



Secular trends in all-cause and cause-specific mortality rates in people with diabetes in Hong Kong, 2001–2016: a retrospective cohort study

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Abstract

Aims/hypothesis The aim of the study was to describe trends in all-cause and cause-specific mortality rates in Hong Kong Chinese people with diabetes from 2001 to 2016.

Methods The Hong Kong Diabetes Surveillance Database (HKDSD) is a territory-wide diabetes cohort identified from the Hong Kong Hospital Authority electronic medical record system. Deaths between 2001 and 2016 were identified from linkage to the Hong Kong Death Registry. We used Joinpoint regression analysis to describe mortality patterns among people with diabetes by age and sex, and standardised mortality ratios (SMRs) to compare all-cause mortality rates in people with and without diabetes.

Results Between 2001 and 2016, a total of 390,071 men and 380,007 women aged 20 years or older with diabetes were included in the HKDSD. There were 96,645 deaths among men and 88,437 deaths among women. Mortality rates for all-cause, cardiovascular disease and cancer among people with diabetes declined by 52.3%, 72.2% and 65.1% in men, respectively, and by 53.5%, 78.5% and 59.6% in women, respectively. Pneumonia mortality rates remained stable. The leading cause of death in people with diabetes has shifted from cardiovascular disease to pneumonia in the oldest age group, with cancer remaining the most common cause of death in people aged 45–74 years. The all-cause SMRs for men declined from 2.82 (95% CI 2.72, 2.94) to 1.50 (95% CI 1.46, 1.54), and for women, they declined from 3.28 (95% CI 3.15, 3.41) to 1.67 (95% CI 1.62, 1.72). However, among people aged 20–44 years, the declines in all-cause mortality rates over the study period were not statistically significant for both men (average annual per cent change [AAPC]: –3.2% [95% CI –7.3%, 1.0%]) and women (AAPC: –1.2% [95% CI –6.5%, 4.4%]). The SMRs in people aged 20–44 years fluctuated over time, between 7.86 (95% CI 5.74, 10.5) in men and 6.10 (95% CI 3.68, 9.45) in women in 2001, and 4.95 (95% CI 3.72, 6.45) in men and 4.92 (95% CI 3.25, 7.12) in women in 2016.

Conclusions/interpretation Absolute and relative mortality has declined overall in people with diabetes in Hong Kong, with less marked improvements in people under 45 years of age, calling for urgent action to improve care in young people with diabetes.

Keywords All-cause mortality · Cause-specific mortality · Diabetes · Standardised mortality ratios · Trends

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Research in context

What is already known about this subject?

- The overall mortality in people with diabetes has declined in developed countries
- The patterns of cause-specific mortality in people with diabetes differ across countries
- Little is known about the trends in all-cause and cause-specific mortality in people with diabetes in Asian countries

What is the key question?

- What are the trends in all-cause and cause-specific mortality rates in people with diabetes in Hong Kong?

What are the new findings?

- Absolute mortality in people with diabetes and relative mortality comparing people with and without diabetes have declined overall in Hong Kong from 2001 to 2016
- The declines in mortality rates were statistically significant only in people aged 45 years and older, but not in younger people
- The leading cause of death in people with diabetes has shifted from cardiovascular disease to pneumonia in the oldest age group, with cancer still being the most common cause of death in those aged 45–74 years

How might this impact on clinical practice in the foreseeable future?

- More focused prevention and care strategies are needed for young people with diabetes in Hong Kong

Abbreviations

AAPC	Average annual per cent change
APC	Annual per cent change
CVD	Cardiovascular disease
HKDSD	Hong Kong Diabetes Surveillance Database
SMR	Standardised mortality ratio

Introduction

According to the WHO, diabetes was the seventh leading cause of death in 2016 worldwide, and was estimated to contribute to about 2.8% of total deaths [1]. People with diabetes are at a higher risk of death from all causes and from a wide range of diabetes-related complications, including cardiovascular disease (CVD), cancer and renal disease, compared with people without diabetes [2]. The overall death rates in people with diabetes have declined in developed countries over time, partly as a consequence of improvements in the control of primary risk factors, as well as acute and chronic management of cardiovascular and other complications of diabetes [3–7]. However, the magnitude of declines in all-cause mortality, the patterns of cause-specific mortality and their association with age and sex vary across countries.

Hong Kong is a cosmopolitan city in southern China, with 7.3 million residents, mainly of Chinese ethnicity, living a westernised lifestyle. During the last few decades, Hong Kong has experienced accelerated socioeconomic growth

accompanied by a rising prevalence of diabetes and other non-communicable diseases. Between 2006 and 2014, the prevalence of diabetes in Hong Kong increased from 7.2% to 10.3% and this increasing trend is expected to continue [8]. Hong Kong has a universal healthcare coverage system provided by the Hong Kong Hospital Authority and currently has the highest life expectancy in the world [9]. Age-standardised (2016 Hong Kong census population) mortality rates decreased by about 20% between 2001 and 2016 in the general population in Hong Kong [10]; however, there are no data on time trends in mortality in people with diabetes. Understanding all-cause and cause-specific mortality trends in diabetes is important to evaluate the impact of provision of diabetes care, identify the changing patterns in causes of death, and inform decision makers in developing new healthcare strategies to address unmet needs. In this study, we used territory-wide data from the Hong Kong Diabetes Surveillance Database (HKDSD) to describe secular trends in all-cause and cause-specific mortality rates in Hong Kong Chinese people with diabetes, from 2001 to 2016.

Methods

Study population The Hong Kong Hospital Authority is a statutory body established in 1990 that currently governs all 43 public hospitals/institutions, 49 specialist clinics and 73 general (primary care) outpatient clinics serving the entire

population of over seven million residents in Hong Kong [11]. In 2000, the Hospital Authority adopted a territory-wide electronic medical record system that continuously captures demographic information, diagnostic and procedure codes, laboratory results, and prescription and consultation records of all people attending public hospitals and clinics. The system provides a longitudinal and lifelong medical follow-up record of people in the public sector until they die or migrate out of Hong Kong. In 2015–2016, the Hospital Authority electronic medical record system recorded about 6.2 million attendees in general outpatient clinics, 7.2 million attendees in specialist clinics and 1.1 million inpatient services, covering about 90% of total medical services in Hong Kong [12]. The HKDSD comprises a population-based cohort of people with diabetes identified from the Hospital Authority electronic medical record system. Diabetes was ascertained based on one or more of the following qualifying criteria: (1) recording of a diagnostic code of diabetes based on ICD-9 code 250.xx (www.icd9data.com/2007/volume1, accessed 18 June 2019); (2) recording of a diagnostic code of diabetes according to the revised edition of the International Classification of Primary Care, World Organization of National Colleges, Academies, and Academic Associations of General Practitioners/Family Physicians code T89 or T90 (www.who.int/classifications/icd/adaptations/icpc2/en/, accessed 8 December 2019); (3) $HbA_{1c} \geq 48$ mmol/mol (6.5%) in any one available measurement; (4) fasting plasma glucose ≥ 7.0 mmol/l in any one available measurement; (5) prescription of blood glucose lowering drugs; or (6) long-term prescription of insulin (≥ 28 days). Women with gestational diabetes were not included in the HKDSD if diagnosis occurred 9 months before or 6 months after delivery (ICD-9 codes 72–75) or within 9 months of any pregnancy-related encounter (ICD-9 codes 630–676). However, women with subsequent episodes that met the criteria of diabetes occurring outside the context of any obstetric events were included. Information on the date and the underlying cause of death was obtained from linkage to the Hong Kong Death Registry, in which causes of death were identified by ICD-10 codes (<http://apps.who.int/classifications/icd10/browse/2016/en>, accessed 18 June 2019). We grouped the underlying cause of death into 12 mutually exclusive categories (see electronic supplementary material [ESM] Table 1). The study was approved by the local clinical research ethics committee.

Statistical analysis To avoid bias from incomplete case records of diabetes in the first year of establishment of the Hong Kong Hospital Authority electronic medical record system, analyses were limited to data from 2001 to 2016. Analyses included adults aged 20 years and older and were performed separately for men and women and for age subgroups: 20–44, 45–59, 60–74 and ≥ 75 years. Age-standardised mortality rates were

calculated for people with diabetes by dividing the number of deaths (numerator) by person-years at risk (denominator) in people included in the HKDSD between 1 January and 31 December in each calendar year from 2001 to 2016. A flow-chart describing the numerator and denominator is shown in ESM Fig. 1. The 2016 Hong Kong Census mid-year population was used as the standard population by 5 year age groups. Joinpoint regression analysis was used to describe the secular trends in age-standardised mortality rates and to investigate whether there were time points at which significant changes in mortality trends occurred. The Joinpoint regression analysis compared models by starting with no joinpoints and subsequently testing whether more joinpoints needed to be added into the model to best fit the data. The best fitting model was selected to report the average annual per cent change (AAPC) in age-standardised mortality rates for the full study period, and annual per cent change (APC) for each linear trend segment detected. Joinpoint regression analysis of cause-specific mortality rates was only performed for causes which contributed more than 10% of total deaths and for age subgroups ≥ 45 years because of small numbers of deaths in the youngest age group.

As trends in absolute mortality rates in people with diabetes cannot directly reflect the contribution of changes in quality of care for diabetes, we calculated standardised mortality ratios (SMRs) to compare all-cause mortality in people in the Hong Kong population with and without diabetes in each calendar year, using Poisson regression models with adjustment for age. We subtracted the number of deaths in people with diabetes from the total number of deaths in the whole Hong Kong population to calculate the number of deaths in people without diabetes (numerator). Risk time in person-years for people without diabetes (denominator) was calculated using a similar method of subtraction of risk time in people with diabetes from mid-year population estimates for the whole Hong Kong population. Numbers of deaths and mid-year population estimates for the whole Hong Kong population by sex, 5 year age groups and calendar year were obtained from the Hong Kong Census and Statistics Department.

We constructed abridged period life tables to estimate life expectancy in people with diabetes between 2001 and 2016 and compared it with the Hong Kong population without diabetes in the same study period. The life tables were constructed based on the Chiang method [13] using 5 year age intervals up to 85 years and an open-ended interval thereafter. In addition, we calculated the expected gains in life expectancy after the hypothetical elimination of diabetes in the general population. Two-sided tests with a p value less than 0.05 were considered statistically significant. All analyses were conducted using R software, version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria), or the Joinpoint Regression Program, version 4.7.0.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Bethesda, MD, USA).

Results

Trends in all-cause mortality rates Between 2001 and 2016, a total of 390,071 men and 380,007 women aged 20 years or older with diabetes were included in the HKDSD. During 2,734,007 and 2,903,052 person-years of follow-up there were 96,645 deaths among men and 88,437 deaths among women, respectively. The age-standardised mortality rates for all causes in people with diabetes were significantly higher for men than for women, and for older than for younger people (Fig. 1). In the whole group the all-cause mortality rates for men declined by 52.3% (AAPC -5.1% [95% CI -5.7% , -4.6%]) and for women by 53.5% (AAPC -5.5% [95% CI -7.2% , -3.7%]) (Table 1). However, among people aged 20–44 years, the declines for men (AAPC -3.2% [95% CI -7.3% , 1.0%]) and women (AAPC -1.2% [95% CI -6.5% , 4.4%]) were not statistically significant ($p < 0.05$ for interaction between age group and study year for both). The Joinpoint regression analysis showed that mortality declines were less marked after 2006 for both sexes, with similar patterns in all age groups of 45 years and older (Table 1). The trends in all-cause mortality rates in people without diabetes are shown in the ESM Table 2.

Trends in cause-specific mortality rates CVD, cancer and pneumonia were the three most common causes of death during the whole study period, which together contributed 71.7% and 69.0% of total deaths in men and women, respectively (ESM Tables 3, 4). The proportions of deaths due to

other causes by study year are shown in ESM Tables 3 and 4. Between 2001 and 2016, CVD and cancer mortality rates declined by 72.2% (AAPC -8.5% [95% CI -9.5% , -7.4%]) and 65.1% (AAPC -7.0% [95% CI -7.8% , -6.1%]) in men, respectively, and by 78.5% (AAPC -9.8% [95% CI -11.4% , -8.2%]) and 59.6% (AAPC -6.1% [95% CI -7.1% , -5.0%]) in women, respectively (Table 1, Fig. 2). However, declines in pneumonia mortality rates were not statistically significant in men (AAPC -3.0% [95% CI -7.6% , 1.8%]) or women (AAPC -2.4% [95% CI -5.6% , 0.9%]) (Table 1, Fig. 2). The declining trends in deaths due to CHD and stroke (ESM Fig. 2), which are the two most common categories of CVD, were generally similar to the trend in CVD deaths (Fig. 2). The AAPC for CHD deaths was -8.0% (95% CI -9.6% , -6.5%) in men and -10.7% (95% CI -15.0% , -6.1%) in women and, for stroke deaths, it was -8.3% (95% CI -10.0% , -6.5%) in men and -11.4% (95% CI -12.4% , -10.5%) in women. The different patterns of changes in cause-specific mortality rates resulted in a shift in the leading cause of death from CVD to pneumonia in the whole group (ESM Table 3 and ESM Table 4). The proportion of deaths due to cancer was approximately stable over time. The significant increase in pneumonia deaths and decrease in CVD deaths mainly occurred in men and women aged ≥ 75 years (ESM Table 5 and ESM Table 6). In men and women aged 45–74 years, the highest proportion of deaths was consistently attributed to cancer. There were too few deaths in people aged 20–44 years to describe patterns over time in cause-specific mortality. Among other specific causes of death, significant declines were observed for the

Fig. 1 Trends in age-stratified and age-standardised all-cause mortality rates and SMRs in men and women with diabetes in Hong Kong between 2001 and 2016. All-cause mortality rates in (a) men and (b) women. SMRs in (c) men and (d) women. For mortality rates, circles indicate observed mortality rates and lines are modelled mortality rates from the Joinpoint regression analyses

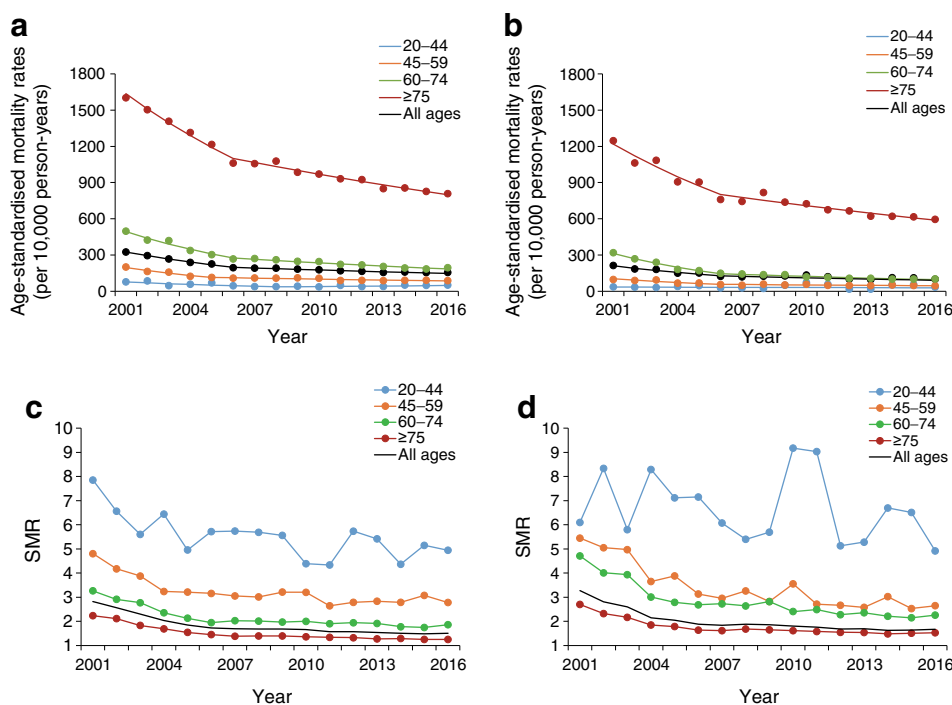


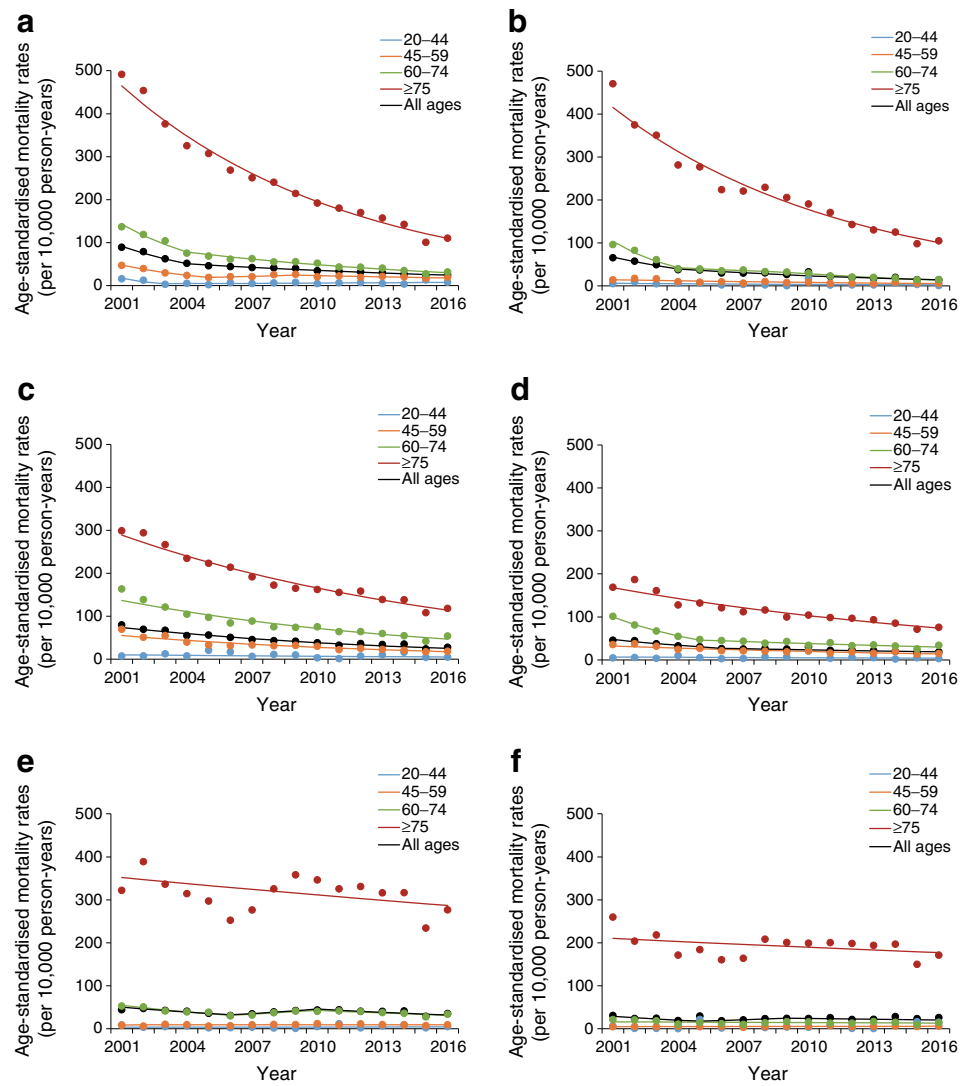
Table 1 Joinpoint analysis of time trends in age-standardised all-cause and cause-specific mortality rates in men and women with diabetes in Hong Kong between 2001 and 2016

Cause of death	Mortality rate (per 10,000 person-years)			Time period 1			Time period 2			Time period 3		
	2001	2016	AAPC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)	
Men												
All-cause												
All ages	325.1	154.9	-5.1 (-5.7, -4.6)*	2001–2006	-9.4 (-11.1, -7.8)*	2006–2016	-2.9 (-3.4, -2.4)*					
20–44 years	76.6	50.7	-3.2 (-7.3, 1.0)	2001–2008	-10.1 (-16.2, -3.5)*	2008–2016	3.2 (-3.4, 10.2)					
45–59 years	199.7	87.9	-5.4 (-7.1, -3.6)*	2001–2005	-12.6 (-18.6, -6.2)*	2005–2016	-2.6 (-3.7, -1.4)*					
60–74 years	497.5	195.0	-6.4 (-7.4, -5.4)*	2001–2006	-11.1 (-13.8, -8.2)*	2006–2016	-3.9 (-4.8, -3.1)*					
≥75 years	1602.3	808.0	-4.7 (-5.3, -4.0)*	2001–2006	-7.6 (-9.5, -5.8)*	2006–2016	-3.1 (-3.6, -2.7)*					
CVD												
All ages	89.1	24.8	-8.5 (-9.5, -7.4)*	2001–2004	-17.7 (-22.4, -12.7)*	2004–2016	-6.0 (-6.7, -5.3)*					
45–59 years	47.0	19.2	-6.4 (-10.2, -2.4)*	2001–2005	-20.4 (-28.4, -11.5)*	2005–2009	6.1 (-7.5, 21.8)			2009–2016	-4.4 (-7.6, -1.1)*	
60–74 years	136.8	31.7	-9.9 (-12.0, -7.7)*	2001–2004	-18.3 (-27.6, -7.8)*	2004–2016	-7.6 (-8.9, -6.4)*					
≥75 years	491.8	110.3	-9.2 (-10.0, -8.4)*	2001–2016	-9.2 (-10.0, -8.4)*							
Cancer												
All ages	80.0	27.9	-7.0 (-7.8, -6.1)*	2001–2016	-7.0 (-7.8, -6.1)*							
45–59 years	69.8	18.6	-7.4 (-8.7, -6.1)*	2001–2016	-7.4 (-8.7, -6.1)*							
60–74 years	163.8	54.3	-6.9 (-8.0, -5.9)*	2001–2016	-6.9 (-8.0, -5.9)*							
≥75 years	299.0	118.5	-6.0 (-6.7, -5.3)*	2001–2016	-6.0 (-6.7, -5.3)*							
Pneumonia												
All ages	44.3	35.3	-3.0 (-7.6, 1.8)	2001–2006	-8.5 (-18.0, 2.0)	2006–2010	9.1 (-5.5, 26.0)					
45–59 years	8.2	8.9	0.3 (-2.1, 2.7)	2001–2016	0.3 (-2.1, 2.7)	2006–2010	8.1 (-7.0, 25.7)					
60–74 years	52.7	33.7	-3.6 (-7.8, 0.7)	2001–2006	-10.5 (-17.8, -2.6)*	2006–2010	8.1 (-7.0, 25.7)					
≥75 years	322.0	276.8	-1.4 (-3.0, 0.3)	2001–2016	-1.4 (-3.0, 0.3)							
Women												
All-cause												
All ages	212.5	98.8	-5.5 (-7.2, -3.7)*	2001–2006	-9.7 (-14.2, -5.0)*	2006–2016	-3.3 (-5.1, -1.5)*					
20–44 years	36.0	33.5	-1.2 (-6.5, 4.4)	2001–2016	-1.2 (-6.5, 4.4)							
45–59 years	97.1	44.5	-5.3 (-7.5, -3.1)*	2001–2006	-11.2 (-16.9, -5.0)*	2006–2016	-2.3 (-4.2, -0.3)*					
60–74 years	319.2	101.2	-7.6 (-8.7, -6.5)*	2001–2006	-14.3 (-17.1, -11.3)*	2006–2016	-4.1 (-5.2, -3.1)*					
≥75 years	1246.3	594.9	-4.7 (-5.9, -3.6)*	2001–2006	-8.1 (-11.3, -4.7)*	2006–2016	-3.0 (-3.9, -2.2)*					
CVD												
All ages	65.8	14.1	-9.8 (-11.4, -8.2)*	2001–2004	-16.2 (-23.3, -8.4)*	2004–2016	-8.2 (-9.2, -7.1)*					
45–59 years	14.2	5.9	-6.2 (-8.6, -3.8)*	2001–2016	-6.2 (-8.6, -3.8)*	2004–2016	-8.2 (-9.2, -7.1)*					
60–74 years	96.4	15.0	-12.5 (-15.1, -9.9)*	2001–2004	-25.7 (-33.3, -17.3)*	2004–2009	-5.7 (-12.1, 1.2)					
≥75 years	471.1	105.1	-9.0 (-9.8, -8.2)*	2001–2016	-9.0 (-9.8, -8.2)*	2004–2009	-5.7 (-12.1, 1.2)			2009–2016	-11.1 (-13.8, -8.3)*	
Cancer												
All ages	45.8	18.5	-6.1 (-7.1, -5.0)*	2001–2006	-10.6 (-13.4, -7.8)*	2006–2016	-3.7 (-4.8, -2.6)*					
45–59 years	35.6	14.9	-5.6 (-7.0, -4.1)*	2001–2016	-5.6 (-7.0, -4.1)*							
60–74 years	101.2	34.0	-7.7 (-10.1, -5.2)*	2001–2005	-17.5 (-25.4, -8.8)*	2005–2016	-3.8 (-5.7, -1.9)*					
≥75 years	169.0	75.7	-5.3 (-6.1, -4.5)*	2001–2016	-5.3 (-6.1, -4.5)*							
Pneumonia												
All ages	30.8	26.0	-2.4 (-5.6, 0.9)	2001–2005	-12.0 (-18.6, -4.8)*	2005–2009	8.7 (-1.2, 19.6)					
45–59 years	4.5	5.8	1.6 (-0.6, 3.7)	2001–2016	1.6 (-0.6, 3.7)	2005–2009	8.7 (-1.2, 19.6)					
60–74 years	21.2	14.3	-1.5 (-3.9, 1.1)	2001–2016	-1.5 (-3.9, 1.1)							
≥75 years	260.0	171.4	-1.1 (-2.6, 0.3)	2001–2016	-1.1 (-2.6, 0.3)							

Joinpoint regression analysis for cause-specific mortality rates was only performed for age subgroups of 45 years and older

**p* < 0.05

Fig. 2 Trends in age-stratified and age-standardised mortality rates due to CVD, cancer and pneumonia in men and women with diabetes in Hong Kong between 2001 and 2016. Mortality rates in men due to (a) CVD, (c) cancer and (e) pneumonia. Mortality rates in women due to (b) CVD, (d) cancer and (f) pneumonia. Circles represent observed mortality rates and lines are modelled mortality rates from the Joinpoint regression analyses



proportions of deaths due to renal disease and diabetes in both men and women (ESM Tables 3 and ESM Table 4), whilst the proportions of deaths due to other causes was stable.

Trends in SMRs SMRs for all-cause mortality comparing people with and without diabetes were significantly higher for women than for men and were greatest in the youngest

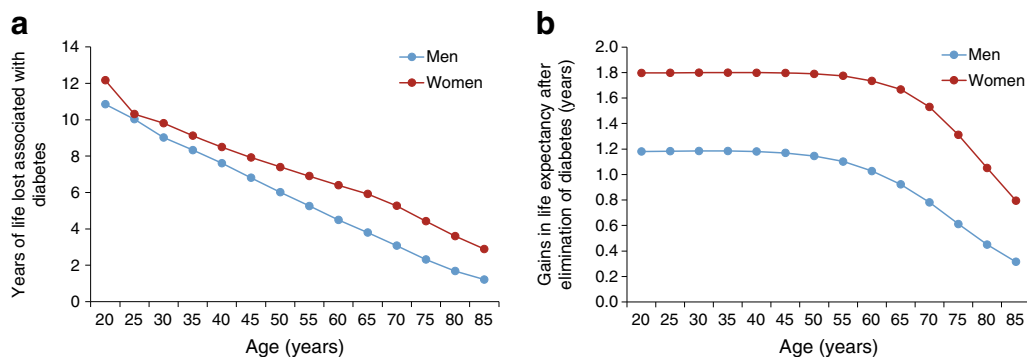


Fig. 3 (a) Years of life lost associated with diabetes and (b) gains in life expectancy after hypothetical elimination of diabetes in men and women in Hong Kong between 2001 and 2016

age group and declined with age (Fig. 1). From 2001 to 2016, SMRs for all-cause mortality for men in the whole group decreased from 2.82 (95% CI 2.72, 2.94) to 1.50 (95% CI 1.46, 1.54), and for women from 3.28 (95% CI 3.15, 3.41) to 1.67 (95% CI 1.62, 1.72). Changes in SMRs for all-cause mortality over time were similar for men and women and across all age groups, except for young people aged 20–44 years, in whom SMRs fluctuated over time, between 7.86 (95% CI 5.74, 10.5) in men and 6.10 (95% CI 3.68, 9.45) in women in 2001, and 4.95 (95% CI 3.72, 6.45) in men and 4.92 (95% CI 3.25, 7.12) in women in 2016.

Abridged life tables The difference in life expectancy between people with and without diabetes was greater for women than for men and declined by age attained (Fig. 3). Men with diabetes at age 40 and 60 years were estimated to have a loss of 7.6 and 4.5 years of life, respectively, compared with those without diabetes. The corresponding years of life lost for women were 8.5 years and 6.4 years, respectively. After a hypothetical elimination of diabetes, the estimated gains in life expectancy were 1.2 and 1.0 years for men at the age of 40 and 60 years, respectively, and 1.8 and 1.7 years for women, respectively, in the whole Hong Kong population (Fig. 3).

Trends in HbA_{1c} and LDL-cholesterol levels Between 2001 and 2016, the mean value of HbA_{1c} decreased from 61.5 mmol/mol (7.8%) to 56.9 mmol/mol (7.4%) in men with diabetes and from 60.5 mmol/mol (7.7%) to 56.3 mmol/mol (7.3%) in women with diabetes in the whole age group (ESM Table 7). The declines were observed in all age subgroups but not in young women aged 20–44 years ($p_{\text{trend}} = 0.12$). LDL-cholesterol levels also decreased significantly in both men and women and among all age subgroups (ESM Table 8).

Discussion

Using population-level data, we provide a comprehensive picture of secular trends in all-cause and cause-specific mortality rates and their associations with age and sex among people with diabetes in Hong Kong from 2001 to 2016. Both all-cause mortality rates and SMRs declined substantially in people with diabetes except in young people aged 20–44 years who had four- to ninefold higher rates of death relative to their counterparts without diabetes. The magnitude of declines was similar for men and women, although overall men had higher absolute but lower relative mortality than women. The decrease in all-cause mortality rates was largely due to significant improvements in mortality rates from CVD and cancer. This resulted in a change in the leading cause of death from CVD to pneumonia in the oldest group of people with diabetes, with cancer still being the most common cause of death in those aged 45–74 years.

Decline in all-cause mortality rates Improvements in all-cause mortality rates in people with diabetes have also been reported in other developed countries [3–7]. In the USA, all-cause mortality rates in diabetes declined by 20% every 10 years from 1988–1994 to 2010–2015, but with non-significant changes in young adults aged less than 45 years [5]. In Australia, all-cause mortality rates in type 2 diabetes declined by 19% from 2000 to 2011 [3]. Mortality rates were unchanged in young men and increased in young women aged below 40 years. Studies from Australia, Canada and the UK reported that SMRs comparing the population with diabetes against the general population have reduced over time in older age groups [6, 14]. Though the magnitude of absolute mortality rates and decline rates between studies may not be comparable owing to differences in the methodology used, the overall trends in all-cause mortality rates and SMRs in our study are generally consistent with the findings from other developed countries.

In our study, the >50% reduction in all-cause mortality rate in the Hong Kong Chinese cohort with diabetes during the 16 year study period is noteworthy and may be related to the many changes that have occurred in the social and healthcare system in Hong Kong during the last two decades. Major healthcare reforms that began in the 1990s, with focused efforts to expand services across primary, secondary and tertiary care, were conceivably the most crucial in lowering morbidity and mortality in both the general population and in people with diabetes [15]. Subsequent establishment of multi-disciplinary diabetes centres in public hospitals to provide patient education and support and, most recently, the implementation of a territory-wide diabetes risk assessment programme, have been linked to improved control of metabolic risk factors and reduction in the incidence of diabetes-related cardiovascular–renal complications in Hong Kong Chinese people with type 2 diabetes [16–18]. Data from our study showed that both HbA_{1c} and LDL-cholesterol levels have improved significantly at the territory-wide level, indicating that people were benefiting from the diabetes care programmes. In addition, reductions in the proportions of deaths due to CVD and renal disease in our study supported previous reports of decreased incident cardiovascular–renal complications in Hong Kong. Government policies and health promotion campaigns have also been effective at lowering exposure to health and behavioural risk factors at a population level. For instance, the prevalence of obesity has been stable in men and has decreased in women since the mid-1990s in Hong Kong, whilst it continues to increase in most areas worldwide [19–21]. Cigarette smoking prevalence also declined by 57% in people aged 15 years and older between 1982 and 2017 [22]. Finally, as people with diabetes are being diagnosed earlier in their disease trajectory, timely implementation of treatment and metabolic legacy may be expected to have had an impact on mortality rates. This is supported by the declining mean HbA_{1c} values observed at diagnosis of

diabetes in a Hong Kong diabetes cohort, reflecting a trend towards earlier detection of diabetes [16].

Notably, we observed faster declines in all-cause mortality rates in the earlier part of the study period and slower declines thereafter. It is conceivable that the impact of healthcare reforms were most prominent when the change was being established and the contrast from baseline care was the greatest, which then diminished over time. Another explanation is that the all-cause mortality rates in Hong Kong people with diabetes later reached a relatively low level such that further advances in medical care did not result in declines in mortality rates as great as previously.

Premature mortality in young people with diabetes The less marked improvements in all-cause mortality rates among young people in Hong Kong and in other regions is concerning since these individuals are at the prime age of economic productivity and the high rates of premature mortality are expected to have major societal impacts [3, 5]. In the Hong Kong Renal Register, 60% of renal replacement therapy was related to diabetes, with the most rapid rate of increase occurring in the 45–64 year age group [23]. In a 7 year prospective cohort of 9509 people with type 2 diabetes from the Hong Kong Diabetes Register and a cross-sectional study of 15,341 people with type 2 diabetes from the Joint Asia Diabetes Evaluation programme, those with diabetes diagnosed before the age of 40 years in Hong Kong were less likely to achieve treatment goals and had higher rates of complications than their counterparts with late-onset diabetes, despite being younger [24, 25]. In our study, the improvements in the control of HbA_{1c} and LDL-cholesterol were also generally less marked in the youngest age group than in other age groups. There is now increasing evidence highlighting poor adherence to treatment and medical follow-up and high levels of psychosocial stress in young people with diabetes [26]. Additionally, the phenotypic heterogeneity and lack of guidance to manage people with young-onset diabetes may also contribute to suboptimal control in this group. However, it is important to note that the non-statistically significant changes in all-cause mortality rates and imprecise SMRs in young people may, in part, be due to the small number of deaths in this age group.

Cause-specific mortality trends As a consequence of improved primary and secondary prevention, as well as advances in acute management of CVD, mortality rates due to CVD in people with diabetes is declining globally [7, 27]. Moreover, the magnitude of declines in CVD mortality rates was shown to be greater than in other causes of death, with a trend towards a decreased proportion of deaths caused by CVD in people with diabetes. For example, the proportion of deaths attributed to CVD in diabetes decreased from 47.8% to 34.1% in the USA between 1988–1994 and 2010–2015 [5]. In

Australia, it declined from 33.8% to 21.1% in men and from 33.7% to 22.8% in women between 1997 and 2010 [14]. Apart from CVD, our group was among the first to report the high mortality rates from cancer, accounting for nearly one in four deaths in Chinese people with diabetes [28]. Trends in cancer mortality rates in people with diabetes vary across countries. In Australia, despite unchanging rates of cancer mortality in people with type 1 or type 2 diabetes, cancer gradually surpassed CVD as the leading cause of death between 2000 and 2011 [3, 14]. In the USA, cancer mortality rates in people with diabetes declined whilst the proportion of total deaths caused by cancer in people with diabetes remained constant over the last 20 years [5]. We also revealed a decrease in cancer mortality rates and an unchanged proportion of deaths attributed to cancer in Hong Kong people with diabetes. Active measures to lower risk factors for cancer, such as anti-smoking campaigns, universal hepatitis B vaccination, progressive implementation of cancer screening programmes and improved cancer therapeutics, are key contributory factors for cancer prevention and prolonging cancer survival rate [29].

We found a considerably higher mortality rates from pneumonia in people with diabetes in Hong Kong compared with other countries. The increased proportion of deaths due to pneumonia is partly explained by the decreased proportion of deaths due to CVD. Hong Kong has particularly high rates of both hospitalisation and mortality due to pneumonia, especially in the elderly. Since 2012, pneumonia has become the second leading underlying cause of death in the general Hong Kong population [30]. However, the underlying cause of death statistics may not be comparable across different countries because of differences in physicians' diagnostic habits and perceptions and judgement of causal sequence of death [31]. Determining the underlying cause of death in people with diabetes can be difficult as multiple morbidities often coexist with diabetes at the time of death, increasing the probability of diagnostic misclassification. Additionally, when the relationship between a chronic disease and cause of death is uncertain, acute presentation of illnesses, such as pneumonia, is a more widely accepted underlying cause of death in Hong Kong than in other areas, suggesting possible over-representation of pneumonia-associated deaths in Hong Kong [32].

Improved diabetes management and patient education also contributed to a substantial reduction in deaths with diabetes as the underlying cause of death in our study. However, due to differences in coding practice, there is a probability that the <1% of total deaths attributed to diabetes in recent years in Hong Kong has been underestimated when compared with the USA (~13% in 2010–2015) and Australia (~15% in 1997–2010) [5, 14].

Strengths and limitations To our knowledge, this is the first analysis of trends in all-cause and cause-specific mortality rates in a Chinese population with diabetes. The major

strengths of this study are the use of a territory-wide database of people with diabetes in Hong Kong and a long observation period. There are several limitations of this study. The HKDSD is derived from an administrative data source that is subject to issues of external and internal validity. People treated in the private sector were not included in the HKDSD. However, the healthcare system in Hong Kong is heavily subsidised such that the majority of Hong Kong people seek care for acute and chronic illnesses in the public sector. Recent estimates show that the Hong Kong Hospital Authority provides about 90% of the total hospital bed days and 80% of outpatient visits in Hong Kong [16]. The number of people with diagnosed diabetes but without any records in the public sector in the 16-year study period is, therefore, expected to be small and unlikely to affect our conclusion. Although the diagnostic criteria for diabetes were consistent across study years in our study, changes in other factors in the study population might have affected the results. For example, earlier detection of diabetes might result in lead-time bias and a shorter diabetes duration in the latter part of the study period, which would partially contribute to declined mortality rates. Additionally, socioeconomic status is known to influence mortality rates in people regardless of diabetes status [33]. However, we were not able to investigate whether diabetes duration and socioeconomic status have changed over time due to a lack of data. The SMRs and difference in life expectancy comparing people with and without diabetes may be underestimated, as a small proportion of people with diabetes treated in the private sector were misclassified as not having diabetes in our study. As with most mortality statistics, our findings are limited by reliance on the accuracy of certification of cause of death, with potential for misclassification bias. This misclassification bias is, however, unlikely to affect the estimates of time trends, as the method for certifying death has not changed over the study period in Hong Kong. We were not able to differentiate between types of diabetes, although over 95% of Hong Kong people with diabetes have type 2 diabetes [25]. Finally, we did not have any data to estimate the number of people in the HKDSD who were lost to follow-up because of external migration; however, the number should be very small [34].

Conclusions Using surveillance data, we revealed major declines in mortality rates from all causes, CVD and cancer, and in mortality relative to the non-diabetic population in men and women with diabetes in Hong Kong between 2001 and 2016. The declines were more marked in older than younger age groups, suggesting that more focused prevention and care strategies are needed for young people. The multiple policy and system changes introduced in response to the growing prevalence of diabetes in Hong Kong might have contributed to these secular changes and may serve as a reference for other developing regions facing similar challenges.

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Data availability The data supporting the findings of this study are available on request from the corresponding author (AOYL).

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