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Original Article

Prevalence and co-occurrence of dementia risk factors in Denmark: A nationwide study

Janet Janbek [a,*], Thomas Munk Laursen [b], Kasper Jørgensen [a], Martin Mejlby Jensen [c], Marie Holm Eliasen [d], Anne Illemann Christensen [e], Sebastian Walsh [f], Andrew Sommerlad [g], Carol Brayne [f], Gunhild Waldemar [a,h]

[a] Danish Dementia Research Centre, Department of Neurology, Copenhagen University Hospital- Rigshospitalet. Blegdamsvej 9, Copenhagen Ø 2100, Denmark
[b] National Centre for Register-Based Research, Aarhus University, Fuglesangs Allé 26, Aarhus V 8210, Denmark
[c] DEFACTUM, Central Denmark Region, Olof Palmes Allé 15, Aarhus N 8200, Denmark
[d] Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Nordre Fasanvej 57, Frederiksberg 2000, Denmark
[e] National Institute of Public Health, University of Southern Denmark, Studiestræde 6, Copenhagen K 1455, Denmark
[f] Cambridge Public Health, University of Cambridge, The Old Schools, Trinity Lane, Cambridge CB2 1TN, United Kingdom
[g] Division of Psychiatry, University College London, Gower Street, London WC1E 6BT, United Kingdom
[h] Department of Clinical Medicine, University of Copenhagen, Blegdamsvej 3B, Copenhagen N 2200, Denmark

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ABSTRACT

Background: The clustering of dementia risk factors is common and has implications for policies targeting risk reduction.
Objectives: To estimate the prevalence of 16 dementia risk factors and their co-occurrence.
Design: Cross-sectional based on a closed cohort on 1 January 2022 with nationwide data on risk factors from 1969/1977.
Setting: Denmark
Participants: Whole population; closed cohort of individuals ≥65 years on 1 January 2022, and a subpopulation of responders in the 2010/2013 Danish National Health Survey.
Intervention (exposures): Sixteen dementia risk factors: hypertension, cardiovascular disease, diabetes, hypercholesterolemia, obesity, smoking, alcohol, physical inactivity, depression, hearing loss, vision impairment, traumatic brain injury, sleep disorders, hospital-diagnosed infections, social isolation, and low education.
Measurements: Period and point prevalence proportions of the dementia risk factors and of all possible combinations of factors (those occurring in ≥10 % of individuals). The prevalence estimates reflect a population-level view of persons who have experienced, were diagnosed, or were treated for the risk factors assessed.
Results: In the whole population ($N = 1{,}214{,}286$) and the subpopulation ($N = 88{,}565$), 5 % had no risk factors, 12 % had only one, and 82 % had multiple. Hypertension was the most prevalent (57 %), and vision impairment the least (2 %). Men, individuals ≥85 years, and those with low education had the highest prevalence of risk factors (with exceptions).
Conclusions: Clustering of risk factors is very common, and findings emphasize the need to focus on multidomain interventions for dementia risk reduction that account for the clustering of risk.

1. Introduction

Recent evidence shows that dementia incidence rates have declined in Europe and the United States over the past 25 years [1], which may be due to various lifestyle interventions and policies. Several potentially modifiable risk factors for dementia have been identified, suggesting promising avenues for risk reduction [2]. However, risk factors have rarely been investigated in a single large, population-based cohort. Differences in population risk profiles, settings, and study methodologies make the true assessment of the impact of these risk factors on

* Corresponding author at: Danish Dementia Research Centre, Department of Neurology, Copenhagen University Hospital- Rigshospitalet, Blegdamsvej 9, Copenhagen Ø 2100, Denmark.
E-mail address: Janet.Janbek@regionh.dk (J. Janbek).

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dementia risk challenging. This in turn challenges the potential for risk reduction in different populations and communities.

Furthermore, risk factors have mostly been studied for their individual impact on dementia risk. These have been summarized in the reports of the Lancet's Commission on dementia, which estimated the population attributable fraction for 14 selected risk factors, drawing upon risk factor prevalence estimates [2]. The risk factors were less education, hearing loss, high LDL cholesterol, depression, traumatic brain injury (TBI), physical inactivity, diabetes, smoking, hypertension, obesity, excessive alcohol, social isolation, air pollution, and visual loss. However, the isolated occurrence of risk factors is uncommon. With the high prevalence of multimorbidity in the adult population worldwide, clustering and co-occurrence of risk factors is common, and the interplay seems likely to affect dementia risk, with implications for policies targeting risk reduction. Most previous studies considered the co-occurrence of risk factors by assessing the number of risk factors, as summarized in a 2019 systematic review which noted that data on particular risk factor clusters are rare, hindering evidence synthesis [3]. Other studies assessed multimorbidity including all chronic conditions [4–6] or specific cardiometabolic factors [7]. In the reports of the Lancet's Commission (and in several studies following the reports' methodology), the co-occurrence of risk factors is accounted for by calculating the communality between risk factors [2].

As such, most studies have focused on single risk factors, and none have to our knowledge explicitly explored the prevalence of risk factor combinations at a national level using data combined from national registries, healthcare data, and population-based studies. Moreover, single-domain interventions have shown little to no success to date in trials, resulting in increasing attention toward multidomain interventions, which target multiple factors acknowledging the interplay between co-occurring factors, and have potentially promising evidence [8,9]. Understanding the co-occurrence of risk factors would inform the application of these interventions.

Our study therefore aims to estimate the prevalence of several potentially modifiable risk factors for dementia, and the most common combinations of these risk factors in middle-aged and older adults in Denmark at a national level using routine health data and population-based health surveys. Our study further aims to estimate the prevalence of the risk factors and their combinations according to important socio-demographic factors for policy and risk reduction efforts, i.e., sex, age, and educational level.

2. Methods

2.1. Data sources

Data used in this study came from the Danish nationwide registries and the Danish National Health Survey.

The National Patient Registry includes inpatient data from 1977 and onwards from somatic wards (medical and surgical) [10], and the Psychiatric Central Research Registry has psychiatric ward records from 1969 [11]. Outpatient and emergency contact data were added to both registries in 1995. Diagnoses until 1994 were registered according to the International Classification of Diseases (ICD) 8th edition, and 10th edition from 1995 onward. The National Prescription Registry contains information on all drug prescriptions dispensed by Danish community pharmacies since 1994 [12]. The registry is commonly used to identify diseases diagnosed in primary care where no diagnostic codes are directly recorded for medications specific to certain diseases e.g., acetylcholinesterase inhibitors for dementia used as proxies for the disease itself. The Population Education Registry provides information on education from annual administrative records of Danish educational institutions [13].

The Danish National Health Survey contains information on risk factors unavailable in the registries (e.g., lifestyle factors) [14]. Data were linked with the national registry datasets using a unique personal identification number from the Danish Civil Registration System. The survey procedures have been described in full elsewhere [14]. Briefly, the Danish National Health Survey is a nationally representative population-based survey which has been conducted in 2010, 2013, 2017, 2021, and 2023. We used data from 2010 and 2013 because of the high number of respondents, especially when combined (under the assumption that the two study phases are sufficiently close to be treated as one fixed time point). The survey is comprised of individuals aged ≥16 years randomly selected from the Danish Civil Registration System using a stratified random sampling approach [14]. Data were collected using either a web- or paper questionnaire, which was completed at least partially by 117,639 (59.5 %) and 162,283 (54.0 %) respondents in 2010 and 2013, respectively.

2.2. Study population

The whole population was the cohort of individuals who were alive in Denmark, aged ≥65 years, and dementia-free on 1 January 2022 (Supplementary Table A1 details how dementia status was classified). Hence, the population comprised all birth cohorts before and including 1957. This was to ensure that the prevalence of risk factors was measured in a cohort of individuals at risk of incident late-life dementia. The cohort was fixed/closed, meaning that no new individuals were added to the cohort from birth cohorts after 1957, to allow for a fixed denominator.

We also established a subpopulation (hereafter the "health survey subpopulation") of individuals from the whole population who had answered the Danish National Health Surveys in 2010 or 2013. Individuals from the health survey subpopulation were excluded from the analyses if they had missing information on any of the risk factors derived from the National Health Survey data (description of missingness shown in Supplementary Table A2). If a person had completed the questionnaire in 2010 and 2013, we included the 2010 data.

2.3. Risk factors

The literature and expert knowledge informed this study's risk factor selection. The 16 risk factors selected in this study were 13 taken from the Lancet Commission's report 2024 (excluding air pollution due to our lack of available data) and three additional factors (cardiovascular disease (CVD), sleep disorders, and hospital-diagnosed infections) (Table 1). The addition of the three new risk factors was based on the evidence of their potential association with dementia (CVD summarized by Brain et al. [15]; and sleep disorders and hospital-diagnosed infections were previously linked to dementia in our study population [16, 17]). Moreover, as this study focuses on the co-occurrence of risk factors, investigating the potential co-occurrence of CVD with other cardiometabolic risk factors was considered relevant. Data on 11 risk factors were based on registry data, and five were based on the National Health Survey data and investigated only for the health survey subpopulation.

Risk factors drawn from the registry data were considered as far back as possible i.e., the earliest risk factor data came from 1969 on depression and sleep disorders or 1977 on, e.g., hypertension. Individuals were considered to have experienced exposure to the risk factors at age ≥65 years on 1 January 2022 if they had any previous record of these risk factors. Risk factors were defined as the first date of either a secondary care registered diagnosis in the National Patient Registry or the Psychiatric Central Research Registry, or a redeemed relevant medication from the National Prescription Registry (medications as primary care diagnoses proxy). We defined risk factors based on available validated algorithms of ICD and Anatomical Therapeutic Chemical (ATC) Classification codes (referenced in Table 1 and Supplementary Table A1) and expert knowledge.

For the five risk factors drawn from the National Health Survey data, these were considered at the time the 2010/2013 surveys were

Table 1
List of selected risk factors and their definitions.

Source, estimate, and timeframe	Risk factor	Definition and earliest possible year for data availability
Registry data. Period prevalence. Prevalent cases are those with a record of the risk factor before study start as far back as 1969 (thus having experienced the risk factor at study start; age ≥65 years on 1 January 2022), and new cases added during 2022.	Hypertension	Secondary care diagnoses (ICD codes), 1977 Medications as primary care diagnoses proxy, 1995
	Hospital-diagnosed infections	Secondary care diagnoses (ICD codes), 1977
	Hypercholesterolemia	Secondary care diagnoses (ICD codes), 1977 Medications as primary care diagnoses proxy, 1995
	Cardiovascular disease (CVD)	Secondary care diagnoses (ICD codes for stroke, ischemic heart disease, Atrial fibrillation), 1977 Medications as primary care diagnoses proxy, 1995
	Low education	Schooling up to 9th grade (obligatory period), 1980
	Depression	Secondary care diagnoses (ICD codes), 1969 Medications as primary care diagnoses proxy, 1995
	Hearing loss	Secondary care diagnoses (ICD codes), 1977
	Diabetes	Secondary care diagnoses (ICD codes), 1977 Medications as primary care diagnoses proxy, 1995
	Traumatic brain injury (TBI)	Secondary care diagnoses (ICD codes), 1977
	Sleep disorders	Secondary care diagnoses (ICD codes), 1969
	Vision impairment	Secondary care diagnoses (ICD codes), 1977
National Health Survey data. Point prevalence at time of survey completion, 2010 or 2013.	Alcohol	>10 units/week, self-reported
	Smoking	Self-reported current smokers
	Obesity	BMI ≥ 30 kg/m^2, based on self- reported weight and height
	Physical inactivity	Self-reported. Based on Saltin questionnaire
	Social Isolation	Inspired by the Social Network Index. Sum score 0–5 (from self-reports), score ≥3 is social isolation

Definitions of the registry-based risk factors relied on previous studies, validation studies, and expert knowledge. Definitions are listed in detail in Supplementary Table A1, and references to previous and validation studies are provided where these were used.

completed. We used national recommendations (for alcohol consumption) issued by the Danish Health Authority (year 2023) [18] and available indices (for social isolation and physical inactivity) to define cutoffs. Detailed definitions of all risk factors are in Table 1 and Supplementary Table A1. All risk factors were treated as binary variables.

We further combined risk factors into clusters based on assumed common mechanistic pathways linking them to dementia: cardiometabolic (hypertension, CVD, diabetes, hypercholesterolemia, obesity, smoking, alcohol, and physical inactivity), neuro-psychosocial (depression, hearing loss, vision impairment, TBI, and sleep disorders), immune (hospital-diagnosed infections), and cognitive reserve (social isolation and low education).

2.4. Data analysis

2.4.1. Main analyses

Period prevalence proportions were calculated for each risk factor using the whole population (for 11 risk factors) and point prevalence proportions using the health survey subpopulation (for five risk factors).

The period prevalence in the whole population was calculated, where the prevalent cases (numerator) were individuals with a record of the risk factor as far back as 1969, thus already having experienced the risk factor at study start on 1 January 2022 (the youngest age with complete data from 1995 onwards is 38 years). New cases occurring from 1 January 2022 until 31 December 2022 (the period) were further added unless a dementia record occurred before. The denominator was the whole population defined above. This prevalence estimate thus provides a population-level reflection of having experienced a risk factor. The point prevalence in the health survey subpopulation was calculated where the prevalent cases (numerator) were individuals with data on risk factors from the surveys in 2010/2013, and the denominator was the health survey subpopulation defined above. See Supplementary Fig. A1 for a graphical illustration of prevalence estimations.

To ensure the subpopulation's representativeness, we re-calculated the prevalence proportions for the 11 registry risk factors exclusively in this subpopulation and compared these with the estimates from the whole population. We also compared individuals with complete data included in our analyses with those excluded due to missing data.

We then calculated the prevalence proportions for the combinations of risk factors using the health survey subpopulation, where data on all 16 risk factors were available. These combined the point prevalence of five risk factors and period prevalence of 11 risk factors. We calculated the prevalence for all possible combinations and reported those occurring in ≥10 % of individuals. We also calculated the prevalence proportions for the four clusters of risk factors and their combinations (e.g., co-occurrence of any cardiometabolic risk factor with any neuro-psychosocial risk factor), again presenting combinations occurring in ≥10 %. All prevalence proportion numbers calculated from the health survey subpopulation were weighted for non-response and different sampling probabilities using weights provided by Statistics Denmark. Results were stratified by sex and by birth cohorts (cohorts aged 65 – 74 years (born 1948–1957), 75 – 84 years (born 1947–1938), and ≥85 years (born ≤1937)).

2.4.2. Sensitivity analyses

Pre-planned sensitivity analyses were conducted. First, we stratified by age at risk factor onset by limiting our populations to those born from 1940 to 1950. This was done to ensure that individuals in this age subgroup had available data on risk factors from 1995 (when prescription data became available in addition to the hospital data) and to allow us to estimate the prevalence of each risk factor (first record; onset) at ages <65 and ≥65 years. Individuals were thus 45 – 55 years old in 1995 and 72 – 82 years old in 2022. For the health survey subpopulation, age was the individual's age when the questionnaire was answered. Second, we removed education from the list of risk factors and treated it as a stratifying variable, using tertiles of education (Supplementary Table A1). Third, we redefined the cutoffs for alcohol, smoking, and physical inactivity. Alcohol consumption was redefined from >10 units/week (women and men) to >14 units/week for women and >21 units/week for men as per previous national recommendations. Smoking was redefined to ever vs never smokers rather than current vs not current smokers and to daily vs no daily smoking. Physical inactivity was redefined to include light physical activity in addition to the "Physically inactive" response category.

3. Results

The whole population comprised 1,214,286 individuals, of whom 88,565 had responded to the 2010/2013 National Health Surveys (health survey subpopulation). In both populations, most were women (53.6 % and 52.5 %, respectively), and born in the period 1948–1957 (51.2 % and 51.8 %, respectively) (Table 2). In the health survey subpopulation, with data on all 16 risk factors, 4828 (5.4 %) had no risk factors, 10,929 (12.3 %) had only one risk factor, and 72,899 (82.2 %) had multiple risk factors.

We present numbers for the period prevalence of 11 risk factors and the point prevalence of five risk factors (smoking, alcohol, obesity, physical inactivity, and social isolation). The prevalence estimates reflect a population-level view of persons who have experienced, were diagnosed, or were treated for the risk factors assessed. For the 11 risk factors drawn from the registries and considered as far back as possible (1969/1977 and more complete information from 1995 onwards), 51.2 % of the population reflect risk factors experienced from ages 38 – 47 years, 37.2 % from ages 48 – 57 years, and 11.6 % from ages ≥58 years (based on the birth cohorts in Table 2). The median age at first record for each risk factor was between 51 and 68 years (Supplementary Table A3).

Fig. 1 shows the prevalence of each of the 16 dementia risk factors and their combinations. Hypertension was the most prevalent (57 %), followed by hospital-diagnosed infections (52 %), hypercholesterolemia (50 %), and CVD (46 %). The least prevalent risk factor was vision impairment (2 %). Men had a higher prevalence of all risk factors apart from low education and depression, which were higher in women, and hypertension, hospital-diagnosed infections, physical inactivity, social isolation, and vision impairment (similar in both). Thirty-two combinations of the 16 risk factors were present in ≥10 % of our population. The most common were those among the four most prevalent risk factors (i.e., hypertension, hospital-diagnosed infections, hypercholesterolemia, and CVD). All combinations were more common in men except for combinations involving low education and depression.

Individuals excluded from our analyses due to missing data on at least one risk factor in the Danish National Health Survey data were older than those included, and among them, there was a higher proportion of women than among the included individuals (60 % vs 53 %) (Supplementary Table A4). The prevalence of risk factors from the registries in the health survey subpopulation was comparable to that of the whole population, except that survey respondents had higher levels of education (24 % of the whole population and 19 % of the subpopulation had low education) (Supplementary Table A3).

Fig. 2 shows the prevalence (%) of the risk factors and their most common combinations, stratified by birth cohorts. The prevalence of risk factors was highest in individuals aged ≥85 years (compared with ages 65 – 74 and 75 – 84 years), except for alcohol consumption, smoking, obesity, diabetes, and sleep disorders, which had lower prevalence in those aged ≥85 years. Most of the identified combinations were also more prevalent in individuals aged ≥85 years. Several combinations did not appear (prevalence <10 %) in the youngest age group, and three combinations (all involving smoking) did not appear in the oldest.

Fig. 3 shows the prevalence (%) of the risk factor clusters and their most common combinations. The cardiometabolic cluster was the most common, with a prevalence of 86 %, followed by the immune cluster (51 %), the neuro-psychosocial cluster (39 %), and the cognitive reserve cluster (29 %). Nine combinations between the four clusters were found in ≥10 % of the health survey subpopulation. Detailed numbers are presented in Supplementary Tables A5 to A7.

In the sensitivity analyses, all risk factors apart from CVD, hearing loss, diabetes, sleep disorders, and vision impairment had a higher prevalence of onset at age <65 years (Supplementary Fig. A2, Table A8). Individuals with low education had the highest prevalence of all risk factors apart from alcohol consumption, which had the highest prevalence in individuals with high education. Twenty-eight combinations that were identified in the main analyses (excluding low education) were more prevalent in the low-education group, except for combinations involving alcohol consumption (Supplementary Fig. A3, Table A9). Twelve of the 28 combinations did not appear in the high education group (prevalence <10 %) (e.g., hypertension and depression). Risk factor prevalence differed according to defined cutoffs for some of the risk factors (Supplementary Table A10), e.g., alcohol consumption prevalence 27 % for >10 units/week and 17 % for >14 units/week (women) and >21 units/week (men); ever smoking was 61 %, daily smoking was 18 %, and current smoking prevalence was 20 %. Finally, physical inactivity, defined as the questionnaire items of light activity or inactivity, was prevalent in 80 % of the population vs 12 % for physically inactive alone.

Table 2
Characteristics of the study populations.

	Whole population		Health survey subpopulation	
	N = 1,214,286		N = 88,656	
Women N, %	651,030	53.6	46,529	52.5
Men N, %	563,256	46.4	42,127	47.5
Age on 1 January 2022, years				
65–74 (born 1948–1957)	621,083	51.2	45,905	51.8
75–84 (born 1938–1947)	452,245	37.2	34,071	38.4
85+ (born ≤1937)	140,958	11.6	8680	9.8
Median birth cohort (IQR)	1948 (1942, 1953)		1948 (1943, 1953)	
Number of risk factors				
No risk factors N, % *	–	–	4828	5.4
At least one risk factor N, %	–	–	83,828	94.6
Only one risk factor N, %*	–	–	10,929	12.3 (13.0 of total with at least one risk factor)
>1 risk factor N, %	–	–	72,899	82.2 (87.0 of total with at least one risk factor)

* Excluding hospital-diagnosed infections from the risk factors, 7683 individuals had no risk factors (8.7 %) and 8074 had only one risk factor (9.1 %). The presented percentages for the health survey subpopulation are unweighted. IQR: Interquartile range; N: Number.

4. Discussion

4.1. Key findings

In this nationwide study in Denmark, we estimated the prevalence of 16 potentially modifiable dementia risk factors and their co-occurrence. Only 5 % of the population had no risk factors, 12 % had only one, and 82 % had multiple risk factors. Thus, the co-occurrence of risk factors is common. Hypertension was the most prevalent risk factor (57 %), and vision impairment was the least prevalent (2 %). The most common combinations were those among the four commonest risk factors (i.e., hypertension, hospital-diagnosed infections, hypercholesterolemia, and CVD). Having at least one cardiometabolic risk factor was the most common (in 86 % of the population). Overall, men, individuals aged ≥85 years, and those with low education had the highest prevalence of risk factors, though with some exceptions, and the prevalence of the combinations also varied.

4.2. Strengths and limitations

Our findings should be interpreted considering some limitations. First, we had decades of available data to determine exposure to the 11 risk factors, while we could only use a single time point for exposure to the five risk factors (smoking, alcohol, obesity, physical inactivity, and social isolation). This may have underestimated the burden of the five risk factors in our population and is particularly noteworthy when

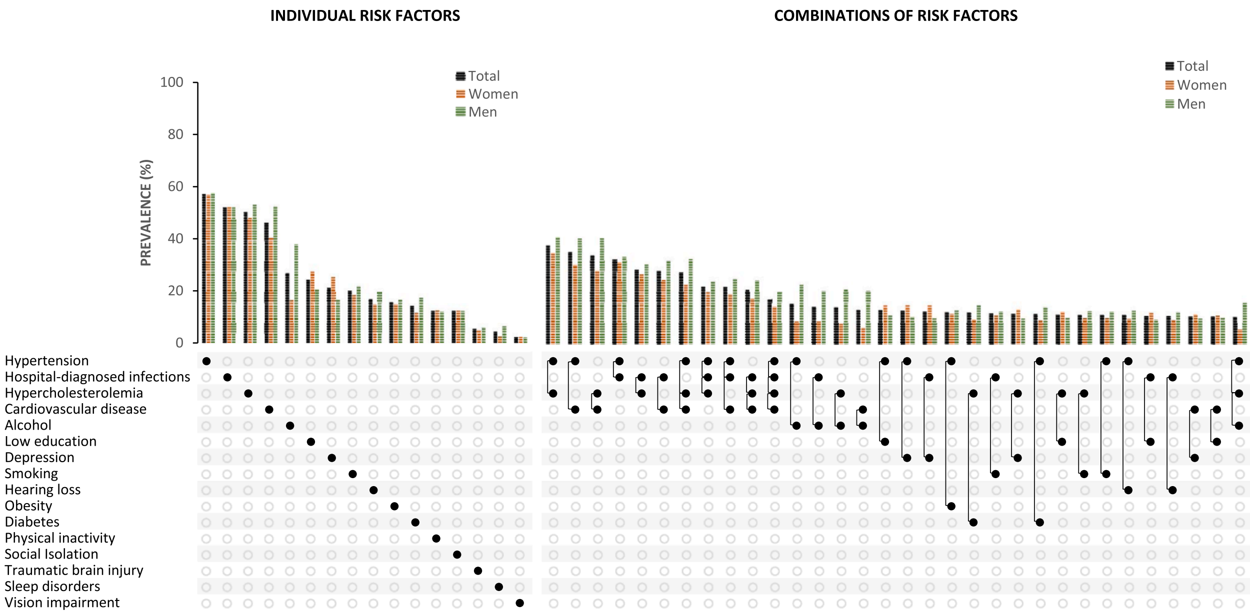

Fig. 1. Prevalence (%) of dementia risk factors and their combinations in the whole population ($N = 1{,}214{,}286$) and the health survey subpopulation ($N = 88{,}656$), and by sex.

The figure shows the prevalence proportion (%) of the 16 dementia risk factors selected in this study and the most common combinations occurring in ≥10 % of the health survey subpopulation. For the whole population, the period prevalences of 11 risk factors were estimated (Hypertension, hospital-diagnosed infections, hypercholesterolemia, cardiovascular disease, low education, depression, hearing loss, diabetes, traumatic brain injury, sleep disorders, and vision impairment). For the health survey subpopulation, the point prevalences of five risk factors were estimated (smoking, alcohol, obesity, physical inactivity, and social isolation). The prevalence estimates reflect a population-level view of persons who have experienced, were diagnosed, or were treated for the risk factors assessed. For the 11 risk factors drawn from the registries and considered as far back as possible (1969/1977 and more complete information from 1995 onwards), 51.2 % of the population reflect risk factors experienced from ages 38 – 47 years, 37.2 % from ages 48 – 57 years, and 11.6 % from ages ≥58 years. The median age at (first) risk factor record ranged between 51 and 68 years. Combination numbers are based on the health survey subpopulation where data on all 16 factors were available. Percentages in the health survey subpopulation were weighted for non-response and different sampling probabilities.

comparing prevalence across age groups at risk factor onset. Similarly, the prevalence of some risk factor combinations that include any of the five risk factors may be less representative of the true burden. Importantly, most of the 11 risk factors assessed using a long retrospective timeframe were chronic conditions such as hypertension and diabetes. For these conditions, whether we had chosen to draw data as far back as possible, or if we pre-specified a period of e.g., 10 years, the prevalence estimates are unlikely to differ substantially [19]. Other risk factors were events experienced by the individuals such as hospital-diagnosed infections, depression, and TBI, but which are not necessarily conditions individuals are living with at the time of our assessment. The prevalence of these events would most likely be lower than estimated in our study if we had pre-specified a timeframe of e.g., 10 years. However, having experienced such events (considered as far back as possible) may have a lasting impact on brain health, and their prevalence is important to reflect for intervention and policy efforts to target. Therefore, it is crucial to stress that the prevalence estimates in our study reflect a population-level view of persons who have experienced, were diagnosed, or were treated for the risk factors assessed.

Second, although we used validated algorithms to define risk factors in the registry data, several were not validated e.g., hearing loss and vision impairment, which may be under-recorded. For these two, we also did not consider the underlying disease. Even where validated algorithms were used, we may have overestimated the disease prevalence (e.g., for hypertension and depression) as medication was used to define the diseases and these may be prescribed for other conditions. Third, we could not differentiate between controlled and uncontrolled conditions or measure severity or temporality. Fourth, we lacked genetic risk data and did not consider ethnicity, both previously shown to contribute to dementia risk profile differences [5,20]. At the start of 2022 in Denmark, only 9 % of the population were non-Western immigrants or their descendants [21]. Fifth, the Danish National Health Survey data were self-reported and there were missing data. Potential consequent biases were limited by applying weights that reduced bias and enhanced representativeness [22,23]. However, if missingness was related to pre-clinical dementia symptoms, this could result in underestimating the risk factors' prevalence due to the overrepresentation of healthier respondents. We cannot exclude this possibility, particularly because excluded individuals due to missing data were older than those included and there was a higher proportion of women among them, which may support that some missingness may be due to preclinical dementia symptoms, hence decreasing the true representativeness of the burden of these risk factors. Further, although the prevalence of all risk factors in the health survey subpopulation was comparable to that in the whole population, the exception was that individuals in the subpopulation had higher education levels.

Despite the limitations, our study was made possible due to the high-quality and nationwide data available for 16 dementia risk factors. Eleven factors were drawn from registry data with negligible selection bias, and five were based on self-reported data in the health survey subpopulation, which was found representative of the whole population, allowing for the exploration of all possible combinations across all 16 dementia risk factors [22,23]. We stratified estimates by sex, age groups, and educational levels, and redefined cutoffs where necessary to provide prevalence measures crucial for policy and research.

4.3. Interpretation and findings in context

Previous reports showed that physical inactivity was the most prevalent factor (prevalence 40 % to 83 %) in Italy [24], Canada, the US, New Zealand, Australia, and Denmark (summarized in [25]), and was reported with a global prevalence of 27.5 % in the 2024 report of the

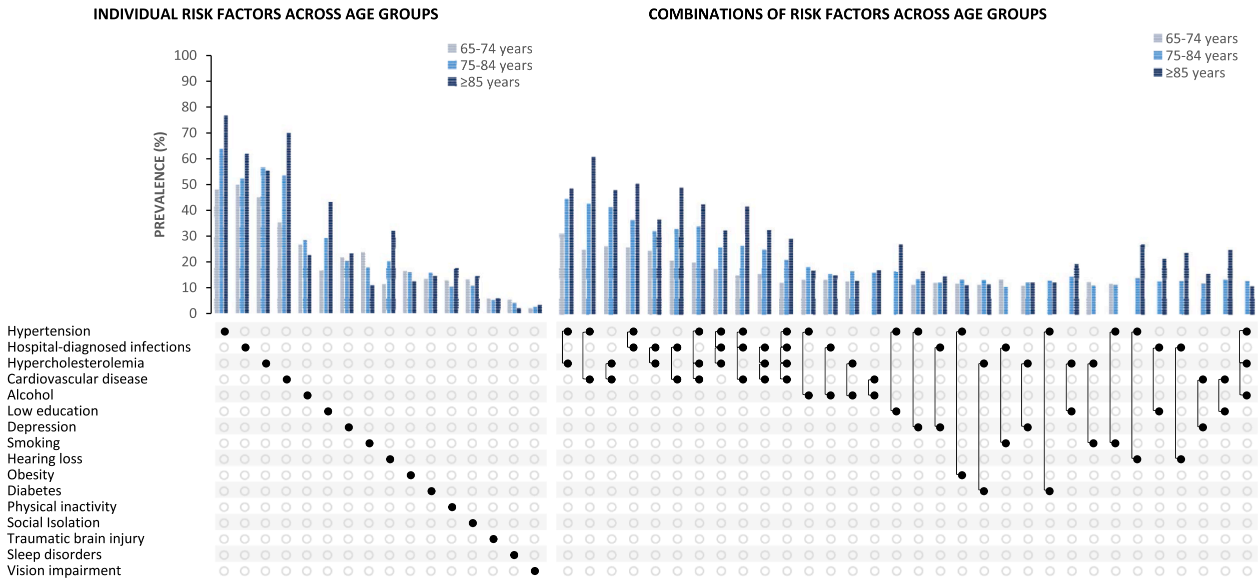

Fig. 2. Prevalence (%) of dementia risk factors in the whole population ($N = 1{,}214{,}286$) and the health survey subpopulation ($N = 88{,}656$) across age groups, and their combinations in the health survey subpopulation.

The figure shows the prevalence proportion (%) of the 16 dementia risk factors and the most common combinations across age groups. Combinations are those identified in the main analysis which had shown a prevalence of ≥10 % in the health survey subpopulation (and ordered in this figure accordingly). For the whole population, the period prevalences of 11 risk factors were estimated (Hypertension, hospital-diagnosed infections, hypercholesterolemia, cardiovascular disease, low education, depression, hearing loss, diabetes, traumatic brain injury, sleep disorders, and vision impairment). For the health survey subpopulation, the point prevalences of five risk factors were estimated (smoking, alcohol, obesity, physical inactivity, and social isolation). The prevalence estimates reflect a population-level view of persons who have experienced, were diagnosed, or were treated for the risk factors assessed. For the 11 risk factors drawn from the registries and considered as far back as possible (1969/1977 and more complete information from 1995 onwards), 51.2 % of the population reflect risk factors experienced from ages 38 – 47 years, 37.2 % from ages 48 – 57 years, and 11.6 % from ages ≥58 years. The median age at (first) risk factor record ranged between 51 and 68 years. Combination numbers are based on the health survey subpopulation where data on all 16 risk factors were available. Percentages in the health survey subpopulation were weighted for non-response and different sampling probabilities.

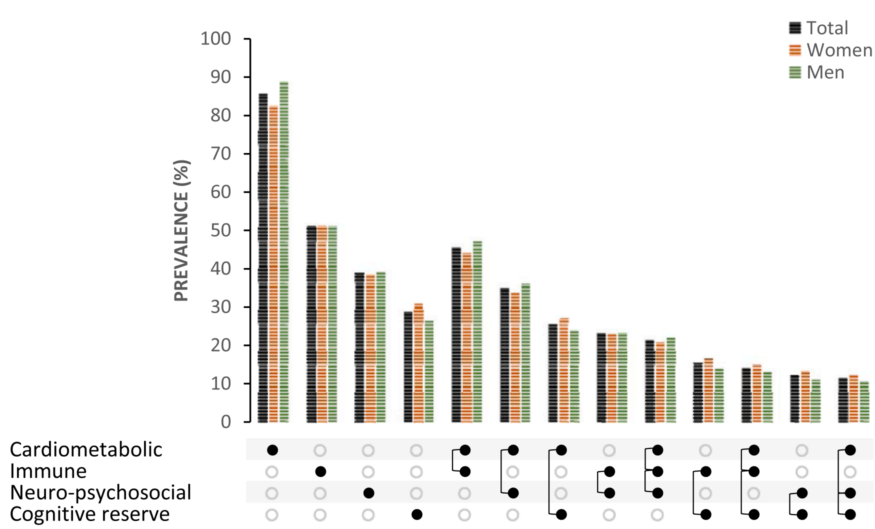

Fig. 3. Prevalence (%) of clusters of dementia risk factors and their combinations in the health survey subpopulation ($N = 88{,}656$), and by sex.

The clusters are groupings of the 16 risk factors: Cardiometabolic (hypertension, cardiovascular disease, diabetes, hypercholesterolemia, obesity, smoking, alcohol, and physical inactivity), neuro-psychosocial (depression, hearing loss, vision impairment, traumatic brain injury, and sleep disorders), immune (hospital-diagnosed infections), and cognitive reserve (social isolation and low education). Percentages were weighted for non-response and different sampling probabilities.

Lancet Commission [2]. In the present study, physical inactivity was also the most common risk factor (80 %) when the definition included light activity and had a prevalence of 12 % when not included. As such, varying prevalence estimates across studies reflect variations in population risk profiles, healthcare systems, policies, and study methodologies including the data sources, risk factor definitions, and the studied population groups (e.g., age cohorts) [21,25,26].

To our knowledge, this study is the first to assess risk factor combinations at a national level using routinely collected administrative and health data, and survey data. Previous studies assessed the number of risk factors [3] or multimorbidity [4–7] but there was considerable variability in the assessed risk factors. Therefore, it is not possible to compare our findings to prior work. The most relevant literature is an abstract of a Canadian study based on a cohort sample of 30,097, where similar risk factors as those in our study were assessed [27]. The most common combinations were reported among the most prevalent risk factors, which involved physical inactivity, hearing loss, sleep disturbance, and obesity [27]. In our study, the most common combinations were those involving cardiometabolic factors (hypertension, hypercholesterolemia, and CVD) in addition to hospital-diagnosed infections (of these, only hypertension was included in the Canadian study). Discrepancies in the combinations between the Canadian study and ours are likely attributed to the prevalence of the single risk factors, as discussed above.

In the present study, men, individuals ≥85 years, and those with low education had the highest prevalence of risk factors. Exceptions were higher prevalence of depression and low education in women, higher prevalence of alcohol consumption, smoking, obesity, diabetes, and sleep disorders in the youngest group (65 – 74 years), and higher prevalence of alcohol consumption in the group with high education. Similar observations were seen in several previous studies across countries [25,28–31], suggesting important implications for policy and research internationally. These can inform multi-country intervention efforts and cross-country joint policies. As for risk factor combinations, the Canadian abstract found no sex differences but reported variations according to age, while educational levels do not seem to have been assessed [27]. In our study, we noted several differences in the prevalence of combinations across the assessed groups e.g., several identified combinations did not appear (prevalence <10 %) in the youngest or oldest age groups, or the high education group. Sex differences may be explained by biological predispositions to disease or societal factors and healthcare-seeking behaviour (e.g., in depression) [28]. Differences across ages and educational levels can be attributed to different risk profiles, generational societal contributions, advancements in disease treatment, and improved lifestyle due to intervention efforts at the individual and population levels.

4.4. Conclusions – Implications for research, practice, and policy

Our findings provide an extensive evidence base at the population-level for policy and dementia risk reduction efforts, both nationally and globally. First, policies and interventions can be tailored and prioritized using the provided evidence on the prevalence of the risk factors and their combinations. Prevalence differences across the sexes, ages, and educational levels for the single risk factors and their co-occurrence are specifically valuable as trends are likely globally informative and can guide multi-country initiatives. We emphasize the need to draw attention toward multidomain interventions, as the co-occurrence of risk factors is common [3]. However, the evidence base is surprisingly scarce on the prevalence of risk factor combinations [3], and our study guides the priorities for future multidomain interventions and thus their implementation. Of particular interest is exploring implementation through policy-driven approaches at the population level [9] as these have great potential for implementation on a large scale across various healthcare systems [32].

Second, our findings on risk factor combinations and the differences across sexes, ages, and educational levels carry important implications for future research. In our population, 86 % had at least one cardiometabolic risk factor. While the interlinks between such factors are well-established, other identified common combinations in the present study are of interest for generating novel hypotheses on risk subgroups and potential underlying mechanisms, as specific combination patterns may impact dementia risk through different pathways. Finally, the impact of co-occurrences of risk factors for the risk of dementia should be investigated in future research with the appropriate dynamic cohort design and longitudinal follow-up periods.

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We have not used any AI.

CRediT authorship contribution statement

Janet Janbek: Writing – review & editing, Writing – original draft, Visualization, Project administration, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Thomas Munk Laursen:** Writing – review & editing, Validation, Formal analysis, Data curation, Conceptualization. **Kasper Jørgensen:** Writing – review & editing, Validation, Conceptualization. **Martin Mejlby Jensen:** Writing – review & editing, Validation, Conceptualization. **Marie Holm Eliasen:** Writing – review & editing, Validation, Conceptualization. **Anne Illemann Christensen:** Writing – review & editing, Validation, Conceptualization. **Sebastian Walsh:** Writing – review & editing, Validation, Conceptualization. **Andrew Sommerlad:** Writing – review & editing, Validation, Conceptualization. **Carol Brayne:** Writing – review & editing, Validation, Conceptualization. **Gunhild Waldemar:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Janet Janbek reports financial support was provided by Alzheimer-forskningsfonden. Janet Janbek reports financial support was provided by KID Foundation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2025.100365.

References

[1] Wolters FJ, Chibnik LB, Waziry R, Anderson R, Berr C, Beiser A, et al. Twenty-seven-year time trends in dementia incidence in Europe and the United States. Neurology 2020;95(5). Aug 4.
[2] Livingston G, Huntley J, Liu KY, Costafreda SG, Selbæk G, Alladi S, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. The Lancet 2024;404(10452):572–628. Aug.
[3] Peters R, Booth A, Rockwood K, Peters J, D'Este C, Anstey KJ. Combining modifiable risk factors and risk of dementia: a systematic review and meta-analysis. BMJ Open 2019;9(1):e022846. Jan.
[4] Grande G, Marengoni A, Vetrano DL, Roso-Llorach A, Rizzuto D, Zucchelli A, et al. Multimorbidity burden and dementia risk in older adults: the role of inflammation and genetics. Alzheimer's Dementia 2021;17(5):768–76. May 6.
[5] Calvin CM, Conroy MC, Moore SF, Kuźma E, Littlejohns TJ. Association of multimorbidity, disease clusters, and modification by genetic factors with risk of dementia. JAMA Netw Open 2022;5(9):e2232124. Sep 20.

[6] Hu HY, Zhang YR, Aerqin Q, Ou YN, Wang ZT, Cheng W, et al. Association between multimorbidity status and incident dementia: a prospective cohort study of 245,483 participants. Transl Psychiatry 2022;12(1):505. Dec 7.

[7] Tai XY, Veldsman M, Lyall DM, Littlejohns TJ, Langa KM, Husain M, et al. Cardiometabolic multimorbidity, genetic risk, and dementia: a prospective cohort study. Lancet Healthy Longev 2022;3(6):e428–36. Jun.

[8] Hafdi M, Hoevenaar-Blom MP, Richard E. Multi-domain interventions for the prevention of dementia and cognitive decline. Cochrane Database Systemat Rev 2021;2021(11). Nov 8.

[9] Röhr S, Kivipelto M, Mangialasche F, Ngandu T, Riedel-Heller SG. Multidomain interventions for risk reduction and prevention of cognitive decline and dementia: current developments. Curr Opin Psychiatry 2022;35(4):285–92. Jul.

[10] Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish national patient registry: a review of content, data quality, and research potential. Clin Epidemiol 2015;7:449–90.

[11] Mors O, Perto GP, Mortensen PB. The Danish psychiatric central research register. Scand J Public Health 2011;39(7_suppl):54–7. Jul.

[12] Wallach Kildemoes H, Toft Sørensen H, Hallas J. The Danish national prescription registry. Scand J Public Health 2011;39(7_suppl):38–41. Jul.

[13] Jensen VM, Rasmussen AW. Danish education registers. Scand J Public Health 2011;39(7_suppl):91–4. Jul 20.

[14] Christensen AI, Lau CJ, Kristensen PL, Johnsen SB, Wingstrand A, Friis K, et al. The Danish national health survey: study design, response rate and respondent characteristics in 2010, 2013 and 2017. Scand J Public Health 2022;50(2):180–8. Mar 8.

[15] Brain J, Greene L, Tang EYH, Louise J, Salter A, Beach S, et al. Cardiovascular disease, associated risk factors, and risk of dementia: an umbrella review of meta-analyses. Front Epidemiol 2023;3. Feb 9.

[16] Damsgaard L, Janbek J, Laursen TM, Erlangsen A, Spira AP, Waldemar G. Hospital-diagnosed sleep disorders and incident dementia: a nationwide observational cohort study. Eur J Neurol 2022;29(12):3528–36. Dec 18 [Internet]Available from: https://onlinelibrary.wiley.com/doi/10.1111/ene.15517.

[17] Janbek J, Laursen TM, Frimodt-Møller N, Magyari M, Haas JG, Lathe R, et al. Hospital-diagnosed infections, autoimmune diseases, and subsequent dementia incidence. JAMA Netw Open 2023;6(9):e2332635. Sep 7 [Internet]Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2809056.

[18] Danish Health Authority. Anbefalinger om alkohol. 2023.

[19] Juul-Larsen HG, Christensen LD, Andersen O, Bandholm T, Kaae S, Petersen J. Development of the "chronic condition measurement guide": a new tool to measure chronic conditions in older people based on ICD-10 and ATC-codes. Eur Geriatr Med 2019;10(3):431–44. Jun 10.

[20] Lee M, Whitsel E, Avery C, Hughes TM, Griswold ME, Sedaghat S, et al. Variation in population attributable fraction of dementia associated with potentially modifiable risk factors by race and ethnicity in the US. JAMA Netw Open 2022;5(7):e2219672. Jul 6.

[21] Jørgensen K, Nielsen TR, Nielsen A, Waldemar G. Potential for prevention of dementia in Denmark. Alzheimer's Dementia 2023;19(10):4590–8. Oct 18.

[22] Jensen HAR, Lau CJ, Davidsen M, Feveile HB, Christensen AI, Ekholm O. The impact of non-response weighting in health surveys for estimates on primary health care utilization. Eur J Public Health 2022;32(3):450–5. Jun 1.

[23] Momen NC, Lasgaard M, Weye N, Edwards J, McGrath J, Plana-Ripoll O. Representativeness of survey participants in relation to mental disorders: a linkage between national registers and a population-representative survey. Int J Popul Data Sci 2022;7(4). Oct 19.

[24] Asta F, Bellomo G, Contoli B, Lombardo FL, Minardi V, Salemme S, et al. Preventing dementia in Italy: estimations of modifiable risk factors and public health implications. J Prev Alzheimers Dis 2025;12(3):100055. Mar.

[25] Son S, Speechley M, Zou GY, Kivipelto M, Mangialasche F, Feldman HH, et al. Potentially modifiable dementia risk factors in Canada: an analysis of Canadian longitudinal study on aging with a multi-country comparison. J Prev Alzheimers Dis 2024.

[26] Lee M, Whitsel E, Avery C, Hughes TM, Griswold ME, Sedaghat S, et al. Variation in population attributable fraction of dementia associated with potentially modifiable risk factors by race and ethnicity in the US. JAMA Netw Open 2022;5(7):e2219672. Jul 6.

[27] Son S, Speechley MR, Montero-Odasso M. What are the most prevalent combinations of modifiable dementia risk factors that can be targeted in multidomain lifestyle intervention in Canada? Alzheimer's & Dementia 2023;19(S23). Dec 25.

[28] Elser H, Horváth-Puhó E, Gradus JL, Smith ML, Lash TL, Glymour MM, et al. Association of early-, middle-, and late-life depression with incident dementia in a Danish cohort. JAMA Neurol 2023;80(9):949. Sep 1.

[29] Sindi S, Kåreholt I, Ngandu T, Rosenberg A, Kulmala J, Johansson L, et al. Sex differences in dementia and response to a lifestyle intervention: evidence from Nordic population-based studies and a prevention trial. Alzheimer's Dementia 2021;17(7):1166–78. Jul 13.

[30] Gong J, Harris K, Lipnicki DM, Castro-Costa E, Lima-Costa MF, Diniz BS, et al. Sex differences in dementia risk and risk factors: individual-participant data analysis using 21 cohorts across six continents from the COSMIC consortium. Alzheimer's Dementia 2023;19(8):3365–78. Aug 15.

[31] Ngandu T, von Strauss E, Helkala EL, Winblad B, Nissinen A, Tuomilehto J, et al. Education and dementia. Neurology 2007;69(14):1442–50. Oct 2.

[32] Walsh S, Wallace L, Kuhn I, Mytton O, Lafortune L, Wills W, et al. Population-level interventions for the primary prevention of dementia: a complex evidence review. EClinicalMedicine 2024;70:102538. Apr.