**Supplemental Table 1.** **Prospective studies of psychosocial factors in associations with cognitive decline and Alzheimer’s disease**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Publication year** | **Studies** | **Follow-up(years)** | **No. of participants** | **Age at baseline (years)** | **Female (%)** | **Risk factor measurements** | **Risk factor** | **Outcomes** |
| Gottesman, R. F.(1) | 2017 | The Atherosclerosis Risk in Communities Cohort | 25 | 15,744 | 44-66 | 55 | In-person visits, hospitalization surveillance,  telephone calls | Lower educational attainment | With increased risk of dementia |
| Wilson, R. S.(2) | 2012 | The Rush Memory and Aging Project | 5 | 1,076 | Mean 80 | 74 | Annual evaluation using a 5-point scale | More frequent mental stimulation | With better cognitive functioning |
| Najar, J.(3) | 2019 | The Gothenburg H70 Birth Cohort Studies | 44 | 800 | Mean 47 | 100 | Semi-structured psychiatric interviews | Cognitive  activity | With a reduced risk of AD |
| Marioni, R. E.(4) | 2015 | The Paquid cohort | 20 | 2,854 | Mean 77 | 59 | A scale for late-life social, intellectual engagement | Social engagement | With a decreased risk of dementia |
| Zhou, Z.(5) | 2018 | The Chinese Longitudinal Healthy Longevity Survey | 9 | 7,511 | ≥65 | 54 | Questions | Social engagement | With a lower risk of dementia |
| Amieva, H.(6) | 2010 | The Paquid cohort | 15 | 2,089 | ≥65 | 60 | Questionnaire | Social network | With a reduced risk of AD |
| Sommerlad, A.(7) | 2019 | The Whitehall II cohort study | 28 | 10,228 | 35-55 | 33 | A self-report questionnaire | Social contact | Conferring higher cognitive reserve |
| Fancourt, D.(8) | 2020 | The English Longitudinal Study of Ageing | 12 | 9,550 | >50 | 45 | Questions | Community engagement | With a lower risk of developing dementia |
| Biddle, K. D.(9) | 2020 | The Harvard Aging Brain Study | 4 | 257 | Mean 74 | 60 | Self-report | Marital status (the widowed) | With accelerated β-amyloid-related cognitive decline |
| Saito, T.(10) | 2018 | The Aichi Gerontological Evaluation Study prospective cohort | 9 | 13,984 | ≥65 | 51 | Questions | Social relationship | With decreased risk of dementia |
| Geda, Y. E.(11) | 2014 | The Mayo Clinic Study of Aging | Median 5 | 1,587 | Median 80 | 50 | NPI-Q | Depression | With an increased risk of MCI |
| Holmquist, S.(12) | 2020 | The Swedish National Patient Register (Matched cohort) | 11 | 238,772 | >50 | 61 | ICD | Depression | With increased risk of dementia |
| Holmquist, S.(12) | 2020 | The Swedish National Patient Register (The sibling cohort) | >20 | 50,644 | >50 | 58 | ICD | Depression | With increased risk of dementia |
| Almeida, O. P.(13) | 2016 | The Health in Men Study | 5 | 4,568 | 70-89 | 0 | The GDS-15 | Depressive symptoms | With increased risk rate of cognitive impairment |
| Almeida, O. P.(14) | 2017 | The Health in Men Study | 14 | 4,922 | 71-89 | 0 | Questions and the Geriatric Depression Scale | Depression | With increased risk of developing dementia |
| Steenland, K.(15) | 2012 | The large National Alzheimer’s Coordinating Center database | Mean 3 | 8,855 | 73 | 61 | The GDS-15 or the NPI-Q | Depression | With an increased risk of MCI |
| Song, H.(16) | 2020 | The Swedish National Patient Register (Matched cohort) | About 5 | 657,083 | <50 | 61 | ICD-9 | Stress-related disorders | With increased risk of AD |
| Song, H.(16) | 2020 | The Swedish National Patient Register (The sibling cohort) | About 5 | 123,321 | <50 | 54 | ICD-9 | Stress-related disorders | With increased risk of AD |
| Sindi, S.(17) | 2017 | The CAIDE study | 30 | 2,000 | Mean 50 | 63 | Questions | Midlife work-related stress | With an increased risk of AD |
| Wang, H. X.(18) | 2012 | The Kungsholmen Project | 6 | 913 | ≥75 | 0 | Questions | Psychosocial stress at work | With an increased risk of AD |
| Gradus, J. L.(19) | 2018 | The Danish National Patient Registry | 17 | 279,188 | ≥40 | NA | The national Danish Psychiatric Central Research Registry | Stress Disorders | With higher risk of dementia |
| Flatt, J. D.(20) | 2018 | The Kaiser Permanente Northern California health system | Mean 8 | 499,844 | >60 | 55 | ICD-9 | Post-traumatic stress disorder | With increased risk of dementia |
| Wang, T. Y.(21) | 2016 | The Taiwan National Health Insurance Research Database | About 7 | 8,750 | >55 | 77 | ICD-9 | Post-traumatic stress disorder | With higher risk of developing dementia |

The CAIDE study = The Cardiovascular Risk Factors, Aging and Dementia study; AD = Alzheimer’s disease; MCI = mild cognitive impairment; NPI-Q=Neuropsychiatric Inventory Questionnaire; ICD-9 = International Classification of Diseases-9th Revision; GDS-15 = Geriatric Depression Scale 15

**Supplemental Table 2.** **Prospective studies of pre-existing diseases in associations with cognitive decline and Alzheimer’s disease**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Publication year** | **Studies** | **Follow-up(years)** | **No. of participants** | **Age at baseline (years)** | **Female (%)** | **Risk factor measurements** | **Risk factor** | **Outcomes** |
| Marseglia, A.(22) | 2019 | The Swedish National Study on Aging and Care-Kungsholmen | 9 | 2,746 | ≥60 | 63 | Using High Performance Liquid Chromatography to measure HbA1c levels and self-report | Diabetes and prediabetes | With faster cognitive decline |
| Zheng, F.(23) | 2018 | The English Longitudinal Study of Ageing | Mean 8 | 5,189 | Mean 66 | 55 | Using a Tosoh G7 analyser to measure HbA1c levels | Diabetes | With faster cognitive decline |
| Marseglia, A.(24) | 2018 | The Swedish Adoption/Twin Study of Aging | 23 | 793 | ≥50 | 59 | Using an enzymatic method to test blood glucose level and self-report | Prediabetes and diabetes | With faster cognitive decline |
| McGrath, E. R.(25) | 2017 | The Framingham Offspring Study | Mean 8 | 1,440 | Mean 69 | 47 | Recorded in a standardized fashion | Systolic hypertension, decreased SBP | With an increased risk of AD |
| Rajan, K. B.(26) | 2018 | The Chicago Health and Aging Project | 18 | 2,137 | ≥65 | 63 | Using mercury sphygmomanometers and using digital oscillometric devices | Late life BP | With a U-shaped association of AD |
| Oishi, E.(27) | 2017 | The Hisayama study | 5 | 1,674 | ≥60 | 56 | Using a validated digital electronic device based on the cuff oscillometric method | BPV | With an increased risk of AD |
| Yoo, J. E.(28) | 2020 | The Korean National Health Insurance Service | 6 | 23,503,802 | Mean 55.5 | 48 | Measured by a trained clinician and using the average of the two brachial BP | BPV | With an increased risk of AD |
| Schilling, S.(29) | 2017 | The 3C Study | 13 | 7,470 | Mean 74 | 61 | Using enzymatic methods | Hypercholesterolemia, LDL-C | With an increased risk of AD |
| Marcum, Z. A.(30) | 2018 | The Adult Changes in Thought study | About 5 | 4,368 | ≥50 | 59 | Using all recorded measures in the laboratory database | non-HDL-C | With a U-shaped association of AD |
| Svensson, T.(31) | 2019 | The Japan Public Health Centre-based prospective Study | 19 | 1,299 | About 54 | NA | Using enzymatic methods | HDL-C | With a decreased risk of MCI |
| Tolppanen, A. M.(32) | 2014 | The CAIDE study | 26 | 1,304 | Mean 50, 71and 79 | 61 | BMI measurements | Late-life high BMI | With a decreased risk of AD |
| LeBlanc, E. S.(33) | 2017 | The Study of Osteoporotic Fractures | 20 | 1,289 | Mean 68 and 88 | 100 | BMI measurements | Late life weight loss | With an increased risk of MCI |
| Alhurani, R. E.(34) | 2016 | The Mayo Clinic Study of Aging | Mean 4 | 1,895 | ≥70 | 49 | BMI measurements | Late life weight loss | With an increased risk of MCI |
| Rusanen, M.(35) | 2014 | The CAIDE study | 26 | 1,510 | Mean 50 | 62 | Questionnaire | Atrial fibrillation | With an increased risk of AD |
| Dublin, S.(36) | 2011 | The ACT study | Mean 7 | 3,045 | Median 74 | 60 | ICD-9 | Atrial Fibrillation | With an increased risk of AD |
| Kim, D.(37) | 2019 | The Korea National Health Insurance Service Senior cohort | About 8 | 262,611 | ≥60 | 56 | ICD-10 | Atrial Fibrillation | With an increased risk of AD |
| Jefferson, A. L.(38) | 2015 | The Framingham Heart Study | Median 8 | 1,039 | Mean 69 | 53 | Brain MRI | Lower cardiac index | With an increased risk of AD |
| Akoudad, S.(39) | 2016 | The Rotterdam Study | Mean 6 | 3,257 | Mean 60 | 55 | Brain MRI | Cerebral microbleeds | With an increased risk of AD |
| Romero, J. R.(40) | 2017 | The Framingham Heart Study | Mean 7 | 1,296 | Mean 72 | 54 | Brain MRI | Cerebral microbleeds | With an increased risk of AD |
| Fann, J. R.(41) | 2018 | The Danish Civil Registration System | 14 | 2,794,852 | >50 | 52 | Using the Danish National Patient Register | Traumatic brain injury | With an increased risk of AD |
| Yaffe, K.(42) | 2019 | The Veterans Health Administration | Mean 4 | 109,140 | ≥55 | 100 | ICD-9 | Traumatic brain injury | With an increased risk of dementia |
| Chen, S.(43) | 2020 | The Hisayama Study, | 10 | 1,588 | 60-99 | 57 | Using the high- performance liquid chromatography method | High serum Hcy | With an increased risk of AD |
| Hooshmand, B.(44) | 2019 | The Swedish National Study on Aging and Care-Kungsholmen | 6 | 2,570 | Mean 73 | 57 | Using tandem mass spectrometry | High serum Hcy | With an increased risk of AD |
| Hooshmand, B.(45) | 2010 | The CAIDE study | 7 | 271 | 65-79 | 62 | Chemiluminescent microparticle immunoassay | High serum Hcy | With an increased risk of AD |
| Osler, M.(46) | 2019 | The Danish National Patient Registry | 39 | 942,567 | ≥65 | 0 | ICD-8, ICD-10 | Hearing loss | With an increased rate of dementia |
| Liu, C. M.(47) | 2019 | The National Health Insurance Research Database | 12 | 16,270 | 45-64 | 43 | ICD-9 | Hearing loss | With higher risk of dementia |
| Saito, S.(48) | 2018 | The Ohasama study | 4 | 140 | ≥65 | 69 | Counting the number of remaining teeth | Tooth loss | With an increased risk of MCI |
| Okamoto, N.(49) | 2015 | The Fujiwara-kyo Study | 5 | 2,335 | >65 | 48 | Using the blinded single observer method | Tooth loss | With an increased risk of MCI |
| Takeuchi, K.(50) | 2017 | The Hisayama Study | 5 | 1,566 | ≥60 | 56 | Following the Third National Health and Nutrition Examination Survey | Tooth loss | With an increased risk of AD |

The CAIDE study = The Cardiovascular Risk Factors, Aging and Dementia study; AD = Alzheimer’s disease; SBP = systolic blood pressure; BP = blood pressure; BPV = blood pressure variability; LDL-C = low-density lipoprotein cholesterol; HDL-C= high-density lipoprotein cholesterol; MCI = Mild cognitive impairment; BMI = body mass index; Hcy = homocysteine; ICD-9 = International Classification of Diseases-9th Revision; MRI = magnetic resonance imaging

**Supplemental Table 3.** **Prospective studies of environmental factors, lifestyle factors in associations with cognitive decline and Alzheimer’s disease.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Publication year** | **Studies** | **Follow-up(years)** | **No. of participants** | **Age at baseline (years)** | **Female (%)** | **Risk factor measurements** | **Risk factor** | **Outcomes** |
| Oudin, A.(51) | 2016 | The Betula study | ≥15 | 1,806 | ≥55 | 57 | Using a land-use regression model with a spatial resolution of 50 m × 50 m | Traffic-related air pollution | With higher risk of risk of AD |
| Chen, H.(52) | 2017 | The Ontario Population Health and Environment Cohort | ≥10 | 2,066,639 | Mean 67 | 53 | Using satellite observations, land-use regression model, and an optimal interpolation method | Ambient air pollution | With higher incidence of dementia. |
| Grande, G.(53) | 2020 | The Swedish National Study on Aging and Care in Kungsholmen | Mean 6 | 2,927 | Mean 74 | 63 | Using dispersion models for outdoor levels at residential addresses | Air pollution | With a higher risk of dementia |
| Oudin, A.(54) | 2018 | The longitudinal Betula study | ≥15 | 1,806 | ≥55 | 57 | Using a land-use regression model with a spatial resolution of 50 m × 50 m | Air pollution | With a higher risk of dementia |
| Kishimoto, H.(55) | 2016 | The Hisayama Study | 17 | 803 | ≥65 | 61 | Questionnaire | Leisure-time physical activity | With lower risk of risk of AD |
| Kulmala, J.(56) | 2014 | The CAIDE study | Mean 30 | 3,559 | Mean 50 | 57 | Question | Poor physical fitness | With higher dementia risk |
| Buchman, A. S.(57) | 2012 | The Rush Memory and Aging Project | Mean 4 | 716 | Mean 82 | 76 | Actigraphy | Total daily physical activity | With lower risk of AD |
| Sabia, S.(58) | 2017 | The Whitehall II study | 28 | 10,308 | 35-55 | 33 | Questionnaire | Physical activity | No association with dementia |
| Tolppanen, A.(59) | 2015 | The CAIDE study | 28 | 3,559 | Mean 50 | 57 | Question | Leisure-time physical activity | With lower risk of AD |
| Benedict, C.(60) | 2015 | The Uppsala Longitudinal Study of Adult Men | 40 | 2,322 | 50 | 0 | Questions | Sleep disturbance | With higher risk of AD |
| Lutsey, P. L.(61) | 2018 | The Atherosclerosis Risk in Communities Study | 15 | 1,667 | Mean 63 | 53 | Polysomnography | OSA | With higher risk of AD |
| Westwood, A. J.(62) | 2017 | The Framingham Heart Study | 10 | 2,457 | Mean 72 | 57 | Self-report | Prolonged sleep duration | With an increased risk of AD |
| Chen, J. C.(63) | 2016 | The Women’s Health Initiative Memory Study | 13 | 7,444 | ≥65 | 100 | Self-report | Sleep duration | V-shaped association with MCI/dementia risk |
| Jørgensen, J. T.(64) | 2020 | The Danish Nurse Cohort | ≥6 | 28,731 | ≥44 | 100 | Questions | Shift work | With increased risk of dementia |
| Deal, J. A.(65) | 2020 | The Atherosclerosis Risk in Communities study | ≥12 | 13,002 | 63 | 57 | Self-report | Cigarette smoking and time of quitting | With benefits to the cognition |
| Choi, D.(66) | 2018 | The Korean National Health Insurance System-National Health Screening Cohort | 8 | 46,140 | ≥60 | 0 | Questionnaire | Smoking cessation | With reduced risk of AD |
| Mons, U.(67) | 2013 | The prospective statewide cohort study in Germany | 5 | 1,697 | ≥65 | 59 | Standardized  questionnaires | Smoking | With increased risk of cognitive impairment |
| Langballe, E. M.(68) | 2015 | The Nord-Trøndelag Health study | >27 | 40,435 | ≥38 | 51 | Questionnaire | Frequent alcohol drinking | With increased risk of AD |
| Sabia, S.(69) | 2018 | The Whitehall II study | 28 | 10,308 | 35-55 | 33 | Questionnaire | Alcohol consumption >14 units/week | With greater risk of dementia |
| Zhang, R.Y.(70) | 2020 | The Health and Retirement Study | 9 | 19,887 | 62 | 60 | Questions | Alcohol drinking (10-14 drinks/week) | With benefits to the cognition |
| Handing, E. P.(71) | 2015 | The population-based Swedish Twin Registry | >43 | 12,326 | Mean 54 | 56 | The Swedish Twin Registry questionnaire | Alcohol consumption (>12 grams/day) | With greater risk of dementia |
| Topiwala, A.(72) | 2017 | The Whitehall II cohort | >30 | 550 | Mean 43 | 20 | The CAGE screening questionnaire | Moderate alcohol consumption | With adverse effects on cognition |
| Sugiyama, K.(73) | 2016 | The Ohsaki Cohort 2006 Study | 6 | 13,137 | ≥65 | 55 | FFQ | Coffee consumption | With a lower risk of dementia |
| Tomata, Y.(74) | 2016 | The Ohsaki Cohort 2006 Study | 6 | 13,645 | ≥65 | 56 | FFQ | Green tea consumption | With a lower risk of incident dementia |
| Noguchi-Shinohara, M.(75) | 2014 | The Nakajima Project | Mean 5 | 490 | >60 | 67 | A self-administered questionnaire | Green tea consumption | With a lower incidence of cognitive decline |

AD = Alzheimer’s disease; The CAIDE study = = The Cardiovascular Risk Factors, Aging and Dementia study; OSA = obstructive sleep apnea; MCI = mild cognitive impairment; FFQ = Food-frequency questionnaire; CAGE = cut-annoyed-guilty-eye.

**Supplemental Table 4. Prospective studies of diets in associations with cognitive decline and Alzheimer’s disease.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Publication year** | **Studies** | **Follow-up(years)** | **No. of participants** | **Age at baseline (years)** | **Female (%)** | **Risk factor measurements** | **Risk factor** | **Outcomes** |
| Mélissa, G.(76) | 2020 | The Three-City Study | 12 | 2,777 | Mean 76 | 61 | FFQ and the 24-hour dietary recall | Refined carbohydrates | With higher risk of risk of AD |
| Tangney, C. C.(77) | 2014 | The Memory and Aging Project | ≥4 | 826 | Mean 82 | 74 | FFQ | DASH- and Mediterranean-like dietary patterns | With a slower rate of cognitive decline |
| Hosking, D. E.(78) | 2019 | The Personality and Total Health Through Life study | 12 | 1,220 | Mean 63 | NA | CSIRO-FFQ | The MIND and Mediterranean diet | With reduced risk of cognitive impairment |
| Morris, M. C.(79) | 2015 | The Rush Memory and Aging Project | ≥5 | 960 | About 81 | 75 | FFQ | The MIND diet | With slower rates of cognitive decline |
| Morris, M. C.(80) | 2015 | The Rush Memory and Aging Project | Mean 5 | 923 | About 81 | 75 | FFQ | Three dietary patterns | With reduced risk of risk of AD |
| Ozawa, M.(81) | 2016 | The Whitehall II cohort study | ≥10 | 5,083 | About 55 | 29 | FFQ | An inflammatory dietary pattern | With accelerated cognitive decline |
| Samieri, C.(82) | 2020 | The Three-City Study | 12 | 627 | Mean 78 | 74 | FFQ | A novel diet pattern | With benefits on cognition |
| Littlejohns, T. J.(83) | 2014 | The Cardiovascular Health Study | Mean 6 | 1,658 | Mean 74 | 69 | Using liquid chromatography-tandem mass spectrometry | Vitamin D deficiency | With an increased risk of AD |
| Miller, J. W.(84) | 2015 | The University of California at Davis Alzheimer’s Disease Center longitudinal community diversity study | Mean 5 | 382 | Mean 76 | 62 | Competitive  immunoassay | Low Vitamin D status | With accelerated decline in cognitive function domain |
| Zhao, C.(85) | 2020 | The Washington Heights-Inwood Columbia Aging Project | Mean 6 | 1,759 | ≥65 | 69 | FFQ | Higher vitamin D intake | With decreased dementia risk |
| Olsson, E.(86) | 2017 | The Uppsala Longitudinal Study | 18 | 1,182 | Mean 71 | 0 | High-performance liquid chromatography-mass spectrometry, 7-day dietary records, a vitamin D-synthesis genetic risk score | Vitamin D | No association with AD |
| Agarwal, P.(87) | 2019 | The Rush Memory and Aging Project | Mean 7 | 925 | Mean 81 | 75 | FFQ | Vitamin C and total flavonoids | With reduced risk of AD |
| Noguchi-Shinohara, M.(88) | 2018 | The Nakajima study | About 7 | 349 | ≥65 | 66 | High-performance liquid chromatography and fluorescence | Vitamin C and vitamin E | With reduced risk of cognitive decline |
| Holland, T. M.(89) | 2020 | The Rush Memory and Aging Project | Mean 6 | 921 | Mean 81 | 75 | FFQ | Dietary intakes of flavonols | With reduced risk of AD |
| Honda, T.(90) | 2019 | The Hisayama study | 10 | 1,628 | ≥60 | NA | Using gas chromatography/mass spectrometry | Serum elaidic acid | With a greater risk of AD |

AD = Alzheimer’s disease; FFQ = Food frequency questionnaire; DASH = Dietary Approach to Stop Hypertension; MIND = Mediterranean-DASH diet Intervention for Neurodegenerative Delay; CSIRO-FFQ = Commonwealth Scientific and Industrial Research Organization semi-quantitative food frequency questionnaire

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