Trends in survival following dementia diagnosis: a multinational cohort study

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Abstract

This multinational cohort study examines the trends in relative mortality risk following dementia diagnosis in the UK, Germany, Finland, Canada (Ontario), New Zealand, South Korea, Taiwan, and Hong Kong. A common protocol was applied to population-based data of individuals aged 60+ with an incident dementia diagnosis recorded between 2000 and 2018. Data from 1,272,495 individuals showed that the standardised mortality ratios (SMRs) for dementia ranged from 1.27 (95% CI 1.27-1.28; UK) to 2.90 (2.87-2.93; New Zealand). Both adjusted SMRs and hazard ratios (HRs) estimated from Cox proportional hazard models declined consistently over the study period in the UK, Canada, South Korea, Taiwan and Hong Kong, which accounted for 84% of all participants. This study found a steady trend of decreasing risk of mortality in five out of eight databases, which signals the potential positive effect of dementia plans and associated policies and provides reference for future policy evaluation.

Introduction

Dementia, which may result from a variety of diseases, is a disabling syndrome that mainly affects older adults.[1] With a prevalence of 55 million worldwide and nearly 10 million new cases a year,[1] dementia has been recognised as a public health priority internationally since 2012.[2] Healthcare systems in high-income countries are under great pressure to refine or reform to cope with the rising needs; systems in many low- and middle-income countries need data to encourage prioritization, and to guide planning and action.

The survival time of people living with dementia may vary between world regions, time periods, and subpopulations within a region.[3] In an earlier systematic review, based on data from 42 studies including more than 11,000 people living with dementia,[4] duration of survival after a diagnosis of dementia ranged from 1.3 to 7.9 years in individuals with younger onset dementia, and 1.8 to 7.2 years in late-onset dementia. The authors noted potential temporal trends by using the year of introduction of cholinesterase inhibitors as an anchor to divide studies into two epochs prior to and after 1997. Although a meta-analysis was not conducted, the findings highlighted variability in survival that might be partially explained by change in practice (the introduction of cholinesterase inhibitors) over time.

Despite the continued absence of either a cure or disease-modifying treatment, progress has been made over recent years in early diagnosis of specific cognitive disorders, risk-reduction, coverage through funding, and quality of health and social care interventions for people living with dementia.[5] Public health strategies and plans, such as increasing diagnostic rates, case-finding, and early diagnosis,[6] and other population-specific contextual factors (e.g., role of primary/secondary/tertiary care in dementia) may also affect survival. Consequently, data on survival of people living with dementia under different contexts (i.e., over time and across systems) may provide clues to inform dementia strategies.

Evidence on survival trends following dementia diagnosis across the world remains scarce or is out-of-date: most previous studies have observational periods that ended by 2012[4,7–13] except for a Chinese study.[14] The WHO *Global Action Plan on the Public Health Response to Dementia 2017-2025*[15] identified routine population-level monitoring of dementia indicators as a key action area to provide data in guiding evidence-based actions. Up-to-date information on survival after dementia diagnosis, stratified by geographical areas and demographic characteristics, can help policymakers understand the real-world impact on health and social care systems,[16] and inform decisions on care and support strategies, and the workforce needed to deliver them.[4]

Population-based electronic medical records (EMR) and administrative data offer an efficient approach to complement primary epidemiological data collection for understanding the full spectrum of dementia in the general

population.[17] Using longitudinal data for people with dementia from eight developed jurisdictions, including the UK, Germany, Finland, Canada (Ontario), New Zealand, South Korea, Taiwan, and Hong Kong, this study aims to: 1) estimate median survival time after the first record of diagnosis of dementia by age group; and 2) examine the relative mortality risk of people diagnosed with dementia over time compared with the general population.

Results

The present study employed medical insurance claims databases from Germany, Canada (Ontario), South Korea and Taiwan; EMR databases from the UK, and Hong Kong; a register-based cohort from Finland; and a claim and EMR combined database from New Zealand. EMRs from Hong Kong and New Zealand included inpatient, outpatient, and accident and emergency department data retrieved from publicly funded hospitals. Details of the data sources are described in the supplementary materials (Supplementary Text 1). The databases were chosen because they had national administrative data or regional databases that are representative of specific populations (e.g., people using public health services, community-dwelling older adults, and people eligible for certain insurance plans). They included jurisdictions from three of the six World Health Organization regions (the Americas, Europe, and the Western Pacific). All eight databases have been used extensively in earlier epidemiological studies (see Supplementary Table 1 for key references of each database). All databases contributed data on dementia diagnosis and vital status.

A total of 1,272,495 individuals with a recorded diagnosis of dementia from eight databases, including both claims data and EMR, were followed for periods between 1 January 2000 and 31 December 2018. The sample representativeness, data type, and study period of each database are summarised in Table 1.

The sample characteristics of each database are shown in Table 2. Females accounted for 60.7% of the total sample. Mean age at the date of the first diagnosis (index date) ranged from 76.8 years (SD 8.9) in South Korea to 82.9 years (8.2) in Germany. In most databases, individuals aged 85 years or older at first diagnosis dominated the study sample (Fig. 1). The South Korean and Taiwanese samples were youngest, with higher proportions of individuals observed in the younger age groups compared to other databases. During the study period, 60% of individuals died.

Annual counts of incident dementia cases in each database are documented in the appendix (Table A2). Changes in the age distribution of incident cases over time in all databases except Germany are also shown in the appendix (Figure A1). The proportion of people aged 85 years or older gradually increased over time for all databases reporting absolute incident numbers. Dementia sub-type was rarely recorded at the time of first diagnosis. For databases providing information on dementia subtypes, the percentage of individuals with Alzheimer's disease ranged from 9.1% in Canada to 42.0% in South Korea, and those with vascular dementia ranged from 3.5% in Canada to 45.7% in Taiwan (see Table 2).

In all databases, median survival was shorter with increased age (Fig. 2). Overall, the longest survival was observed in the UK for those aged 65–69, 70–74 and 80–84 years. The median survival time for people aged 60–64 years at diagnosis in the UK was 10.8 years, falling to 3.5 years in those aged 85 years or over. Survival in Canada started at a low level (4.9 at age 60–64) and only gradually decreased with age increased (2.4 at age 85+). The shortest survival years was observed in New Zealand with 1.7 years at age 85+.

Highest overall standardised mortality ratios (SMRs) for people with dementia were found in New Zealand (2.90; 95% confidence interval (CI): 2.87–2.93) and Hong Kong (2.79; 95% CI: 2.77–2.81). The lowest SMR of 1.27 (95% CI: 1.27–1.28) was observed in the UK. Figure 3 shows the aggregated and calendar-year-specific SMRs. An overall decreasing

trend was observed in the UK, Canada, South Korea, Taiwan, and Hong Kong, while an increasing trend was observed in Finland and New Zealand, and no clear trend was identified in Germany. The most substantial reductions in SMRs were seen in South Korea (from 4.04 in 2003 to 1.67 in 2013) and Taiwan (from 2.77 in 2003 to 1.82 in 2015).

Results from Cox proportional hazard models examining the effect of calendar year on mortality risk, adjusting for sex and age, are summarised in Table 3. Compared with the first study year at each study site (the reference year), the mortality risk decreased over time in the UK, Canada, South Korea, Taiwan and Hong Kong. In Canada, using 2000 as the reference year, the HRs decreased from 0.95 (95% CI: 0.93–0.97) in 2001 to 0.70 (95% CI: 0.68–0.72) in 2016. Similarly, in the UK, HRs dropped from 0.97 (95% CI: 0.92–1.02) in 2001 (2000 as baseline) to 0.72 (95% CI: 0.65–0.79) in 2016. A more substantial decline in mortality risk was observed in South Korea, where HRs dropped from 0.87 (95% CI: 0.78–0.98) in 2004 to 0.55 (95% CI: 0.48–0.64) in 2013. In Germany, the HRs were statistically significantly lower in the years 2013–2015 compared to 2007: ranged between 0.84 (95% CI: 0.80–0.87) in 2014 and 0.93 (95% CI: 0.88–0.98) in 2015.). In Finland, no significant association was observed between mortality risk and calendar year. In New Zealand, no significant association was observed between 2001 and 2013 and an increased risk of mortality was observed from 2014 onwards, compared with year 2000.

Discussion

To our knowledge, this is the largest epidemiological study of dementia survival, using a common protocol applied to individual-level EMR and administrative data from eight ethnically diverse regions with developed health systems. Despite the considerable variations in survival time following dementia diagnosis over time and across databases, we found a consistent decline in relative mortality risk in people with dementia diagnosis in the UK, Canada (Ontario), South Korea, Taiwan and Hong Kong. No clear trend could be identified in Germany or Finland, and an increasing trend was observed in New Zealand. These findings reflect real-world survival of people living with dementia after a diagnosis is first recorded in administrative or electronic medical record data in eight developed jurisdictions.

EMR and administrative data are becoming increasingly available across the globe, providing an excellent opportunity to examine real-life impacts of dementia at different periods on health and care systems.[18] Our findings provide information to complement data available from other sources, such as population-based epidemiolocal research and the Global Burden of Disease study.[19] However, it is important to note some differences between individual databases included in this study. We analysed data from general practice databases (UK), EMRs from publicly funded hospitals (Hong Kong and New Zealand), claims data (Germany, Canada, South Korea, Taiwan, and New Zealand), and national register of chronic diseases (Finland). Each has its strengths and limitations. For instance, medical claims data typically have the advantage of covering the total population. However, their linkage to reimbursement may have an influence on diagnostic, help-seeking, and recording behaviour.[20] Previous studies have suggested that using claims data may lead to an inflated estimation of dementia prevalence.[21] The higher proportion of people diagnosed with dementia at the younger age groups in the South Korean and Taiwanese databases concurs with this observation suggested by previous studies. Primary care datasets often include a wider pool of people living with dementia, including those with milder dementia, as compared with data from secondary/tertiary care. Although their record linkage of specialist care data may not be as detailed or accurate as hospital records, the impact on our findings is likely minimal. Hospital records, though typically having high diagnostic accuracy,[22] are nevertheless skewed towards dementia cases at the more severe end of the spectrum, leading to potential underestimates of survival times. The higher SMRs in Hong Kong and New Zealand may be interpreted in this context against this background. Although it is difficult to assess to what extent the context of each individual database may have affected our findings, these database-specific properties should be taken into consideration when interpreting trends.

Dementia is a symptom diagnosis which can be caused by several diseases with varied survival rates following diagnosis.[4,23] Although examining mortality risks associated with various subtypes of dementia diagnoses is of interest, the purpose of our study was to examine the mortality risk associated with the *whole variety* of cognitive disorders causing dementia, rather than any specific diagnosis. This is because we observed substantial heterogeneity in the prevalence of dementia subtypes, and that half or more patients were coded as having unspecific or other dementias. This may reflect the complexity in ascertaining the specific cause of dementia and be partially explained by variations in coding practice across jurisdictions and between clinicians with different levels of expertise. Survival trends by subtype of dementia were hence not further explored, despite the known effect of subtype on survival.[3,23] Future studies with precise subgroup diagnoses should examine trends in survival following various subtypes of dementia to inform more targeted dementia plans.

Previous evidence on dementia survival from the same data sources are available in the UK, Taiwan, and Germany. The earlier UK study, using 1990–2007 data, reported median survival following dementia diagnosis of 6.7 years in those aged 60 to 69 years.[24] Our findings from the 2000–2016 data indicate a median survival time of approximately ten years in the same age group, suggesting a marked increase. The earlier Taiwanese study using the 2001–2010 data reported median survival of 3.4 years for people aged over 65.[25] Our study of the 2003–2015 data showed median survival of 5.1 years for people aged 60 years or over, also suggesting an increase in survival following dementia diagnosis. The earlier German study, examining the short-term trend in dementia mortality between 2006/07 and 2009/10, observed an increased mortality risk and a shorter life expectancy in people with dementia in more recent years, particularly in women.[13] Our analysis identified no clear trend in Germany.

National dementia strategies have now been developed in a number of jurisdictions to advance dementia prevention, care, and support.[26] By the end of the study period, four jurisdictions in this study (UK, Finland, South Korea, and Taiwan) had national dementia strategies in place, and two (Canada and Germany) had national plans in development. Assuming that some progress has been made in priority areas highlighted by such strategies, such as raising dementia awareness, increasing diagnosis rates, and improving care and support,[27] longer survival following dementia diagnosis could be expected over recent years. A key finding in this study is the steady trend of decreasing risk of mortality in five databases, accounting for 84% of all participants in this study, signalling the potential positive effect of dementia plans and associated policies.

Another noteworthy finding is the steady increase in SMR and HRs between 2014 and 2018 in New Zealand. According to the New Zealand Framework for Dementia Care published in 2013, recommendations were made to shift assessment, diagnosis, and management of uncomplicated dementia to primary care to free-up specialist services (to respond to episodic events and provide support and advice to primary care services in complex cases).[28] We used hospital admission data from New Zealand to identify cases of dementia. As such, the increase in SMRs and HRs observed since 2014 in New Zealand may reflect the increasing involvement of primary care, so that by the time people living with dementia first present to hospitals they have more advanced dementia and thus an elevated risk of mortality. However, whether the shortened survival for people in the hospital database is due to the impact of task-shifting needs to be verified using primary care data collected before hospital admission, which at present is lacking on a national level in New Zealand. This highlights the future need for data linkage across care settings. In addition, national guidelines regarding prescription and reimbursement of anti-dementia drugs may influence physicians' incentives to record a dementia diagnosis. These findings illustrate how variations in national dementia policies may affect demands within health systems.

Although we could not examine incidence of dementia due to lack of data from the general population, a steady increase in the proportion of people diagnosed at an older age (85 years or over) was observed in all databases reporting absolute incident numbers. This concurs with previous studies and may indicate delayed onset of dementia. A general improvement in population health may have contributed to reduction in modifiable vascular and lifestyle-related risk factors of dementia. This risk reduction, together with longer education, might have contributed to the decline in the incidence of dementia, particularly among younger people.[29–31] Another possibility is that increased dementia awareness, greater emphasis on diagnosis, or the development of symptomatic treatments might mean that people whose dementia was not previously recognised are now being formally diagnosed, but at a later age.

This study has several limitations. First, in contrast to clinical studies, information on dementia severity and time since symptom onset is typically not available in routinely-collected data. Findings from this study cannot directly address the question of compression or expansion of morbidity, since dementia diagnosis may be affected by a collection of contextual factors (attitudes towards dementia, levels of public awareness and stigma, accessibility to diagnostic services, levels of medical and social care for dementia and socioeconomic inequalities).[14] However, findings from this study are important as they reflect the burden of dementia that is currently carried by the healthcare system. Second, given that dementia is often underdiagnosed and undertreated, many diagnoses of dementia are likely to be made at moderate or sometimes severe stage of the disease, resulting in underestimation of survival time. Third, while it is reasonable to assume record accuracy,[32] a certain level of coding errors is expected. It is possible that some first recordings of a dementia diagnosis differed from the actual date of diagnosis, and errors may occur when a dementia assessment is coded as diagnosis, leading to overestimation of survival after diagnosis of dementia. However, understanding population-level trends in survival based on EMR and administrative data will aid healthcare policy and planning. These data complement knowledge about dementia survival based on analyses of other clinical data sources and highlight international differences and changes over time in models of primary and secondary care for people living with dementia.

In developing a common protocol, some compromises in data treatment were necessary, requiring precaution in interpretation. First, comorbidities and multimorbidity, despite their known impact on survival, were not included in the current investigation. However, the aim of this study was to provide timely epidemiological data on trends in survival of an average older person with a dementia diagnosis. The specific impact of comorbidity on survival and trends in survival is considered beyond the scope and may be better investigated in-depth within a database under its own context. Second, only few databases reported whether a dementia diagnosis was the incident diagnosis. For the other databases, we used the first year of the study period as the lookback period to identify incident cases (to exclude individuals with a prior record of dementia before study entry). It is possible that a longer lookback period may be needed for certain databases. Specifically, the markedly high SMR in Hong Kong in 2002 and in the UK in 2000 may suggest inclusion of existing dementia cases. However, as stable trends of increased survival were robustly observed in the five databases over an observational period of at least 11 years (South Korea), extending the lookback period may not affect our conclusions. In Finland, incident cases of Alzheimer's disease were included between 2005 and 2011, yet no more Alzheimer's disease cases entered the cohort after 2011. Thus, the Finnish data after 2011 included an increasing number of people with longer duration and more advanced Alzheimer's disease, while this kind of calendar year phenomenon did not occur in the comparison cohort. This possibly caused the increase in SMR.

Notwithstanding these limitations, the real-world information from settings with varied practices and policy contexts presented here provides a reference for advancing dementia health and social care services. The steady decrease in mortality risk observed in five databases are encouraging as they suggest that dementia policies and public health campaigns may be having effects. Many governments across the world aim at developing national dementia

strategies.[33] Our findings, based on multinational comparisons of population-based longitudinal survival data, provide evidence for future policy evaluation and provide reference points for lower- and middle-income countries where no secular trend data are currently available. Future studies should investigate the impact of specific practices and policy context on the changes of survival following dementia diagnosis.

Online Methods

Procedure

We used a common protocol to examine the trend in dementia survival for each site. The protocol was prepared by the primary authors (HL, MKo, CR, and CB), and reviewed and revised by the research team. Data analyses were performed separately within each database using the common protocol by collaborators or data custodians, and no raw data transfer was needed. For all databases, only aggregated results from de-identified records were submitted to the research group, and no individuals were contacted. Ethical approval for the use of data was obtained through the respective contributing authors in each participating site, and from: The Health Improvement Network Scientific Review Committee (UK), Sungkyunkwan University Institutional Review Board (Korea), Taiwan National Cheng Kung University Hospital Institutional Review Board (Taiwan) and Institutional Review Board of the Hospital Authority HK West Cluster (Hong Kong) (see Supplementary Table 3 for details). German, Ontario (Canada), Finnish and New Zealand legislation did not require ethics committee approval.

Study Participants

We included individuals aged 60 years and older with an incident record of dementia diagnosis during the study period. The overall study period was set between 1 January 2000 and 31 December 2018 based on data availability across all databases; database-specific study periods varied from 7 (Finland) to 19 years (New Zealand) (see Table 1 for details). Cases were identified using ICD-9 (290, 294.1, 294.2, 331.0, 331.1, 331.82), ICD-10 (F00-F03, G30, G31.1, G31.83), or Read codes for dementia as published in a previous UK study,[34] whichever was applicable for each database. Details of codes used in each site are listed in Supplementary Table 4. The Finnish MEDALZ (MEDication use and ALZheimer's disease) cohort included only individuals diagnosed with Alzheimer's disease; other types of dementia were not included.[35]

Individuals with a documented history of dementia before study entry were excluded. For databases without a variable indicating whether the diagnosis was the incident one, the year before the study period was set as the lookback period. Patients with a dementia diagnosis during the lookback period were excluded. The date of the first diagnosis was defined as the date when follow-up started, i.e., the index date. Individuals were followed from the index date until death (all causes), the end of the site-specific study period, or the end of insurance (if applicable), whichever came first.

Data analysis

We stratified individuals into subgroups by age at diagnosis using five-year age bands (60–64, 65–69, 70–74, 75–79, 80–84, and 85+) and sex. Sample characteristics and the annual number of incident cases were tabulated for each group. We used the Kaplan-Meier estimator to estimate the survival rate by age group. The impact of the dementia diagnosis on mortality risk was assessed using the standardised mortality ratio (SMR), which was quantified as the ratio of the observed number of deaths in the study population to the expected number of deaths in the study group,

based on age- and sex-specific mortality rates in the general population. Mortality data of the corresponding general population were retrieved from official statistics during the study period or the population of the medical insurance claims database from which the dementia cases were obtained (see Supplementary Table 5 for details). Cox proportional hazards regression was used to assess the association of mortality in dementia patients with calendar year of incident dementia diagnosis, taking time at risk into account. The model was adjusted for sex and age, and hazard ratios (HRs) and 95% CIs (confidence intervals) were reported. Calendar year was treated as categorical variable as its association with mortality risk may not be linear. All sites used Statistical Analysis System (SAS) v9.4 (SAS Institute, Cary, NC, USA) for data management and analysis.

Declarations

Contributors

HLu and ICKW initiated the study. HLu, ICKW, MKo, JSB, CSLC, SH, JI, ECCL, KKL, TYSL, KKCM, AT and GHYW collaboratively designed the study. HLu prepared the common protocol, the syntax, and the first draft of the manuscript. MKo, CR, and CB commented, tested, and revised the syntax. MKo, AT, and SH analysed and cross-checked the Finnish data; ATH and EK analysed the Canadian (Ontario) data; CR, CB, and BH analysed the German data; KKCM and WCYL led the UK data management; KB and AHYC analysed the New Zealand data; ECCL and TCL analysed the Taiwan data; JYS led the Korea team and JYS, JHK, and HLe analysed the Korean data; HLu, CSLC, KKL, and YC analysed the Hong Kong data and summarized aggregated data from all study sites. JSB, MKn, GHYW, AT, SH, and ICKW substantially revised the drafts of the manuscript. All authors critically reviewed the common protocol, reviewed all drafts, and approved the final version of the manuscript.

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Other authors have no conflict of interest to declare.

Data sharing

The study protocol and syntax are available in the Supplementary Material. All data requests should be directed to the corresponding author (wongick@hku.hk). De-identified **data of each study site may be shared separately with qualified researchers after reviewing the research proposal. The proposal needs to comply with site-specific legislations and/or within the scope of the ethical approval.**

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Tables

Table 1. The sample representativeness and study period of each database contributing data to the survival analysis of patients diagnosed with incident dementia between 2000 and 2018.

Sites	Database	Type of data	Representativeness	Study period
United Kingdom	The Health Improvement Network (THIN) electronic recording scheme	Primary care EMR	6% representative sample of the total population	Jan 1 2000 – Dec 31, 2016
Germany	Allgemeine Ortskrankenkasse (AOK)	Claims data	Random sample of 5% of AOK records which cover a third of the German population	Jan 1, 2007 - Dec 31, 2016
Finland	MEDALZ (Medication use and Alzheimer's disease) cohort	National register	Community-dwelling older adults	Jan 1, 2005 – Dec 31, 2015 With new diagnosis between Jan 1, 2005 – Dec 31, 2011
Canada (Ontario)	A dementia cohort created using the Discharge Abstract Database (DAD), Ontario Health Insurance Plan (OHIP) physician billing claims database, and the Ontario Drug Benefit (ODB) Program database	Claims data	All Ontario residents who are eligible for services covered by the universal, provincial medical insurance plan (OHIP)	Jan 1, 2000 - Dec 31, 2016
New Zealand	The National Minimum Dataset (NMDS), National Non-Admitted Patient Collection (NNPAC), and the Mortality Collection (MORT)	Hospital EMR (including inpatient, outpatient, and accident & emergency department data) and claims data combined	A national collection of publicly funded New Zealand hospital admissions	Jan 1, 2000 – Dec 31, 2018
South Korea	National Insurance Service-National Sampled Cohort (NHIS-NSC) database	Claims data	2.2% random sample of the total population	Jan 1, 2003 - Dec 31, 2013
Taiwan	National Health Insurance Research Database (NHIRD)	Claims data	99% of the total population	Jan 1, 2003 - Dec 31, 2015
Hong Kong	Clinical Data Analysis and Reporting System (CDARS)	Hospital EMR (including inpatient, outpatient, and accident & emergency department data)	All patients using public healthcare services	Jan 1, 2002 – Dec 31, 2018

Table 2. Sample characteristics of the sites contributing medical insurance claims data and electronic medical records data to the survival analysis of people living with dementia at the first recording of dementia diagnosis between 2000 and 2018.

	Total		UK		Germany		Finland		Canada (Ontario)	
	N	%	N	%	N	%	N	%	N	%
Study period	**2000-2018**		**2000-2016**		**2007-2016**		**2005-2015**[1]		**2000-2016**	
Total N	1272495		171025		88075		69834		483981	
Alzheimer's disease			48569	28.4	-	-	69834	100.0	44023	9.1
Vascular dementia			34124	20.0	-	-	-	-	16928	3.5
Lewy body dementia			-	-	-	-	-	-	682	0.1
Unspecific or other dementias			88332	51.7	-	-	-	-	422348	87.3
Female	772047	60.7	111803	65.4	59183	67.2	45619	65.3	296282	61.2
Age in years at diagnosis, Mean (sd)			81.7 (7.6)		82.9 (8.2)		80.4 (6.5)		81.3 (7.9)	
Number of deaths	763843	60.0	70181	41.0	53420	60.7	44253	63.4	333378	68.9
			New Zealand		**South Korea**		**Taiwan**		**Hong Kong**	
Study period			**2000-2018**		**2003-2013**		**2003-2015**		**2002-2018**	
Total N			47410	100	30730		235228		146212	
Alzheimer's disease			18930	39.9	12915	42.0	52291	22.2	26283	18.0
Vascular dementia			12156	25.6	4619	15.0	107384	45.7	20152	13.8
Lewy body dementia			260	0.6	-	-	23	0.0	-	-
Unspecific or other dementias			16064	33.9	13196	42.9	75530	32.1	99777	68.2
Female			27071	57.1	20334	66.2	123323	52.4	88432	60.5
Age in years at diagnosis, Mean (sd)			82.4 (7.2)		76.8 (8.9)		78.6 (7.9)		82.7 (7.9)	
Number of deaths			38000	80.2	9179	29.9	114216	48.6	101216	69.2

[1] With incident diagnosis between 2005-2011

Table 3. Adjusted hazard ratios (HRs) of the Cox proportional hazard models examining the mortality risk associated with sex, age, and calendar year of people living with dementia after an incident dementia diagnosis from eight study

sites.

	UK			Germany			Finland			Canada (Ontario)		
	HR[1]	SE[2]	95% CI[3]	HR	SE	95% CI	HR	SE	95% CI	HR	SE	95% CI
Female *(ref. Male)*	0.72	0.008	(0.71-0.73)	0.72	0.010	(0.70-0.73)	0.65	0.010	(0.64-0.66)	0.71	0.004	(0.70-0.71)
Age at diagnosis (ref: 60-64)												
65-69	1.14	0.041	(1.05-1.24)	1.32	0.053	(1.19-1.46)	1.22	0.057	(1.09-1.36)	1.16	0.016	(1.12-1.20)
70-74	1.52	0.037	(1.41-1.63)	1.63	0.048	(1.49-1.79)	1.46	0.052	(1.31-1.61)	1.51	0.015	(1.47-1.56)
75-79	2.09	0.036	(1.95-2.25)	2.19	0.047	(2.00-2.40)	1.97	0.050	(1.79-2.18)	1.94	0.014	(1.89-1.99)
80-84	2.88	0.035	(2.69-3.08)	3.07	0.046	(2.80-3.36)	2.88	0.050	(2.61-3.17)	2.65	0.014	(2.58-2.72)
85+	4.85	0.035	(4.53-5.19)	5.77	0.046	(5.28-6.31)	4.68	0.050	(4.24-5.16)	4.34	0.014	(4.23-4.46)
Calendar Year (ref.: first year of respective study year)												
2001	0.97	0.024	(0.92-1.02)	-	-	-	-	-	-	0.95	0.009	(0.93-0.97)
2002	0.99	0.024	(0.95-1.04)	-	-	-	-	-	-	0.91	0.009	(0.89-0.93)
2003	0.98	0.023	(0.94-1.03)	-	-	-	-	-	-	0.88	0.009	(0.86-0.89)
2004	0.96	0.023	(0.92-1.01)	-	-	-	-	-	-	0.85	0.009	(0.83-0.86)
2005	0.92	0.023	(0.88-0.96)	-	-	-	-	-	-	0.83	0.009	(0.82-0.85)
2006	0.92	0.022	(0.88-0.97)	-	-	-	1.01	0.017	(0.98-1.05)	0.79	0.009	(0.78-0.81)
2007	0.87	0.023	(0.83-0.91)	-	-	-	1.01	0.017	(0.98-1.05)	0.76	0.010	(0.75-0.77)
2008	0.81	0.023	(0.78-0.85)	1.00	0.014	(0.97-1.03)	0.98	0.018	(0.95-1.02)	0.76	0.010	(0.75-0.77)
2009	0.77	0.023	(0.73-0.80)	0.98	0.015	(0.95-1.01)	0.99	0.018	(0.96-1.03)	0.74	0.010	(0.73-0.75)
2010	0.76	0.023	(0.73-	1.00	0.016	(0.97-	0.99	0.019	(0.95-	0.74	0.010	(0.72-

			0.79)			1.03)			1.03)			0.75)
2011	0.70	0.023	(0.67-0.73)	1.01	0.017	(0.98-1.05)	0.99	0.020	(0.95-1.03)	0.72	0.010	(0.71-0.74)
2012	0.73	0.024	(0.69-0.76)	1.03	0.018	(0.99-1.07)	-	-	-	0.73	0.010	(0.72-0.75)
2013	0.67	0.025	(0.64-0.70)	0.92	0.018	(0.89-0.95)	-	-	-	0.73	0.011	(0.72-0.75)
2014	0.70	0.027	(0.66-0.74)	0.84	0.021	(0.80-0.87)	-	-	-	0.72	0.011	(0.71-0.74)
2015	0.77	0.031	(0.73-0.82)	0.93	0.026	(0.88-0.98)	-	-	-	0.72	0.012	(0.70-0.73)
2016	0.72	0.050	(0.65-0.79)	1.04	0.034	(0.97-1.11)	-	-	-	0.70	0.015	(0.68-0.72)
2017	-	-	-	-	-	-	-	-	-	-	-	-
2018	-	-	-	-	-	-	-	-	-	-	-	-

[1]HR = Hazard Ratio; [2]SE = Standard Error; [3]CI = Confidence Interval

Table 3 *Continued.* Adjusted hazard ratios (HRs) of the Cox proportional hazard models examining the mortality risk associated with sex, age, and calendar year of people living with dementia after an incident dementia diagnosis from eight study sites.

	New Zealand			South Korea			Taiwan			Hong Kong		
	HR	SE	95% CI	HR	SE	95% CI	HR	SE	95% CI	HR	SE	95% CI
Female *(ref.: Male)*	0.69	0.011	(0.68-0.71)	0.55	0.022	(0.53-0.58)	0.71	0.006	(0.70-0.72)	0.62	0.006	(0.61-0.63)
Age at diagnosis (ref: 60-64)												
65-69	1.27	0.057	(1.13-1.41)	1.35	0.070	(1.18-1.55)	1.24	0.021	(1.19-1.29)	1.3	0.034	(1.21-1.39)
70-74	1.54	0.053	(1.39-1.70)	2.20	0.064	(1.95-2.50)	1.63	0.020	(1.57-1.70)	1.64	0.031	(1.54-1.74)
75-79	1.96	0.051	(1.77-2.16)	3.29	0.062	(2.91-3.71)	2.15	0.019	(2.07-2.23)	2.02	0.030	(1.90-2.15)
80-84	2.32	0.051	(2.11-2.57)	4.93	0.062	(4.37-5.56)	2.94	0.019	(2.83-3.05)	2.56	0.030	(2.42-2.72)
85+	3.45	0.050	(3.13-3.81)	8.40	0.062	(7.44-9.47)	4.59	0.019	(4.43-4.76)	3.98	0.300	(3.75-4.22)
Calendar Year												
2001	1.02	0.032	(0.96-1.08)	-	-	-	-	-	-	-		-
2002	0.96	0.032	(0.90-1.02)	-	-	-	-	-	-	-		-
2003	0.97	0.032	(0.91-1.03)	-	-	-	-	-	-	1	0.017	(0.96-1.03)
2004	0.95	0.032	(0.89-1.01)	0.87	0.060	(0.78-0.98)	1.00	0.014	(0.97-1.03)	0.95	0.017	(0.91-0.98)
2005	0.95	0.032	(0.90-1.02)	0.93	0.060	(0.83-1.04)	0.97	0.014	(0.94-1.00)	0.93	0.017	(0.90-0.96)
2006	0.94	0.031	(0.88-1.00)	0.95	0.056	(0.85-1.06)	0.93	0.014	(0.90-0.96)	0.92	0.017	(0.89-0.95)
2007	0.93	0.031	(0.87-0.99)	0.97	0.055	(0.87-1.08)	0.90	0.014	(0.88-0.93)	0.92	0.017	(0.89-0.95)
2008	0.98	0.031	(0.92-1.04)	0.73	0.053	(0.66-0.82)	0.89	0.015	(0.86-0.91)	0.90	0.017	(0.87-0.93)
2009	0.95	0.031	(0.90-1.01)	0.79	0.054	(0.71-0.88)	0.86	0.015	(0.83-0.88)	0.88	0.016	(0.85-0.91)
2010	0.99	0.031	(0.93-1.05)	0.73	0.056	(0.65-0.82)	0.86	0.015	(0.83-0.88)	0.86	0.016	(0.84-0.89)
2011	0.98	0.031	(0.92-1.04)	0.76	0.055	(0.68-0.84)	0.84	0.015	(0.82-0.87)	0.83	0.016	(0.80-0.86)

2012	0.98	0.031	(0.92-1.04)	0.65	0.061	(0.58-0.73)	0.84	0.016	(0.82-0.87)	0.82	0.017	(0.79-0.85)
2013	0.98	0.031	(0.93-1.05)	0.55	0.076	(0.48-0.64)	0.83	0.017	(0.81-0.86)	0.82	0.017	(0.79-0.85)
2014	1.06	0.031	(1.00-1.13)	-	-	-	0.85	0.019	(0.81-0.88)	0.80	0.018	(0.78-0.83)
2015	1.09	0.031	(1.03-1.16)	-	-	-	0.76	0.027	(0.72-0.80)	0.77	0.019	(0.74-0.80)
2016	1.08	0.033	(1.01-1.15)	-	-	-	-	-	-	0.78	0.020	(0.75-0.81)
2017	1.16	0.036	(1.08-1.24)	-	-	-	-	-	-	0.78	0.023	(0.75-0.81)
2018	1.20	0.044	(1.10-1.30)	-	-	-	-	-	-	0.79	0.029	(0.75-0.84)

Figures

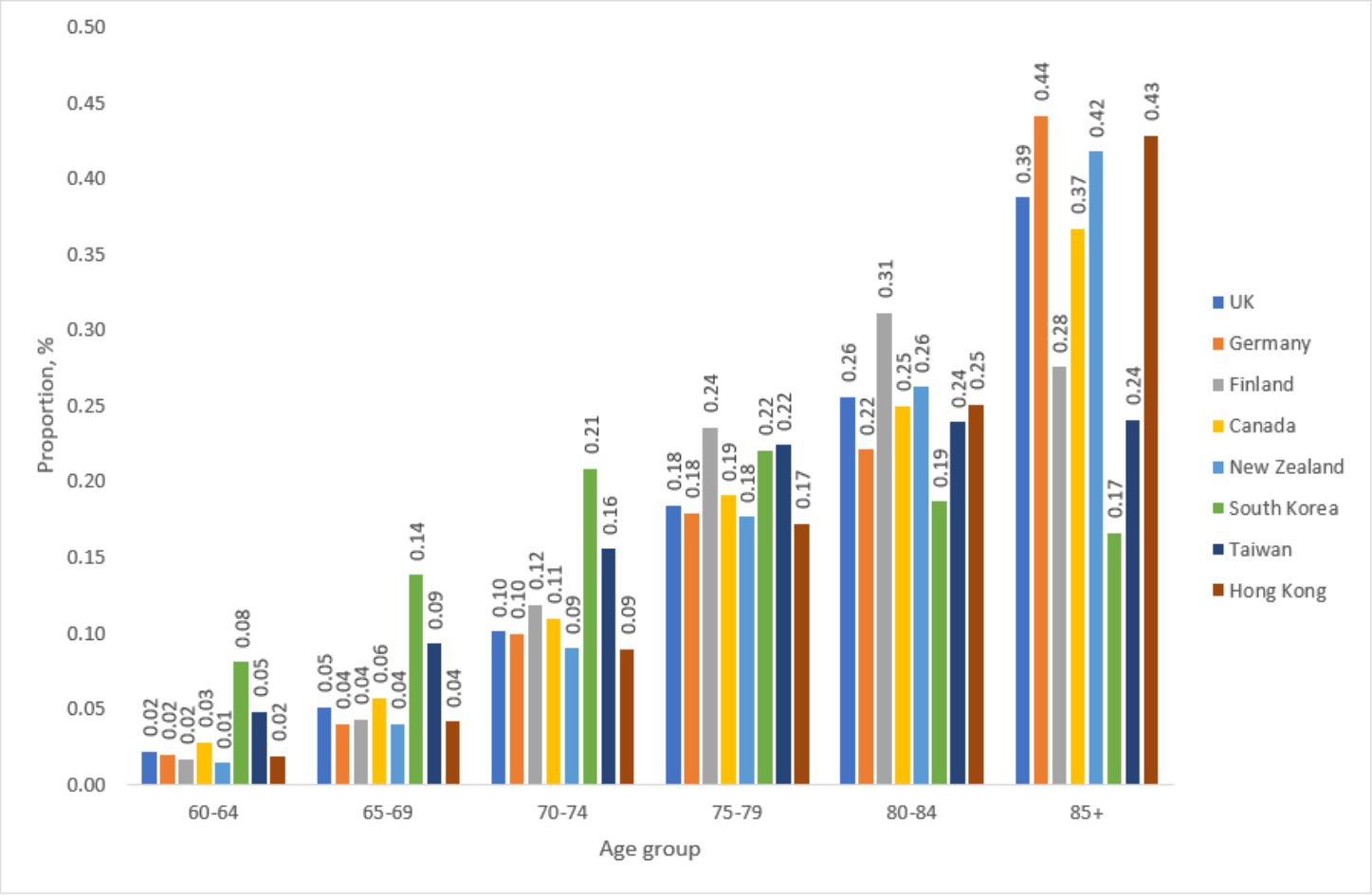


Figure 1

Distribution of age at the recording of incident diagnosis of dementia (index date) by database

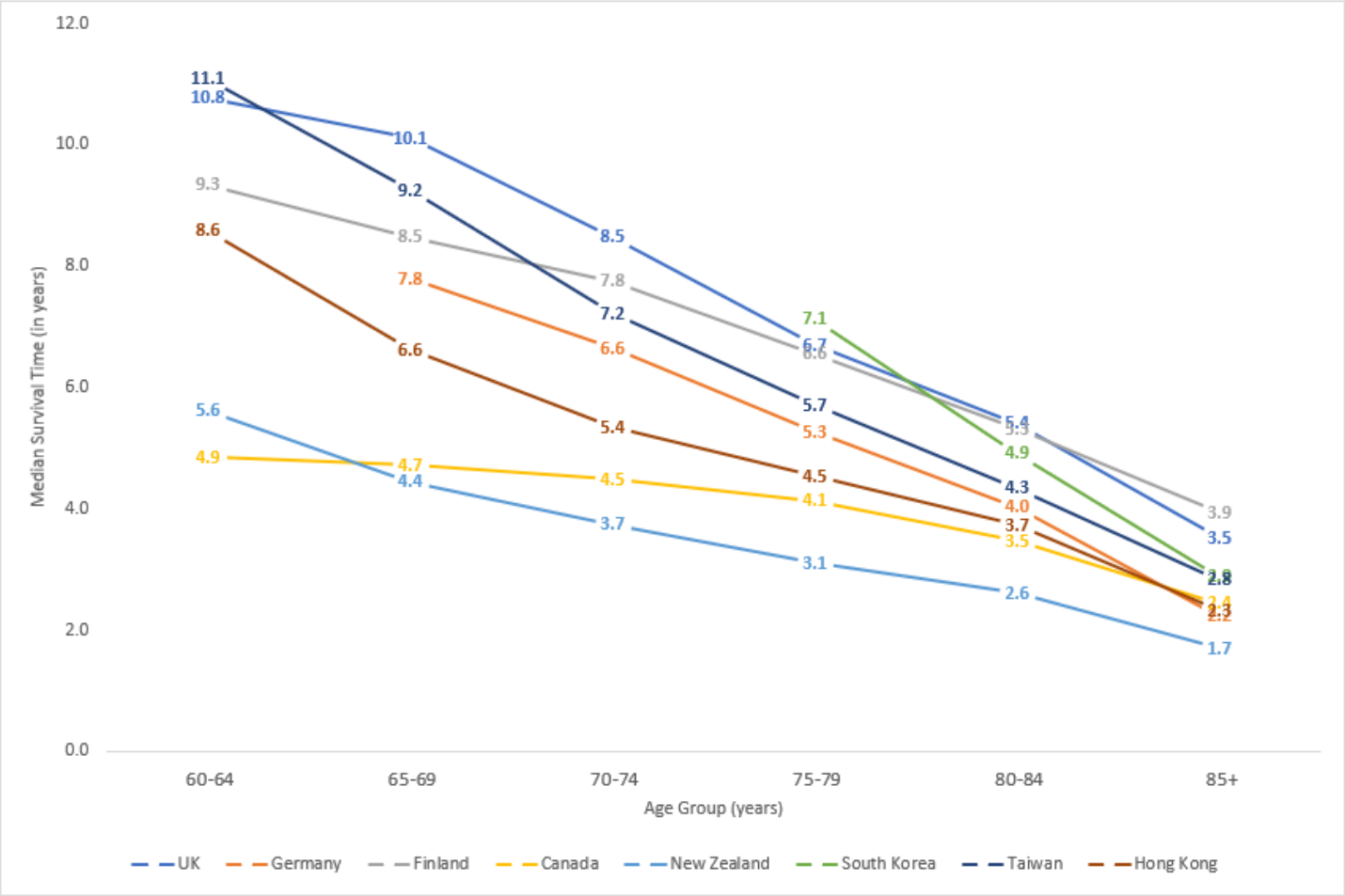
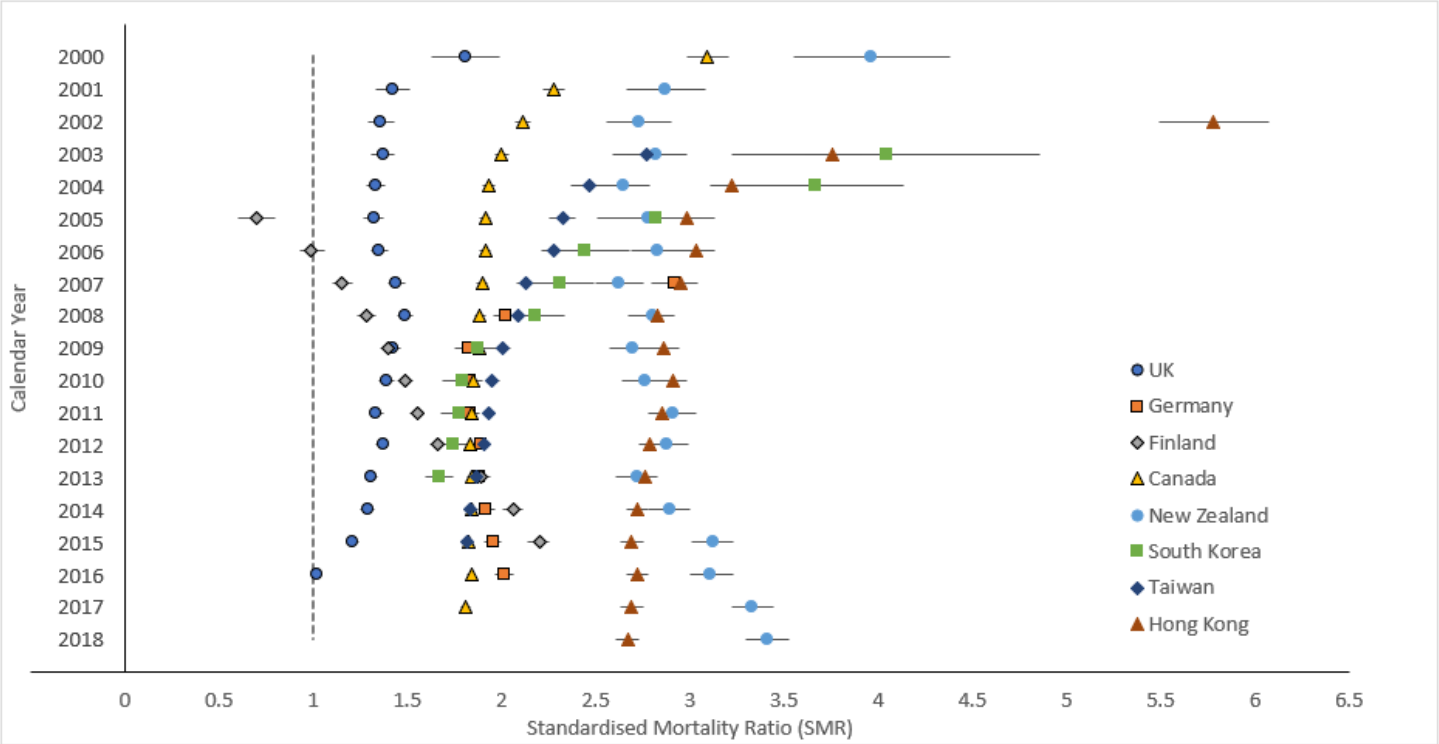


Figure 2

Median survival time after incident diagnosis of dementia in years by age group and database



Aggregated SMR (95% confidence interval)

UK	Germany	Finland	Canada	New Zealand	South Korea	Taiwan	Hong Kong
1.27 (1.27-1.28)	1.91 (1.89-1.92)	1.63 (1.61-1.64)	1.85 (1.84-1.85)	2.90 (2.87-2.93)	1.75 (1.71-1.79)	1.90 (1.89-1.91)	2.79 (2.77-2.81)

Figure 3

Standardized mortality ratio with 95% confidence interval by calendar year and study site, comparing patients with incident dementia diagnosis to the general population.

Supplementary Files

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