Supplemental materials for

Ebell MH, Barry HC, Baduni K, Grasso G. Clinically important benefits and harms of monoclonal antibodies targeting amyloid for the treatment of Alzheimer Disease: a systematic review and meta-analysis. *Ann Fam Med*. 2024;22(1):50-58.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Pg 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Pg 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pg 4, para 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pg 4, para 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pg 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pg 5 final para and pg 6 first para
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Same
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 6, “Data abstraction”
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pg 6, “Data abstraction”
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pg 6, para 3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pg 6, para 3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 6, para 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pg 7, para 2
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pg 6 para 2 and pg 5, “Inclusion and exclusion criteria”
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pg 7, para 1
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pg 7 final para and pg 8 initial para
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pg 7, para 2
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA (too few studies to do this)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA (too few studies to do this)

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Pg 7, para 2 and 3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pg 8, para 3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Pg 8, para 3
Study characteristics	17	Cite each included study and present its characteristics.	Pg 9, para 1 and Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figures 1-5 and Appendix Figures 1-16
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 9-11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 9-11 and Figures 1-5 and Appendix Figures 1-16
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pg 11, final para
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Pg 12, para 2 and CI's in pg 9-11
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pg 12, para 3
	23b	Discuss any limitations of the evidence included in the review.	Pg 13, para 3
	23c	Discuss any limitations of the review processes used.	NA
	23d	Discuss implications of the results for practice, policy, and future research.	Pg 13/14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Pg 5, para 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pg 5, para 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pg 14
Competing	26	Declare any competing interests of review authors.	Pg 14

Section and Topic	Item #	Checklist item	Location where item is reported
interests			
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Pg 14

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Supplemental Appendix 2

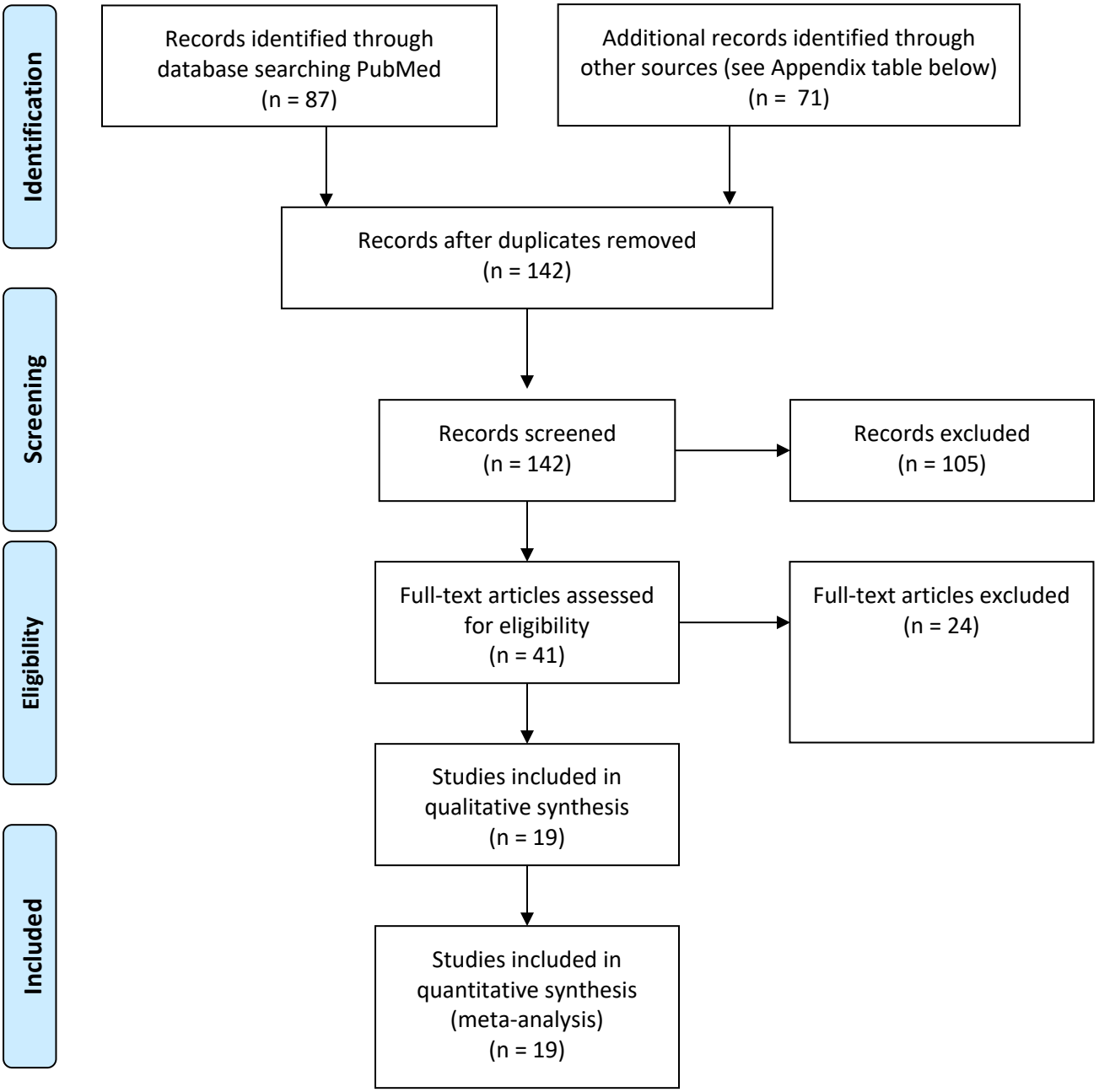
Search strategy for PubMed.

("monoclonal antibody" OR "Antibodies, Monoclonal and Immunoglobulins" OR "lecanemab" “donanemab” OR “ponezumab” OR "crenezumab" OR "aducanumab" OR "gantenerumab" OR "solanezumab" OR "bapineuzumab") AND ("Alzheimer"[tiab] OR "Alzheimer disease"[MeSH]) Filters: Abstract, Clinical Trial, Randomized Controlled Trial, Humans

Data Preparation

For continuous outcomes such as functional or cognitive scales, we compared the difference between baseline and final measurements in treatment and placebo groups. Where only the standard error (SE) or a 95% confidence interval (CI) was reported we calculated standard deviations (SD). One study did not report the SD, SE, or 95% CI for the difference between final measurement and baseline for the ADAS-cog-14.[17] We therefore calculated weighted means of the SE for other studies using the ADAS-cog-14 and used that to impute the SD. Finally, one study reported the ADAS-cog-12 changes as negative numbers instead of positive, so we reversed the direction to make this study’s results align with the others using the same scale.[21]

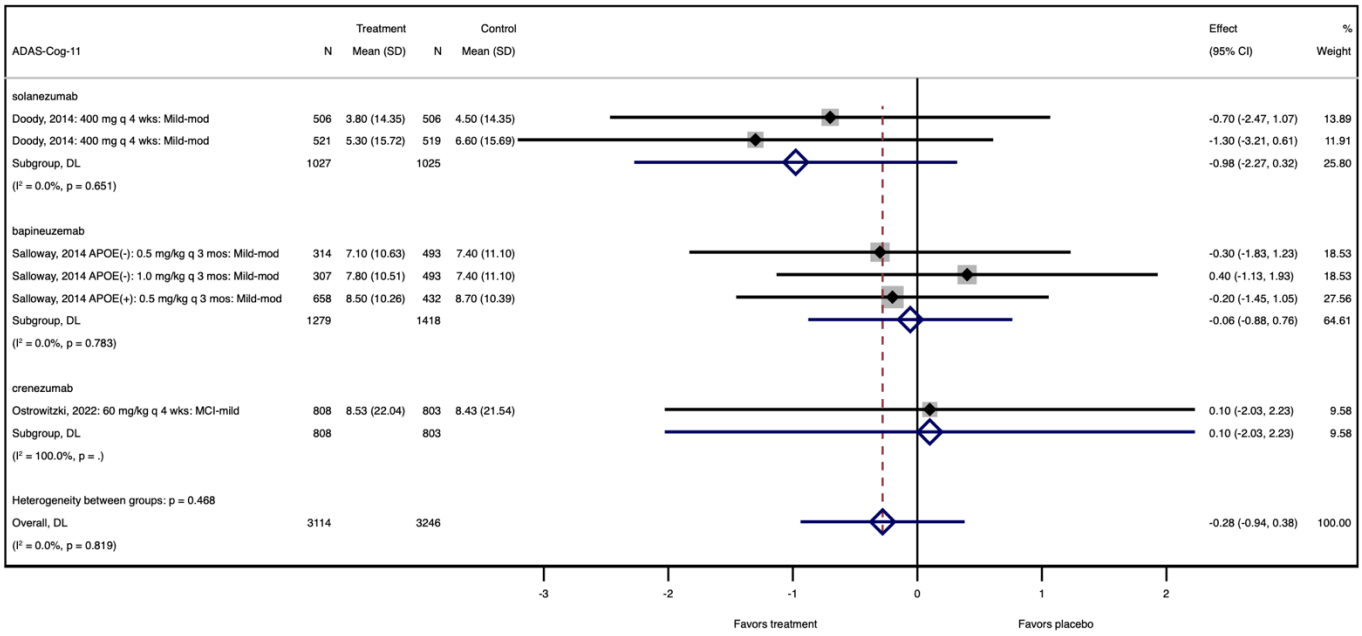
Supplemental Figure 1. PRISMA flow diagram for literature search.



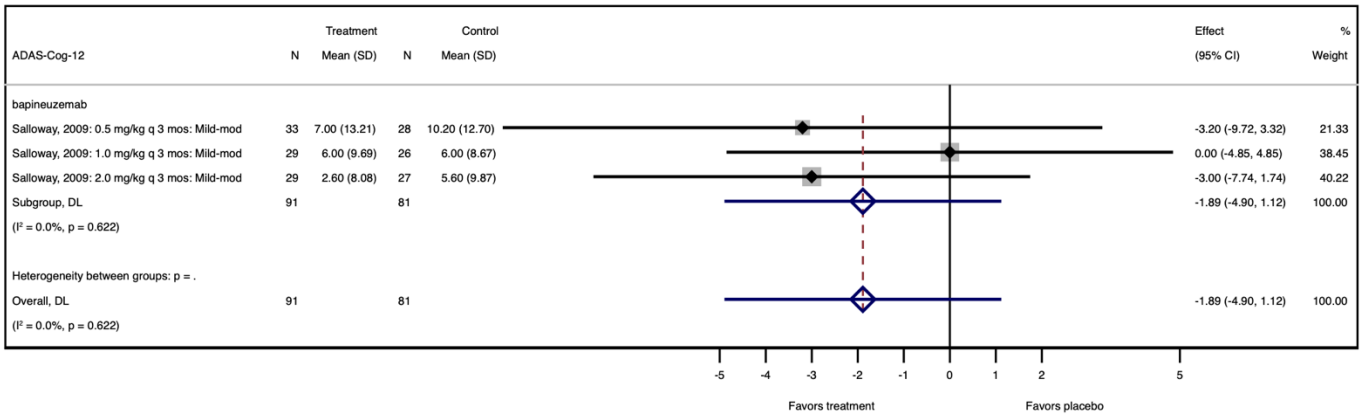
Supplemental Table 1. Summary of Pubmed and other sources searched.

Database	Number of publications	Duplicates	Records screened
PubMed	90	0	90
Cochrane CENTRAL	23	7	16
Clinicaltrials.gov	42	5	37
NEJM early online publication	1	0	1
ISRTCN trial registry (www.isrctn.com)	0	0	0
YODA trial registry (yoda.yale.edu)	2	2	0
Clinicalstudydatarequest.com	1	0	1
Vivli trial registry (vivli.org)	2	2	0
Totals	**161**	**16**	**145**

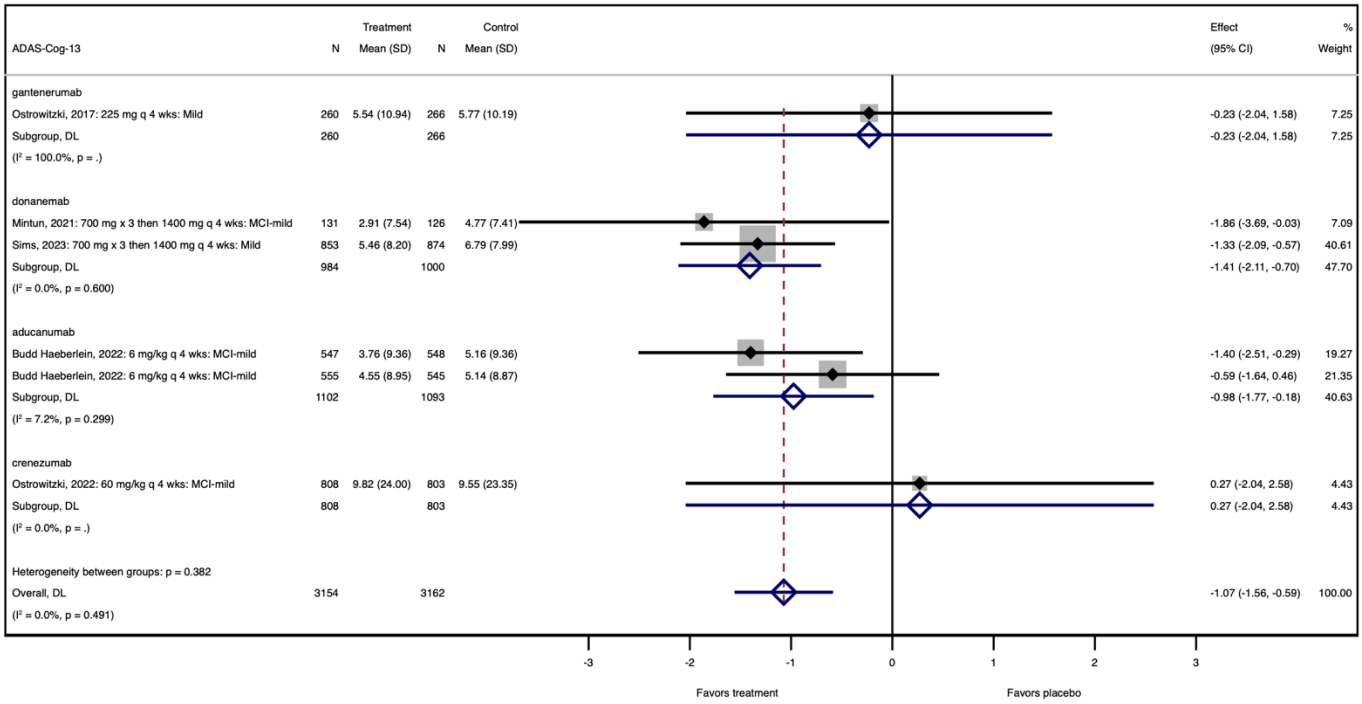
Supplemental Figure 2. Forest plot for the ADAS-Cog-11 cognitive scale



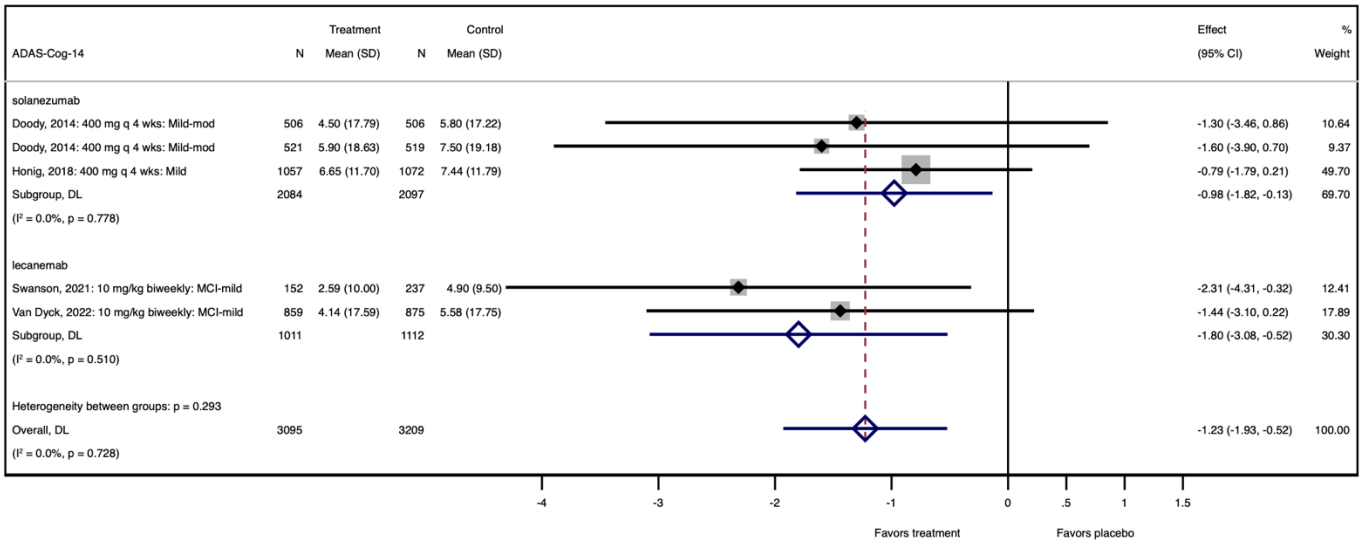
Supplemental Figure 3. Forest plot for the ADAS-Cog-12 cognitive scale



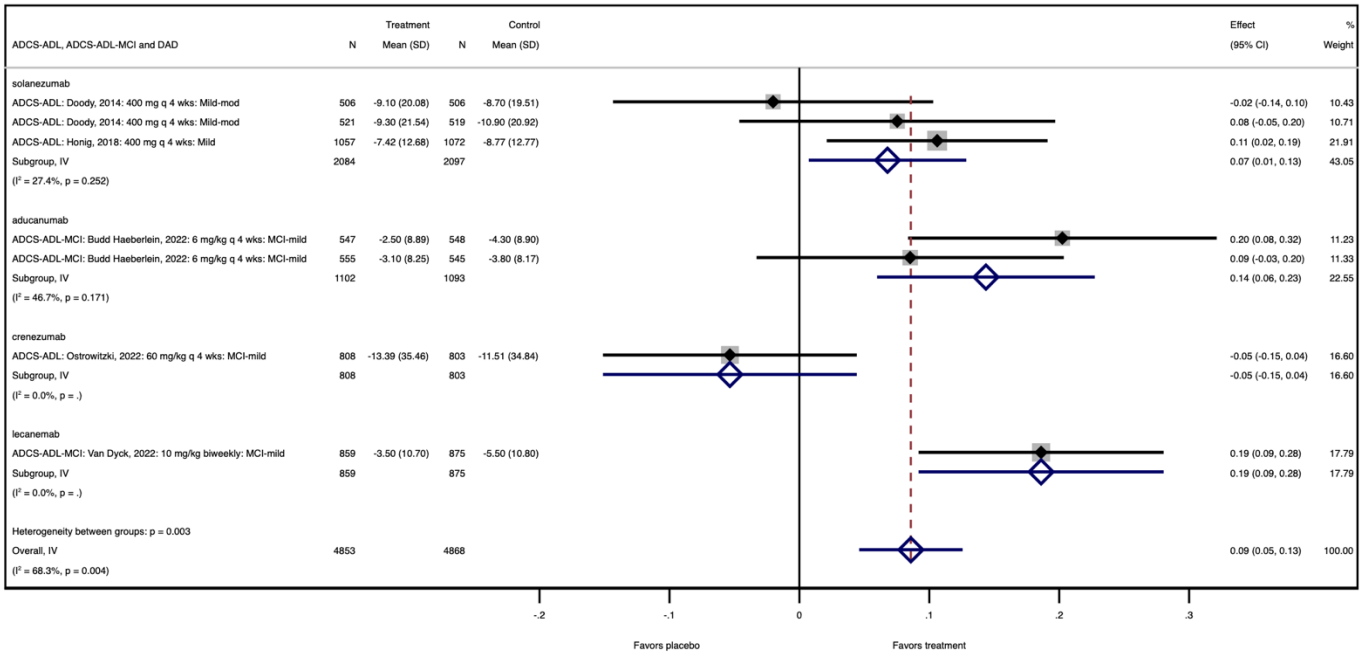
Supplemental Figure 4. Forest plot for the ADAS-Cog-13 cognitive scale



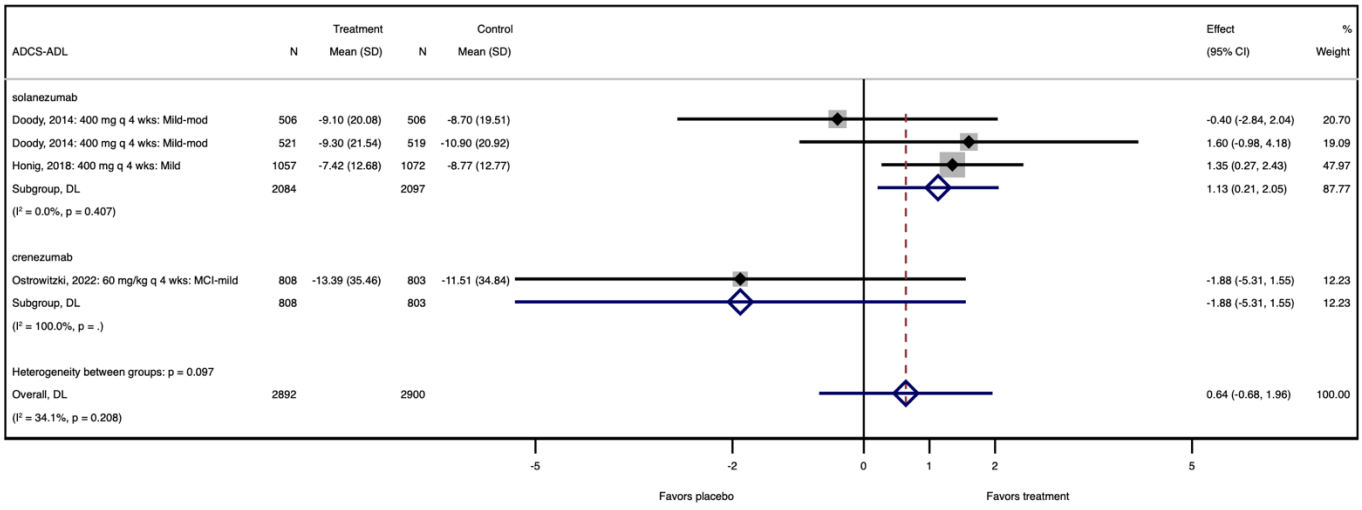
Supplemental Figure 5. Forest plot for the ADAS-Cog-14 cognitive scale



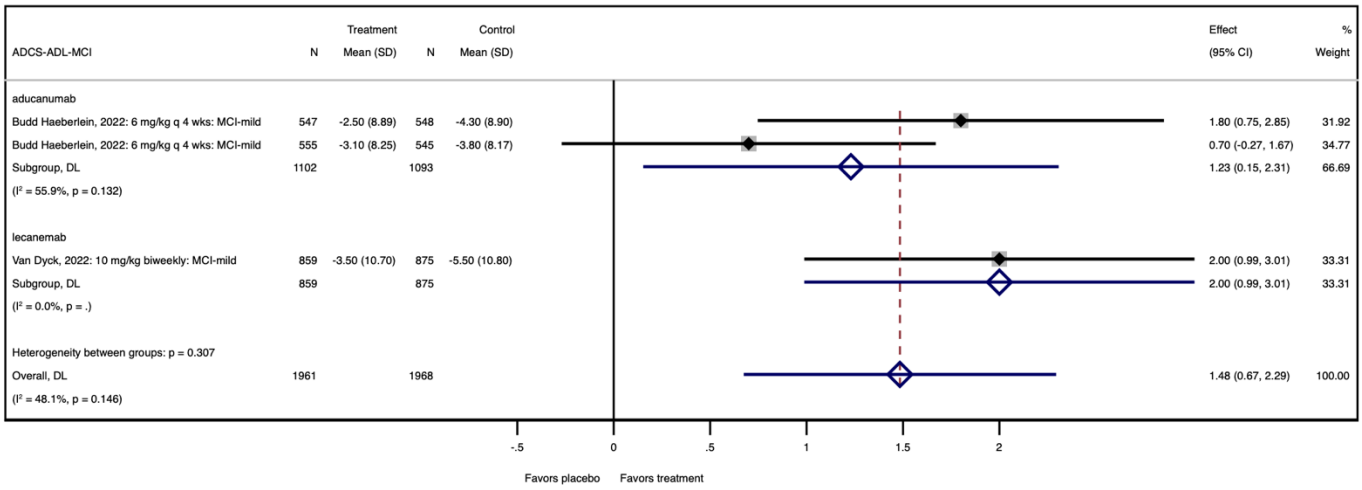
Supplemental Figure 6. Forest plot for Forest plot for the mean differences for the 3 functional scales: ADCS-ADL, ADCS-ADL-MCI and DAD.



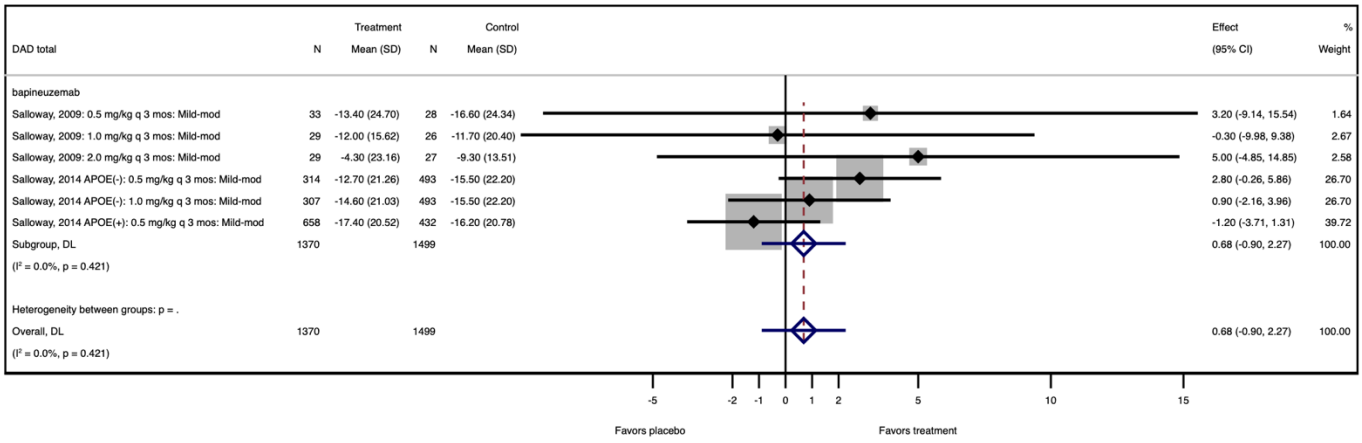
Supplemental Figure 7. Forest plot for the ADCS-ADL functional scale



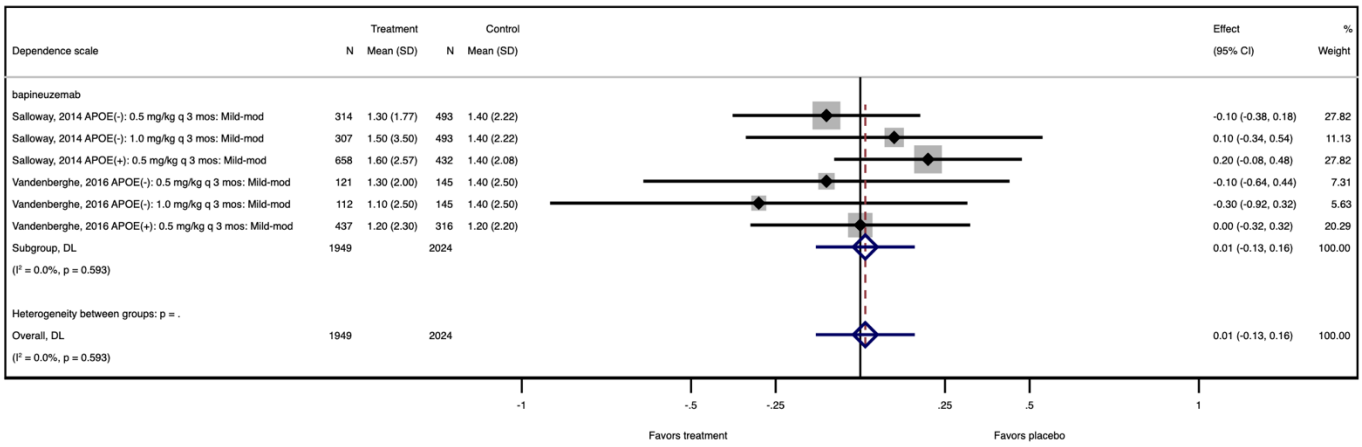
Supplemental Figure 8. Forest plot for the ADCS-ADL-MCI functional scale



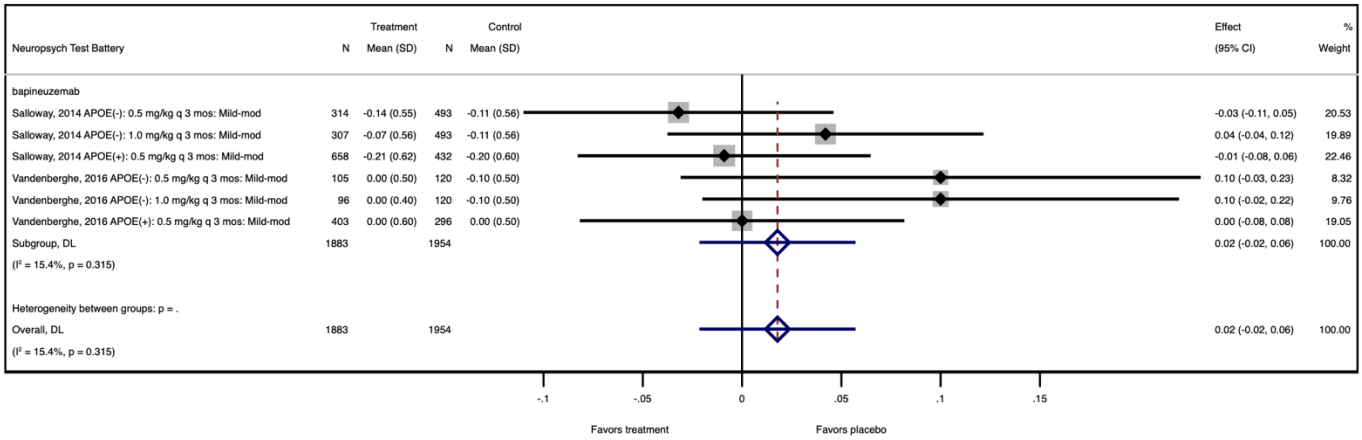
Supplemental Figure 9. Forest plot for the DAD functional scale



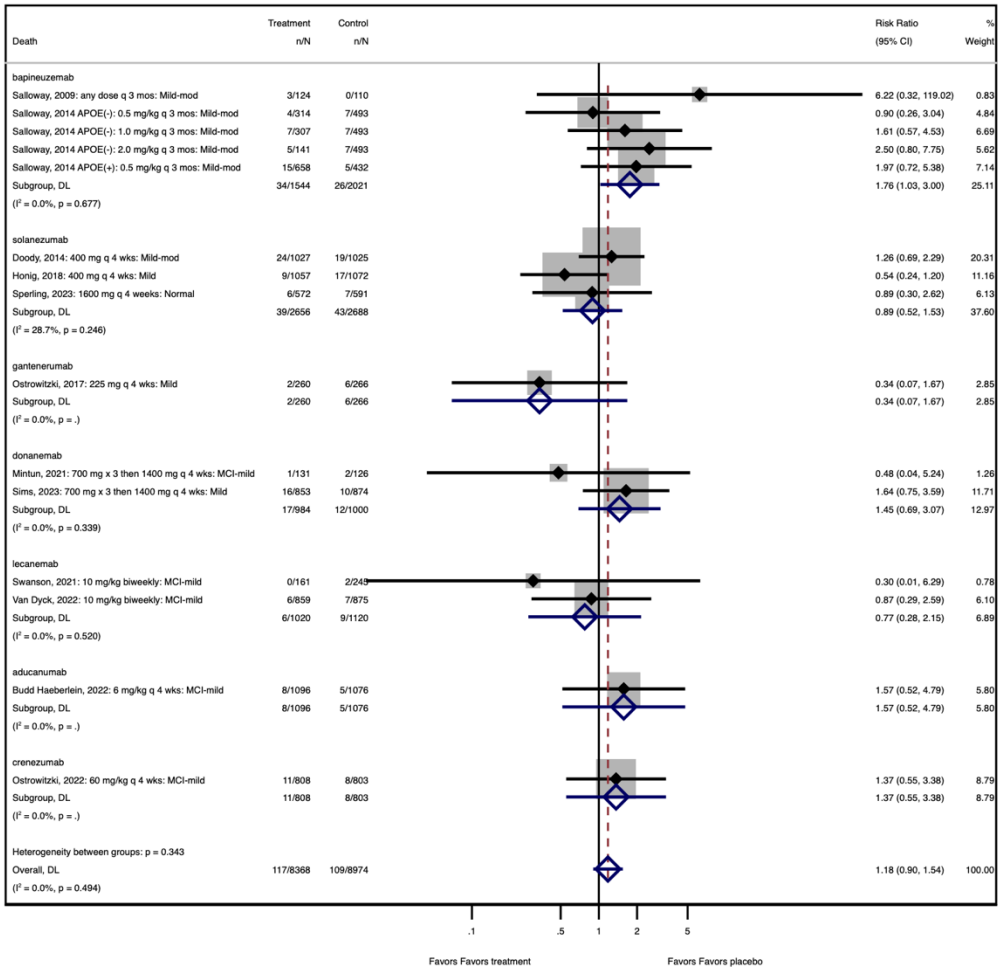
Supplemental Figure 10. Forest plot for the Dependence Scale, a combined scale



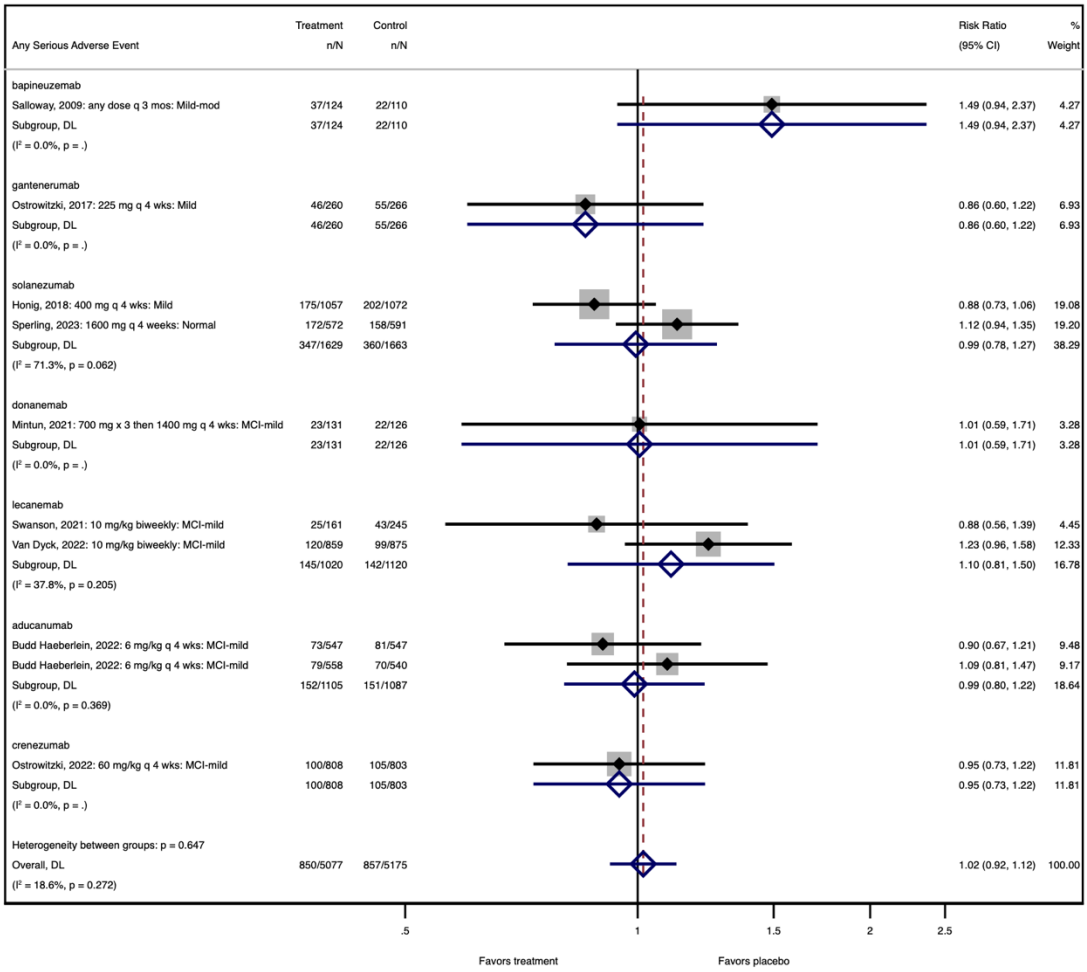
Supplemental Figure 11. Forest plot for the Neuropsychological Test Battery scale



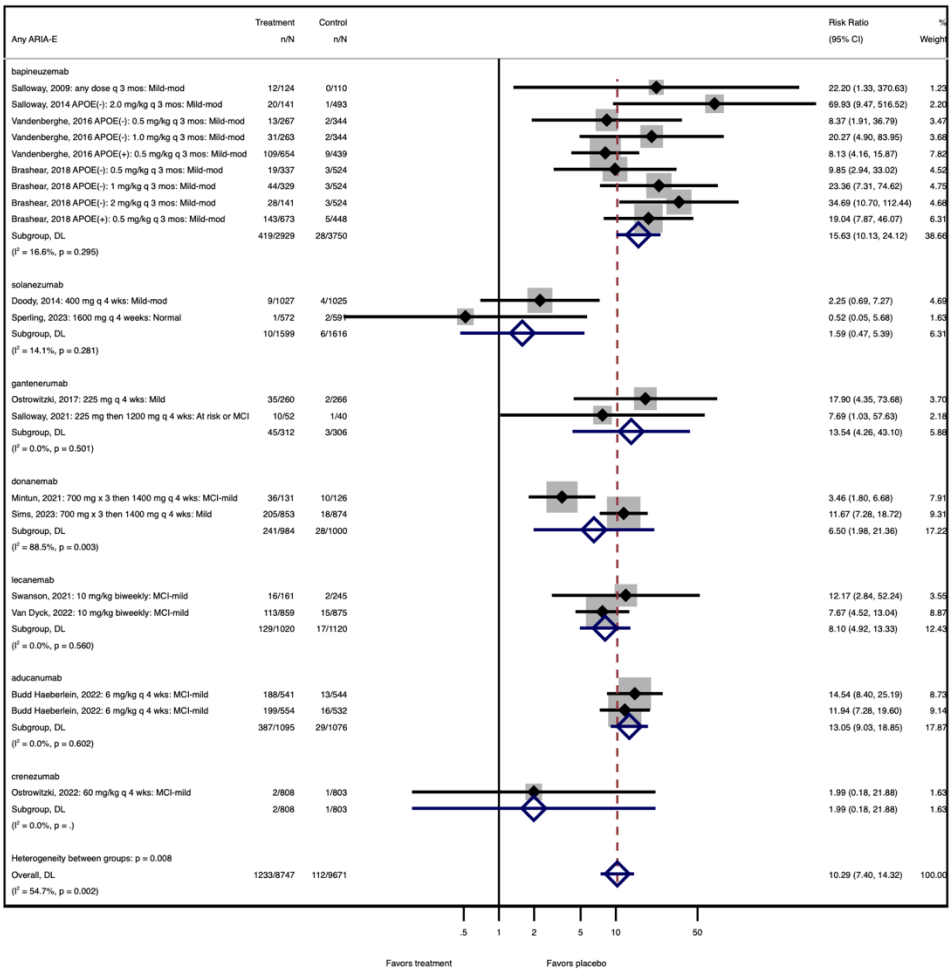
Supplemental Figure 12. Forest plot for mortality



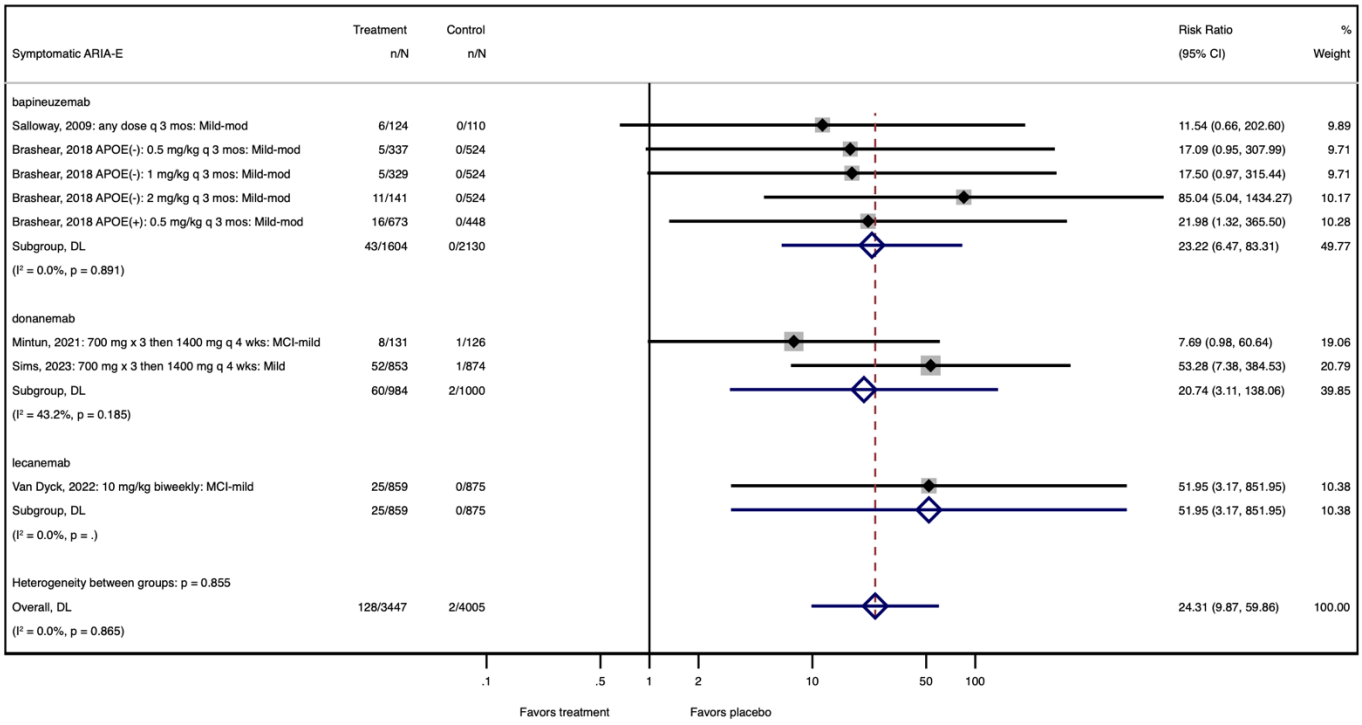
Supplemental Figure 13. Forest plot for serious adverse events



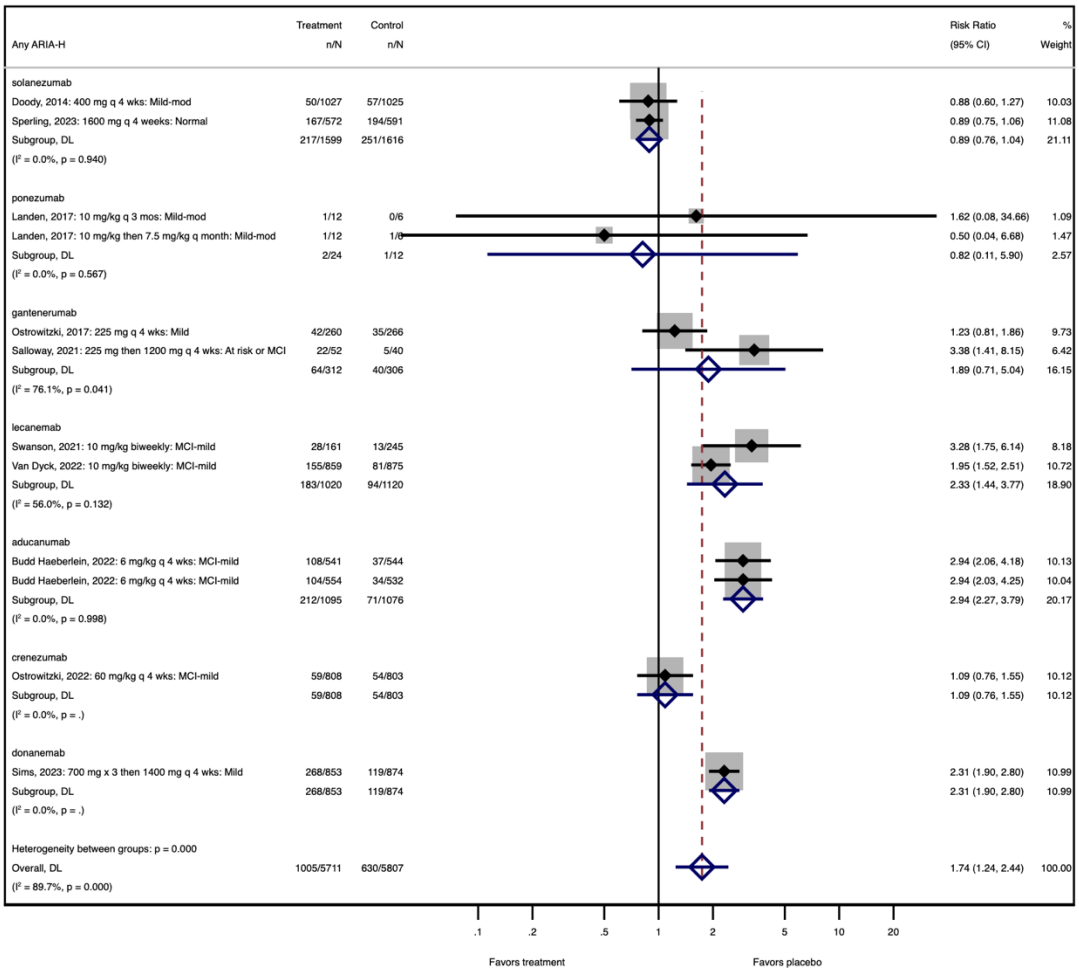
Supplemental Figure 14. Forest plot for any ARIA-E (amyloid related imaging abnormality – edema)



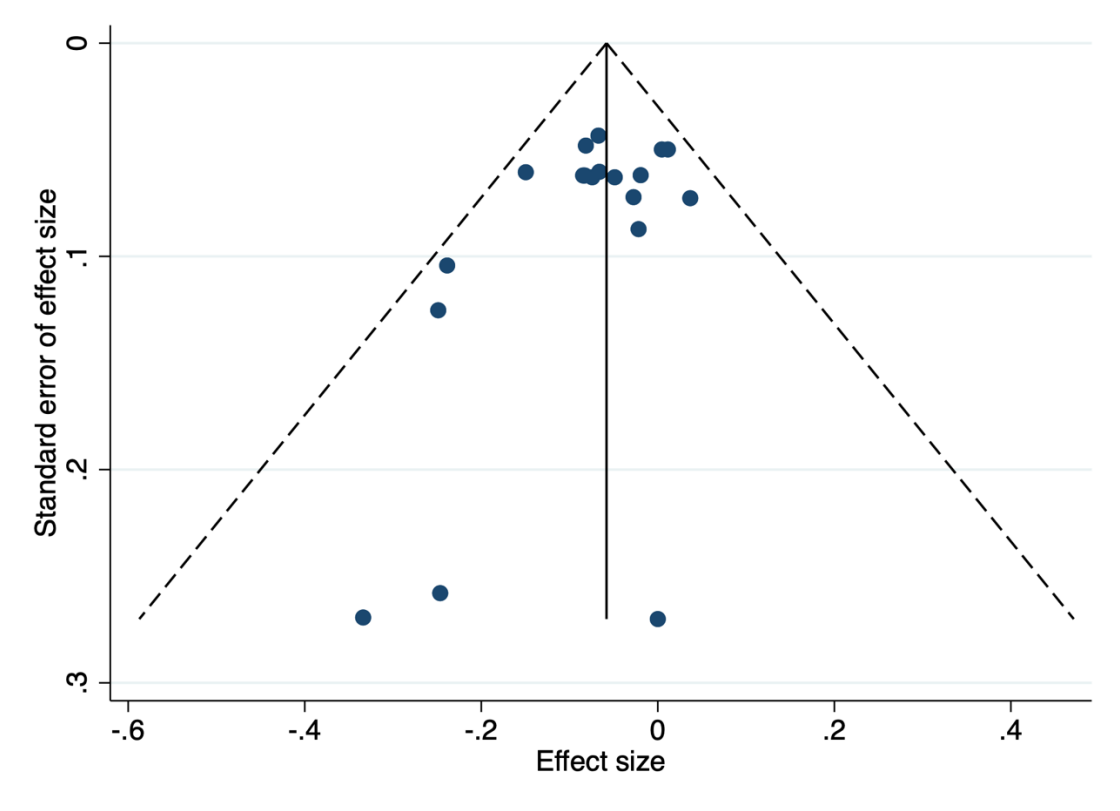
Supplemental Figure 15. Forest plot for symptomatic ARIA-E (amyloid related imaging abnormality – edema)



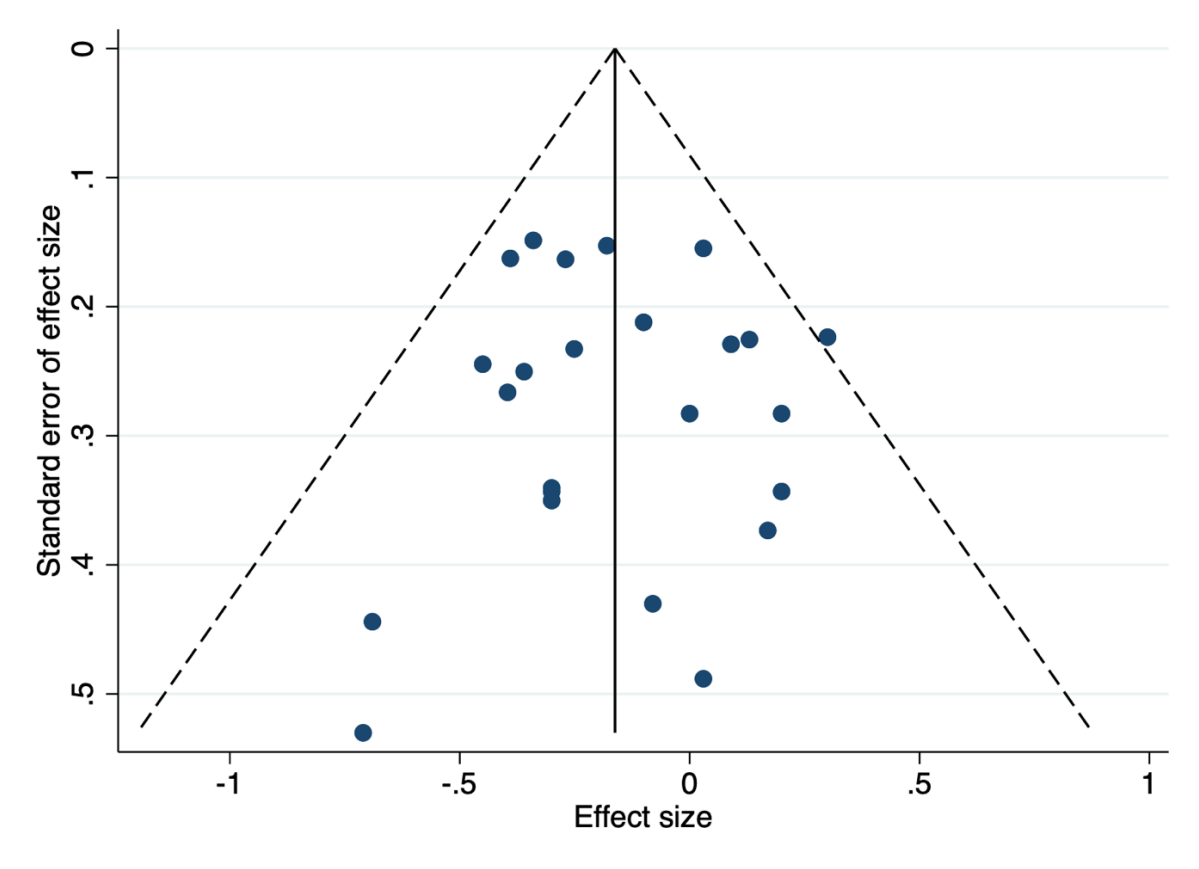
Supplemental Figure 16. Forest plot for any ARIA-H (amyloid related imaging abnormality – hemorrhage)



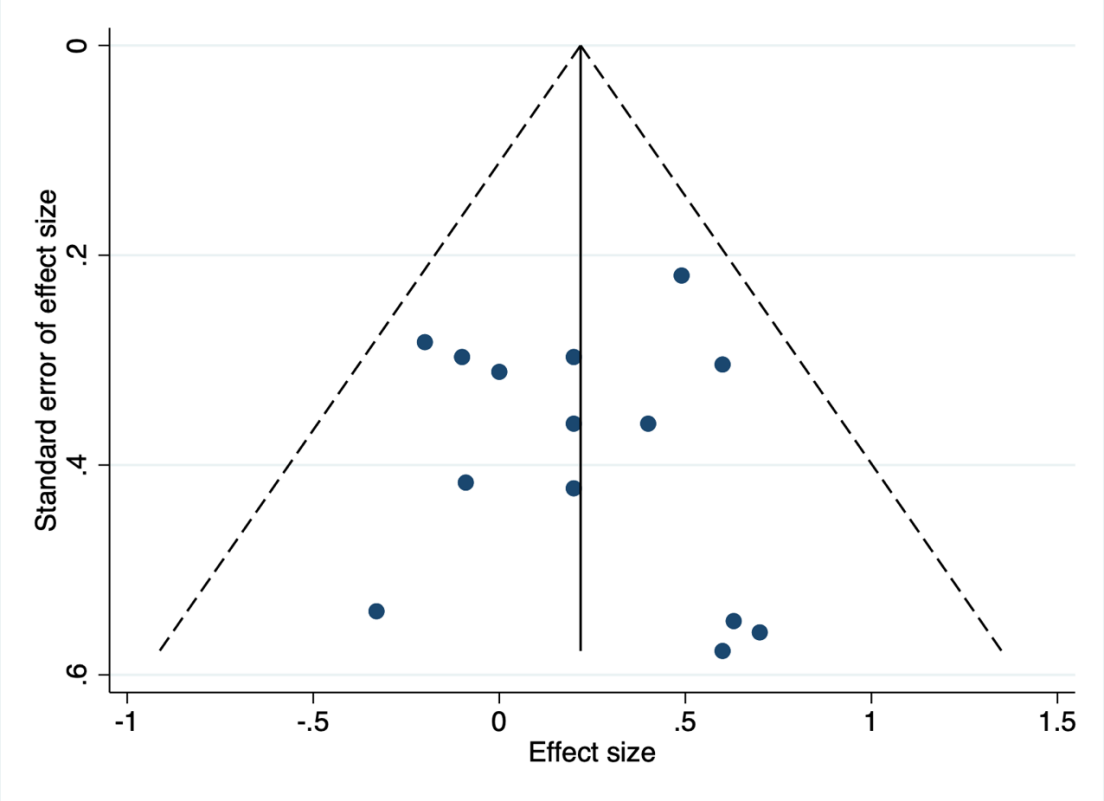
Supplemental Figure 17. Funnel plot for studies reporting ADAS-Cog-11 through -14 scores



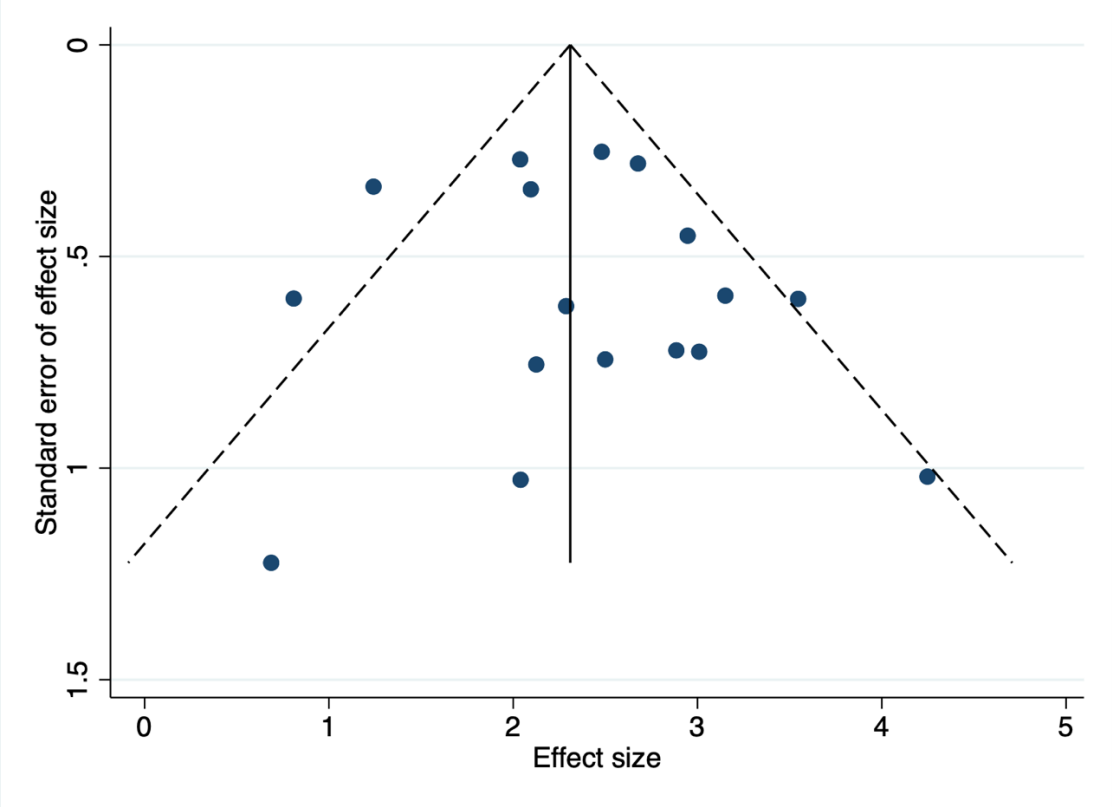
Supplemental Figure 18. Funnel plot for CDR-SB score



Supplemental Figure 19. Funnel plot for MMSE score



Supplemental Figure 20. Funnel plot for ARIA-E outcome



Supplemental Figure 21. Funnel plot for ARIA-H outcome