

Guideline: "Diagnosis and treatment of dementia and Mild cognitive impairment"

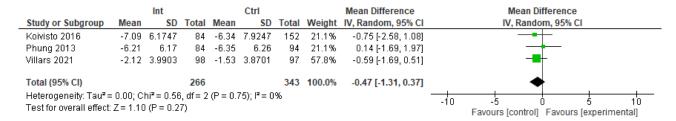
Supplementary material

Meta-analysis

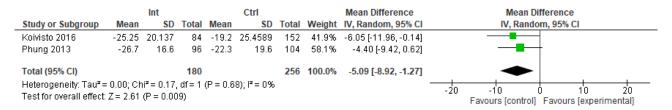
REVIEW QUESTION 5. How effective are pre-, peri- and post-diagnostic counselling and support on outcomes for people living with dementia and their caregivers?

Outcomes of people with dementia

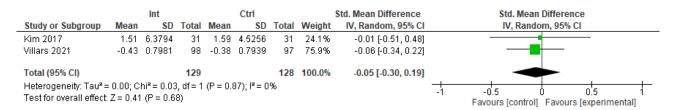
MMSE



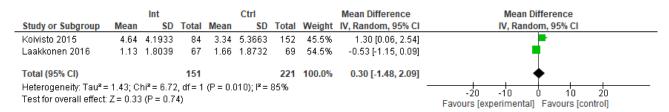
ADCS-ADL



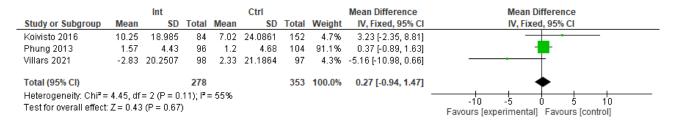
ADL



CDR-SB



NPI



Qol-AD

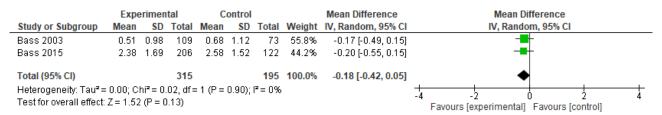
		Int			Ctrl			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Koivisto 2016	-0.36	7.8336	84	1.22	10.0463	152	25.3%	-1.58 [-3.89, 0.73]	
Phung 2013	-2.89	4.89	96	-2.84	2	103	43.4%	-0.05 [-1.10, 1.00]	
Villars 2021	1.32	6.2348	98	-0.5	6.8967	97	31.3%	1.82 [-0.03, 3.67]	-
Total (95% CI)			278			352	100.0%	0.15 [-1.46, 1.76]	-
Heterogeneity: Tau² = Test for overall effect				(P = 0.0	07); I * = 63	%			-4 -2 0 2 4 Favours [control] Favours [experimental]

REVIEW QUESTION 7a. What are the most effective methods of care planning, focusing upon improving outcomes for people with dementia and their carers?

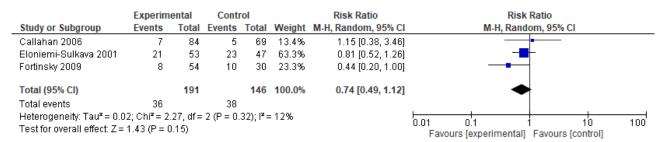
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings

	Expe	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Bass 2003	0.18	0.56	109	0.26	0.59	73	76.4%	-0.08 [-0.25, 0.09]			
Bass 2015	1.8	1.22	206	1.77	1.46	122	23.6%	0.03 [-0.28, 0.34]			
Total (95% CI)			315			195	100.0%	-0.05 [-0.20, 0.10]	•		
Heterogeneity: Tau²: Test for overall effect				-0.5 -0.25 0 0.25 0.5 Favours [experimental] Favours [control]							

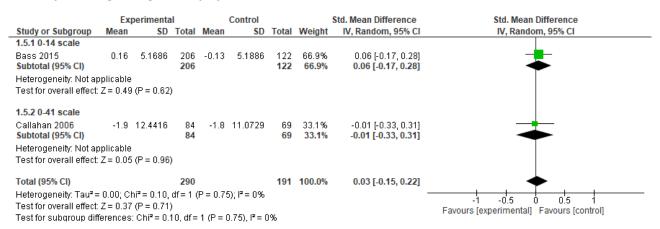
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – ER admission



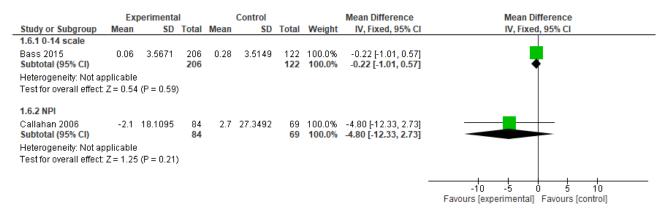
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – institutionalization rate



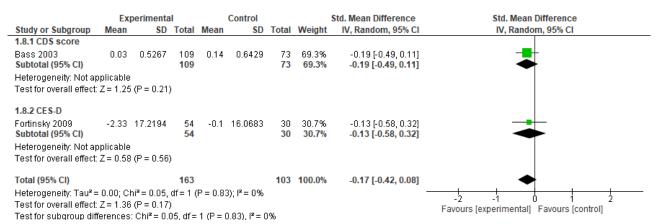
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – cognitive symptoms



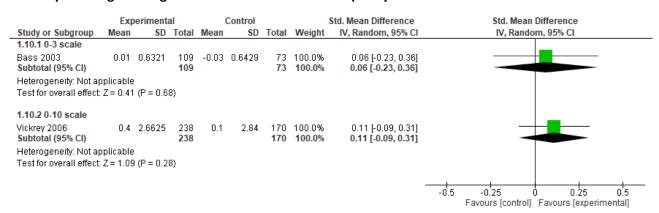
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – behavioural symptoms



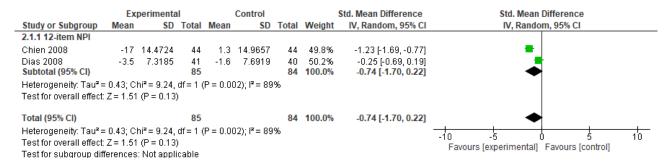
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – caregivers' depressive symptoms



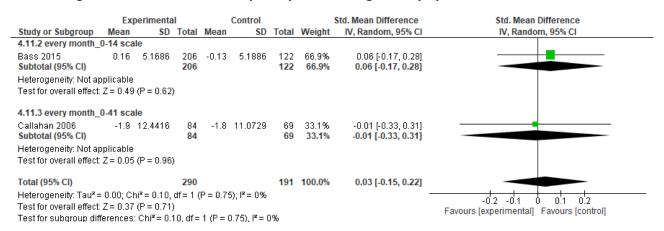
Care coordination/management using a protocol/action plan (including training for caregivers) and monthly meetings – caregivers' satisfaction on services quality



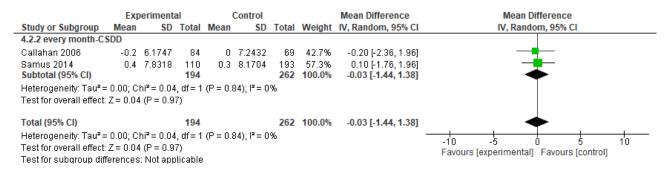
Case management, follow-up every 2 months - NPI



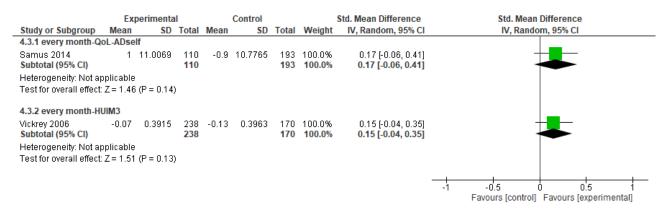
Case management: combined, follow-up every month - cognitive symptoms



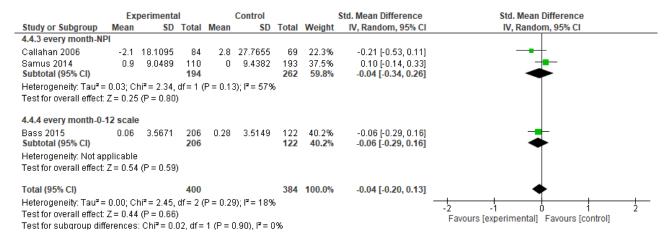
Case management: combined, follow-up every month - CSDD



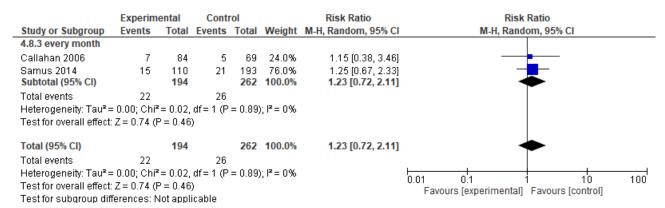
Case management: combined, follow-up every month - quality of life of people with dementia



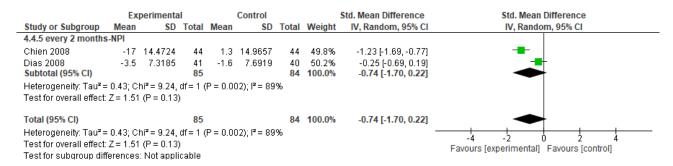
Case management: combined, follow-up every month - behavioural symptoms



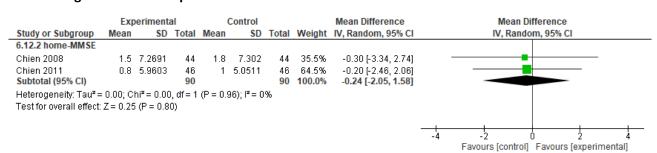
Case management: combined, follow-up every month - institutionalization rate



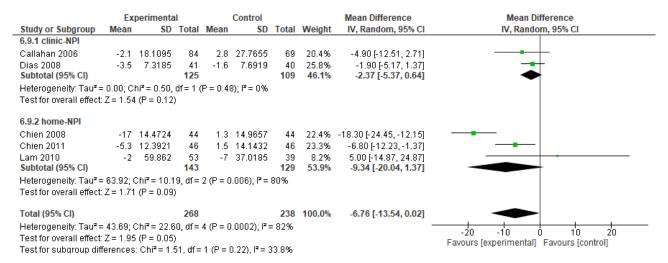
Case management: combined, follow-up every 2 months - behavioural symptoms



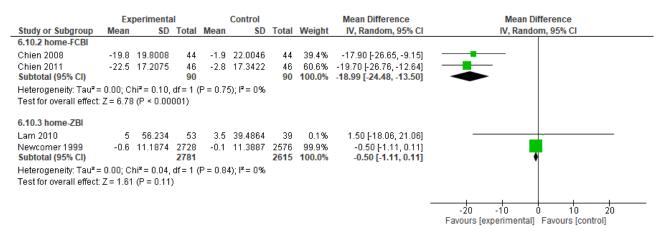
Case management: follow-up visits at home - MMSE



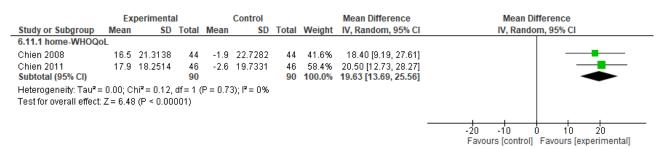
Case management: follow-up at home or in clinics- behavioural symptoms



Case management: follow-up visits at home - caregivers' burden



Case management: follow-up visits at home - caregivers' quality of life

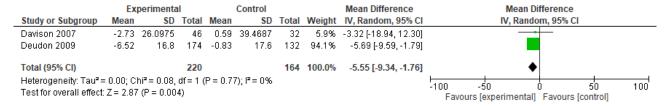


Case management: follow-up visits at home – institutionalization rate

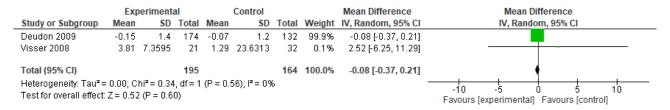
	Experimental			Control			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
6.8.1 home											
Chien 2008	-2.5	2.0541	44	0.5	3.643	44	28.7%	-3.00 [-4.24, -1.76]			
Chien 2011 Subtotal (95% CI)	-2.2	1.3815	46 90	0.9	2.3353	46 90	71.3% 100.0%	-3.10 [-3.88, -2.32] -3.07 [-3.73, -2.41]	<u>+</u>		
Heterogeneity: Tau² :	= 0.00; C	$hi^2 = 0.02$, df = 1	(P = 0.3)	89); I² = 0	%					
Test for overall effect	Z = 9.09	P < 0.0	0001)								
									-4 -2 0 2 4		
									Favours [experimental] Favours [control]		

REVIEW QUESTION 9. What effect does training for staff working with people living with dementia have upon the experiences of people living with dementia in their care?

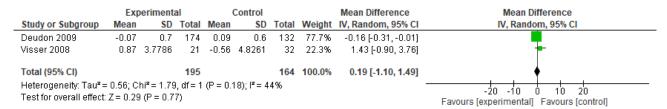
BPSD Training – CMAI



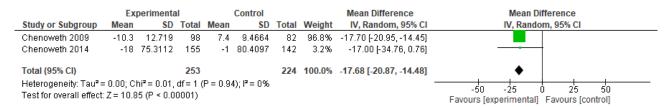
BPSD Training - CMAI-PA



BPSD Training - CMAI-VA



Person-Centered - CMAI



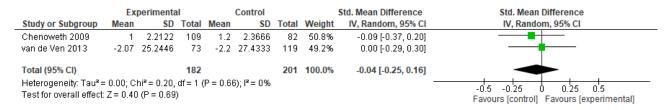
Care Mapping - CMAI

	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Chenoweth 2009	-2.4	9.1121	109	7.4	9.4664	82	55.5%	-9.80 [-12.47, -7.13]		
van de Ven 2013	1.57	25.116	73	0.52	27.1579	119	44.5%	1.05 [-6.50, 8.60]	+	
Total (95% CI)			182			201	100.0%	-4.97 [-15.54, 5.59]	•	
Heterogeneity: Tau² = Test for overall effect				-100 -50 0 50 10 Favours [experimental] Favours [control])O					

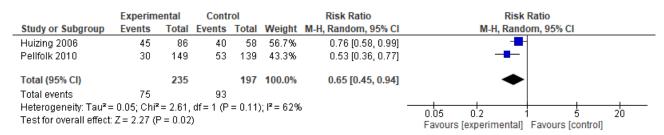
Care Mapping - NPI

	Ex	perimenta	ıl	(Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Chenoweth 2009	0.8	7.1106	109	-1.6	7.3729	82	73.7%	2.40 [0.32, 4.48]	
van de Ven 2013	0.93	11.0579	73	-2.15	13.276	119	26.3%	3.08 [-0.40, 6.56]	 -
Total (95% CI)			182			201	100.0%	2.58 [0.79, 4.36]	•
Heterogeneity: Tau² : Test for overall effect			,	-	-50 -25 0 25 50 Favours [experimental] Favours [control]				

Care Mapping - quality of life of people with dementia



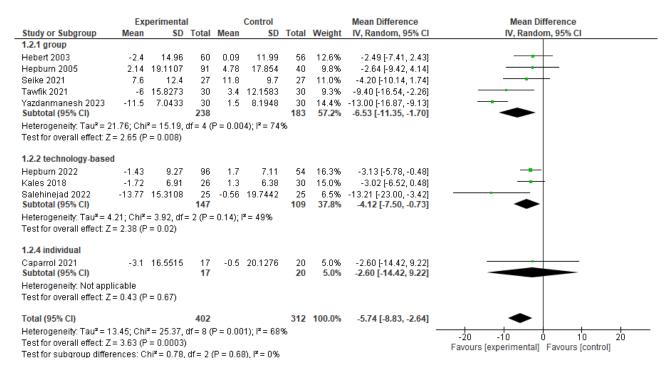
Reducing physical restraint frequency use



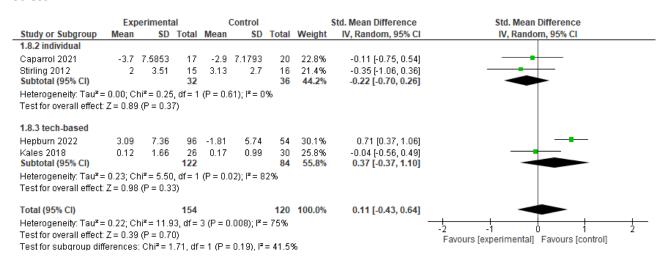
REVIEW QUESTION 14b. How effective are carers' assessments in identifying the needs of informal carers of people living with dementia?

PSYCHOEDUCATIONAL INTERVENTIONS

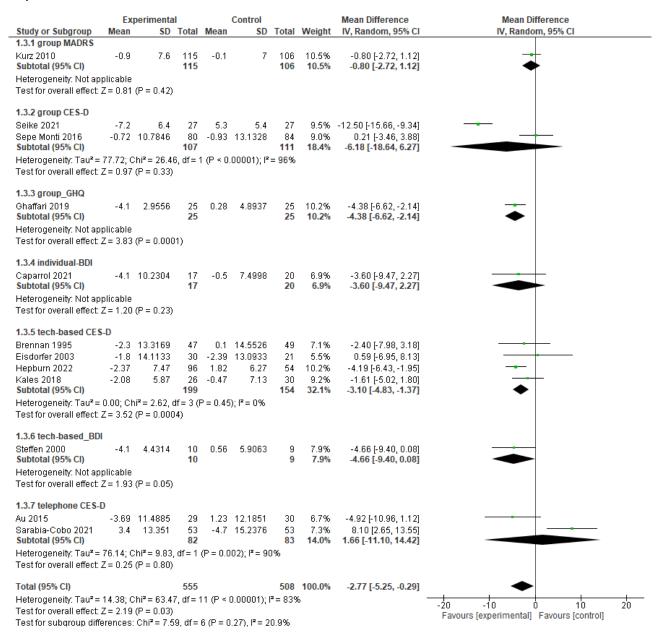
ZBI



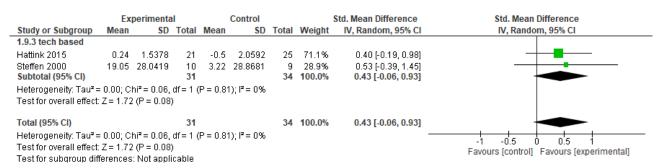
Stress



Depression

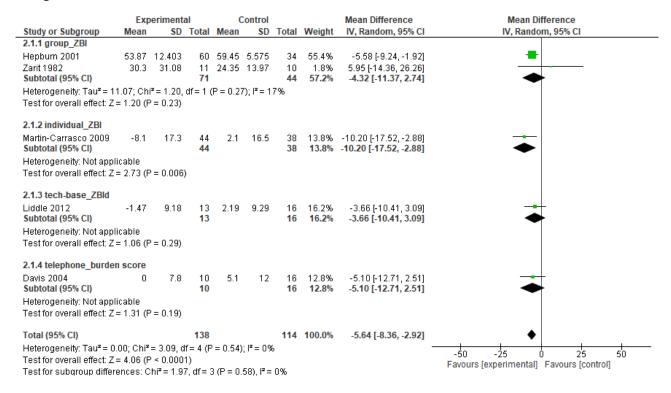


Self-efficacy

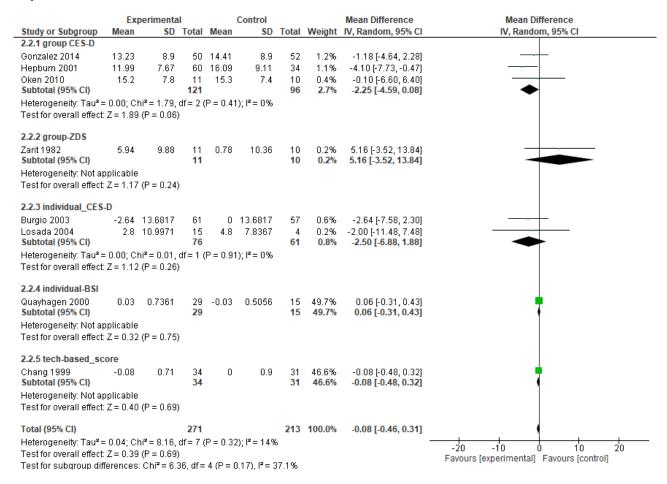


SKILL TRAINING

Caregiver burden

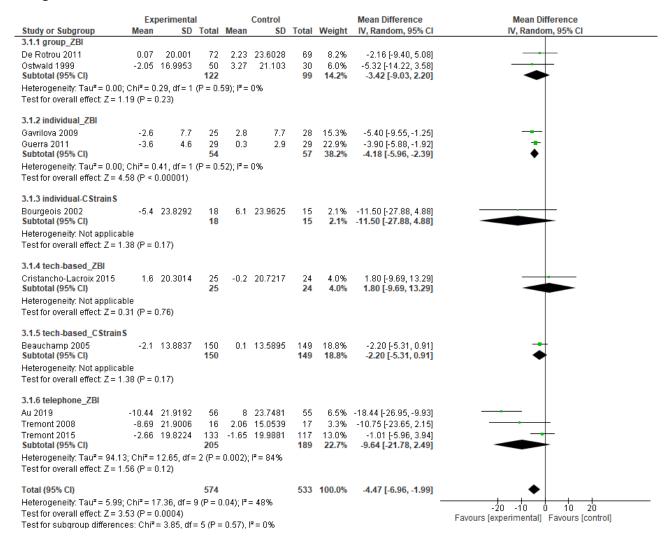


Depression



PSYCHOEDUCATIONAL INTERVENTIONS AND SKILL TRAINING

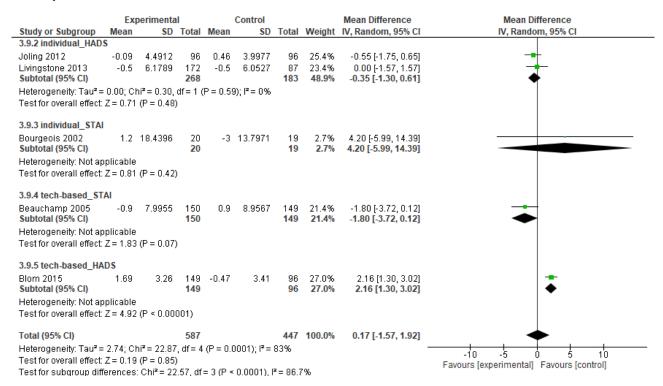
Caregiver burden



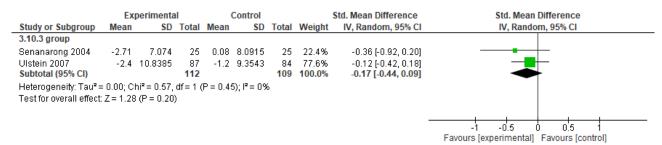
Depression

Study or Subgroup	Ex Mean	perimental SD		Mean	Control	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
3.3.1 group_MADRS De Rotrou 2011		10.6814	72		13.5705	69	3.2%	-1.41 [-5.45, 2.63]	
Subtotal (95% CI)		10.0011	72	1.21	10.0100	69	3.2%	-1.41 [-5.45, 2.63]	
Heterogeneity: Not applicable Test for overall effect: Z = 0.68		49)							
3.3.2 group_CES-D									
Losada 2011 Ostwald 1999		15.6578 11.0932	68 51		16.9953 11.4621	50 30	1.5% 2.1%	-3.98 [-9.98, 2.02] -2.05 [-7.16, 3.06]	
Subtotal (95% CI)			119			80	3.6%	-2.86 [-6.75, 1.03]	
Heterogeneity: $Tau^2 = 0.00$; C Test for overall effect: $Z = 1.44$			= 0.63); I² = 0'	%				
3.3.3 individual_CES-D									
Bourgeois 2002 Burns 2003		13.2261 13.2647	20 38	3.2	9.8343 16.2559	19 37	1.1% 1.2%	0.90 [-6.39, 8.19] -1.30 [-8.02, 5.42]	
Joling 2012		10.6604	96	2.91	9.4759	96	6.0%	-1.40 [-4.25, 1.45]	
Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; C	hi≅ – 0.3	2 df = 2 /P	154 - 0.95	\- I≅ — ∩•	04.	152	8.3%	-1.12 [-3.59, 1.35]	
Test for overall effect: Z = 0.89			- 0.00,),1 – 0	70				
3.3.4 individual_CES-D short		4 6 4 0 4	50	0.00	4 7400	50	40.00	0.701.2.47.0.041	
Judge 2012 Subtotal (95% CI)	-0.72	4.6431	59 59	0.06	4.7199	59 59	13.2% 13.2%	-0.78 [-2.47, 0.91] - 0.78 [-2.47, 0.91]	•
Heterogeneity: Not applicable Test for overall effect: Z = 0.90		37)							
3.3.5 individual_HADS									
Livingstone 2013	-0.2	5.5145	172	0.6	5.6304	87	16.0%	-0.80 [-2.24, 0.64]	<u> </u>
Subtotal (95% CI) Heterogeneity: Not applicable	9		172			87	16.0%	-0.80 [-2.24, 0.64]	\blacksquare
Test for overall effect: $Z = 1.09$		28)							
3.3.6 tech-based_CES-D									
Beauchamp 2005 Blom 2015	-1.4 -2.35	14.7514 8.21	150 149		15.5043 7.51	149	4.4%	-2.40 [-5.83, 1.03]	
Gallagher-Thompson 2010		14.0387	36	0.34 -0.8	15.6198	96 34	10.5% 1.2%	-2.69 [-4.69, -0.69] -1.45 [-8.42, 5.52]	
Kajiyama 2013 Subtotal (95% CI)	-2.52	10.7421	46 381	-0.77	11.9094	57 336	2.8% 18.8%	-1.75 [-6.13, 2.63] - 2.45 [-4.01, -0.88]	
Heterogeneity: Tau ² = 0.00; C	hi² = 0.2	3, df = 3 (P); I² = 0°	%	330	10.0%	-2.43 [-4.01, -0.00]	
Test for overall effect: Z = 3.06	6 (P = 0.1	002)							
3.3.7 tech-based_BDI									
Cristancho-Lacroix 2015 Subtotal (95% CI)	1.2	14.6083	25 25	-0.2	9.7806	24 24	1.2% 1.2%	1.40 [-5.54, 8.34] 1.40 [-5.54, 8.34]	
Heterogeneity: Not applicable Test for overall effect: Z = 0.40		69)	20			2.4	11270	1140 [-0.04, 0.04]	
3.3.8 telephone_CES-D		·							
Au 2019	-4.67	11.2023	56	1.63	14.2044	55	2.4%	-6.30 [-11.06, -1.54]	
Tremont 2015 Subtotal (95% CI)	-2.89	14.1672	133 189	0.43	14.09	117 172	4.2% 6.6%	-3.32 [-6.83, 0.19] -4.37 [-7.19, -1.54]	
Heterogeneity: Tau² = 0.00; C Test for overall effect: Z = 3.03); I² = 0'	%	172	0.076	-4.07 [-7.10, -1.04]	
3.3.9 telephone_GD\$		-							
Tremont 2008	-0.56	7.0938	16	1.88	8.9857	17	1.8%	-2.44 [-7.95, 3.07]	
Subtotal (95% CI)			16			17	1.8%	-2.44 [-7.95, 3.07]	
Heterogeneity: Not applicable Test for overall effect: Z = 0.83		39)							
3.3.10 group_MAACL									
Coon 2003 Subtotal (95% CI)	-1.4	1.7742	41 41	1.9	1.7762	44 44	27.4% 27.4 %	-3.30 [-4.06, -2.54] - 3.30 [-4.06, -2.54]	‡
Heterogeneity: Not applicable	e		71			44	21.4/0	-5.50 [-4.00, -2.54]	•
Test for overall effect: Z = 8.56		00001)							
Total (95% CI)			1228			1040	100.0%	-2.14 [-2.90, -1.38]	◆
Heterogeneity: Tau ² = 0.40; C			(P = 0.	23); l² =	:19%			-	-10 -5 0 5 10
Test for overall effect: Z = 5.52 Test for subgroup differences			9 (P =	0.04), P	²= 50.0%				Favours [experimental] Favours [control]

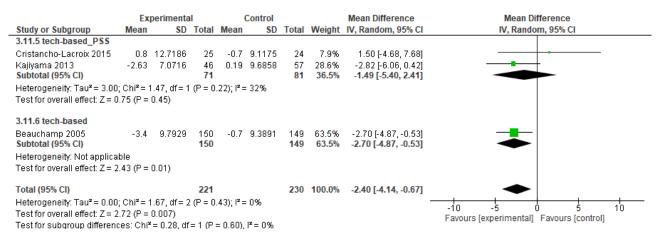
Anxiety



Caregiver stress - group interventions



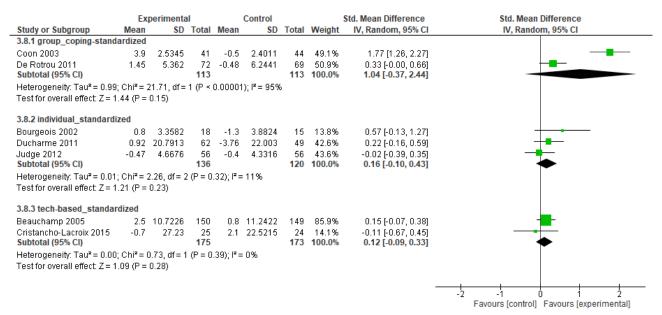
Caregiver stress – interventions on technological support



Quality of life - Interventi individuali

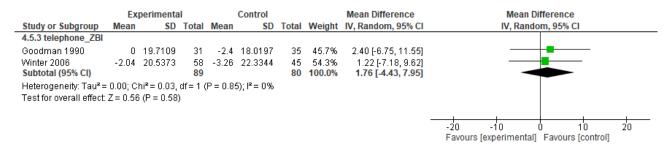
	Experimental			Control			Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
3.12.1 individual_sta	ndardize	ed								
Burns 2003	-0.7	19.6246	36	-4.1	20.0334	34	16.1%	0.17 [-0.30, 0.64]	-	
Gavrilova 2009	4	9.3	25	2.7	12	28	12.2%	0.12 [-0.42, 0.66]		
Joling 2012	-3.44	22.604	96	-2.69	22.8014	96	44.4%	-0.03 [-0.32, 0.25]		
Judge 2012 Subtotal (95% CI)	0.04	3.9908	59 216	-0.23	4.9501	59 217	27.3% 100.0%	0.06 [-0.30, 0.42] 0.04 [-0.15, 0.23]	•	
Heterogeneity: Tau ² :	= 0.00; Cl	$hi^2 = 0.64$,	df = 3 (P = 0.89	3); I² = 0%					
Test for overall effect	Z = 0.45	6 (P = 0.65))							
								_	-0.5 -0.25 0 0.25 0.5 Favours [control] Favours [experimental]	

Self-efficacy

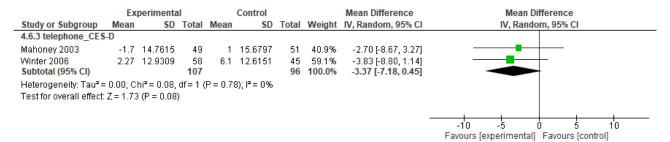


SUPPORTIVE INTERVENTIONS

Caregiver burden

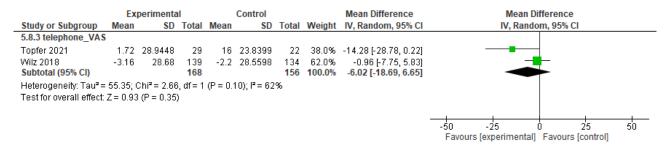


Depression

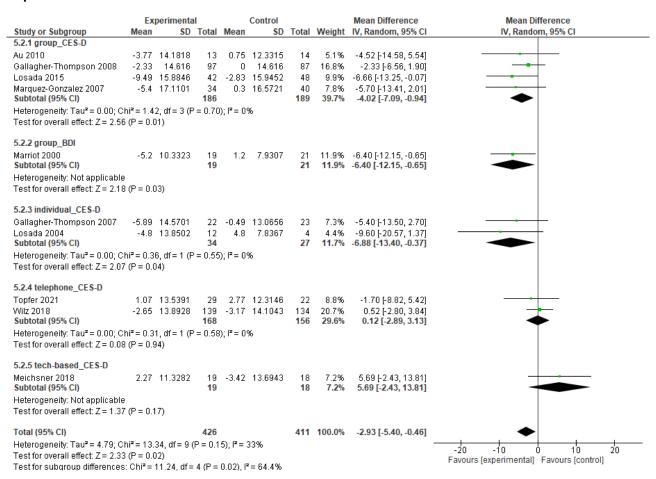


COGNITIVE BEHAVIORAL INTERVENTIONS

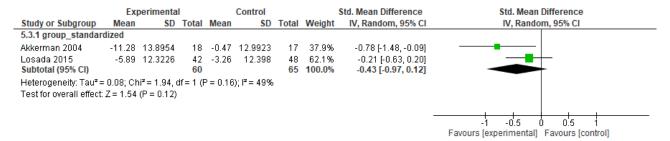
Caregiver burden



Depression

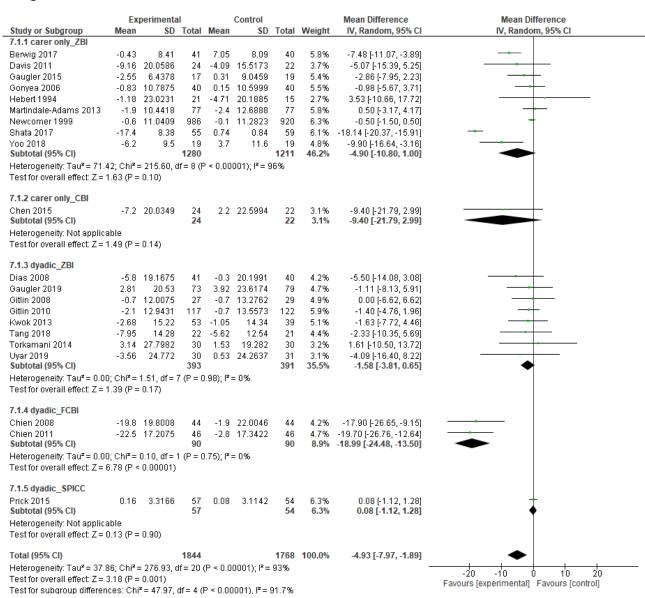


Anxiety

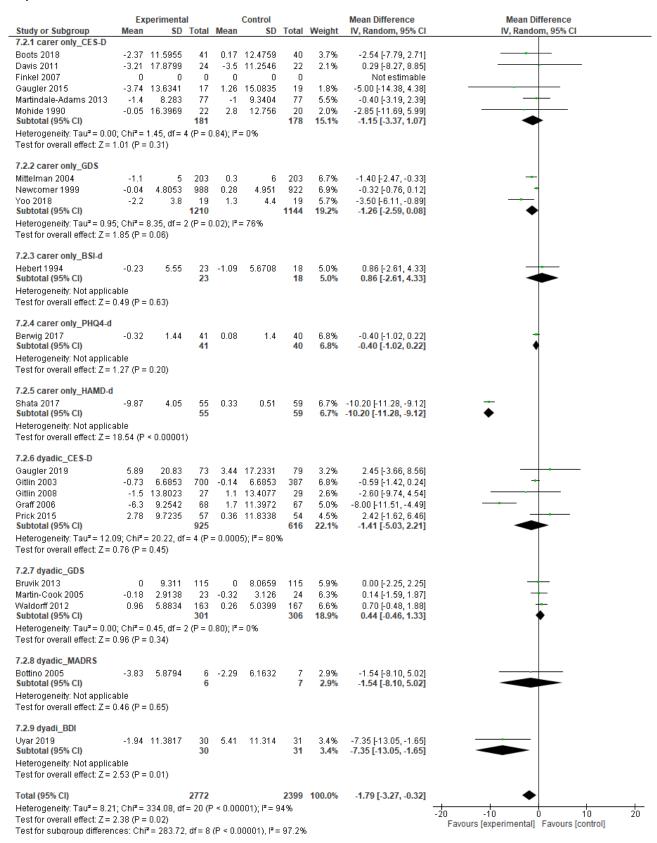


MULTICOMPONENT INTERVENTIONS

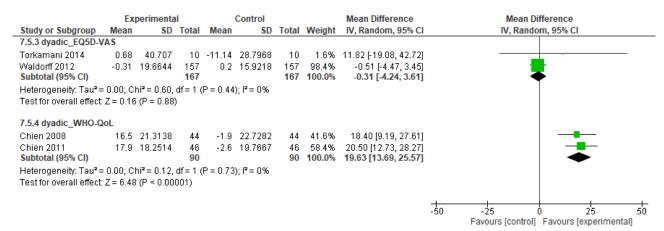
Caregiver burden



Depression

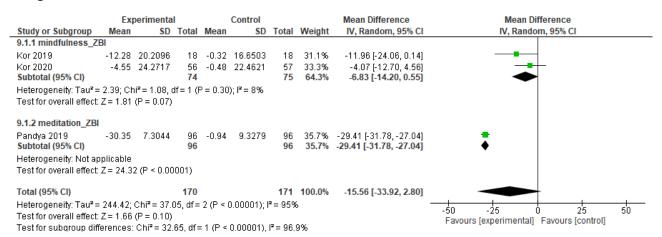


Quality of life

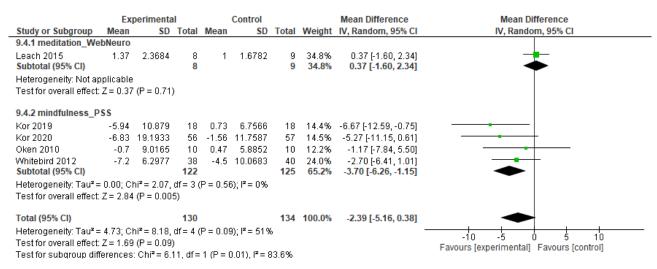


MEDITATION/MINDFULNESS

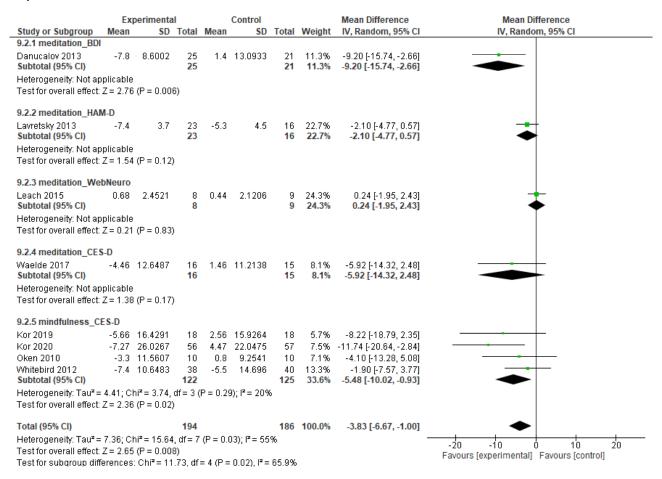
Caregiver burden



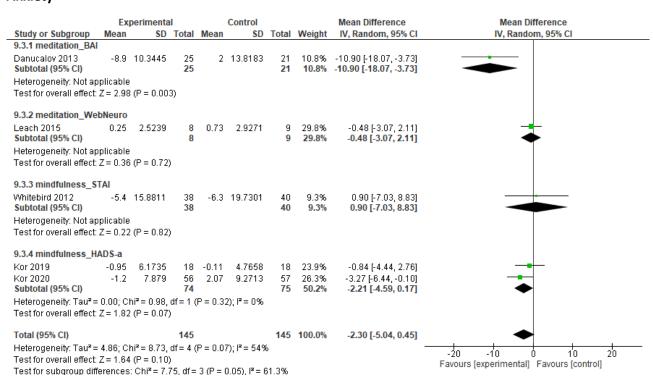
Caregiver stress



Depression



Anxiety

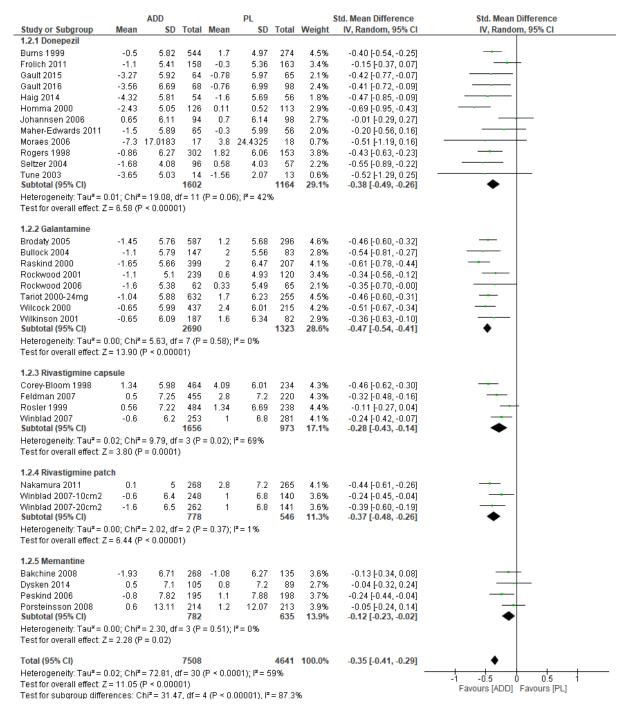


REVIEW QUESTION 15a. What is the safety and efficacy of acetylcholinesterase inhibitors and memantine for the treatment of cognitive symptoms in people with Alzheimer's dementia and how should they be monitored?

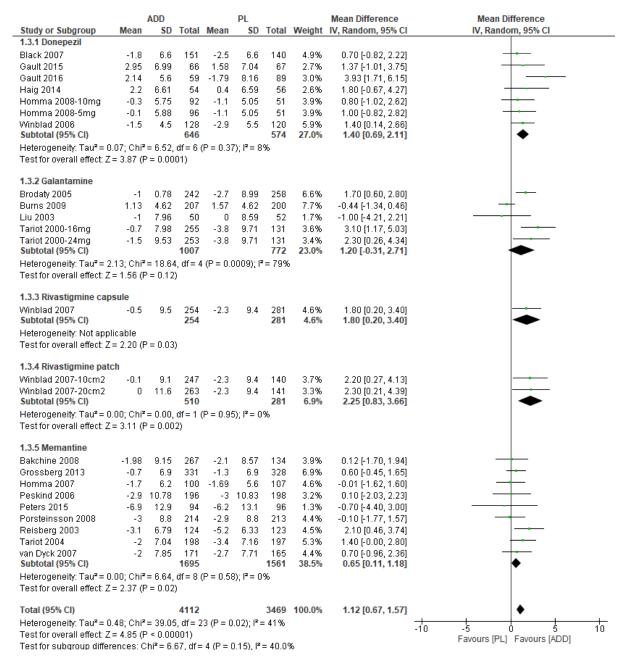
Acetylcholinesterase inhibitors vs placebo – MMSE (AD not stratified for severity)

		ADD			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean		Total	Mean		Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Donepezil	0.6	2.2	450		2.2	4.44	2.40	0.001.046.4.001	<u> </u>
Black 2007 Courtney 2004	0.6 0.93	3.3 3.24	150 245	0	3.3 2.96	141 263	3.4% 4.0%	0.60 [-0.16, 1.36] 0.93 [0.39, 1.47]	
Feldman 2001	1.4	3.24	131	-0.4	2.30	139	2.9%	1.80 [0.85, 2.75]	
Frolich 2011	0.9	3.29	138	-0.4	3.37	145	3.3%	1.00 [0.03, 2.73]	
Gault 2015	1	2.68	66	0.47	2.7	67	3.0%	0.53 [-0.38, 1.44]	
Gault 2016	1.29	2.76	69	0.56	2.83	98	3.1%	0.73 [-0.13, 1.59]	
Gauthier 2002	1.5	4.29	91	-0.56	4	100	2.3%	2.06 [0.88, 3.24]	
Haig 2014	1.4	2.71	54	1.1	2.69	56	2.7%	0.30 [-0.71, 1.31]	
Holmes 2004	-0.1	3.84	41	-1.8	3.71	55	1.7%	1.70 [0.17, 3.23]	
Jia 2017	1.7	3.3	150	1	3.4	151	3.4%	0.70 [-0.06, 1.46]	
Johannsen 2006	1.41	3.18	93	0.58	3.18	99	3.0%	0.83 [-0.07, 1.73]	
Maher-Edwards 2015	0.5	3.1	128	-0.3	3.2	118	3.3%	0.80 [0.01, 1.59]	-
Mazza 2006	1.2	4.4576	25	-0.25	4.9021	26	0.8%	1.45 [-1.12, 4.02]	
Mohs 2001	1.8	4.21	111	0.45	4.29	96	2.4%	1.35 [0.19, 2.51]	
Rogers 1998	0.31	3.57	303	-0.97	3.47	154	3.6%	1.28 [0.60, 1.96]	→
Seltzer 2004	1.35	3.34	91	0.1	3.15	55	2.6%	1.25 [0.17, 2.33]	
Tariot 2001	-0.1	4	103	-0.8	4	102	2.5%	0.70 [-0.40, 1.80]	+
Winblad 2001	0.4	3.74	121	-1.09	3.72	120	2.9%	1.49 [0.55, 2.43]	
Winblad 2006	1.1	3.3	120	0.1	3.3	120	3.2%	1.00 [0.17, 1.83]	
Subtotal (95% CI)			2230			2105	53.9%	0.99 [0.79, 1.19]	♦
Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	•			(P = 0.6	69); I² = 0	%			
1.1.2 Galantamine									
Liu 2003 Subtotal (95% CI)	2	4	50 50	0.1	0.3	52 52	2.5% 2.5%	1.90 [0.79, 3.01] 1.90 [0.79, 3.01]	•
Heterogeneity: Not appli Test for overall effect: Z=		= 0.000	8)						
1.1.3 Rivastigmine-caps	sule								
Agid 1998	0.14	3.21	214	0	2.6	117	3.7%	0.14 [-0.50, 0.78]	+
Corey-Bloom 1998	0.2	3	231	-0.9	3	235	4.0%	1.10 [0.56, 1.64]	-
Feldman 2007	-0.15	3.6	454	-1.4	3.6	220	3.9%	1.25 [0.67, 1.83]	
Mowla 2007	1.1	1.4	34	-0.5	0.5	32	4.1%	1.60 [1.10, 2.10]	-
Rosler 1999	0.2	3.5	242	-0.5	3.6	239	3.7%	0.70 [0.07, 1.33]	-
Winblad 2007 Subtotal (95% CI)	0.8	3.2	256 1431	0	3.5	281 1124	3.9% 23.3%	0.80 [0.23, 1.37] 0.95 [0.55, 1.36]	-
Heterogeneity: Tau ² = 0. Test for overall effect: Z=				(P = 0.01	l); l² = 66	%			
	·		,						
1.1.4 Rivastigmine patc		2.0	240	0.0	2.0	254	4.400	0.001.000.000	\perp
Nakamura 2011	0	2.9	246	-0.3	2.8	251	4.1%	0.30 [-0.20, 0.80]	T
Winblad 2007-10cm2	1.1	3.3	250	0	3.5	140	3.5%	1.10 [0.39, 1.81]	
Winblad 2007-20cm2 Subtotal (95% CI)	0.9	3.4	262 758	0	3.5	141 532	3.5% 11.1%	0.90 [0.19, 1.61] 0.71 [0.20, 1.22]	•
Heterogeneity: Tau² = 0. Test for overall effect: Z =		•	lf= 2 (F	9 = 0.14)	; I² = 499			0.7 [0.20, 1.22]	ľ
1.1.5 Memantine									
Fox 2012	0.9	9.05	72	-0.5	8.72	77	0.7%	1.40 [-1.46, 4.26]	
Porsteinsson 2008	-0.2	6.42	210	-6	6.17	198	2.3%	5.80 [4.58, 7.02]	
Reisberg 2003	-0.5	2.4	124	-1.2	3.02	124	3.6%	0.70 [0.02, 1.38]	
Wang 2013	1.2	2.6	11	-0.4	4	11	0.7%	1.60 [-1.22, 4.42]	
Wilkinson 2012 Subtotal (95% CI)	-0.43	5.65	133 550	-0.74	5.76	144 554	2.0% 9.2%	0.31 [-1.03, 1.65] 2.00 [-0.36, 4.35]	
Heterogeneity: Tau² = 6. Test for overall effect: Z=				(P < 0.00	0001); l² :			,	
Total (95% CI)			5019			4367	100.0%	1.09 [0.84, 1.34]	
Heterogeneity: Tau ² = 0.	33: Chi≅	= 100.76		3 (P < 0	000011				
Test for overall effect: Z=			•		.55551),	. – 01			-4 -2 0 2 4
Test for subgroup differe				4 (P = 0.	35), I² = 9	9.7%			Favours [PL] Favours [ADD]

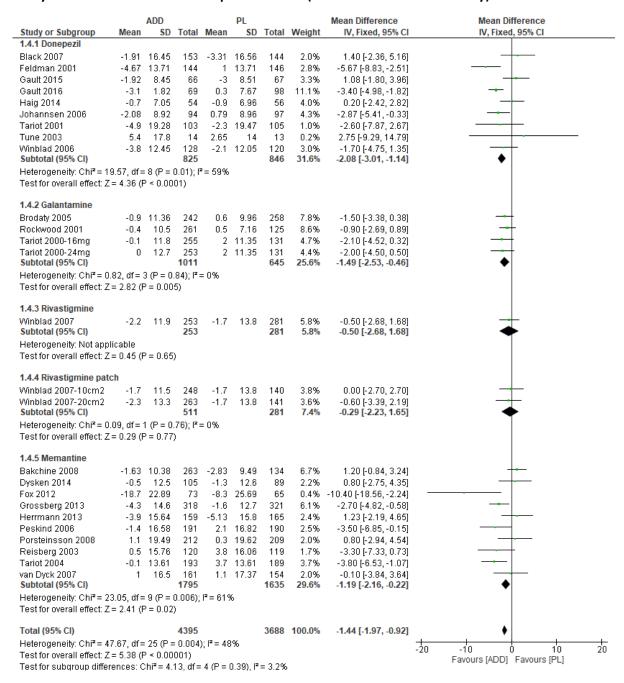
Acetylcholinesterase inhibitors vs placebo - ADAS-Cog (AD not stratified for severity)



Acetylcholinesterase inhibitors vs placebo - ADCS-ADL (AD not stratified for severity)



Acetylcholinesterase inhibitors vs placebo - NPI (AD not stratified for severity)



Acetylcholinesterase inhibitors vs placebo – CIBIC+ (AD not stratified for severity)

		ADD			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.5.1 Donepezil									
Burns 1999	4.18	0.99	544	4.52	0.99	274	9.4%	-0.34 [-0.48, -0.20]	
Gauthier 2002	4	1.19	98	4.55	1.08	105	2.7%	-0.55 [-0.86, -0.24]	
Rogers 1998	4.11	0.98	298	4.51	0.99	152	6.2%	-0.40 [-0.59, -0.21]	
Subtotal (95% CI)			940			531	18.3%	-0.38 [-0.49, -0.28]	•
Heterogeneity: Tau² = Test for overall effect:					0.48);	I= 0%			
1.5.2 Galantamine									
Brodaty 2005	4.21	1.08	593	4.35	1.14	301	8.5%	-0.14 [-0.30, 0.02]	
Raskind 2000	4.13	0.96	357	4.38	0.99	196	7.4%	-0.25 [-0.42, -0.08]	
Rockwood 2001	3.92	0.8	240	4.26	0.9	123	6.4%	-0.34 [-0.53, -0.15]	
Rockwood 2006	3.67	1	61	4.12	0.99	65	2.2%	-0.45 [-0.80, -0.10]	
Wilcock 2000	4.22	0.99	437	4.51	0.99	215	8.0%	-0.29 [-0.45, -0.13]	
Subtotal (95% CI)			1688			900	32.5%	-0.26 [-0.34, -0.17]	◆
Heterogeneity: Tau ² =	0.00; C	hi² = 4	.27, df=	= 4 (P =	0.37);	$I^2 = 6\%$			
Test for overall effect:	Z = 5.99	9 (P < 0	0.00001	1)					
1.5.3 Rivastigmine									
Corey-Bloom 1998	4.22	1.24	464	4.49	1.25	234	6.0%	-0.27 [-0.47, -0.07]	
Feldman 2007	4	1.3	444	4.5	1.3	216	5.3%	-0.50 [-0.71, -0.29]	
Rosler 1999	4.08	1.62	452	4.38	1.24	230	5.0%	-0.30 [-0.52, -0.08]	
Subtotal (95% CI)			1360			680	16.3%	-0.35 [-0.50, -0.21]	•
Heterogeneity: Tau* = Test for overall effect:					0.25);	I ² = 28°	%		
1.5.4 Memantine		. (,		,					
Grossberg 2013	3.8	1.2	333	4.1	1.2	328	6.7%	-0.30 [-0.48, -0.12]	
Peskind 2006		0.96	196		1.06	197	5.8%	-0.32 [-0.52, -0.12]	
Porsteinsson 2008	4.38	0.90	214		0.96	213	6.5%	-0.04 [-0.23, 0.15]	
Reisberg 2003		1.12	118		1.09	118	3.2%	-0.30 [-0.58, -0.02]	
Tariot 2004		1.04	198		1.05	196	5.5%	-0.25 [-0.46, -0.04]	
van Dyck 2007	4.3	1.04	171	4.66	1.03	163	5.2%	-0.30 [-0.51, -0.09]	
Subtotal (95% CI)	4.3	'	1230	4.0	'	1215	32.9%	-0.24 [-0.34, -0.15]	•
Heterogeneity: Tau² = Test for overall effect:			.95, df =		0.31);			,	Ť
Total (95% CI)		-	5218			3336	100.0%	-0.29 [-0.35, -0.24]	A
	0.00:0	hiz = 0		F = 4 G /F	0 2			-0.23 [-0.33, -0.24]	—
Heterogeneity: Tau² =					= 0.2	1), (*=)	2170		-1 -0.5 0 0.5 1
Test for overall effect:		,			0 - 0 4	G7 12 -	44.00		Favours [ADD] Favours [PL]
Test for subgroup diff	erences	. Oni*:	= 5.16,	u(= 3 ()	r = 0.1	b), I*=	41.9%		

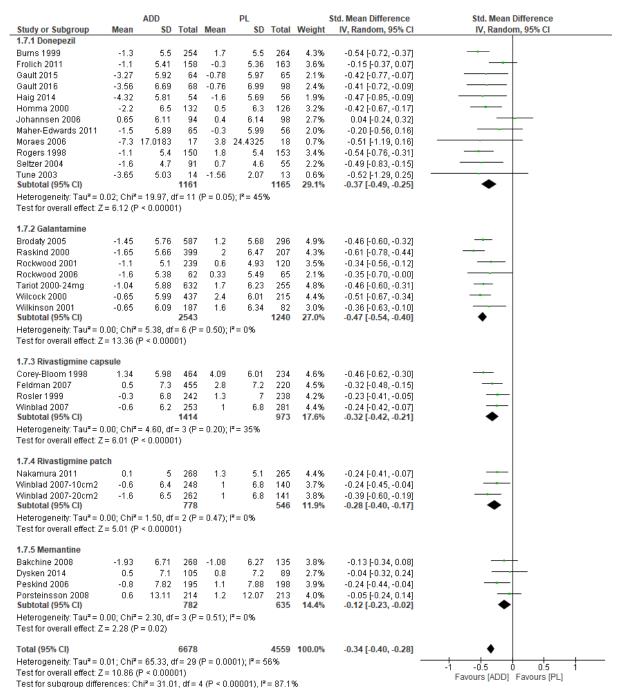
Acetylcholinesterase inhibitors vs placebo – adverse events (AD not stratified for severity)

-							
Study or Subgroup	ADD		PL	Total	Woight	Risk Ratio	Risk Ratio
Study or Subgroup 2.1.1 Donepezil	Events	Total	Events	TOTAL	weight	M-H, Random, 95% CI	M-H, Random, 95% CI
•	24	170	10	107	260	4 70 (4 05 0 05)	
Black 2007 Burns 1999	34 74	176 544	18 27	167 274	3.6% 4.2%	1.79 [1.05, 3.05]	<u> </u>
Feldman 2001	12	144	9	146	2.3%	1.38 [0.91, 2.09] 1.35 [0.59, 3.11]	
Gault 2015	5	68	2	68	0.8%	2.50 [0.50, 12.44]	
Gault 2016	7	76	3	104	1.2%	3.19 [0.85, 11.95]	
Haig 2014	4	60	3	63	1.0%	1.40 [0.33, 6.00]	
Homma 2000	2	136	1	131	0.4%	1.93 [0.18, 20.99]	
Homma 2008-5+10mg	21	197	11	105	2.8%	1.02 [0.51, 2.03]	+
Jia 2017	14	157	10	156	2.4%	1.39 [0.64, 3.04]	+-
Krishnan 2003	0	34	1	33	0.2%	0.32 [0.01, 7.68]	· ·
Maher-Edwards 2011	4	67	2	62	0.8%	1.85 [0.35, 9.75]	- ·
Mazza 2006	4	25	0	26	0.3%	9.35 [0.53, 165.12]	
Mohs 2001	23	214	16	217	3.2%	1.46 [0.79, 2.68]	
Rogers 1998	34 15	311 96	11	162	3.0%	1.61 [0.84, 3.09]	
Seltzer 2004 Tariot 2001	11	103	5 19	57 105	1.9% 2.8%	1.78 [0.68, 4.64] 0.59 [0.30, 1.18]	
Winblad 2001	10	142	9	144	2.1%	1.13 [0.47, 2.69]	
Winblad 2006	20	128	8	120	2.4%	2.34 [1.07, 5.12]	<u> </u>
Subtotal (95% CI)		2678		2140	35.3%	1.42 [1.18, 1.72]	♦
Total events	294		155				
Heterogeneity: Tau² = 0.0 Test for overall effect: Z =				= 0.62); I² = 0%		
2.1.2 Galantamine							
Brodaty 2005	24	326	15	320	3.1%	1.57 [0.84, 2.94]	+-
Burns 2009	30	207	31	200	3.9%	0.94 [0.59, 1.49]	-
Liu 2003	2	50	0	52	0.3%	5.20 [0.26, 105.62]	-
Raskind 2000	116	423	16	213	3.7%	3.65 [2.22, 6.00]	
Rockwood 2001	66	261	5	125	2.1%	6.32 [2.61, 15.30]	
Tariot 2000-16+24mg	46	552	20	286	3.7%	1.19 [0.72, 1.97]	T <u>.</u>
Wilcock 2000 Wilkinson 2001	79 53	438 198	19 8	215 87	3.9% 2.8%	2.04 [1.27, 3.28] 2.91 [1.45, 5.86]	
Subtotal (95% CI)	33	2455	0	1498	23.4%	2.12 [1.34, 3.36]	•
Total events	416		114				
Heterogeneity: Tau ² = 0.3 Test for overall effect: Z =	3.21 (P =			: 0.000	1);	Xo	
2.1.3 Rivastigmine capsi Feldman 2007		456	20	222	2.00	1 50 10 05 0 471	
Rosler 1999	63 55	456 242	20 16	239	3.8% 3.6%	1.53 [0.95, 2.47] 3.39 [2.00, 5.75]	
Winblad 2007	26	294	18	302	3.3%	1.48 [0.83, 2.65]	
Subtotal (95% CI)	20	992		763	10.7%	1.98 [1.16, 3.36]	•
Total events	144		54			. , .	
Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	5; Chi² = 6		= 2 (P =	0.05); P	²= 67%		
2.1.4 Rivastigmine patch	1						
Nakamura 2011	34	287	21	288	3.6%	1.62 [0.97, 2.73]	
Winblad 2007 patch	62	594	18	302	3.7%	1.75 [1.06, 2.91]	-
Subtotal (95% CI)		881		590	7.3%	1.69 [1.18, 2.43]	•
Total events	96		39				
Heterogeneity: Tau² = 0.0 Test for overall effect: Z =				0.84); P	²= 0%		
2.1.5 Memantine							
Bakchine 2008			6	152	2.2%	2.23 [0.94, 5.27]	
Dalleriirie 2000	28	318					
Grossberg 2013	28 3 4	318 342	21	335	3.6%	1.59 [0.94, 2.67]	
Grossberg 2013 Herrmann 2013	34 15	342 182	21 10	187	2.5%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34]	-
Grossberg 2013 Herrmann 2013 Peskind 2006	34 15 19	342 182 201	21 10 10	187 202	2.5% 2.6%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00]	+
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008	34 15 19 13	342 182 201 217	21 10 10 17	187 202 216	2.5% 2.6% 2.8%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53]	
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003	34 15 19 13 22	342 182 201 217 126	21 10 10 17 13	187 202 216 126	2.5% 2.6% 2.8% 3.0%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21]	
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004	34 15 19 13 22 15	342 182 201 217 126 203	21 10 10 17 13 25	187 202 216 126 201	2.5% 2.6% 2.8% 3.0% 3.2%	1.59 (0.94, 2.67) 1.54 (0.71, 3.34) 1.91 (0.91, 4.00) 0.76 (0.38, 1.53) 1.69 (0.89, 3.21) 0.59 (0.32, 1.09)	
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007	34 15 19 13 22	342 182 201 217 126 203 178	21 10 10 17 13	187 202 216 126 201 172	2.5% 2.6% 2.8% 3.0% 3.2% 3.5%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21] 0.59 [0.32, 1.09] 0.92 [0.54, 1.60]	
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007 Subtotal (95% CI)	34 15 19 13 22 15	342 182 201 217 126 203	21 10 10 17 13 25 23	187 202 216 126 201	2.5% 2.6% 2.8% 3.0% 3.2%	1.59 (0.94, 2.67) 1.54 (0.71, 3.34) 1.91 (0.91, 4.00) 0.76 (0.38, 1.53) 1.69 (0.89, 3.21) 0.59 (0.32, 1.09)	•
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007	34 15 19 13 22 15 22 168 1; Chi ^z = 1	342 182 201 217 126 203 178 1767	21 10 10 17 13 25 23	187 202 216 126 201 172 1591	2.5% 2.6% 2.8% 3.0% 3.2% 3.5% 23.2%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21] 0.59 [0.32, 1.09] 0.92 [0.54, 1.60]	
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	34 15 19 13 22 15 22 168 1; Chi ^z = 1	342 182 201 217 126 203 178 1767 (3.74, (0.19)	21 10 10 17 13 25 23	187 202 216 126 201 172 1591 : 0.06);	2.5% 2.6% 2.8% 3.0% 3.2% 3.5% 23.2%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21] 0.59 [0.32, 1.09] 0.92 [0.54, 1.60] 1.24 [0.90, 1.72]	•
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	34 15 19 13 22 15 22 168 1; Chi ² = 1 1.30 (P =	342 182 201 217 126 203 178 1767	21 10 10 17 13 25 23 125 4f = 7 (P =	187 202 216 126 201 172 1591 : 0.06);	2.5% 2.6% 2.8% 3.0% 3.2% 3.5% 23.2%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21] 0.59 [0.32, 1.09] 0.92 [0.54, 1.60]	•
Grossberg 2013 Herrmann 2013 Peskind 2006 Porsteinsson 2008 Reisberg 2003 Tariot 2004 van Dyck 2007 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	34 15 19 13 22 15 22 168 1; Chi ² = 1 1.30 (P =	342 182 201 217 126 203 178 1767 (3.74, (0.19) 8773	21 10 10 17 13 25 23 125 4f = 7 (P =	187 202 216 126 201 172 1591 : 0.06);	2.5% 2.6% 2.8% 3.0% 3.2% 3.5% 23.2% *= 49%	1.59 [0.94, 2.67] 1.54 [0.71, 3.34] 1.91 [0.91, 4.00] 0.76 [0.38, 1.53] 1.69 [0.89, 3.21] 0.59 [0.32, 1.09] 0.92 [0.54, 1.60] 1.24 [0.90, 1.72]	0.005 0.1 1 10 200

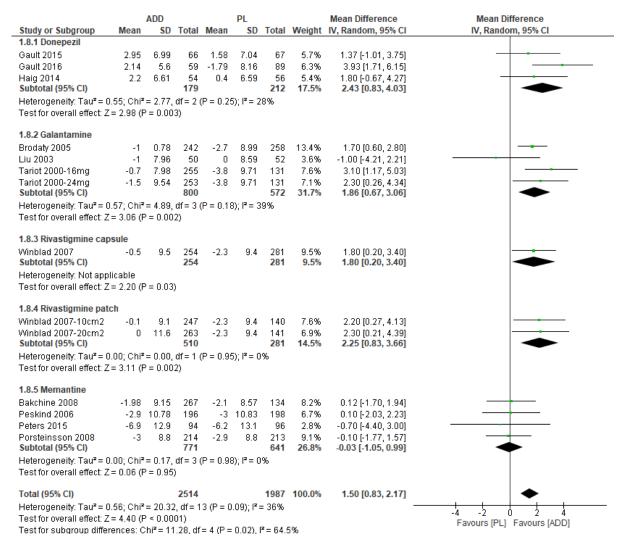
Acetylcholinesterase inhibitors vs placebo – MMSE (AD mild-moderate)

Study or Subgroup	Mean	ADD SD	Total	Mean	PL SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
1.6.1 Donepezil	mean	35	rotui	mean	35	Total	TTOIGHT	TV, Random, 55% Ci	TV, Rundoni, 00% GI
Frolich 2011	0.9	3.29	138	-0.1	3.37	145	5.7%	1.00 [0.22, 1.78]	
Gault 2015	1	2.68	66	0.47	2.7	67	4.6%	0.53 [-0.38, 1.44]	
Gault 2016	1.29	2.76	69	0.56	2.83	98	5.0%	0.73 [-0.13, 1.59]	
Haig 2014	1.4	2.71	54	1.1	2.69	56	4.0%	0.30 [-0.71, 1.31]	
Mazza 2006		4.4576	25		4.9021	26	0.8%	1.45 [-1.12, 4.02]	
Rogers 1998	0.4	3.1	150	-1	3.1	154	6.5%	1.40 [0.70, 2.10]	
Tariot 2001	-0.1	4	103	-0.8	4	102	3.6%	0.70 [-0.40, 1.80]	
Subtotal (95% CI)			605			648	30.3%	0.88 [0.53, 1.23]	•
Heterogeneity: Tau² = 0 Test for overall effect: Z				= 0.61)	; I² = 0%				
1.6.2 Galantamine									
Liu 2003	2	4	50	0.1	0.3	52	3.5%	1.90 [0.79, 3.01]	
Subtotal (95% CI)			50			52	3.5%	1.90 [0.79, 3.01]	-
Heterogeneity: Not appl Test for overall effect: Z		P = 0.000	8)						
1.6.3 Rivastigmine cap	sule								
Agid 1998	0.14	3.21	214	0	2.6	117	7.1%	0.14 [-0.50, 0.78]	
Feldman 2007	-0.2	3.6	454	-1.4	3.6	227	7.9%	1.20 [0.63, 1.77]	 -
Mowla 2007	1.1	1.4	34	-0.5	0.5	32	8.8%	1.60 [1.10, 2.10]	_ -
Rosler 1999	0.2	3.5	242	-0.5	3.6	239	7.2%	0.70 [0.07, 1.33]	-
Winblad 2007 Subtotal (95% CI)	0.8	3.2	256 1200	0	3.5	281 896	8.0% 39.0%	0.80 [0.23, 1.37] 0.91 [0.42, 1.40]	<u>→</u>
Heterogeneity: Tau² = 0 Test for overall effect: Z				P = 0.00)7); I² = 7	2%			
1.6.4 Rivastigmine pate	ch								
Nakamura 2011	0	2.9	246	-0.3	2.8	251	8.8%	0.30 [-0.20, 0.80]	 -
Winblad 2007-10cm2	1.1	3.3	250	0	3.5	140	6.4%	1.10 [0.39, 1.81]	
Winblad 2007-20cm2 Subtotal (95% CI)	0.9	3.4	262 758	0	3.5	141 532	6.4% 21.6%	0.90 [0.19, 1.61] 0.71 [0.20, 1.22]	<u>.</u>
Heterogeneity: Tau ² = 0 Test for overall effect: Z	•			= 0.14)	; I² = 499	6			
1.6.5 Memantine									
Porsteinsson 2008	-0.2	6.42	210	-0.6	6.17	198	3.0%	0.40 [-0.82, 1.62]	
Wilkinson 2012	-0.43	5.651		-0.74	5.76	144	2.6%	0.31 [-1.03, 1.65]	
Subtotal (95% CI)	-0.43	3.031	343	-0.74	3.70	342	5.6%	0.36 [-0.54, 1.26]	•
Heterogeneity: Tau² = 0 Test for overall effect: Z				= 0.92)	; I² = 0%	0.2	0.0.0	5,55 [5,5 1, 1,25]	
Total (95% CI)			2956			2/170	100.0%	0.86 [0.62, 1.10]	_
	10: Obiz	- 20.46		/D = 0.0	10\-18 - 4		100.0%	0.00 [0.02, 1.10]	
Heterogeneity: Tau ² = 0 Test for overall effect: Z				(~= 0.0	J3), I== 4	270			-4 -2 0 2 4
Test for overall effect: Z	,			1/0 - 0	20) 12 - 1	10 70%			Favours [PL] Favours [ADD]
restror subdroub gillet	ences. C	an = 4.9.	د, ui = 4	, (r = U.	50), F=1	10.770			

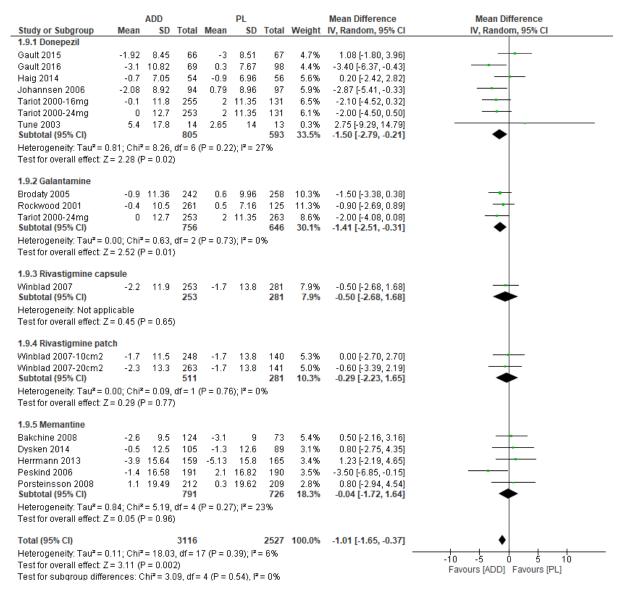
Acetylcholinesterase inhibitors vs placebo - ADAS-Cog (AD mild-moderate)



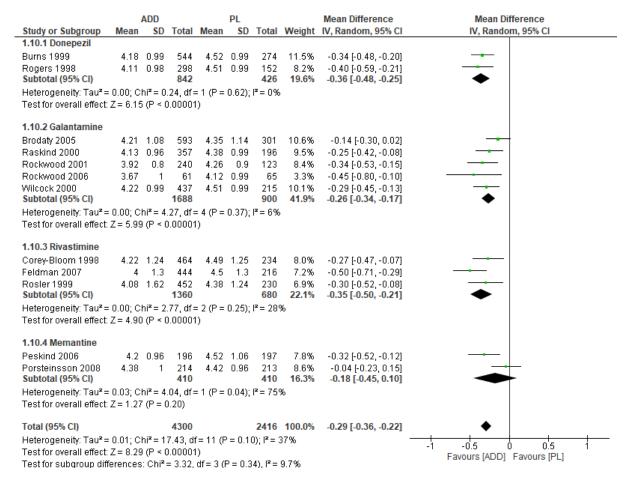
Acetylcholinesterase inhibitors vs placebo - ADCS-ADL (AD mild-moderate)



Acetylcholinesterase inhibitors vs placebo - NPI (AD mild-moderate)



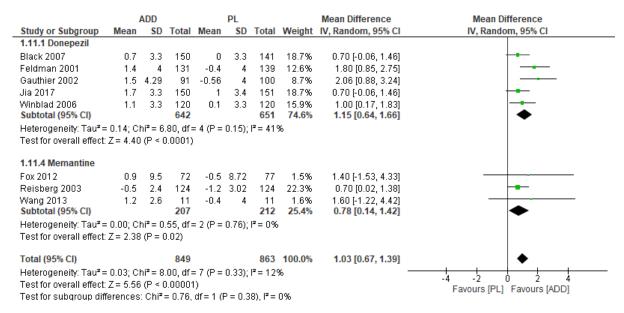
Acetylcholinesterase inhibitors vs placebo - CIBIC+ (AD mild-moderate)



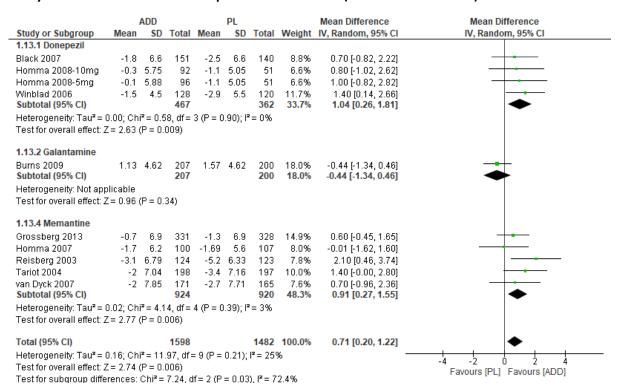
Acetylcholinesterase inhibitors vs placebo – Discontinuation due to adverse events (AD mild-moderate)

	ADD)	PL			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.2.1 Donepezil							
Burns 1999	74	544	27	274	6.0%	1.38 [0.91, 2.09]	-
Gault 2015	5	68	2	68	1.1%	2.50 [0.50, 12.44]	
Gault 2016	7	76	3	104	1.5%	3.19 [0.85, 11.95]	
Haig 2014	4	60	3	63	1.3%	1.40 [0.33, 6.00]	
Homma 2000	2	136	1	131	0.5%	1.93 [0.18, 20.99]	
Krishnan 2003	0	34	1	33	0.3%	0.32 [0.01, 7.68]	
Maher-Edwards 2011	4	67	2	62	1.0%	1.85 [0.35, 9.75]	 _,
Mazza 2006	4	25	0	26	0.4%	9.35 [0.53, 165.12]	
Mohs 2001	23	214	16	217	4.3%	1.46 [0.79, 2.68]	
Rogers 1998	34	311	11	162	4.0%	1.61 [0.84, 3.09]	<u> </u>
Seltzer 2004	15	96	5	57	2.5%	1.78 [0.68, 4.64]	
Tariot 2001 Winblad 2001	11 10	103	19 9	105 144	3.8% 2.8%	0.59 [0.30, 1.18]	
Subtotal (95% CI)	10	142 1876	9	1446	29.5%	1.13 [0.47, 2.69] 1.36 [1.07, 1.72]	•
Total events	193	1070	99	1440	23.370	1.50 [1.07, 1.72]	\
Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	00; Chi²=			P = 0.5	0); l² = 0%	6	
2.2.2 Galantamine							
Brodaty 2005	24	326	15	320	4.2%	1.57 [0.84, 2.94]	+-
Liu 2003	2	50	0	52	0.3%	5.20 [0.26, 105.62]	
Raskind 2000	116	423	16	213	5.2%	3.65 [2.22, 6.00]	
Rockwood 2001	66	261	5	125	2.8%	6.32 [2.61, 15.30]	
Tariot 2000-16+24mg	46	552	20	286	5.2%	1.19 [0.72, 1.97]	 -
Wilcock 2000	79	438	19	215	5.4%	2.04 [1.27, 3.28]	
Wilkinson 2001	53	198	8	87	3.7%	2.91 [1.45, 5.86]	
Subtotal (95% CI)		2248		1298	26.9%	2.43 [1.57, 3.75]	•
Total events	386	47.70	83	0.00	71.17 00	01	
Heterogeneity: Tau² = 0.: Test for overall effect: Z =				= 0.00	/); i== bb	%	
2.2.3 Rivastigmine							
Feldman 2007	63	456	20	222	5.4%	1.53 [0.95, 2.47]	-
Nakamura 2011	34	287	21	288	5.0%	1.62 [0.97, 2.73]	 • -
Rosler 1999	55	242	16	239	5.0%	3.39 [2.00, 5.75]	_
Winblad 2007	26	294	18	302	4.6%	1.48 [0.83, 2.65]	
Subtotal (95% CI)		1279		1051	20.0%	1.88 [1.28, 2.77]	•
Total events	178		75				
Heterogeneity: Tau ² = 0.1		6.49.		= 0.09):	l² = 54%		
Test for overall effect: Z =	•			,			
2.2.4 Rivastigmine patc	h						
Nakamura 2011	34	287	21	288	5.0%	1.62 [0.97, 2.73]	<u> </u>
Winblad 2007 patch	62	594	18	302	5.2%	1.75 [1.06, 2.91]	
Subtotal (95% CI)		881		590	10.2%	1.69 [1.18, 2.43]	•
Total events	96		39				
Heterogeneity: Tau² = 0.1 Test for overall effect: Z =	00; Chi ² =		df=1 (P=	0.84);	² = 0%		
	v		•				
2.2.5 Memantine							
Bakchine 2008	28	318	6	152	2.9%	2.23 [0.94, 5.27]	
Herrmann 2013	15	182	10	187	3.3%	1.54 [0.71, 3.34]	
Peskind 2006	19	201	10	202	3.5%	1.91 [0.91, 4.00]	
Porsteinsson 2008 Subtotal (95% CI)	13	217 918	17	216 757	3.7%	0.76 [0.38, 1.53]	
	75	310	40	131	13.4%	1.45 [0.89, 2.35]	
Total events Heterogeneity: Tau² = 0.1 Test for overall effect: Z=	•			= 0.19);	I²= 38%		
Total (95% CI)		7202		5142	100.0%	1.75 [1.47, 2.09]	•
Total events	928	1202	339	0142	100.070	1110 [1141, 2.00]	▼
Heterogeneity: Tau² = 0.1		รถ ฉว		P = n n	07)·J≥ = 4	396	
Test for overall effect: Z=				0.0	01/,1 - 4	5,0	0.01 0.1 1 10 100
Test for subgroup differe				(P = 0.1	8), I²= 36	3.1%	lowerrisk [PL] higherrisk [ADD]

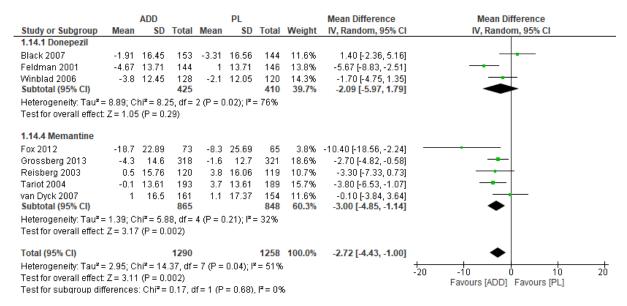
Acetylcholinesterase inhibitors vs placebo - MMSE (AD moderate-severe)



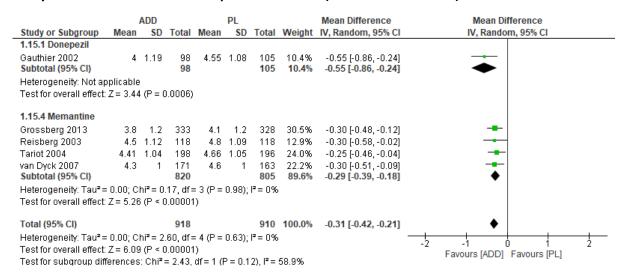
Acetylcholinesterase inhibitors vs placebo - ADCS-ADL (AD moderate-severe)



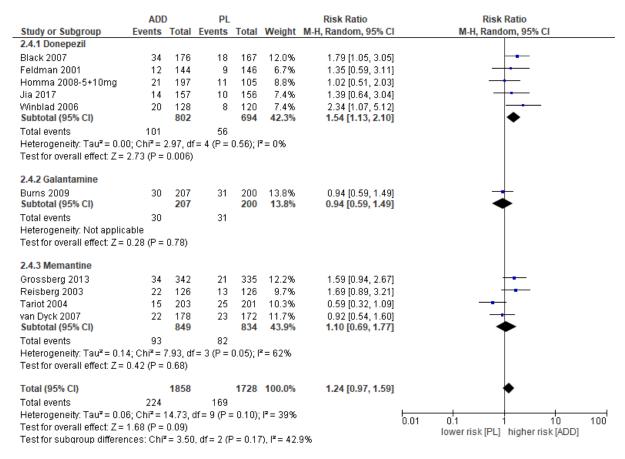
Acetylcholinesterase inhibitors vs placebo - NPI (AD moderate-severe)



Acetylcholinesterase inhibitors vs placebo - CIBIC+ (AD moderate-severe)

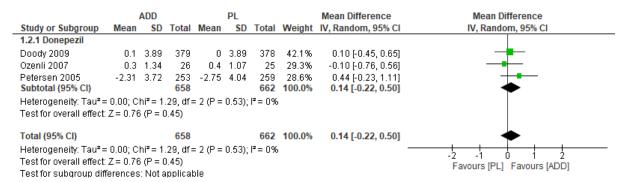


Acetylcholinesterase inhibitors vs placebo – Discontinuation due to adverse events (AD moderate-severe)

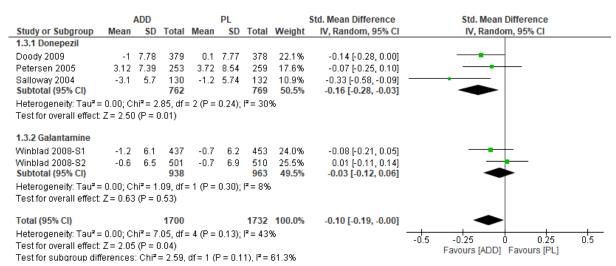


REVIEW QUESTION 15b. What is the safety and efficacy of acetylcholinesterase inhibitors and memantine for the treatment of cognitive symptoms in people with Mild cognitive impairment (MCI) and how should they be monitored?

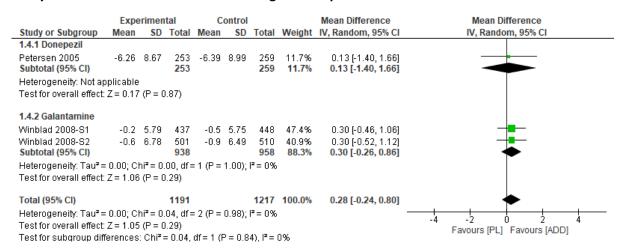
Donepezil for Mild cognitive impairment – MMSE



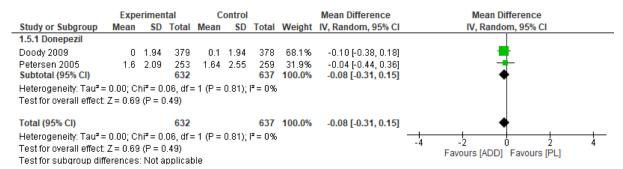
Acetylcholinesterase inhibitors for Mild cognitive impairment - ADAS-Cog



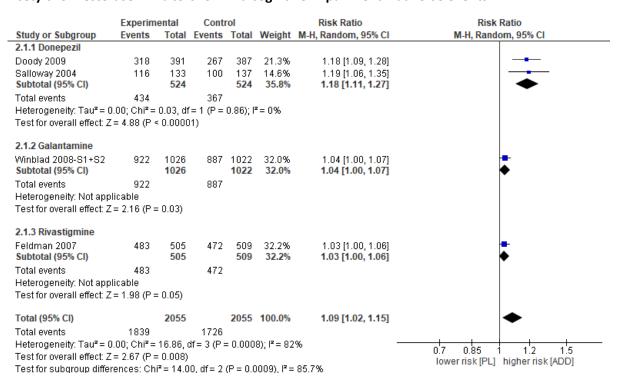
Acetylcholinesterase inhibitors for Mild cognitive impairment - ADCS-ADL-MCI



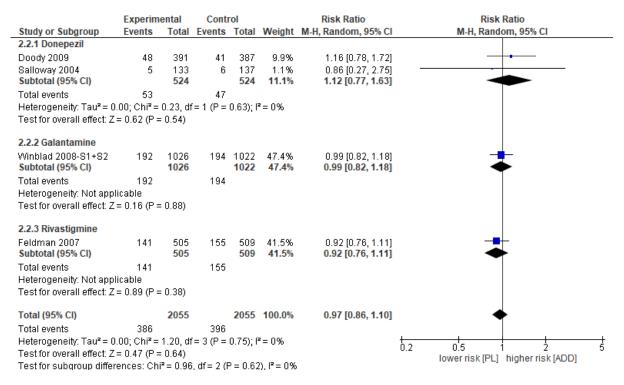
Donepezil for Mild cognitive impairment - CDR-SB



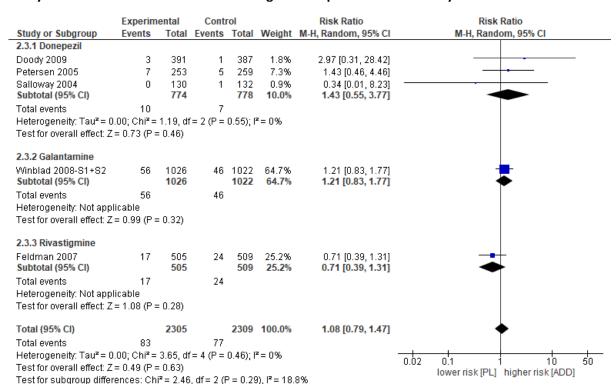
Acetylcholinesterase inhibitors for Mild cognitive impairment – adverse events



Acetylcholinesterase inhibitors for Mild cognitive impairment – serious adverse events



Acetylcholinesterase inhibitors for Mild cognitive impairment - mortality

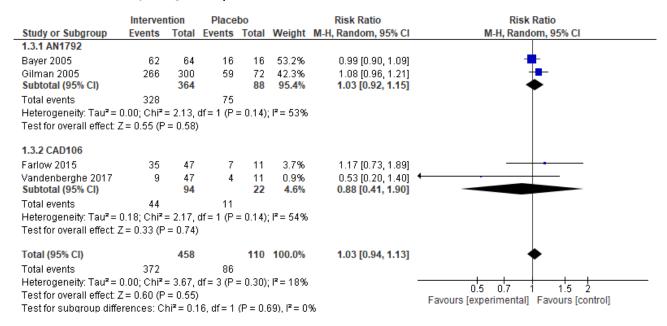


Acetylcholinesterase inhibitors for Mild cognitive impairment – withdrawal due to adverse events

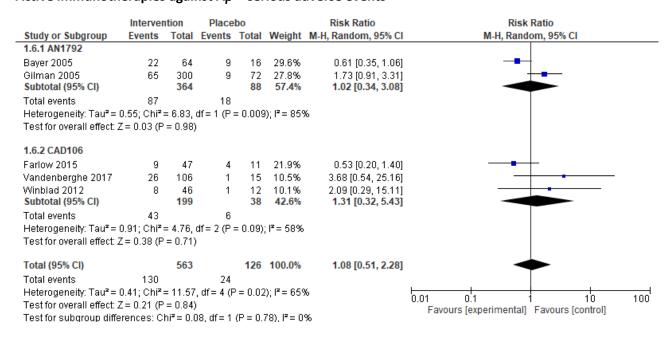
	ADD)	PL			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.4.1 Donepezil							
Doody 2009	72	409	32	412	17.6%	2.27 [1.53, 3.36]	
Salloway 2004	29	132	10	137	5.9%	3.01 [1.53, 5.93]	
Subtotal (95% CI)		541		549	23.5%	2.43 [1.73, 3.42]	•
Total events	101		42				
Heterogeneity: Tau² =	0.00; Chi	r = 0.50	0, df= 1 (P = 0.4	8); I² = 09	6	
Test for overall effect:	Z = 5.13 ((P < 0.0	10001)				
2.4.2 Galantamine							_
Winblad 2008-S1	107	494	51	496	28.4%	2.11 [1.55, 2.87]	<u>†</u>
Winblad 2008-82	125	532	54	526	31.1%	2.29 [1.70, 3.08]	🕇
Subtotal (95% CI)		1026		1022	59.5%	2.20 [1.78, 2.72]	▼
Total events	232		105			,	
Heterogeneity: Tau ² =				P = 0.7	U); I*= U9	6	
Test for overall effect:	Z = 7.23	P < U.U	10001)				
2.4.3 Rivastigmine							
Feldman 2007	62	505	34	509	17.0%	1.84 [1.23, 2.74]	
Subtotal (95% CI)		505		509	17.0%	1.84 [1.23, 2.74]	•
Total events	62		34				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 2.98 (P = 0.0	003)				
Total (95% CI)		2072		2080	100.0%	2.19 [1.85, 2.58]	•
Total events	395		181				
Heterogeneity: Tau² =	0.00; Chi	$r^2 = 1.70$	6, df = 4 (P = 0.7	8); I² = 09	6	0.01 0.1 1 10 100
Test for overall effect:		•					lower risk [PL] higher risk [ADD]
Test for subgroup diff	erences:	Chi²= '	1.11, df=	2 (P=	0.57), I ² =	: 0%	

REVIEW QUESTION 15c. What is the safety and efficacy of biological drugs (active and passive immunotherapy) for the treatment of cognitive symptoms in people with Alzheimer's dementia or Mild cognitive impairment (MCI) and how should they be monitored?

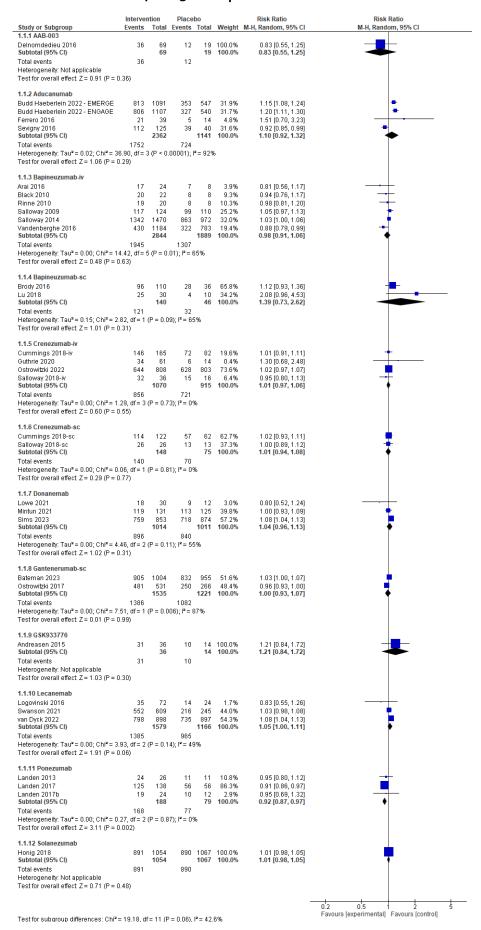
Active immunotherapies against $A\beta$ – adverse events



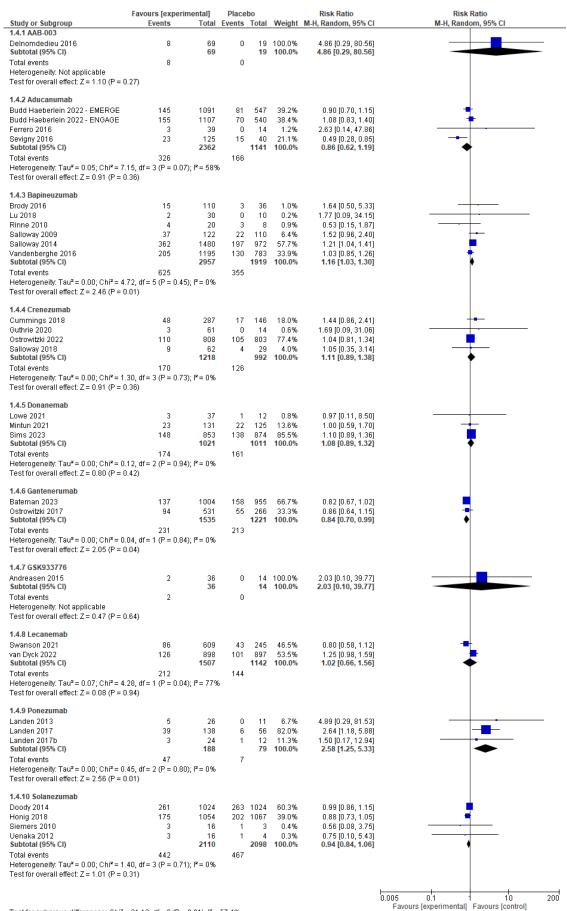
Active immunotherapies against $A\beta$ – serious adverse events



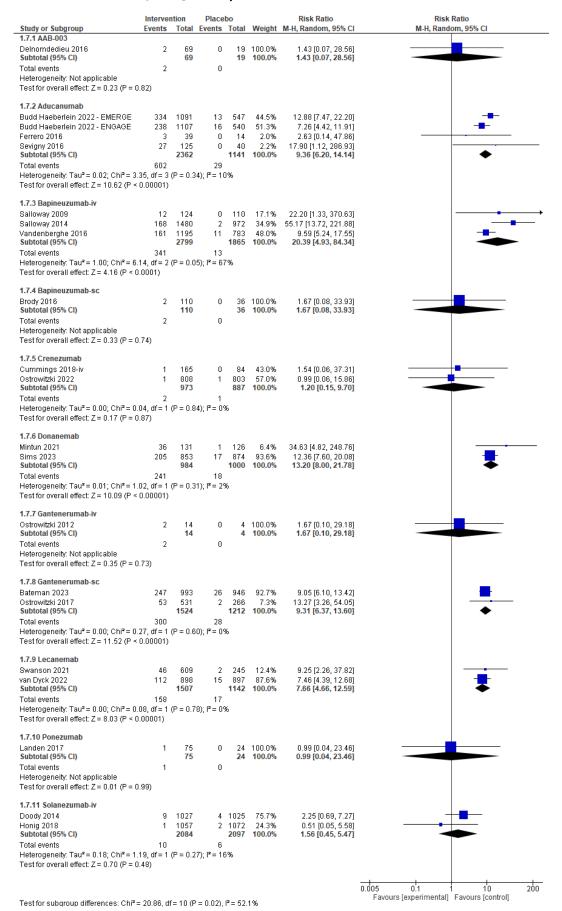
Passive immunotherapies against $A\beta$ – adverse events



Passive immunotherapies against $A\beta$ – serious adverse events



Passive immunotherapies against $A\beta$ – ARIA-E



Passive immunotherapies against A β – ARIA-E in subjects homozygous for *ApoE &* genotype

Charles on Cale and a	Interve		Place		18/-:	Risk Ratio		Ratio
Study or Subgroup 1.8.1 Aducanumab	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	om, 95% CI
Budd Haeberlein 2022 Subtotal (95% CI)	117	182 182	6		100.0% 100.0 %	20.89 [9.43, 46.27] 20.89 [9.43, 46.27]		-
Total events	117		6					
Heterogeneity: Not applic	able							
Test for overall effect: Z=	7.49 (P ≤	0.0000	1)					
1.8.2 Donanemab								
Mintun 2021	11	25	4	28	16.7%	40 00 (4 74 00 77)		
Sims 2023	58	143	1 5	146	83.3%	12.32 [1.71, 88.77] 11.84 [4.89, 28.67]		
Subtotal (95% CI)	20	168	5		100.0%	11.92 [5.32, 26.71]		•
Total events	69		6		1001070	11102 [0102, 2011 1]		
Heterogeneity: Tau ² = 0.0		0.00. df	_	0.97): I ²	= 0%			
Test for overall effect: Z=				,,				
1.8.3 Lecanemab								
van Dyck 2022 Subtotal (95% CI)	46	141 141	5		100.0% 100.0%	8.68 [3.56, 21.17] 8.68 [3.56, 21.17]		
Total events	46		5					
Heterogeneity: Not applic	able							
Test for overall effect: Z=	4.75 (P <	0.0000	1)					
1.8.4 Gantenerumab								
Bateman 2023	86	180	7	150	93.5%	10.24 [4.89, 21.44]		
Ostrowitzki 2017	11	103	0	53	6.5%	11.94 [0.72, 198.81]	_	· · ·
Subtotal (95% CI)		283		203	100.0%	10.34 [5.06, 21.14]		-
Total events	97		7					
Heterogeneity: Tau ² = 0.0			•	0.92); l²	= 0%			
Test for overall effect: Z=	6.40 (P <	0.0000	1)					
							0.01 0.1	1 10 100
							Favours [experimental]	Favours [control]

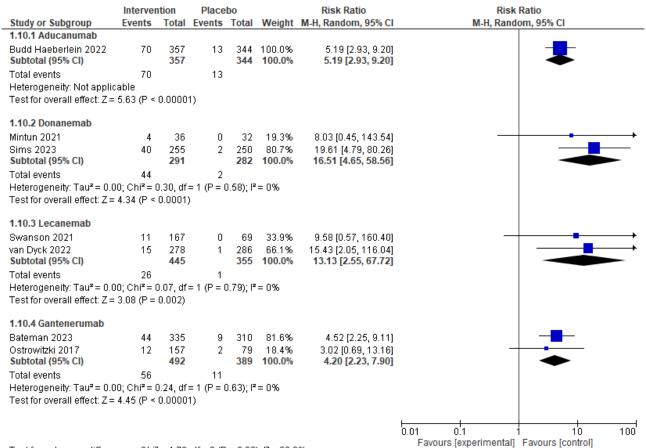
Test for subgroup differences: Chi² = 2.52, df = 3 (P = 0.47), l² = 0%

Passive immunotherapies against A β – ARIA-E in subjects heterozygotes for ApoE ϵ 4 genotype

	Interver		Place			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.9.1 Aducanumab							_
Budd Haeberlein 2022 Subtotal (95% CI)	200	564 564	10		100.0% 100.0%	19.29 [10.34, 36.01] 19.29 [10.34, 36.01]	
Total events	200		10				
Heterogeneity: Not applic	able						
Test for overall effect: Z=	9.29 (P <	0.0000	1)				
1.9.2 Donanemab							
Mintun 2021	21	70	0	64	5.5%	39.37 [2.43, 636.83]	
Sims 2023	103	452	9	474	94.5%	12.00 [6.15, 23.43]	
Subtotal (95% CI)		522		538	100.0%	12.81 [6.68, 24.54]	•
Total events	124		9				
Heterogeneity: Tau² = 0.0			•	0.41); I²	= 0%		
Test for overall effect: Z=	7.68 (P <	0.0000	1)				
1.9.3 Lecanemab							
van Dyck 2022	52	479	9	478	100.0%	5.77 [2.87, 11.57]	-
Subtotal (95% CI)		479		478	100.0%	5.77 [2.87, 11.57]	•
Total events	52		9				
Heterogeneity: Not applic							
Test for overall effect: Z=	4.93 (P <	0.0000	1)				
1.9.4 Gantenerumab							_
Bateman 2023	117	478	10	486	95.1%	11.90 [6.31, 22.41]	
Ostrowitzki 2017	30	271	0	134	4.9%	30.28 [1.87, 491.35]	
Subtotal (95% CI)		749		620	100.0%	12.45 [6.72, 23.09]	•
Total events	147		10				
Heterogeneity: Tau² = 0.0			•	0.51); I²	= 0%		
Test for overall effect: Z=	8.00 (P <	0.0000	1)				
							0.002 0.1 1 10 500
							Favours [experimental] Favours [control]

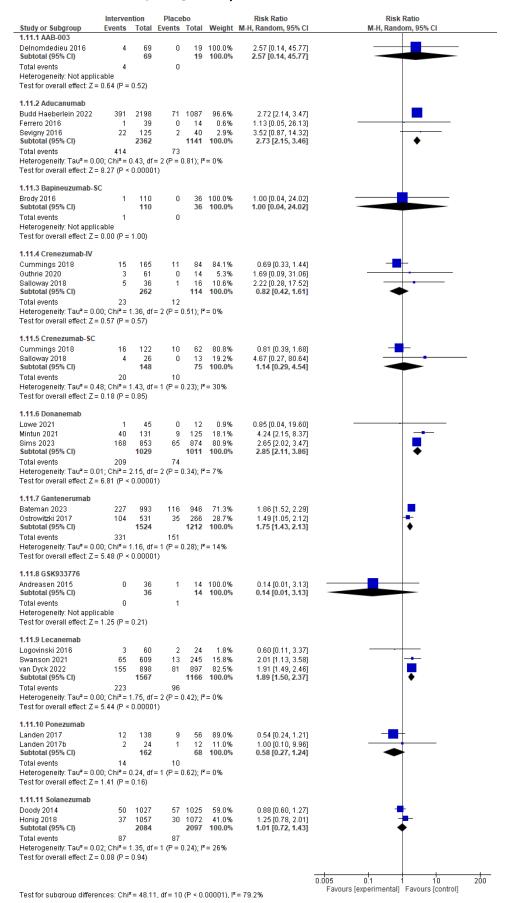
Test for subgroup differences: $Chi^2 = 6.53$, df = 3 (P = 0.09), $I^2 = 54.1\%$

Passive immunotherapies against A β – ARIA-E in subjects not carrying the ApoE ϵ 4 genotype



Test for subgroup differences: $Chi^2 = 4.70$, df = 3 (P = 0.20), $I^2 = 36.2\%$

Passive immunotherapies against Aβ – ARIA-H

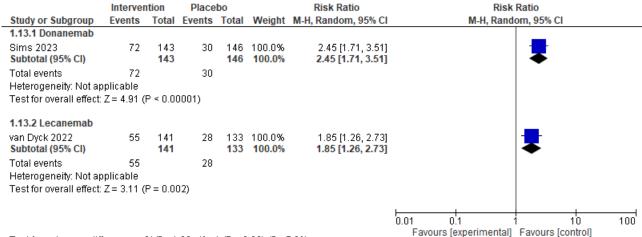


Passive immunotherapies against A β – ARIA-H in subjects not carrying the ApoE ϵ 4 genotype

	Interven	tion	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.12.2 Donanemab							
Sims 2023 Subtotal (95% CI)	48	255 255	28	250 250	100.0% 100.0%	1.68 [1.09, 2.59] 1.68 [1.09, 2.59]	
Total events	48		28				
Heterogeneity: Not appl	licable						
Test for overall effect: Z	= 2.35 (F	P = 0.02	2)				
1.12.4 Lecanemab							
van Dyck 2022 Subtotal (95% CI)	33	278 278	12	286 286	100.0% 100.0 %	2.83 [1.49, 5.36] 2.83 [1.49, 5.36]	🖶
Total events	33		12				
Heterogeneity: Not appl	licable						
Test for overall effect: Z	= 3.19 (F	P = 0.00	01)				
							0.01 0.1 1 10 100
T1/	_				4.00		Favours [experimental] Favours [control]

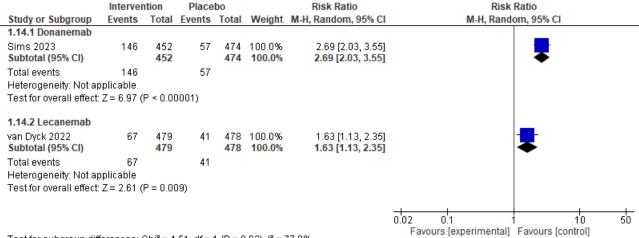
Test for subgroup differences: $Chi^2 = 1.75$, df = 1 (P = 0.19), $I^2 = 42.8\%$

Passive immunotherapies against A β – ARIA-H in subjects homozygous for ApoE \mathcal{A} genotype



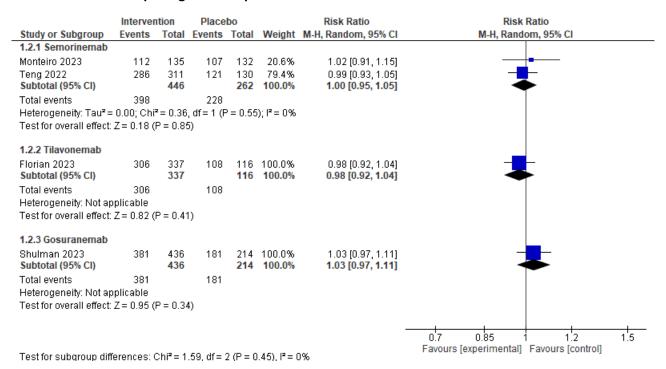
Test for subgroup differences: $Chi^2 = 1.08$, df = 1 (P = 0.30), $I^2 = 7.0\%$

Passive immunotherapies against A β – ARIA-H subjects heterozygotes for ApoE ϵ 4 genotype

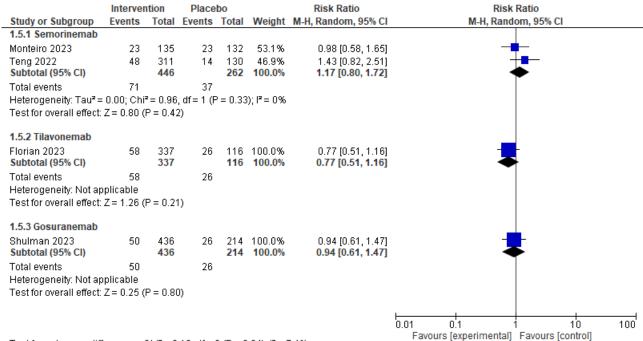


Test for subgroup differences: $Chi^2 = 4.51$, df = 1 (P = 0.03), $I^2 = 77.8\%$

Passive immunotherapies against Tau protein – adverse events



Passive immunotherapies against Tau protein – serious adverse events



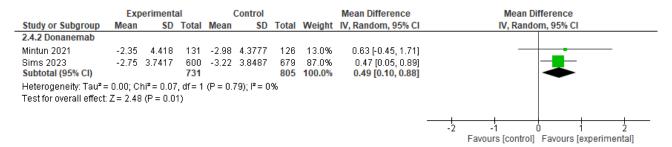
Passive immunotherapies against A β – CDR-SB

tudy or Subgroup	Mean	mAb SD	Total	Mean	PL SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
7.1 AAB-003-IV									
elnomdedieu 2016 - 1mg/kg	1.75	1.708	6	-0.35	1.935	4	22.8%	2.10 [-0.24, 4.44]	
elnomdedieu 2016 - 2mg/kg	1	2.449	16	-0.35	1.935	4	24.7%	1.35 [-0.89, 3.59]	 • -
elnomdedieu 2016 - 4mg/kg	1.86	3.371		-0.35	1.935	4	20.2%	2.21 [-0.27, 4.69]	
elnomdedieu 2016 - 8mg/kg	0.79	2.84	24	-0.35	1.935	3	20.5%	1.14 [-1.33, 3.61]	
elnomdedieu 2016 -0.5mg/kg ubtotal (95% CI)	1	3.286	6 69	-0.35	1.935	4 19	11.8% 100.0%	1.35 [-1.89, 4.59] 1.65 [0.54, 2.77]	
eterogeneity: Tau² = 0.00; Chi² = 0.60, df = 4 (P : est for overall effect: Z = 2.90 (P = 0.004)	= 0.96);	I²= 0%	03			13	100.0%	1.03 [0.34, 2.77]	
7.2 Aducanumab									
idd Haeberlein 2022 (EMERGE) -High Dose	1.35	2.69	547	1.74	2.69	274	43.5%	-0.39 [-0.78, 0.00]	-
ıdd Haeberlein 2022 (ENGAGE) -High Dose	1.59	2.61	555	1.56	2.52	273	48.6%	0.03 [-0.34, 0.40]	•
vigny 2016 - 01mg/kg	1.72	2.56	31	1.87	2.59	10	2.0%	-0.15 [-1.99, 1.69]	
vigny 2016 - 03mg/kg	1.37	2.43	32	1.87	2.59	10	2.0%	-0.50 [-2.31, 1.31]	
igny 2016 - 06mg/kg	1.11	2.41	30	1.87	2.59	10	2.0%	-0.76 [-2.58, 1.06]	
vigny 2016 -10mg/kg	0.63	2.66	32	1.87	2.59	10	1.9%	-1.24 [-3.09, 0.61]	
btotal (95% CI)	0.5		1227			587	100.0%	-0.21 [-0.46, 0.05]	₹
terogeneity: Tau² = 0.00; Chi² = 4.08, df = 5 (P : st for overall effect: Z = 1.58 (P = 0.11)	= 0.54);	I*= U%							
3 Bapineuzumab									
lloway 2014 - 0.5mg/kg	3.3	2.57	658	3	4.16	432	26.5%	0.30 [-0.14, 0.74]	 - -
lloway 2014 - 0.5mg/kg	2.6	3.54	314	2.6	4.44	246	11.1%	0.00 [-0.68, 0.68]	+
lloway 2014 - 1 mg/kg	2.8	3.5	307	2.6	4.44		11.1%	0.20 [-0.48, 0.88]	+
ndenberghe 2016 - 0.5mg/kg	2.23	3.67	255	2.59	3.62		10.0%	-0.36 [-1.07, 0.35]	
ndenberghe 2016 - 1 mg/kg	2.41	3.66	253	2.59	3.62	164	10.0%	-0.18 [-0.89, 0.53]	
ndenberghe 2016 -0.5mg/kg btotal (95% CI)	2.44	3.31	650 2437	2.59	3.32	431 1684	31.3% 100.0%	-0.15 [-0.55, 0.25] 0.00 [-0.23, 0.23]	7
	- 0.573	J≥ — ∩ 04.	2431			1004	100.070	0.00 [-0.23, 0.23]	Ť
terogeneity: Tau² = 0.00; Chi² = 3.88, df = 5 (P : st for overall effect: Z = 0.01 (P = 0.99)	- 0.57);	i – U%							
.4 Crenezumab-IV									
ımmings 2018 - 15mgkg	2.49	3.21	165	2.57	3.21	84	36.1%	-0.08 [-0.92, 0.76]	-
trowitzki 2022 - 60mg/kg (Cread)	3.59	2.45	86	3.42	2.47	88	40.8%	0.17 [-0.56, 0.90]	
trowizki 2022 - 60mg/kg (Cread 2)	1.89	1.63	12	3.19	1.68	15	23.1%	-1.30 [-2.55, -0.05]	
btotal (95% CI)			263			187	100.0%	-0.26 [-1.01, 0.48]	~
terogeneity: Tau ² = 0.22; Chi ² = 3.99, df = 2 (P =	= 0.14);	I² = 50%							
st for overall effect: Z = 0.68 (P = 0.49)									
7.5 Crenezumab-SC							400.5::	0.0011.50.5.55	_
mmings 2018 - 300mg	2.01	2.87	122	2.7	2.83		100.0%	-0.69 [-1.56, 0.18]	
btotal (95% CI)			122			62	100.0%	-0.69 [-1.56, 0.18]	
terogeneity: Not applicable st for overall effect: Z = 1.56 (P = 0.12)									
7.6 Donanemab									
ntun2021	1.22	2.01	131	1.58	1.99	125	30.6%	-0.36 [-0.85, 0.13]	-
ns 2023		2.3658	598		2.3764	672	69.4%	-0.70 [-0.96, -0.44]	<u> </u>
btotal (95% CI)	1.62	2.3030	729	2.72	2.5104		100.0%	-0.60 [-0.90, -0.29]	-
terogeneity: Tau² = 0.02; Chi² = 1.44, df = 1 (P =	= 0.23):	I² = 31%						,	,
st for overall effect: Z = 3.80 (P = 0.0001)	/								
7.7 Gantenerumab									
teman 2023 (Graduate I)		3.1274	499		3.5236		30.8%	-0.30 [-0.72, 0.12]	***
teman 2023 (Graduate II)		3.1242	498	3.01	3.276	477	33.0%	-0.19 [-0.59, 0.21]	7
trowitzki 2017 - 105mg	1.69	2.68	271	1.6	2.61	133	17.9%	0.09 [-0.46, 0.64]	†
trowitzki 2017 - 225mg	1.73	2.54	260	1.6	2.61	133	18.3%	0.13 [-0.41, 0.67]	<u>_</u>
btotal (95% CI)	- 0.500	IZ COY	1528			1228	100.0%	-0.12 [-0.35, 0.12]	₹
terogeneity: Tau² = 0.00; Chi² = 2.22, df = 3 (P : st for overall effect: Z = 0.98 (P = 0.33)	= 0.53);	r= U%							
.8 Lecanemab									
anson 2021 - 05mg/kgB	1.46	2.36	89	1.5	2.47	48	5.0%	-0.04 [-0.89, 0.81]	
vanson 2021 - 05mg/kgM	1.71	2.31	48	1.5	2.47	48	4.0%	0.21 [-0.75, 1.17]	
ranson 2021 - 10mg/kgB	1.1	2.63	152	1.5	2.47	48	5.5%	-0.40 [-1.21, 0.41]	-+
anson 2021 - 10mg/kgM	1.25	2.65	246	1.5	2.47	46	5.9%	-0.25 [-1.04, 0.54]	-+
anson 2021 -02.5mg/kgB	1.23	2.44	52	1.5	2.47	48	3.9%	-0.27 [-1.23, 0.69]	
n Dyck 2022	-0.45	2.337	859	0	2.337	875	75.6%	-0.45 [-0.67, -0.23]	<u>.</u>
btotal (95% CI)			1446			1113	100.0%	-0.38 [-0.57, -0.19]	•
terogeneity: Tau² = 0.00; Chi² = 2.62, df = 5 (P : st for overall effect: Z = 3.91 (P < 0.0001)	= 0.76);	l² = 0%							
.9 Solanezumab									
ody 2014 (Expedition 1)	2	5.7247	506	1.9	5.7247	506	12.4%	0.20 [-0.51, 0.91]	-
lody 2014 (Expedition 1) lody 2014 (Expedition 2)	2.3	3.93	521	2.7	3.96	519	25.7%	-0.40 [-0.88, 0.08]	<u> </u>
nig 2018 (Expedition 3)	1.87		1057	2.21		1072	61.9%	-0.34 [-0.63, -0.05]	_
btotal (95% CI)	1.07	3.23	2084	2.21	5.0		100.0%	-0.29 [-0.54, -0.04]	•
terogeneity: Tau² = 0.00; Chi² = 2.17, df = 2 (P =	= 0.34):	l² = 8%						,,	1
st for overall effect: Z = 2.24 (P = 0.03)	,,								
								_	-4 -2 0 2 4
t for outbaroun difforonces: Chiz = 25.04, Af = 0	2 /D = 0	002) 12 -	ളാവം						Favours [mAb] Favours [PL]
t for subgroup differences: Chi² = 25.01, df = 8	5 (F = U.	002), IT=	00.0%						

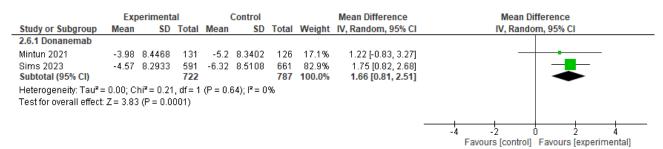
Donanemab - iADRS

	Ex	perimenta	erimental Control					Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI
Mintun 2021	-6.86	12.9907	131	-10.06	12.8077	126	18.5%	3.20 [0.05, 6.35]	
Sims 2023	-10.19	13.2772	583	-13.22	11.2576	444	81.5%	3.03 [1.53, 4.53]	ı -
Total (95% CI)			714			570	100.0%	3.06 [1.70, 4.42]	•
Heterogeneity: Tau²: Test for overall effect			,	P = 0.92)	; I² = 0%		-10 -5 0 5 10 Favours [control] Favours [experimental]		

Donanemab - MMSE



Donanemab - ADCS-ADL



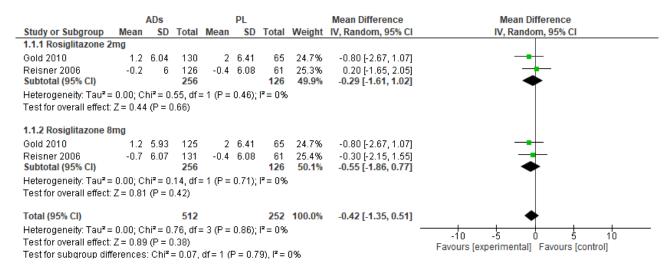
Passive immunotherapies against A β – amyloid PET

Study or Subgroup	Mean	mAb SD	Total	Mean	PL SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
L.2.1 BAPINEUZUMAB-IV Salloway 2014 - 0.5 mg/kg Salloway 2014 - 0.5 mg/kg Salloway 2014 - 1 mg/kg /andenberghe 2016 - 0.5 mg/kg /andenberghe 2016 - 1 mg/kg /andenberghe 2016 - 0.5 mg/kg /andenberghe 2016 - 0.5 mg/kg bubtotal (95% Cl) Heterogeneity: Tau² = 0.00; Chi² = 5.04, df = 5 (l	0.039 0.001 -0.094 -0.04 0 -0.04 P = 0.41); F	0.1566 0.1793 0.1632 0.196 0.1658 0.1697	75	-0.046 0.102 -0.046 0.02 0.02 0.03	0.1172 0.1716 0.1253 0.1442 0.1442 0.196	7 40 8 13 13 24 105	7.4% 43.3% 8.3% 7.1% 10.4% 23.4% 100.0%	0.56 [-0.39, 1.52] -0.57 [-0.96, -0.18] -0.31 [-1.21, 0.59] -0.36 [-1.33, 0.62] -0.13 [-0.93, 0.68] -0.38 [-0.91, 0.15] -0.36 [-0.62, -0.10]	•
est for overall effect: Z = 2.69 (P = 0.007)	0.41),1	- 170							
2.2.2 BAPINEUZUMAB-SC Brody 2016 - 20mg Brody 2016 - 20mg Brody 2016 - 7mg Subtotal (95% CI)	-0.021 -0.014 -0.066	0.1803 0.1863 0.1777	36 35 34 105	0 0 0	0.1749 0.1749 0.1749	11 11 11 33	33.7% 33.5% 32.8% 100.0%	-0.12 [-0.79, 0.56] -0.07 [-0.75, 0.60] -0.37 [-1.05, 0.32] -0.18 [-0.58, 0.21]	
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 2 (1 est for overall effect: Z = 0.92 (P = 0.36)	r = 0.81), I	-= 0%							
2.2.3 SOLANEZUMAB-IV -lonig 2018 Subtotal (95% CI) -leterogeneity: Not applicable Fest for overall effect: Z = 1.41 (P = 0.16)	-0.01	0.1419	805 805	0	0.1406	791 791	100.0% 100.0 %	-0.07 [-0.17, 0.03] - 0.07 [-0.17, 0.03]	•
2.2.4 GANTENERUMAB-IV Ostrowitzki 2012 - 60mg Ostrowitzki 2012 200mg Subtotal (95% CI) Heterogeneity, Tau" = 0.00; Chi" = 0.05, df=1 (i	0.03 -0.27 P = 0.83):1	0.24 0.45 =- 0%	6 6 12	0.24 0.24	0.15 0.15	2 2 4	52.0% 48.0% 100.0 %	-0.80 [-2.50, 0.89] -1.07 [-2.83, 0.69] - 0.93 [-2.15, 0.29]	•
Fest for overall effect: Z = 1.49 (P = 0.14)	, - 0.03),1	- 0.00							
2.2.5 GANTENERUMAB-SC Bateman 2023 (Graduate I) Bateman 2023 (Graduate II) Distrowitzki 2017 - 105mg Distrowitzki 2017 - 225mg	-66.44 -56.46 0 -0.09	19.9355 18.45 0.2 0.14	49 44 32 30	0 0 -0.02 -0.02	19.9355 18.45 0.13 0.13	41 40 18 17	24.9% 24.9% 25.1% 25.0% 100.0 %	-3.30 [-3.95, -2.66] -3.03 [-3.67, -2.40] 0.11 [-0.47, 0.69] -0.50 [-1.11, 0.10] -1.68 [-3.39, 0.03]	÷ _
Heterogeneity: Tau² = 2.94; Chi² = 92.54, df = 3		01); I² = 97	155 7%			116	100.0%	-1.00 [-3.39, 0.03]	
Heterogeneity: Tau ^z = 2.94; Chi ^z = 92.54, df = 3 Fest for overall effect: Z = 1.93 (P = 0.05)		01); I² = 97				110	100.0%	-1.00 [-3.35, 0.03]	
Heterogeneity: Tau ² = 2.94; Chi ² = 92.54, df = 3 Fest for overall effect: Z = 1.93 (P = 0.05) H.2.6 LECANEMAB-IV Bwanson 2021 - 02.5mg/kgB Bwanson 2021 - 05mg/kgB Bwanson 2021 - 05mg/kgB Bwanson 2021 - 10mg/kgB Bwanson 2021 - 10mg/kgM an Dyck 2022 Subtotal (95% CI) Heterogeneity: Tau ² = 0.48; Chi ² = 43.17, df = 5	-0.094 -0.197 -0.131 -0.306 -0.225 -59.12	0.1111 0.1091 0.1111 0.126 0.1179 23.7218	28 27 28 44 89 354 570	0.004 0.004 0.004 0.004 0.004 0	0.1244 0.1244 0.1244 0.1244 0.1244 23.7218	20 20 20 20 20 19 344	16.4% 15.7% 16.2% 15.7% 16.8% 19.2%	-0.83 [-1.42, -0.23] -1.71 [-2.39, -1.03] -1.14 [-1.76, -0.52] -2.44 [-3.13, -1.75] -1.91 [-2.47, -1.35] -2.49 [-2.99, -2.29] -1.77 [-2.37, -1.16]	+ + + + •
Heterogeneity: Tau ² = 2.94; Chi ² = 92.54, df = 3 Test for overall effect: Z = 1.93 (P = 0.05) 2.2.6 LECANEMAB-IV Swanson 2021 - 02.5mg/kgB Swanson 2021 - 05mg/kgB Swanson 2021 - 05mg/kgB Swanson 2021 - 10mg/kgM Swanson 2021 - 10mg/kgM and Dyck 2022 Subtotal (95% CI) Heterogeneity: Tau ² = 0.48; Chi ² = 43.17, df = 5 Test for overall effect: Z = 5.74 (P < 0.00001)	-0.094 -0.197 -0.131 -0.306 -0.225 -59.12 (P < 0.000	0.1111 0.1091 0.1111 0.126 0.1179 23.7218 01); F= 88	28 27 28 44 89 354 570	0.004 0.004 0.004 0.004	0.1244 0.1244 0.1244 0.1244 23.7218	20 20 20 20 19 344 443	16.4% 15.7% 16.2% 15.7% 16.8% 19.2% 100.0%	-0.83 [-1.42, -0.23] -1.71 [-2.39, -1.03] -1.14 [-1.76, -0.52] -2.44 [-3.13, -1.75] -1.91 [-2.47, -1.35] -2.49 [-2.69, -2.29] -1.77 [-2.37, -1.16]	+ + + + •
Heterogeneity: Tau ² = 2.94; Chi ² = 92.54, df = 3 'est for overall effect: Z = 1.93 (P = 0.05) ### 2.26 LECANEMAB-IV ### 3.25 LECANE	-0.094 -0.197 -0.131 -0.306 -0.225 -59.12 (P < 0.000 -0.002 -0.009 -0.002	0.1111 0.1091 0.1111 0.126 0.1179 23.7218 01); P= 98 0.0719 0.1036 0.1375	28 27 28 44 89 354 570	0.004 0.004 0.004 0.004	0.1244 0.1244 0.1244 0.1244	20 20 20 20 20 19 344	16.4% 15.7% 16.2% 15.7% 16.8% 19.2%	-0.83 [-1.42, -0.23] -1.71 [-2.39, -1.03] -1.14 [-1.76, -0.52] -2.44 [-3.13, -1.75] -1.91 [-2.47, -1.35] -2.49 [-2.69, -2.29]	+ + + + •
Subtotal (95% CI) Heterogeneity: Tau* = 2.94; Chi* = 92.54, df = 3 Test for overall effect: Z = 1.93 (P = 0.05) 2.2.6 LECANEMAB-IV Swanson 2021 - 02.5mg/kgB Swanson 2021 - 05mg/kgB Swanson 2021 - 10mg/kgB Swanson 2021 -	-0.094 -0.197 -0.131 -0.306 -0.225 -59.12 (P < 0.000 -0.002 -0.009 -0.002	0.1111 0.1091 0.1111 0.126 0.1179 23.7218 01); P= 98 0.0719 0.1036 0.1375	28 27 28 44 89 354 570 3%	0.004 0.004 0.004 0.004 0	0.1244 0.1244 0.1244 0.1244 23.7218 0.0719 0.1036 0.136	20 20 20 20 34 443 120 55 10 185	16.4% 15.7% 16.2% 15.7% 16.8% 19.2% 100.0%	-0.83 [-1.42, -0.23] -1.71 [-2.39, -1.03] -1.14 [-1.76, -0.52] -2.44 [-3.13, -1.75] -1.91 [-2.47, -1.35] -2.49 [-2.89, -2.29] -1.77 [-2.37, -1.16] -0.08 [-0.34, 0.17] -0.16 [-0.54, 0.21] 0.36 [-0.40, 1.12]	+++++++++++++++++++++++++++++++++++++++
Heterogeneity: Tau" = 2.94; Chi" = 92.54, df = 3 Test for overall effect: Z = 1.93 (P = 0.05) ### 2.26 LECANEMAB-IV ### Swanson 2021 - 02.5mg/kgB ### Swanson 2021 - 05mg/kgB ### Swanson 2021 - 10mg/kgB ### Swanson 2021 - 10mg/kgM ### Swanson	(P < 0.000 -0.094 -0.197 -0.131 -0.306 -0.225 -59.12 (P < 0.000 -0.002 -0.002 -0.029 -0.029 -0.236 -0.236 -0.236 -0.236 -0.135 -0.21 -0.263	0.1111 0.1091 0.1111 0.126 0.1179 23.7218 01); IF = 88 0.0719 0.1036 0.1375 F = 0% 0.1862 0.1239 0.1246 0.1246 0.1246 0.1246 0.1246 0.1217	28 27 28 44 570 33% 120 55 21 196 24 24 24 460	0.004 0.004 0.004 0.004 0 0	0.1244 0.1244 0.1244 0.1244 23.7218 0.0719 0.1036 0.136	200 200 200 200 199 344 443 120 55 100 185	16.4% 15.7% 16.2% 15.7% 16.8% 19.2% 100.0%	-0.83 [-1.42, -0.23] -1.71 [-2.39, -1.03] -1.14 [-1.76, -0.52] -2.44 [-3.13, -1.75] -1.91 [-2.47, -1.35] -2.49 [-2.69, -2.29] -1.77 [-2.37, -1.16] -0.08 [-0.34, 0.17] -0.16 [-0.54, 0.21] 0.36 [-0.40, 1.12] -0.07 [-0.28, 0.13]	++++++++++++++++++++++++++++++++++++++

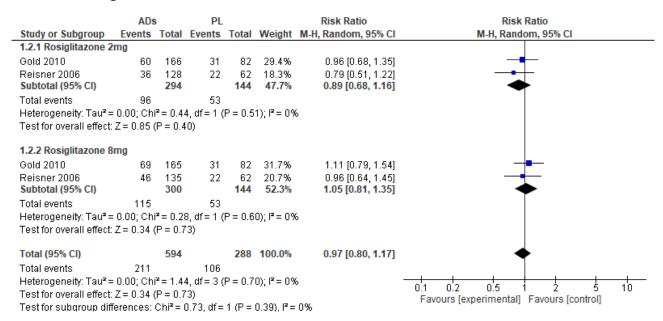
Test for subgroup differences: Chi² = 417.46, df = 9 (P < 0.00001), l² = 97.8%

REVIEW QUESTION 16a. What effect does modifying risk factors (repositioning drugs acting on possible etiological causes of dementia) have on slowing the progression of dementia?

Antidiabetic drugs - ADAS-Cog



Antidiabetic drugs - adverse events



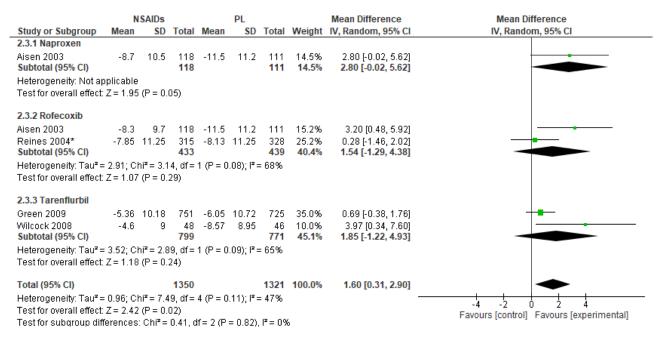
Non steroidal anti-inflammatory drugs – ADAS-Cog

	N	SAIDs			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.1.1 Celecoxib									
Soininen 2007* Subtotal (95% CI)	4.39	16.03	278 278	5	16.03	135 135	9.6% 9.6%	-0.61 [-3.91, 2.69] - 0.61 [-3.91, 2.69]	-
Heterogeneity: Not ap	plicable	!							
Test for overall effect:	Z = 0.36	(P = 0.	72)						
2.1.2 Diclofenac									
Scharf 1999 Subtotal (95% CI)	0.25	4.5	17 17	1.93	5.55	14 14	8.9% 8.9 %	-1.68 [-5.29, 1.93] - 1.68 [-5.29, 1.93]	-
Heterogeneity: Not ap Test for overall effect:	•		36)						
2.1.3 lbuprofen									
Pasqualetti 2009* Subtotal (95% CI)	-3	10.56	51 51	-3.1	10.56	46 46	7.6% 7.6%	0.10 [-4.11, 4.31] 0.10 [-4.11, 4.31]	
Heterogeneity: Not ap Test for overall effect:			96)						
2.1.4 Indomethacin									
De Jong 2008 Subtotal (95% CI)	7.8	7.6	19 19	9.3	10	19 19	5.3% 5.3%	-1.50 [-7.15, 4.15] - 1.50 [-7.15, 4.15]	
Heterogeneity: Not ap Test for overall effect:			60)						
2.1.5 Naproxen									
Aisen 2003 Subtotal (95% CI)	-5.8	8	118 118	-5.7	8.2	111 111	12.9% 12.9 %	-0.10 [-2.20, 2.00] - 0.10 [-2.20, 2.00]	*
Heterogeneity: Not ap Test for overall effect:	•		93)						
2.1.6 Rofecoxib									
Aisen 2003	-7.6	7.7	122	-5.7	8.2	111	13.1%	-1.90 [-3.95, 0.15]	
Reines 2004*	4.84	8.44	321	5.44	8.44	327	15.1%	-0.60 [-1.90, 0.70]	-
Subtotal (95% CI)			443			438	28.2%	-1.00 [-2.17, 0.18]	•
Heterogeneity: Tau ² = Test for overall effect:				1 (P = 0	l.29); l ^z =	= 9%			
2.1.7 Tarenflurbil									
Green 2009	4.24	7.99	786	1.73	5.74	746	16.3%	2.51 [1.82, 3.20]	-
Wilcock 2008 Subtotal (95% CI)	2.67	6.72	48 834	4.02	6.72	46 792	11.2% 27.5 %	-1.35 [-4.07, 1.37] 0.81 [-2.94, 4.57]	
Heterogeneity: Tau ² = Test for overall effect:				1 (P = 0	.007); l²	²= 86%			
Total (95% CI)			1760			1555	100.0%	-0.37 [-1.94, 1.19]	•
Heterogeneity: Tau ² = Test for overall effect:			.38, df=	= 8 (P <	0.0000			-	-10 -5 0 5 10
Test for subgroup diff				lf=6 (P	= 0.95),	I² = 0%	6		Favours [experimental] Favours [control]

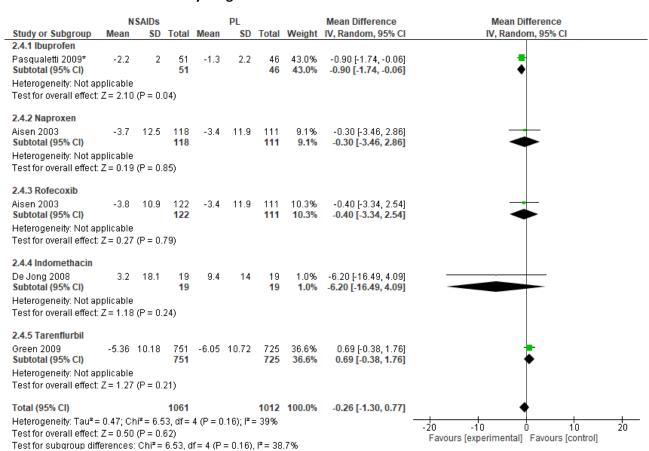
Non steroidal anti-inflammatory drugs – MMSE

		SAIDs			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.2.1 Aspirin	0.7	4.00	00	0.0	4.00	0.4	20.00	0.40 (0.57 0.27)	_
Bentham 2008* Subtotal (95% CI)	-0.7	1.66	98 98	-0.6	1.66	94 94	28.8% 28.8%	-0.10 [-0.57, 0.37] - 0.10 [-0.57, 0.37]	•
Heterogeneity: Not a									
Test for overall effect	Z = 0.42	(P = 0.1)	68)						
2.2.2 Celecoxib									
Soininen 2007* Subtotal (95% CI)	-2.3	2.37	255 255	-2	2.37	128 128	25.1% 25.1%	-0.30 [-0.80, 0.20] - 0.30 [-0.80, 0.20]	*
Heterogeneity: Not a	pplicable							,,	
Test for overall effect		(P = 0.1)	24)						
2.2.4 lbuprofen									
Pasqualetti 2009* Subtotal (95% CI)	2.7	3.57	51 51	2.1	3.39	46 46	3.3% 3.3%	0.60 [-0.79, 1.99] 0.60 [-0.79, 1.99]	
Heterogeneity: Not a	nnlicable					40	0.070	0.00 [-0.70, 1.00]	
Test for overall effect		(P = 0.4)	40)						
2.2.5 Indomethacin									
De Jong 2008 Subtotal (95% CI)	-3.4	4.3	19 19	-5.4	5.5	19 19	0.6% 0.6%	2.00 [-1.14, 5.14] 2.00 [-1.14, 5.14]	
Heterogeneity: Not a	nnlicable						0.070	2.00 [-1.14, 5.14]	
Test for overall effect		(P = 0.1)	21)						
2.2.7 Rofecoxib									
Reines 2004* Subtotal (95% CI)	-2.57	4.784	322 322	-2.13	4.78	329 329	11.8% 11.8%	-0.44 [-1.17, 0.29] - 0.44 [-1.17, 0.29]	<u> </u>
Heterogeneity: Not a	nnlicable		JEE			323	11.070	-0.44 [-1.17, 0.23]	—
Test for overall effect		(P = 0.1)	24)						
		`	•						
2.2.8 Tarenflurbil									
Green 2009	-2.36	4.1	630	-2.04	4.11	615	30.5%	-0.32 [-0.78, 0.14]	*
Subtotal (95% CI)	ماطممنامم		630			615	30.5%	-0.32 [-0.78, 0.14]	T
Heterogeneity: Not a Test for overall effect		/P = 0 :	17)						
, cotion overall ellect	. == 1.50	v. – o.	,						
Total (95% CI)			1375			1231	100.0%	-0.22 [-0.47, 0.03]	•
Heterogeneity: Tau² :			-	5 (P = 0	.53); [= 0%		-	-4 -2 0 2 4
Test for overall effect		•							Favours [control] Favours [experimental]
Test for subgroup dit	terences:	Chi*=	4.14, d	t=5(P	= 0.53	$ \cdot ^2 = 0$	%		· · · · · · · · · · · · · · · · · · ·

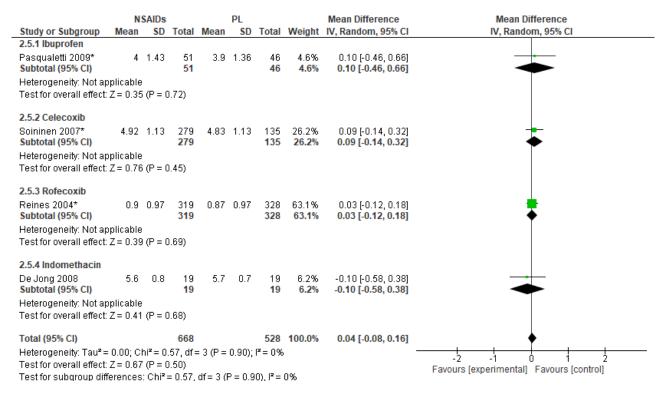
Non steroidal anti-inflammatory drugs - ADCS-ADL



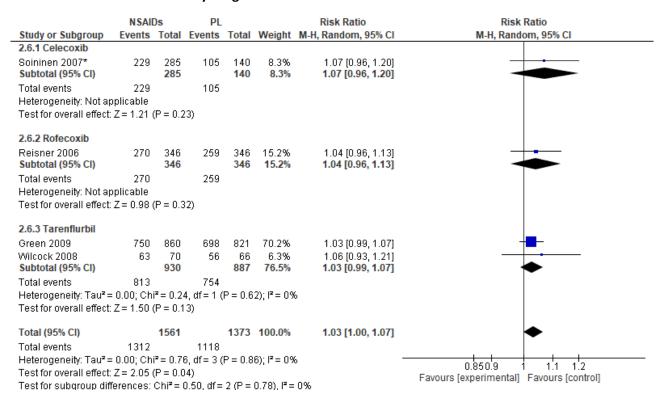
Non steroidal anti-inflammatory drugs - NPI



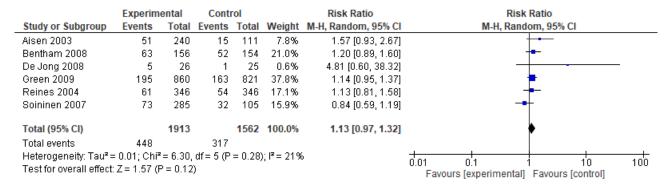
Non steroidal anti-inflammatory drugs - CIBIC+



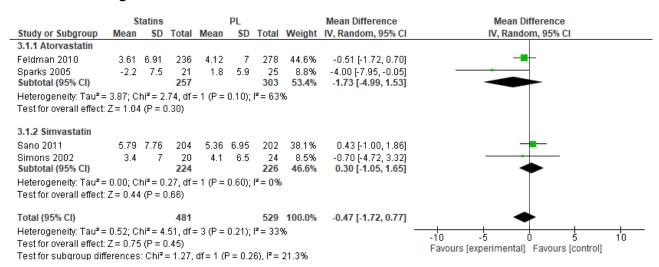
Non steroidal anti-inflammatory drugs - adverse events



Non steroidal anti-inflammatory drugs - serious adverse events



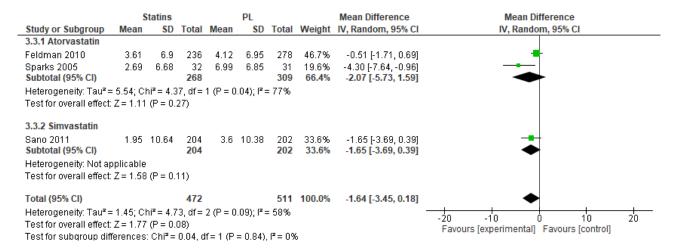
Statins - ADAS-Cog



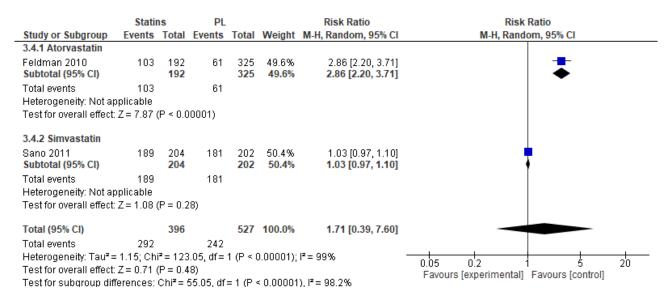
Statins - MMSE

	S	tatins			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.2.1 Atorvastatin									
Feldman 2010	-0.96	3.38	236	-1.35	3.5	278	35.9%	0.39 [-0.21, 0.99]	-
Sparks 2005 Subtotal (95% CI)	-0.77	2.7	32 268	-2.42	3.2	31 309	18.8% 54.7%	1.65 [0.19, 3.11] 0.84 [-0.35, 2.02]	•
Heterogeneity: Tau ² =				= 1 (P =	0.12);	l² = 599	%		
Test for overall effect:	Z=1.39	1 (P = t	J.17)						
3.2.2 Simvastatin									
Sano 2011	-2.47	3.8	204	-2.28	4.08	202	32.1%	-0.19 [-0.96, 0.58]	-+
Simons 2002 Subtotal (95% CI)	-0.6	3.1	24 228	-2.7	3.39	20 222	13.2% 45.3 %		
Heterogeneity: Tau² = Test for overall effect:	•		•	= 1 (P =	0.03);	I = 789	%		
Total (95% CI)			496			531	100.0%	0.67 [-0.17, 1.51]	•
Heterogeneity: Tau ² =	0.42; CI	hi = 8.	.04, df=	3 (P =	0.05);	$I^2 = 639$	%	_	-4 -5 0 5 4
Test for overall effect:			•	•					-4 -2 0 2 4
Test for subgroup diff		•		df = 1 (F	9 = 0.9	6), I²=	0%		Favours [control] Favours [experimental]

Statins - NPI



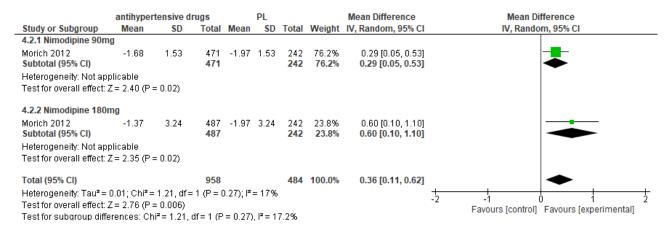
Statins - adverse events



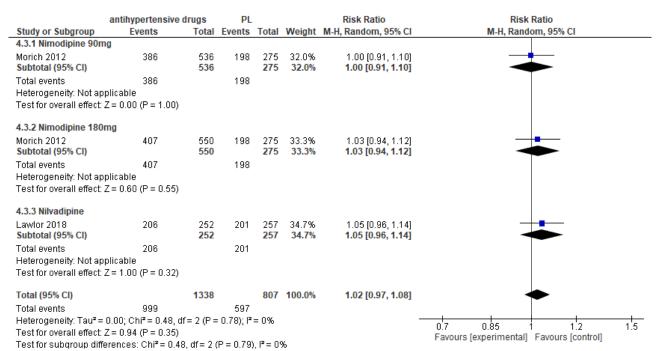
Antihypertensive drugs - ADAS-Cog

	antihype	rtensive d	Irugs		PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.1.1 Nimodipine 90m	g								
Morich 2012 Subtotal (95% CI)	2.59	5.95	471 471	3.03	5.95	242 242	43.7% 43.7%	-0.44 [-1.36, 0.48] - 0.44 [-1.36, 0.48]	•
Heterogeneity: Not app	plicable								
Test for overall effect: 2	Z= 0.93 (P	= 0.35)							
4.1.2 Nimodipine 180r	mg								
Morich 2012 Subtotal (95% CI)	2.58	5.87	487 487	3.03	5.87	242 242	45.4% 45.4%		*
Heterogeneity: Not app Test for overall effect: 2		= 0.33)							
4.1.3 Nilvadipine									
Lawlor 2018 Subtotal (95% CI)	9.41	10.53	247 247	9.63	10.46	251 251	10.9% 10.9%	-0.22 [-2.06, 1.62] - 0.22 [-2.06, 1.62]	
Heterogeneity: Not app Test for overall effect: 2		= 0.82)							
Total (95% CI)			1205			735	100.0%	-0.42 [-1.03, 0.19]	•
Heterogeneity: Tau ² =	0.00; Chi ^z =	= 0.05, df=	= 2 (P = 0	.97); P :	= 0%				
Test for overall effect: 2			- 0	///					-4 -2 0 2 4
Test for subgroup diffe	,		df = 2 (P	= 0.97)	$J^2 = 0\%$,			Favours [experimental] Favours [control]

Antihypertensive drugs - MMSE

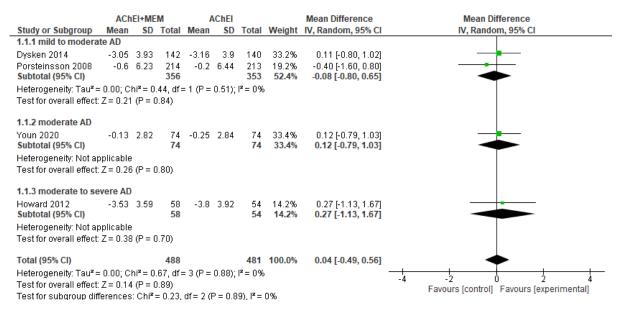


Antihypertensive drugs - adverse events

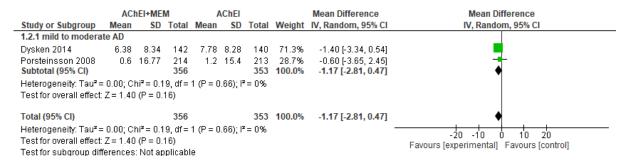


REVIEW QUESTION 17a. How effective is the co-prescription of cholinesterase inhibitors and memantine for the treatment of Alzheimer's disease?

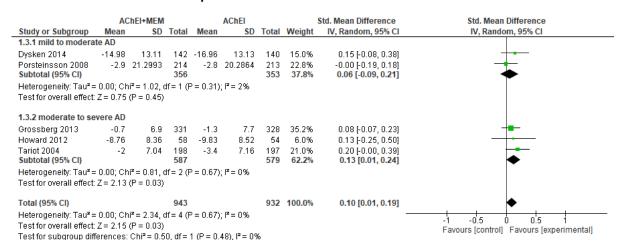
AChEI + memantine vs AChEI + placebo – MMSE



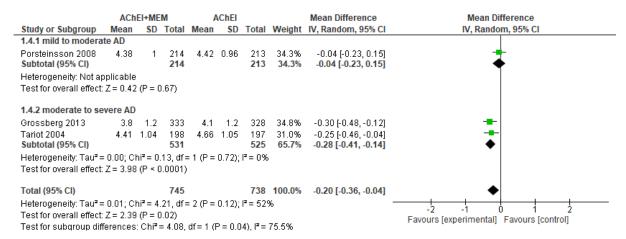
AChEI + memantine vs AChEI + placebo - ADAS-Cog



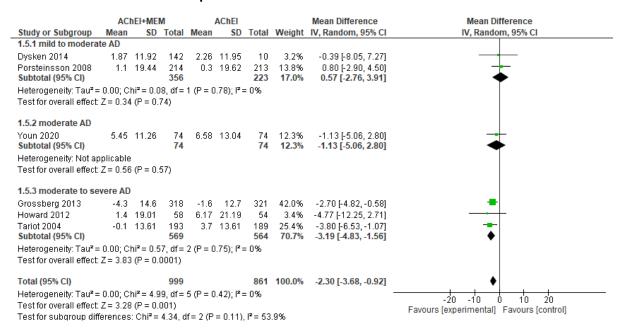
AChEI + memantine vs AChEI + placebo - ADL



AChEI + memantine vs AChEI + placebo - CIBIC+



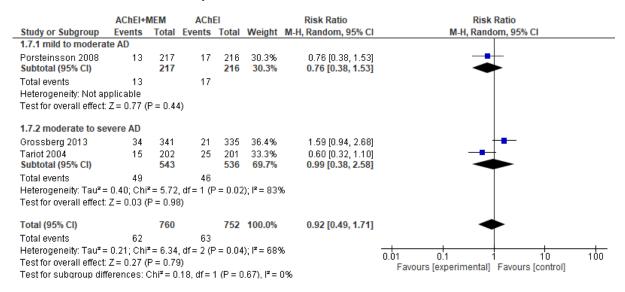
AChEI + memantine vs AChEI + placebo - NPI



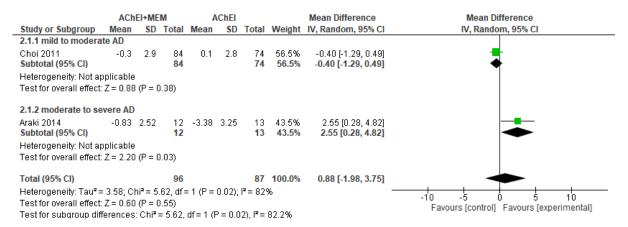
AChEI + memantine vs AChEI + placebo - adverse events

	AChEI+I	MEM	AChl	3		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.6.1 mild to modera	te AD						
Dysken 2014	18	155	19	152	11.7%	0.93 [0.51, 1.70]	
Porsteinsson 2008 Subtotal (95% CI)	27	217 372	30	216 368	18.2% 29.8%	0.90 [0.55, 1.45] 0.91 [0.62, 1.33]	*
Total events	45		49				
Heterogeneity: Tau ² = Test for overall effect:				= 0.93	i); I²= 0%		
1.6.2 moderate to se	vere AD						
Grossberg 2013	28	341	21	335	14.3%	1.31 [0.76, 2.26]	 -
Howard 2012 Subtotal (95% CI)	40	76 417	46	73 408	55.8% 70.2%	0.84 [0.63, 1.10] 0.99 [0.63, 1.57]	*
Total events	68		67				
Heterogeneity: Tau ² = Test for overall effect:				= 0.12	?); I² = 589	6	
Total (95% CI)		789		776	100.0%	0.91 [0.74, 1.12]	•
Total events Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diff	Z = 0.86 (P = 0.39	3)				0.02 0.1 10 50 Favours [experimental] Favours [control]

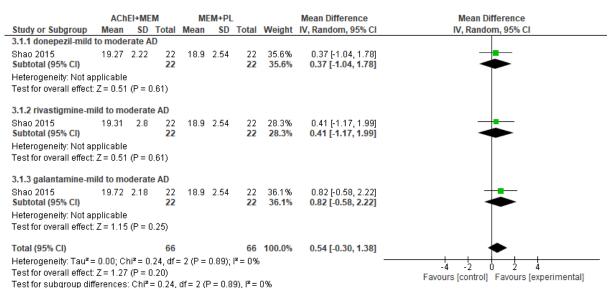
AChEI + memantine vs AChEI + placebo - withdrawal due to adverse events



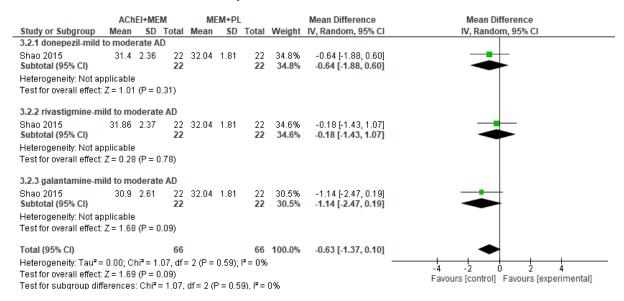
AChEI + memantine vs AChEI as monotherapy - MMSE



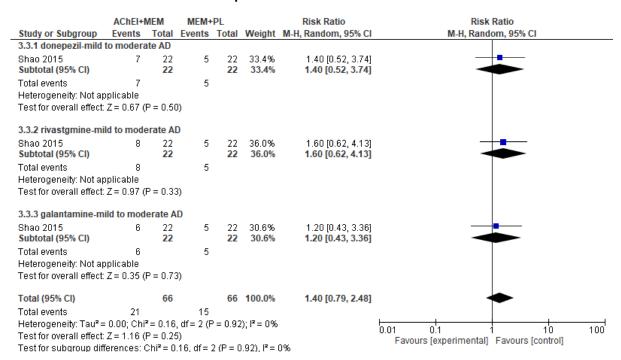
AChEI + memantine vs memantina + placebo - MMSE



AChEI + memantine vs memantine + placebo - ADCS-ADL

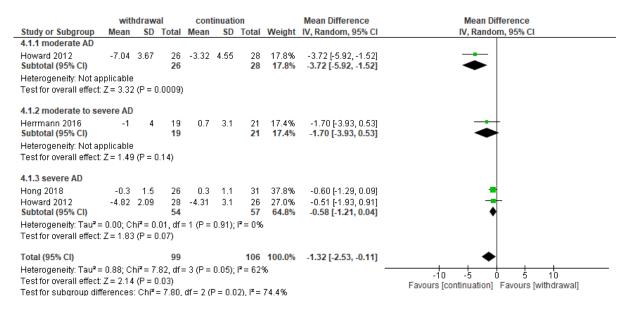


AChEI + memantine vs memantine + placebo - adverse events



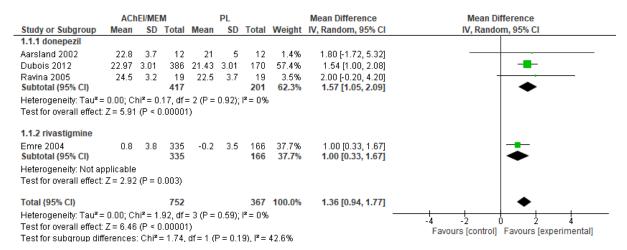
REVIEW QUESTION 17b. When should treatment with donepezil, galantamine, rivastigmine, memantine be withdrawn for people with Alzheimer's disease?

AChEI withdrawal vs continuation - MMSE

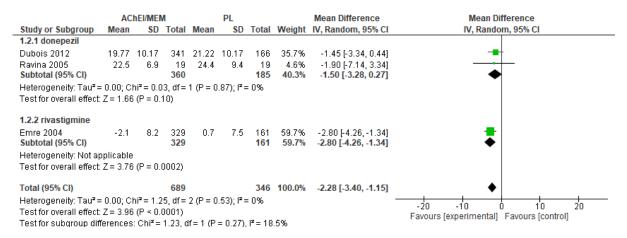


REVIEW QUESTION 18a. What is the comparative effectiveness of donepezil, galantamine, memantine and rivastigmine for cognitive enhancement in dementia associated with Parkinson's disease?

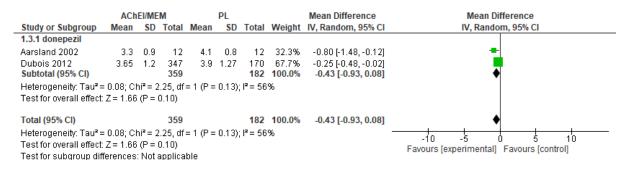
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - MMSE



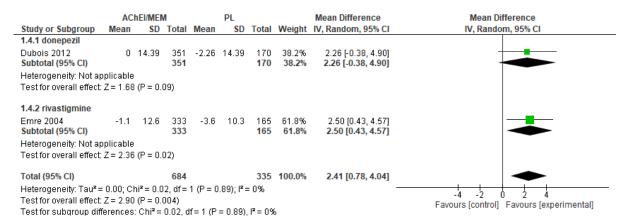
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - ADAS-Cog



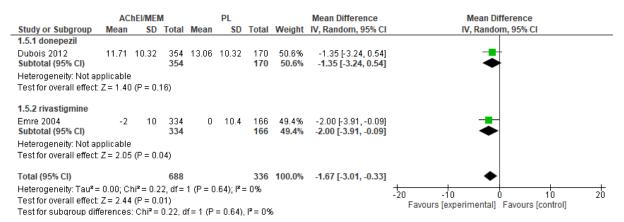
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - CIBIC+



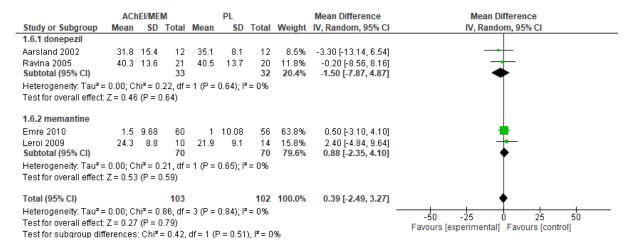
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - ADL



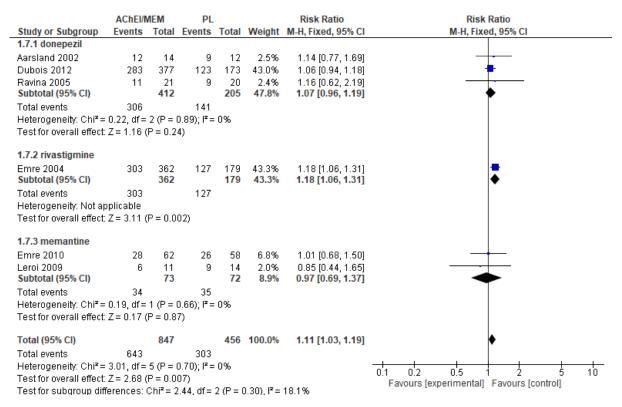
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - NPI-10 items



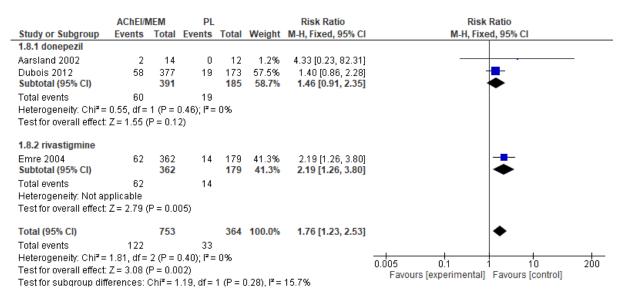
Acetylcholinesterase inhibitors and memantine for the treatment of PDD - UPDRS-III



Acetylcholinesterase inhibitors and memantine for the treatment of PDD - adverse events

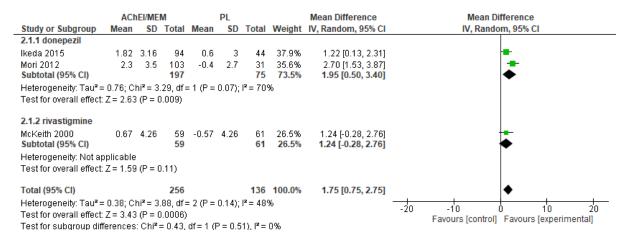


Acetylcholinesterase inhibitors and memantine for the treatment of PDD – withdrawal due to adverse events

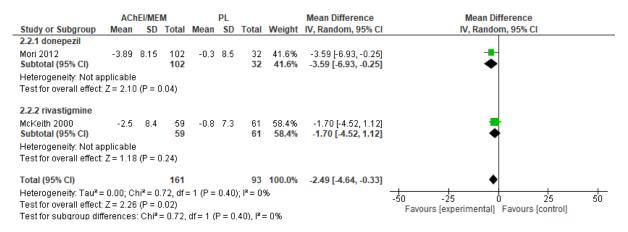


REVIEW QUESTION 18b. What is the comparative effectiveness of donepezil, galantamine, memantine and rivastigmine for cognitive enhancement in dementia with Lewy bodies?

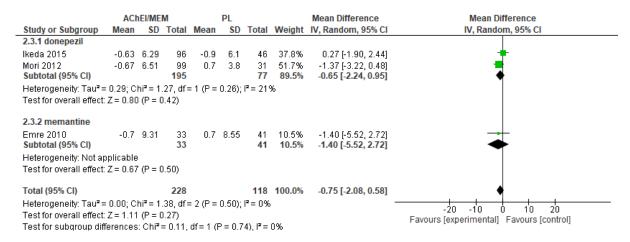
Acetylcholinesterase inhibitors and memantine for the treatment of DLB - MMSE



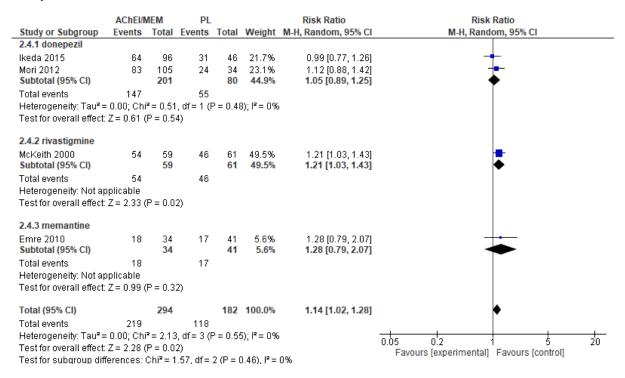
Acetylcholinesterase inhibitors and memantine for the treatment of DLB - NPI-10 items



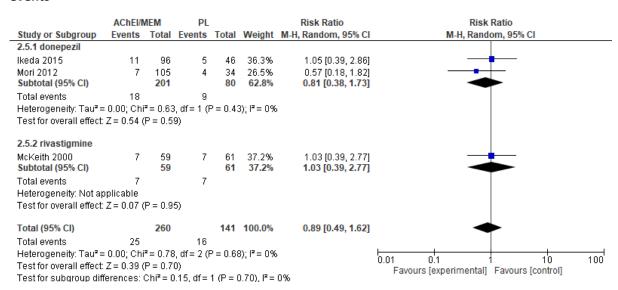
Acetylcholinesterase inhibitors and memantine for the treatment of DLB - UPDRS-III



Acetylcholinesterase inhibitors and memantine for the treatment of DLB - adverse events



Acetylcholinesterase inhibitors and memantine for the treatment of DLB – withdrawal due to adverse events



REVIEW QUESTION 20a. What are the most effective non-pharmacological interventions for supporting cognitive functioning in people living with dementia?

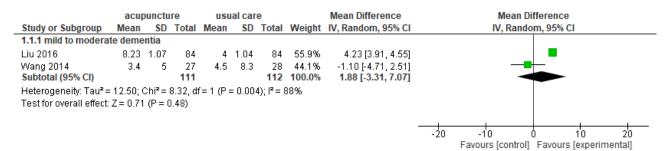
REVIEW QUESTION 20b. What are the most effective non-pharmacological interventions for supporting functional ability in people living with dementia?

REVIEW QUESTION 20c. What are the most effective non-pharmacological interventions to support wellbeing in people living with dementia?

REVIEW QUESTION 20d. What are the most effective methods of supporting people living with dementia to reduce harm and stay independent?

ACUPUNCTURE

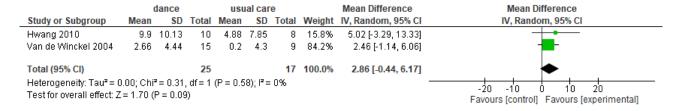
MMSE



PHYSICAL EXERCISE

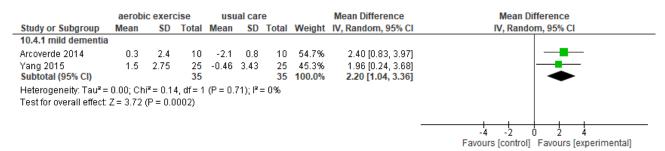
Dance

MMSE

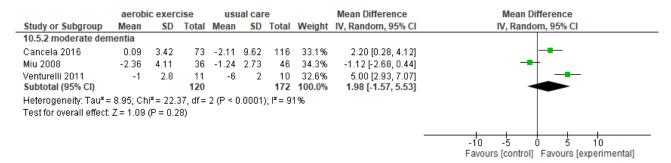


Aerobic exercise

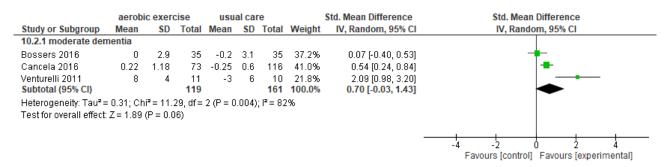
MMSE



MMSE

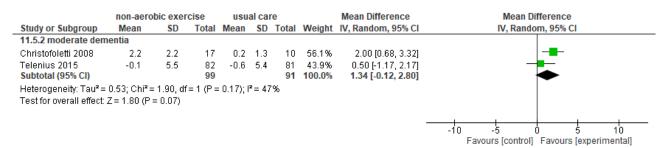


Functional activities

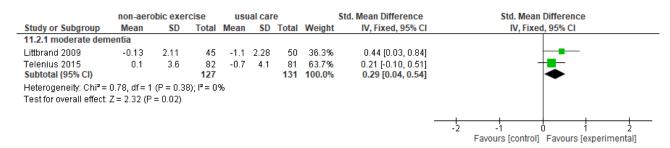


Non-aerobic exercise

MMSE

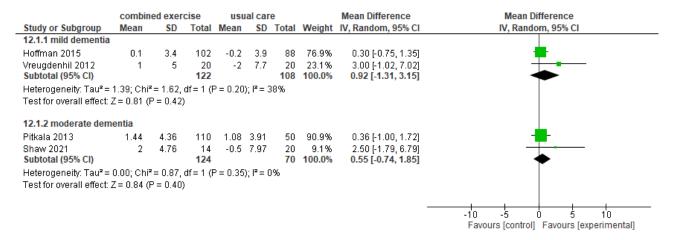


Functional activities

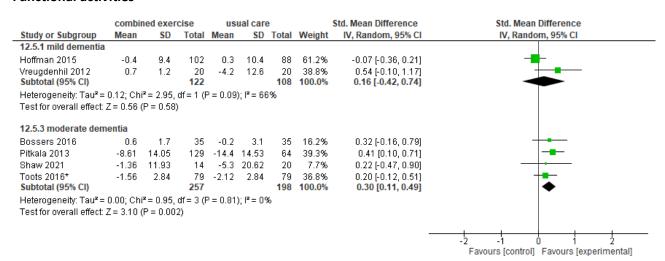


Aerobic/non-aerobic combined exercise

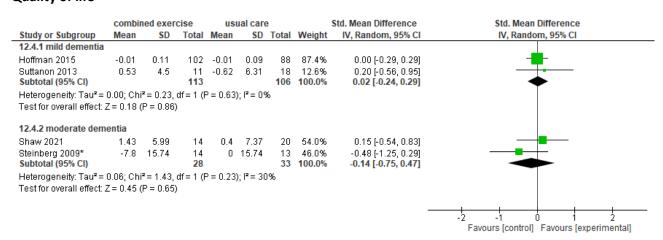
MMSE



Functional activities

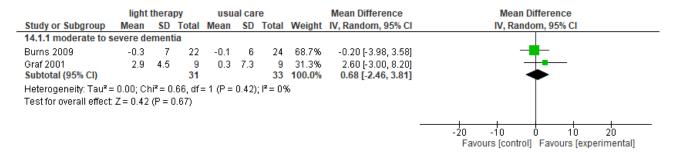


Quality of life



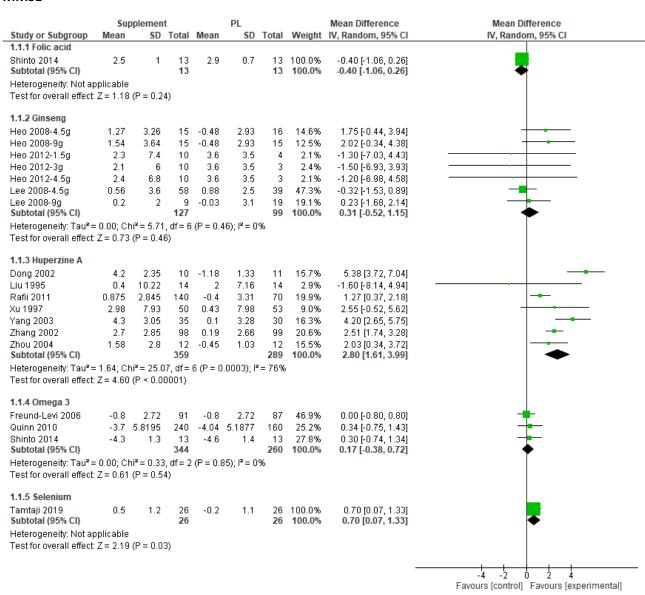
Light therapy

MMSE

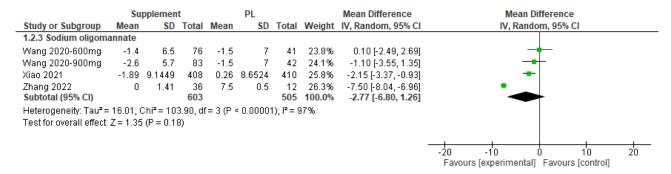


NUTRITIONAL INTERVENTIONS

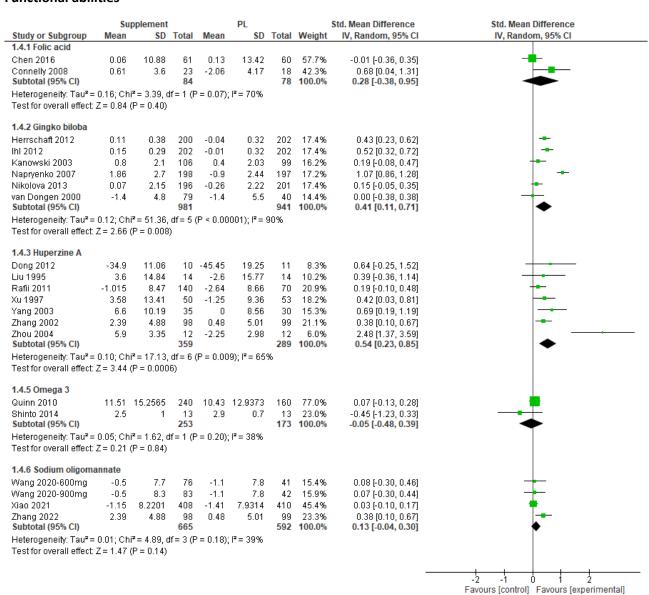
MMSE



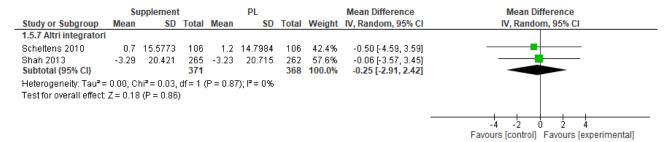
ADAS-Cog



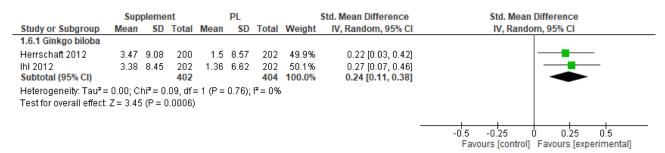
Functional abilities



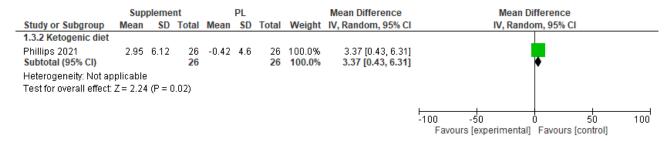
ADCS-ADL - other supplements



Quality of life - Ginkgo biloba



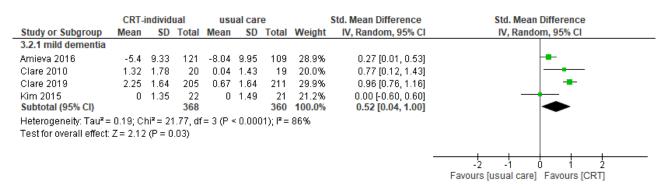
Quality of life - Ketogenic diet



COGNITIVE INTERVENTIONS

Cognitive rehabilitation (individual)

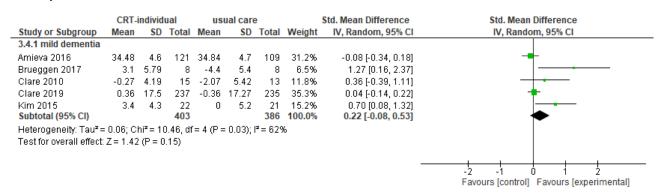
ADL



Functional activities

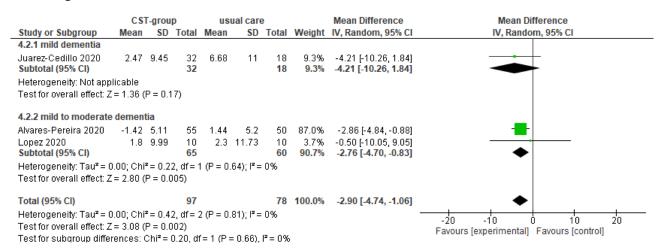
	CRT-individual			us	ual care	е		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.3.1 mild dementia									
Brueggen 2017	-0.52	0.94	8	0.26	1.1	8	30.6%	-0.72 [-1.74, 0.30]	
Clarkson 2021 Subtotal (95% CI)	2.5	14.83	234 242	1.1	12.58	234	69.4% 100.0%	0.10 [-0.08, 0.28] - 0.15 [-0.89, 0.59]	
Heterogeneity: Tau² =	0.20; C	hi² = 2.4	11, df=	1 (P = 0	l.12); l² =	= 59%			
Test for overall effect:	Z = 0.40) (P = 0.	69)						
									Favours [experimental] Favours [control]

Quality of life

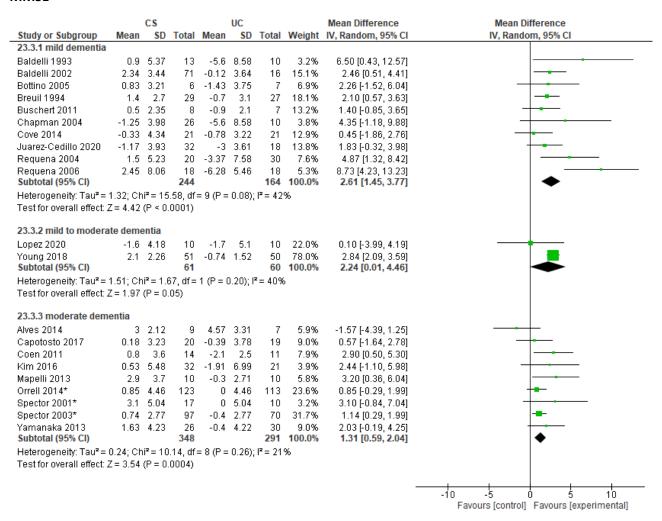


Cognitive stimulation (group)

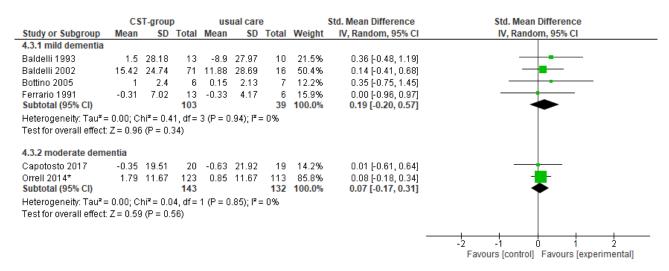
ADAS-Cog



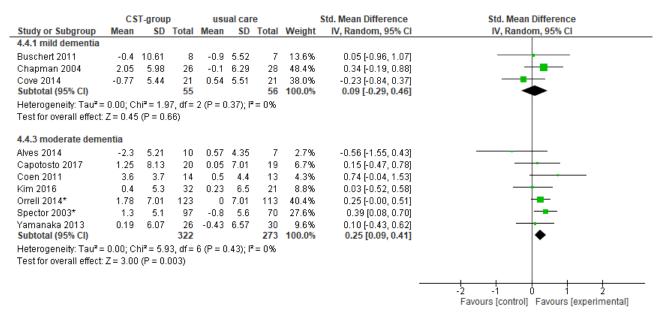
MMSE



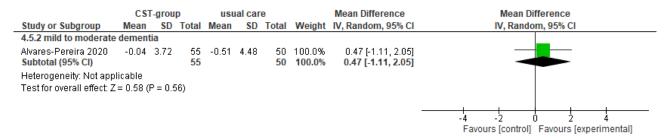
Functional abilities



Quality of life

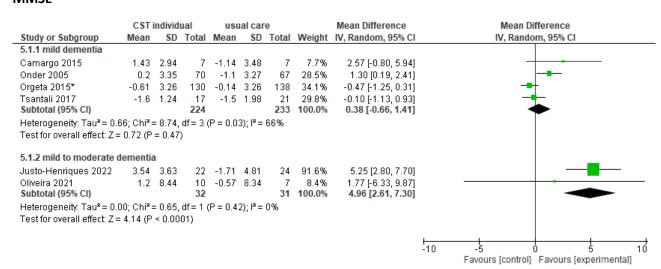


Quality of life

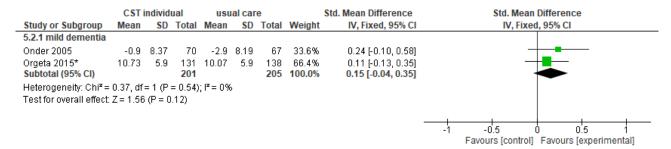


Cognitive stimulation (individual)

MMSE

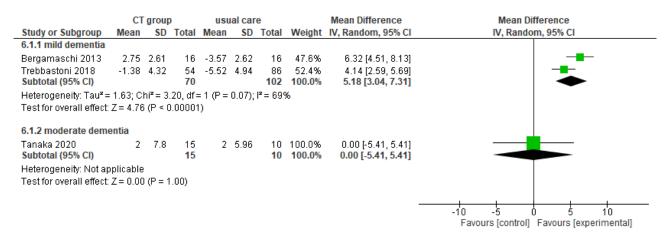


ADL

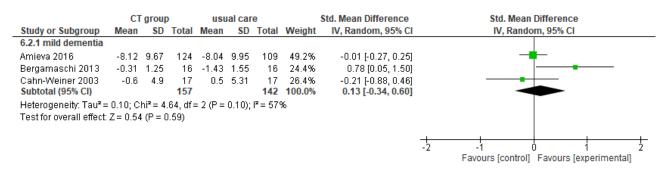


Cognitive training (group)

MMSE

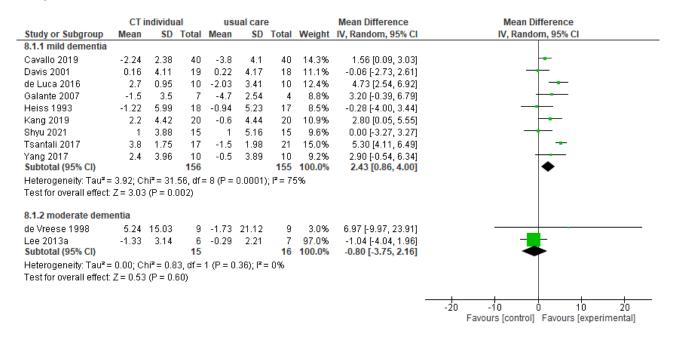


ADL

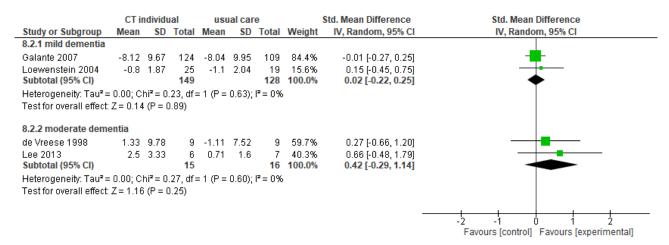


Cognitive training (individual)

MMSE

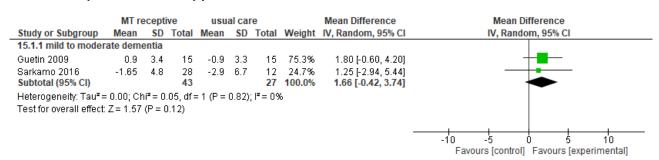


ADL

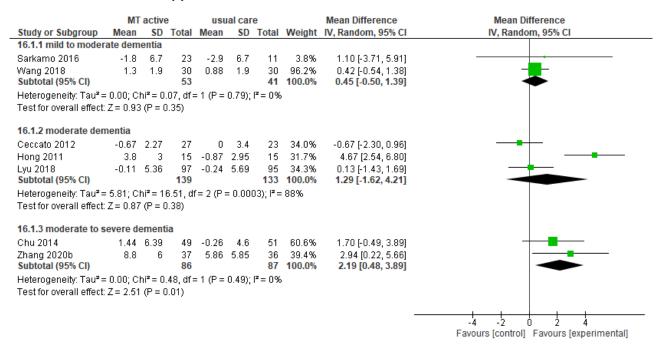


MUSIC THERAPY

MMSE - receptive music therapy

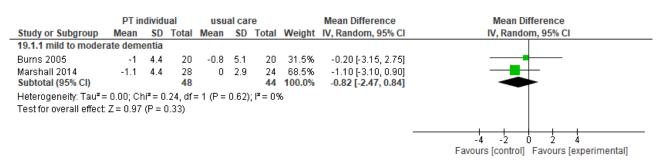


MMSE - active music therapy



PSYCHOTHERAPY

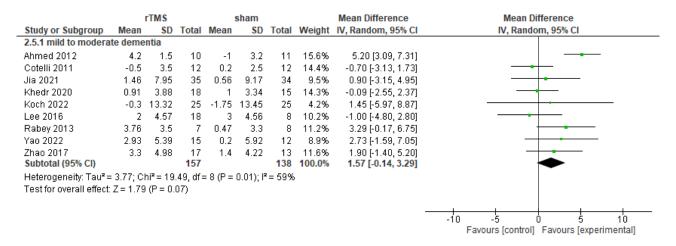
MMSE



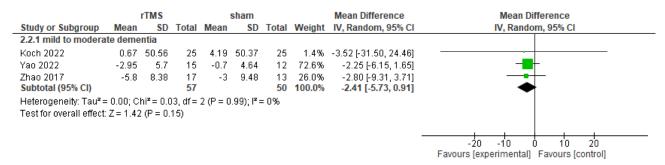
TRANSCRANICAL STIMULATION

Repetitive Transcranial Magnetic Stimulation

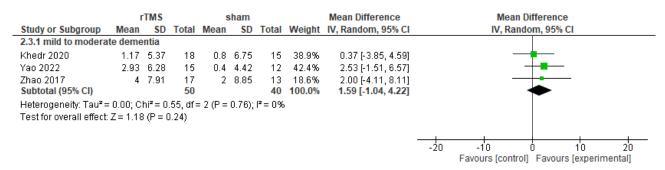
MMSE



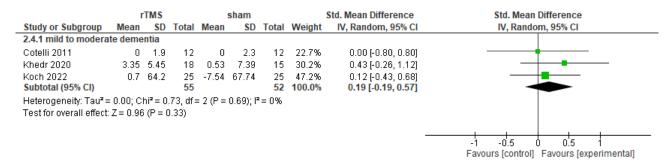
ADAS-Cog



MoCA

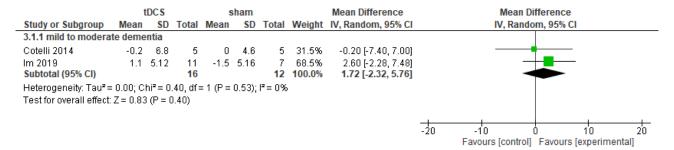


ADL



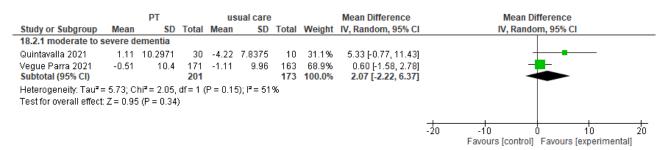
Transcranial Direct-Current Stimulation

MMSE



PET THERAPY

MMSE

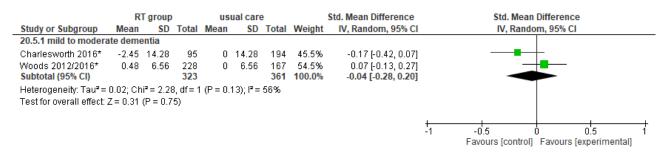


REMINESCENCE THERAPY (group)

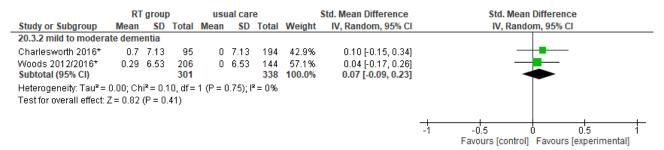
MMSE

	RT	group)	usu	al car	е		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
20.4.2 moderate den	nentia								
to 2007	0	4.73	17	-0.8	3.93	17	4.8%	0.80 [-2.12, 3.72]	•
.ok 2019	2.82	3.88	30	-0.57	3.32	30	12.3%	3.39 [1.56, 5.22]	
Fadaka 2007	2.04	1.53	28	-0.22	1.55	27	61.8%	2.26 [1.45, 3.07]	——
Гапака 2017	1.5	2.5	13	-1.4	3.3	14	8.5%	2.90 [0.70, 5.10]	
Vang 2007	1.75	4.94	51	-0.13	4.3	51	12.7%	1.88 [0.08, 3.68]	•
Subtotal (95% CI)			139			139	100.0%	2.33 [1.69, 2.97]	•
Heterogeneity: Tau ^z =	0.00; C	hi = 2.	.87, df=	4 (P =	0.58);	$I^2 = 0\%$			
Test for overall effect:	Z = 7.15	i (P < 0	0.00001	l)					
									-4 -2 0 2 4
									Favours [control] Favours [experimental]

Functional abilities

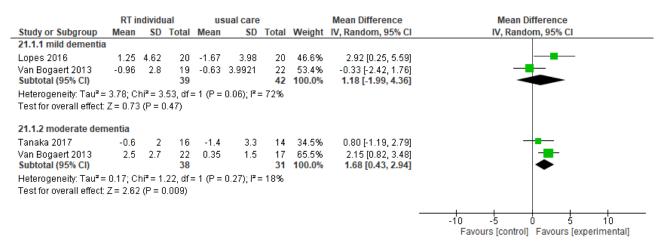


Quality of life



REMINESCENCE THERAPY (individual)

MMSE

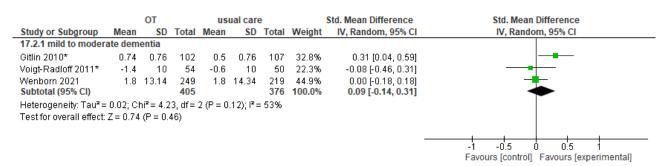


OCCUPATIONAL THERAPY

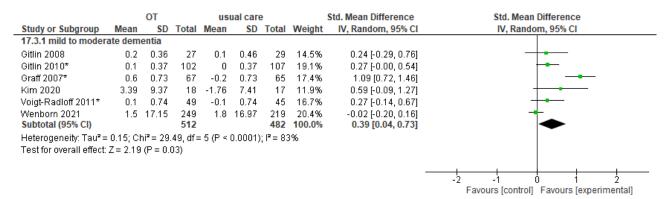
MMSE

		OT		usu	al car	e		Mean Difference		Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Veight IV, Random, 95% CI		IV, Random, 95% CI			
17.1.1 mild to moder	ate dem	entia											
Kim 2020	0.86	2.55	18	-0.42	2.1	17	44.6%	1.28 [-0.26, 2.82]		 			
Wenborn 2021 Subtotal (95% CI)	-0.3	8.01	249 267	-0.5	7.21	219 236	55.4% 100.0%	0.20 [-1.18, 1.58] 0.68 [-0.37, 1.73]		*			
Heterogeneity: Tau ² = Test for overall effect:				= 1 (P =	0.31);	l² = 4%							
									-10	-5 0 5 10			

ADL



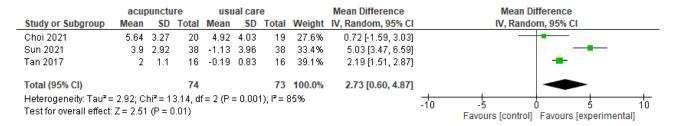
Quality of life



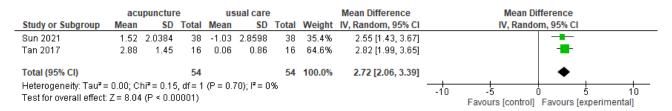
REVIEW QUESTION 20e. What are the most effective non-pharmacological interventions for supporting cognitive functioning, functional ability and wellbeing in people with Mild Cognitive Impairment?

ACUPUNCTURE

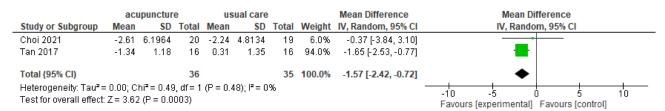
MoCA



MMSE

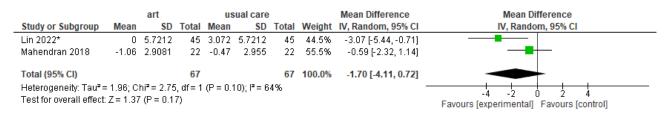


ADAS-Cog

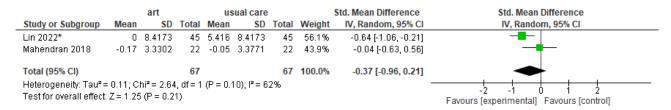


ART THERAPY

GDS



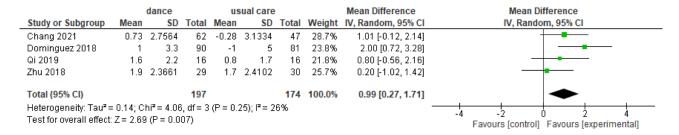
Anxiety



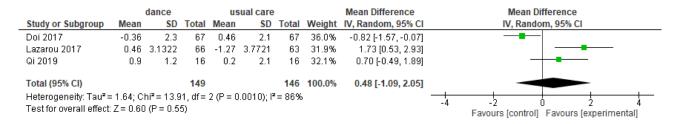
PHYSICAL EXERCISE

Dance

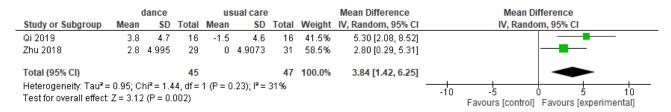
MoCA



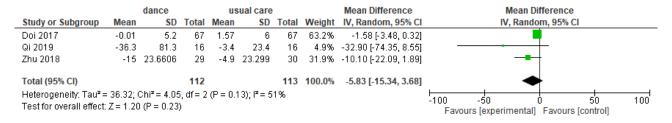
MMSE



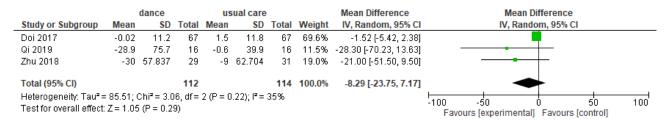
WMS-R LM



TMT-A



TMT-B

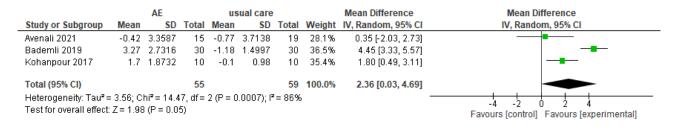


GDS

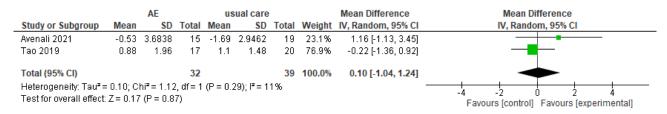
		dance		us	sual care			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Chang 2021	-0.66	1.772	62	0.17	2.2819	47	42.8%	-0.83 [-1.62, -0.04]	-
Dominguez 2018	-0.4	2	90	0.5	2.6	81	54.1%	-0.90 [-1.60, -0.20]	
Zhu 2018	-2.1	5.5208	29	-3.2	5.9978	31	3.1%	1.10 [-1.81, 4.01]	
Total (95% CI)			181			159	100.0%	-0.81 [-1.32, -0.29]	•
Heterogeneity: Tau² = Test for overall effect				(P = 0.	42); I² = 0	%		-	-4 -2 0 2 4 Favours [experimental] Favours [control]

Aerobic exercise

MMSE

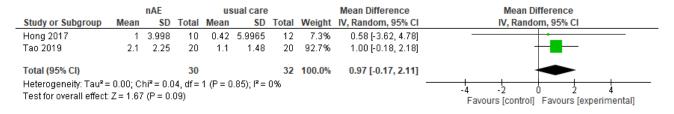


MoCA

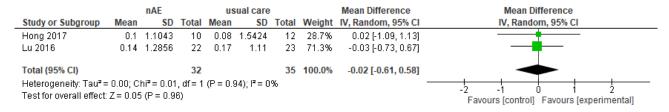


Non-aerobic exercise

MoCA



Digit Span Forward

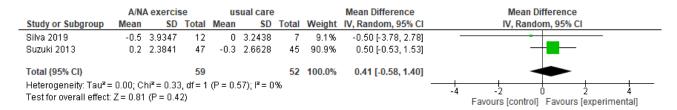


Digit Span Backward

		nAE		us	ual care			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hong 2017	0	1.8592	10	-1.42	1.1804	12	36.8%	1.42 [0.09, 2.75]	-
Lu 2016	0.41	0.7894	22	0.22	0.9019	23	63.2%	0.19 [-0.30, 0.68]	-
Total (95% CI)			32			35	100.0%	0.64 [-0.52, 1.81]	
Heterogeneity: Tau² : Test for overall effect				(P = 0.0	09); I² = 6	5%			-2 -1 0 1 2 Favours [control] Favours [experimental]

Aerobic/non-aerobic combined exercise

MMSE



GAMES AND VIDEOGAMES

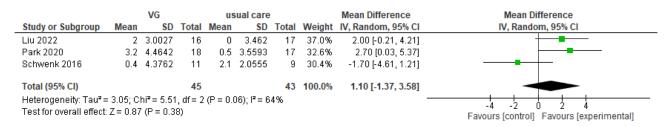
Games and board games

MoCA

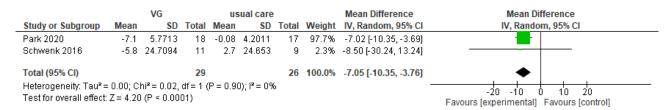
		games		us	ual car	е		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Xue 2021	0.41	1.92	36	0.28	3.04	36	51.8%	0.13 [-1.04, 1.30]	
Zhang 2020	1.69	2.7073	35	-0.18	2.952	34	48.2%	1.87 [0.53, 3.21]	-
Total (95% CI)			71			70	100.0%	0.97 [-0.73, 2.67]	-
Heterogeneity: Tau² : Test for overall effect				(P = 0.0	06); I²=	73%			-4 -2 0 2 4 Favours [control] Favours [experimental]

Videogames

MoCA



TMT-A

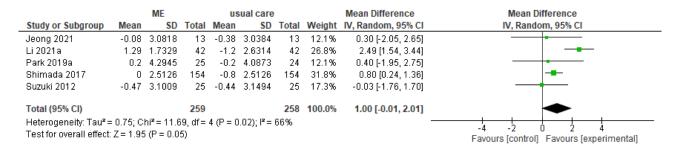


TMT-B

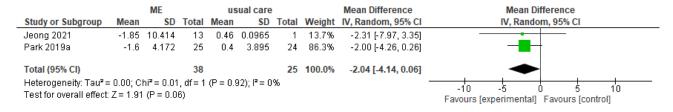
		VG		u	sual care			Mean Difference		M	ean Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV,	Random, 959	6 CI	
Park 2020	-7.9	11.0801	18	-1.7	14.451	17	98.8%	-6.20 [-14.77, 2.37]			-		
Schwenk 2016	6.4	118.9028	11	0.9	49.6313	9	1.2%	5.50 [-71.89, 82.89]					_
Total (95% CI)			29			26	100.0%	-6.06 [-14.57, 2.46]			•		
Heterogeneity: Tau² = Test for overall effect:			,	9 = 0.77)	; I² = 0%				-100 Fav	-50 ours [experim	0 ental] Favou	50 irs [control]	100

MULTIMODAL INTERVENTIONS

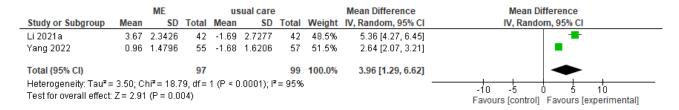
MMSE



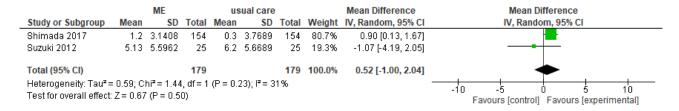
ADAS-Cog



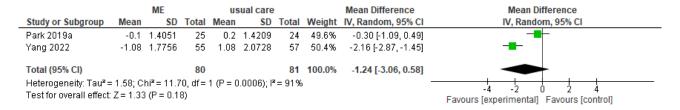
MoCA



WMS-R LM



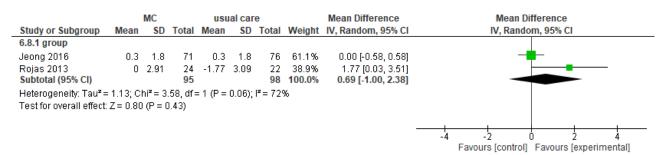
GDS



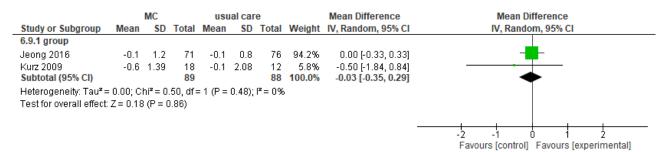
COGNITIVE INTERVENTIONS

Multimodal cognitive intervention (group) in residential care setting

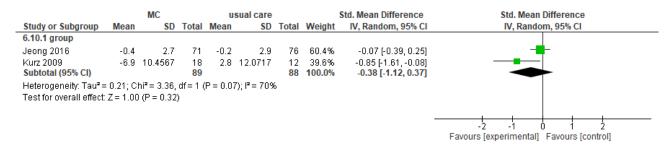
MMSE



BADL

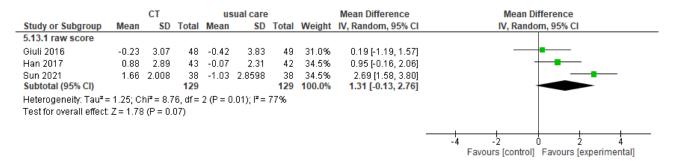


GDS

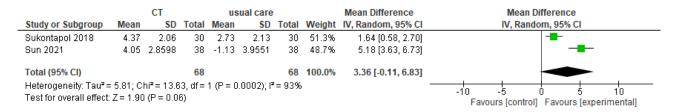


Cognitive training

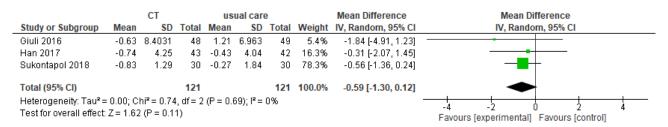
MMSE



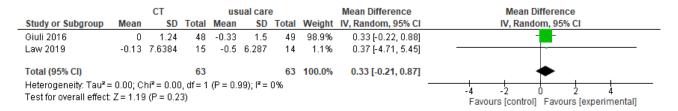
MoCA



GDS



IADL



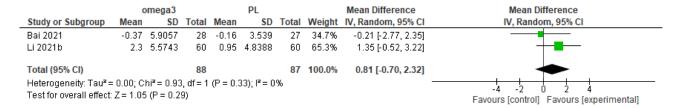
NUTRITIONAL INTERVENTIONS

Polyunsaturated fatty acids

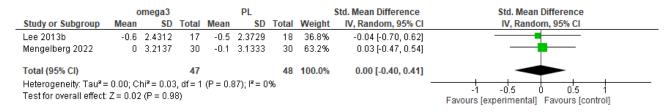
Digit Span

	C	mega3			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bai 2021	0.47	1.96	28	-1.11	2.1487	27	25.2%	1.58 [0.49, 2.67]	
Lee 2013b	1.6	2.7651	17	-0.5	2.7431	18	11.5%	2.10 [0.27, 3.93]	
Li 2021b	0.53	1.7807	60	-0.15	2.2452	60	39.6%	0.68 [-0.05, 1.41]	
Mengelberg 2022	1.2	2.3	30	0.9	2.2	30	23.7%	0.30 [-0.84, 1.44]	- •
Total (95% CI)			135			135	100.0%	0.98 [0.30, 1.66]	•
Heterogeneity: Tau² =	= 0.16; C	hi² = 4.58	l, df = 3	(P = 0.3)	21); I² = 3	4%		-	
Test for overall effect	Z = 2.84	P = 0.0	04)						-4 -2 U 2 4 Favours [control] Favours [experimental]

WAIS

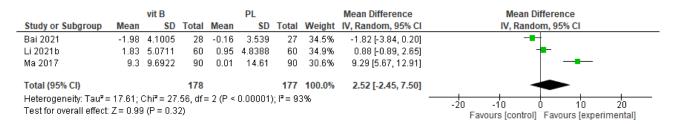


Depressive symptoms

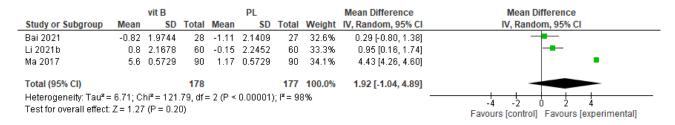


Vitamin B

WAIS

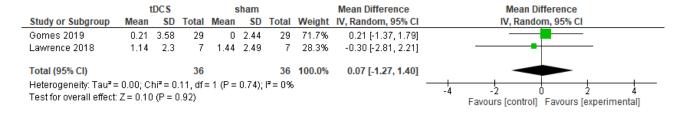


Digit Span



TRANSCRANIAL DIRECT-CURRENT STIMULATION

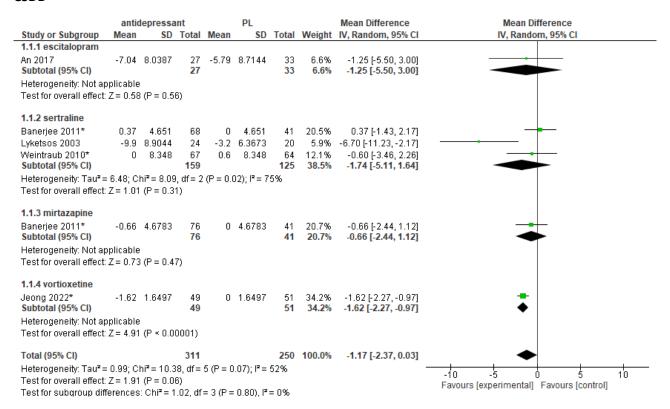
MMSE



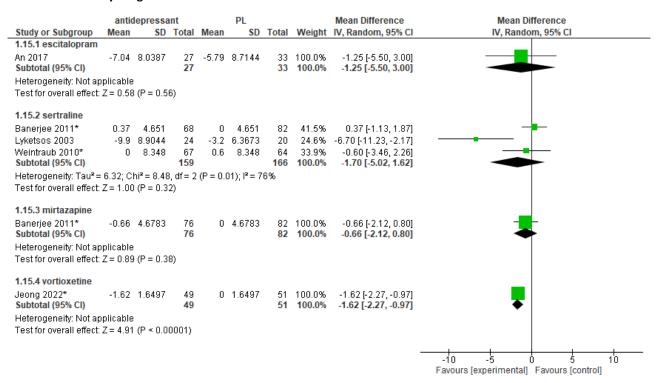
REVIEW QUESTION 21a. Quali sono gli interventi farmacologici più efficaci per gestire i sintomi non cognitivi della malattia, come disturbi dello spettro della schizofrenia e altri disturbi psicotici, disturbi depressivi, cambiamenti comportamentali in persone con demenza?

ANTIDEPRESSANTS

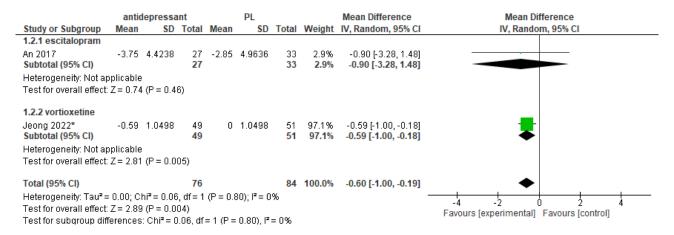
CSDD



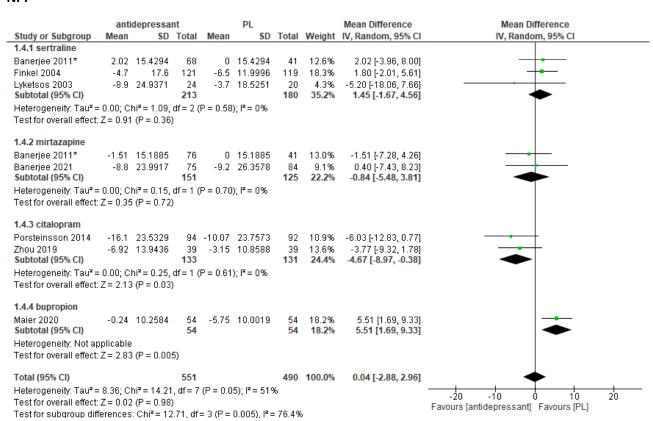
CSDD - stratified by drug



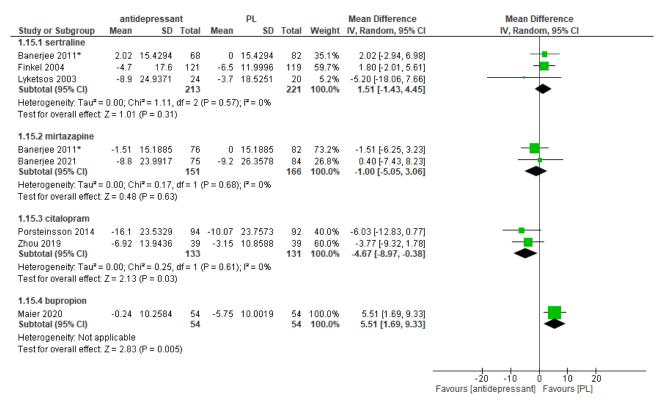
GDS



NPI



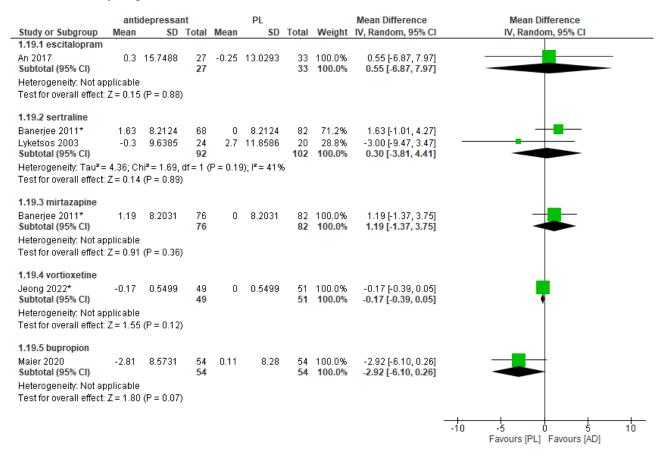
NPI - stratified by drug



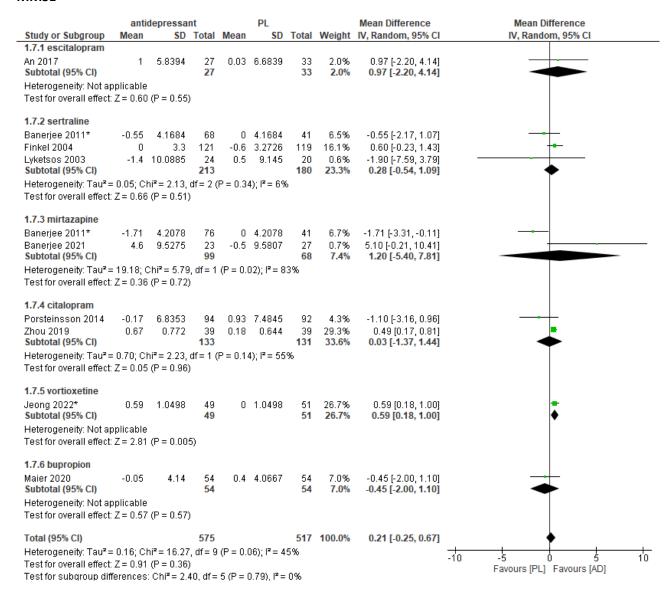
ADL

	anti	depressa	nt		PL			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean			Mean		Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.5.1 escitalopram								,	i li
An 2017 Subtotal (95% CI)		15.7488	27 27	-0.25	13.0293	33 33	12.9% 12.9 %	0.04 [-0.47, 0.55] 0.04 [-0.47, 0.55]	
Heterogeneity: Not a Test for overall effect)						
1.5.2 sertraline									
Banerjee 2011*	1.63	8.2124	68	0	8.2124	41	19.1%	0.20 [-0.19, 0.59]	
Lyketsos 2003 Subtotal (95% CI)	-0.3	9.6385	24 92	2.7	11.8586	20 61	10.0% 29.1 %	-0.28 [-0.87, 0.32] 0.02 [-0.43, 0.47]	
Heterogeneity: Tau²: Test for overall effect				(P = 0.19	9); I² = 41%	1			
1.5.3 mirtazapine									
Banerjee 2011* Subtotal (95% CI)	1.19	8.2031	76 76	0	8.2031	41 41	19.6% 19.6%	0.14 [-0.24, 0.52] 0.14 [-0.24, 0.52]	
Heterogeneity: Not a Test for overall effect)						
1.5.4 vortioxetine									
Jeong 2022* Subtotal (95% CI)	-0.17	0.5499	49 49	0	0.5499	51 51	18.7% 18.7%	-0.31 [-0.70, 0.09] - 0.31 [-0.70, 0.09]	
Heterogeneity: Not a Test for overall effect)						
1.5.5 bupropion									
Maier 2020 Subtotal (95% CI)	-2.81	8.5731	54 54	0.11	8.28	54 54	19.7% 19.7%	-0.34 [-0.72, 0.04] - 0.34 [-0.72, 0.04]	
Heterogeneity: Not a Test for overall effect								3.2. [22, 2.0 1]	
Total (95% CI)			298			240	100.0%	-0.08 [-0.29, 0.13]	•
Heterogeneity: Tau ² :				P = 0.22	2); I²= 29%	•		-	-1 -0.5 0 0.5 1
Test for overall effect Test for subgroup dit			,	4 (P = 0	0.31), I² = 1	6.0%			Favours [PL] Favours [AD]

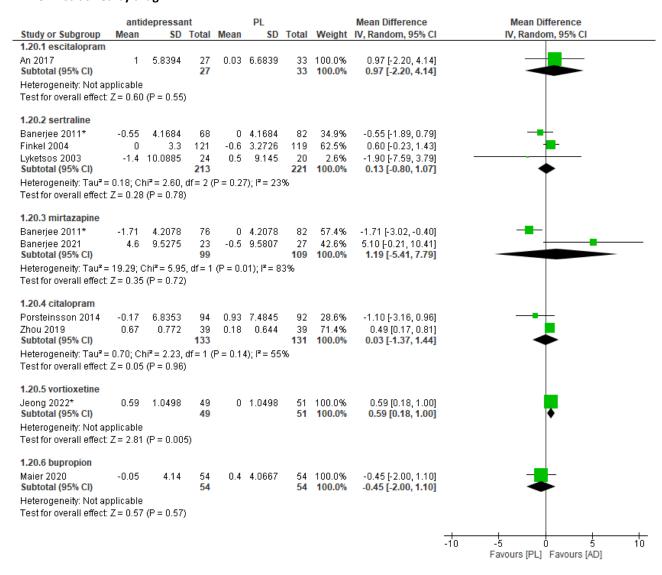
ADL - stratified by drug



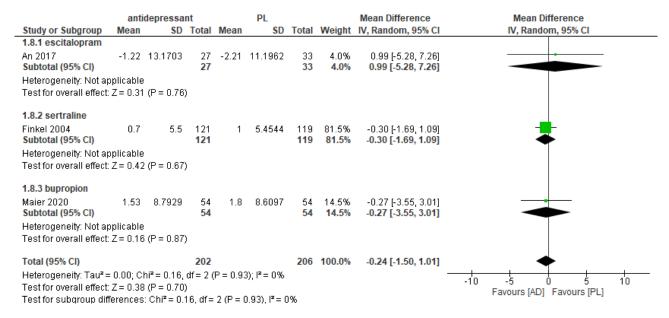
MMSE



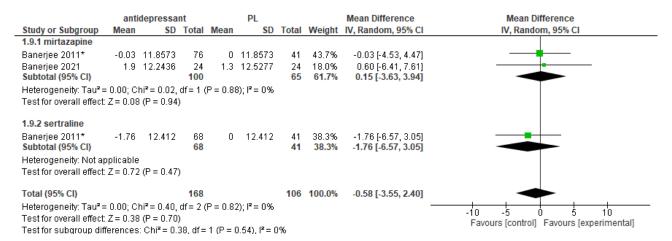
MMSE - stratified by drug



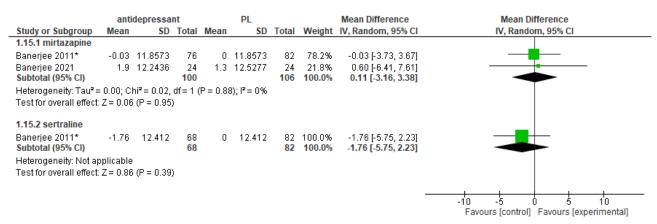
ADAS-Cog



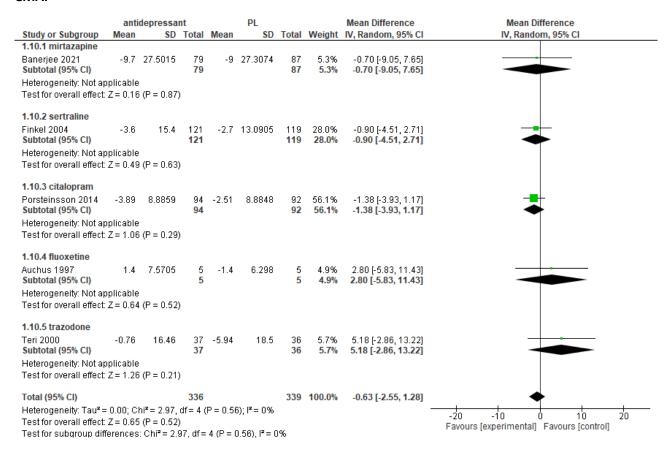
DEM-QoL



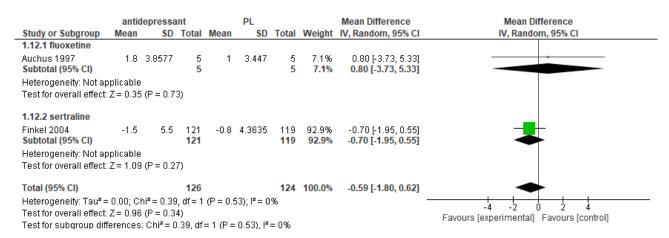
DEM-QoL - stratified by drug



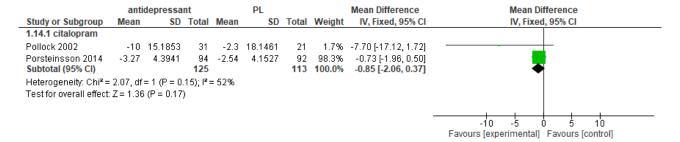
CMAI



BEHAVE-AD



NBRS

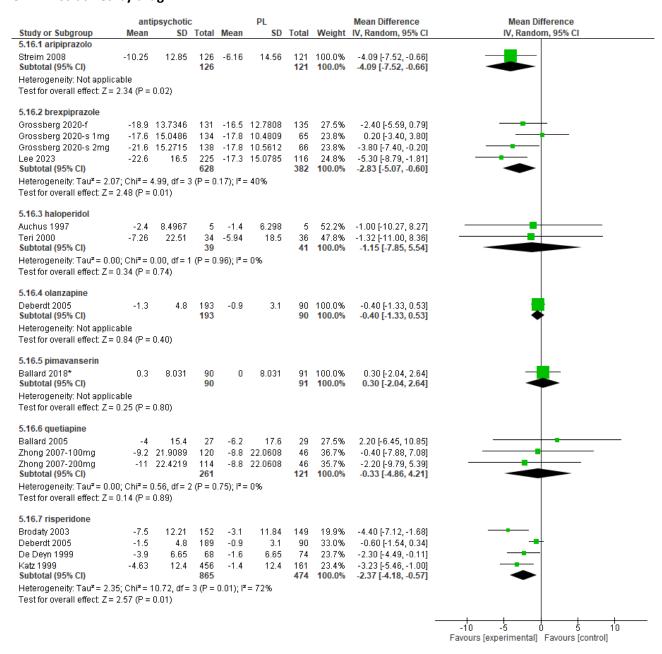


ANTIPSYCHOTICS

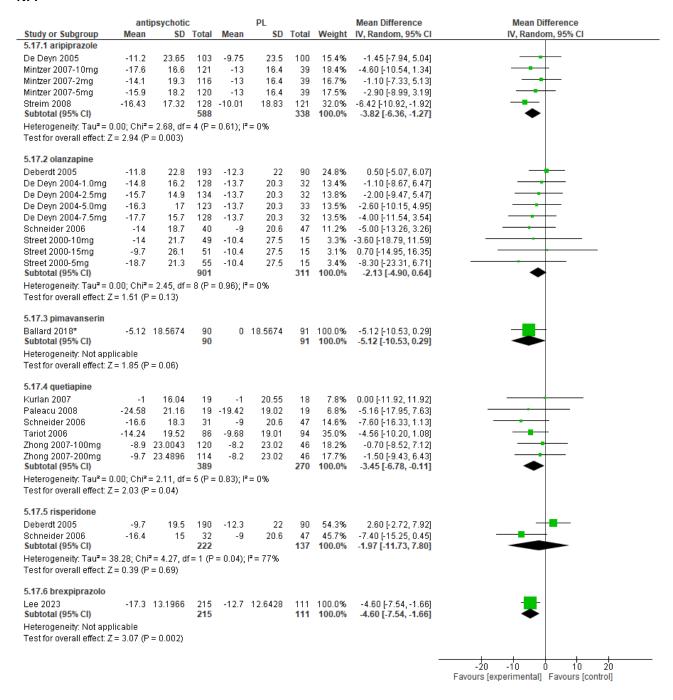
CMAI

	ant	ipsychotic			PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
5.1.1 aripiprazolo									
Streim 2008 Subtotal (95% CI)	-10.25	12.85	126 126	-6.16	14.56	121 121	5.6% 5.6%	-4.09 [-7.52, -0.66] - 4.09 [-7.52, -0.66]	
Heterogeneity: Not applic Fest for overall effect: Z=		0.02)							
5.1.2 brexpiprazole									
Grossberg 2020-f		13.7346	131		12.7808	135	6.2%	-2.40 [-5.59, 0.79]	
Grossberg 2020-s 1mg		15.0486	134		10.4809	65	5.2%	0.20 [-3.40, 3.80]	
Grossberg 2020-s 2mg		15.2715	138		10.5612	66	5.2%	-3.80 [-7.40, -0.20]	
.ee 2023 Subtotal (95% CI)	-22.6	16.5	225 628	-17.3	15.0785	116 382	5.4% 21.9%	-5.30 [-8.79, -1.81] - 2.83 [-5.07, -0.60]	<u> </u>
Heterogeneity: Tau² = 2.0 Test for overall effect: Z =			3 (P = 0	.17); l² =	= 40%				
5.1.3 haloperidol									
Auchus 1997	-2.4	8.4967	5	-1.4	6.298	5	1.0%	-1.00 [-10.27, 8.27]	
Teri 2000 Subtotal (95% CI)	-7.26	22.51	34 39	-5.94	18.5	36 41	0.9% 1.9%	-1.32 [-11.00, 8.36] - 1.15 [-7.85, 5.54]	
Heterogeneity: Tau² = 0.0 Test for overall effect: Z =				.96); [*=	= 0%	71	21070		
5.1.4 olanzapine	v								
Deberdt 2005	-1.3	4.8	193	-0.9	3.1	45	15.4%	-0.40 [-1.53, 0.73]	
Subtotal (95% CI)	-1.3	4.0	193	-0.8	3.1	45 45	15.4%	-0.40 [-1.53, 0.73]	•
Heterogeneity: Not applic Test for overall effect: Z =		0.49)							
5.1.5 pimavanserin									
Ballard 2018* Subtotal (95% CI)	0.3	8.031	90 90	0	8.031	91 91	9.0% 9.0%	0.30 [-2.04, 2.64] 0.30 [-2.04, 2.64]	
Heterogeneity: Not applic Test for overall effect: Z=		0.80)							
5.1.6 quetiapine									
Ballard 2005	-4	15.4	27	-6.2	17.6	29	1.2%	2.20 [-6.45, 10.85]	
Zhong 2007-100mg		21.9089	120		22.0608	46	1.5%	-0.40 [-7.88, 7.08]	+
Zhong 2007-200mg Subtotal (95% CI)	-11	22.4219	114 261	-8.8	22.0608	46 121	1.5% 4.1%	-2.20 [-9.79, 5.39] - 0.33 [-4.86, 4.21]	
Heterogeneity: Tau² = 0.0				.75); ² =	= 0%	121	~4.1 70	-0.55 [-4.00, 4.21]	
Test for overall effect: Z =	u.14 (P =	u.89)							
5.1.7 risperidone									
Brodaty 2003	-7.5	12.21	152	-3.1	11.84	149	7.6%	-4.40 [-7.12, -1.68]	
Deberdt 2005	-1.5	4.8	189	-0.9	3.1	45	15.3%	-0.60 [-1.74, 0.54]	 †
De Deyn 1999	-3.9	6.65	68	-1.6	6.65	74	9.7%	-2.30 [-4.49, -0.11]	
	-4.63	12.4	456 865	-1.4	12.4	161 429	9.5% 42.1%	-3.23 [-5.46, -1.00] - 2.38 [-4.15 , - 0.62]	
		9.49 df= 3		.02); l² =	= 68%	723	72.1/0	-2.00 [-7.10, -0.02]	
Katz 1999 Subtotal (95% CI) Heterogeneity: Tau ² = 2.1									I I
Subtotal (95% CI)									
Subtotal (95% CI) Heterogeneity: Tau² = 2.1 Test for overall effect: Z = Total (95% CI)	2.65 (P =	0.008)	2202	0.5.11		1230	100.0%	-1.87 [-2.83, -0.92]	•
Subtotal (95% CI) Heterogeneity: Tau² = 2.1 Test for overall effect: Z =	2.65 (P = 2; Chi² = :	0.008) 25.63, df=		= 0.04);	I²= 41%	1230	100.0%	-1.87 [-2.83, -0.92]	-10 -5 0 5 10

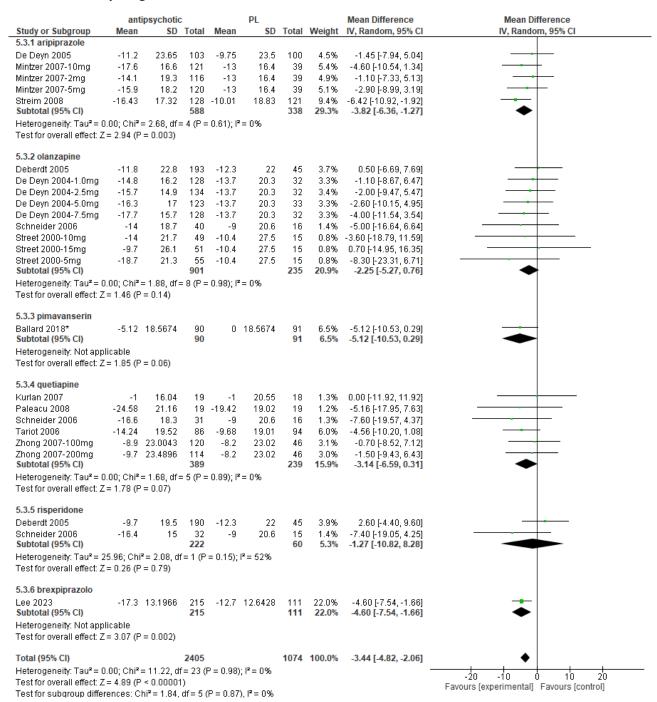
CMAI - stratified by drug



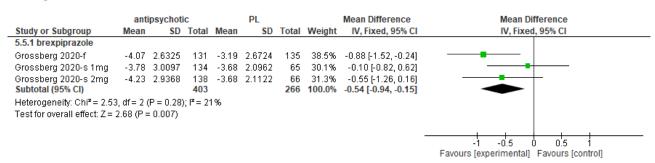
NPI



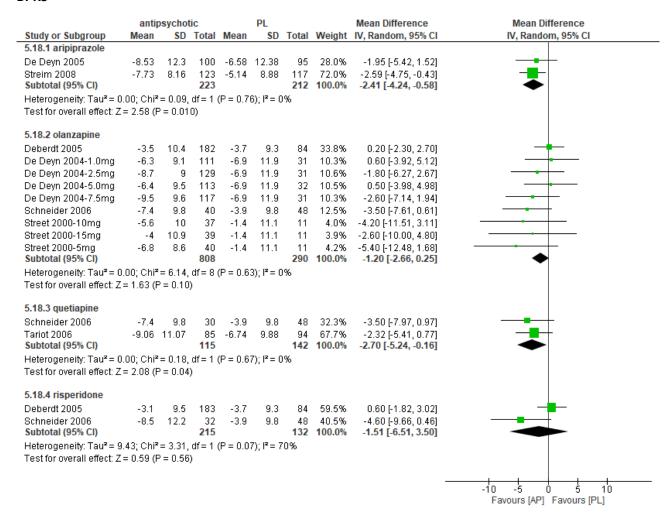
NPI - stratified by drug



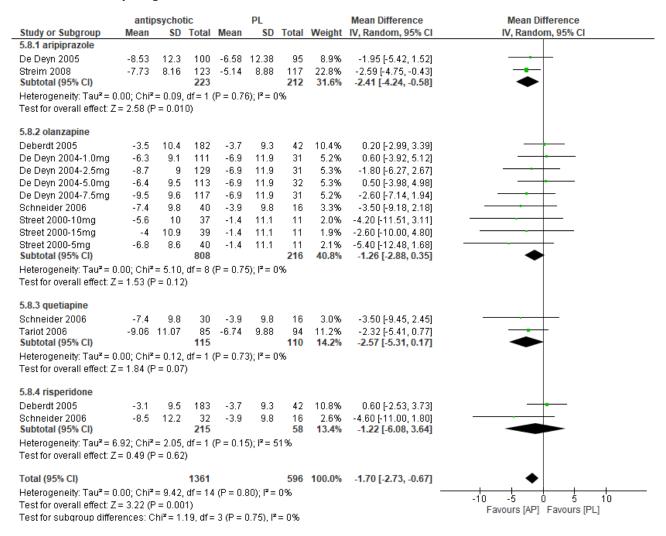
NPI-Ag



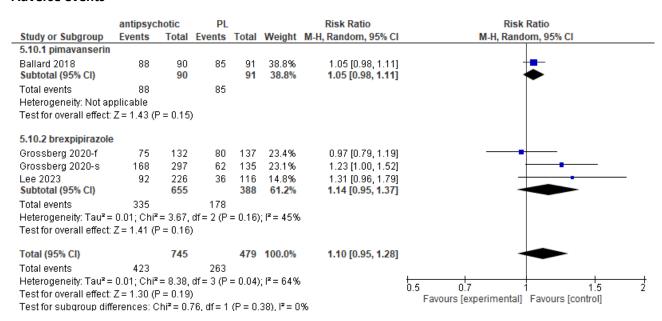
BPRS



BPRS - stratified by drug



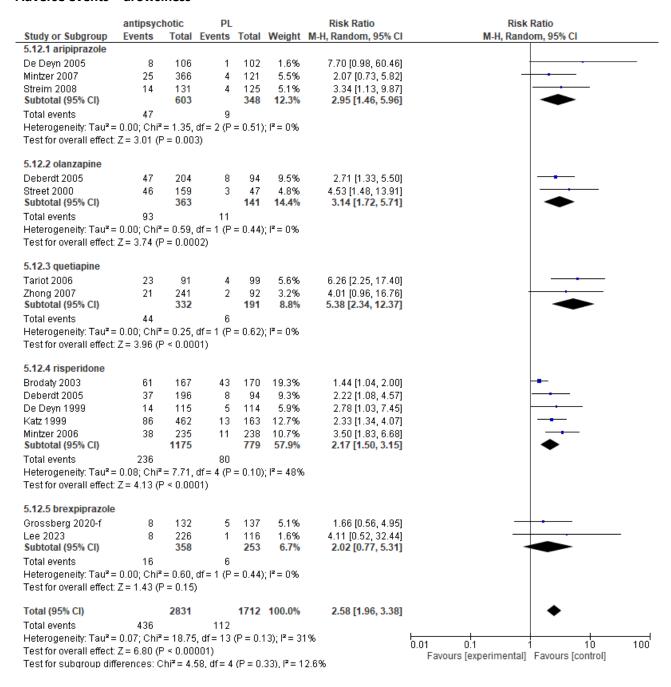
Adverse events



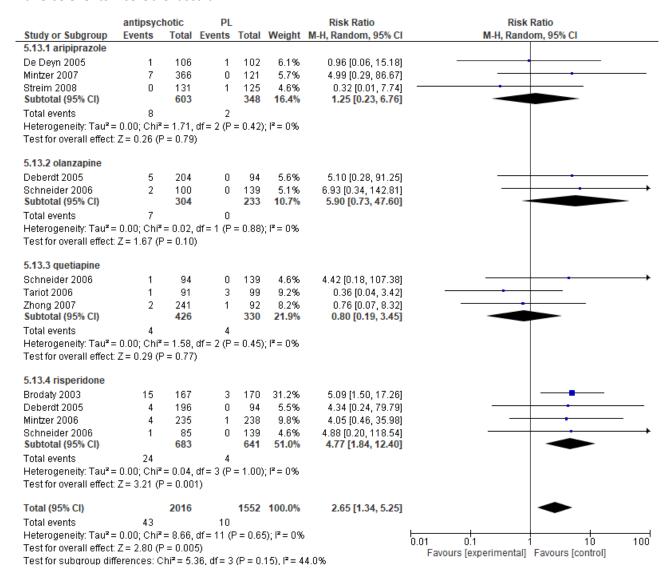
Adverse events - extrapyramidal

	antipsyc	hotic	PL			Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
5.11.1 aripiprazole							
Streim 2008	7	131	5	125	3.6%	1.34 [0.44, 4.10]	
Mintzer 2007	27	366	7	121	6.3%	1.28 [0.57, 2.85]	
De Deyn 2005	5	106	4	102	2.8%	1.20 [0.33, 4.35]	- -
Subtotal (95% CI)		603		348	12.8%	1.28 [0.71, 2.29]	◆
Total events	39		16				
Heterogeneity: Tau ² =	= 0.00; Chi ²	= 0.01,	df = 2 (P :	= 0.99)	$ I^2 = 0\% $		
Test for overall effect	Z = 0.82 (F	9 = 0.41					
5.11.2 brexpiprazole							
Lee 2023	2	226	0	116	0.6%	2.58 [0.12, 53.24]	
Grossberg 2020-s	2	297	0	135	0.6%	2.28 [0.11, 47.21]	
Grossberg 2020-f	1	132	0	137	0.5%	3.11 [0.13, 75.74]	
Subtotal (95% CI)		655		388	1.6%	2.62 [0.44, 15.52]	
Total events	5		0				
Heterogeneity: Tau² =				= 0.99)	; I² = 0%		
Test for overall effect	Z = 1.06 (F	P = 0.29					
5.11.3 olanzapine							
-	40	400		400	0.000	04.05 (0.00.570.50)	
Schneider 2006	12	100	0	139	0.6%	34.65 [2.08, 578.53]	
Deberdt 2005 Subtotal (95% CI)	73	204 304	28	94 233	16.6% 17.2%	1.20 [0.84, 1.72]	
	05	304	20	233	17.270	5.06 [0.13, 191.77]	
Total events	85 - 5 00: Obiz	- 6 70	28 df = 1.70	_ 0.040	N: 12 = 0.50	v	
Heterogeneity: Tau² =				= 0.010	J); IT= 85%	70	
Test for overall effect	. Z = 0.87 (F	-= 0.38)					
5.11.4 quetiapine							
Zhong 2007	14	241	5	92	4.5%	1.07 [0.40, 2.88]	
Tariot 2006	9	91	12	99	6.2%	0.82 [0.36, 1.85]	
Schneider 2006	2	94	0	139	0.6%	7.37 [0.36, 151.77]	
Paleacu 2008	1	20	5	20	1.2%	0.20 [0.03, 1.56]	
Subtotal (95% CI)		446		350	12.4%	0.87 [0.40, 1.87]	•
Total events	26		22				
Heterogeneity: Tau² =	= 0.16; Chi ²	= 4.07	df= 3 (P :	= 0.25)	; I² = 26%		
Test for overall effect	Z = 0.37 (F	P = 0.72					
5.11.5 risperidone							
Schneider 2006	10	85	0	139	0.6%	2/ 10 [2 02 676 041	
Mintzer 2006	20	235	8	238	6.3%	34.19 [2.03, 576.01]	
Minizer 2006 Katz 1999	20 64	462	12	163	9.8%	2.53 [1.14, 5.63]	-
De Deyn 1999	17	115	13	114	8.2%	1.88 [1.04, 3.39] 1.30 [0.66, 2.54]	<u> </u>
Deberdt 2005	97	196	28	94	17.3%	1.66 [1.18, 2.34]	-
Brodaty 2003	39	167	27	170	13.7%	1.47 [0.95, 2.29]	
Subtotal (95% CI)	33	1260	21	918	56.0%	1.71 [1.29, 2.26]	•
Total events	247	.200	88		00.070	[, £]	•
Heterogeneity: Tau ² =		= 6.76		= 0.241	: 2 ± 28%		
Test for overall effect				J.24)	,. 2070		
. SST.S. STORAN ONOOL	5.10 (1	5.00	,				
Total (95% CI)		3268		2237	100.0%	1.47 [1.17, 1.85]	♦
Total events	402		154				
Heterogeneity: Tau² =	= 0.05; Chi²	= 22.43	, df = 17	(P = 0.1)	$(7); l^2 = 24$	4%	0.002 0.1 1 10 500
Test for overall effect							Favours [experimental] Favours [control]
Test for subgroup dif	ferences: C	>hi²= 3.8	35, df = 4	(P = 0.	43), $I^2 = 0$	%	r arouro (experimentar) i arouro (control)

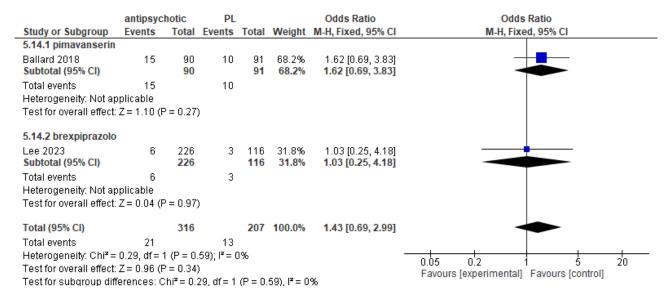
Adverse events - drowsiness



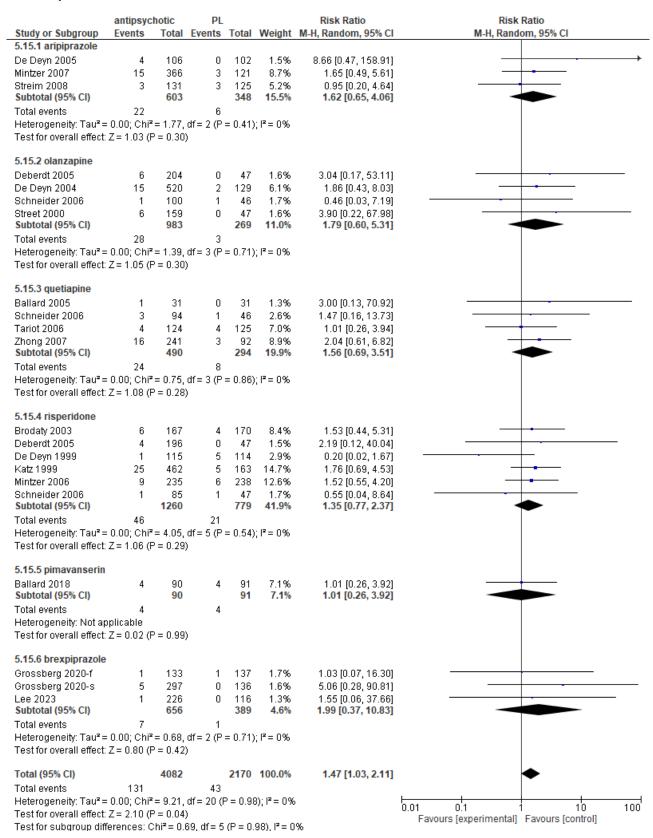
Adverse events - cerebrovascular



Serious adverse events

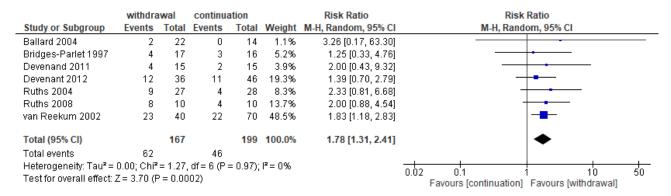


Mortality

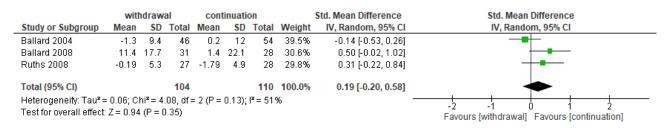


ANTIPSYCHOTIC SUSPENSION

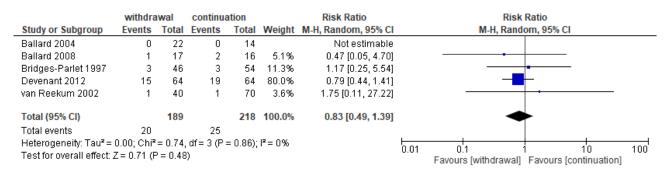
Behavioral symptoms worsening



Behavioral symptoms severity

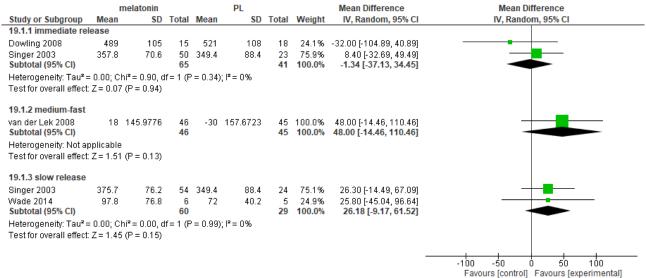


Mortality

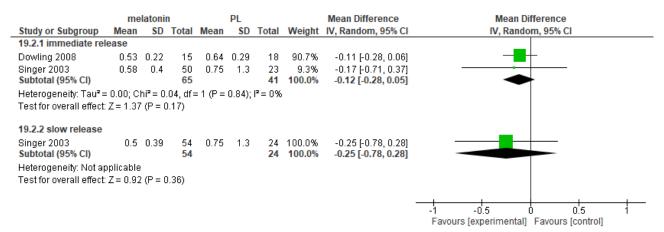


MELATONIN

Average of total night-time sleep time

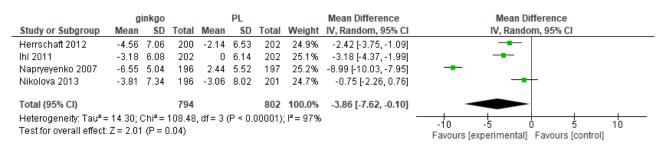


Ratio between daytime and night-time sleep time

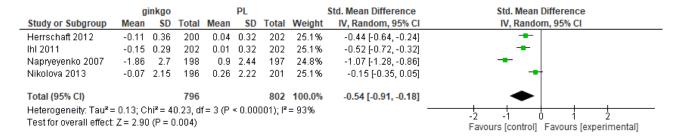


GINKGO BILOBA

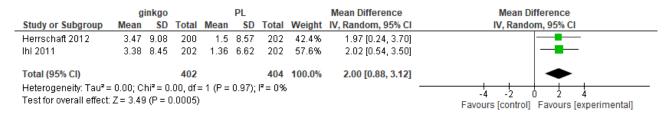
NPI



ADL

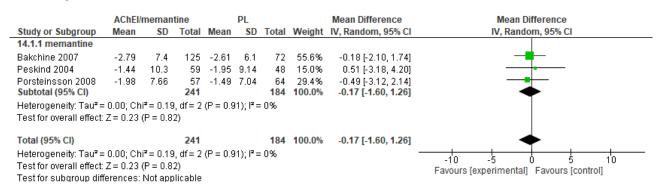


Quality of life

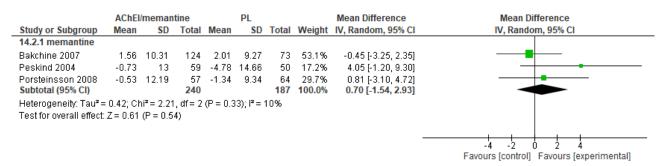


ACHEI/MEMANTINE

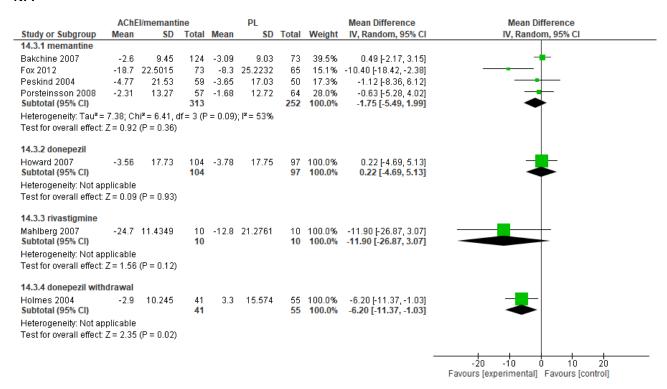
ADAS-Cog



ADL



NPI



METHYLPHENIDATE

AES

	meth	nylphenid	ate		PL			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Herrmann 2008	-2.31	5.11	13	0.5	3.87	12	33.9%	-2.81 [-6.35, 0.73]	-	
Padala 2018	-14.1	6.9629	30	-4.2	6.9629	29	33.9%	-9.90 [-13.45, -6.35]		
Rosenberg 2013	-1.9	8.0777	29	0.6	7.7949	31	32.2%	-2.50 [-6.52, 1.52]		
Total (95% CI)			72			72	100.0%	-5.11 [-9.93, -0.29]	•	
Heterogeneity: Tau² : Test for overall effect				2 (P =	0.006); l²	= 80%			-20 -10 0 10 20 Favours [experimental] Favours [control]	

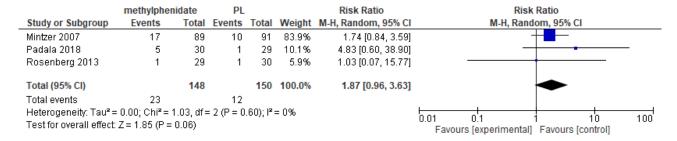
NPI

	meth	ylphenid	ate		PL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Herrmann 2008	0.38	4.19	13	-1.69	2.93	12	21.8%	2.07 [-0.75, 4.89]	
Mintzer 2021	-4.5	4.1	89	-3.1	3.6	91	42.9%	-1.40 [-2.53, -0.27]	
Rosenberg 2013	-4.4	3.2311	29	-2.6	3.3407	31	35.3%	-1.80 [-3.46, -0.14]	
Total (95% CI)			131			134	100.0%	-0.78 [-2.50, 0.94]	-
Heterogeneity: Tau² = Test for overall effect			•	(P = 0.0	16); I² = 69	5%			-4 -2 0 2 4 Favours [experimental] Favours [control]

MMSE

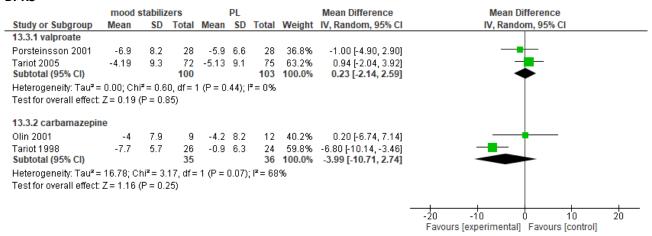
	methylphenidate PL							Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Herrmann 2008	-0.58	2.53	13	-1.08	2.81	12	42.4%	0.50 [-1.60, 2.60]	-		
Padala 2018	2.2	2.678	30	-0.4	2.629	29	57.6%	2.60 [1.25, 3.95]			
Total (95% CI)			43			41	100.0%	1.71 [-0.32, 3.74]	•		
Heterogeneity: Tau² = Test for overall effect:				1 (P = 0.	.10); l²=	63%			-10 -5 0 5 10 Favours [control] Favours [experimental]		

Serious adverse events

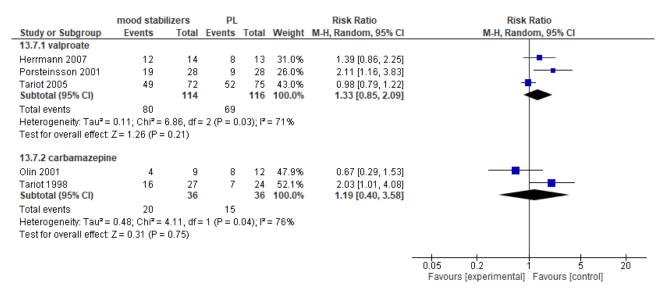


MOOD STABILIZERS

BPRS



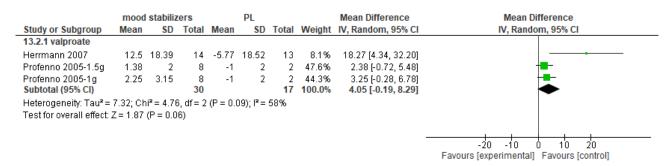
Adverse events



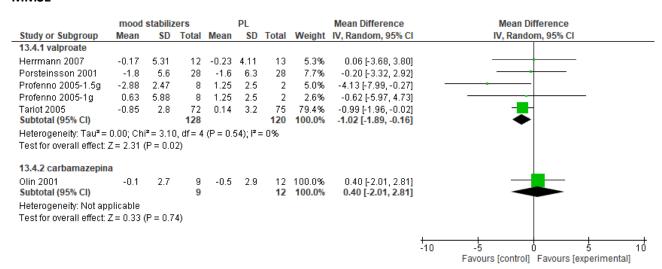
CMAI

	mood	PL			Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
13.1.1 valproate									
Herrmann 2007	10.38	16.74	14	-5	17.44	13	25.2%	15.38 [2.47, 28.29]	
Porsteinsson 2001	-9.5	22.2	28	-7.3	12.3	28	32.4%	-2.20 [-11.60, 7.20]	
Tariot 2005 Subtotal (95% CI)	-6.7	15.6	72 114	-3.5	14.5	75 116	42.3% 100.0%		
Heterogeneity: Tau ² = Test for overall effect				2 (P =	0.03); l²	= 72%			
			,						
								-	-20 -10 0 10 20
									Favours [experimental] Favours [control]

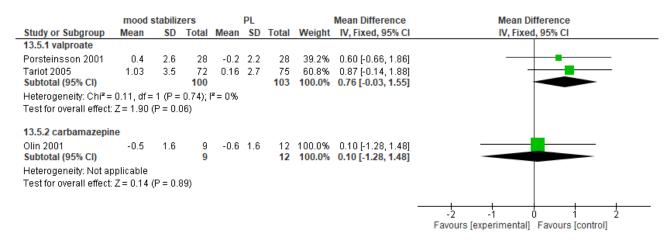
NPI



MMSE



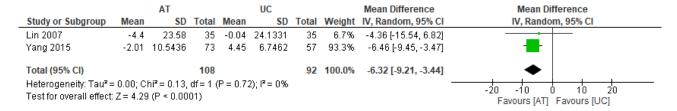
PSMS



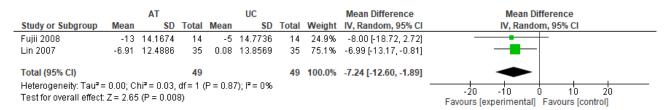
REVIEW QUESTION 21b. What are the most effective non-pharmacological interventions for managing illness emergent non-cognitive symptoms, such as psychosis, depression, behavioral changes in people living with dementia?

AROMATHERAPY (lavender)

CMAI

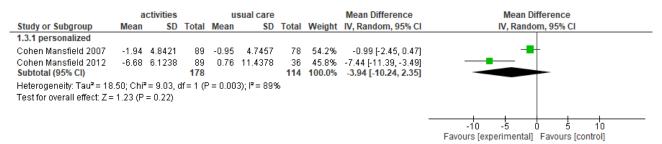


NPI



RECREATIONAL ACTIVITIES

ABMI

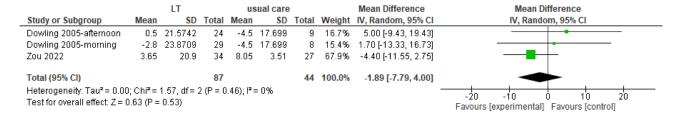


LIGHT THERAPY

CMAI



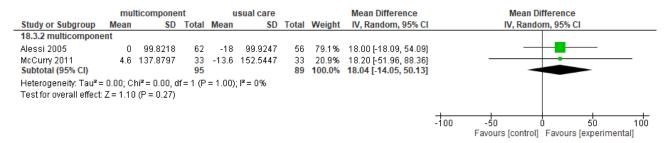
NPI



SLEEP INTERVENTIONS

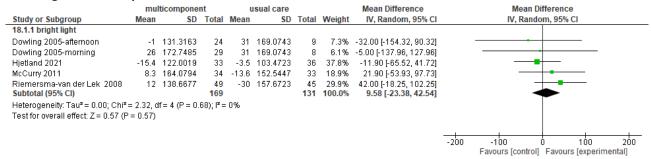
Multicomponent interventions including improving sleep hygiene, exposure to light, and physical activity

Total night-time sleep time

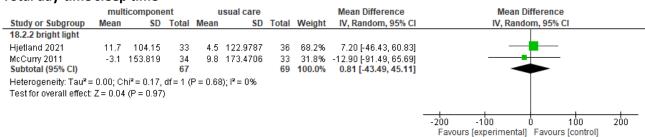


Interventions based on exposure to bright light and controlled light

Total night-time sleep time



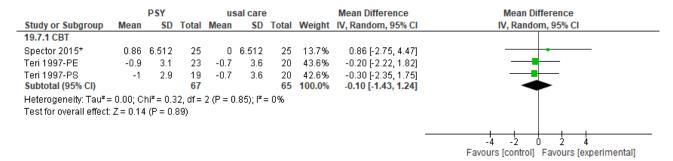
Total day-time sleep time



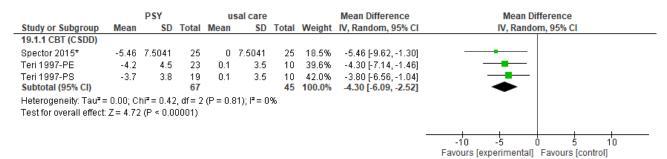
PSYCHOLOGICAL INTERVENTIONS

Cognitive Behavioral Therapy for the treatment of psychological and behavioral disorders

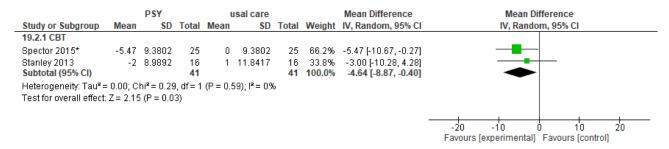
MMSE



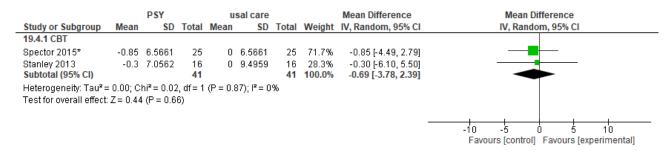
CSDD



RAID

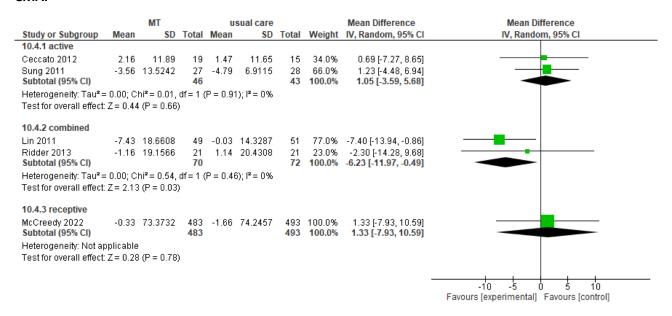


QoL-AD

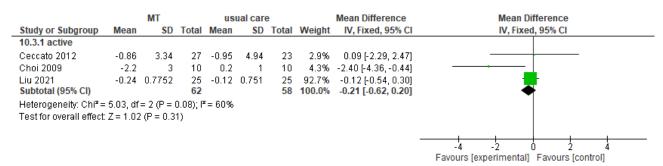


MUSIC THERAPY

CMAI



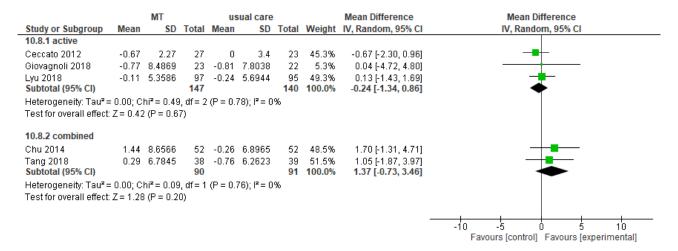
GDS



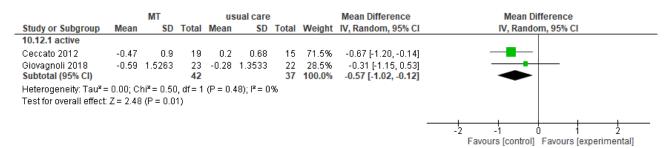
NPI

		MT		u	sual care			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
10.6.1 active									
Baker 2022-choir	-4.4	9.4664	82	-1	8.403	40	18.9%	-3.40 [-6.71, -0.09]	
Baker 2022-group	-4.7	9.2963	77	-1	8.403	40	18.7%	-3.70 [-7.03, -0.37]	
Choi 2009	-3.2	3.1	10	0.5	0.8	10	52.6%	-3.70 [-5.68, -1.72]	
Giovagnoli 2018	-0.36	22.5469	23	6.28	18.2915	22	1.4%	-6.64 [-18.61, 5.33]	
Lyu 2018 Subtotal (95% CI)	-6.82	17.8124	97 289	-0.4	17.2303	95 207	8.4% 100.0%	-6.42 [-11.38, -1.46] -3.92 [-5.35, -2.48]	<u>→</u>
Heterogeneity: Tau² = Test for overall effect:			•	P = 0.86); I*= 0%				
10.6.2 combined									
Baker 2022 Subtotal (95% CI)	-4.1	8.5719	79 79	-1	8.403	80 80	100.0% 100.0 %	-3.10 [-5.74, -0.46] - 3.10 [-5.74, -0.46]	-
Heterogeneity: Not ap Test for overall effect:		(P = 0.02)							
10.6.3 receptive									
D'Aniello 2021 Subtotal (95% CI)	-13.76	9.9356	30 30	-3.76	14.9435	30 30		-10.00 [-16.42, -3.58] - 10.00 [-16.42, -3.58]	
Heterogeneity: Not ap Test for overall effect:		/P = 0.003)\						
restion overall ellect.	∠ = 3.00	(F = 0.002	-)						
									-20 -10 0 10 2
									Favours [experimental] Favours [control]

MMSE

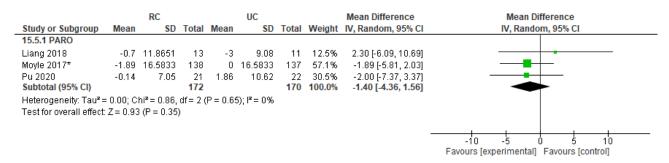


ADL

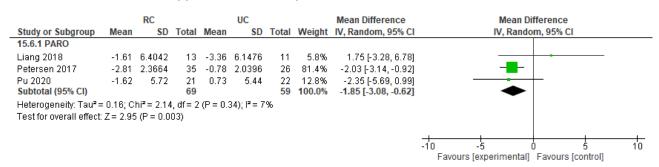


ROBOT THERAPY

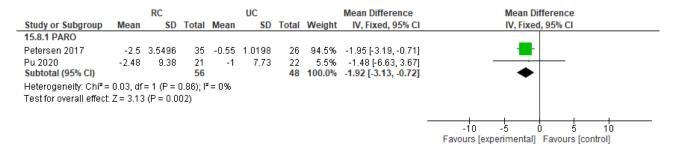
interactive robot with the appearance of a baby seal - CMAI-SF



interactive robot with the appearance of a baby seal - CSDD

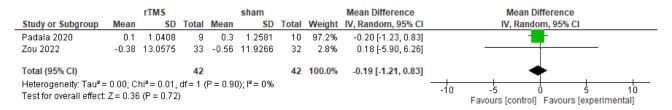


interactive robot with the appearance of a baby seal - RAID



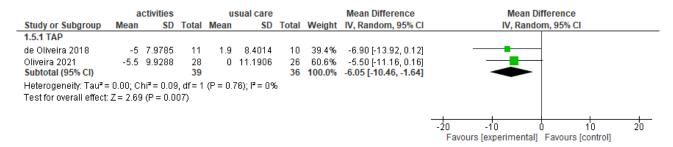
TRANSCRANIAL STIMULATION

ADL

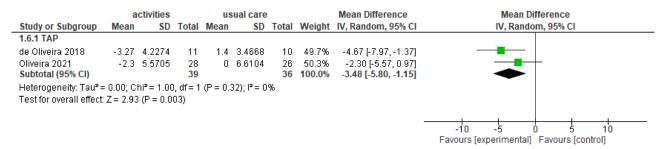


TAILORED ACTIVITY PROGRAM

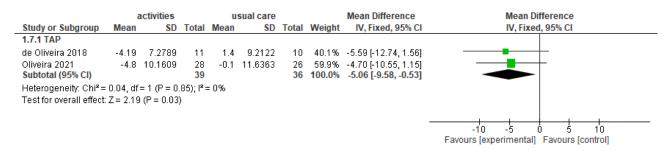
NPI-Ag



NPI-aggressività

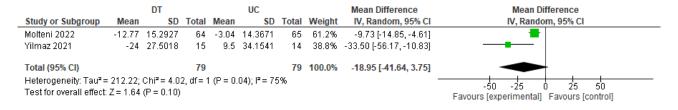


NPI-ansia



DOLL THERAPY

NPI

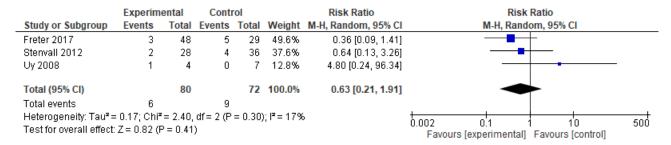


REVIEW QUESTION 22b. Are there effective methods for treating intercurrent illness in people living with dementia that are different from those already in use for people who do not have dementia?

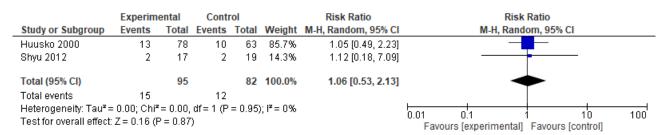
HIP FRACTURE REHABILITATION

Intervention to enhance inpatient and home care compared with standard care

In-hospital mortality

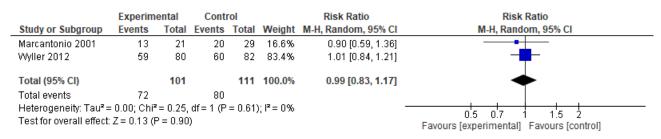


Mortality at 12 months



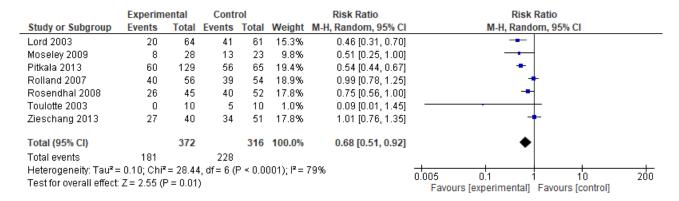
Implementation of inpatient care management coordinated by a geriatrician vs coordinated by an orthopedist

Incidence of delirium during hospitalization



PHYSICAL EXERCISE FOR FALL PREVENTION

Fall risk

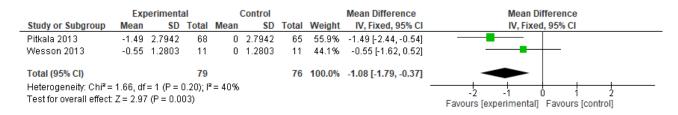


Hip fracture risk



PHYSICAL EXERCISE-BASED REHABILITATION AT HOME VS STANDARD CARE

Number of falls



REVIEW QUESTION 24. What models of palliative care are effective for people with dementia? MULTIDIMENSIONAL AND MULTIDISCIPLINARY END-OF-LIFE EDUCATION INTERVENTIONS FPCS

