**Appendix Table N1. Characteristics of eligible studies: lipid lowering** **interventions in adults with normal cognition**

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| **Intervention Type** | **Study****DesignCountry****RoB** | **N=** | **Population****Inclusion****Age (mean)****Sex (% female)****Race (% White)****Education (mean years)****Baseline Cog** | **Intervention (INT)****Mode****Components****Frequency****Duration** | **Comparison****Mode****Components****Frequency****Duration** | **Outcome measurement****Timing** | **Outcome (Instrument)** |
| *Statins Versus Placebo*  | Trompet 2010[1](#_ENREF_1), [2](#_ENREF_2)RCTMultinationalHigh | 5804 | Adults aged 70 to 82 years with preexisting vascular disease or at increased risk of vascular disease and normal cognition.Mean age (SD): 75 (3)52% FemaleRace: NRMean years of education (SD): 15.1 (2)Mean MMSE (SD): 28 (1.5) | Pravastatin | Placebo | 42 months mean follow up | Brief Cognitive Test Performance [MMSE]Executive/Attention/Processing Speed [SCWT] [Letter-Digit Coding Test]Memory [15-Picture Learning Test Immediate And Delayed] |
| Parale 2006[3](#_ENREF_3)ObservationalIndiaHigh | 97 | Adults age ≥40 years with cardiovascular indications for statin use and normal cognition.Mean age (SD): 56.5 (8)67% FemaleRace: NRMean years education (SD): 11 (2.9)Mean MMSE (SD): 28.4 (1.8) | Atorvastatin 10 mg daily | Placebo | 6 months | Brief Cognitive Test Performance [MMSE]Executive/Attention/Processing Speed [DSST] [DVT] [TMT B]Memory [Picture-Word Learning] [COWAT] [Auditory Vigilance]Adverse Events |
| Muldoon2004[4](#_ENREF_4)RCTUnited StatesMedium | 308 | Adults aged 35 to 70 years with low-density lipoprotein cholesterol level between 160 and 220 mg/dL and normal cognition.Mean age (SD): 53.7 (9.1)52% Female86% WhiteMean years education (SD): 14.8 (3.4)Mean Digit Vigilance (errors), and Recurring Words (errors): 6.6, 81.84. | Simvastatin 10 mg daily or Simvastatin 40 mg daily | Placebo | 6 months | Executive/Attention/Processing Speeda [Composite]Memory [Memory Composite 1] [Memory Composite 2]Adverse Events |
| Heart Protection Study 2002[5](#_ENREF_5)RCTUnited KingdomMedium | 20,536 | Adults aged 40-80 years with total cholesterol concentrations ≥ 135 mg/dL and with substantial 5-risk of death from coronary heart disease and normal cognition. 28% > 70 years28% FemaleRace: NREducation: NRMean TICS-M (SD): 24.07 (NR) | Simvastatin 40 mg daily | Matching-placebo | 5 years mean follow up | DiagnosisBrief Cognitive Test Performance [TICS]Adverse Events [Hospitalizations] |
| Muldoon 2000[6](#_ENREF_6)RCTUnited StatesMedium | 209 | Adults aged 24 to 60 with hypercholesterolemia (serum low-density-lipoprotein cholesterol level ≥160 md/dL) and normal cognition.Mean age (SD): 46.4 (8.9)46% Female88% WhiteMean years education (SD): 15 (3)Mean Digit Span (SD), Digit Symbol (SD), Trailing Making B (SD): 7 (1.3), 11.8 (2.5), 65 (21). | Lovastatin 20 mg daily | Matching placebo | 6 months | Executive/Attention/Processing Speedb [Composite Measure of Attention] [Composite of Mental Flexibility] [Composite Measure of Psychomotor Speed]Executive/Attention/Processing Speedb Memory [Working Memory Composite] [Memory Retrieval Composite] |
| Santanello 1997[7](#_ENREF_7)RCTUnited StatesMedium | 431 | Adults aged ≥65 years with low-density lipoprotein-cholesterol >159 md/dL and < 221 mg/dL and normal cognition and MMSE ≥ 24.Mean age (SD): 71.2 (NR)71% Female24% WhiteEducation: NRMean Digit Symbol Substation Score (SD): 41.86 (13.88) | (I1) lovastatin 20 mg daily(I2) lovastatin 40 mg daily | Placebo | 6 months | Executive/Attention/Processing Speed [DSST]Adverse Events [Number of Events] |
| *Statin Plus Ezetimibe Versus Placebo* | Tendolkar 2010[8](#_ENREF_8)RCTNetherlandsLow | 34 | Elderly stroke-free patients with chronic or paroxysmal atrial fibrillation and normal cognition.Mean age (SD): 74 (4)24% FemaleRace: NREducation: NRMean MMSE (SD): 27.4 (2) | Atorvastatin 20mg for 2 weeks then increased to 40mg, after 4 weeks ezetimibe 10mg was added. Standard anticoagulant therapy | Matching-placebo and standard anticoagulant therapy | 1 year | Biomarker [Brain Volume Change]Brief Cognitive Test Performance [MMSE]Executive/Attention/Processing Speed [DSST]Memory [Dutch Modified Version RAVLT]Immediate and Delayed Word Recall] |
| *Statin Plus Fenofibrate Versus Statin Plus Placebo* |  |  |  |  |  |  |
| Willamson 2014[9](#_ENREF_9)(ACCORD Lipid trial)RCTUnited StatesMedium | 1538 | Middle-aged and older adults with diabetes at high risk of cardiovascular events with low-density lipoprotein cholesterol levels of less than 100 mg/dL and normal cognition.Mean age (SD): 62.5 (5.7)38.9% Female73% White13% <High school 25% High school graduate33% Some college 28% college graduate or moreMedian MMSE (25th and 75th percentile): 28 (26-29) | Fenofibrate plus statin | Placebo plus statin | 40 months | Brief Cognitive Test Performance [MMSE]Executive/Attention/Processing Speed [SCWT] [DSST]Memory [RAVLT] |
| *Comparative Effectiveness* | Muldoon2004[4](#_ENREF_4)RCTUnited StatesMedium | 189 | Adults aged 35 to 70 years with low-density lipoprotein cholesterol level between 160 and 220 mg/dL and normal cognition.Mean age (SD): 53.7 (9.1)52% Female86% WhiteMean years education (SD): 14.8 (3.4)Mean Digit Vigilance (errors), and Recurring Words (errors): 6.6, 81.84. | Simvastatin 10 mg daily | Simvastatin 40 mg daily | 6 months | Executive/Attention/Processing Speeda [Composite 1] [Composite 2]Memory [Memory Composite]Adverse Events |
| Carlsson 2002[10](#_ENREF_10)RCT-CrossoverUnited StatesMedium | 41 | Adults ≥70 years with low-density lipoprotein-cholesterol ≥140 mg/dl and tri-glyceride levels ≤140 mg/dl and normal cognition.Mean age (SD): 76.3 (4.3)68% FemaleRace: NREducation: NRMean Digit Symbol Substitution (SD): 42.45 (9.69) | Pravastatin 20 mg daily | Tocopherol 440 IU daily | 6 months | Executive/Attention/Processing Speed [DSST]Adverse Events [Physical Adverse Events] [Hospitalizations] |

aMuldoon 20043 grouped tests into composite measures and if there was a significant difference in the composite measure individual items were evaluated. The composite measures were: 1) composite Executive/Attention/Processing Speed 1: Elithorn mazes, digit vigilance, recurring words, grooved pegboard; 2) memory composite 1: mirror tracing, 4-word short term memory, 3) memory composite 1: digit symbol, stroop interference, trail making B, digit span, complex figure, letter rotation;
bMuldoon 20005 grouped tests into composite measures and if there was a significant difference in the composite measure individual items were evaluated. The composite measures were: 1) composite measure of attention: digit vigilance, letter rotation, digit span, recurring words; 2) composite measure of psychomotor speed: grooved pegboard, Elithorn Maze, Digit Symbol; 3) composite of mental flexibility: Stroop Interference, Trail Making Digit Vigilance, Letter Rotation; 4) working memory composite: Associative Learning, Digit Span, 5) memory retrieval composite: Controlled Oral Word Association, Digit Symbol Recall, Verbal Recall, Complex Figure.

DVT=Digit Vigilance Test; COWAT=Controlled Oral Word Association Test; DSST=Digit Symbol Substitution Test; IU=international units; mg=milligrams; MMSE=Mini-Mental State Examination; NR=not reported; RCT=randomized controlled trial; RAVLT=Rey’s Auditory Verbal Learning Test; SCWT = Stroop Color Word Test; SD=standard deviation; TICS=Telephone Interview for Cognitive Status