

Supplementary material

Supplementary table 1. Search terms used

| | | |
|-----------------|------------|---|
| | | exp marital status/ OR marriage.tw. OR married.tw. OR marital status.tw. OR spouse.tw |
| Medline | AND | exp Dementia/ OR dementia.tw. OR alzheimer*.tw |
| | AND | Epidemiologic studies/ OR exp case control studies/ OR exp cohort studies/ OR Case control.tw. OR (cohort adj (study or studies)).tw. OR Cohort analy\$.tw. OR (Follow up adj (study or studies)).tw. OR (observational adj (study or studies)).tw. OR Longitudinal.tw. OR Retrospective.tw. OR Cross sectional.tw. OR Cross-sectional studies/ |
| | | exp marriage/ OR marriage.tw. OR married.tw. OR marital status.tw. OR spouse.tw |
| Embase | AND | exp Dementia/ OR dementia.tw. OR alzheimer*.tw |
| | AND | Clinical study/ OR Case control study OR Case control study OR Longitudinal study/ OR Retrospective study/ OR Prospective study/ OR Cohort analysis/ OR (Cohort adj (study or studies)).mp. OR (Case control adj (study or studies)).tw. OR (follow up adj (study or studies)).tw. OR (observational adj (study or studies)).tw. OR (epidemiologic\$ adj (study or studies)).tw. OR (cross sectional adj (study or studies)).tw. NOT Randomized controlled trials/ |
| | | exp marriage/ OR marriage.tw. OR married.tw. OR marital status.tw. OR spouse.tw |
| PsycINFO | AND | exp dementia/ OR dementia.mp. OR Alzheimer.mp |
| | AND | exp Longitudinal studies/ OR cohort.mp OR prospective.mp OR longitudinal.mp OR retrospective.mp OR ((case* adj5 control*) or (case adj3 comparison*) or case-comparison or control group*).ti,ab.id. NOT "literature review".md |

Supplementary table 2. Full data extracted from cohort, case-control and cross-sectional studies

| Study | Recruitment source and population at start (response rate) Mean population age at baseline | n of participant at study inception n of cases at follow-up | Mean/range of years follow-up | n un-explained loss to follow-up / missing data % | Measurements of marital status (%) At what age, and approx. what year was marital status recorded? | Analysis adjusted for: | Statistical model used | Outcome How was dementia assessed? | Results | Adjusted results (95% Confidence interval) | Un-adjusted results |
|---------------|---|--|--|---|---|--|---|--|--|--|---------------------|
| COHORT | | | | | | | | | | | |
| Amieva 2010 | PAQUID, France: Longitudinal population-based study of randomly selected older adults (69%) 73.7 years | 2089 461 all Dementia 373 Alzheimer's Disease | 5-15 Cases excluded if dementia detected within 3yr 'latent period' | 1264 38% | Married (60.7%) Widowed (32.5%) Divorced (2.7%) Single (4.2%) Assessed for over 65s in 1988 | Age; Sex; Edu; baseline cognition; positive affect; ADLs; Chronic diseases; quality and quantity of social network contact | Cox regression (with age as time-scale) | Dementia Alzheimer's Disease (Clinical assessment by neurologist using valid criteria) | Married Widowed Divorced Single Married Widowed Divorced Single | HR 1 HR 0.88 (0.7, 1.1) HR 0.94 (0.5, 1.7) HR 1.29 (0.7, 2.1) HR 1 HR 0.92 (0.7, 1.1) HR 0.88 (0.4, 1.7) HR 1.36 (0.7, 2.3) | Not provided |
| Arai 2004 | Hokkaido, Japan. Community-based prospective study 69 years | 853 34 | 5 | No data provided | Living with spouse 71% Not living with spouse 29% Living with others 15% Assessed in 1998 | Age; Sex | Mantel-Haentzel | Dementia Clinical assessment based on algorithm | Living with spouse Not living with spouse | RR 1 RR 2.0 (1.0, 5.0) | 1 2.2 |
| Bae 2014 | Korean Longitudinal Study on Cognitive Aging and Dementia (71.6%) 71.7 | 359 45 all dementia 9 Alzheimer's Disease | 3.5 | 144 40% | Married 70.2% Widowed 29.8% Divorced 0% Single 0% Assessed in 2008 | Age, sex | Cox regression | Dementia Alzheimer's Disease Clinical assessment by psychiatrist using valid criteria | Married Widowed Divorced Single Married Widowed Divorced Single | HR 1 HR 1.79 (0.5, 6.5) HR 0 HR 0 HR 1 HR 4.40 (0.8, 24.7) HR 0 HR 0 | Not provided |

| | | | | | | | | | | | |
|------------------|--|---|------|---------------|--|---|---------------------|---|---|--|--|
| Bickel 1994 | Mannheim, Germany. Longitudinal population-based cohort of elderly persons in private households (82.1%) 73.8 years | 331 34 | 7-8 | 12 4% | Married 42.4% Widowed 47.5% Divorced 3.8% Single 6.4% Assessed in 1992 | Age, sex | Cox regression | Dementia Clinical assessment by trained physicians based using valid criteria | Married Widowed Divorced Single | HR 1 HR 1.59 (0.7, 3.5) HR 3.17 (0.6, 16.4) HR 2.90 (0.8, 10.5) | 1 1.86 3.21 3.56 |
| Fratiglioni 2000 | Kungsholmen, Sweden: Longitudinal population-based study of community-dwelling people born before 1913 (76%) 81.5 years | 1368 176 | 3 | 165 12% | Married 27.8% Widowed 45.4% Divorced 5.9% Single 20.9% Assessed in 1987 | Age; Sex; BL cognition | Cox regression | Dementia Clinical assessment by 2 independent physicians using valid criteria | Married Widowed Divorced Single | HR 1 HR 1.45 (0.9, 2.2) HR 1.04 (0.5, 2.4) HR 1.77 (1.1, 2.9) | 1 1.6 (wid or div) 1.8 |
| Håkansson 2009 | CAIDE project. Longitudinal population-based study derived from random sampling in two regions in Eastern Finland (82-90%) 71.3 years | 2000 44 | 20.9 | 511 2.7% | Married 80.1% Widowed 7.8% Divorced 4.4% Single 7.8% Mid-life – people aged 50.5 between 1972-87 Late life – people aged 71.3 in 1998 | Age; Sex; Edu; ApoE; BMI; BP; Cholesterol; Occupation; Physical activity; Region; Smoking; Depression | Logistic regression | Alzheimer's Disease Clinical assessment by expert board using valid criteria | <i>Mid-life marital status</i> Married Widowed Single/divorced <i>Mid-and late-life marital status change</i> Remained married Became single Remained single | OR 1 OR 2.52 (0.8, 7.7) OR 1.78 (0.7, 4.9) OR 1 OR 1.60 (0.7, 3.8) OR 2.83 (1.1, 7.4) | Not provided |
| Hatch 2013 | Cache County Memory Study. Longitudinal population based study of all residents aged over 65, identified from Medicare records (90%) 74.6 years | 5092 548 all dementia 369 Alzheimer's disease | 12 | 1459 28.7% | Married 65.9% Widowed 29.9% Divorced 4.1% Measured in 1995 | Age; Sex; Occupation; ApoE | Cox regression | Dementia Alzheimer's Disease (Clinical assessment by expert board using valid criteria) | Married Widowed Divorced Married Widowed Divorced | HR 1 HR 0.99 (0.81, 1.22) HR 0.65 (0.37, 1.16) HR 1 HR 1.04 (0.82, 1.33) HR 0.59 (0.28, 1.25) | 1 1.75 0.67 1 2.05 0.64 |
| Sundström 2014 | Betula prospective cohort study, Umeå Sweden: Longitudinal population-based study | 1677 354 | 8.6 | 32 2% | Married 57.6% Widowed 14.2% Divorced 5.7% Single 32.6% | Age; Sex; Alcohol; mental illness; availability of a close friend; | Cox regression | Dementia Clinical assessment by | Married Widowed Divorced Single | 1 HR 1.30 (1.0, 1.7) HR 1.32 (0.9, 2.1) HR 1.09 (0.6, 1.9) | 1.42 1.48 1.59 |

| | | | | | | | | | | | |
|---------------------|--|---------------------------|-----|-------------|--|--|---------------------|---|---|---|--|
| | derived from general population stratified by age and sex. (87%) 74.7 years | | | | Assessed in 1993-5 | parental status | | 2 independent physicians using valid criteria | | | |
| Sundström 2016 | Linnaeus database, Sweden: Linked population data from healthcare and death records for entire population 69.4 years (other group of people aged 50-64, mean age 56.1) | 750129 25722 | 6 | 32065 1% | Men: Married 68.1% Widowed 3.5% Divorced 15.0% Single 13.5% Women: Married 61.8% Widowed 13.1% Divorced 17.0% Single 8.2% Total: Married 64.9% Widowed 8.4% Divorced 16.0% Single 10.8% Assessed in 1997 | Age; Sex; Parental status; Edu; Income; CVD | Cox regression | Dementia Derived from clinical records or death certificates: Specificity 98% Sensitivity 55% | All aged 65-74 Married Widowed Divorced Single | HR 1 HR 1.12 (1.1, 1.2) HR 1.42 (1.4, 1.5) HR 1.23 (1.2, 1.3) | (Age-adjusted) 1 1.11 1.42 1.25 |
| | | | | | | | | | Men aged 65-74 Married Widowed Divorced Single | HR 1 HR 1.10 (1.0, 1.2) HR 1.47 (1.4, 1.6) HR 1.29 (1.2, 1.4) | (Age-adjusted) 1 1.10 1.48 1.32 |
| | | | | | | | | | Women aged 65-74 Married Widowed Divorced Single | HR 1 HR 1.10 (1.1, 1.4) HR 1.36 (1.3, 1.4) HR 1.16 (1.1, 1.3) | (Age-adjusted) 1 1.11 1.36 1.18 |
| | | | | | | | | | All aged 50-64 Married Widowed Divorced Single | HR 1 HR 1.28 (1.1, 1.4) HR 1.79 (1.7, 1.9) HR 1.71 (1.6, 1.9) | Not provided |
| CASE-CONTROL | | | | | | | | | | | |
| Beard 1992 | Rochester, USA. Epidemiology Project. Cases selected from records of Mayo Clinic which delivered medical care to most residents. 80.4 years | 241 cases 241 controls | N/A | 0 | Married 28.8% Widowed 48.0% Divorced 5.4% Single 17.8% Assessed at point of diagnosis (1975-79) | Matched by age and sex | Logistic regression | Alzheimer's Disease Clinical diagnoses confirmed against valid criteria by psychiatrist. | Married Widowed Divorced Single | OR 1 OR 1.10 (0.7, 1.7) OR 1.25 (0.5, 2.9) OR 1.07 (0.6, 1.8) | Not provided |
| | | | | | | | | | Men Married Widowed Divorced Single | OR 1 OR 1.24 (0.8, 1.8) OR 3.45 (0.9, 14.0) OR 1.73 (0.3, 9.7) | Not provided |
| | | | | | | | | | Women Married Widowed Divorced Single | OR 1 OR 0.98 (0.8, 1.2) OR 0.77 (0.4, 1.4) OR 0.94 (0.7, 1.2) | Not provided |

| | | | | | | | | | | | |
|----------------------------|---|---------------------------|------|---------------------|--|---|-------------------------|---|------------------------|------|---|
| Seidler 2003 | Frankfurt, Germany. Cases selected from general practice registers: (77% agreed to participation) Controls selected as random sample of population register >65 years (61%) AND sample from general practice register (90%) Cases: 79.5 years Controls: 75.4 years | 195 cases 229 controls | N/A | 29 6% | Married 78.5% Widowed 11.1% Divorced 3.8% Single 6.6% Derived in c2001 from interview with patient or next-of-kin based on marital status when 50yrs | Age; sex; edu; region; family history; smoking | Logistic regression | Dementia Clinical diagnoses confirmed against valid criteria by psychiatrist. | <i>Status at 30yrs</i> | | |
| | | Married | | | | | | | OR 1 | 1 | |
| | | Widowed | | | | | | | OR 2.1 (0.7, 6.2) | 2.50 | |
| | | Divorced | | | | | | | OR 1.0 (0.2, 4.1) | 1.14 | |
| Single | OR 1.1 (0.6, 2.0) | 1.23 | | | | | | | | | |
| <i>Status at 50yrs</i> | | | | | | | | | | | |
| Married | OR 1 | 1 | | | | | | | | | |
| Widowed | OR 1.2 (0.6, 2.3) | 1.69 | | | | | | | | | |
| Divorced | OR 0.6 (0.2, 1.8) | 0.58 | | | | | | | | | |
| Single | OR 1.1 0.5, 2.5) | 1.36 | | | | | | | | | |
| <i>Status 10y earlier</i> | | | | | | | | | | | |
| Married | OR 1 | 1 | | | | | | | | | |
| Widowed | OR 1.0 (0.6, 1.6) | 1.47 | | | | | | | | | |
| Divorced | OR 0.5 (0.2, 1.7) | 0.57 | | | | | | | | | |
| Single | OR 1.7 (0.7, 4.2) | 1.99 | | | | | | | | | |
| Alzheimer's Disease | <i>Status at 30yrs</i> | | | | | | | | | | |
| | Married | OR 1 | 1 | | | | | | | | |
| | Widowed | OR 4.3 (1.4, 12.9) | 4.14 | | | | | | | | |
| | Divorced | OR 1.3 (0.2, 7.2) | 1.04 | | | | | | | | |
| Single | OR 0.7 (0.3, 1.5) | 0.99 | | | | | | | | | |
| Vascular dementia | <i>Status at 30yrs</i> | | | | | | | | | | |
| | Married | OR 1 | 1 | | | | | | | | |
| | Widowed | OR 1.7 (0.2, 14.9) | 0.73 | | | | | | | | |
| | Divorced | OR 1.5 (0.2, 13.7) | 0.92 | | | | | | | | |
| Single | OR 1.7 | 1.43 | | | | | | | | | |
| CROSS-SECTIONAL | | | | Missing data | | | | | | | |
| Correa Ribeiro 2013 | Rio de Janeiro, Brazil. Age and sex-stratified sample selected from clients of a private health-care plan: (98%) 78.2 years | 683 | N/A | 108 12.5% | Married 41.6% Widowed 40.8% Divorced 7.5% Single 10.1% Derived from interview by researcher in 2009 | Age; Sex; edu; Personal income | Log-binomial regression | Dementia Clinical diagnoses by consensus panel on valid criteria | <i>Status at 30yrs</i> | | |
| | | 115 | | | | | | | Married | RR 1 | 1 |
| | | | | | | | | Widowed | RR 1.43 (0.9, 2.3) | 2.97 | |
| | | | | | | | | Divorced/separated | RR 0.31 (0.1, 2.0) | 0.24 | |
| | | | | | | | | Single | RR 0.81 (0.3, 2.1) | 1.17 | |
| Fan 2015 | Taiwan. Nationwide population-based cross-sectional study (36.5%) 75.7 years | 10432 | N/A | 419 5.0% | Married 64.2% Widowed 31.0% Divorced/single 4.8% Derived from researcher interview in 2012 | Age; sex; edu; BMI; Hypertension; Diabetes; CVD; Smoking; alcohol; exercise; social engagement; sleep | Logistic regression | Dementia Clinical diagnoses confirmed against valid criteria by psychiatrist. | <i>Status at 30yrs</i> | | |
| | | 929 | | | | | | | Married | OR 1 | 1 |
| | | | | | | | | Widowed | OR 1.42 (1.2, 1.8) | 2.65 | |
| | | | | | | | | Divorced/single | OR 1.20 (0.7, 2.0) | 1.67 | |
| Guaita 2015 | Abbiategrosso, Italy. Survey of all residents | 1321 | N/A | 2 0.2% | Married 67.1% Widowed 24.6% | Age; Sex; Area of birth; | Logistic regression | All dementia Clinical | Married | RR 1 | 1 |
| | | | | | | | | Widowed | RR 1.17 (0.5, 2.7) | 1.18 | |

| | | | | | | | | | | | |
|------------|--|---|-----|------------|--|---|---------------------|--|--|--|---------------------------|
| | aged 70-74 yr. (80.4%) 71.7 years | 39 all dementia 15 Alzheimer's disease 18 vascular dementia | | | Divorced 2.2% Single 6.1% Assessed in 2011 | Occupation; Education | | diagnoses confirmed against valid criteria by geriatrician | Divorced Single | RR 0.87 (0.1, 7.2) RR 2.52 (0.8, 7.8) | 1.26 2.44 |
| | | | | | | | | Alzheimer's Disease | Married Widowed Divorced Single | RR 1 RR 1.05 (0.3, 3.8) RR 2.42 (0.3, 23.0) RR 1.31 (0.2, 11.0) | 1 1.18 3.09 1.18 |
| | | | | | | | | Vascular dementia | Married Widowed Divorced Single | RR 1 RR 1.8 (0.5, 6.2) RR -- RR 5.63 (1.3, 23.8) | 1 1.45 -- 1.45 |
| Zhang 2006 | China: prevalence study conducted across four different communities. (94%) 68.2 years | 34807 732 Alzheimer's Disease 295 vascular dementia | N/A | 59 0.1% | Married 77.4% Widowed 20.8% Divorced/single 1.6% Assessed in over 55s in 1997 | Age; Sex; Edu; Rural/urban dwelling; ethnicity; occupation; age/region interaction; sex/education interaction | Logistic regression | Alzheimer's Disease | Married Widowed Divorced/Single | OR 1 OR 1.4 (1.1, 1.7) OR 2.0 (0.8, 5.0) | 1 5.2 2.3 |
| | | | | | | | | Vascular Dementia | Married Widowed Divorced/Single | OR 1 OR 0.6 (0.5, 0.9) OR 1.0 (0.4, 2.4) | 1 1.1 0.9 |

Key: ADLs = Activities of daily living; BMI = body mass index; CVD = cardiovascular disease; Edu = education; HR = Hazard ratio; OR = Odds ratio; RR = Risk ratio

Notes: Shaded results are those which have been provided on request by study authors. *Italicised results* are those which we calculated from study data e.g. when confidence intervals were not provided.

Supplementary table 3. Rating criteria for quality of included studies and results from quality rating.

* Indicates a point for methodological quality

Supplementary table 3a - COHORT STUDIES

Selection

- 1) Representativeness of the exposed cohort
 - a. truly representative of the average person over 65 years in the community with initial response rate over 70% *
 - b. selected group of users e.g. nurses, volunteers
 - c. no description of the derivation of the cohort
- 2) Selection of the non-exposed cohort
 - a. drawn from the same community as the exposed cohort *
 - b. drawn from a different source
 - c. no description of the derivation of the non-exposed cohort
- 3) Ascertainment of exposure
 - a. secure record (e.g. public records) *
 - b. structured questionnaire with details on timing of potential changes of marital status *
 - c. written self-report
 - d. no description
- 4) Demonstration that outcome of interest was not present at start of study
 - a. yes *
 - b. no

Comparability

- 5) Comparability of cohorts on the basis of the design or analysis (2 * possible)
 - a. As well as **age and sex**, the study controls for **Education or baseline cognition***
 - b. Study additionally controls for a **measure of physical illness AND socio-economic status** *
 - c. Only adjusts for **age and sex**

Outcome

- 6) Assessment of outcome (*dementia*)
 - a. Systematic blind assessment using standard diagnostic criteria *
 - b. Record linkage
 - c. Self- or carer- report
 - d. no description
- 7) Was follow-up long enough for outcomes to occur
 - a. At least 5 years *
 - b. no
- 8) Adequacy of follow up of cohorts
 - a. complete follow up - all subjects accounted for *
 - b. Less than <30 % lost to follow up *
 - c. follow up rate < 70% (select an adequate %) and no description of those lost
 - d. no statement

| | | 1 * | 2 * | 3 * | 4 * | 5 * / ** | 6 * | 7 * | 8 * | Total |
|---|----------------|--------|--------|--------|--------|-------------|--------|--------|--------|-------|
| 1 | Amieva | c | * | d | * | * | * | * | c | 5 |
| 2 | Arai | c | * | d | * | c | c | * | d | 3 |
| 3 | Bae | b | * | d | * | c | * | b | c | 3 |
| 4 | Bickel | b | * | d | * | c | * | * | * | 5 |
| 5 | Fratiglioni | * | * | d | * | * | * | b | * | 6 |
| 6 | Håkansson | * | * | d | * | ** | * | * | * | 8 |
| 7 | Hatch | b | * | * | * | ** | * | * | * | 5 |
| 8 | Sundström 2014 | * | * | d | * | * | * | * | * | 7 |
| 9 | Sundström 2016 | * | * | * | * | ** | b | * | * | 8 |

Supplementary table 3b - CASE-CONTROL STUDIES

Selection

- 1) Is the case definition (*dementia diagnosis*) adequate?
 - a. yes, with independent validation *
 - b. Record linkage
 - c. no description
- 2) Representativeness of the cases
 - a. consecutive or obviously representative series of cases *
 - b. potential for selection biases or not stated
- 3) Selection of Controls
 - a. community controls *
 - b. hospital controls
 - c. no description
- 4) Definition of Controls
 - a. no history of disease (endpoint) *
 - b. no description of source

Comparability

- e. Comparability of cases and controls on the basis of the design or analysis (2 * possible)
 - a. As well as **age and sex**, the study controls for **Education or baseline cognition***
 - b. study also controls for a **measure of physical illness AND socio-economic status ***
 - c. Only adjusts for **age and sex**

Exposure

- f. Ascertainment of exposure
 - a. secure record (eg public records) *
 - b. structured questionnaire with details on timing of potential changes of marital status AND independent verification (notes OR informant) *
 - c. interview not blinded to case/control status
 - d. written self-report or medical record only
 - e. no description
- g. Same method of ascertainment for cases and controls
 - a. yes *
 - b. no
- h. Non-Response rate
 - a. same rate for both groups *
 - b. non respondents described
 - c. rate different and no designation

| | | 1 * | 2 * | 3 * | 4 * | 5 * / ** | 6 * | 7 * | 8 * | Total |
|---|---------|--------|--------|--------|--------|-------------|--------|--------|--------|-------|
| 1 | Beard | b | b | * | b | - | c | * | * | 3 |
| 2 | Seidler | b | b | b | b | * | c | b | b | 1 |

Supplementary table 3c - CROSS-SECTIONAL STUDIES

Selection

- 1) Were the criteria for inclusion in the sample clearly defined?
 - a. truly representative of the average person over 65 years in the community *
 - b. selected group of users eg volunteers
 - c. no description of the derivation of the sample
- 2) Was the initial response rate reported?
 - a. Reported and > 70% *
 - b. Reported and < 70%
 - c. Not reported

Measurements

- 3) Ascertainment of exposure
 - a. secure record (eg public records) *
 - b. structured questionnaire with details on timing of potential changes of marital status AND independent verification (notes OR informant) *
 - c. interview not blinded to dementia status
 - d. written self-report or medical record only
 - e. no description
- 4) Assessment of Dementia
 - a. Systematic blind assessment using standard diagnostic criteria *
 - b. Record linkage *
 - c. Self- or carer- report
 - d. no description

Comparability

- 5) Comparability of cases and controls on the basis of the design or analysis (2 * possible)
 - a. As well as **age** and **sex**, the study controls for **Education** or **baseline cognition** *
 - b. study controls for a measure of **physical illness** AND **socio-economic status** *
 - c. Only adjusts for **age and sex**

| | | 1 * | 2 * | 3 * | 4 * | 5 * / ** | |
|---|----------------|--------|--------|--------|--------|-------------|---|
| 1 | Correa-Ribeiro | b | * | c | * | * | 3 |
| 2 | Fan | * | * | c | * | * | 4 |
| 3 | Guaita | * | * | c | * | * | 4 |
| 4 | Zhang | * | * | e | * | * | 4 |

Supplementary figure 1. Begg's funnel plots for main meta-analyses showing risk for publication bias in published studies.

