

Association of comorbidity with healthcare utilization in people living with dementia, 2010-2019: A population-based cohort study

Running title: Comorbidity in dementia and healthcare utilization

Yingyang Zhang MSc¹, Hao Luo PhD^{1,2*}, Terry Y.S. Lum PhD^{1,2}, Martin Knapp PhD³, Davide L. Vetrano PhD^{4,5}, Celine C.S. Chui PhD^{6,7,8}, Pengcheng Wang MSc¹, Gloria H.Y. Wong PhD^{1,2}

¹Department of Social Work and Social Administration, The University of Hong Kong, Hong Kong, China.

²Sau Po Centre on Ageing, The University of Hong Kong, Hong Kong, China.

³Department of Health Policy, London School of Economics and Political Science, London, UK.

⁴Aging Research Center, NVS Department, Karolinska Institutet, Stockholm University, Stockholm, Sweden.

⁵Stockholm Gerontology Research Center, Stockholm, Sweden.

⁶School of Nursing, The University of Hong Kong, Hong Kong, China.

⁷School of Public Health, The University of Hong Kong, Hong Kong, China.

⁸Laboratory of Data Discovery for Health (D²4H), Hong Kong Science and Technology Park, Hong Kong, China.

* Corresponding author

Room 521, The Jockey Club Tower, The Centennial Campus, The University of Hong Kong, Pokfulam Road, Hong Kong, China.

E-mail address: haoluo@hku.hk

Tel: (852) 39174373

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Abstract

Evidence on the healthcare utilization associated with comorbidity in people with dementia is lacking in Chinese societies. This study aimed to quantify healthcare utilization associated with comorbidity that is common in people living with dementia. We conducted a cohort study using population-based data from Hong Kong public hospitals. Individuals aged 35+ with a dementia diagnosis between 2010 and 2019 were included. Among 88,151 participants, people with at least two comorbidities accounted for 81.2%. Estimates from negative binomial regressions showed that compared to those with one or no comorbid condition other than dementia, adjusted rate ratios of hospitalizations among individuals with six or seven and eight or more conditions were 1.97 [98.75% CI, 1.89-2.05] and 2.74 [2.63-2.86], respectively; adjusted rate ratios of Accident & Emergency department visits among individuals with six or seven and eight or more conditions were 1.53 [1.44-1.63] and 1.92 [1.80-2.05], respectively. Comorbid chronic kidney diseases were associated with the highest adjusted rate ratios of hospitalizations (1.81 [1.74-1.89]), whereas comorbid chronic ulcer of the skin was associated with the highest adjusted rate ratios of Accident & Emergency department visits (1.73 [1.61-1.85]). Healthcare utilization for individuals with dementia differed substantially by both the number of comorbid chronic conditions and the presence of some specific comorbid conditions. These findings further highlight the importance of taking account of multiple long-term conditions in tailoring the care approach and developing healthcare plans for people with dementia.

Keywords

comorbidity, healthcare utilization, hospitalizations, Accident & Emergency, dementia, electronic health records

Introduction

Dementia is a major challenge faced by health and social care systems across the world, particularly with population ageing (GBD 2019 Dementia Forecasting Collaborators, 2022). A large body of research on healthcare utilization reveals that people living with dementia have significantly higher rates of hospital admissions, longer hospital stays, and more frequent primary care consultations and emergency department visits compared to those without dementia (Zhu et al., 2015; Phelan et al., 2012).

The fact that people living with dementia often live with comorbidity (Kingston et al., 2018; Chen et al., 2017) has been identified as a key contributor to healthcare utilization among this population (Browne et al., 2017). The relationship between comorbidity and healthcare utilization in people living with dementia is complex. First, dementia is associated with poorer access to services, and hence lower healthcare utilizations, in some countries (Bunn et al., 2014). Second, the presence of dementia may complicate the management of other chronic conditions and further increase their burdens (Callahan et al., 2014). Third, differences in individual behavioural/cultural factors (e.g., awareness), provider/healthcare system factors (e.g., accessibility), and policy context (e.g., the role of primary/secondary/tertiary care) may result in different patterns of healthcare utilization. The complex nature of these relationships thus requires population-based evidence from different contexts with a sufficient sample size and follow-up period to understand observed patterns and so inform policy.

Most current evidence on the associations between comorbidity and healthcare utilization in people living with dementia has been generated from Western studies (Browne et al., 2017; MacNeil-Vroomen et al., 2020; Kaczynski et al., 2019; Afonso-Argiles et al., 2020; Mondor et al., 2017; Griffith et al., 2016). For instance, a UK study using primary care data found that higher numbers of co-occurring chronic conditions were associated with earlier death, a greater number of primary care consultations, hospital admissions, and prescribing (Browne et al.,

2017). A population-based Canadian cohort of community-dwelling people living with dementia in 2008 followed up for five years showed that healthcare utilization increased consistently with the number of co-occurring conditions (Griffith et al., 2016). A US study using claims data found that patients with dementia who were diagnosed with atrial fibrillation and chronic kidney diseases had the highest significant healthcare use (MacNeil-Vroomen et al., 2020). However, it is unclear whether similar findings from these Western populations may be observed in other (e.g., Asian) populations.

With Chinese communities aging at an unprecedented rate, Chinese populations are a major driving force of the global burden of dementia (Jia et al., 2020). Earlier estimates suggested a prevalence of 9.5 million in mainland China, Hong Kong, and Taiwan (Wu et al., 2018). In mainland China, an updated estimate of 15.3 million in 2019, and projected to increase to 45.5 million by 2050 (GBD 2019 Dementia Forecasting Collaborators, 2022). Initial evidence from China suggests that a greater comorbidity burden was associated with length of hospitalization and daily expenditures (Wang et al., 2017; Yan et al., 2019). However, there are no high-quality, up-to-date longitudinal data on the healthcare utilization of dementia. More importantly, to our best knowledge, no study investigates the association of specific comorbid chronic conditions with healthcare utilization in this vulnerable group. Among Chinese regions, Hong Kong has a population-based electronic health records system, policies on dementia awareness and dementia-friendly communities, a relatively developed healthcare system (Choy et al., 2022), and the world's highest life expectancy at birth (Ni et al., 2021). These features make evidence from Hong Kong a useful reference for dementia policy and plans in other Chinese regions. The present study aimed to examine healthcare utilization associated with the number of comorbidity and specific comorbid chronic conditions among individuals living with dementia, using 10-year population-based electronic health records in Hong Kong.

Methods

Data source, study design, and participants

We conducted a population-based cohort study utilizing data from the Clinical Data Analysis and Reporting System (CDARS), managed by the Hong Kong Hospital Authority. CDARS collects territory-wide electronic health records from all public hospitals, which provide 80% of all inpatient services and almost all Accident and Emergency (A&E) services in Hong Kong (Food and Health Bureau of Hong Kong Special Administrative Region Government, 2017). The database contains demographics, diagnosis (stored in International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes), and admission/discharge information from inpatient, A&E, and outpatient settings. CDARS has been widely used in epidemiological studies (Lau et al., 2017; Man et al., 2017; Chai et al., 2020).

We included all individuals with a diagnosis of dementia (of any subtype) between 1 January 2010 and 30 June 2019. All-cause dementia was ascertained using ICD-9-CM codes 290, 294.[1,2,8], and 331.[0,1,82]. We considered both primary and secondary diagnoses and interrogated diagnostic records from all settings. The date of the first dementia diagnosis was defined as the index date. The follow-up period was defined as the period between the index date to the date of death or 31 December 2019, whichever was earlier. Individuals were excluded if they: (1) had a record of dementia diagnosis before 1 January 2010 (i.e., prevalent cases); (2) did not have a record of age; (3) were younger than 35 years at the index date; (4) had an incorrect record indicated by the date of death preceding the index date; or (5) had died on the index date (Detailed information can be found in Figure 1).

Patient records were de-identified in CDARS to ensure privacy. This study was approved by Institutional Review Board of XXX (reference number: XXX) (Blind for review).

Variables

Outcome measures. Rates of all-cause hospitalizations and Accident and Emergency (A&E) department visits were measured by the average number of admissions or visits per person per

year during the follow-up period.

Comorbidity. Comorbidity prior to or on the index date were classified into 60 categories (including dementia) as proposed by a previous study (Calderón-Larranaga et al., 2017). This classification has been used extensively in epidemiological studies (Vetrano et al., 2020). We define an individual as having comorbidity if they simultaneously have one or more chronic diseases out of a total of 59 categories of interest (in addition to dementia). The original work included 918 four-digit level ICD-10-CM codes, which were then mapped into ICD-9-CM codes in our study (see Supplementary Table 1). The total number of comorbid chronic conditions was collapsed into five groups (0-1, 2-3, 4-5, 6-7, and 8+).

Specific comorbid chronic conditions of interest.

We included conditions with a prevalence $\geq 5\%$ when examining the impact of specific comorbid chronic conditions on utilization. As certain conditions are more likely to co-occur than others, we combined categories that were moderately or highly correlated (determined by polychoric correlation coefficient > 0.5 and/or those with established etiological associations, see Supplementary Table 2) when building models. Specifically, we combined hypertension, diabetes, and dyslipidemia into a variable of traditional cardiovascular risk factors; ischemic heart disease, heart failure, atrial fibrillation, other cardiovascular diseases, and cardiac valve diseases into chronic cardiovascular diseases; cerebrovascular disease and other neurological diseases into chronic neurological diseases.

Covariates. Covariates included age, sex, and history of healthcare utilization. Healthcare utilization history was measured by the total number of visits to inpatient, A&E, and outpatient settings between 1995 and the index date.

Statistical analysis

We tabulated the sample characteristics and the prevalence of each comorbid chronic condition and the distribution of the number of conditions. We fitted eight negative binomial regression

models to estimate the adjusted rate ratios and confidence intervals for healthcare utilization associated with the number of conditions and specific comorbid conditions. Given that there were four outcomes, we used the Bonferroni-adjusted significance level of 0.0125 ($= 0.05/4$) and 98.75% CIs to counteract the problem of inflated type I errors. We also conducted subgroup analysis to investigate the possible differences by sex and age in the association.

Three sets of sensitivity analyses were conducted to investigate the robustness of the associations. First, individuals with a follow-up time of less than one year (likely due to vulnerabilities prior to the initial dementia diagnosis) may have high healthcare service utilization rates. We excluded these individuals because their inclusion may lead to an overestimation of healthcare utilization by the cohort. Second, we excluded those with chronic disease conditions with a prevalence $< 2\%$ in the sample to observe whether it could generate potential effects on the association between the number of comorbid conditions with utilization. Finally, we combined chronic kidney diseases with the traditional cardiovascular disease risk factors (including hypertension, diabetes, and dyslipidemia) into one category since our preliminary analysis showed its moderate correlation with diabetes, and the clinical evidence indicated an association between chronic kidney disease and elevated risk of cardiovascular disease (Gansevoort et al., 2013). Listwise deletion was used to handle missing values. All analyses were conducted using R Version 4.0.5 (R Core Team, 2021).

Findings

A total of 88,151 individuals were included in the analysis (Figure 1). The mean age for the overall sample was 82.9 (SD 8.6) years; 59.3% were women. After the index date, 57.7% died, resulting in 272,685 person-years of follow-up with a median follow-up time of 2.5 years (interquartile range 1.0-4.7 years) (see Figure 1 for details).

We summarized the sample characteristics by sex and age (Table 1). Men participants had a

higher percentage of comorbidity, and as the increase of age at diagnosis, the percentage of comorbidity increased as well (Table 1), women and men displaying similar patterns of comorbidity in different age groups (Supplementary Figure 1). Table 2 shows the prevalence of each condition. Hypertension was the most prevalent condition (51.3%), followed by cerebrovascular disease (30.7%). In addition to dementia, 81.2% of patients had two or more co-occurring chronic conditions, and 16.0% had eight or more comorbid conditions.

Figure 2 shows that the adjusted rate ratios across inpatient and A&E settings increased substantially as the number of comorbid chronic conditions increased. Compared with individuals with one or no co-occurring chronic condition, individuals with eight or more conditions had almost three times the rate of hospital admission (rate ratio 2.74 [98.75% CI, 2.63-2.86]) and twice the rate of A&E visits (1.92 [1.80-2.05]).

Figure 3 and Figure 4 presents the adjusted rate ratios for healthcare utilization by specific comorbid chronic conditions. We excluded prostate diseases in the models because these are specific to males. Compared to dementia patients without comorbid chronic kidney diseases, individuals with comorbid chronic kidney diseases had the highest adjusted rate ratios of hospitalization (1.81 [1.74-1.89]) (Figure 3), whereas individuals with chronic ulcer of the skin were associated with the highest adjusted rate ratios of A&E department visits (1.73 [1.61-1.85]) (Figure 4). Anemia and COPD were also significantly associated with higher rate ratios of hospital admissions and A&E department visits, respectively (Figure 3 and Figure 4).

Similar association patterns were found in the subgroup analysis (Supplementary Table 3-4) and in three sensitivity analyses (Supplementary Table 5-7).

Discussion

This study systematically presents the first population-based evidence from a Chinese society on the association between comorbid chronic conditions and healthcare utilization in people

living with dementia. We found a high prevalence of comorbid chronic conditions among people with dementia and that healthcare utilization for individuals with dementia differed substantially by both the number of comorbid chronic conditions and the presence of some specific comorbid conditions.

The above findings can be compared with findings in other contexts. The high prevalence of two or more comorbid chronic conditions among people living with dementia observed in our study is similar to that reported in Western countries (78.5% - 89.01%) (Browne et al., 2017; Kaczynski et al., 2019; Mondor et al., 2017; Griffith et al., 2016). Our findings that the number of comorbid chronic conditions was significantly associated with higher rates of hospitalization and A&E department visits are similar to findings from a Canadian study in which the risk of hospital admission and emergency department visits also increased monotonically with the number of chronic conditions among community-dwelling older people living with dementia (Mondor et al., 2017). In a UK cohort study, Browne and colleagues not only found a significant association between the number of chronic conditions and hospitalization, but also a higher risk of death among people living with dementia who had two or more comorbid chronic conditions (Browne et al., 2017).

We also observed substantial differences in healthcare utilization by specific comorbid chronic conditions among people living with dementia. Specifically, individuals with comorbid chronic kidney diseases presented the highest rate ratio for all-cause hospitalizations, which is consistent with findings from a US study in which the prevalence of chronic kidney diseases was 29.4%, and was significantly associated with the highest risk ratio for the number of hospitalizations among people with dementia with two or more chronic conditions (MacNeil-Vroomen et al., 2020). As suggested in this US study, complications and concomitants of chronic kidney diseases among people with dementia may increase the probability of hospitalization. Chronic kidney diseases cluster with other conditions such as hypertension,

ischemic heart disease, diabetes, and eye diseases (Akugizibwe et al., 2020). In light of this evidence, comorbid chronic kidney diseases might be considered as a proxy for a more complex clinical picture. Further analysis of the association between clusters of comorbid chronic conditions with healthcare utilization among people living with dementia is warranted. However, a UK dementia cohort showed that chronic kidney diseases had no significant association with hospitalizations, while it was significantly associated with primary care consultations and medication (Browne et al., 2017). This may reflect differences in how healthcare systems respond to comorbid chronic kidney diseases among people living with dementia, which has healthcare implications.

Although the prevalence was low, comorbid chronic ulcer of the skin made considerable demands on emergency medical resources in our sample. Pressure ulcer is common among people with advanced dementia (Mitchell et al., 2009). People with dementia and pressure ulcers also have a much lower survival time than those with pressure ulcers but without dementia (Jaul et al., 2017). As individuals with chronic ulcers are more likely to be bedbound, the presence of ulceration may be regarded as a marker of very severe stage chronic conditions – including other motor impairments, nutritional issues, vascular insufficiency – or even the end of life. The higher levels of healthcare utilization and costs are hence to be expected.

We also found that anaemia and respiratory diseases played a significant role in utilization of inpatient and A&E department services. The heterogeneity of the patterns of healthcare utilization among participants with different specific comorbid chronic conditions in different public hospital settings may need to be considered when identifying high-risk individuals needing targeted clinical care and allocating public medical resources.

Our results should be interpreted within the specific context of Hong Kong. As an affluent city, public health sectors provide almost-free medical care (97% of treatment is subsidized) to all permanent residents. Extensive government subsidization of healthcare services provided in

public hospitals has overburdened the public healthcare system since the beginning of this century (Parry et al., 2002). As the proportion of older adults and life expectancy continue to grow, the number of people living with dementia and comorbid chronic conditions will also increase. A better understanding of the impact of comorbid chronic conditions on healthcare use is urgently needed for health system planning. Our findings underline the sizable current impact of dementia care on the public health system in Hong Kong, whose main contributors are co-occurring chronic conditions due to increased hospitalization and A&E use. These findings inform dementia plans including resources allocation, by providing estimates for economic analyses, such as in projecting for potential cost-saving from policy interventions targeting unnecessary hospitalization. For example, models of collaborative care involving primary care are emerging, with initial data suggesting a reduction in acute healthcare service utilization, among other benefits (Heintz et al., 2020). In Hong Kong, policy recommendations have been made recently regarding the roles of primary healthcare, which include consolidation of resources, such as care voucher (a kind of personal budget or consumer-directed care) subsidised services for older people (Health Bureau, Hong Kong SAR Government, 2022). Our findings can inform detailed coordination of related resources, for example through simulation modelling, to enable evidence-informed dementia policy and plan.

This study has several limitations. First, there are inherent limitations with the database employed. Disease diagnoses in electronic medical records may be affected by many factors, including potential coding bias, the context of clinical diagnosis, and individual clinician factors (Luo et al., 2020). Our data are derived from public hospital records. This may underestimate diagnoses (both dementia and comorbidities) as public hospitals only provide 30% of outpatient services in Hong Kong. Second, we used fixed, not time-varying, covariates. New-onset chronic conditions developed during follow-up and their potential role in healthcare outcomes could not be captured. Third, we investigated all-cause instead of cause-specific

healthcare utilization, which may limit the potential clinical implications. Information on the severity of dementia (Zhu et al., 2017) and continuity of care (Mondor et al., 2017) was not available, which may be associated with utilization. Lastly, we only investigated the healthcare utilization of inpatient and A&E settings and we did not include outpatient service use because of its low representativeness (30%) in Hong Kong.

Clinical and policy implications. With global population aging and the projected increase in the number of people living with dementia, the findings from an aged Chinese society with the highest longevity have reference value for service providers and policymakers both locally and elsewhere. We have illustrated the challenging nature of current healthcare utilization patterns associated with comorbid chronic conditions in people living with dementia, confirming previous warnings based on simulation modelling in England, for example, regarding comorbidity when the number of very old people with medium or high dependency continues to grow (Kingston et al., 2018). The good news is that the key drivers of this healthcare use, namely hospitalization and A&E visits that are potentially linked to late diagnosis and a suboptimal balance between primary/secondary/tertiary healthcare, can be addressed, in part at least. Timely diagnosis and care coordination across disciplines and sectors would help reduce need for utilization of these services. Improved access to services and continuity of care (Bunn et al., 2016) could address previously identified issues among people living with dementia and comorbid chronic conditions, such as polypharmacy (Clague et al., 2017) and inappropriate prescribing (Delgado et al., 2020). Well-planned actions to prevent unnecessary hospitalization could reduce costs without harming patient health or wellbeing (Anderson et al., 2020; Bunn et al., 2017).

Declaration of Conflicting Interests

We declare no competing interests.

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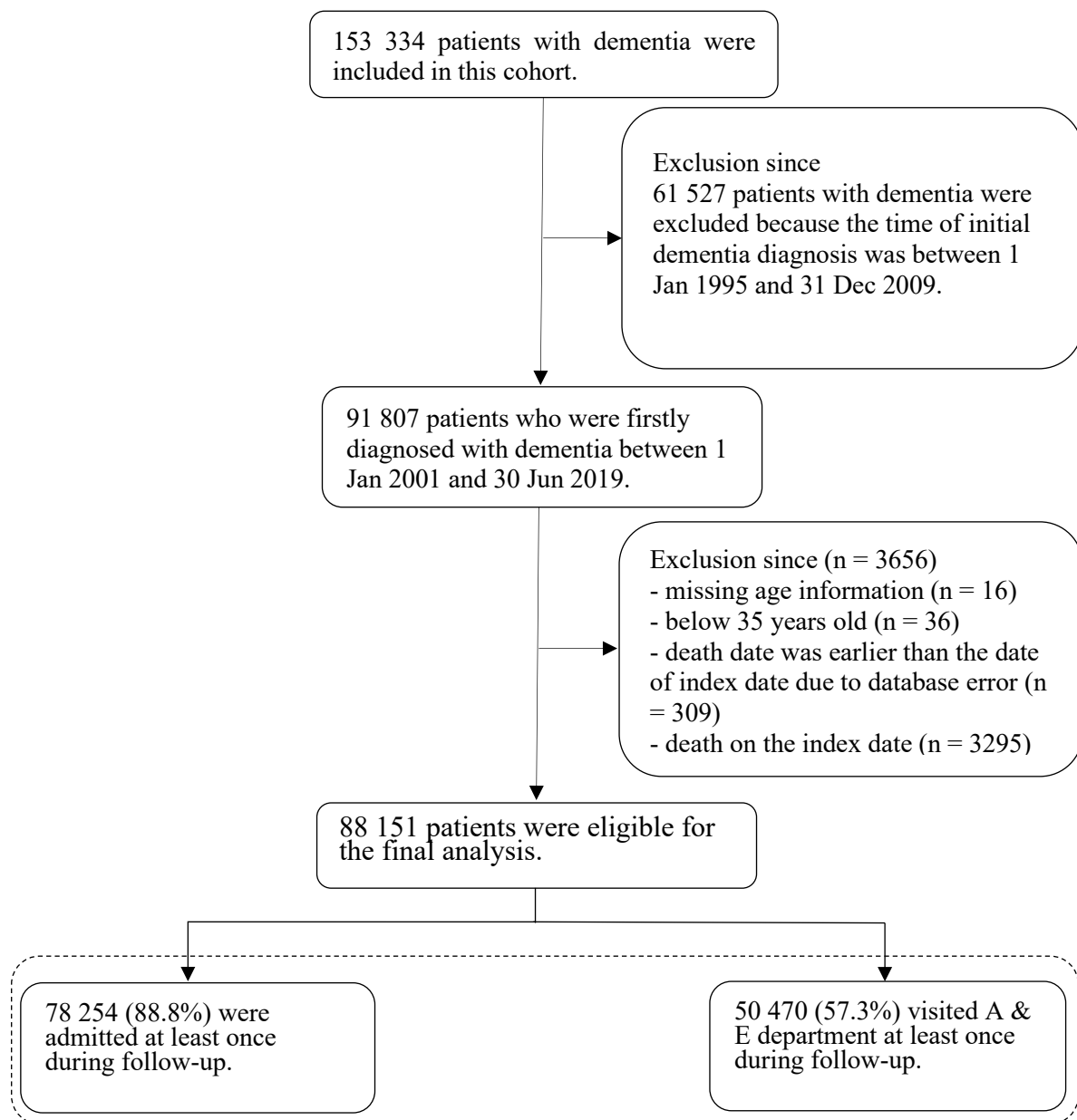


Figure 1 Flow chart of study population selection

Note: A & E = Accident & Emergency.

Table 1 Sample characteristics of the dementia cohort (n = 88 151)

	Number of chronic condition categories				
	0-1	2-3	4-5	6-7	≥8
Total participants	16561 (18.8%)	22608 (25.6%)	20742 (23.5%)	14093 (16.0%)	14147 (16.0%)
Sex					
Women	10,496 (20.1%)	13,453 (25.7%)	12,228 (23.4%)	8,008 (15.3%)	8,107 (15.5%)
Men	6,065 (16.9%)	9,155 (25.5%)	8,514 (23.7%)	6,085 (17.0%)	6,040 (16.8%)
Age at diagnosis, y					
35-64	893 (29.7%)	853 (28.3%)	615 (20.4%)	318 (10.6%)	330 (11.0%)
65-74	2,270 (23.2%)	2,563 (26.2%)	2,106 (21.5%)	1,436 (14.7%)	1,423 (14.5%)
75-84	6,653 (19.2%)	8,902 (25.6%)	8,172 (23.5%)	5,546 (16.0%)	5,458 (15.7%)
≥85	6,745 (16.6%)	10,290 (25.3%)	9,849 (24.3%)	6,793 (16.7%)	6,936 (17.1%)

Note: Numbers may not add exactly because of rounding.

Table 2 Prevalence of comobird chronic conditions in addition to dementia prior to or on the date of the initial dementia diagnosis (n = 88 151)

Disease name	N (%)	95% CI	Disease name	N (%)	95% CI
Hypertension	45 223 (51.3)	51.0-51.6	Other psychiatric and behavioral diseases	3899 (4.4)	4.3-4.6
Cerebrovascular disease	27 081 (30.7)	30.4-31.0	Migraine and facial pain syndromes	3342 (3.8)	3.7-3.9
Cataract and other lens diseases	23 050 (26.1)	25.9-26.4	Thyroid diseases	3335 (3.8)	3.7-3.9
Diabetes	22 883 (26.0)	25.7-26.2	Chronic pancreas biliary tract and gallbladder diseases	3235 (3.7)	3.5-3.8
Colitis and related diseases	21 412 (24.3)	24.0-24.6	Chronic infectious diseases	3200 (3.6)	3.5-3.8
Anemia	16 448 (18.7)	18.4-18.9	Ear nose throat diseases	2963 (3.4)	3.2-3.5
Ischemic heart disease	14 911 (16.9)	16.7-17.2	Allergy	2869 (3.3)	3.1-3.4
Dyslipidemia	13 433 (15.2)	15.0-15.5	Glaucoma	2861 (3.2)	3.1-3.4
Solid neoplasms	13 171 (14.9)	14.7-15.2	Asthma	2461 (2.8)	2.7-2.9
Heart failure	12 571 (14.3)	14.0-14.5	Schizophrenia and delusional diseases	2073 (2.4)	2.3-2.5
Esophagus stomach and duodenum diseases	12 153 (13.8)	13.6-14.0	Epilepsy	2032 (2.3)	2.2-2.4
Atrial fibrillation	11 427 (13.0)	12.7-13.2	Neurotic stress-related and somatoform diseases	2012 (2.3)	2.2-2.4
Osteoarthritis and other degenerative joint diseases	8691 (9.9)	9.7-10.1	Deafness hearing impairment	1920 (2.2)	2.1-2.3
Other neurological diseases	8404 (9.5)	9.3-9.7	Sleep disorders	1750 (2.0)	1.9-2.1
Inflammatory arthropathies	7951 (9.0)	8.8-9.2	Peripheral neuropathy	1683 (1.9)	1.8-2.0
Prostate diseases	7496 (8.5)	8.3-8.7	Bradycardias and conduction diseases	1320 (1.5)	1.4-1.6
Other cardiovascular diseases	7120 (8.1)	7.9-8.3	Peripheral vascular disease	1280 (1.5)	1.4-1.5
Dorsopathies	6997 (7.9)	7.8-8.1	Venous and lymphatic diseases	1267 (1.4)	1.4-1.5
COPD emphysema chronic bronchitis	6476 (7.3)	7.2-7.5	Cardiac valve diseases	1211 (1.4)	1.3-1.5
Depression and mood diseases	6160 (7.0)	6.8-7.2	Blood and blood forming organ diseases	1072 (1.2)	1.1-1.3
Chronic kidney diseases	5736 (6.5)	6.3-6.7	Autoimmune diseases	964 (1.1)	1.0-1.2
Other genitourinary diseases	5695 (6.5)	6.3-6.6	Blindness visual impairment	890 (1.0)	0.9-1.1
Other respiratory diseases	4827 (5.5)	5.3-5.6	Obesity	498 (0.6)	0.5-0.6
Chronic ulcer of the skin	4559 (5.2)	5.0-5.3	Hematological neoplasms	460 (0.5)	0.5-0.6
Osteoporosis	4552 (5.2)	5.0-5.3	Other digestive diseases	418 (0.5)	0.4-0.5
Other eye diseases	4306 (4.9)	4.7-5.0	Other skin diseases	140 (0.2)	0.1-0.2
Parkinson and parkinsonism	4118 (4.7)	4.5-4.8	Inflammatory bowel diseases	40.0 (0.0)	0.0-0.1
Other metabolic diseases	4112 (4.7)	4.5-4.8	Chromosomal abnormalities	36.0 (0.0)	0.0-0.1
Other musculoskeletal and joint diseases	4006 (4.5)	4.4-4.7	Multiple sclerosis	11.0 (0.0)	0.0-0.0
Chronic liver diseases	3943 (4.5)	4.3-4.6	2+ chronic diseases	71 590 (81.2)	81.0-81.5
			4+ chronic diseases	48 982 (55.6)	55.2-55.9
			6+ chronic diseases	28 240 (32.0)	31.7-32.3
			8+ chronic diseases	14 147 (16.0)	15.8-16.3

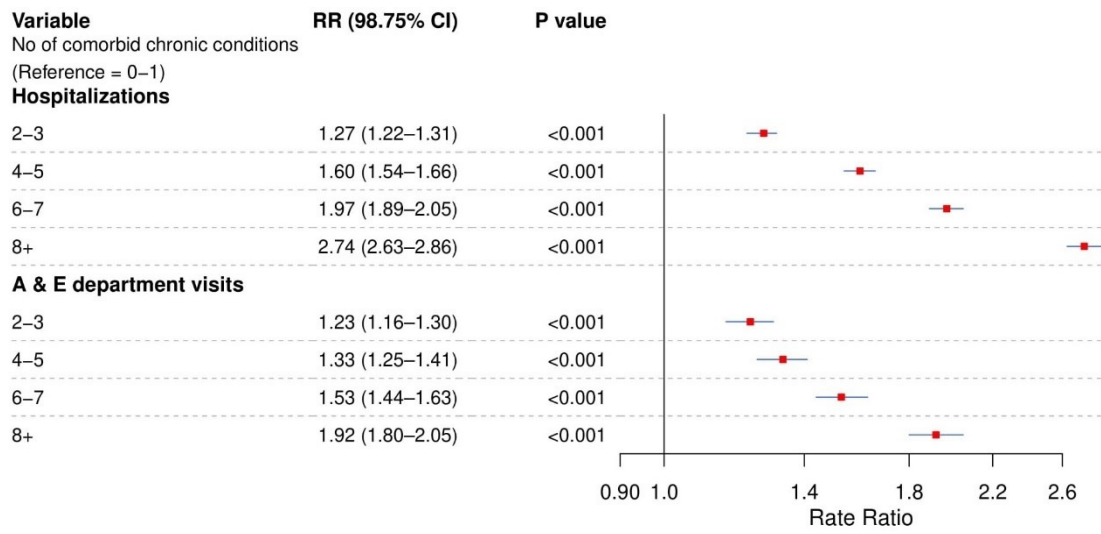


Figure 2 Adjusted rate ratios for healthcare utilization by number of comorbid chronic conditions in people with dementia (n = 88 151)

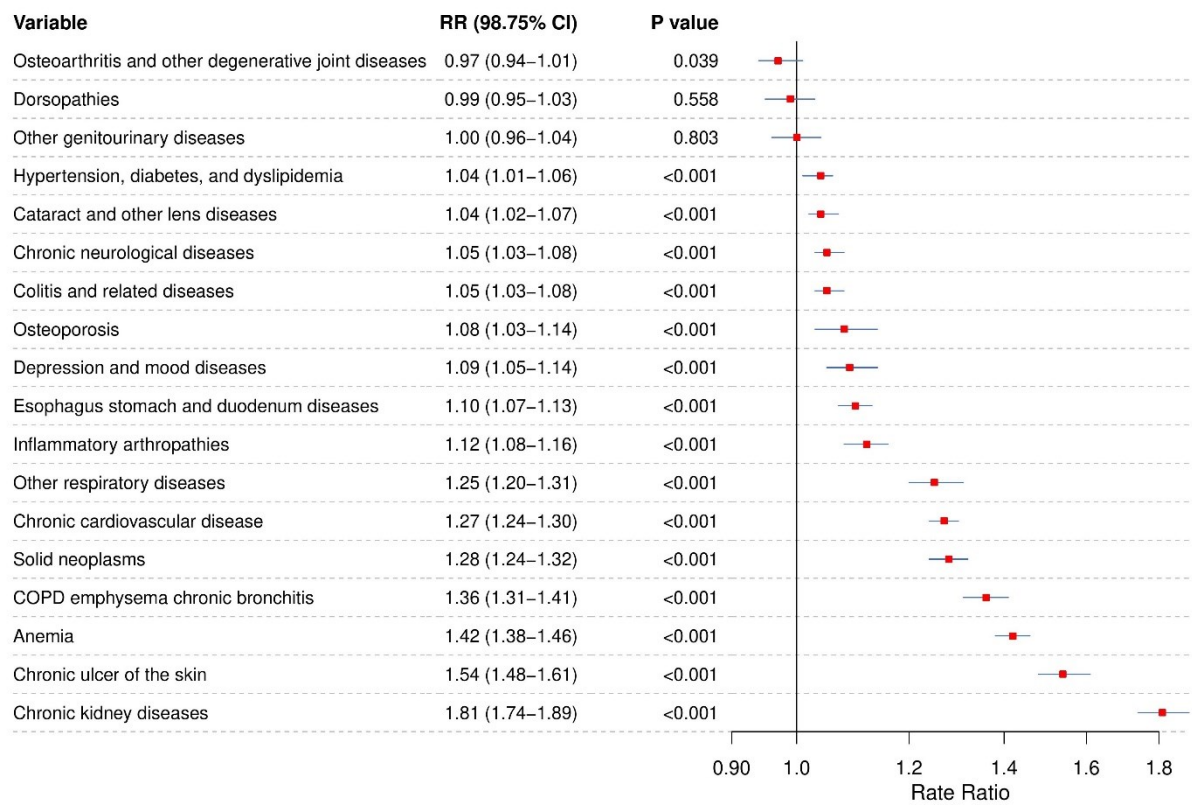


Figure 3 Adjusted rate ratios for hospitalizations by specific comorbid chronic conditions in people with dementia (n = 88 151)

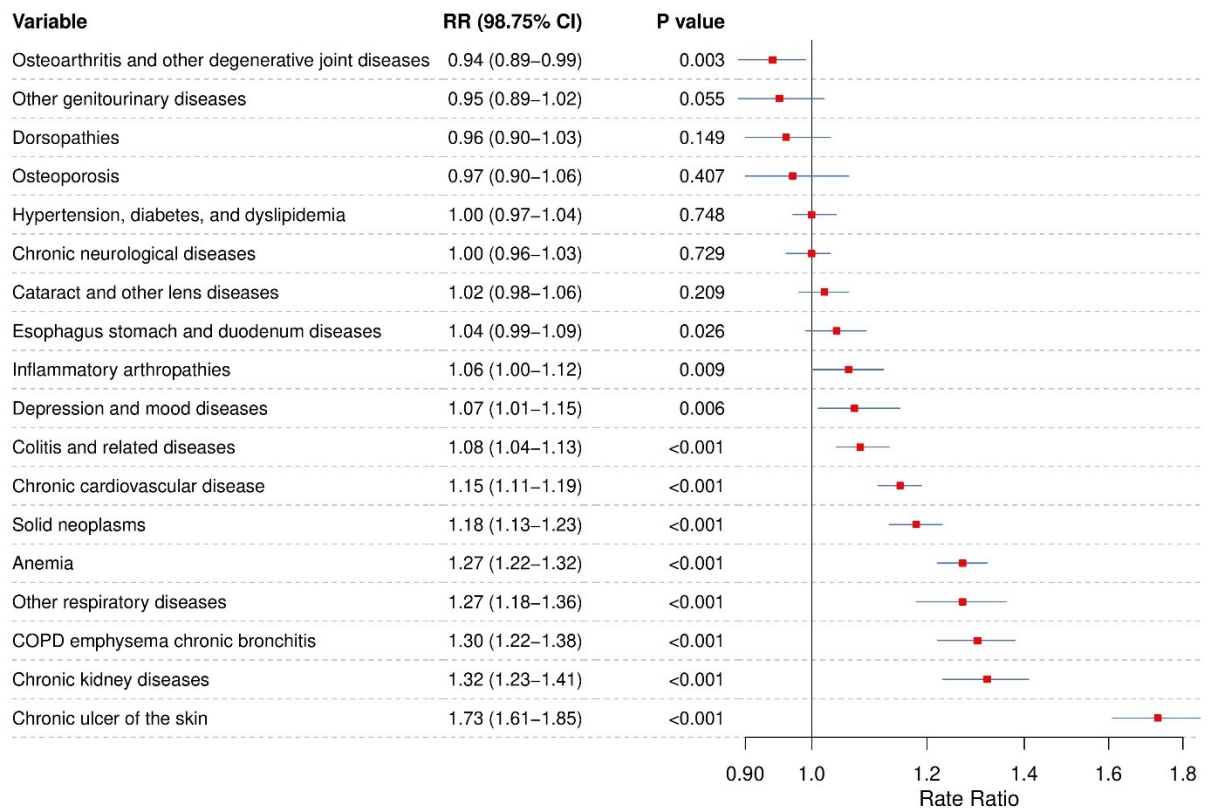


Figure 4 Adjusted rate ratios for Accident and Emergency department visits by specific comorbid chronic conditions in people with dementia (n = 88 151)