

Appendix Table 1. Detailed Eligibility Criteria for Systematic Review

Category	Inclusion	Exclusion
Language	English language publications	Non-English language publications
Age	Study subjects who were 18 years or older	Study subjects younger than 18 years
Populations	<p>1) Diagnostic model used to determine dementias: The diagnosis of dementia using any of these criteria: i) ICD 9 or 10. (85, 86), ii) DSM III, III-R, and IV. (87-89), iii) NINCDS.(90), iv) NINCDS-ADRDA(6) or NINCDS-AIREN.(91)</p> <p>2) Diagnostic criteria used to determine cognitive impairment (pre-dementias): In the case of not yet diagnosed dementia, specific diagnostic categories were accepted for the following: i) mild cognitive impairment (MCI).(92), ii) cognitive impairment not dementias (CIND).(93), iii) cognitive loss no dementias (CLOND).(94)</p> <p>3)Disease classifications for dementias: These included AD, senile dementia of the Alzheimer’s type (SDAT), Lewy body disease, VaD, multi-infarct dementia (MID), AIDS/HIV dementia, Parkinson’s disease dementia (PDD), progressive supranuclear palsy (PSP), mixed diagnosis dementia, encephalopathy, Mesulam syndrome, progressive non-fluent aphasia, Binswanger disease, subcortical leukoencephalopathy, circumscribed lobar brain atrophy, Pick disease, amyloid beta-protein (not Down’s syndrome or trisomy), cerebral amyloid angiopathy, neurofibrillary tangles, threads, senile plaques, corticobasil ganglionic degeneration, cerebral autosomal dominant ischemia with subcortical leukoencephalopathy (CADASIL), Huntington’s disease with dementia, hydrocephalus</p> <p>4) Severity classification: This was accepted in whichever classification system the studies specified. The majority of studies specified threshold criteria using the MMSE as follows: mild > 22, moderate 14 – 21, and 10 – 14 as severe. Many studies used the definition of mild to moderate as a range from 10 to 26 based on criteria established by Folstein et al.(95) Some studies specified a category (i.e. mild to moderate) but did not report the baseline MMSE values for the groups compared. Some studies specified two categories (mild to moderate) and (moderate to severe) based on the DSM-III-R criteria. Cambridge Examination for Mental Disorders in the Elderly (CAMDEX) specifies levels of severity (minimal, mild, moderate, severe). Similarly, some studies reported a category of severity without stating which method was used. In these instances, the category of severity specified was accepted as reported by the study authors.</p>	<p>1) Dementias disease classification: i) alcohol caused dementia/Korsakoff’s syndrome, ii) Creutzfeldt-Jakob syndrome, c) spongiform encephalopathy, iii) hypothyroidism, iv) vitamin B12 deficiency, v) neurosyphilis.</p> <p>2) Dementias diagnosed using only Lowb, Hachinski (specific for VaD) criteria.(96)</p> <p>3) All organically caused dementias which includes “Delirium, Dementia, Amnesic Disorders, and Cognitive Disorder Otherwise Specified. The predominant disturbance is a clinically significant deficit in cognition that represents a significant change from a previous level of functioning. For each disorder in this section, the etiology is either a general medical condition (although the specific general medical condition may not be identifiable) or a substance (i.e., a drug of abuse, medication, or toxin), or a combination of these factors.”(87)</p> <p>4) Temporary dementia (e.g. side effect of anesthesia) classified as follows: Delirium: a delirium is characterized by a disturbance of consciousness and a change in cognition that develop over a short period of time. The disorders included in the "Delirium" section are listed according to presumed etiology: delirium due to a general medical condition, substance-induced delirium (i.e. due to a drug of abuse, a medication, or toxin exposure), delirium due to multiple etiologies, or delirium not otherwise specified (if the etiology is indeterminate).</p> <p>5) Normal or healthy volunteers: studies that deal with healthy people (i.e. prevention is limited to people who have any form of the above); volunteer study population</p> <p>6) General population of elderly persons.</p> <p>7) Study subjects selected for depression (some patients may have dementia but not all) and where there is no stratified analysis by disease subgroup (i.e. the dementia subjects).</p>
Study Design and Control	Parallel arm randomized controlled trial; both placebo and other drug control were acceptable	Cross-over randomized control trials Studies that re-analyzed data (post-hoc) analyses combining data from several trials
Quality Score	Modified Jadad score greater than or equal to 3 out of 5	Modified Jadad score less than 3 out of 5

Category	Inclusion	Exclusion
Study Outcomes	<p>1) General cognitive function (e.g., ADAS-cog). Specific cognitive function (e.g., Wechsler Memory Tests).</p> <p>2) Global clinical assessment (e.g., CIBIC). Behavior/mood (disturbances characterized by agitation, wandering, sleep cycle disturbance, depression, obsessive compulsive activities).</p> <p>3) Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE_AD).</p> <p>4) Quality of life/ADL (e.g., Instrumental Activities of Daily Living (IADL)).</p> <p>5) Effects on primary caregiver (also referred to as caregiver burden).</p> <p>6) Safety as measured by the incidence of adverse effects (e.g., particularly serious adverse events).</p> <p>7) Acceptability of treatment as measured by withdrawal rate from trial due to side effects of the medication. (e.g., dropouts due to adverse events).</p> <p>8) Mortality.</p> <p>9) Dependency or rate of institutionalization or continued residence in own home.</p> <p>10) Use of services.</p>	None

AD = Alzheimer disease; ADAS-cog = Alzheimer's Disease Assessment Scale–cognitive subscale; ADL = activities of daily living; CIBIC = clinician-based impression of change scale; DSM = Diagnostic and Statistical Manual of Mental Disorders; MMSE = Mini-Mental Status Examination; NINCDS = National Institute of Neurological and Communicative Disorders and Stroke; NINCDS-AIREN = National Institute of Neurological and Communicative Disorders and Stroke and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences; NINCDS-ARDA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Diseases Association; VaD = vascular dementia.