**Supplementary Materials**

**Supplementary Table 1.** Articles meeting criteria but not providing data for meta-analysis

|  | Study (no. of subjects) | Study name (source) | Observation period, years (SD) | Cholesterol measures | Outcome | Outcome Measure(s) | Mean age, years (SD) | Female (%) | Education (years) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | Kalmijn et al., 1996 [1](n = 718) | Zutphen Elderly Study (Zutphen, the Netherlands)  | Up to 8 years | TC, HDL-C | Cognitive decline | MMSE | APOE ε4 absent: 74.7 (4.2)APOE ε4 present: 74.5 (4.3) | 0 | *APOE ε4*, absent (higher education): 25%*APOE ε4*, present (higher education): 50% |
| 2 | Kivipelto et al., 2001## [2](n = 1,352)  | N/A (Random sample studied within the framework of the North Karelia Project and the FINMONICA study during 1972, 1977, 1982, and 1987) | 21 | TC | MCI | MMSE, detailed neuropsychological evaluation, CDR Scale  | MCI (midlife) = 51.7 (5.8)MCI (late-life) = 72.8 (4.1)No MCI (midlife) = 50.1 (6.0)No MCI (late-life) = 71.0 (3.9) | 38.3%No MCI females = 61.7% | MCI = 6.8 (2.04)No MCI = 8.8 (3.5) |
| 3 | Tan, et al., 2003\* [3](n = 1,026) | Framingham Study (Framingham, Massachusetts) | Up to 40 years | TC, HDL-C | Incident AD | MMSE, CDR scale, DSM-IV, NINCDS-ADRDA | At exam 20 Men = 75.7 (5.2)Women = 76.4 (5.4)Total = 76.1 (5.3) | 63.0 | Data not available |
| 4 | Piguet et al., 2003 [4](n = 377) | Sydney Older Persons Study (Sydney, Australia) | 6 | TC | Cognitive decline | MMSE, ICD-9, DSM-IIIR | 80.4 (3.7) | 46.7 | 10.1 (1.9) |
| 5 | Karlamangla et al., 2004 [5](n = 267) | MacArthur Studies of Successful Aging (USA) | 4.5 | TC, HDL-C | Cognitive function | SPMSQ | 74 (median) | 58.4 | Data not available |
| 6 | Reitz et al., 2005 [6](n = 1,147) | (Random sample of Medicare recipients aged 65+ years, residing in Manhattan, USA) | 7 | Fasting TC and TG levels, HDL-C and LDL-C | Memory decline | Benton visual retention test, Selective reminding test | 76.3 (5.8) | 68.4 | 8.6 (4.6)  |
| 7 | Komulainen et al., 2007 [7](n = 101) | N/A (women examined as part of a large population-based risk factor survey, North Karelia and other areas in Finland) | 12 | TC, HDL-C, LDL-C | Cognitive function | MMSE | Age at follow up. No metabolic syndrome = 74.9 (3.0)Metabolic syndrome = 75.5 (3.0) |  100 | No metabolic syndrome = 9.0 (3.6)Metabolic syndrome = 8.2 (3.7) |
| 8 | Stewart et al., 2007 [8](n = 1,027) | The Honolulu-Asia Aging Study (Japanese American men born on the island of Oahu, Hawaii) | 26 | TC | Incident dementia | DSM-IIIR, NINCDS-ADRDA | Total = 80.2 (4.2)No dementia = 80.0 (4.0)Incident dementia = 83.7 (4.9) | 0 | Total = 10.8 (3.1)No dementia = 10.9 (3.0)Incident dementia = 9.2 (3.5) |
| 9 | Artero et al., 2008 [9](n = 6892) | Three City Study (Bordeaux, Dijon and Montpellier, France) | 4 | TC | MCI, dementia | Benton Visual retention Test, the Trail Making Test, the Isaacs’ Set Test and a word recall, DSM-IV | MCI = 74.6 (5.7)Normal = 73.1 (4.9) | MCI = 64.6Normal = 56.6 | Low Edu (MCI) = 24.7%Low Edu Normal = 22.5%Medium Edu (MCI) = 62.2%Medium Edu (Normal) = 54.2%High Edu (MCI) = 13.1%High Edu (Normal) = 24.3% |
| 10 | Mielke et al., 2008 [10](n = 436) | The Women’s Health and Ageing Study II (Baltimore, Maryland) | Up to 9 years | TC, HDL-C | Cognitive decline | MMSE, Trail Making Test, Hopkins Verbal Test Revised, Ourdue Pegboard | 74.5 (2.8) | 100 | 12.5 (3.3) |
| 11 | van Vliet et al., 2010 [11](n = 599) | Leiden 85-plus Study (the Netherlands) | 5 | TC, HDL-C | Cognitive decline | MMSE | 85 | Survivors = 72%Non-survivors = 59% | Survivors (>6 years education) = 37.0%Non-survivors (>6 years education) = 33.0% |
| 12 | Infurna, 2013[12](n = 4,177) | Health and Retirement Study (USA) | 4 | HDL-C | Memory change | Immediate and delayed free-recall tests | 67 (10.4) | 59% | 13 (3.0) |
| 13 | de Bruijn et al., 2014 [13](n = 984) | Rotterdam Study (Rotterdam, the Netherlands) | 8.7 (3.4) | TC, HDL-C | Dementia/AD | MMSE, GMS, CAMDEX, DSM-IIIR, NINCDS-ADRDA | Incident dementia = 72.0 (7.1) | 55.8 | Data not available |
| 14 | Yaffe et al., 2014 [14](n = 3,381) | Coronary Artery Risk Development in Young Adults (CARDIA) Study | 25 | TC | Cognitive Function | Digit Symbol Substitution Test, Stroop test, Rey Auditory Verbal Learning Test | 50.2 (3.6) | 56.4 | 15.5 (2.5) |
| 15 | Hogenkamp et al., 2014 [15](n = 652) | Uppsala Longitudinal Study of Adult Men (Uppsala County, Sweden) | 7 | HDL-C, LDL-C | Cognitive function | MMSE, Trail making tests A and B | 70 | 0 | Primary = 50.0%Secondary = 32.0%University = 18.0% |
| 16 | Thacker et al., 2014 [16](n = 17,761) | The Reasons for Geographic and Racial Differences in Stroke Study (South-east USA) | 4 | TC | Incident cognitive impairment | Six item screener and verbal learning, memory and fluency tests | Cognitive Impairment = 58.8Not impaired = 57.3 | 55 | Cognitive impairment (high school graduate) = 24.3%Not impaired (high school graduate) = 25.2% |
| 17 | Wendell et al., 2014 [17](n = 1601) | Baltimore Longitudinal Study of Aging (Baltimore, USA) | 6.4 (5.3) | TC | Neuropsychological function | Multiple tests including MMSE, Trail Making Test, Fluency tests and Boston Naming Test, CVLT | 54.4 (16.4) | 49 | 16.7 (2.5) |

\*Age at baseline unclear in manuscript

AD, Alzheimer’s disease; APOE, apolipoprotein; CAMDEX, Cambridge Mental Disorders of the Elderly Examination; CDR, Clinical Dementia Rating; CVLT, California Verbal Learning Test; DSM, Diagnostic and Statistical Manual of Mental Disorders; GMS, Geriatric Mental State; HDL-C, high density lipoprotein; ICD-9, 9th revision of the International Statistical Classification of Diseases and Related Health Problems; LDL-C, low density lipoprotein; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; SPMSQ, Short Portable Mental Status Questionnaire; TC, total cholesterol; TG, triglycerides

**Supplementary Table 2.** Descriptive statistics for baseline serum cholesterol measure for each study included in meta-analyses.

|  | Study (no. of subjects) | Study name (source) | Mean serum cholesterol at baseline (SD) | Mean Serum Cholesterol Range at Baseline | Year of Baseline Serum Cholesterol Measurement |
| --- | --- | --- | --- | --- | --- |
| 1 | Yoshitake et al., 1995 [18](n = 828) | N/A (non-demented residents of Hisayama Town, Kyushu, Japan | MenTC (mg/dl): 177 (34)TG (mg/dl): 110 (79)HDL (mg/dl): 50 (15)LDL (mg/dl): 412 (121)VLDL (mg/dl): 113 (126)WomenTC (mg/dl): 198 (34)TG (mg/dl): 110 (53)HDL (mg/dl): 52 (14)LDL (mg/dl): 490 (131)VLDL (mg/dl): 113 (90) | N/A | 1985 |
| 2 | Hyman et al., 1996 [19](n = 1,899) | Iowa 65+ Rural Health Study (Iowa, USA) | Not provided | N/A | 1982 |
| 3 | Notkola et al., 1998 [20](n = 444) | Seven Countries Study (444 men in the Finnish Cohorts) | Men 6.6 mmol/l | N/A | 1959 |
| 5 | Slooter et al., 1999 [21](n = 244 (dementia cases, 1,002 controls) | Rotterdam Study (Rotterdam, the Netherlands) | TC (all dementia) mmol/L: 6.26 (1.16) TC (controls) mmol/L: 6.69 (1.22)HDL (all dementia) mmol/L: 1.34 (0.38)HDL (controls) mmol/L: 1.34 (0.38) | N/A | Not provided |
| 6 | Kivipelto et al., 2001 [22](n = 1,449) | N/A (participants derived from random population-based samples in Kuopio and Joensuu, Eastern Finland) | Subjects with MCITC midlife: 7.2 (1.2) mmol/LTC late-life: 5.9 (1.2)Subjects without MCITC midlife: 6.7 (1.2)TC late-life: 5.8 (1.0) | N/A | 1972 |
| 7 | Reitz et al., 2004 [23](n = 1,168) | N/A (Random sample of Medicare recipients aged 65+ years, residing in Manhattan, USA) | TC: 198.8 mg/dL (5.1 mmol/L)Non-HDL-C: 151.4 mg/dL (3.9 mmol/L)HDL-C: 47.4 mg/dL (1.2 mmol/L)TG: 155.9 mg/dL (1.8 mmol/L)LDL-C: 120.1 mg/dL (3.1 mmol/L) | N/A | 1992 |
| 8 | Solfrizzi et al., 2004 [24](n = 2,963; n = 1,555 without impairment and n = 121 with MCI) | Italian Longitudinal Study on Aging (Eight municipalities in Italy) | Normal SubjectsTC: 221.1 (40.9) mg/dL or 5.7 (1.1) mmol/LHDL-L: 49.0 (11.2) mg/dL or 1.3 (0.3) mmol/L | N/A | 1992-1993, 1995-1996 |
| 9 | Li et al., 2005 [25](n = 2,112) | The Adult Changes in Thought Study (Seattle, USA) | Subjects with dementiaTC: 231.1 (39.0) mg/dLSubjects without dementiaTC: 230.7 (37.7) mg/dL | N/A | 1994-1996 |
| 10 | Mielke et al., 2005 [26](n = 382) | N/A (Sample of 70-year old residents of Gothenburg, Sweden) |  | Quartile 1TC age 70: 3.51-6.07 mmol/L or 136–234 mg/dLTC age 75: 3.21–5.30 mmol/L or 124–204 mg/dLTC age 79: 3.05–5.17 mmol/L or 118–199 (mg/dL)TG age 70: 0.44–0.79 mmol/L or 39–70 (mg/dL)TG age 75: 0.41–1.01 mmol/L or 36–89 (mg/dL)TG age 79: 0.10–0.99 mmol/L or 9–88 mg/dLQuartile 2TC age 70: 6.08–7.18 mmol/L or 235–277 mg/dLTC age 75: 5.31–6.12 mmol/L or 205–236 mg/dLTC age 79: 5.18–6.10 mmol/L or 200–235 mg/dLTG age 70:0.80–1.06 mmol/L or 71–93 mg/dLTG age 75: 1.02–1.30 mmol/L or 90–115 mg/dLTG age 79: 1.00–1.29 mmol/L or 89–114 mg/dLQuartile 3TC age 70: 7.19–8.02 mmol/L or 278–310 mg/dLTC age 75: 6.13–7.02 mmol/L or 237–271 mg/dLTC age 79: 6.11–6.81 mmol/L or 236–263 mg/dLTG age 70: 1.07–1.43 mmol/L or 94–126 mg/dLTG age 75: 1.31–1.78 mmol/L or 116–157 mg/dLTG age 79: 1.30–1.69 mmol/L or 115–149 mg/dLQuartile 4 TC age 70: 8.03–11.44 mmol/L or 311–442 mg/dLTC age 75: 7.03–9.29 mmol/L or 272–359 mg/dLTC age 79: 6.82–9.10 mmol/L or 264–352 mg/dLTG age 70: 1.44–2.54 mmol/L or 127–225 mg/dLTG age 75: 1.79–3.90 mmol/L or 158–345 mg/dLTG age 79: 1.70–3.80 mmol/L or 150–336 mg/dL | 1901-1902 |
| 11 | Reitz et al., 2008 [27](n = 854) | N/A (Random sample of Medicare recipients aged 65+ years, residing in Manhattan, USA) | TC (mg/dl)No MCI: 200.6 (41.2)Incident total MCI: 195.5 (40.9)HDL-C (mg/dl)No MCI: 47.6 (15.8)Incident total MCI: 46.9 (15.5)TG (mg/dl)No MCI: 163.5 (88.5)Incident total MCI: 157.5 (87.5)LDL-C (mg/dl)No MCI: 120.2 (36.4)Incident total MCI: 116.6 (34.3) | N/A | 1992 - 1994 |
| 12 | Raffaitan et al., 2009 [28](n = 7,738) | French Three City Study (Bordeaux, Dijon and Montpellier, France) | Not provided | N/A | 1999 - 2000 |
| 13 | Reitz et al., 2010 [29](n = 1,130) | N/A (Random sample of Medicare recipients aged 65+ years, residing in Manhattan, USA) | TC: 199.2 (38.2) mg/dLHDL-C: 48.3 (14.6) mg/dLNon-HDL-C: 150.9 (37.0) mg/dL | N/A | 1999 - 2001 |
| 14 | Mielke et al., 2010 [30](n = 1,462) | The Prospective Population Study of Women (Gothenburg, Sweden) | Mean cholesterol level by birth cohortAll-cause dementia1968: 7.2 (1.0) mmol/L1974: 7.2 (1.2) mmol/L1980: 7.3 (1.2) mmol/L1992: 6.4 (1.2) mmol/L2000: 6.2 (1.3) mmol/LNo dementia1968: 6.8 (1.1) mmol/L1974: 6.9 (1.2) mmol/L1980: 7.0 (1.2) mmol/L1992: 6.3 (1.0) mmol/L2000: 6.1 (1.0) mmol/L | N/A | 1968 - 1969 |
| 15 | Beydoun et al., 2011 [31](n = 1,604) | Baltimore Longitudinal Study of Aging (Baltimore, USA) | TC: 219.9 (40.6) mg/dlHDL-C: 49.0 (13.0) mg/dl | N/A | 1958 |
| 16 | Ancelin et al., 2013 [32](n = 7,053) | French Three-City Study (Bordeaux, Dijon and Montpellier, France) | MenTG: 1.28 mmol/lTC: 5.52 mmol/lLDL-C: 3.50 mmol/lHDL-C: 1.44 mmol/lWomenTG: 1.21 mmol/lTC: 5.99 mmol/lLDL-C: 3.70 mmol/lHDL-C: 1.73 mmol/l | N/A | 1999 - 2001 |
| 17 | Taniguchi et al., 2014 [33](n = 682) | N/A (sample of participants aged 70+ years who lived in Kusatsu, Japan in 2002) | Cognitive declineTC: 201 (34) mg/dLHDL-C: 59.0 (14.0) mg/dLTG: 139 (68) mg/dLNo cognitive declineTC: 207 (34) mg/dLHDL-C: 62.4 (15.8) mg/dLTG: 135 (90) mg/dL | N/A | 2002 |
| 18 | Toro et al., 2014 [34](n = 381) | Interdisciplinary Longitudinal Study on Adults Development and Ageing (Germany) | TC in those with AD: 246.1 (40.7) mg/dlTC in those with MCI: 247.0 (43.8) mg/dlTC in cognitively healthy participants: 233.0 (38.0) mg/dl | N/A | 1993 - 1994 |

DDL

HDL-C, high density lipoprotein; LDL-C, low density lipoprotein; MCI, mild cognitive impairment; TC, total cholesterol; TG, triglycerides; VLDL, very low density lipoprotein

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**Supplementary Figure 1.** Forest plot of studies with exposure to high TC in late-life and AD, Any Dementia, MCI, or Cognitive decline as an outcome.



**Supplementary Figure 2.** Funnel plot of studies included in meta-analysis of late-life high TC and risk of AD, VaD, MCI, or cognitive decline.

