Supplementary Material

Real-World Use of Symptomatic Treatments in Early Alzheimer's Disease

Supplementary Table 1. Summary of guidelines for the treatment of Alzheimer's disease

Society/Organization	Year	Recommended therapy for MCI due to AD	Recommended therapy for AD dementia	Monitoring	Treatment discontinuation
American Academy of Family Physicians and American College of Physicians [1]	2008	No recommendations	AChE inhibitors for mild to moderate disease Memantine for moderate to severe disease	No recommendations	Discontinue if slowing decline is no longer a goal
American Psychiatric Association [2]	2007	No recommendations	AChE inhibitors for mild to moderate disease Memantine plus donepezil for moderate to severe disease	Every 3 to 6 months if patient is clinically stable or taking stable doses of medication	Discontinue according to patient's preferences or if rapid decline
California Workgroup on Guidelines for Alzheimer's Disease Management [3, 4]	2008	No recommendations	AChE inhibitors for mild to moderate disease Memantine plus an AChE inhibitor for moderate to severe disease	As initial treatment: after 2 to 4 weeks (for adverse effects) Upon diagnosis of probable or possible disease: every 3-6 months (for effect on cognition and function) Upon duration of AD symptoms for >6 months: every 6 months (for effect on disease progression)	Discontinue before surgery, or if poor tolerance, or if continued deterioration at pre-treatment rate after 6 months
Canadian Consensus Conference on the Diagnosis and Treatment of Dementia [5]	2020	Deprescribe AChE inhibitors and memantine	AChE inhibitors for mild to moderate disease Memantine plus an AChE inhibitor for moderate to severe disease	Assessment of cognition, functional autonomy, behavior, as well as caregiver burden every 6-12 months	Discontinue acc. to patient's preferences and/or family; if clinically meaningful worsening of dementia; if no clinically meaningful benefit was observed at any time during treatment; if severe or end-stage

Society/Organization	Year	Recommended therapy for MCI due to AD	Recommended therapy for AD dementia	Monitoring	Treatment discontinuation
					dementia; if intolerable side; if poor medication adherence
European Federation of Neurological Societies [6]	2010	No effective treatments available	AChE inhibitors for mild to moderate disease Memantine monotherapy for moderate to severe disease	Regular follow-up to monitor response to treatment and adverse effects as well as disease progression	No recommendations
British Association for Psychopharmacology [7]	2017	Neither AChE inhibitors nor meantime are effective for MCI	AChE inhibitors for mild to moderate AD dementia Memantine monotherapy for moderate to severe AD Combination therapy (AChE inhibitors and memantine) may be beneficial	No recommendations	No recommendations
French National Authority for Health [8]	2018	No recommendations	None of the available drugs have shown to slow progression toward dependence, yet all carry a risk of life-threatening adverse effects and severe drug interactions	N/A	N/A
German Society for Neurology [9]	2016	No effective pharmacotherapy available	AChE inhibitors for mild to moderate Alzheimer's dementia Memantine monotherapy for moderate to severe disease	No recommendations	No recommendations
Italian Association of Psychogeriatrics [10]	2005	AChE inhibitors on a case-by-case basis	AChE inhibitors for mild to severe disease Memantine monotherapy or in combination with donepezil for moderate to severe disease	Cognitive function, activities of daily living, and behavioral and psychological symptoms	No recommendations
National Institute for Health and Clinical Excellence [11]	2018	No recommendations	AChE inhibitors for mild to moderate AD dementia Memantine monotherapy for moderate AD patients intolerant of or	No recommendations	No recommendations

Society/Organization	Year	Recommended therapy for MCI due to AD	Recommended therapy for AD dementia	Monitoring	Treatment discontinuation
			contraindicated to AChE inhibitors **or** severe AD Memantine plus an AChE inhibitor for moderate to severe disease, for established AD patients who are already taking an AChE inhibitor		
Spanish Ministry of Health, Social Services and Equality [12]	2011	AChE inhibitors not recommended	AChE inhibitors for mild to moderate disease Memantine monotherapy or in combination with AChE inhibitors for moderate to severe disease	Periodic assessment of cognitive, functional, motor and behavioral aspects is recommended, as well as of the degree of strain on the caregiver when monitoring patients with dementia	No recommendations

AChE inhibitor, acetylcholinesterase inhibitor; AD, Alzheimer's disease; MCI, mild cognitive impairment
Adapted, updated, and complemented from Bradford et al. 2011

Supplementary Table 2. PRISMA checklist for abstract

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g., databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e., which group is favored).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g., study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

Supplementary Table 3. PRISMA checklist for manuscript

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Supplementary Table 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 8, Supplementary Table 7
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 8, Supplementary Tables 4 to 6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Tables 4 to 6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8 to 9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 8 to 9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8, Supplementary Table 6
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8, Supplementary Table 7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9

Section and Topic	Item #	Checklist item	Location where item is reported
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Page 9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	Page 9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 9
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 11, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary Table 8
Study characteristics	17	Cite each included study and present its characteristics.	Table 1 Supplementary Table 10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary Table 9
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary Table 10, Tables 2, 3 & 4
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	Tables 2, 3 & 4
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical	Tables 2, 3 & 4

Section and Topic	Item #	Checklist item	Location where item is reported
		heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Tables 2, 3 & 4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 14 & 15
	23b	Discuss any limitations of the evidence included in the review.	Pages 14 & 15
	23c	Discuss any limitations of the review processes used.	Pages 14 & 15
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 8
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 8
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 35
Competing interests	26	Declare any competing interests of review authors.	Page 35
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

Supplementary Table 4. Search strategy for Embase (Ovid) from 1974 to 2021 November 29 (search date: November 30, 2021)

#	Searches	Results
1	mild cognitive impairment/	31017
2	(MCI or aMCI or mild cognit$ impair$ or CIND or cognitive impair$ no dementia).ti,ab,hw.	55074
3	((early or mild$ or prodromal) adj6 (alzheimer$ or alzeimer$ or AD)).mp.	37948
4	Alzheimer disease/	218391
5	(early or mild$ or prodromal).ti,ab.	2820145
6	(dementia adj2 stage adj2 ('2' or '3' or II or III or two or three)).ti,ab.	50
7	4 and 5	52136
8	1 or 2 or 3 or 6 or 7	92919
9	donepezil plus memantine/ or memantine/	11485
10	('1 amino 3, 5 dimethyladamantane' or '1, 3 dimethyl 5 adamantanamine' or '1, 3 dimethyl 5 aminoadamantane' or '3, 5 dimethyl 1 adamantamine' or '3, 5 dimethyl 1 adamantanamine' or '3, 5 dimethylaminoadamantane' or '5 amino 1, 3 dimethyladamantane' or 'adamantane, 5 amino 1, 3 dimethyl' or akatinol or alzantin or axura or d 145 or d145 or ebix or ebixa or ebixza or marixino or maruxa or memantine or memantine hcl or memantine hydrochloride or memantine nitrate or memary or "mn 08" or mn08 or namenda or namenda xr or nemdatine or nsc 102290 or nsc102290 or sun y7017 or suny701).ti,ab,tn.	6427
11	donepezil/	13975
12	(aricept or asenta or doneliquid geriasan or donepezil or donepezil hydrochloride or e 2020 or e2020 or eranz or memac or memorit).ti,ab,tn.	7173
13	rivastigmine/	7875
14	(alzest or ena 713 or ena713 or exelon or nimvastid or prometax or rivastigmin or rivastigmine or sdz 212 713 or sdz 212-713 or sdz 212713 or sdz ena 713 or sdz ena713 or sdz212 713 or sdz212-713 or sdz212713).ti,ab,tn.	3750
15	galantamine/	7892
16	(acumor or alenzo or aneprosil or bergal or consion or elmino or galantex or galanthamine or galanthen or galanyl or galatamin$ or galema or galnora or galsya or gamyl or gatalin or gazylan or girlamen or jilkon or lotprosin or loxifren or luventa or lycoremin$ or margal or masparen or memoton life or natagal or nivalin$ or razadyne or reminyl or spegal or vertusal or zentan or zoroflog).ti,ab,tn.	1697
17	exp cholinesterase inhibitor/	87121
18	(((acetylcholinesterase or cholinesterase or phosphoorganic choline esterase or ache) adj3 (inhibit$ or block$)) or anticholesterinase or anticholinesterase or anticholinesterase or achei$ or chei$).ti,ab,hw.	44409
19	or/9-18	109263
20	clinical study/	156689
21	case control study/	180428
22	family study/	25353
23	longitudinal study/	163936
24	retrospective study/	1164452
25	Prospective study/	728159
26	Randomized controlled trials/	215239
27	25 not 26	719765
28	Cohort analysis/	778204

29	(Cohort adj (study or studies)).mp.	375556
30	(Case control adj (study or studies)).tw.	149065
31	(follow up adj (study or studies)).tw.	67656
32	(observational adj (study or studies)).tw.	203862
33	(epidemiologic$ adj (study or studies)).tw.	113453
34	(cross sectional adj (study or studies)).tw.	269609
35	20 or 21 or 22 or 23 or 24 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34	3239368
36	(RWE or real world or (treatment adj2 pattern$)).ti,ab.	108363
37	"medical record review"/	146071
38	((record$ or chart$) adj2 review$).ti,ab.	172469
39	(register$ or registr$ or survey$ or questionaire$ or database$).ti,ab.	2212471
40	or/36-39	2484258
41	35 or 40	5089510
42	8 and 19 and 41	1067
43	limit 42 to yr="2009 -Current"	824

Supplementary Table 5. Search strategy for Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R) from 1946 to November 29, 2021 (search date: November 30, 2021)

#	Searches	Results
1	Cognitive Dysfunction/	26476
2	(MCI or aMCI or mild cognit$ impair$ or CIND or cognitive impair$ no dementia).ti,ab,hw.	28244
3	((early or mild$ or prodromal) adj6 (alzheimer$ or alzeimer$ or AD)).mp.	24691
4	Alzheimer Disease/	104707
5	(early or mild$ or prodromal).ti,ab.	2048109
6	4 and 5	25242
7	(dementia adj2 stage adj2 ('2' or '3' or II or III or two or three)).ti,ab.	26
8	1 or 2 or 3 or 6 or 7	67204
9	Memantine/	2440
10	('1 amino 3, 5 dimethyladamantane' or '1, 3 dimethyl 5 adamantanamine' or '1, 3 dimethyl 5 aminoadamantane' or '3, 5 dimethyl 1 adamantamine' or '3, 5 dimethyl 1 adamantanamine' or '3, 5 dimethylaminoadamantane' or '5 amino 1, 3 dimethyladamantane' or 'adamantane, 5 amino 1, 3 dimethyl' or akatinol or alzantin or axura or d 145 or d145 or ebix or ebixa or ebixza or marixino or maruxa or memantine or memantine hcl or memantine hydrochloride or memantine nitrate or memary or "mn 08" or mn08 or namenda or namenda xr or nemdatine or nsc 102290 or nsc102290 or sun y7017 or suny701).ti,ab.	3898
11	Donepezil/	2658
12	(aricept or asenta or doneliquid geriasan or donepezil or donepezil hydrochloride or e 2020 or e2020 or eranz or memac or memorit).ti,ab.	4007
13	Rivastigmine/	1185
14	(alzest or ena 713 or ena713 or exelon or nimvastid or prometax or rivastigmin or rivastigmine or sdz 212 713 or sdz 212-713 or sdz 212713 or sdz ena 713 or sdz ena713 or sdz212 713 or sdz212-713 or sdz212713).ti,ab.	1861
15	Galantamine/	1611
16	(acumor or alenzo or aneprosil or bergal or consion or elmino or galantex or galanthamine or galanthen or galanyl or galatamin$ or galema or galnora or galsya or gamyl or gatalin or gazylan or girlamen or jilkon or lotprosin or loxifren or luventa or lycoremin$ or margal or masparen or memoton life or natagal or nivalin$ or razadyne or reminyl or spegal or vertusal or zentan or zoroflog).ti,ab.	759
17	exp Cholinesterase Inhibitors/	52590
18	(((acetylcholinesterase or cholinesterase or phosphoorganic choline esterase or ache) adj3 (inhibit$ or block$)) or anticholesterinase or anticholinesterase or anticholinesterase or achei$ or chei$).ti,ab,hw.	36711
19	or/9-18	68715
20	Epidemiologic studies/	8909
21	exp case control studies/	1256790
22	exp cohort studies/	2257018
23	Case control.tw.	138769
24	(cohort adj (study or studies)).tw.	254614
25	Cohort analy$.tw.	9691
26	(Follow up adj (study or studies)).tw.	52439
27	(observational adj (study or studies)).tw.	131366

28	Longitudinal.tw.	279758
29	Retrospective.tw.	627679
30	Cross sectional.tw.	424021
31	Cross-sectional studies/	401248
32	or/20-31	3393163
33	(RWE or real world or (treatment adj2 pattern$)).ti,ab.	63241
34	((record$ or chart$) adj2 review$).ti,ab.	90079
35	(register$ or registr$ or survey$ or questionaire$ or database$).ti,ab.	1631579
36	or/33-35	1756973
37	32 or 36	4572772
38	8 and 19 and 37	708
39	limit 38 to yr="2009 -Current"	443

Supplementary Table 6. Search strategy for EBM Reviews (Ovid) (search date: November 30, 2021)

#	Searches	Results
1	Cognitive Dysfunction/	1926
2	(MCI or aMCI or mild cognit$ impair$ or CIND or cognitive impair$ no dementia).ti,ab,hw.	4995
3	((early or mild$ or prodromal) adj6 (alzheimer$ or alzeimer$ or AD)).mp.	4860
4	Alzheimer Disease/	3636
5	(early or mild$ or prodromal).ti,ab.	201989
6	4 and 5	1631
7	(dementia adj2 stage adj2 ('2' or '3' or II or III or two or three)).ti,ab.	10
8	1 or 2 or 3 or 6 or 7	10063
9	Memantine/	420
10	('1 amino 3, 5 dimethyladamantane' or '1, 3 dimethyl 5 adamantanamine' or '1, 3 dimethyl 5 aminoadamantane' or '3, 5 dimethyl 1 adamantamine' or '3, 5 dimethyl 1 adamantanamine' or '3, 5 dimethylaminoadamantane' or '5 amino 1, 3 dimethyladamantane' or 'adamantane, 5 amino 1, 3 dimethyl' or akatinol or alzantin or axura or d 145 or d145 or ebix or ebixa or ebixza or marixino or maruxa or memantine or memantine hcl or memantine hydrochloride or memantine nitrate or memary or "mn 08" or mn08 or namenda or namenda xr or nemdatine or nsc 102290 or nsc102290 or sun y7017 or suny701).ti,ab.	1415
11	Donepezil/	604
12	(aricept or asenta or doneliquid geriasan or donepezil or donepezil hydrochloride or e 2020 or e2020 or eranz or memac or memorit).ti,ab.	1790
13	Rivastigmine/	243
14	(alzest or ena 713 or ena713 or exelon or nimvastid or prometax or rivastigmin or rivastigmine or sdz 212 713 or sdz 212-713 or sdz 212713 or sdz ena 713 or sdz ena713 or sdz212 713 or sdz212-713 or sdz212713).ti,ab.	765
15	Galantamine/	228
16	(acumor or alenzo or aneprosil or bergal or consion or elmino or galantex or galanthamine or galanthen or galanyl or galatamin$ or galema or galnora or galsya or gamyl or gatalin or gazylan or girlamen or jilkon or lotprosin or loxifren or luventa or lycoremin$ or margal or masparen or memoton life or natagal or nivalin$ or razadyne or reminyl or spegal or vertusal or zentan or zoroflog).ti,ab.	100
17	exp Cholinesterase Inhibitors/	1857
18	(((acetylcholinesterase or cholinesterase or phosphoorganic choline esterase or ache) adj3 (inhibit$ or block$)) or anticholesterinase or anticholinesterase or anticholinesterase or achei$ or chei$).ti,ab,hw.	2756
19	or/9-18	6080
20	Epidemiologic studies/	43
21	exp case control studies/	14915
22	exp cohort studies/	157995
23	Case control.tw.	10247
24	(cohort adj (study or studies)).tw.	19804
25	Cohort analy$.tw.	1058
26	(Follow up adj (study or studies)).tw.	10195
27	(observational adj (study or studies)).tw.	16907
28	Longitudinal.tw.	21004

29	Retrospective.tw.	31860
30	Cross sectional.tw.	19540
31	Cross-sectional studies/	5444
32	or/20-31	257227
33	(RWE or real world or (treatment adj2 pattern$)).ti,ab.	8844
34	((record$ or chart$) adj2 review$).ti,ab.	6595
35	(register$ or registr$ or survey$ or questionaire$ or database$).ti,ab.	184327
36	or/33-35	195413
37	32 or 36	408655
38	8 and 19 and 37	313
39	limit 38 to yr="2009 -Current" [Limit not valid in DARE; records were retained]	196

ACP Journal Club 1991 to November 2021, EBM Reviews - Cochrane Central Register of Controlled Trials October 2021, Cochrane Database of Systematic Reviews 2005 to November 23, 2021, Cochrane Methodology Register 3rd Quarter 2012, Database of Abstracts of Reviews of Effects 1st Quarter 2016

Supplementary Table 7. Inclusion and exclusion criteria

Criteria	Inclusion	Exclusion
Population	Patients with early AD, comprising: Prodromal AD/MCI due to AD Mild AD dementia	Moderate AD Severe AD Any other dementia not caused by AD (e.g., vascular dementia, Lewy body dementia, mixed dementia, etc.)
Intervention & comparators	AD symptomatic treatments as monotherapy or in combination: AChEis (licensed for use in patients with mild AD dementia): ● Donepezil ● Rivastigmine ● Galantamine ● Memantine (licensed for use in patients with moderate to severe AD)	Non-pharmacological Palliative therapy Plant-based therapies (e.g., Ginkgo biloba) Nutritional therapies
Outcomes	Proportion of patients receiving treatment at baseline Frequency of treatment(s) used Prescription rates of treatments	Safety outcomes Discontinuations Adherence/persistence Switching treatments Change in treatment use over time
Study design	Prospective/retrospective observational studies, to include: Registries Medical record reviews Surveys SLRs of observational data and meta-analysis publications (for reference checking) Full publications only	Randomized controlled trials and/or meta-analyses Comparative, non-randomized clinical studies and/or meta-analyses Preclinical early phase studies investigating the prevention of AD in patients without the disease Narrative reviews Studies reported as abstracts/poster only
Geography	No restriction	
Date of publication	2009 onwards	Pre-2009
Language	No restriction	

Supplementary Table 8. Studies excluded at full paper screening and reason for exclusion

Author	Title	Citation	DOI
Not relevant population (n=87)			
Ah, Y. M.	Effect of anticholinergic burden on treatment modification, delirium and mortality in newly diagnosed dementia patients starting a cholinesterase inhibitor: A population-based study	Basic & Clinical Pharmacology & Toxicology. 2019, 124(6):741-748.	https://dx.doi.org/10.1111/bcpt.13184
Ban, C. X.	Clinicians' prescription preferences for treating patients with Alzheimer's disease in Shanghai	Translational Neurodegeneration. 2016, 5(1) (8).	http://dx.doi.org/10.1186/s40035-016-0055-3
Behl, P.	Treatment effects in multiple cognitive domains in Alzheimer's disease: a two-year cohort study	Alzheimer's Research & Therapy. 2014, 6(4):48.	https://dx.doi.org/10.1186/alzrt280
Bent-Ennakhil, N.	a real-world analysis of treatment patterns for cholinesterase inhibitors and memantine among newly-diagnosed Alzheimer's disease patients	Neurol Ther. 2017 6(1):131-144.	10.1007/s40120-017-0067-7
Bohlken, J.	Relevance of Coded Prodromal Mild Cognitive Impairment in the Routine Treatment of Patients with Dementia in Germany	J Alzheimers Dis. 2018, 65(2):393-399.	http://dx.doi.org/10.3233/JAD-180567
Bracco, L.	Do cholinesterase inhibitors act primarily on attention deficit? A naturalistic study in Alzheimer's disease patients	Journal of Alzheimer's Disease. 2014, 40(3):737-742.	http://dx.doi.org/10.3233/JAD-131154
Calabria, M.	Efficacy of acetyl-cholinesterase-inhibitor (ACHEI) treatment in Alzheimer's disease: A 21-month follow-up real world study	Archives of Gerontology and Geriatrics. 2009, 49(1):e6-e11.	http://dx.doi.org/10.1016/j.archger.2008.07.006
Carcaillon, L.	Diagnosis of Alzheimer's disease patients with rapid cognitive decline in clinical practice: interest of the Deco questionnaire	Journal of Nutrition, Health & Aging. 2011, 15(5):361-6.	
Carney, G.	Comparison of cholinesterase inhibitor safety in real-world practice	Alzheimer's and Dementia: Translational Research and Clinical Interventions. 2019, 5:732-739.	http://dx.doi.org/10.1016/j.trci.2019.09.011
Chang, C. C.	A 48-week, multicenter, open-label, observational study evaluating oral rivastigmine in patients with mild-to-moderate Alzheimer's disease in Taiwan	Advances in Therapy. 2019, 36(6):1455-1464.	http://dx.doi.org/10.1007/s12325-019-00939-0
Chang, Y. P.	Clinical compliance of donepezil in treating Alzheimer's disease in Taiwan	American Journal of Alzheimer's Disease & Other Dementias. 2015, 30(4):346-51.	https://dx.doi.org/10.1177/1533317514556875
Cheng, Y. W.	Hippocampal atrophy but not white-matter changes predicts the long-term cognitive response to cholinesterase inhibitors in Alzheimer's disease	Alzheimer's Research and Therapy. 2015, 7(1) (72).	http://dx.doi.org/10.1186/s13195-015-0155-9
Cherubini, A.	Underrecognition and Undertreatment of Dementia in Italian Nursing Homes	Journal of the American Medical Directors Association. 2012, 13(8):e7-759.	http://dx.doi.org/10.1016/j.jamda.2012.05.015
Cho, H. S.	Suboptimal baseline serum vitamin B12 is associated with cognitive decline in people with Alzheimer's disease undergoing cholinesterase inhibitor treatment	Frontiers in Neurology. 2018, 9 (325).	http://dx.doi.org/10.3389/fneur.2018.00325
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Not relevant outcome (n=18)			
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Not relevant intervention (n=2)			
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Not relevant study design (n=16)			
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MCI not specifically due to AD (n=15)			
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Epstein, N. U.	Differences in medication use in the Alzheimer's disease neuroimaging initiative: Analysis of baseline characteristics	Drugs and Aging. 2010, 27(8):677-686.	http://dx.doi.org/10.2165/11538260-000000000-00000
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Lee, L.	Enhancing dementia care: A primary care-based memory clinic	Journal of the American Geriatrics Society. 2010, 58(11):2197-2204.	http://dx.doi.org/10.1111/j.1532-5415.2010.03130.x
Na, S.	The effect of dizziness in patients with cognitive impairments	Journal of Prevention of Alzheimer's Disease. 2018, 5(1):S125-S126.	http://dx.doi.org/10.14283/jpad.2018.40
Pyun, J. M.	Change in cognitive function according to cholinesterase inhibitor use and amyloid PET positivity in patients with mild cognitive impairment	Alzheimer's Research & Therapy. 2021, 13(1):10.	https://dx.doi.org/10.1186/s13195-020-00749-5
Roberts, J. S.	Mild cognitive impairment in clinical care: A survey of American Academy of Neurology members	Neurology. 2010, 75(5):425-431.	http://dx.doi.org/10.1212/WNL.0b013e3181eb5872
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Tifratene, K.	Mild cognitive impairment and anti-Alzheimer disease medications: A cross sectional study of the French National Alzheimer Databank (BNA)	Journal of Alzheimer's Disease. 2014, 38(3):541-549.	http://dx.doi.org/10.3233/JAD-131103
Weinstein, A. M.	Treatment practices of mild cognitive impairment in California Alzheimer's Disease Centers	Journal of the American Geriatrics Society. 2009, 57(4):686-90.	https://dx.doi.org/10.1111/j.1532-5415.2009.02200.x
Yu, X.	Usage and adherence of antidementia drugs in a memory clinic cohort in Chongqing, Southwest China	Psychogeriatrics: The Official Journal of the Japanese Psychogeriatric Society. 2020, 20(5):706-712.	https://dx.doi.org/10.1111/psyg.12568

Supplementary Table 9. Summary of risk of bias assessments using Joanna Briggs Institute Prevalence Checklist

Study	Q1. Was the sample frame appropriate to address the target population?	Q2. Were study participants sampled in an appropriate way?	Q3. Was the sample size adequate?	Q4. Were the study subjects and the setting described in detail?	Q5. Was the data analysis conducted with sufficient coverage of the identified sample?	Q6. Were valid methods used for the identification of the condition?	Q7. Was the condition measured in a standard, reliable way for all participants?	Q8. Was there appropriate statistical analysis?	Q9. Was the response rate adequate, and if not, was the low response rate managed appropriately?
Besser 2016 [13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bruno 2018 [14]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Calvo-Perxas 2017 [15]	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Chaves 2014 [16]	Yes	Unclear	No	Yes	No	Yes	Yes	Yes	Yes
Chiu 2009 [17]	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes
Droogsma 2015 [18]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Epelbaum 2019 [19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hessmann 2018 [20]	Unclear	Yes	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes
Kongpakwatta 2019 [21]	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes
Martinez-Moreno 2016 [22]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Mesterton 2010 [23]	Yes	Yes	No	Yes	Yes	Yes	Unclear	Yes	Yes
Olazaran 2017 [24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Podhorna 2020 [25]	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes
Reed 2018 [26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rojas 2010 [27]	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Unclear
Schneider 2011 [28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tormalehto 2015 [29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear

Study	Q1. Was the sample frame appropriate to address the target population?	Q2. Were study participants sampled in an appropriate way?	Q3. Was the sample size adequate?	Q4. Were the study subjects and the setting described in detail?	Q5. Was the data analysis conducted with sufficient coverage of the identified sample?	Q6. Were valid methods used for the identification of the condition?	Q7. Was the condition measured in a standard, reliable way for all participants?	Q8. Was there appropriate statistical analysis?	Q9. Was the response rate adequate, and if not, was the low response rate managed appropriately?
Vinuela 2021 [30]	Yes	Yes	No	Yes	Yes	Yes	Unclear	Yes	Yes
Wang 2014 [31]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Wattmo 2016 [32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
Wimo 2013 [33]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Supplementary Table 10. Treatment patterns by study

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
MCI due to AD						
Europe	Germany	Hessmann 2018 [20]	Cross-sectional study including patients from five study sites in Marburg-Biedenkopf.	N=51 Diagnostic criteria: MMSE score: 27-30	*Prescription rates of treatments* *Type of treatment received as a proportion of total population (n=51)* **AChEi monotherapy:** 16 (31.4%) ● Rivastigmine: 9 (17.6%) **Memantine monotherapy:** 4 (7.8%)	●●
North America	Canada & USA	Schneider 2011 [28]	Prospective Cohort ADNI database May 2009	N=402 % Male=259 (64.4%) Mean age (SD)=74.8 (7.42) Diagnostic criteria: MMSE score: 24-30 Mean MMSE (SD)=27.0 (1.78) *APOE* ε4 genotype carriers, 1 or 2 alleles=215 (53.5%)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=402)* **AChEi(s) monotherapy:** 141 (35.1%) o Median AChEi exposure: 0.97; IQR: 0.41 to 2.14 **Memantine**:** 46 (11.4%) o Median memantine exposure: 0.88; IQR: 0.30 to 1.42 **AChEi(s) + Memantine:** 36 (9%) o Median AChEi exposure: 1.54; IQR: 0.78 to 2.75 o Median memantine exposure: 0.80; IQR:0.33 to 1.35 o Most frequently reported dosing regimen: 20 mg memantine **Other** ● **AChEi monotherapy or in combination with memantine:** 177 (44.0%) **No AD symptomatic treatment**: 215 (53.5%) *Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving AChEi* **Other** ● **Donepezil monotherapy or in combination with memantine:** 150 (84.7%) o Most frequently reported dosing regimen: >10 mg donepezil ● **Galantamine monotherapy or in combination with memantine:** 18 (10.2%) o Most frequently reported dosing regimen: 16-24 mg galantamine ● **Rivastigmine monotherapy or in combination with memantine:** 9 (5.1%) o Most frequently reported dosing regimen: 6-12 mg rivastigmine	●
North America	USA	Besser 2016 [13]	Case series NACC UDS September 2005 to March 2015	N=191 % Male=95 (49.7) Mean age (SD)=79.1 (10.3)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=178)* **AChEi monotherapy:** 33 (18.5%)	●

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
				Diagnostic criteria: MCI (according to the Petersen criteria) Mean age of onset (SD)=76.5 (10.8) ≥1 *APOE* ε4 allele= 64 (41.8%)	**Memantine monotherapy**: 12 (6.7%)	
Multinational	France, Germany, Japan, UK & USA	Podhorna 2020 [25]	Survey of online questionnaires and patient record forms from a survey of physicians	N=331	*Prescription rates of treatments* *Treatment received as a proportion those receiving any AD treatment (n=128)* **AChEi monotherapy:** NR (87%)* ● Donepezil: NR (63.0%) ● Galantamine: NR (9.0%) ● Rivastigmine: NR (15.0%) ○ Most frequently reported dosing regimen: Patch (10%) **Memantine monotherapy**: NR (10%) **AChEi(s) + Memantine:** ● Donepezil and Memantine: NR (4%) *Prescription rates of treatments* *Type of treatment received as a proportion of total population (n=331)* **No AD symptomatic treatment:** NR (41%)	●●
Mild AD dementia						
Asia	Thailand	Kongpakwatta 2019 [21]	Cross-sectional study conducted in a tertiary hospital in Thailand November 2017 to April 2018	N=35 % Male=17 (48.6) Mean age (SD)=77.6 (6.3) Diagnostic criteria: MMSE score: ≥20 Mean MMSE (SD)= 22.6 (2.0)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=35)* **Other:** ● AD medications (including donepezil, galantamine, rivastigmine, and memantine): 33 (94.3%) **No AD symptomatic treatment:** 2 (5.7%)	●●●
Europe	Finland	Tormalehto 2015 [29]	Prospective cohort study conducted over three hospital districts in middle and eastern Finland 2002 to 2006	N=236 % Male=115 (48.7) Mean age (SD)=75.7 (6.5) Diagnostic criteria: CDR: 0.5 to 1	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=236)* **AChEi monotherapy:** 210 (89.0%) **Memantine monotherapy**: 16 (7.0%) **AChEi(s) + Memantine:** 1 (0.4%) *Frequency of treatment use (Mean utilization rates)* *Type of treatment received as a proportion of total population* **AChEi monotherapy**: NR (91%)* ● Donepezil: NR (46%) ● Galantamine: NR (28%) ● Rivastigmine: NR (17.0%)	●●
Europe	France	Wimo 2013 [33]	GERAS (an 18-month, prospective, observational study of patients with	N=138 % Male=NR (45.7) Mean age (SD)=79.3 (5.93) Diagnostic criteria: MMSE 21−26	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=138)* **AChEi monotherapy:** NR (81.9%)	●

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
			probable AD dementia of all severities) October 2010 to September 2011		**Memantine monotherapy**: NR (13.8%)	
Europe	Germany	Hessmann 2018 [20]	Cross-sectional study	N=130 Diagnostic criteria: MMSE: 20 to 26	*Prescription rates of treatments* *Type of treatment received as a proportion of total population (n=130)* **AChEi monotherapy:** ● Donepezil: 17 (13.1%) **Memantine monotherapy**: 27 (20.8%)	●●
Europe	Germany	Wimo 2013 [33]	GERAS October 2010 to September 2011	N=228 % Male=NR (57.9) Mean age (SD)= 74.7 (6.89) Diagnostic criteria: MMSE 21−26	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=228)* **AChEi monotherapy:** NR (73.7%) **Memantine monotherapy**: NR (19.7%)	●
Europe	Italy	Bruno 2018 [14]	GERAS II (a prospective, multicenter, observational study) April 2013 to January 2014	N=29 % Male=15 (51.7) Mean age (SD)=76.2 (7.12) Diagnostic criteria: Diagnosis of probable AD and a MMSE score of ≤26 Mean MMSE (SD)= 23.0	*Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving any AD treatment (n=21)* **AChEi monotherapy:** 13 (61.9%) **Memantine monotherapy**: 7 (33.3%) **AChEi + Memantine:** 1 (4.8%)	●●●
Europe	Multinational (France, Germany, UK)	Reed 2018 [26]	GERAS October 2010 to September 2011	N=566 % Male=295 (52.1) Mean age (SD)=77.3 (6.9) Diagnostic criteria: MMSE score: 20 to 26 Mean MMSE (SD)= 23.3 (1.6)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=566)* **AChEi monotherapy:** 411 (72.6%) **Memantine monotherapy**: 41 (7.2%) **AChEi + Memantine:** 26 (4.6%) **No AD symptomatic treatment:** 88: (15.5%)	●
Europe	Netherlands	Droogsma 2015 [18]	Retrospective Cohort Memory clinic of the medical center Leeuwarden 2002 to 2012	N=335 % Male=122 (36.4) Mean age (SD)=Median: 80, IQR: 75.0-83.0 Diagnostic criteria: MMSE: ≥21 to 26 Mean MMSE (SD)= 23.0	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of those receiving AChEi (n=335)* **AChEi monotherapy: 335 (100%)** ● Galantamine: 327 (97.6%) ○ Frequency of administration: Daily ● Rivastigmine: 8 (2.4%) ○ Frequency of administration: Daily	●●
Europe	Spain	Calvo-Perxas 2017 [15]	Retrospective Cohort ReDeGi Pharmacy Unit Database -Public Health Catalan Healthcare Service 2007 to 2014	N=2028 Diagnostic criteria: CDR score: 1	*Prescription rates of treatments* *Type of treatment received as a proportion of total population (n=2028)* **AChEi monotherapy:** 1249 (61.6%) **Memantine monotherapy**: 83 (4.1%) **AChEi + Memantine:** 170 (8.4%) **No AD symptomatic treatment:** 526 (25.9%)	●●

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
Europe	Spain	Martinez-Moreno 2016 [22]	Retrospective observational cohort study conducted at an outpatient clinic. May 2004 to March 2012	N=60 % Male=25 (42) Mean age (SD)=75.1 (6.35) Diagnostic criteria: Diagnosis of mild AD dementia and a MMSE score of≥20	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population* **AChEi monotherapy:** 33 (55%)	●●●
Europe	Spain	Olazaran 2017 [24]	GERAS II April 2013 to December 2013	N=116 % Male=53 (45.7) Mean age (SD)=74.7 (7.9) Diagnostic criteria: MMSE 21−26	*Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving any AD treatment (n=96)* **AChEi monotherapy:** 71 (74%) ● Galantamine: 10 (10.4%) ● Rivastigmine: 43 (44.8%) ● Donepezil: 33 (34.4%) **Memantine monotherapy**: 10 (10.4%) **AChEi + Memantine:** 11 (11.5%) *Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=116)* **No AD symptomatic treatment:** 20 (17.2%)	●
Europe	Spain	Vinuela 2021 [30]	Single center, prospective, non-interventional cohort study May 2017 to June 2018	N=60 % Male= 23 (38.3) Mean age (SD)= 75.8 (9.0) Diagnostic criteria: Mild AD dementia and an MMSE >20	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=60)* **AChEi monotherapy:** 35 (58.3%) **Memantine monotherapy**: 11 (18.3%)	●●●
Europe	Sweden	Mesterton 2010 [23]	Cross-sectional study using medical records, interviews, self-administered questionnaires August 2007	N=91 % Male=45 (49) Mean age (SD)=76.8 (7.4) Diagnostic criteria: MMSE 20−26 Mean MMSE (SD)= 23.7 (2.6)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=91)* **AChEi monotherapy:** 69 (76%) **Memantine monotherapy**: 10 (11%)	●●●
Europe	Sweden	Wattmo 2016 [32]	SATS - a 3-year, prospective, open, non-randomized multicenter study	N=734 % Male=261 (36) Mean age (SD)=75.2 (6.8) Diagnostic criteria: MMSE score: 20 to 26 Mean MMSE (SD)= 23.4 (2.0) Mean age of onset (SD)=72.3 (7.1) *APOE* ε4 carrier= 241 (31)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of those receiving AChEi (n=734)* **AChEi monotherapy:** NR (100%) ● Donepezil: NR (48.0%) o Mean dosage: 6.9 ± 1.7 mg ● Galantamine: NR (30.0%) o Mean dosage: 15.3 ± 3.6 mg ● Rivastigmine: NR (22.0%) o Mean dosage: 6.2 ± 2.1 mg	●●
Europe	UK	Wimo 2013 [33]	GERAS October 2010 to September 2011	N=201 % Male=NR (50.2) Mean age (SD)= 78.8 (6.85) Diagnostic criteria: MMSE 21−26	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=201)* **AChEi monotherapy:** NR (82.6%) **Memantine monotherapy**: NR (1.0%)	●

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
North America	Multinational (Canada, USA)	Schneider 2011 [28]	Prospective Cohort using ADNI database May 2009	N=188 % Male=99 (52.7%) Mean age (SD)=75.3 (7.56) Diagnostic criteria: MMSE score: 21-26 Mean MMSE (SD)= 23.3 (2.04) *APOE* ε4 genotype carriers, 1 or 2 alleles=124 (66.0%)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=188)* **AChEi(s) monotherapy:** 86 (45.7%) o Median AChEi exposure: 0.97; IQR: 0.33 to 2.15 **Memantine**:** 86 (45.7%) o Median memantine exposure: 0.94; IQR: 0.32 to 1.93 **AChEi(s) + Memantine:** 73 (38.8%) o Median AChEi exposure: 2.20; IQR: 1.00 to 3.66 o Median memantine exposure: 1.03; IQR: 0.38 to 1.97 o Most frequently reported dosing regimen: 20 mg memantine **Other** ● **AChEi monotherapy or in combination with memantine:** 159 (84.6%) **No AD symptomatic treatment:** 16 (8.5%) *Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving AChEi (n=159)* **Other** ● **Donepezil monotherapy or in combination with memantine:** 123 (77.4%) o Most frequently reported dosing regimen: >10 mg donepezil ● **Galantamine monotherapy or in combination with memantine:** 25 (15.7%) o Most frequently reported dosing regimen: 16-24 mg galantamine ● **Rivastigmine monotherapy or in combination with memantine:** 11 (6.9%) o Most frequently reported dosing regimen: 6-12 mg rivastigmine	●
South America	Argentina	Chaves 2014 [16]	Retrospective Cohort using computerized medical records of Hospital Italiano de Buenos Aires. January 2002 to January 2010	N=23 % Male=1 (4.4) Diagnostic criteria: CDR: 1 Mean age of onset (SD)=82.4 (4.9)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (N=23)* **AChEi mixed**:** 22 (96.0%) **Memantine mixed***: 5 (23.0%)	●●●
Worldwide	Multinational (France, Germany,	Podhorna 2020 [25]	Online questionnaires and patient record forms	N=1175	*Prescription rates of treatments* *Treatment received as a proportion those receiving any AD treatment (n=809)* **AChEi monotherapy:** NR (88%)*	●●

Region	Country	Study	Study details	Patient details	Treatment patterns	Quality assessment
	Japan, UK & USA)		from a survey of physicians		● Donepezil: NR (63.0%) ● Galantamine: NR (7.0%) ● Rivastigmine: NR (18.0%) o Most frequently reported dosing regimen: Patch (11%) ● Donepezil and Galantamine: NR (1.0%) **Memantine monotherapy**: NR (7.0%) **AChEi(s) + Memantine:** ● Donepezil and Memantine: NR (3%) *Prescription rates of treatments* *Type of treatment received as a proportion of total population (n=1,175)* **No AD symptomatic treatment:** NR (19%)	
Early AD						
Europe	France	Epelbaum 2019 [19]	Retrospective Cohort using electronic clinical records database from 11 memory research and resource centers 2	N=195 % Male=87 (44.9) Mean age (SD)=70.8 (0.6) Diagnostic criteria: MMSE ≥20 Mean MMSE (SD)= 24.7 (0.2)	*Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving any AD treatment (n=60)* **AChEi monotherapy:** 48 (80%)* ● Donepezil: 18 (30%) o Most frequently reported dosing regimen: 10 mg, 16 (26.7%) ● Galantamine: 9 (15%) o Most frequently reported dosing regimen: 24 mg, 6 (10%) ● Rivastigmine: 21 (35%) o Most frequently reported dosing regimen: 9.5 mg patch, 17 (28.3%) *Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=195)* **No AD symptomatic treatment: 135 (69.2%)**	●
North America	USA	Wang 2014 [31]	Cross-sectional study of community dwelling volunteers enrolled in studies of ageing and memory at Washington University in St Louis.	N=44 Diagnostic criteria: Very mild or mild AD dementia (CDR 0.5 and CDR 1)	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of total population (n=44)* **AChEi monotherapy:** 25 (56.8%) ● Donepezil: 21 (47.7%) ● Galantamine: 3 (6.8%) ● Rivastigmine: 1 (2.3%) **No AD symptomatic treatment:** 19 (43.2%)	●●●

AChEi, acetylcholinesterase inhibitor; AD, Alzheimer's disease; ADNI, Alzheimer's Disease Neuroimaging Initiative; *APOE*, Apolipoprotein E; CDR, Clinical Dementia Rating; IQR, interquartile range; MCI, mild cognitive impairment; MMSE, Mini-Mental State Exam; N, number; NR, not recorded; NACC, National Alzheimer's Coordinating Center's; ReDeGi, Registry of Dementias of Girona; SATS, The Swedish Alzheimer Treatment Study; SD, standard deviation; UDS, Uniform Data Set; UK, United Kingdom; USA, United States of America

*Calculated value; ** Likely to report mixed population of monotherapy and combination therapy; •, low risk of bias; ••, unclear risk of bias; •••, high risk of bias

Supplementary Table 11. Studies which report proportion per dose received

Mild AD dementia/eAD dementia						
Region	**Country**	**Study**	**Study details**	**Patient details**	**Treatment patterns**	**Quality assessment**
Asia	Taiwan	Chiu 2009 [17]	Prospective Cohort Non-interventional post-marketing surveillance study December 2004 to December 2006	N=264 Diagnostic criteria: CDR score: 1	*Proportion of patients receiving treatment at baseline* *Treatment received as a proportion those receiving rivastigmine (n=264)* **AChEi only:** Rivastigmine: 109 (100%) Mean exposure: 0.41; SD: 0.14 <6 mg daily: 63 (23.9%) 6-121 mg daily: 201 (76.1%) **Memantine only**: NR **AChEi(s) + Memantine:** NR **No AD symptomatic treatment:** NR	●●
South America	Argentina	Rojas 2010 [27]	Prospective Cohort study at the Memory Laboratory at Hospital Zubizarreta March 2008 to March 2009	N=38 % Male=16 (42.1) Mean age (SD)=71.0 (9.83) Diagnostic criteria: CDR: 1	*Proportion of patients receiving treatment at baseline* *Type of treatment received as a proportion of those receiving donepezil (n=38)* **AChEi only:** Donepezil: 38 (100%) Exposure: NR 5 mg 16 (42.1%) 10 mg: 22 (57.9%) **Memantine only**: NR **AChEi(s) + Memantine:** NR **No AD symptomatic treatment:** NR	●●●

AChEi, acetylcholinesterase inhibitor; AD, Alzheimer's disease; CDR, Clinical Dementia Rating; MCI, mild cognitive impairment; MMSE, Mini-Mental State Exam; N, number; NR, not recorded; SD, standard deviation; ••, unclear risk of bias; •••, high risk of bias

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