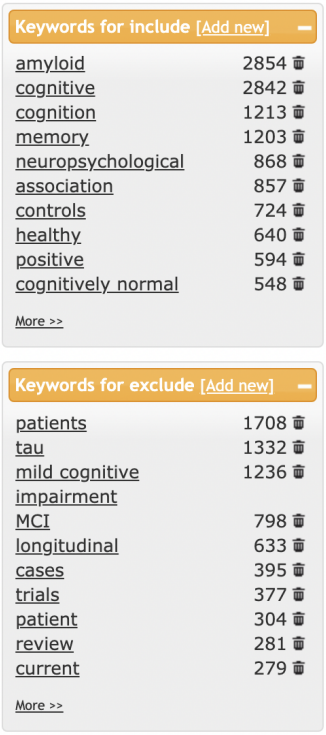
Register protocol on PROSPERO
https://www.crd.york.ac.uk/prospero/

Remove duplicates in EndNote

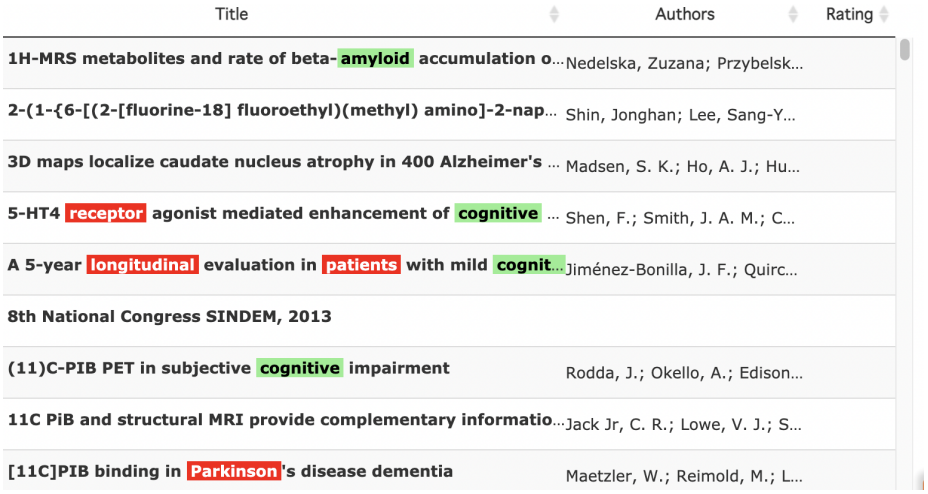


Go to EndNote -> Preferences -> Duplicates and compare references based on ‘Author’, ‘Year’, ‘Title’. For quick duplicate deletion, we advise you to select different combinations to aid in deleting as much as possible.
This article by Bramer et al. explains more in-depth the order and combinations to use during the duplicate removal in EndNote. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4915647/

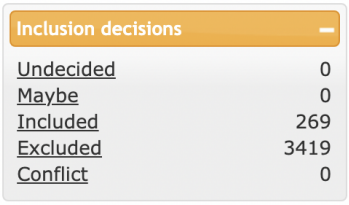
Export from Endnote to **Rayyan and begin title/abstract screening (blinded)**
https://rayyan.ai/guides/endnote



In Rayyan, both reviewers can create keywords in the title and/or abstract to make screening easier (see Figure above).



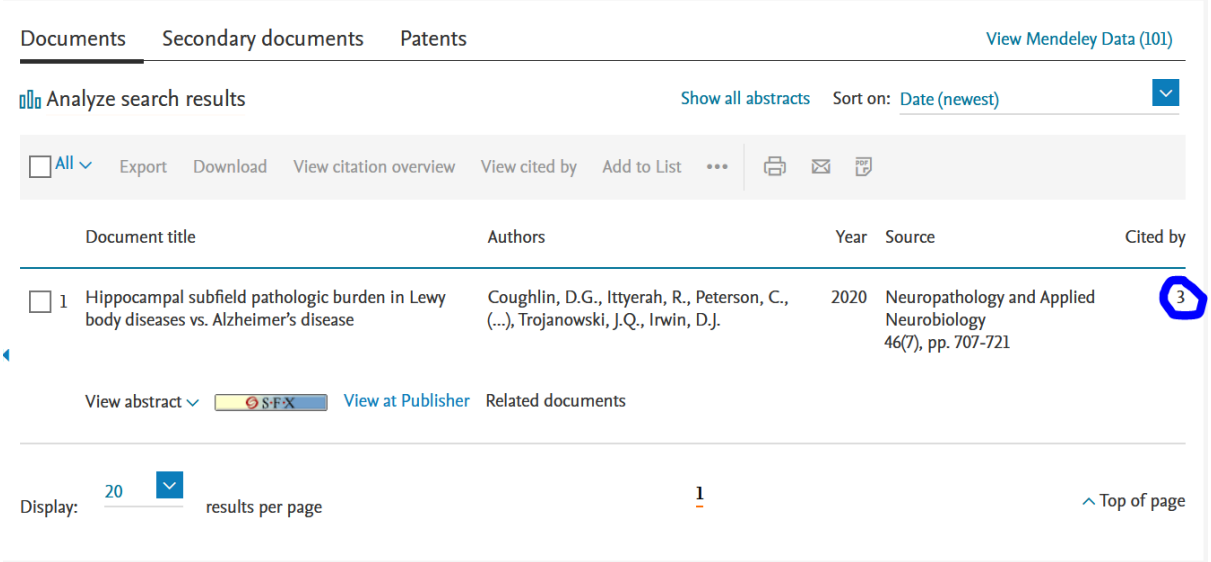
As you can see above, included words will then be highlighted in green and excluded words highlighted in red.



You can start including and excluding articles, or deciding 'maybe' to make a further decision at a later time. Once both reviewers have made a decision on all articles, then blinding is turned off and reviewers can discuss any discrepancies in decision-making.

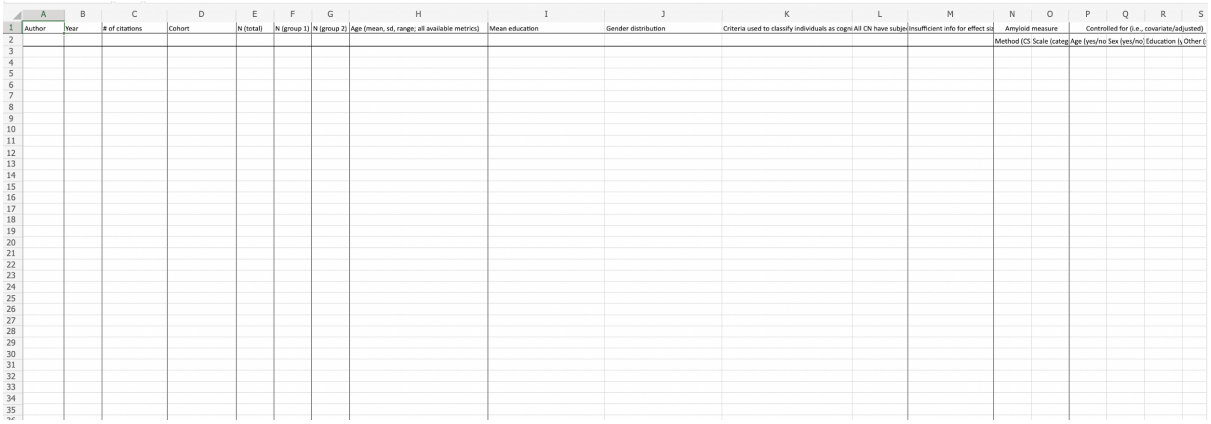
Full-text screening

- We would advise you to create PDF folders in your DropBox or shared reviewer area, for easy access of the full-text PDFs to screen.
- Snowballing (check the reference lists of the selected articles for additional articles of interest) and reverse snowballing (using Scopus, look up the selected articles and check for other articles that have cited those)



Data extraction

- Make sure to keep track of further excluded articles based on data extraction difficulties, for example if based on insufficient info for any data extraction (perhaps try to contact the corresponding author for data availability).
- Decide upon effect metric for data pooling and check what variables you will need to have for effect size transformations (see section data synthesis/meta-analysis)
- See '***Sample Table Data Extraction***' in the DropBox folder.



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	Author	Year	# of citations	Cohort	N (total)	N (group 1)	N (group 2)	Age (mean, sd, range; all available metrics)	Mean education	Gender distribution	Criteria used to classify individuals as cogni	All CN have subje	Insufficient info for effect si	Amyloid measure		Controlled for (i.e., covariate/adjusted)			
2														Method (CS	Scale (categ	Age (yes/no	Sex (yes/no)	Education (y	Other (
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Risk of bias assessment

- Newcastle-Ottawa Quality Assessment Scale for Cohort Studies
- Cochrane Risk-of-Bias Tool for Randomized Trials
- See '***Risk of Bias Assessment***' folder for more information and sample Excel documents

Table x. Newcastle-Ottawa scale for assessment of quality of included studies (each star represents if individual criterion within the subsection was fulfilled)

	Selection			*Comparability*				*Outcome*		*Overall quality score*
	1. Representativeness of th	*2. Selection of the n*	*3. Ascertainment of*	*Study controls for*	*Study controls for*	*Study controls for*	*Study controls for*	*1. Ascertainment of*	*2. Same method of a*	*(max. 9)*
Study	truly or somewhat represer	drawn from the sam	continuous or categ	age	sex/gender	education	other factors	independent neurop	yes	
Amariglio-2012	-	*	-	-	-	-	-	*	*	3
Bennett	-	*	*	-	-	-	-	*	*	4
Bos	*	*	-	-	-	-	-	*	*	4
Clark	*	*	-	-	-	-	-	*	*	4
Doraiswamy-2014	*	*	-	-	-	-	-	*	*	4
Dubois-2018	-	*	*	-	-	-	-	*	*	4
Edmonds	*	*	*	-	-	-	-	*	*	5
Harrington	-	*	*	*	-	-	*	*	*	6
Hassentab-2016	-	*	*	-	-	-	-	*	*	4
Hilal	*	*	*	*	*	*	*	*	*	9
Jicha	*	*	*	-	-	-	-	*	*	5
Lee-2020	*	*	*	*	*	*	-	*	*	8
Li et al. (2014)	-	*	*	*	*	*	*	*	*	8
Li-2007	-	*	-	-	-	-	-	*	*	3
Lim-2013c	*	*	-	-	-	-	-	*	*	4
Mathis	*	*	-	-	-	-	-	*	*	4
Mielke-2016	-	*	*	*	*	*	-	*	*	7
Oh-2011	*	*	-	-	-	-	-	*	*	4
Oh-2012	*	*	-	-	-	-	-	*	*	4
Papp-2017	*	*	*	-	-	-	-	*	*	5
Payoux-2015	*	*	-	-	-	-	-	*	*	4
Price-2009	-	*	*	-	-	-	-	*	*	4
[illegible]		*	*					*	*	

Data synthesis/meta-analysis

Please discuss with your supervisor if the number and type of studies that you have found are suitable for conducting a meta-analysis.

First, you need to transform the effect measures you have gathered into a summary statistic. Commonly used effect metrics for pooling are (see e.g. Cochrane Handbook for more information):

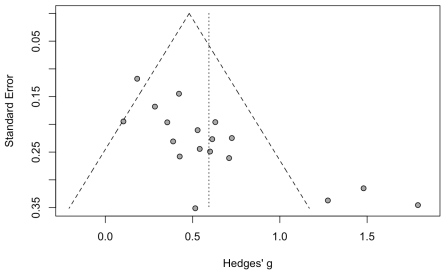
- For dichotomous outcomes
    - risk ratio (RR)
    - odds ratio (OR)
    - risk difference (RD)
- For continuous outcomes
    - (mean difference)
    - standardized mean difference/Cohen's d/Hedges' g
    - standardized regression coefficient
    - correlation coefficient (r)

Make sure that you correct for differences in direction of scales if necessary. There are different online calculators that you can make use of:

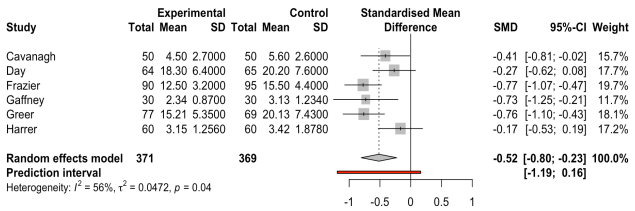
- https://www.campbellcollaboration.org/research-resources/effect-size-calculator.html (online effect size calculator)
- http://vassarstats.net/median_range.html (a tool to calculate mean, SD from median + range)
- https://www.statstodo.com/CombineMeansSDs_Pgm.php (a tool to combine means + SDs from multiple groups)
- https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/a.html#a (a great tutorial for doing meta-analyses in R and computing effect sizes there)

We would recommend you to use R for pooling your data. The book by Mathias Harrer gives great guidance (including R codes) on what packages to use and how to conduct the analyses. Make sure that you also derive measures for between-study heterogeneity and explore it if significant heterogeneity is found. Aside from that, you can explore a type/source of publication bias, small sample bias, by creating funnel plots, and test for funnel plot-asymmetry using Egger's test.

Funnel plot



Forest plot (to display results of pooling)



Source of both images: Harrer, M., Cuijpers, P., Furukawa, T.A, & Ebert, D. D. (2019). Doing Meta-Analysis in R: A Hands-on Guide. DOI: 10.5281/zenodo.2551803

Additional resources

- YouTube video for steps from the search until title/abstract screenin Rayyan -> https://www.youtube.com/watch?v=YFfzH4P6YKw
- Cochrane Handbook for Systematic Reviews
- Practical Meta-Analysis by Mark Lipsey & David Wilson (2001) - not sure if there's a more recent version
- PRISMA guidelines
- MOOSE guidelines

Example search string (in PsycInfo)

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(

(exp Tau Proteins/ OR tau.ab,ti. OR flortaucipir.ab,ti. OR FTP PET.ab,ti. OR T-807.ab,ti. OR T807.ab,ti. OR AV-1451.ab,ti. OR AV1451.ab,ti. OR Tauvid.ab,ti. OR MK-6240.ab,ti. OR MK6240.ab,ti. OR FDDNP.ab,ti. OR GTP-1.ab,ti. OR GTP1.ab,ti. OR RO-948.ab,ti. OR RO948.ab,ti. OR PI-2620.ab,ti. OR PI2620.ab,ti. OR THK-523.ab,ti. OR THK523.ab,ti. OR THK-5105.ab,ti. OR THK5105.ab,ti. OR THK-5117.ab,ti. OR THK5117.ab,ti. OR THK-5351.ab,ti. OR THK5351.ab,ti. OR T-808.ab,ti. OR T808.ab,ti. OR methyl lansoprazole.ab,ti. OR PBB3.ab,ti. OR neurofibrillary.ab,ti. OR tangles.ab,ti.)

AND

(PET.ab,ti. OR Positron emission tomograph*.ab,ti. OR exp Positron Emission Tomography/)

)

OR

(

(exp Tau Proteins/ OR tau.ab,ti. OR ptau.ab,ti. OR neurofibrillary.ab,ti. OR tangles.ab,ti.)

AND

(CSF.ab,ti. OR exp Cerebrospinal Fluid/ OR cerebrospinal fluid*.ab,ti. OR cerebro spinal fluid*.ab,ti. OR plasma.ab,ti.)

)

OR

(

(exp Tau Proteins/ OR tau.ab,ti. OR neurofibrillary.ab,ti. OR tangles.ab,ti.)

AND

(exp Neuropathology/ OR neuropatholog*.ab,ti. OR neurofibrillary pathology.ab,ti. OR tau pathology.ab,ti. OR neurofibrillary tangles.ab,ti. OR tau tangles.ab,ti. OR Braak.ab,ti.)

)

)

AND

(exp Semantics/ OR exp Episodic Memory/ OR exp Semantic Memory/ OR memory.ab,ti. OR episodic.ab,ti. OR cognition.ab,ti. OR semantic*.ab,ti. OR cognitive domain*.ab,ti. OR cognitive batter*.ab,ti. OR cognitive test*.ab,ti. OR neuropsychological.ab,ti. OR psychometric.ab,ti. OR exp Neuropsychology/ OR exp Psychometrics/ OR exp Neuropsychological Assessment/ OR exp Test Performance/ OR exp Cognitive Ability/ OR exp Cognitive Impairment/ OR exp Performance Tests/ OR exp Cognition/)

AND

(

(human.po. OR individuals.ab,ti. OR participants.ab,ti. OR older adults.ab,ti. OR subjects.ab,ti.)

AND

(normal.ab,ti. OR healthy.ab,ti. OR non demented.ab,ti. OR nondemented.ab,ti. OR aging.ab,ti. OR Aged.ab,ti. OR elderly.ab,ti. OR Prodromal Symptoms.ab,ti. OR older.ab,ti. OR preclinical.ab,ti. OR pre-clinical.ab,ti. OR unimpaired.ab,ti.)

)

)

NOT

(exp Mice/ OR exp Animal Models/ OR animal model*.ab,ti. OR transgenic.ab,ti. OR mice.ab,ti. OR mouse.ab,ti. OR rat.ab,ti. OR rats.ab,ti. OR rodent.ab,ti. OR rodents.ab,ti. OR primate*.ab,ti. OR canine.ab,ti. OR murine.ab,ti. OR rabbit*.ab,ti. OR transgenic mice.ab,ti.)