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ORIGINAL ARTICLE

Dementia increases mortality beyond effects of comorbid conditions: A national registry-based cohort study

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Abstract

Background and purpose: Mortality is known to be markedly increased in people with dementia. However, the association between multiple chronic conditions and mortality in dementia is not well clarified. The aim of this study was to investigate the impact of somatic and psychiatric diseases on mortality in dementia compared with the general elderly population.

Methods: Using a cohort study design, nationwide registry data from 2006 to 2015 on dementia and psychiatric and somatic comorbidities defined by the Charlson Comorbidity Index (CCI) were linked. Impact of chronic conditions was assessed according to mortality rate ratios (MRRs) in all Danish residents aged ≥ 65 years with and without dementia.

Results: Our population comprised 1,518,917 people, of whom 114,109 people were registered with dementia. The MRRs was 2.70 (95% confidence interval 2.68, 2.72) in people with dementia after adjusting for sex, age, calendar year, and comorbidities. MRRs increased with higher CCI score, and when comparing people with a similar comorbidity load, MRRs were significantly higher for people with dementia.

Conclusions: The comorbidity load was associated with increased mortality in both people with and without dementia. Mortality in dementia remained increased, even after adjusting for psychiatric and chronic somatic comorbidities. Our findings suggest that dementia disorders alone contribute to excess mortality, which may be further increased by comorbidities.

KEYWORDS

cohort study, comorbidity, dementia, mortality

INTRODUCTION

Mortality is markedly increased in people with dementia [1]. This excess mortality is complex and associated with multiple factors, such as age [2–8], being male [6–9], dementia subtype and severity [10], reduction in activities of daily living [2,4,11,12], institutionalization [3], and possibly low cognitive performance [2,3,6,9,13,14].

Concurrent chronic comorbidities have also been linked to increased mortality in people with dementia [1,15,16], just as specific comorbidities have been found to increase mortality in dementia, including cerebrovascular disease [15], diabetes [16], and hypertension [16]. It is possible that insufficient treatment of comorbidities could contribute to excess mortality in dementia. However, studies investigating the association between the load

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of chronic comorbidities and mortality in people with and without dementia are scarce [17,18].

Globally, the number of people living with dementia is increasing, and due to higher life expectancy, it is expected to increase more rapidly during the next decades [19]. The prevalence of comorbidities also increases with age. Therefore, to understand the association between comorbidities and mortality in the growing population of people with dementia, more knowledge is needed.

The present study examined three hypotheses: (i) the presence of other somatic diseases and psychiatric conditions is associated with increased mortality in people with dementia; (ii) after adjusting for comorbidities, people with dementia will have higher mortality compared with people without dementia; and (iii) people with chronic somatic or psychiatric conditions and dementia have excess mortality compared with people with the same chronic somatic or psychiatric conditions without dementia.

Denmark's longstanding practice of assigning all residents an individual personal identification number means that Danish national registries represent unique data sources for investigating the three hypotheses in an entire national population. The aim of this study was to investigate the impact of psychiatric and somatic conditions on mortality in people with dementia compared to people without dementia.

METHODS

Study design and data sources

The study was designed as a registry-based cohort study using data from Danish national registries: the Danish Civil Registration System; the Danish National Patient Registry; the Psychiatric Central Register; the National Prescription Registry; and Statistics Denmark [20–23]. Denmark has universal free access to healthcare. The second and third registries listed above include information on all contacts to the secondary healthcare system since 1995. The registries have previously been described [24].

We obtained data on all hospital-based psychiatric diagnoses from 1970 to 2015 and on all somatic diagnoses from 1977 to 2015, and dementia medications from 1995 to 2015. Data were made available through Statistics Denmark, which also provided data on immigration and date of death. Data were linked using anonymized personal identification numbers.

Study period and study population

The study period was defined as 1 January 2006 to 31 December 2015. Within this 10-year period all Danish residents and immigrants to Denmark aged ≥ 65 years were included. Each person was considered at risk of death from time of inclusion until death, emigration, loss to follow-up, the day they turned 110 years old, or the study period ended, whichever occurred first. People were censored

at the age of 110 as the risk of accidental misregistration at this age was considered high (although rare).

Definition of dementia

Dementia was defined as being registered with a dementia diagnosis in the Danish National Patient Registry or the Psychiatric Central Register or as having filled a prescription for an anti-dementia medication. Tables S1 and S2 in the Supporting Information present the diagnosis codes and Anatomical Therapeutic Chemical codes for this identification. Date of dementia onset was defined as either the date of the first hospital contact (in- or outpatient) where a dementia diagnosis was registered, or the date an anti-dementia drug prescription was filled for the first time, whichever occurred first. Dementia is usually diagnosed in a hospital setting in Denmark. As we wanted to examine late-onset dementia, we excluded people registered with dementia prior to age 65 years.

Definition of comorbidities

Comorbidities were defined as continuous variables. Risk time was delineated as the disease being absent or present. We included information on 19 somatic diseases and four categories of psychiatric conditions (Tables S3 and S4 present the diagnostic codes).

Somatic conditions

In accordance with the Charlson Comorbidity Index (CCI) method, all comorbidities were defined as continuous variables based on weighted comorbidity scores. Comorbidity scores assign weights, from 1 to 6, to each comorbidity for every individual, who are then given a sum of the weights based on all present comorbidities. A CCI score of zero represents no comorbidities, and a score from 1 to ≥ 6 represents a gradually higher load of comorbidities [25].

To examine the load of comorbidities, we used a modified version of the CCI in which dementia was excluded, leaving 18 chronic somatic conditions: (i) myocardial infarction; (ii) congestive heart disease; (iii) peripheral vascular disease; (iv) cerebrovascular disease; (v) chronic pulmonary disease; (vi) connective tissue disease; (vii) ulcer disease; (viii) mild liver disease; (ix) diabetes mellitus; (x) hemiplegia; (xi) moderate/severe renal disease; (xii) diabetes mellitus with chronic complications; (xiii) any tumor; (xiv) leukemia; (xv) lymphoma; (xvi) moderate/severe liver disease; (xvii) metastatic solid tumor; and (xviii) AIDS. This modified CCI is referred to hereafter as the CCI.

As atrial fibrillation is a known risk factor for developing dementia and could have an impact on mortality in dementia, we added it to the list of investigated somatic diseases without including it in the CCI.

Psychiatric conditions

A recent study investigating psychiatric diseases and mortality found that all classes of psychiatric diseases were related to excess mortality, even single episodes of depression [26]. Thus, we believe that the psychiatric diseases listed can have a potential effect on mortality, even after being declared cured.

We included data on four groups of psychiatric conditions: (i) mental and behavioral disorders due to psychoactive substance abuse; (ii) schizophrenia and related disorders; (iii) affective disorders; and (iv) neurotic, stress-related and somatoform disorders.

Statistics

We used Poisson regression to calculate mortality rate ratios (MRRs) with SAS, version 9.4 (SAS Institute Inc.). First, we assessed MRRs comparing women and men, respectively, with and without dementia, stratified by CCI scores of 0 to ≥ 6 . The reference group was defined as people without dementia with a CCI score of zero (reference value was 1.00). Second, we quantified the excess mortality by assessing the MRRs for men and women by CCI score stratified into 5-year age groups. For each age- and CCI score-stratified group, the reference groups were defined as 1.00 in the same age- and CCI score group without dementia. Thus, in these analyses, the effect of an increasing CCI score on mortality was annulled. Third, we assessed MRRs for the selected 23 comorbidities in combination with dementia by defining the reference as 1.00 for women and men who had the specific comorbidity but not dementia. Fourth, we assessed MRRs using three different models adjusting for the listed covariates: Model 1: age and calendar year; Model 2: Model 1 plus selected psychiatric conditions (substance abuse disorders, schizophrenia, affective disorders, and neurotic, stress-related, and somatoform disorders); Model 3: Model 2 plus atrial fibrillation and somatic diseases included in the CCI. Additionally, we performed a sensitivity analysis equivalent to Models 1–3, including only incident cases diagnosed with dementia at age ≥ 65 years from 1 January 2006 to 31 December 2015. Statistical significance was defined according to a 5% significance level.

Data approvals

This study was approved by the Danish Data Protection Agency, Statistics Denmark, and the Danish Health Data Authority. Using anonymized registry data, no ethics committee approval was required by Danish law.

RESULTS

Our population comprised 1,518,917 people (women: 820,758; men: 698,159) observed over 9,433,208 person-years (women: 5,008,459;

men: 4,209,921). There were 114,109 people (women: 71,528; men: 42,581) registered with dementia, accounting for 326,112 person-years (women: 214,828; men: 111,284). The mean follow-up time for people without dementia was 6.48 years and for people with dementia it was 2.86 years. During the 10-year period, 439,205 people died (women: 234,517; men: 204,688), of whom 77,409 were registered with dementia (women: 48,295; men: 29,114). Tables 1 and 2 show descriptive data of the population. Additionally, we calculated the distribution of person-years for the 5-year age groups by CCI score (Tables S5 and S6). In people with dementia aged < 85 years, the percentage of years lived with low CCI scores was markedly lower than in those without dementia, whereas in people aged ≥ 85 years, the distribution was similar in people with and without dementia.

Mortality rate ratio stratified by Charlson Comorbidity Index score

The age- and calendar year-adjusted MRRs increased with higher CCI scores and were significantly higher for men and women with dementia for all CCI scores compared to those without dementia (Figure 1). Additionally, the highest difference in MRRs between people with and without dementia was observed in the groups with zero or few comorbidities.

Excess mortality stratified by age and Charlson Comorbidity Index score

Excess mortality was most predominant in the youngest age groups with a low CCI score (Figure 2). The mortality was significantly higher for women and men in all age and CCI score groups compared with those without dementia.

Excess mortality in dementia and concurrent comorbidities

For women and men with any of the chronic somatic and psychiatric conditions, also having dementia was associated with a significantly higher mortality (Figure 3).

Table 3 presents three models of MRRs for women and men with dementia adjusted for age and divided into 5-year age groups. The reference groups were women and men, respectively, in the same age groups without dementia. Model 1 was adjusted for age and calendar year. The MRRs were highest in the age groups 65–69 years (women: 5.39 [95% confidence interval {CI} 4.84, 6.01]; men: 5.41 [95% CI 4.98, 5.88]) and lowest in the age groups ≥ 90 years (women: 2.06 [95% CI 2.03, 2.10]; men: 2.21 [95% CI 2.15, 2.28]). In Model 3, we adjusted for psychiatric and chronic somatic diseases and observed a decline in MRRs for the age groups 65–69 years (women: 2.73 [95% CI 2.44, 3.05]; men: 3.34 [95% CI 3.07, 3.63]), whereas the MRRs in the age groups ≥ 90 years were stable (women: 2.04 [95% CI

TABLE 1 Demographic data for the Danish elderly population, 2006 to 2015, stratified by sex and dementia status; number of persons, number of deaths, person-years, crude mortality rates, mean age in 2006 and 2015, and the average mean age at death. Number of deaths, person-years, and crude mortality rates are presented in 5-year age strata

Variables	Women		Men	
	Dementia	No dementia	Dementia	No dementia
Persons, N	71,528	749,230	42,581	655,578
Number of deaths	48,295	186,222	29,114	175,574
Person-years	214,828	5,008,459	111,284	4,098,637
Mortality rate, per 100 person-years	22.5	3.7	26.2	4.3
Mean (SD) age: 1 January 2006, years	83.8 (6.5)	75.9 (7.7)	81.1 (6.5)	74.1 (6.8)
Mean (SD) age: 1 January 2015, years	84.3 (6.9)	75.0 (7.6)	81.4 (6.7)	73.7 (6.6)
Average mean (SD) age at death, years	87.1 (6.5)	83.1 (9.0)	84.1 (6.5)	79.6 (8.3)
Age group				
65–69 years				
Number of deaths	331	18422	576	27,506
Person-years	4902	1,590,642	5477	1,526,855
Mortality rate, per 100 person-years	6.8	1.2	10.5	1.8
70–74 years				
Number of deaths	1758	22145	2198	30497
Person-years	17,026	1,198,014	15,918	1,076,665
Mortality rate, per 100 person-years	10.3	1.8	13.8	2.8
75–79 years				
Number of deaths	4717	28,035	4795	33,492
Person-years	34,827	896,874	25,295	727,928
Mortality rate, per 100 person-years	13.5	3.1	19.0	4.6
80–84 years				
Number of deaths	10,032	33,916	7775	34,441
Person-years	54,791	656,181	30,535	452,816
Mortality rate, per 100 person-years	18.3	5.2	25.5	7.6
85–89 years				
Number of deaths	14,710	36,770	8334	28,582
Person-years	59,912	420,858	23,640	226,193
Mortality rate, per 100 person-years	24.6	8.7	35.3	12.6
≥90 years				
Number of deaths	16,747	46,934	5436	21,056
Person-years	43,370	245,889	10,419	88,180
Mortality rate, per 100 person-years	38.6	19.1	52.2	23.9

2.00, 2.08]; men 2.17 [95% CI 2.10, 2.24]). The sensitivity analysis of incident cases did not change the results (Table S7).

DISCUSSION

This is the first nationwide study to investigate the impact of comorbid psychiatric and somatic conditions on mortality in dementia compared with the general elderly population. We found that a higher load of somatic comorbidities was associated with a higher

mortality. Although the excess mortality in people with dementia was most pronounced in groups with no or few comorbidities compared with the general elderly population, it was, nonetheless, significantly higher for all CCI score groups.

In our fully adjusted model, where we adjusted for calendar year, age, and psychiatric and somatic comorbidities, mortality remained more than double that in people with dementia compared with the general elderly population. Thus, our data suggest that the excess mortality in dementia cannot solely be explained by the comorbidity load. Finally, for each of the investigated somatic and psychiatric

TABLE 2 Descriptive data for the Danish elderly population, 2006 to 2015, stratified by sex and dementia status; number of deaths, person-years, and crude mortality rates, stratified by Charlson Comorbidity Index score and by occurrence of psychiatric comorbidity

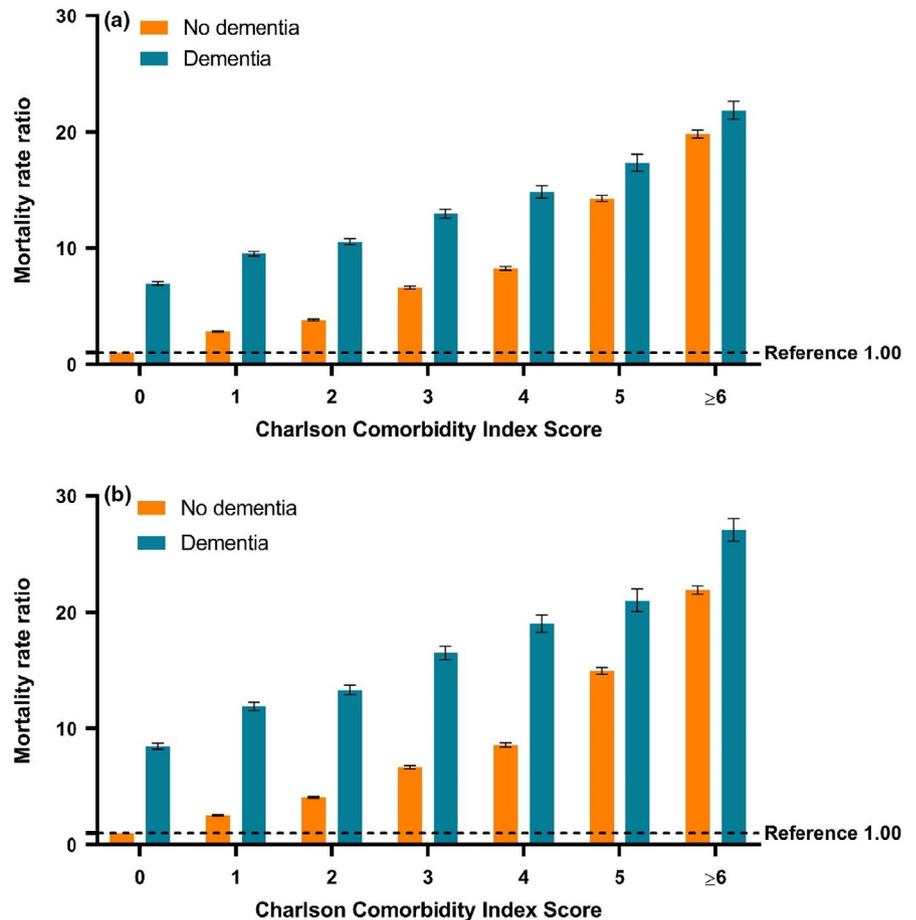
	Women		Men	
	Dementia	No dementia	Dementia	No dementia
Charlson Comorbidity Index				
0				
Number of deaths	13,056	27,597	5698	20,677
Person-years	83,297	2,775,629	34,631	2,089,297
Mortality rate, per 100 person-years	15.7	1.0	16.5	1.0
1				
Number of deaths	10,935	29,733	5967	21,420
Person-years	48,683	803,780	25,524	709,212
Mortality rate, per 100 person-years	22.5	3.7	23.4	3.0
2				
Number of deaths	9154	36,495	5362	30,477
Person-years	37,838	768,855	19,704	614,165
Mortality rate, per 100 person-years	24.2	4.7	27.2	5.0
3				
Number of deaths	5886	26,957	4020	24,729
Person-years	19,573	282,883	11,939	270,484
Mortality rate, per 100 person-years	30.1	9.5	33.7	9.1
4				
Number of deaths	3421	17,640	2600	18,748
Person-years	10,453	156,391	7160	165,885
Mortality rate, per 100 person-years	32.7	11.3	36.3	11.3
5				
Number of deaths	2438	19,761	1984	21,015
Person-years	6917	111,188	4919	110,479
Mortality rate, per 100 person-years	35.2	17.8	40.3	19.0
≥6				
Number of deaths	3405	28,039	3483	38,508
Person-years	8067	109,732	7407	139,115
Mortality rate, per 100 person-years	42.2	25.6	47.0	27.7
Psychiatric comorbidity				
No				
Number of deaths	39,494	165,189	24,916	161,592
Person-years	172,784	4,631,956	94,412	3,895,119
Mortality rate, per 100 person-years	22.9	3.6	26.4	4.1
Yes				
Number of deaths	8801	21,033	4198	13,982
Person-years	42,044	376,503	16,873	203,517
Mortality rate, per 100 person-years	20.9	5.6	24.9	6.9

conditions, having a coexisting dementia disease was associated with a significantly higher mortality, even in terms of metastatic cancer.

It is difficult to compare our results with other studies because, to the best of our knowledge, there are no studies available investigating the impact of multiple comorbidities in people with dementia

in a complete nationwide population. However, a Canadian study based on data from physicians, hospital admissions, ambulatory care utilization, and clinical laboratory results included the entire elderly population of Alberta ($N = 610,457$) for practical purposes [17]. The study investigated the impact of 29 comorbidities, as well

FIGURE 1 Mortality by Charlson Comorbidity Index (CCI). (a) Age- and calendar year-adjusted mortality by CCI in women. (b) Age- and calendar year-adjusted mortality by CCI in men. Mortality rate ratios adjusted for age and calendar year for women (a) and men (b) stratified by CCI. The reference is defined as 1.00 for women and men without dementia with a CCI score of zero. Error bars represent 95% confidence intervals



as occurrence of multiple comorbidities on the risk of mortality in people with dementia compared with people without [17]. In line with our results, they reported that (i) mortality increased with the number of comorbidities for all elderly people but was significantly higher in people with dementia, and that (ii) differences in hazard ratios for mortality comparing people with and without dementia were reduced with an increasing number of comorbidities and were attenuated with increasing age [17]. When comparing the hazard ratios from the Canadian study with our MRRs, our values were markedly higher, especially in the youngest age groups with few comorbidities. These differences could be explained by (i) the fact that the Canadian study included more comorbidities, thus increasing the risk of having comorbidities; (ii) the fact that our study only included data on comorbidity diagnoses from the secondary health sector, possibly reflecting more severe diseases or disease stages; and (iii) the fact that our study adjusted for calendar year. Overall, our findings give weight to the existing knowledge that mortality in people with dementia increases with the number of comorbidities. The importance of including information about comorbidities when assessing risk of mortality was also emphasized by Haaksmas *et al.* [18]. They introduced a survival prediction table, estimating 3-year survival probability after dementia diagnoses [18]. Using the four strongest predictors of mortality in their model (age, sex, comorbidities, and global cognition), they were able to predict 3-year survival probability accurately 70%–71% of the time [18].

This study also assessed mortality in people with dementia compared with the general elderly population. In our fully adjusted model (age, calendar year, psychiatric and somatic comorbidities), the MRRs was 2.70 (95% CI 2.68, 2.72). Other studies have assessed mortality in smaller populations comparing people and without dementia, adjusted for multiple comorbidities [27–29]. They found hazard ratios of mortality of 1.47 (95% CI 1.35, 1.60) [27] and 2.07 (95% CI 1.62, 2.66) [28], and a relative risk of 1.80 (95% CI 1.46, 2.21) [29]. However, these results all included adjustments for activities of daily living or level of care. Furthermore, two of these studies assessed comorbidities at time of diagnosis of dementia or baseline only [27,28], whereas our comorbidities were continuous variables, allowing the number of comorbidities to increase throughout the study period. These two factors may explain why we found a higher MRRs.

Our data suggest that the excess mortality in dementia cannot solely be explained by the comorbidity load. We believe that the excess mortality is caused by the dementia disorder per se, as most dementia disorders are progressive, fatal brain diseases. There are several possible explanations for the excess mortality in dementia. First, there may be an association between frailty, dementia, and mortality. Frailty, identified as a risk factor for developing dementia [30], has also been associated with increased risk of mortality in people with dementia [31,32]. Furthermore, an autopsy study by Wallace *et al.* [33] reported that people with less frailty were less

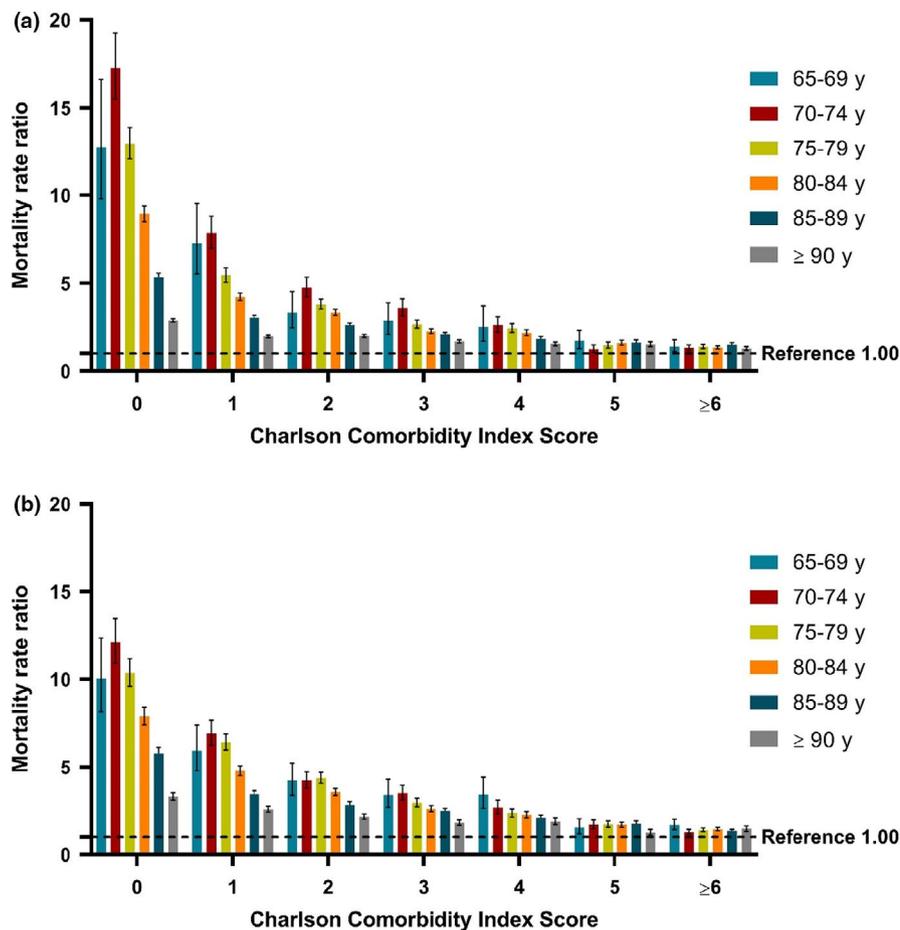


FIGURE 2 Excess mortality by Charlson Comorbidity Index (CCI). (a) Excess mortality in women with dementia by CCI. (b) Excess mortality in men with dementia by CCI. The age- and calendar year-adjusted mortality rate ratios (MRRs) are presented for women (a) and men (b) with dementia in 5-year age groups stratified by CCI. For each of the age groups and CCI scores, the reference is defined as 1.00 for women and men without dementia in the same age group and with the same CCI score. Thus, the MRRs becomes a measure of the excess mortality stratified by CCI score. Error bars represent 95% confidence intervals

likely to develop Alzheimer's dementia clinically, despite similar neuropathological Alzheimer's pathology in their brains, whereas people who were more frail were more likely to express both neuropathological changes and clinical dementia symptoms. Frailty may be a moderator of the Alzheimer's disease pathology and a risk factor for Alzheimer's dementia. In our study, we did not assess frailty. However, we believe that increased frailty could lead to a higher risk of dementia, further increasing mortality. Hereby, frailty could potentially explain some of the observed excess mortality in dementia in our study.

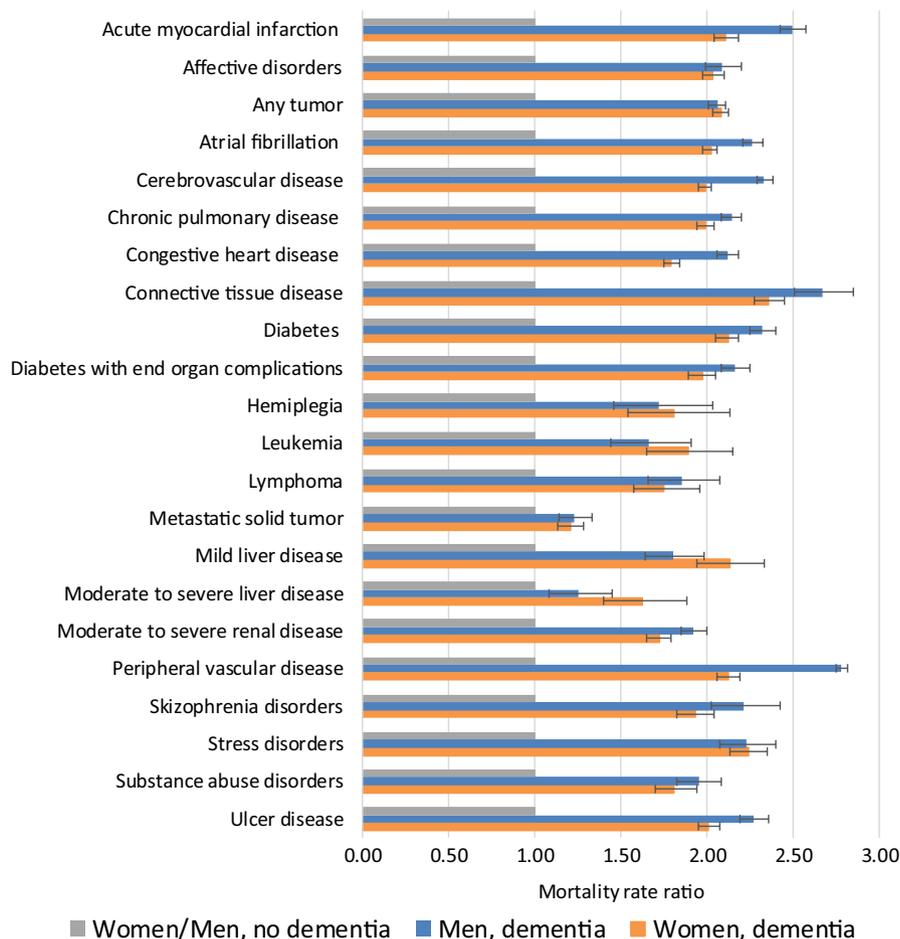
Second, people with dementia have a different risk factor profile from people without dementia. A review identified nine comorbidities to be more frequent in people with dementia (falls, delirium, epilepsy, weight loss and nutritional disorders, incontinence, sleep disturbances, visual dysfunction, oral disease, and frailty) [30], whereas a population-based study found that other comorbidities were less frequent (hypertension, type 2 diabetes mellitus, ischemic heart disease, angina, and myocardial infarction) [34]. There is also the issue of whether comorbidities were actually less prevalent or just underdiagnosed [34].

Third, we believe that there might be a higher risk of inappropriate or insufficient treatment of other diseases in people with dementia and that this could increase mortality. For example, a review by Bunn et al. [35] found some evidence that people with dementia and diabetes or visual impairment did not have the same access to

care as people with diabetes or visual impairment without dementia. We believe that a difference in management of comorbidities could be attributed to the excess mortality in dementia.

We found that in the youngest age groups, MRRs were reduced significantly when adjusting for comorbidities, whereas the adjustments did not change much in the oldest age groups. Younger age was associated with higher MRRs after adjusting for comorbidities. We believe that there are three possible explanations for this. First, mortality for people aged ≥ 85 years is already high, which is why concurrent conditions do not increase mortality as much proportionally. Second, since comorbidities were more frequent in the oldest age groups and the distribution of comorbidities was similar in people aged ≥ 85 years with and without dementia, our results suggest that comorbidities represent an equally great risk of mortality for people with and without dementia. In other words, the effect of dementia becomes diluted by having more comorbidities. Third, there may be a difference in the distribution of dementia subtypes in the various age groups. Onset of frontotemporal dementia and Lewy body dementia usually occurs earlier compared with Alzheimer's disease and vascular dementia. These two first-mentioned dementia subtypes have been reported to have significantly higher mortality than in Alzheimer's disease [3]. Thus, an unequal distribution of dementia subtypes favoring the ones with the highest mortality rate in the youngest age groups may partially explain the persistent excess mortality in our fully adjusted model.

FIGURE 3 Excess mortality in dementia and concurrent comorbidities. Excess mortality in women and men with dementia and selected comorbidities. The reference is defined as 1.00 for women and men without dementia but with the selected comorbidities. Error bars represent 95% confidence interval. Results for AIDS are not presented due to low sample size



This study has some limitations. First, different comorbidities may increase the risk of dying from the various dementia subtypes. However, even though the validity of dementia diagnoses in the Danish national registries is high, the specific dementia subtypes are not useful, as a large proportion of people have an unspecific dementia diagnosis [36]. Second, the severity stage of dementia has been associated with mortality in dementia, and including this variable would have been preferable [10]. Unfortunately, no data for assessing severity stage are available from the Danish national registries. Third, as diagnoses are often made months or years after symptom onset, our population may include some people with dementia symptoms prior to the age of 65 years. However, the definition of early- and late-onset dementia is arbitrary. A review found comparable survival in early- and late-onset dementia, so we do not believe this will have affected our result substantially [10]. Fourth, the study aims of providing an overview of how a range of multiple different conditions is associated with mortality in dementia led to broadly defining disease groups. One example of this is cancer comorbidity because different cancer types and additional subtypes are associated with different mortality risks [37]. Thus, when interpreting our results, the differential mortality risks for each disease group should be considered. Fifth, in Denmark, as in many other countries, the estimated number of people living with dementia is substantially higher than the number of people that are registered with a diagnosis. A study based on findings

from population-based studies estimated that Denmark would have approximately 87,000 people with dementia in Denmark in 2015 [38]. However, in our previous study, only 36,000 people were registered with dementia in 2015 [39]. Thus, our study may underestimate the prevalence of dementia. Sixth, we included all diagnoses on comorbidities registered from the 1970s to 2015. It is possible that the use of diagnoses changed during this period, and also in terms of the use of dementia diagnoses in the study period. Seventh, treatments for comorbid conditions may have had an effect; for example, antipsychotics have been associated with increased mortality in older people [40].

Strengths of the present study include the fact that it uses data from an entire, unselected national cohort. The population is large and represents many person-years at risk. The dates of diagnoses and deaths are continuous variables, for which the time intervals are days. The risk time that each person in this study contributes is therefore quite accurate. Furthermore, due to follow-up in national registries, this large cohort has minimal dropouts and no missing data. Our information on comorbidities covered continuous variables over a long period from the 1970s to 2015, allowing us to track changes in comorbidities until time of death, instead of assessing a comorbidity status at baseline only. Finally, the registered dementia diagnoses and somatic conditions have a high validity in the national registries, making them beneficial for use in epidemiological studies [25,41].

TABLE 3 Mortality rate ratios are presented for women and men in 5-year age strata and an age-adjusted average

Age	Model 1 Adjusted for age and calendar year		Model 2 Adjusted for age, calendar year and psychiatric conditions		Model 3 Adjusted for age, calendar year, and psychiatric and chronic somatic conditions	
	Women with dementia		Women with dementia		Women with dementia	
	MRRs	95% CI	MRRs	95% CI	MRRs	95% CI
Age-adjusted average	2.78	(2.75, 2.81)	2.66	(2.63, 2.68)	2.61	(2.59, 2.64)
65–69 years	5.38	(4.82, 6.00)	3.97	(3.55, 4.43)	2.70 ^a	(2.41, 3.01)
70–74 years	5.33	(5.08, 5.60)	4.51	(4.29, 4.74)	3.29 ^b	(3.12, 3.46)
75–79 years	4.16	(4.04, 4.29)	3.79	(3.67, 3.91)	3.24 ^b	(3.14, 3.35)
80–84 years	3.46	(3.38, 3.54)	3.31	(3.24, 3.39)	3.12 ^b	(3.05, 3.19)
85–89 years	2.77	(2.71, 2.82)	2.70	(2.65, 2.76)	2.67 ^b	(2.61, 2.72)
≥90 years	2.06	(2.03, 2.10)	2.04	(2.01, 2.08)	2.04 ^b	(2.00, 2.08)

Age	Men with dementia		Men with dementia		Men with dementia	
	MRRs	95% CI	MRRs	95% CI	MRRs	95% CI
Age-adjusted average	3.09	(3.05, 3.13)	2.93	(2.89, 2.97)	2.83 ^b	(2.79, 2.87)
65–69 years	5.40	(4.97, 5.87)	4.26	(3.92, 4.63)	3.34 ^b	(3.07, 3.63)
70–74 years	4.69	(4.49, 4.90)	4.10	(3.92, 4.28)	3.39 ^b	(3.24, 3.54)
75–79 years	4.00	(3.88, 4.12)	3.73	(3.61, 3.84)	3.44 ^b	(3.33, 3.55)
80–84 years	3.28	(3.20, 3.36)	3.18	(3.10, 3.26)	3.01 ^b	(2.93, 3.09)
85–89 years	2.76	(2.69, 2.83)	2.71	(2.64, 2.78)	2.64 ^b	(2.57, 2.70)
≥90 years	2.21	(2.15, 2.28)	2.19	(2.13, 2.26)	2.17 ^b	(2.10, 2.24)

In each of the three models presented, the reference is defined as 1.00 for women and men without dementia in each of the 5-year age stratum.

Abbreviations: MRRs, mortality rate ratio.

^aLeukemia, lymphoma, and AIDS have been excluded from the model due to low sample size.

^bAIDS has been excluded from the model due to low sample size.

This study identifies people with dementia as a vulnerable group with increased mortality, especially those who have concurrent chronic comorbidities. Without any existing disease-modifying treatments for dementia disorders, attempts to moderate their course through better access to care and treatment of comorbidities should be strengthened. We believe that the findings from our study are generalizable to other high-income Western countries with similar access to healthcare.

In conclusion, the findings of the present study emphasize the severity of dementia disorders. Having an additional dementia disease in combination with any of a wide range of somatic or psychiatric conditions was associated with a significantly higher mortality rate. Mortality in dementia remained high, even after adjusting for psychiatric and somatic comorbidities, which indicates that dementia disorders alone contribute to excess mortality.

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CONFLICT OF INTERESTS

None declared.

AUTHOR CONTRIBUTIONS

Lærke Taudorf: Conceptualization (lead); Formal analysis (equal); Methodology (equal); Writing-original draft (lead); Writing – review and editing (lead). **Ane Nørgaard:** Writing – review and editing (supporting). **Henry Brodaty:** Supervision (supporting); Writing – review and editing (supporting). **Thomas Munk Laursen:** Formal analysis (equal); Methodology (equal); Supervision (supporting); Writing –review and editing (supporting). **Gunhild Waldemar:** Conceptualization (equal); Methodology (equal); Supervision (lead); Writing – original draft (equal); Writing –review and editing (equal).

DATA AVAILABILITY STATEMENT

This study was based on data from nationwide public registries and according to Danish law, it is now allowed to share such datasets. To gain access to Danish registry data, individual research projects must seek approval from the Danish Health Data Authority. Hence, further data sharing of this project is not possible.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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