Trends in all-cause mortality among people with diagnosed diabetes in high-income settings: a multicountry analysis of aggregate data

Dianna J Magliano,

Department of Diabetes and Population Health, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia

Lei Chen,

Department of Diabetes and Population Health, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia

Bendix Carstensen,

Clinical Epidemiology, Steno Diabetes Center Copenhagen, Gentofte, Denmark

Edward W Gregg,

Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK

Meda E Pavkov,

Division of Diabetes Translation, Centers for Diseases Control and Prevention, Atlanta, GA, USA

Agus Salim,

Department of Diabetes and Population Health, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, VIC, Australia

Linda J Andes,

Division of Diabetes Translation, Centers for Diseases Control and Prevention, Atlanta, GA, USA

Ran Balicer,

Clalit Research Institute, Clalit Health Services, Tel Aviv, Israel

Marta Baviera,

Correspondence to: Prof Dianna J Magliano, Baker Heart and Diabetes Institute, Melbourne, VIC 3004, Australia Dianna.magliano@baker.edu.au.

Laboratory of Cardiovascular Prevention, Mario Negri Institute for Pharmacological Research IRCCS, Milan, Italy

Juliana C N Chan,

Department of Medicine and Therapeutics, Li Ka Shing Institute of Health Sciences, Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong Special Administrative Region, China

Yiling J Cheng,

Division of Diabetes Translation, Centers for Diseases Control and Prevention, Atlanta, GA, USA

Helene Gardiner,

Centre for Surveillance and Applied Research, Public Health Agency of Canada, Ottawa, ON, Canada

Hanne L Gulseth,

Department for Chronic Diseases and Ageing, Norwegian Institute of Public Health, Oslo, Norway

Romualdas Gurevicius,

Center of Health Information, Institute of Hygiene, Vilnius, Lithuania; Faculty of Public Governance and Business, Mykolas Romeris University, Vilnius, Lithuania

Kyoung Hwa Ha,

Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, South Korea

György Jermendy,

3rd Medical Department, Bajcsy-Zsilinszky Hospital, Budapest, Hungary

Dae Jung Kim,

Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, South Korea

Zoltán Kiss,

2nd Department of Medicine and Nephrological Center, Medical Faculty, University of Pécs, Pécs, Hungary

Maya Leventer-Roberts,

Clalit Research Institute, Clalit Health Services, Tel Aviv, Israel; Departments of Pediatrics and Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Chun-Yi Lin,

General Clinical Research Center, Taipei Veterans General Hospital, Taipei, Taiwan

Andrea O Y Luk,

Department of Medicine and Therapeutics, Li Ka Shing Institute of Health Sciences, Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong Special Administrative Region, China

Stefan Ma,

Epidemiology and Disease Control Division, Public Health Group, Ministry of Health, Singapore

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Manel Mata-Cases,
CIBER of Diabetes and Associated Metabolic Diseases, Instituto de Salud Carlos III (ISCIII), Barcelona, Spain; Institut Català de la Salut, Unitat de Suport a la Recerca Barcelona Ciutat, Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol), Barcelona, Spain

Didac Mauricio,
CIBER of Diabetes and Associated Metabolic Diseases, Instituto de Salud Carlos III (ISCIII), Barcelona, Spain; Institut Català de la Salut, Unitat de Suport a la Recerca Barcelona Ciutat, Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol), Barcelona, Spain; Department of Endocrinology and Nutrition, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain

Gregory A Nichols,
Science Programs Department, Kaiser Permanente Center for Health Research, Portland, OR, USA

Santa Pildava,
Research and Health Statistics Department, Centre for Disease Prevention and Control, Riga, Latvia

Avi Porath,
Research Institute, Maccabi Healthcare Services, Tel Aviv, Israel; Faculty of Health, Ben Gurion University, Beer-Sheva, Israel

Stephanie H Read,
Usher Institute, University of Edinburgh, Edinburgh, UK

Cynthia Robitaille,
Centre for Surveillance and Applied Research, Public Health Agency of Canada, Ottawa, ON, Canada

Maria Carla Roncaglioni,
Laboratory of Cardiovascular Prevention, Mario Negri Institute for Pharmacological Research IRCCS, Milan, Italy

Paz Lopez-Doriga Ruiz,
Department for Chronic Diseases and Ageing, Norwegian Institute of Public Health, Oslo, Norway; Department of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo University Hospital, Oslo, Norway

Kang-Ling Wang,
General Clinical Research Center, Taipei Veterans General Hospital, Taipei, Taiwan

Sarah H Wild,
Usher Institute, University of Edinburgh, Edinburgh, UK

Naama Yekutiel,
Research Institute, Maccabi Healthcare Services, Tel Aviv, Israel

Jonathan E Shaw

Department of Diabetes and Population Health, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; School of Life Sciences, Latrobe University, Melbourne, VIC, Australia

Summary

Background—Population-level trends in mortality among people with diabetes are inadequately described. We aimed to examine the magnitude and trends in excess all-cause mortality in people with diabetes.

Methods—In this retrospective, multicountry analysis, we collected aggregate data from 19 data sources in 16 high-income countries or jurisdictions (in six data sources in Asia, eight in Europe, one from Australia, and four from North America) for the period from Jan 1, 1995, to Dec 31, 2016, (or a subset of this period) on all-cause mortality in people with diagnosed total or type 2 diabetes. We collected data from administrative sources, health insurance records, registries, and a health survey. We estimated excess mortality using the standardised mortality ratio (SMR).

Findings—In our dataset, there were approximately 21 million deaths during 0·5 billion person-years of follow-up among people with diagnosed diabetes. 17 of 19 data sources showed decreases in the age-standardised and sex-standardised mortality in people with diabetes, among which the annual percentage change in mortality ranged from –0·5% (95% CI –0·7 to –0·3) in Hungary to –4·2% (–4·3 to –4·1) in Hong Kong. The largest decreases in mortality were observed in east and southeast Asia, with a change of –4·2% (95% CI –4·3 to –4·1) in Hong Kong, –4·0% (–4·8 to –3·2) in South Korea, –3·5% (–4·0 to –3·0) in Taiwan, and –3·6% (–4·2 to –2·9) in Singapore. The annual estimated change in SMR between people with and without diabetes ranged from –3·0% (95% CI –3·0 to –2·9; US Medicare) to 1·6% (1·4 to 1·7; Lombardy, Italy). Among the 17 data sources with decreasing mortality among people with diabetes, we found a significant SMR increase in five data sources, no significant SMR change in four data sources, and a significant SMR decrease in eight data sources.

Interpretation—All-cause mortality in diabetes has decreased in most of the high-income countries we assessed. In eight of 19 data sources analysed, mortality decreased more rapidly in people with diabetes than in those without diabetes. Further longevity gains will require continued improvement in prevention and management of diabetes.

Funding—US Centers for Disease Control and Prevention, Diabetes Australia Research Program, and Victoria State Government Operational Infrastructure Support Program

Editorial note:

the *Lancet* Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Introduction

Mortality among people with diabetes, and how it changes over time, is an important indicator of quality of and access to health care.[1] Reports examining all-cause mortality among people with diabetes have shown decreasing rates in some countries for the past decade,[2] with similar trends observed in general populations, but whether these trends differ

by age and sex is not known.[3] Data from these studies are also complicated by differences in how mortality analyses are conducted. The most robust method to examine mortality draws both the numerator and the denominator from those with diabetes. However, many studies use a general population denominator in the calculation of mortality and identify deaths due to diabetes using diabetes-specific International Classification of Disease (ICD) codes on death certificates,[4] rather than ascertaining mortality among people with verified diabetes status.

To address these limitations, we previously did a systematic review of the scientific literature and found that decreasing mortality was reported in nearly 80% of populations of predominantly European descent from 2000 to 2016, and that, in over half the populations studied, the annual reduction in mortality was greater than or similar to that of people without diabetes.[3] These findings were limited by differences in study periods, definitions of age and sex strata, and there was a paucity of data on younger age groups and non-European populations. Furthermore, we were not able to provide comparisons with mortality trends in the general population.

One substantial limitation of systematic reviews is publication bias and inappropriate influence of studies with notable findings. Consequently, we established the first ever, multicountry assembly of individual-level data to investigate diabetes incidence and all-cause mortality in this population.[5] With this resource, we aimed to examine the magnitude and trends in excess all-cause mortality related to diabetes.

Methods

Study design and data sources

In this multicountry analysis, data custodians (centres or institutions responsible for the data) provided us with aggregate data on all-cause mortality in people with diagnosed total (type 1 and type 2 diabetes) or type 2 diabetes (hereafter referred to as diabetes) from an international diabetes consortium across 16 high-income countries or jurisdictions.[5] The details of the consortium database have been described elsewhere.[5] The consortium includes 24 data sources, among which 19 had adequate mortality data for the current analysis. We collected aggregate data from 19 data sources from these 16 jurisdictions (with one data source for each of Australia, Canada, Denmark, Hong Kong, Hungary, Italy [Lombardy], Latvia, Lithuania, Norway, Scotland, Singapore, South Korea, Spain, and Taiwan; two for Israel; and three for the USA) on population size, counts of prevalent diabetes, death counts, and person-years of follow-up in people with and without diagnosed diabetes by sex and age group (<20, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 79–80, 80–84, and 85 years) for each individual calendar year between Jan 1, 1995, and Dec 31, 2016 (or a subset of this period).

The Human Ethics Committee of Alfred Health, Melbourne, VIC, Australia approved this study. Only one data source (US National Health Interview Survey [NHIS]) required individual participant consent for inclusion. For all other data sources, data were collected as part of routine clinical care and individual data were only visible to data custodians.

Assessment of diabetes status and vital status

Diabetes status and, where available, type of diabetes was determined by data custodians using various definitions, including blood glucose concentration, HbA_{1c}, linkage to medication or reimbursement registries, clinical diagnosis records provided by physicians, self-report in health surveys, or algorithms based on several of these elements. Type of diabetes was determined using clinical diagnosis (by ICD codes or health-care professional diagnosis) or algorithms using age at diabetes onset and age at starting insulin treatment. Death in people with diabetes was determined via linkage to national death registries or national population registers.

Quality of the included data

Two authors (DJM and LC) independently assessed risk of bias using a modified Newcastle-Ottawa Scale (NOS) (appendix pp 1-4).[6] Disagreements were resolved by discussion with a third author (JES). Risk of bias was classified as high (score 0–5), medium (6–7), or low (8–9).

Statistical analysis

We modelled mortality rates, using age (defined as the midpoint of each age group) and calendar time as continuous variables, and calendar time interval (1 year) separately by sex for each data source. We used Poisson regression for multiplicative models with death as the outcome and log(person-years) as the offset. We fitted age-period-cohort models using cubic splines for the effects. We placed knots for the splines at evenly spaced quantiles of the marginal distribution of the event times for each of the three variables in the model (age, period [calendar time], and cohort [period minus age]). For each data source and sex, we plotted the estimated mortality rates by age for a select set of dates 4 years apart, spanning the observation period, as well as mortality rates by period for five ages (40, 50, 60, 70, and 80 years). We used the estimated rates from the age-period-cohort models for each data source to calculate age-standardised mortality rates using direct standardisation (using the total diabetes population formed by pooling the consortium data) by calendar time, separately by sex and jointly. We also fitted a set of age-period models with smooth age effects but a linear effect of calendar time for each data source, providing an overall summary of the annual changes in mortality rates by sex for each data source. We calculated 95% CIs using Wald CIs (back transformed from log rates within 1·96 SE above and below the point estimate). We calculated the standardised mortality ratio (SMR) by calculating the ratio of the observed number of deaths in the diabetes population to the expected number if mortality was the same as in the population without diabetes. An SMR of 1 implies identical mortality in people with and without diabetes.

We modelled the SMR similarly to how we modelled the mortality rates, using Poisson regression for multiplicative models with observed number of deaths as the outcome and the log(expected number of deaths) as the offset. We modelled SMR by fitting models with a linear effect of calendar time for each data source, providing an overall summary of the annual changes in SMR by sex for each data source. A description of statistical models used is in the appendix (pp 5-7).

We used Stata software (version 15.1) for data management and R software (version 3.6.3) for statistical analyses and graphics.

Role of the funding source

Results

Mortality data in people with diagnosed diabetes were available from 19 data sources from 16 jurisdictions (table). Three of the data sources were from east Asia (Hong Kong, South Korea, and Taiwan) and one was from southeast Asia (Singapore). Data were included from a variety of sources: nine (47%) of 19 data sources were administrative data, four (21%) were registries, five (26%) were health insurance databases, and one (5%) was a nationally representative survey. 12 (63%) data sources included the whole population with diabetes in the relevant country or jurisdiction, three (16%) were nationally representative samples (South Korea, Taiwan, USA [NHIS]), and the remaining four (21%) included two health insurers from Israel, which collectively covered 70% of the national population, a US health insurer (Kaiser Permanente Northwest [KPNW]) and the US Medicare (table; appendix pp 2-4).

Diabetes status was defined by algorithms incorporating at least two different criteria in nine (47%) data sources, clinical diagnosis in seven (37%), diabetes medication use in two (11%), and by self-report of a health-care provider diagnosis in one (5%). Ten (53%) data sources provided death counts specifically in people with type 2 diabetes while the nine (47%) other data sources had counts in people with all types of diabetes. Quality scores ranged from 5 to 9, with a median of 7 (IQR 6–8; appendix pp 2-4). In our dataset, there were approximately 21 million deaths during 0·5 billion person-years of follow-up in people with diabetes (appendix pp 8-10, 17).

Age-standardised and sex-standardised all-cause mortality rates in people with diabetes ranged from 13·3 deaths per 1000 person-years in Spain in 2011 and 2012 to 42·1 deaths per 1000 person-years in Latvia in 2000 (figure 1; appendix pp 11-13). During the period for which data were available, all-cause mortality in people with diabetes decreased in all data sources except Spain and Norway (figure 1; appendix p 14). Trends in age-standardised all-cause mortality did not differ substantially by sex (appendix pp 15-16, 18). In the data sources with decreasing mortality, the annual estimated change in all-cause mortality among people with diabetes over the whole study period ranged from −0·5% (95% CI −0·7 to −0·3) for Hungary to −4·2% (−4·3 to −4·1) for Hong Kong (figure 2; appendix p 14). For Spain, annual percentage change in all-cause mortality in those with diabetes increased in both men and women, whereas for Norway, the annual percentage change decreased in men but was stable in women (appendix pp 15-16, 22). All-cause mortality in people with diabetes

decreased more rapidly in countries in east and southeast Asia. The four jurisdictions in these regions had the four largest reductions in mortality, with a change of −4·2% (95% CI −4·3 to −4·1) in Hong Kong, −4·0% (−4·8 to −3·2) in South Korea, −3·5% (−4·0 to −3·0) in Taiwan, and −3·6% (−4·2 to −2·9) in Singapore; and Hong Kong and Singapore were also among those jurisdictions with the largest decreases in SMR (figure 2).

Age-specific and calendar time-specific all-cause mortality by sex are shown for each data source in the appendix (pp 25-43). Among the 17 data sources with decreasing mortality in people with diabetes, 16 had decreasing rates at most ages in both sexes. In Spain, all-cause mortality in people with diabetes increased for all age and sex groups, whereas mortality was relatively stable at all ages for women and slightly decreasing in men in Norway. In some countries, the rate of decrease in all-cause mortality appears to have been greater at younger ages than at older ages (eg, Italy, Lithuania, and South Korea; appendix pp 63-64).

Over the study period, the SMRs between people with and without diabetes decreased in nine (47%) of 19 data sources, were stable in four, and increased in six data sources (figure 2; appendix p 14). The annual estimated change in SMR between people with and without diabetes ranged from −3·0% (95% CI −3·0 to −2·9; US Medicare) to 1·6% (1·4 to 1·7; Lombardy, Italy; appendix p 14).

Among the 17 data sources with decreasing mortality among people with diabetes, we found a significant SMR increase in five (29%), no significant SMR change in four (24%), and a significant SMR decrease in eight (47%; figure 2; appendix pp 14, 21). In Spain, mortality among people with diabetes increased annually (1·1% [95% CI 0·9 to 1·3]), but at a slower rate than in those without diabetes (1·9% [1·8 to 2·0]; appendix p 14). Trends in the SMRs were broadly similar in men and women (appendix pp 15-16, 20).

In most data sources, women had a higher SMR than did men at the five selected ages (appendix pp 44-62). The SMRs were highest in the youngest ages in all countries except for Australia (women) and Israel (MHS), both of which had the highest SMR at age 50 years. The trends in SMR over calendar time were similar across ages for most countries. Denmark had a slight decrease in SMR at older ages, but stable SMRs at younger ages (appendix p 46), Hungary had an increase at younger ages and stability at older ages (appendix p 48), whereas South Korea and Taiwan both had a decrease in SMRs at younger ages (<50 years) and a slight increase at older ages (appendix pp 57, 59).

Discussion

Among people with diabetes from 19 data sources from 16 high-income countries or jurisdictions, we found that absolute mortality decreased across all available years in all but two countries (Spain and Norway) over the study period of 1995 to 2016. Spain showed increases in mortality and in Norway there was a non-significant decrease in mortality. The greatest decreases in mortality over the study period were among people with diabetes in east Asia (Hong Kong, South Korea, and Taiwan) and southeast Asia (Singapore), among which Hong Kong and Singapore also had significant reductions in SMR. Annual decreases in mortality among those with diabetes were greater or similar to those without diabetes in

12 of 17 data sources with an overall trend of decreasing mortality, including all of the data sources from east and southeast Asia.

These findings are consistent with our previous systematic review,[3] in which we found decreasing mortality in nearly 80% of predominantly European populations with diabetes from 2000 to 2016. In that analysis, nearly 60% of the populations with diabetes we assessed had greater or similar annual reductions in mortality as people without diabetes.[3]

We found substantial variation in mortality between populations with diabetes, although much of this reflects similar levels of variation in the general populations (data not shown). For instance, in Catalonia, Spain, mortality in people with diabetes increased from approximately 2012 to 2016; however, mortality increased more rapidly in populations without diabetes (in both Catalonia and Spain).[7] Increasing mortality in Spain has been attributed to increased influenza activity during this period and restrictions in the health-care system since the global financial crisis in 2008.[8] In Norway, mortality decreased, but this was not significant, which might be due to the small number of years of data from this country.

The reduction in mortality in people with diabetes surpassed or was similar to the reduction in the population without diabetes in two-thirds of data sources examined. The narrowing of the gap in mortality between people with and without diabetes suggests that health care in diabetes continues to improve over time, at least in the high-income countries investigated here. The absence of this narrowing of the mortality difference in some countries observed here warrants further research.

Although our findings are consistent with several country-specific publications of all-cause mortality in people with diabetes, such as those from Scotland,[9] the USA,[10] the UK,[11] and Denmark,[12] the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) reported an increase in global death rates due to diabetes from 1990 to 2015.[4] However, GBD uses the total national population as the denominator for estimating mortality, and therefore does not account for increases in the prevalence of diabetes.

An unexpected finding from our study is that the greatest decreases in mortality in people with diabetes were seen in east and southeast Asia. Additionally, in these regions, reductions in mortality in people with diabetes were greater than or similar to changes in mortality in people without diabetes. Possible reasons for these observations are that these jurisdictions have had stronger improvements in models of care for those with diabetes than other jurisdictions, or that each jurisdiction has improved their health-care system, which might have led to improved management of risk factors. A study in Hong Kong showed improvements in metabolic control in patients with diabetes.[13] Furthermore, in Hong Kong, universal health coverage was introduced in 1993, and major changes have been made to integrate diabetes management into health care, expanding services across primary, secondary, and tertiary care. These services included regular and structured risk assessment and education programmes delivered by non-physician staff. Systematic data collection was also implemented in Hong Kong, which helped the government identify trends and unmet needs to inform decision making.[14] In 2016, the Singapore government established the

National Diabetes Prevention and Care Taskforce, which includes a government and primary care network collaboration providing increased services to people with diabetes and support for primary care;[15] similar programmes exist in Taiwan.[16,17] Whether these programmes have been more effective than programmes and policies in other countries is unclear. The high prevalence of diabetes in high-income east and southeast Asian countries and the high burden of renal complications of diabetes in Asia might have led to more concerted efforts towards improving diabetes management in these regions than in other regions.[18] Increased screening for diabetes in these countries could also lead to apparent reductions in mortality because of an increase in the number of individuals with lower mortality being included in the population with diabetes. However, since the incidence of diabetes is decreasing in three of the Asian jurisdictions in which we observed rapid decreases in mortality (Hong Kong, South Korea, and Taiwan),[5] this explanation seems unlikely.

Improvements in survival were similar across all ages, by contrast with the findings of our previous systematic review on mortality trends.[3] US national data also showed significant decreases in mortality in older people and no decrease in mortality among people aged 20–44 years from 1988–94 to 2010–15.[10] Similarly, in the Hong Kong Diabetes Surveillance Database, all-cause death rates decreased by approximately 50% in people with diabetes between 2001 and 2016, except for those aged 20–44 years in which they remained stable.[19]

Several factors could explain the decreasing mortality we observed in people with diabetes. Population-level health promotion on tobacco cessation and lifestyle modification have led to reductions in levels of some risk factors, including smoking,[20] blood pressure,[21] and cholesterol,[22] which might have translated into improved mortality. Furthermore, the use of antihypertensive[23] and lipid-lowering medications[24] for the prevention of cardiovascular disease events among high-risk people has increased in the past few decades. Hypertension, hypercholesterolaemia, and hyperglycaemia have been managed more aggressively in recent decades,[25-27] and might have contributed to reductions in the rates of diabetes-related complications[10] and, ultimately, improved survival. Finally, substantial advances have been made in medical interventions and care for individuals with acute cardiovascular disease events and chronic diseases.[28] There have also been major changes in the way health is managed in some countries that could contribute to decreasing mortality for people with and without diabetes.[14] Changing diagnostic criteria over the past two decades, particularly lowering the diagnostic threshold for fasting glucose, might have identified people at an earlier stage in the natural disease course of diabetes who have an inherently lower risk of mortality. However, the reduction in the fasting glucose diagnostic criterion first recommended in 1997[29] and the more recent shift towards use of HbA_{1c} as a diagnostic test might have partially offset this by leading to diagnoses later in the disease course.[30] Irrespective of diagnostic criteria, increases in screening activity might also lead to more early diagnoses of diabetes, again resulting in decreasing mortality due to lead-time bias. Also, earlier diagnosis of diabetes, with such changes particularly occurring in the late 1990s and early 2000s, might have facilitated earlier use of interventions with long-term benefits for survival.

Our study has several strengths. Most data sources we used are large and population based, enabling stratification by age and sex. Furthermore, we used a standardised approach for

collection and assembly of these data. We also did a rigorous assessment of quality of these data sources and showed most sources were of good quality. Additionally, among the centres that collected and provided the 19 data sources, reports validating the approaches to diabetes diagnosis are available for ten (53%) sources, eight of which have been published.[31-38] Sensitivities and specificities were over 85% for all but one data source, which had a sensitivity of 75%.[38] A further two (11%) centres are registries of patients with pharmacologically treated type 2 diabetes, and so are likely to be highly specific for people with diabetes. Finally, the a priori decision to report on all data sources that met our criteria restricts the effect of publication bias that can arise from the perceived interest in results from a single source. Publication bias refers to the propensity to publish positive rather than non-positive findings.[39] Systematic reviews, especially those that do not examine the grey literature, are particularly prone to such bias. Our inclusion of datasets without knowledge of their mortality trends, has, at least in part, overcome this bias.

Our study also has several limitations. First, we were unable to obtain data on diabetes treatment patterns and whether changes in parameters used to assess quality of diabetes care (ie, HbA_{1c} levels, blood pressure, and LDL cholesterol levels) were greater in the data sources with larger decreases in mortality among those with diabetes than in the other data sources. Second, methods of diagnosing diabetes varied across the data sources and could even be subject to variation over time within a data source. Although each data custodian applied the same diagnostic criteria to their data over time, this approach does not rule out the possibility of changes in coding and clinical practice that might affect diagnostic practice. Also, our data sources reported only on clinically diagnosed diabetes and so are susceptible to influences from changes in diagnostic behaviour. Third, although we report on diabetes as a whole, our findings mainly represent type 2 diabetes because the prevalence of type 2 diabetes is much higher than that of type 1 diabetes. Fourth, we were not able to obtain data on the age at diabetes diagnosis and thus could not examine the association between mortality with duration of diabetes. Fifth, not all of the data sources can be confidently extrapolated to the full national population of people with diabetes because some of them are geographically restricted and some might have socioeconomic biases (eg, employment related to health insurance). Sixth, data were only available from high-income countries, and mortality trends might be different in low-income and middle-income countries. Interestingly, data from the PURE study, which began in 2003, show that mortality in people with diabetes from middle-income countries has also decreased, whereas mortality in low-income countries is unchanged.[40]

In summary, we found that in most of the high-income countries that we assessed, mortality among people with diabetes has decreased, with jurisdictions in east and southeast Asia showing the greatest decreases. The gap in mortality between people with and without diabetes is narrowing in the majority of data sources examined. Our findings highlight the progress in managing diabetes over the past couple of decades and indicate that further longevity gains and reductions in disparities will require continued improvement in prevention and management of diabetes. Finally, this international analysis emphasises the value of systematic data collection in driving policies to improve detection, diagnosis, and management of diabetes, and in identifying trends and unmet needs for continuing improvement.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Data sharing

Aggregated data might be made available upon reasonable request to the corresponding author. There might be limitations on what the data can be used for, subject to approval from the data custodians.

References

1. Chan JCN, Lim LL, Wareham NJ, et al. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. Lancet 2021; 396: 2019–82. [PubMed: 33189186]

2. Sacre JW, Harding JL, Shaw JE, Magliano DJ. Declining mortality in older people with type 2 diabetes masks rising excess risks at younger ages: a population-based study of all-cause and cause-specific mortality over 13 years. Int J Epidemiol 2021; 50: 1362–72. [PubMed: 33462587]

3. Chen L, Islam RM, Wang J, et al. A systematic review of trends in all-cause mortality among people with diabetes. Diabetologia 2020; 63: 1718–35. [PubMed: 32632526]

4. Lin X, Xu Y, Pan X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep 2020; 10: 14790. [PubMed: 32901098]

5. Magliano DJ, Chen L, Islam RM, et al. Trends in the incidence of diagnosed diabetes: a multicountry analysis of aggregate data from 22 million diagnoses in high-income and middle-income settings. Lancet Diabetes Endocrinol 2021; 9: 203–11. [PubMed: 33636102]

6. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2014. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed April 11, 2019).

7. Statistical Institute of Catalonia (IDESCAT). Annual indicators: death and crude death rates. 2021. https://www.idescat.cat/indicators/?id=anuals&n=10344&lang=en (accessed Aug 20, 2021).

8. Bosch X, Moreno P, López-Soto A. The painful effects of the financial crisis on Spanish health care. Int J Health Serv 2014; 44: 25–51. [PubMed: 24684083]

9. Read SH, Kerssens JJ, McAllister DA, et al. Trends in type 2 diabetes incidence and mortality in Scotland between 2004 and 2013. Diabetologia 2016; 59: 2106–13. [PubMed: 27465219]

10. Gregg EW, Cheng YJ, Srinivasan M, et al. Trends in cause-specific mortality among adults with and without diagnosed diabetes in the USA: an epidemiological analysis of linked national survey and vital statistics data. Lancet 2018; 391: 2430–40. [PubMed: 29784146]

11. Pearson-Stuttard J, Bennett J, Cheng YJ, et al. Trends in predominant causes of death in individuals with and without diabetes in England from 2001 to 2018: an epidemiological analysis of linked primary care records. Lancet Diabetes Endocrinol 2021; 9: 165–73. [PubMed: 33549162]

12. Carstensen B, Rønn PF, Jørgensen ME. Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996–2016. BMJ Open Diabetes Res Care 2020; 8: e001071.

13. Luk AOY, Hui EMT, Sin MC, et al. Declining trends of cardiovascular-renal complications and mortality in type 2 diabetes: the Hong Kong Diabetes Database. Diabetes Care 2017; 40: 928–35 [PubMed: 28490423]

14. The Government of the Hong Kong Special Administrative Region's Education Bureau. 10: healthcare system. Health management and social care (secondary 4– 6). 2016. www.edb.gov.hk/attachment/en/curriculum-development/kla/technology-edu/resources/hmsc/HMSC_Booklet10_E_p52.pdf (accessed Aug 11, 2021).

15. Singapore Ministry of Health. Speech by Minister for Health, Mr Gan Kim Yong, at the MOH Committee of Supply Debate 2016. 2016. https://www.moh.gov.sg/news-highlights/details/speech-by-minister-for-health-mr-gan-kim-yong-at-the-moh-committee-of-supply-debate-2016 (accessed Oct 1, 2021).

16. Kim H, Cheng S-H. Assessing quality of primary diabetes care in South Korea and Taiwan using avoidable hospitalizations. Health Policy 2018; 122: 1222–31. [PubMed: 30274936]

17. Chang JC-J, Hwang S-J, Chen T-J, et al. Team-based care improves quality of diabetes care - Family Practice Integrated Care Project in Taiwan. BMC Fam Pract 2020; 21: 209. [PubMed: 33059587]

18. Ma RCW, Chan JCN. Type 2 diabetes in east Asians: similarities and differences with populations in Europe and the United States. Ann N Y Acad Sci 2013; 1281: 64–91. [PubMed: 23551121]

19. Wu H, Lau ESH, Ma RCW, et al. Secular trends in all-cause and cause-specific mortality rates in people with diabetes in Hong Kong, 2001-2016: a retrospective cohort study. Diabetologia 2020; 63: 757–66. [PubMed: 31942668]

20. Hopkins DP, Razi S, Leeks KD, Priya Kalra G, Chattopadhyay SK, Soler RE. Smokefree policies to reduce tobacco use. A systematic review. Am J Prev Med 2010; 38 (suppl 2): S275–89. [PubMed: 20117612]

21. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension 2006; 47: 296–308. [PubMed: 16434724]

22. Uusitalo U, Feskens EJ, Tuomilehto J, et al. Fall in total cholesterol concentration over five years in association with changes in fatty acid composition of cooking oil in Mauritius: cross sectional survey. BMJ 1996; 313: 1044–46. [PubMed: 8898594]

23. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2008. JAMA 2010; 303: 2043–50. [PubMed: 20501926]

24. Kuklina EV, Yoon PW, Keenan NL. Trends in high levels of low-density lipoprotein cholesterol in the United States, 1999–2006. JAMA 2009; 302: 2104–10. [PubMed: 19920234]

25. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 2004; 364: 685–96. [PubMed: 15325833]

26. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998; 317: 703–13. [PubMed: 9732337]

27. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008; 359: 1577–89. [PubMed: 18784090]

28. Mensah GA, Wei GS, Sorlie PD, et al. Decline in cardiovascular mortality: possible causes and implications. Circ Res 2017; 120: 366–80. [PubMed: 28104770]

29. No authors listed. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997; 20: 1183–97. [PubMed: 9203460]

30. Malkani S, Mordes JP. Implications of using hemoglobin A1C for diagnosing diabetes mellitus. Am J Med 2011; 124: 395–401. [PubMed: 21531226]

31. Anwar H, Fischbacher CM, Leese GP, Lindsay RS, McKnight JA, Wild SH. Assessment of the under-reporting of diabetes in hospital admission data: a study from the Scottish Diabetes Research Network Epidemiology Group. Diabet Med 2011; 28: 1514–19. [PubMed: 21883441]

32. No authors listed. Design and estimation for the National Health Interview Survey, 1995–2004. Vital Health Stat 2000; 2: 1–31.

33. Hux JE, Ivis F, Flintoft V, Bica A. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. Diabetes Care 2002; 25: 512–16. [PubMed: 11874939]

34. Kristensen JK, Drivsholm TB, Carstensen B, Steding-Jensen M, Green A. Validation of methods to identify known diabetes on the basis of health registers. Ugeskr Laeger 2007; 169: 1687–92 (in Danish). [PubMed: 17532878]

35. Mata-Cases M, Mauricio D, Real J, Bolibar B, Franch-Nadal J. Is diabetes mellitus correctly registered and classified in primary care? A population-based study in Catalonia, Spain. Endocrinol Nutr 2016; 63: 440–48. [PubMed: 27613079]

36. Nichols GA, Desai J, Elston Lafata J, et al. Construction of a multisite DataLink using electronic health records for the identification, surveillance, prevention, and management of diabetes mellitus: the SUPREME-DM project. Prev Chronic Dis 2012; 9: E110. [PubMed: 22677160]

37. Sung SF, Hsieh CY, Lin HJ, Chen YW, Yang YH, Li CY. Validation of algorithms to identify stroke risk factors in patients with acute ischemic stroke, transient ischemic attack, or intracerebral hemorrhage in an administrative claims database. Int J Cardiol 2016; 215: 277–82. [PubMed: 27128546]

38. Hebert PL, Geiss LS, Tierney EF, Engelgau MM, Yawn BP, McBean AM. Identifying persons with diabetes using Medicare claims data. Am J Med Qual 1999; 14: 270–77 [PubMed: 10624032]

39. Duyx B, Urlings MJE, Swaen GMH, Bouter LM, Zeegers MP. Scientific citations favor positive results: a systematic review and meta-analysis. J Clin Epidemiol 2017; 88: 92–101. [PubMed: 28603008]

40. Anjana RM, Mohan V, Rangarajan S, et al. Contrasting associations between diabetes and cardiovascular mortality rates in low-, middle-, and high-income countries: cohort study data from 143 567 individuals in 21 countries in the PURE Study. Diabetes Care 2020; 43: 3094–101. [PubMed: 33060076]

Research in context

Evidence before this study

We previously published a systematic review of studies published between Jan 1, 1980, to Dec 31, 2019, on trends in all-cause mortality in people with diabetes. We found that decreasing mortality was reported in nearly 80% of populations of predominantly European descent from 2000 to 2016, and nearly 60% of the reported populations with diabetes had a greater or similar annual reduction in mortality compared with populations without diabetes. However, our previous systematic review was limited by different study periods, different age and sex structures of the populations studied, and a paucity of data on young age groups and non-White populations.

Added value of this study

To our knowledge, this is the first multicountry, unit-record (ie, individual personal data) analysis of trends in all-cause mortality in people with diagnosed total (type 1 and type 2 diabetes) or type 2 diabetes. We found that all-cause mortality in people with diabetes has decreased in the majority of high-income countries we assessed. In nearly 50% of the datasets analysed, mortality decreased more rapidly in people with diabetes than in those without diabetes.

Implications of all the available evidence

Maintaining and continual improvement of cardiometabolic management in diabetes is crucial for achieving ongoing reductions in mortality in people with this condition. Notably, little published data from low-income and middle-income countries are available, where trends of all-cause mortality among those with diabetes might be different. Establishing and maintaining the infrastructure for such data collection should be a priority for all countries.
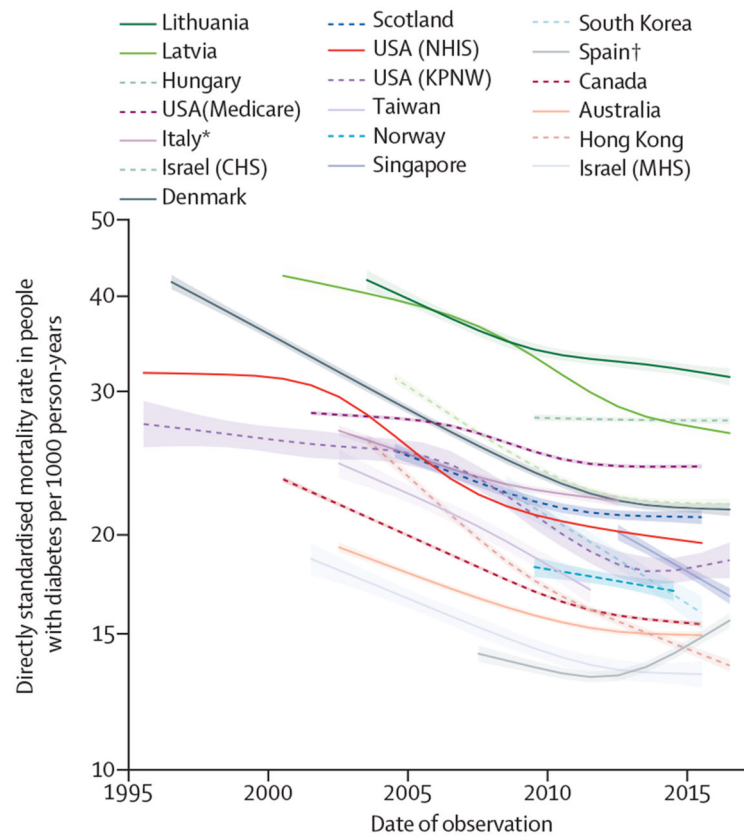
Figure 1: Age-standardised and sex-standardised all-cause mortality among people with diagnosed diabetes per 1000 person-years

The standard population was derived from a pooled study population with diagnosed diabetes, with equal weights for men and women. Standardisation is based on annual age-specific mortality from age-period-cohort models fitted separately for each data source and sex. Shaded areas show 95% CIs. CHS=Clalit Health Services. KPNW=Kaiser Permanente Northwest. MHS=Maccabi Healthcare Services. NHIS=National Health Interview Survey. *Data are from Lombardy, Italy. †Data are from Catalonia, Spain.
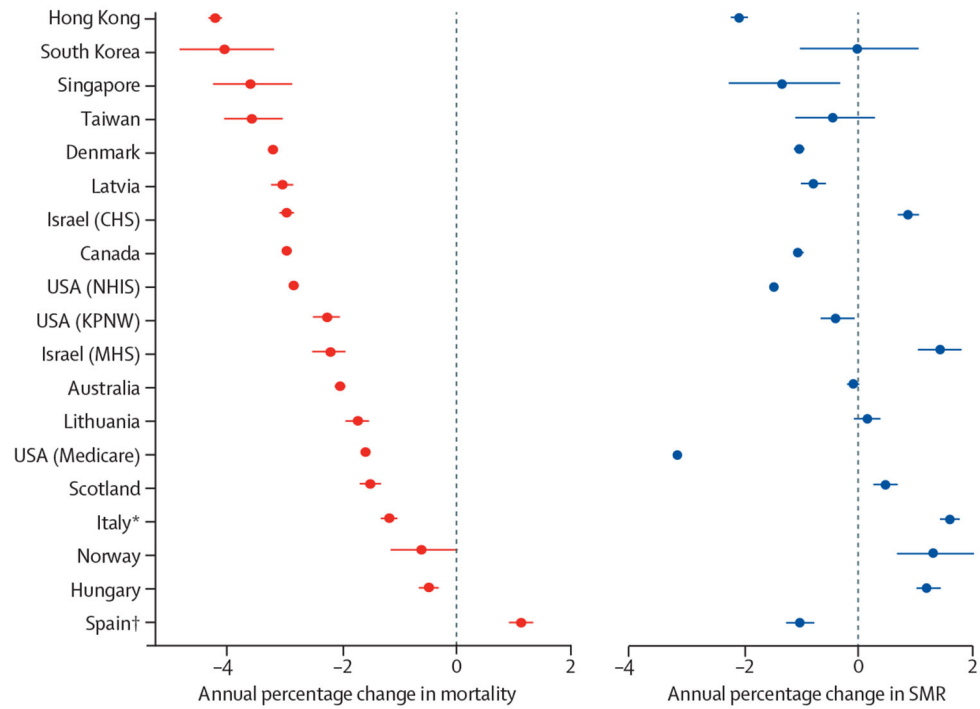
Figure 2: Estimated annual percentage changes in all-cause mortality in people with diagnosed diabetes and estimated annual percentage changes in SMR

Datapoints are estimated percentage changes, with error bars showing 95% CIs. MHS=Maccabi Healthcare Services. NHIS=National Health Interview Survey. SMR=standardised mortality ratio. CHS=Clalit Health Services. KPNW=Kaiser Permanente Northwest. *Data are from Lombardy, Italy. †Data are from Catalonia, Spain.

Table:

Summary characteristics of the 19 data sources and their data

	Origin of data	Type of data	Years analysed for mortality	Age range (years)	Person-years in people with diabetes (in thousands)	Number of deaths in people with diabetes	Diabetes status definition	Diabetes type
Australia	National Diabetes Services Scheme	Registry	2002–15	0	10 222	292 628	Clinical diagnosis	Type 2 diabetes
Canada	Canadian Chronic Disease Surveillance System*	Administrative	2000–15	1	27 111	789 710	Algorithm	All diabetes
Denmark	National Register, prescription database, health insurance database, diabetes quality database, and eye screening database	Registry	1996–2016	0	3517	158 749	Algorithm	Type 2 diabetes
Hong Kong	Hong Kong Hospital Authority (Hong Kong Diabetes Surveillance Database)	Administrative	2003–16	0	5375	171 749	Algorithm	All diabetes
Hungary	National Institute of Health Insurance Fund Management database	Administrative	2009–16	0	5906	246 429	Hypoglycaemic medications	Type 2 diabetes
Israel	Clalit Health Services	Health insurance	2004–16	0	4252	172 182	Algorithm	All diabetes
Israel	Maccabi Healthcare Services	Health insurance	2001–15	0	1160	26 033	Algorithm	Type 2 diabetes
Lombardy, Italy	Administrative health databases	Administrative	2002–12	0	3962	182 439	Algorithm	All diabetes
Latvia	Latvian Diabetes Registry	Registry	2000–16	0	986	47 446	Clinical diagnosis (ICD-10)	Type 2 diabetes
Lithuania	National Compulsory Health Insurance Fund Information System	Administrative	2003–16	0	1274	58 625	Clinical diagnosis (ICD-10)	All diabetes
Norway	Norwegian Registry, Primary Care Database, and Norwegian Prescription Database	Administrative	2009–14	0	1116	39 452	Clinical diagnosis (ICD-10, ICPC-2)	Type 2 diabetes
Scotland	Scottish Care Information-Diabetes database	Registry	2004–15	0	2393	95 285	Clinical diagnosis (Read codes)	Type 2 diabetes
Singapore	National administrative data held by the Ministry of Health of Singapore	Administrative	2012–16	0	1436	37 959	Clinical diagnosis (ICD-10)	All diabetes
South Korea	National Health Insurance Service – National Sample cohort	Health insurance	2008–15	0	414	10 431	Hypoglycaemic medications	All diabetes
Catalonia, Spain	Information System for the Development of Research in Primary Care	Administrative	2007–16	0	3265	114 294	Clinical diagnosis (ICD-10)	Type 2 diabetes
Taiwan	National Health Insurance Research Database (LHID 2000)	Health insurance	2002–11	0	656	17 630	Algorithm	Type 2 diabetes
USA	KPNW (Integrated managed care consortium)	Health Insurance	1995–2016	0	589	18 011	Algorithm	Type 2 diabetes
USA	Medicare (claims data for beneficiaries)	Administrative	2001–15	68	83 231	6 979 017	Algorithm	All diabetes
USA	National Health Interview Survey†	Survey	1995–2015	20	325 319	11 463 555	Self-report of health-care provider	All diabetes

ICD-10=International Classification of Diseases, 10th edition. ICPC-2=International Classification of Primary Care, second version. KPNW=Kaiser Permanente Northwest. LHID 2000=Longitudinal Health Insurance Database randomly sampled from the registered beneficiaries in the year 2000. *This Canadian data source excluded data from Yukon Territory, Saskatchewan, and Quebec; data from Nova Scotia excluded people younger than 20 years. †The weighted numbers of death were generated from a sample of 226 698 people aged 20 years in 1995–2015.