**Supplementary Material**

**Search strategy**

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| 1. Alzheimer\*.mp. |  |

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| 2. AD.mp. |  |

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| 3. exp Alzheimer Disease/ |  |

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| 4. Dement\*.mp. |  |

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| 5. exp Dementia/ |  |

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| 6. exp Dementia/ |  |

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| 7. anti-depres\*.mp. |  |

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| 8. antidepres\*.mp. |  |

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| 9. exp Antidepressive Agents/ |  |

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| 10. citalopram.mp. |  |

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| 11. exp Citalopram/ |  |

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| 12. escitalopram.mp. |  |

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| 13. paroxetine.mp. |  |

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| 14. exp Paroxetine/ |  |

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| 15. fluoxetine.mp. |  |

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| 16. exp Fluoxetine/ |  |

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| 17. fluvoxamine.mp. |  |

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| 18. exp Fluvoxamine/ |  |

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| 19. trazodone.mp. |  |

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| 20. exp Trazodone/ |  |

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| 21. nefazodone.mp. |  |

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| 22. venlafaxine.mp. |  |

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| 23. duloxetine.mp. |  |

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| 24. reboxetine.mp. |  |

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| 25. bupropion.mp. |  |

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| 26. exp Bupropion/ |  |

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| 27. amoxapine.mp. |  |

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| 28. exp Amoxapine/ |  |

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| 29. amitriptyline.mp. |  |

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| 30. exp Amitriptyline/ |  |

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| 31. nortriptyline.mp. |  |

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| 32. exp Nortriptyline/ |  |

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| 33. desipramine.mp. |  |

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| 34. exp Desipramine/ |  |

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| 35. trimipramine.mp. |  |

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| 36. exp Trimipramine/ |  |

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| 37. imipramine.mp. |  |

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| 38. exp Imipramine/ |  |

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| 39. protriptyline.mp. |  |

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| 40. exp Protriptyline/ |  |

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| 41. doxepin.mp. |  |

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| 42. exp Doxepin/ |  |

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| 43. clomipramine.mp. |  |

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| 44. exp Clomipramine/ |  |

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| 45. mirtazapine.mp. |  |

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| 46. mianserin.mp. |  |

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| 47. exp Mianserin/ |  |

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| 48. moclobemide.mp. |  |

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| 49. exp Moclobemide/ |  |

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| 50. phenelzine.mp. |  |

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| 51. exp Phenelzine/ |  |

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| 52. tranylcypromine.mp. |  |

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| 53. exp Tranylcypromine/ |  |

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| 54. SSRI\*.mp. |  |

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| 55. selective serotonin reuptake inhibitor.mp. |  |

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| 56. TCA\*.mp. |  |

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| 57. depress\*.mp. |  |

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| 58. dysthymi\*.mp. |  |

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| 59. adjustment disorder\*.mp. |  |

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| 60. mood disorder\*.mp. |  |

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| 61. affective disorder.mp. |  |

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| 62. affective symptom\*.mp. |  |

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| 63. exp Depression/ |  |

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| 64. exp Depressive Disorder, Major/ |  |

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| 65. exp Depressive Disorder/ |  |

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| 66. exp Dysthymic Disorder/ |  |

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| 67. exp Alzheimer Disease/ or exp Dementia/ |  |

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| 68. (behavioural and psychological symptoms of dementia).mp. |  |

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| 69. neuropsychiatric symptom\*.mp. |  |

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| 70. NPS.mp. |  |

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| 71. exp Behavioral Symptoms/ |  |

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| 72. exp Psychomotor Agitation/ |  |

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| 73. randomized controlled trial.pt. |  |

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| 74. controlled clinical trial.pt. |  |

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| 75. randomized.ab. |  |

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| 76. randomised controlled trial.tw. |  |

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| 77. placebo.ab. |  |

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| 78. random\*.ab. |  |

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| 79. drug therapy.fs. |  |

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| 80. randomly.ab. |  |

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| 81. trial.ab. |  |

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| 82. 1 or 2 or 3 or 4 or 5 or 6 |  |

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| 83. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 |  |

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| 84. 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 |  |

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| 85. 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 |  |

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| 86. 82 and 83 and 84 and 85 |  |

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| 87. limit 86 to humans |  |

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**Supplementary Table 1**. Characteristics of excluded studies.

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| 1 | Rozzini 2010 | Not a RCT, observational study on the use of SSRIs on cognition in patients with AD of which some were depressed |
| 2 | Mowla 2007 | Double-blind placebo-controlled RCT of fluoxetine in mild to moderate AD, patients with major or minor depression were excluded |
| 3 | de Vasconcelos 2007 | Double-blind placebo-controlled RCT study of venlafaxine for depression in dementia, no separate data available for patients with AD |
| 4 | Rao 2006 | Not a RCT, open label treatment study of escitalopram for depression in AD |
| 5 | Finkel 2004 | Double-blind placebo-controlled RCT on efficacy of sertraline in people with AD and behavioral disturbances, patients with AD were not depressed and those with psychiatric disorders were excluded |
| 6 | Oslin 2003 | Double blind controlled trial of venlafaxine versus sertraline in depressed nursing home residents, no placebo arm or separate data for patients with AD |
| 7 | Moretti 2002 | Study on efficacy of SSRIs in patients with AD, randomization unclear. Patients with AD were not depressed and those with psychiatric disorders were excluded |
| 8 | Lanctot 2002 | Double-blind placebo-controlled cross-over RCT of sertraline in nondepressed patients with severe probable AD and behavioral disturbances, those with major depression were excluded |
| 9 | Raji 2001 | Not a RCT, report on three case studies on the use of mirtazapine in the treatment of depression in AD |
| 10 | Streim 2000 | Double-blind RCT of nortriptyline in nursing home residents with depression (of which some had dementia), no placebo arm and no separate data available for patients with AD |
| 11 | Karlsson 2000 | Double-blind RCT on efficacy of citalopram compared to mianserin in depressed patients with or without dementia, no placebo arm and no separate data for patients with AD |
| 12 | Katona 1998 | Double-blind RCT comparing paroxetine with imipramine in depressed patents with dementia, no placebo arm and no separate data for patients with AD |
| 13 | Trappler 1998 | Not a RCT, open label trial on use of SSRIs (fluoxetine, sertraline, and paroxetine) in depressed nursing home residents of which some had AD |
| 14 | Pfeiffer 1997 | Not a RCT, open label study on use of venlafaxine in depressed patients with AD |
| 15 | Taragano 1997 | Double-blind RCT of fluoxetine versus amitriptyline in the treatment of major depression in AD, no placebo arm |
| 16 | Roth 1996 | Double-blind placebo-controlled RCT of moclobemide in older people with dementia and/or depression, no separate data available for patients with AD |
| 17 | Volicer 1994 | Not a RCT, report on case studies on use of sertraline in people with advanced AD and depression |
| 18 | Fuchs 1993 | Double-blind placebo-controlled RCT of the effect of maprotiline in patients with dementia and mild depression, no separate data for patients with AD, excluded patients in need of antidepressant therapy |
| 19 | Passeri 1993 | Double-blind RCT of 5’-methlytetrahydrofolic acid versus trazodone on depressive symptoms in normofolatemic older people with mild to moderate dementia and depression, no placebo arm or separate data for patients with AD |
| 20 | Nyth 1992 | Double-blind placebo-controlled RCT of citalopram in depressed older people and/or dementia, no separate data available for patients with AD |
| 21 | Haupt 1991 | Not a RCT, report on a case study on use of mianserine for treating depression in AD |
| 22 | Lawlor 1991 | Double-blind placebo-controlled RCT crossover trial of meta-chlorophenylpiperasine in patients with moderate to severe AD, behavioral disturbances and levels of mild depression, patients did not meet criteria for major depression |
| 23 | Reynolds 1987 | Not a RCT, open trial of nortriptyline in older people with depression and/or dementia, no separate data available for patients with AD |
| 24 | Jenike 1985 | Not a RCT, report on case studies on use of standard antidepressants and monoamine oxidase inhibitors in depressed patients with AD |
| 25 | Mokhber 2014 | Double-blind RCT of sertraline, venlafaxine, and desipramine in depressed patients with moderate AD, no placebo arm |
| 26 | Passeri 1987 | Double-blind placebo-controlled RCT of minaprine in patients with AD and multi-infarct dementia, patients were not depressed and those with a psychiatric illness were excluded |
| 27 | Mizukami 2006 | Not a RCT, open label trial of milnacipran in treating depression in AD |

| **Supplementary Figure 1.** Summary of findings table: antidepressants versus placebo for depression in Alzheimer’s disease. | | | | | |
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| **Antidepressants compared to placebo for depression in Alzheimer's disease** | | | | | | | |
| **Patient or population**: Depression in Alzheimer's disease  **Setting**: Community and nursing home care  **Intervention**: Antidepressants  **Comparison**: Placebo | | | | | | | |
| Outcome № of participants (studies) | Relative effect (95% CI) | **Anticipated absolute effects (95% CI)** | | | Quality | | |
| **Without Antidepressants** | **With Antidepressants** | **Difference** |
| Treatment response assessed with: Depression rating scale or clinician-rated global impression of change scale Follow up: range 6 to 13 weeks № of participants: 520 (6 RCTs) | **OR 1.95** (0.97 to 3.92) | 42.2% | **58.7%** (41.4 to 74.1) | **16.5% more** (0.7 fewer to 31.9 more) | ⨁⨁⨁◯ MODERATE 1 | |  |
| Mean Depression scores  assessed with: Depression Rating Scales (Cornell Scale for Depression in Dementia or Hamilton Depression Rating Scale) Follow up: range 6 to 13 weeks № of participants: 311  (5 RCTs) | - | - | - | SMD **0.13 fewer** (0.49 fewer to 0.24 more) | ⨁⨁⨁◯ MODERATE 1 | |  |
| \***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).  CI, confidence interval; OR, odds ratio; SMD, standardized mean difference | | | | | | | |
| **GRADE Working Group grades of evidence** **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect | | | | | | | |

1Studies included few participants and events and evidence of inconsistency in whether there was an effect.