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A multinational cohort study of trends in survival following dementia diagnosis

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Background Information on the survival of people living with dementia over time and across systems can help policymakers understand the real-world impact of dementia on health and social care systems. This multinational cohort study examines the trends in relative mortality risk following a dementia diagnosis.

Methods A common protocol was applied to population-based data from the UK, Germany, Finland, Canada (Ontario), New Zealand, South Korea, Taiwan and Hong Kong. Individuals aged 60+ with an incident dementia diagnosis recorded between 2000 and 2018 were followed until death or the end of the study period. Cox proportional hazards regression was used to assess the association of mortality in dementia patients with the year of dementia diagnosis.

Results Data from 1,272,495 individuals, with the mean age at diagnosis ranging from 76.8 years (South Korea) to 82.9 years (Germany), show that the overall median length of survival following recorded diagnosis ranges from 2.4 years (New Zealand) to 7.9 years (South Korea). Hazard ratios (HRs) estimated from Cox proportional hazard models decline consistently over the study period in the UK, Canada, South Korea, Taiwan and Hong Kong, which accounted for 84% of all participants. For example, the HR decreases from 0.97 (95% CI: 0.92–1.02) in 2001 to 0.72 (0.65–0.79) in 2016 in comparison to year 2000 in the UK.

Conclusions This study shows 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.

Plain language summary

How long people live after being diagnosed with dementia can vary between countries and over time. Understanding recent trends in survival following dementia diagnosis across countries can help policymakers better plan support and services for dementia. This multinational study analysed data from over 1.2 million people aged 60 years and older who were diagnosed with dementia between 2000 and 2018 in eight regions: the UK, Germany, Finland, Canada (Ontario), New Zealand, South Korea, Taiwan and Hong Kong. In five of these regions, people diagnosed with dementia in more recent years had a lower risk of dying compared to those diagnosed in earlier years. These improvements in survival may be due to earlier diagnosis and better dementia care.

Dementia, which may result from a variety of diseases, is a disabling syndrome that mainly affects older adults[1]. With a prevalence of 57 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 high-quality epidemiological data on dementia, including the prevalence, incidence, cost and trends, to encourage prioritisation and to guide planning and action[3]. Together with incidence, the survival with dementia is one of the two forces that determine the prevalence of dementia. Knowledge of survival after the diagnosis of dementia is also important for people with dementia and their family members for making informed decisions about the subsequent care arrangement; for clinicians to improve their prognosis and care for people living with dementia; and for policy makers to improve estimation of the real-world disease burden currently carried by health systems[4,5].

The survival time of people living with dementia may vary between world regions, time periods and subpopulations with different socio-demographic characteristics within a region[5,6]. In an earlier systematic review, based on data from 42 studies including more than 11,000 people

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living with dementia[7], 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 suggested a slight increase 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[8]. Public health strategies and plans, such as increasing diagnostic rates, case-finding and early diagnosis[9] and other population-specific contextual factors (e.g. role of primary/secondary/tertiary care in dementia) may also affect survival[10]. 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, scattered, or is out-of-date. A systematic review identified only four studies that reported changes in survival among people living with dementia, all of which were conducted over 10 years ago[5]. According to the review, relatively stable mortality ratios for dementia were observed across 9 years in the US and 14 years in Sweden[11–13]. Assuming reducing mortality rates in the general population, the stable mortality ratio suggests that there were similar rates of decrease in mortality in people with dementia. In contrast, a German study using insurance claims data reported an increase in mortality rates among people living with dementia between 2004 and 2007, particularly in women[14]. Similarly, using data from the National Center for Health Statistics multiple cause-of-death public-use data files, a previous study in the US showed an increasing trend in dementia mortality rates[13]. More recent evidence based on data from the mortality surveillance system in China[15], a cross-sectional survey in Japan[16], a community-based research cohort in France[17] and hospital-based research cohort in the Netherlands[18], suggests a declining trend in mortality among people living with dementia. However, in France, the increase in dementia survival was only evident in women. In China, dementia mortality increased by 24% in rural areas between 2006 and 2012[19]. Additionally, a US study utilised Medicare claims data to examine racial/ethnic difference in survival by year of incident dementia diagnosis between 2001 and 2013. The study identified a decreasing mortality advantage among Asians and Hispanics over Whites[20]. However, the study focused on between racial/ethnic differences and did not examine the survival trend within each race/ethnicity. The lack of congruence across these studies can be attributable to their use of different outcome measures —including absolute risk of mortality or survival rate within certain years, hazard ratios (HRs) for mortality, age-standardised mortality, years of life lost due to dementia and life expectancy with dementia. All previous studies have been limited to a single database and region/country. There has yet to be a cross-national study conducted with a common protocol.

The WHO Global Action Plan on the Public Health Response to Dementia 2017–2025 identified routine population-level monitoring of dementia indicators as a key action area to provide data in guiding evidence-based actions[21]. 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, provide the basis for future studies on 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[22]. The widespread adoption of EMR and administrative data presents a unique opportunity for generating large-scale evidence with a common analytical protocol from multiple databases that span diverse geographic regions and healthcare systems. This approach can improve the understanding on whether any trends identified are due to systematic bias or specific to the unique context of the database[23]. Using longitudinal data between 2000 and 2018 of 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 difference in survival by year of the first dementia diagnosis.

National dementia strategies have now been developed in many 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[24], longer survival following dementia diagnosis could be expected over recent years. The primary goal of this current investigation is to examine whether an increase in dementia survival can be observed in multiple databases by applying a common analytical protocol. Substantial differences in median survival time and mortality risk were observed across databases. Nevertheless, a consistent decreasing trend in the relative risk of mortality was evident in the UK, Canada, South Korea, Taiwan and Hong Kong, suggesting encouraging progress in dementia care and the potential positive impact of national dementia strategies.

Methods

Data sources

The present study employed three medical insurance claims databases, two EMR databases, two databases combining claims and EMR data and a register-based cohort. The claims-based databases were the 'Allgemeine Ortskrankenkasse' (AOK) data sourced from Germany's largest public health insurance[14], the National Insurance Service-National Sampled Cohort (NHIS-NSC) database from South Korea[25], and National Health Insurance Research Database (NHIRD) from Taiwan[26]. The EMR databases consisted of priamry care data from the Health Improvement Network (THIN) in the UK[27] and public hospital records stored in the Clinical Data Analysis and Reporting System (CDARS) in Hong Kong[28,29]. The claims and EMR combined databases included data from the national Ministry of Health databases in New Zealand and the dementia cohort held at the Institute for Clinical Evaluative Science (ICES) in Ontario, Canada. The register-based cohort utilised was the MEDALZ (Medication use and Alzheimer's disease) cohort from Finland[30]. The MEDALZ cohort included residents of Finland who were newly diagnosed with Alzheimer's disease between 2005 and 2011, and were community-dwelling at the time of diagnosis. Individuals with other types of dementia or were residing in long-term care facilities were not included. Details of the data sources are described in Supplementary Note 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 Data 1 for key references of each database). All databases contributed data on dementia diagnosis and vital status. The sample representativeness, data type and study period of each database are summarised in Table 1.

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 iteratively revised by the research team. Data analyses were performed separately within each database using the common protocol by collaborators or data custodians. 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.

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	EMR and claims data combined	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

Study participants

We included individuals aged 60 years and older with an incident record of dementia diagnosis during the study period. Individuals with missing data on sex or date/year of birth were excluded. 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[31], whichever was applicable for each database. Details of codes used in each site are listed in Supplementary Table 1.

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. We additionally conducted sensitivity analyses in two databases (UK THIN and Hong Kong CDARS database) to investigate the possible impact of the length of lookback period by extending the lookback period to 2 years. 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.

Vital status

In six databases, information on vital status was derived from the relevant death registries. Specifically, the date of death was retrieved from Statistics Korea for NHIS-NSC[25], the National Death Registry for NHIRD, the Ontario provincial death registry for the ICES cohort, regional deaths registry from the Immigration Department of Hong Kong for the CDARS[28], the Mortality Collection (MORT) database managed by the Ministry of Health for New Zealand, and Statistics Finland for MEDALZ. For the German AOK data, the date of death is based on the record of the health insurance company as Germany does not have national mortality registries at the time of data sampling[32]. For the UK THIN data, the date of death was based on the General Practitioner' records. A previous validation study showed that the death recording on the THIN database is highly reliable, with a positive predictive value of 99.6% and a sensitivity of 99.7%[33].

Statistics and reproducibility

We stratified individuals into subgroups by age at diagnosis using 5-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. 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 HRs and 95% CIs (confidence intervals) were reported. Since interventions such as the introduction of cholinesterase inhibitors and policies that occurred at any point during the study period may have disrupted the overall trend, calendar year was treated as categorical variable to account for the potential non-linear relationship between time and mortality risk. We tested the proportional hazards assumption by inspecting the graph of the survival function against time for different levels of the predictors (Supplementary Figs. 1–8).

We supplemented the trends in HR by calculating the standardised mortality ratio (SMR). This provides additional information on the changes in mortality among dementia patients relative to the general population. The SMR was quantified as the ratio of the observed number of deaths in the study population (i.e. people with dementia) to the expected number of deaths in the study group calculated 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 (Supplementary Data 2). SMRs for the first 2 years were excluded to account for the possibility of an over-representation

of incident cases. For Finland, SMRs after 2011 were excluded because no cases were added between 2012 and 2015. It is important to note that SMRs in the early years and SMR trends obtained from datasets with a shorter observational period for dementia diagnoses should be interpreted with caution due to the dominance of newly diagnosed patients in the sample. These patients are likely to have a lower risk of mortality compared to those who have been diagnosed for a longer period of time.

All sites used Statistical Analysis System (SAS) v9.4 (SAS Institute, Cary, NC, USA) for data management and analysis. Statistical significance was defined as a two-sided p value of less than 0.05. The study protocol and common syntax are available at GitHub (https://github.com/yvonne840429/NeuroGEN-Dementia-Survival)[34].

Ethics and Inclusion statement

Ethical approval for data use was obtained by the contributing authors at each participating site. In the UK, THIN data were accessed through coauthors from University College London (KKCM and WCYL), with study approval granted by The Health Improvement Network (THIN) Scientific Review Committee. In Germany, AOK data were accessed via coauthors at the German Center for Neurodegenerative Diseases (CR, CB and BH), with legal approval provided by the 'Wissenschaftliches Institut der Ortskrankenkassen' (WIdO). In Finland, MEDALZ data were accessed by coauthors from the University of Eastern Finland (AT, SH and MKo). In Canada, Ontario data were accessed by an ICES-based coauthor (ATH), with approval from ICES' Privacy and Legal Office. In New Zealand, data were accessed by coauthors at the University of Auckland (AHYC and KB). In South Korea, NHIS-NSC data were accessed through coauthors at Sungkyunkwan University (JYS, JHK and HLe), with ethical approval obtained from the Sungkyunkwan University Institutional Review Board (IRB). In Taiwan, NHIRD data were accessed via coauthors at National Cheng Kung University (ECCL and TCL), and approved by the IRB of National Cheng Kung University Hospital. In Hong Kong, the CDARS data were accessed by coauthors from the University of Hong Kong (HLu and CSLC), with approval from the IRB of the Hospital Authority Hong Kong West Cluster. IRB approval was not required for data use in Germany, Finland, Ontario (Canada), or New Zealand, in accordance with respective national legislations. As all data were anonymized and contained no identifiable information, the need for informed consent was waived by all IRBs (see Supplementary Table 2 for details).

Local researchers were engaged throughout the research process, with roles and responsibilities collaboratively defined in advance. Relevant local and regional research has been acknowledged and taken into account in citations. The study poses no risk of stigmatisation, discrimination or other personal risk to participants.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Results

A total of 1,272,495 individuals with a recorded diagnosis of dementia from eight databases were followed for periods between 1 January 2000 and 31 December 2018. 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 the 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 Supplementary Table 3. Changes in the age distribution of incident cases over time in all databases except Germany are also shown in Supplementary Fig. 9. The proportion of people aged 85 years or older gradually increased over time for all databases reporting absolute incident numbers. The subtype of dementia 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).

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		2000–2016	
Total *N*	1,272,495		171,025		88,075		69,834		483,981	
Alzheimer's disease			48,569	28.4	-	-	69,834	100.0	44,023	9.1
Vascular dementia			34,124	20.0	-	-	-	-	16,928	3.5
Lewy body dementia			-	-	-	-	-	-	682	0.1
Unspecific or other dementias			88,332	51.7	-	-	-	-	422,348	87.3
Female	772,047	60.7	111,803	65.4	59,183	67.2	45,619	65.3	296,282	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	763,843	60.0	70,181	41.0	53,420	60.7	44,253	63.4	333,378	68.9
			New Zealand		**South Korea**		**Taiwan**		**Hong Kong**	
Study period			2000–2018		2003–2013		2003–2015		2002–2018	
Total *N*			47,410	100	30,730		235,228		146,212	
Alzheimer's disease			18,930	39.9	12,915	42.0	52,291	22.2	26,283	18.0
Vascular dementia			12,156	25.6	4619	15.0	107,384	45.7	20,152	13.8
Lewy body dementia			260	0.6	-	-	23	0.0	-	-
Unspecific or other dementias			16,064	33.9	13,196	42.9	75,530	32.1	99,777	68.2
Female			27,071	57.1	20,334	66.2	123,323	52.4	88,432	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			38,000	80.2	9179	29.9	114,216	48.6	101,216	69.2

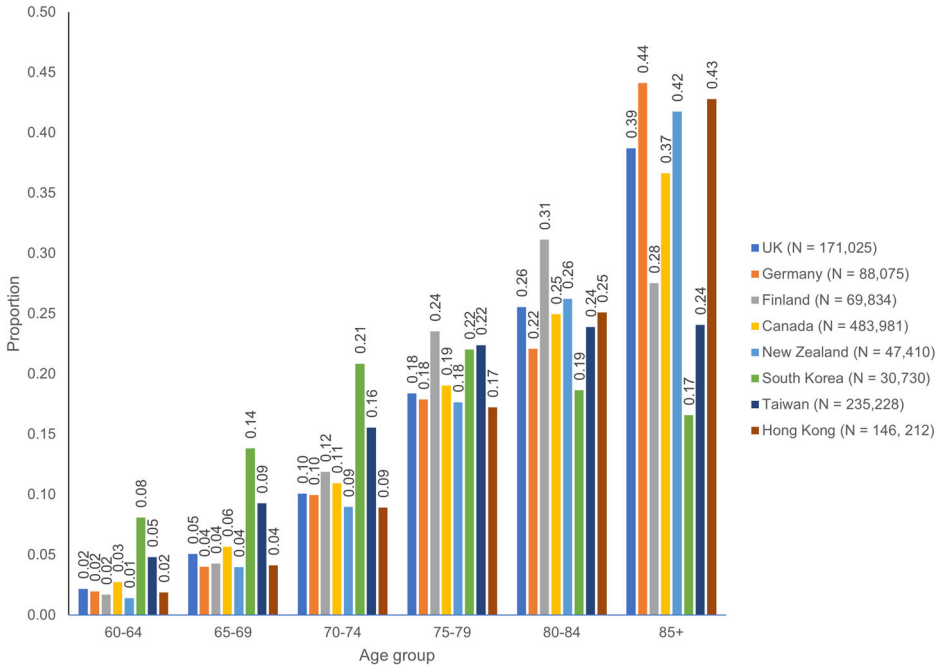

Fig. 1 | Age distribution at the recording of incident diagnosis of dementia (index date), by database.

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+.

Results from Cox proportional hazard models examining the effect of calendar year on mortality risk, adjusting for sex and age, are shown in Fig. 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 (Supplementary Data 3). 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. The sensitivity analysis, which set the lookback period to 2 years instead of 1 year for the UK and Hong Kong databases, yielded consistent results (Supplementary Table 4).

The highest overall SMRs for people with dementia were found in Hong Kong (2.35; 95% confidence interval (CI): 2.34–2.36) and New Zealand (2.34; 95% CI: 2.32–2.37), while the lowest SMR of 1.08 (95% CI: 1.07–1.09) was observed in the UK. Supplementary Fig. 10 shows the aggregated and calendar-year-specific SMRs. An overall decreasing trend was observed in the UK from 2008 to 2016, Canada, South Korea, Taiwan and Hong Kong, while an increasing trend was observed in the UK from 2002 to 2008, Finland, Germany and New Zealand. Calendar-year-specific SMRs for the first 2 years were excluded from the results due to the over-representation of individuals who were newly diagnosed.

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, results from Cox models suggested 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[23]. Our findings provide information to complement data available from other sources, such as population-based epidemiological research and the Global Burden of Disease study[35]. However, it is important to note some differences between individual databases included in this study and database-specific properties may have affected the trends observed. We analysed data from general practice databases (UK and Canada), 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[14]. Previous studies conducted in the US have suggested that using claims data may lead to an inflated estimation of dementia prevalence as approximately half of those with dementia record in claims did not have dementia in the cohort evaluation[36]. More recent findings suggested that individual in the false-positive group were more likely to have reported memory concerns, MCI and/or multiple chronic conditions[37]. While the extent to which these US findings can be generalised to Germany, Taiwan and South Korea claims data is unknown, the possibility of overidentification of dementia cases in these databases should be considered when interpreting our results. Primary care datasets often include a wider pool of people living with dementia, including those with milder dementia, as compared with data from

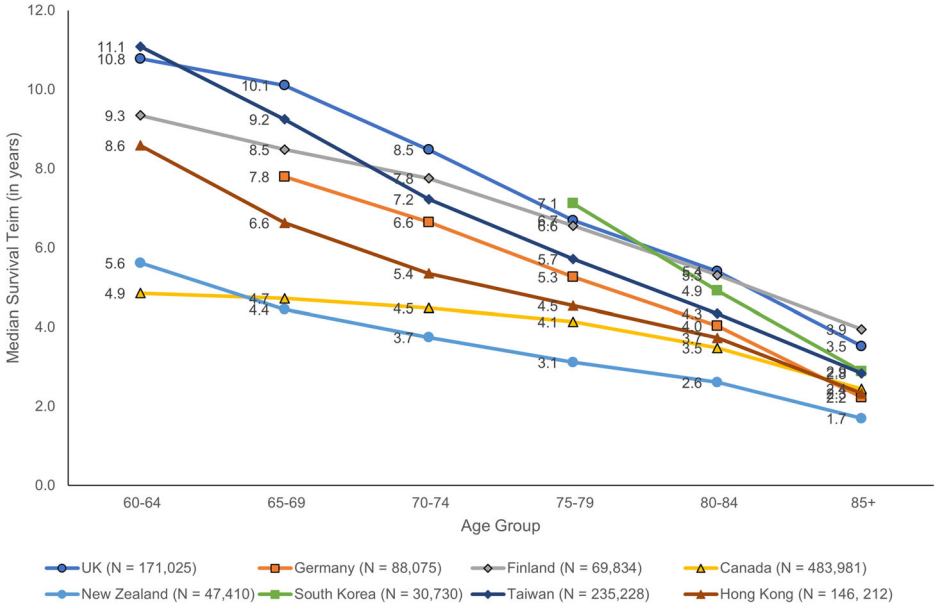

Fig. 2 | Median survival time (in years) following incident diagnosis of dementia, by age group and database (Note: Median survival time was not available among people aged 60–64 in Germany and people aged 60–74 in South Korea because more than 50% of individuals in these age groups survived until the end of the study period).

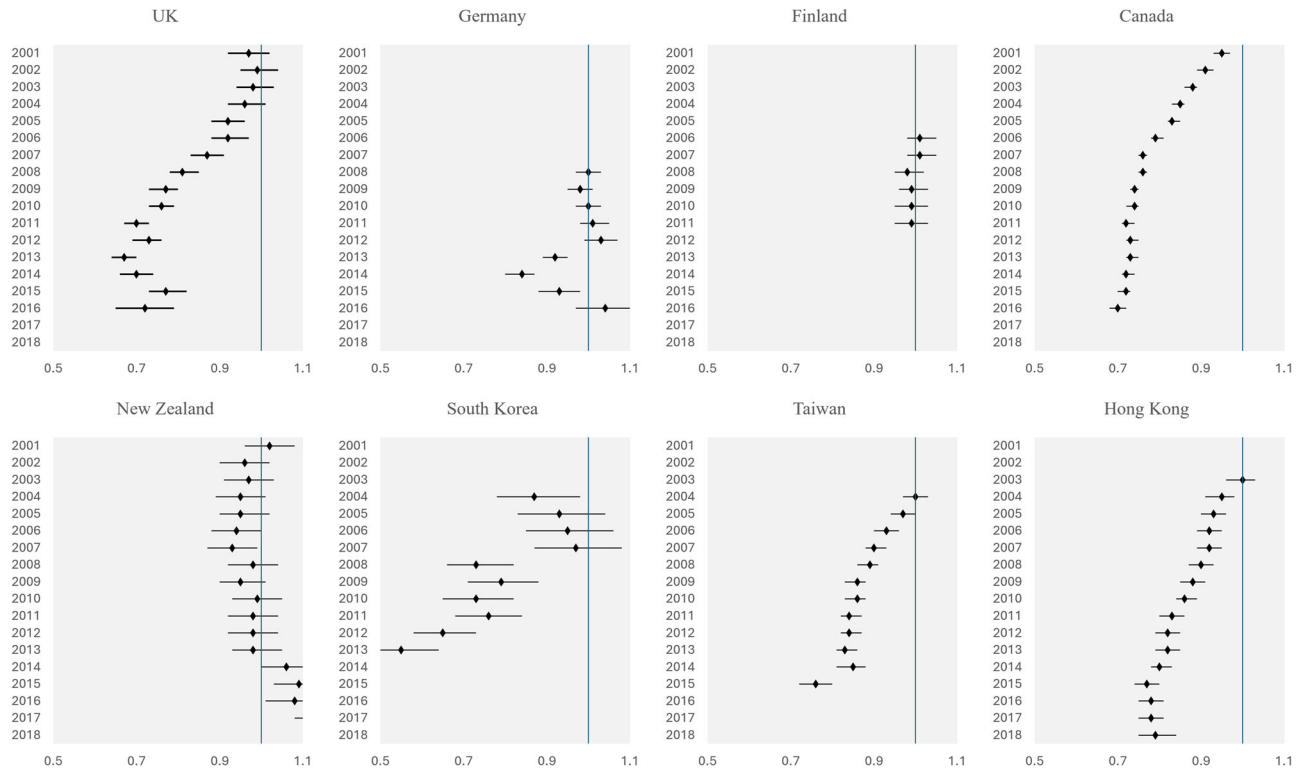

Fig. 3 | Adjusted hazard ratios (HRs) and 95% confidence intervals estimated from the Cox proportional hazard models examining the mortality risk associated with calendar year of people living with dementia after an incident dementia diagnosis from eight study sites, adjusting for sex and age.

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[38], 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. National registers provide comprehensive linkage with multiple data sources, resulting in higher accuracy when identifying incident cases. However, they may have a shorter observation period since maintaining these registers can be challenging. In the case of the MEDALZ cohort, although the observation period ended in 2015, no new cases were added to the cohort after 2011. 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. Therefore, it is essential to interpret the trend within the context of each individual database and comparing outcomes measures between databases is not recommended.

This study reported HRs estimated from Cox models, supplemented by SMRs, for each calendar year. The HR and SMR measure two different relative risks of mortality, and trends estimated based on these measures may

not necessarily align. Specifically, the HR compares mortality risks of people who received the diagnosis at different years within the dementia population (reference group: people with first dementia record in the first year of data availability), while the SMR compares mortality risks between people with dementia and the general population (reference group: mortality rate of the general population at a particular year). The HR is more reliable than the SMR as the SMR does not consider the time at risk of event when calculating the number of deaths in the study population, which likely results to lower estimates than HR during the first few years due to the impact of incident dementia cases. In Finland and Germany, no clear trend was observed in HRs, yet an increase was observed in SMRs. This discrepancy may be attributed to multiple reasons. In Finland, the MEDALZ cohort was restricted to people with incident Alzheimer's disease who were community-dwelling at the time of AD diagnosis. The general population obtained from the national statistics contained both people with and without dementia, with varying types and stages of dementia and both community-dwelling and institutionalised people. Towards the later observation years, Alzheimer's disease progressed from mild/moderate to more severe stages increasing mortality in the MEDALZ cohort. Thus, it is logical that the SMR, standardised into relatively stable general population, is higher in the later years for the MEDALZ cohort even when no change was observed in the HRs. We plotted the observed and expected number of deaths by sex and age in each calendar year (Supplementary Fig. 11). It is evident that as the number of deaths increased substantially over year, the observed number of deaths increased at a faster rate than the expected number of deaths derived from the general population. In Germany, there are several reasons for the increase in SMR over time. First, the observed death rate in the dementia cohort might have increased for similar reasons as observed in Finland. Additionally, the increased knowledge of the disease, along with reduced stigma/psychological barriers for making a dementia diagnosis, may have led clinicians to make more diagnoses over the years. Second, the death rate in the general population has indeed decreased[39]. From 2006 to 2016, the life expectancy in Germany at birth increased from 82.4 to 83.5 for women and 77.2 to 78.6 for men. Third, changes in the decomposition of age groups might also have contributed to the observed increase in SMR over time. Specifically, there has been a decrease of over 6% in the proportion of individuals aged 85 and above among both dementia patients and dementia-related deaths between 2007 and 2016. This age group has consistently exhibited the lowest SMR among all age categories, as the difference in survival between patients with and without dementia is relatively smaller. The diminishing influence of the lower SMR in the 85+ age group might have contributed to an overall increase in the composite SMR across calendar years.

Dementia is a symptom diagnosis which can be caused by several diseases with varied survival rates following diagnosis[7,40]. 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. 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 60–69 years[41]. Our findings from the 2000–2016 data indicate a median survival time of ~10 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[42]. 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[14]. Our analysis identified no clear trend in Germany.

Another noteworthy finding is the steady increase in 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)[43]. We used hospital admission data from New Zealand to identify cases of dementia. As such, the increase in 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.

A key finding of this study is the consistently observed decrease in mortality risk across five databases, which accounted for 84% of all participants. While the specific causes for this decrease may vary and cannot be systematically examined using the current data, it may in part be associated with both earlier dementia diagnosis and better dementia care[10]. Dementia awareness campaigns and initiatives that have been taking place in different parts of the world may have changed the help seeking behaviour of individuals with dementia. Coupled with recent advancements in dementia diagnostic knowledge and tools, people with dementia may have been diagnosed at an earlier stage, allowing more timely interventions[10]. Meanwhile, cholinesterase inhibitors and memantine have been shown to have a useful role in treating patients with mild-to-moderate and moderate and severe Alzheimer's disease, respectively[44,45]. Evidence is also accumulating for the effectiveness of person-centred psychosocial intervention tailored to the person's need[10]. The earlier diagnosis and improved dementia care may have both played a role in the observed decreases in mortality risk, collectively signalling the potential positive effect of dementia plans and associated policies.

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)[15]. 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[46], 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 an overestimation of survival after diagnosis of dementia. While it would be beneficial to conduct a thorough examination of the accuracy in identifying dementia cases (measured by sensitivity and specificity) of each database, such an analysis would necessitate individual-level data linkage with other databases that possess an expert-derived reference standard for dementia[47], which is beyond the scope of the current study. Similarly, although most data sourced information on vital status from death

certificates, not all databases were linked to regional- or national-level death registries, which may have affected the estimation of mortality risk. We did not perform further analysis on the potential impact because six out of databases were linked to death registries and we do not have access to external databases or alternative ways to ascertain death. Although we acknowledge the potential impact of differences in dementia coding and death recording accuracy across databases, such differences should not have affected the interpretation of results and conclusions. This is because our study primarily aimed to evaluate trends within each database rather than difference between databases, which is a perspective that many other multinational studies have adopted[48,49]. It is important to note that the current study is descriptive in nature, with a focus on identifying possible changes of dementia survival over the past two decades and generating hypotheses for subsequent investigations into the underlying causes of any observed changes.

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 accounted for in the current investigation. Given that comorbid conditions are often more prevalent among people living with dementia than those without, the SMRs reported in this study might be overestimated. Deaths observed in the dementia cohort might be attributable to comorbid conditions rather than dementia itself. As such, the observed trends in SMRs likely reflect the combined effects of dementia and comorbid conditions, rather than the impact of dementia alone. However, the aim of this study was to provide epidemiological data on trends in survival of an average older person with a dementia diagnosis rather than the independent effect of dementia on the risk of mortality. The specific impact of comorbidity on survival and trends in survival 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). We then examined the possible impact of lookback period by extending the lookback period to 2 years. The results obtained from this sensitivity analysis were highly consistent with the previous results. This indicates that the effect of the lookback period definition is minimal. The high SMRs observed in most databases during the first few years may suggest the inclusion of existing dementia cases for which no identifiable records were available. In contrast, the Finnish MEDALZ is the only register-based cohort with fully verified information on the incident diagnosis of Alzheimer's disease, and its SMRs were less than or equal to 1 during the first 2 years. Therefore, caution is advised when interpreting SMR values in the first 2–3 years.

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. A focus for policymakers is the economics of dementia. Against a background of population ageing and budget pressure, data that help to gauge service needs are important to support rational resources planning. Our data from eight developed jurisdictions showed that, while there is an overall increase in survival time as expected as healthcare advances, a trend observed within our study period as well as compared with earlier studies, countries vary greatly in this trend. For example, the increase in HRs between 2014 and 2018 in New Zealand—a country among the world's top healthcare systems—illustrated how service needs at different care levels (specialist care in this case) could change, possibly in relation to policies affecting care service configurations (e.g. task-shifting to primary care). Many governments across the world aim at developing national dementia strategies[3]. Policymakers need evidence to deal with complex issues including equity and affordability, with long-term commitment[50]. Although it is beyond the scope of our study to provide cost estimates, the survival data presented here, by country and by age group over 18 years, can be useful in for reference in supporting rational policy plans, for example in economic modelling analyses. While up-to-date local data are ideal, in countries where such data is not yet available, the evidence we present in different settings (jurisdictions with medical insurance claims, different age of incident diagnosis, hospitals) helps to fill the current evidence gaps.

Data availability

All databases used in this study contain sensitive clinical information and are not openly available to protect patient privacy. General data requests may be directed to the corresponding author (wongick@h-ku.hk). For access to specific databases, requests should be directed to the respective local partners. Please contact K.K.C.M. (kenneth.man@ucl.ac.uk) for the UK THIN data; B.H. (britta.haenisch@bfarm.de) for the German AOK data; A.M.T. (anna-maija.tolppanen@uef.fi) for the Finnish MEDALZ data; A.T.H. (AHsu@bruyere.org) for the Ontario (Canada) ICES data; A.H.Y.C. (a.chan@auckland.ac.nz) for the New Zealand data; J.Y.S. (shin.jy@skku.edu) for the NHIS-NSC data from South Korea; E.C.C.L. (edward_lai@email.ncku.edu.tw) for the Taiwan NHIRD data; and C.S.L.C. (cslchui@hku.hk) for the Hong Kong CDARS data. 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. The source data for Figs. 1 and 2 can be found in Supplementary Data 4 and 5, respectively. The numerical values underlying Fig. 3 are referenced in the main text and can be found in Supplementary Data 3.

Code availability

The code used for data analysis is available on GitHub (https://github.com/yvonne840429/NeuroGEN-Dementia-Survival)[34].

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Author contributions

H.Lu. and I.C.K.W. initiated the study. H.Lu., I.C.K.W., M.Ko., J.S.B., C.S.L.C., S.H., J.I., E.C.C.L., K.K.L., T.Y.S.L., K.K.C.M., A.T. and G.H.Y.W. collaboratively designed the study. H.Lu. prepared the common protocol, the syntax and the first draft of the manuscript. M.Ko., C.R. and C.B. commented, tested and revised the syntax. M.Ko., A.T. and S.H. analysed and cross-checked the Finnish data; A.T.H. and E.K. analysed the Canadian (Ontario) data; C.R., C.B. and B.H. analysed the German data;

K.K.C.M. and W.C.Y.L. led the UK data management; K.B. and A.H.Y.C. analysed the New Zealand data; E.C.C.L. and T.C.L. analysed the Taiwan data; J.Y.S. led the Korea team and J.Y.S., J.H.K. and H.Le. analysed the Korean data; H.Lu., C.S.L.C., K.K.L. and Y.C. analysed the Hong Kong data and summarised aggregated data from all study sites. J.S.B., M.Kn., G.H.Y.W., A.T., S.H. and I.C.K.W. 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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Additional information

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