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	ltem #	Checklist item	Location where item is reported					
TITLE	-							
Title	1	Identify the report as a systematic review.						
ABSTRACT								
Abstract	2	See the PRISMA 2020 for Abstracts checklist.						
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.						
METHODS								
Eligibility criteria	5 Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.							
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.						
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	ltem #	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	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 9-11
syntheses	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 Cl'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 INFORMA	TION		
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



PRISMA 2020 Checklist

Section and Topic	ltem #	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

For more information, visit: <u>http://www.prisma-statement.org/</u>

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.



|--|

Database	Number of publications	Duplicates	Records screened
PubMed	90	0	90
Cochrane CENTRAL	23	7	16
<u>Clinicaltrials.gov</u>	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 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

	Treatment	Control	Risk Ratio	%
Death	n/N	n/N	(95% Cl)	Weight
bapineuzemab				
Salloway, 2009: any dose q 3 mos: Mild-mod	3/124	0/110	6.22 (0.32, 119.02) 0.83
Salloway, 2014 APOE(-): 0.5 mg/kg q 3 mos: Mild-mod	4/314	7/493	0.90 (0.26, 3.04)	4.84
Salloway, 2014 APOE(-): 1.0 mg/kg q 3 mos: Mild-mod	7/307	7/493	1.61 (0.57, 4.53)	6.69
Salloway, 2014 APOE(-): 2.0 mg/kg q 3 mos: Mild-mod	5/141	7/493	2.50 (0.80, 7.75)	5.62
Salloway, 2014 APOE(+): 0.5 mg/kg q 3 mos: Mild-mod	15/658	5/432	1.97 (0.72, 5.38)	7.14
Subgroup, DL	34/1544	26/2021	1.76 (1.03, 3.00)	25.11
(l ² = 0.0%, p = 0.677)				
solanezumab				
Doody, 2014: 400 mg q 4 wks: Mild-mod	24/1027	19/1025	1.26 (0.69, 2.29)	20.31
Honig, 2018: 400 mg q 4 wks: Mild	9/1057	17/1072	0.54 (0.24, 1.20)	11.16
Sperling, 2023: 1600 mg q 4 weeks: Normal	6/572	7/591	0.89 (0.30, 2.62)	6.13
Subgroup, DL	39/2656	43/2688	0.89 (0.52, 1.53)	37.60
(l ² = 28.7%, p = 0.246)			₩.	
gantenerumab				
Ostrowitzki, 2017: 225 mg q 4 wks: Mild	2/260	6/266	0.34 (0.07, 1.67)	2.85
Subgroup, DL	2/260	6/266	0.34 (0.07, 1.67)	2.85
(l ² = 0.0%, p = .)			× 1	
			1	
donanemab				
Mintun, 2021: 700 mg x 3 then 1400 mg q 4 wks: MCI-mild	1/131	2/126	0.48 (0.04, 5.24)	1.26
Sims, 2023: 700 mg x 3 then 1400 mg q 4 wks: Mild	16/853	10/874	1.64 (0.75, 3.59)	11.71
Subgroup, DL	17/984	12/1000	1.45 (0.69, 3.07)	12.97
(l ² = 0.0%, p = 0.339)				
			1	
lecanemab				
Swanson, 2021: 10 mg/kg biweekly: MCI-mild	0/161	2/245	0.30 (0.01, 6.29)	0.78
Van Dyck, 2022: 10 mg/kg biweekly: MCI-mild	6/859	7/875	0.87 (0.29, 2.59)	6.10
Subgroup, DL	6/1020	9/1120	0.77 (0.28, 2.15)	6.89
(l ² = 0.0%, p = 0.520)			* i	
			I. Contraction of the second se	
aducanumab				
Budd Haeberlein, 2022: 6 mg/kg q 4 wks: MCI-mild	8/1096	5/1076	1.57 (0.52, 4.79)	5.80
Subgroup, DL	8/1096	5/1076	1.57 (0.52, 4.79)	5.80
(l ² = 0.0%, p = .)				
			1	
crenezumab				
Ostrowitzki, 2022: 60 mg/kg q 4 wks: MCI-mild	11/808	8/803	1.37 (0.55, 3.38)	8.79
Subgroup, DL	11/808	8/803	1.37 (0.55, 3.38)	8.79
(I* = 0.0%, p = .)				
Heterogeneity between groups: p = 0.343			I.	
Overall. DL	117/8368	109/8974		100.00
$(l^2 = 0.0\% \text{ p} = 0.494)$	1170000	.00/00/4	Y 1.10 (0.50, 1.54)	100.00
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			.1 .5 1 2 5	

Favors Favors treatment

Favors Favors placebo

Supplemental Figure 13. Forest plot for serious adverse events

Any Serious Adverse Event	Treatment n/N	Control n/N			Risk Ratio (95% CI)	% Weight
bapineuzemab						
Salloway, 2009: any dose q 3 mos: Mild-mod	37/124	22/110		*	1.49 (0.94, 2.37)	4.27
Subgroup, DL	37/124	22/110	- i	\longrightarrow	1.49 (0.94, 2.37)	4.27
(I ² = 0.0%, p = .)			1			
gantenerumab						
Ostrowitzki, 2017: 225 mg q 4 wks: Mild	46/260	55/266			0.86 (0.60, 1.22)	6.93
Subgroup, DL	46/260	55/266			0.86 (0.60, 1.22)	6.93
(I ² = 0.0%, p = .)						
solanezumab						
Honig, 2018: 400 mg q 4 wks: Mild	175/1057	202/1072			0.88 (0.73, 1.06)	19.08
Sperling, 2023: 1600 mg q 4 weeks: Normal	172/572	158/591		•	1.12 (0.94, 1.35)	19.20
Subgroup, DL	347/1629	360/1663			0.99 (0.78, 1.27)	38.29
(I ² = 71.3%, p = 0.062)						
donanemab						
Mintun, 2021: 700 mg x 3 then 1400 mg q 4 wks: MCI-mild	23/131	22/126	*		1.01 (0.59, 1.71)	3.28
Subgroup, DL	23/131	22/126			1.01 (0.59, 1.71)	3.28
(I ² = 0.0%, p = .)			1			
lecanemab			1			
Swanson, 2021: 10 mg/kg biweekly: MCI-mild	25/161	43/245	• · ·		0.88 (0.56, 1.39)	4.45
Van Dyck, 2022: 10 mg/kg biweekly: MCI-mild	120/859	99/875	- 1 ;	^ +	1.23 (0.96, 1.58)	12.33
Subgroup, DL	145/1020	142/1120		\rightarrow —	1.10 (0.81, 1.50)	16.78
(I ² = 37.8%, p = 0.205)						
aducanumab			_			
Budd Haeberlein, 2022: 6 mg/kg q 4 wks: MCI-mild	73/547	81/547	• i	_	0.90 (0.67, 1.21)	9.48
Budd Haeberlein, 2022: 6 mg/kg q 4 wks: MCI-mild	79/558	70/540	,	•	1.09 (0.81, 1.47)	9.17
Subgroup, DL	152/1105	151/1087			0.99 (0.80, 1.22)	18.64
(I ² = 0.0%, p = 0.369)						
crenezumab						
Ostrowitzki, 2022: 60 mg/kg q 4 wks: MCI-mild	100/808	105/803			0.95 (0.73, 1.22)	11.81
Subgroup, DL	100/808	105/803			0.95 (0.73, 1.22)	11.81
(l ² = 0.0%, p = .)			•			
Heterogeneity between groups: p = 0.647						
Overall, DL	850/5077	857/5175		←	1.02 (0.92, 1.12)	100.00
(l ² = 18.6%, p = 0.272)			۴	,		
		.5	I 1	I I 1.5 2	2.5	
			Favors treatment	Favors placebo		

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

	Treatment	Control		Risk Ratio	%
Any ARIA-E	n/N	n/N		(95% CI)	Weight
-					
bapineuzemab					
Salloway, 2009; any dose g 3 mos; Mild-mod	12/124	0/110		22.20 (1.33. 370.63)	1.23
Salloway, 2014 APOE(-): 2.0 mg/kg g 3 mos: Mild-mod	20/141	1/493		69.93 (9.47, 516.52)	2.20
Vandenberghe, 2016 APOE(-): 0.5 mg/kg g 3 mgs; Mild-mgd	13/267	2/344	·	8.37 (1.91, 36.79)	3.47
Vandenberghe, 2016 APOE(-): 1.0 mg/kg q 3 mos: Mild-mod	31/263	2/344		20 27 (4 90 83 95)	3.69
Vandenberghe, 2010 APOE(-): 0.5 metric 0.0 metrical	100/054	0/400		20.27 (4.50, 55.55)	7.00
Vandenbergne, 2016 APOE(+): 0.5 mg/kg q 3 mos: Mild-mod	109/654	9/439		8.13 (4.16, 15.87)	1.02
Brashear, 2018 APOE(-): 0.5 mg/kg q 3 mos: Mild-mod	19/337	3/524		9.85 (2.94, 33.02)	4.52
Brashear, 2018 APOE(-): 1 mg/kg q 3 mos: Mild-mod	44/329	3/524		23.36 (7.31, 74.62)	4.75
Brashear, 2018 APOE(-): 2 mg/kg q 3 mos: Mild-mod	28/141	3/524		34.69 (10.70, 112.44)	4.68
Brashear, 2018 APOE(+): 0.5 mg/kg q 3 mos: Mild-mod	143/673	5/448		19.04 (7.87, 46.07)	6.31
Subgroup, DL	419/2929	28/3750		15.63 (10.13, 24.12)	38.66
(l ² = 16.6%, p = 0.295)					I
			1		I
solanezumab					I
Doody, 2014: 400 mg q 4 wks: Mild-mod	9/1027	4/1025		2.25 (0.69, 7.27)	4.69
Sperling, 2023: 1600 mg q 4 weeks: Normal	1/572	2/59		0.52 (0.05, 5.68)	1.63
Subgroup, DL	10/1599	6/1616		1.59 (0.47, 5.39)	6.31
$(l^2 = 14.1\%, p = 0.281)$					- 1
(- · · · · · · · · · · · · · · · · · ·			I I		- 1
contenerimet			I I		- 1
Ostrowitzki 2017: 225 ma a 4 wire: Mild	35/260	2/266		17.00 (4.35, 73.68)	3 70
Collower 2004 205	33/200	2/200		77.50 (4.35, 73.66)	3.70
Salloway, 2021: 225 mg then 1200 mg q 4 wks: At risk or MC1	10/52	1/40		7.69 (1.03, 57.63)	2.18
Subgroup, DL	45/312	3/306		13.54 (4.26, 43.10)	5.88
(I* = 0.0%, p = 0.501)			I I		- 1
			1		- 1
donanemab					- 1
Mintun, 2021: 700 mg x 3 then 1400 mg q 4 wks: MCI-mild	36/131	10/126		3.46 (1.80, 6.68)	7.91
Sims, 2023: 700 mg x 3 then 1400 mg q 4 wks: Mild	205/853	18/874		11.67 (7.28, 18.72)	9.31
Subgroup, DL	241/984	28/1000		6.50 (1.98, 21.36)	17.22
(l ² = 88.5%, p = 0.003)			• I		- 1
			1		- 1
lecanemab					- 1
Swanson, 2021: 10 mg/kg biweekly: MCI-mild	16/161	2/245		12.17 (2.84, 52.24)	3.55
Van Dyck, 2022; 10 mg/kg biweekly; MCI-mild	113/859	15/875		7.67 (4.52, 13.04)	8.87
Subaroup, DL	129/1020	17/1120		8.10 (4.92, 13.33)	12.43
$(l^2 = 0.0\%, p = 0.560)$					
(r = 0.0 m, p = 0.000)					- 1
aducanimah					- 1
Budd Hasharlain 2022: 6 malka o 4 wks: MCI	100/541	12/5/4		14 64 (9 40 26 10)	. 74
Budd Hecharlein, 2022; 6 mg/kg q 4 wks; MCI-Mild	100/241	10/044		14.04 (8.40, 25.19)	./3
buou maebenein, 2022: 6 mg/kg q 4 wks: MGI-mild	199/554	16/532		11.94 (7.28, 19.60)	9.14
Subgroup, DL	387/1095	29/10/6	$\overline{\mathbf{\nabla}}$	13.05 (9.03, 18.85)	17.87
(r = 0.0%, p = 0.602)					I
			i i		
crenezumab					I
Ostrowitzki, 2022: 60 mg/kg q 4 wks: MCI-mild	2/808	1/803		1.99 (0.18, 21.88)	1.63
Subgroup, DL	2/808	1/803		1.99 (0.18, 21.88)	1.63
(l ² = 0.0%, p = .)			•		
			l i		
Heterogeneity between groups: p = 0.008					I
Overall, DL	1233/8747	112/9671		10.29 (7.40, 14.32)	100.00
(l ² = 54.7%, p = 0.002)			×		
			.5 1 2 5 10 50		

Favors treatment Favors placebo

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)

	Treatment	Control		Risk Ratio	%
Any ARIA-H	n/N	n/N		(95% CI)	Weight
solanezumab					
Doody, 2014: 400 mg q 4 wks: Mild-mod	50/1027	57/1025		0.88 (0.60, 1.27)	10.03
Sperling, 2023: 1600 mg q 4 weeks: Normal	167/572	194/591		0.89 (0.75, 1.06)	11.08
Subgroup, DL	217/1599	251/1616		0.89 (0.76, 1.04)	21.11
(l° = 0.0%, p = 0.940)			I I		I
ponezumab	4/40	0.00		1 00 (0 00 04 00)	1.00
Landen, 2017: 10 mg/kg q 3 mos: Mild-mod	1/12	0/6		1.62 (0.08, 34.66)	1.09
Landen, 2017: 10 mg/kg then 7.5 mg/kg q month: Mild-mod	1/12	1/8		0.50 (0.04, 6.68)	1.47
	2/24	1/12		0.82 (0.11, 5.90)	2.57
$(1^{\circ} = 0.0\%, p = 0.567)$					I
aantonorumah					
gamenerumad	10/000	05/000		1 00 (0 01 1 00)	0.70
Costrownizki, 2017: 225 mg q 4 wks: Mild	42/260	35/266		1.23 (0.81, 1.86)	9.73
Salloway, 2021: 225 mg then 1200 mg q 4 wks: At hisk or MCI	22/52	5/40		3.38 (1.41, 8.15)	6.42
Subgroup, DL	64/312	40/306		1.89 (0.71, 5.04)	16.15
(r = 76.1%, p = 0.041)					I
lannanah			1		I
Command Contractor biometric MOL with	00/4.04	10/015		0.00 /4 75 0.44	
Swanson, 2021: 10 mg/kg biweekiy: MCI-mild	28/161	13/245		3.28 (1.75, 6.14)	8.18
Van Dyck, 2022: 10 mg/kg biweekiy: MCI-mild	155/859	81/8/5		1.95 (1.52, 2.51)	10.72
(12 - 56 0%, 0.100)	163/1020	94/1120		2.33 (1.44, 3.77)	10.90
(r = 30.0%, p = 0.132)					I
aducanumab					I
Budd Haeberlein, 2022: 6 ma/ka a 4 wks: MCI-mild	108/541	37/544		2 94 (2 06 4 18)	10.13
Budd Haeberlein, 2022: 6 mg/kg q 4 mks: MCL-mild	104/554	34/532		2 94 (2 03 4 25)	10.04
Subaroup DI	212/1095	71/1076		2.04 (2.27, 3.79)	20.17
$(l^2 = 0.0\% \text{ p} = 0.998)$	2121000	/ // 0/0		2.04 (2.27, 0.70)	20.17
(i = 0.0 %, p = 0.000)					I
crenezumab					I
Ostrowitzki 2022: 60 ma/ka a 4 wks: MCI-mild	59/808	54/803		1 09 (0 76 1 55)	10.12
Subaroup, DL	59/808	54/803		1.09 (0.76, 1.55)	10.12
$(l^2 = 0.0\%, p = .)$			Y	(
· · · · · · · · · · · · · · · · · · ·					
donanemab					
Sims, 2023; 700 mg x 3 then 1400 mg g 4 wks: Mild	268/853	119/874		2.31 (1.90, 2.80)	10.99
Subaroup, DL	268/853	119/874	\mathbf{A}	2.31 (1.90, 2.80)	10.99
(l ² = 0.0%, p = .)			\mathbf{v}	, , , , , , , , , , , , , , , , , , , ,	
			i i		
Heterogeneity between groups: $p = 0.000$					
Overall, DL	1005/5711	630/5807		1.74 (1.24, 2.44)	100.00
(l ² = 89.7%, p = 0.000)			V		
			.1 .2 .5 1 2 5 10 20		
			Favors treatment Favors placebo		



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 20. Funnel plot for ARIA-E outcome





