Age-Specific Trends From 2000–2011 in All-Cause and Cause-Specific Mortality in Type 1 and Type 2 Diabetes: A Cohort Study of More Than One Million People

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OBJECTIVE

To analyze changes by age-group in all-cause and cause-specific mortality rates from 2000–2011 in people with diabetes.

RESEARCH DESIGN AND METHODS

A total of 1,189,079 (7.3% with type 1 diabetes) Australians with diabetes registered on the National Diabetes Service Scheme between 2000 and 2011 were linked to the National Death Index. Mortality rates in the total population were age standardized to the 2001 Australian population. Mortality rates were calculated for the following age-groups: 0 to <40 years, ≥ 40 to <60 years, and ≥60 to ≤85 years. Annual mortality rates were fitted using a Poisson regression model including calendar year as a covariate and age and sex where appropriate, with P_{trend} reported.

RESULTS

For type 1 diabetes, all-cause, cardiovascular disease (CVD), and diabetes age-standardized mortality rates (ASMRs) decreased each year by 0.61, 0.35, and 0.14 per 1,000 person-years (PY), respectively, between 2000 and 2011, $P_{trend} < 0.05$, while cancer mortality remained unchanged. By age, significant decreases in all-cause, CVD, and diabetes mortality rates were observed in all age-groups, excluding diabetes mortality in age-group 0–40 years. For type 2 diabetes, all-cause, CVD, and diabetes ASMRs decreased per year by 0.18, 0.15, and 0.03 per 1,000 PY, respectively, $P_{trend} < 0.001$, while cancer remained unchanged. By age, these decreases were observed in all age-groups, excluding 0–40 years, where significant increases in all-cause and cancer mortality were noted and no change was seen for CVD and diabetes mortality.

CONCLUSIONS

All-cause, CVD, and diabetes ASMRs in type 1 and type 2 diabetes decreased between 2000 and 2011, while cancer ASMRs remained unchanged. However, younger populations are not benefiting from the same improvements as older populations. In addition, the absence of a decline in cancer mortality warrants urgent attention.

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People with diabetes have higher all-cause mortality rates compared with people without diabetes, mainly attributable to cardiovascular disease (CVD) (1). However, some evidence suggests that patterns of mortality may be changing (2,3). Declines in age-standardized all-cause and CVD mortality rates have been noted among people with type 2 diabetes, with some evidence that mortality may be approaching that of the general population, particularly at older ages (2–4). For type 1 diabetes, data are inconsistent, with some studies reporting a decrease in all-cause and CVD mortality over time (5–8), while others report no change (9–11).

Data on the effects of diabetes on other causes of death over time are mixed with studies reporting increased, unchanged, or reduced mortality for complications of diabetes (5,12,13), cancer mortality (3,8), and acute complications of diabetes (3,14). Many of these studies are based on small sample sizes and do not distinguish between type 1 and type 2 diabetes. To date, there have been no age-specific analyses of trends in cause-specific mortality among people with diabetes. Examining age-specific trends in mortality identifies which age-groups are driving observed changes in mortality. These are important data to inform public health to prioritize where prevention and treatment efforts are most needed.

Using a large cohort of Australians registered on the National Diabetes Service Scheme (NDSS), we examine trends in age-specific mortality rates for all-cause and the three most common causes of death, CVD, diabetes, and cancer, among people with type 1 and type 2 diabetes.

RESEARCH DESIGN AND METHODS

The NDSS was set up in 1987 to deliver diabetes-related products at subsidized prices and provide information to people with diabetes. Registration of patients is free and is completed by a medical practitioner or credentialed diabetes nurse educator. The NDSS captures 80–90% of all Australians with known diabetes (15).

We included all people with type 1 or type 2 diabetes who were registered on the NDSS between 2000 and 2011 (including all those registered before 2000 and still alive on 1 January 2000). The year 2000 was chosen as the start date, as it followed a unification of state-based registries, as well as an improvement in data quality. After exclusion of 833 registrants, because registration date and date of death were the same, the sample size for these analyses was 1,189,079. Diabetes type is classified by the health practitioner completing registration. However, for the current study, type 1 diabetes status was assigned to registrants who satisfied all three of the following conditions: were recorded as having type 1 diabetes on the NDSS registry, were diagnosed at $<$45 years of age, and were taking insulin. Registration date was used as a proxy for diagnosis date, as a large proportion of registrants (54.4% type 1 diabetes and 32.8% type 2 diabetes) were missing date of diagnosis, many of whom registered in the early years of the operation of the NDSS and had had diabetes for a number of years. We chose 45 years as the cutoff to minimize the number of people with type 1 diabetes that we would miss, without misclassifying significant numbers of people with type 2 as having type 1 diabetes (16). Additionally, registrants who were recorded as having type 2 diabetes on the registry, were diagnosed before the age of 30 years, and were taking insulin within 1 year of diagnosis date were reclassified as having type 1 diabetes. All others were classified as having type 2 diabetes.

The NDSS was linked to the National Death Index using data up to and including 31 December 2011 and used the general framework of Fellegi and Sunter (17). First name, second name, third name, sex, and date of birth were used to conduct the linkage. We set a match link rate of 98.63% (true matches/correct links) with link accuracy of 98.97% (1.03% expected to be false positive links).

Cause of death (COD) was classified according to the ICD-10. Deaths were attributed to CVD if the underlying COD was coded I10–I25 or I60–I69. In addition, participants with a COD of uncomplicated diabetes (ICD-10 codes E109, E119, E12.9, E13.9, or E149) or diabetes with circulatory complications (E105, E11.5, E12.5, E13.5, or E14.5), and where a CVD code also appeared in the first line of the death certificate, were attributed a CVD code for COD. Diabetes and cancer deaths were defined by underlying ICD-10 codes E10–E14 and C00–C97, respectively.

Statistical Analysis

Individuals were followed from 1 January 2000, or registration date if thereafter, to 31 December 2011 or date of death—whichever occurred first. Age-specific mortality rates and 95% CIs were calculated using a Poisson regression model, with a Poisson error distribution, a log link function, and the natural log of population treated as an offset (18). This was done for the following age-groups: 0 to $<$40, $\geq$40 to $<$60, and $\geq$60 to $\leq$85 years in the total population and in men and women separately. We also examined smaller age-groups—0 to $<$40, $\geq$40 to $<$50, $\geq$50 to $<$60, $\geq$60 to $<$70, and $\geq$70 to $\leq$85 years—in the total population to tease out mortality patterns in more specific age-groups. For analyses of the total population, we calculated age-standardized mortality rates (ASMRs), standardized to the 2001 Australian population, obtained from the Australian Institute of Health and Welfare.

For the assessment of changes in all-cause and cause-specific mortality over time, annual mortality rates were fitted using a Poisson regression model including calendar year as a covariate and age and sex where appropriate, with P_{trend} reported. For each annual percentage change estimate, the corresponding 95% CI was calculated. Statistical significance was established at $P < 0.05$.

All analysis used STATA, version 12.1 (StataCorp, College Station, TX). Graphs were generated using GraphPad Prism, version 6.0, for Windows (GraphPad Software, La Jolla, CA [www.graphpad.com]). This study was approved by the Alfred Health Human Research Ethics Committee and the Australian Institute for Health and Welfare Human Research Ethics Committee.

RESULTS

This study included 1,189,049 (7.3% with type 1) individuals with type 1 or type 2 diabetes who were registered on the NDSS between 2000 and 2011. There was a greater proportion of males with type 1 and type 2 diabetes compared with females—52.6% and 53.9%, respectively; median age at diagnosis was 20.1 years (interquartile range

11.1–30.4) and 58.5 years (49.3–67.8) for type 1 and type 2 diabetes, respectively; median follow-up time was 15.2 years and 7.2 years for type 1 and type 2 diabetes, respectively; and 27.9% of people with type 2 diabetes were on insulin.

Among 87,047 people with type 1 diabetes, a total of 5,578 deaths occurred during 825,777 person-years (PY) of follow-up between 2000 and 2011; ASMR was 16.2 per 1,000 PY. In the total population with type 1 diabetes, all-cause, CVD, and diabetes ASMRs significantly decreased each year by 0.61, 0.35, and 0.14 per 1,000 PY, respectively, between 2000 and 2011 ($P_{trend} < 0.05$) (Fig. 1*A* and Supplementary Table 1), while cancer ASMRs remained unchanged. When data were examined by age, significant decreases in all-cause, CVD, and diabetes mortality rates were observed in all age-groups, excluding diabetes mortality in age-group 0–40 years (Table 1). No declines in cancer mortality rates were observed in any age-group. The largest declines in mortality rates were consistently observed in the 60–85 year age-groups, with declines per year of 0.08, 0.11, and 0.10 per 1,000 PY for all-cause, CVD, and diabetes, respectively. Similar patterns were observed in men and women (Table 1).

When examined in smaller age-groups, all-cause mortality significantly decreased in all age-groups, excluding 70–85 years with a borderline significant 0.03 per 1,000 PY decrease in the annual rate ($P_{trend} = 0.098$) (Table 2). Significant improvements in CVD mortality were noted in all age-groups, with annual rate declines between 0.05 and 0.09 per 1,000 PY. For diabetes mortality, significant decreases in mortality were observed in age-groups 50–60 and 60–70 years and no change in mortality for age-groups 0–40, 40–50, and 70–85 years. Significant decreases in cancer mortality rates were observed in age-group 40–50 years, $P_{trend} = 0.023$, but this trend was not observed in any other age-group.

Among 1,102,002 people with type 2 diabetes, a total of 206,974 deaths occurred during 7,309,921 PY of follow-up between 2000 and 2011; ASMR was 8.6 per 1,000 PY. In the total population with type 2 diabetes, all-cause, CVD, and diabetes ASMRs significantly decreased per year by 0.18, 0.15, and 0.03 per 1,000 PY, respectively, between 2000 and 2011 (Fig. 1*B* and Supplementary Table 1), while cancer ASMRs remained unchanged. By age, significant decreases in all-cause, CVD, diabetes, and cancer mortality rates were observed in all age-groups, excluding age-group 0–40 years, where significant increases in mortality were observed for all-cause and cancer and there was no change for CVD and diabetes mortality (Table 3). The largest declines in mortality rates were consistently observed in the 40–60 year age-groups, with annual rate declines of 0.02, 0.05, 0.05, and 0.03 per 1,000 PY for all-cause, CVD, diabetes, and cancer mortality, respectively. Similar patterns were observed in men and women; however, diabetes mortality in women aged 0–40 years could not be estimated due to too few observations to derive meaningful trends (Table 3). By smaller age-groups, in those aged 40–50 years there was no change in mortality rates from all-cause and diabetes mortality, while significant increases in cancer mortality rates were noted (Table 4). Significant declines in mortality from all causes, CVD, diabetes, and cancer were noted in all age-groups >50 years, with the greatest declines consistently observed in the 50–60 and 60–70 year age-groups.

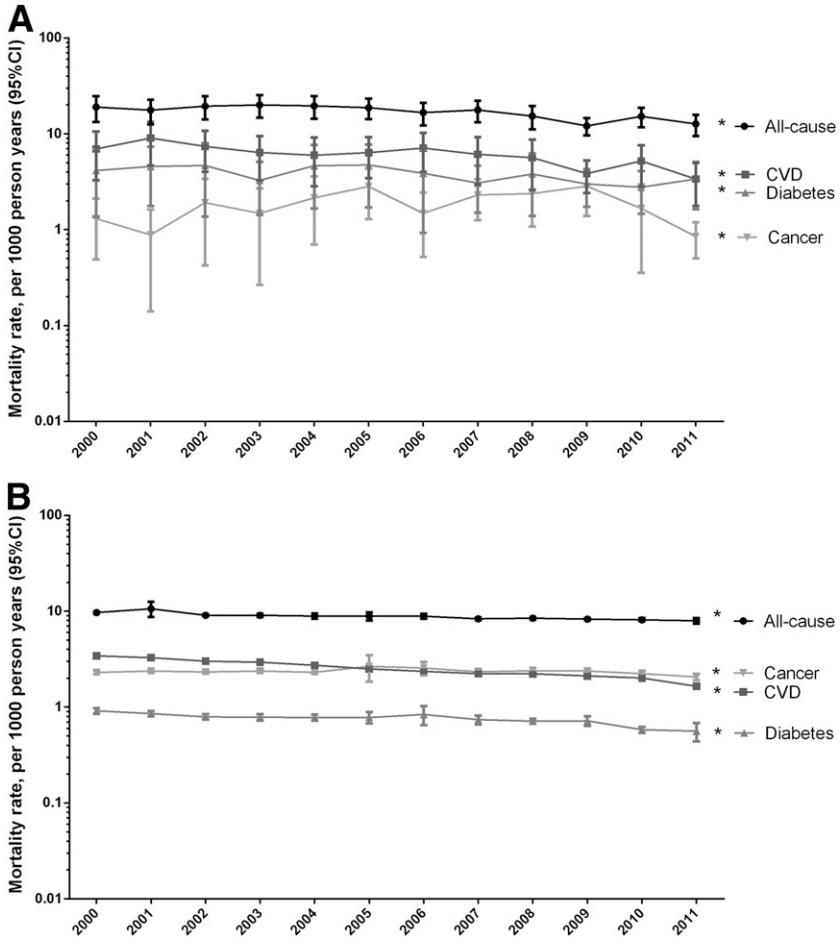

Figure 1—ASMRs in people with type 1 (*A*) and type 2 (*B*) diabetes between 2000 and 2011. Note: rates were standardized to the 2001 Australian population. *$P_{trend} < 0.05$.

CONCLUSIONS

Summary

Our findings of an analysis of age-specific mortality trends among Australians with diabetes are threefold. First, ASMRs for all-cause, CVD, and diabetes mortality have decreased in people with type 1 and type 2 diabetes in the last decade, while cancer ASMRs remain unchanged. Second, improvements in mortality rates are not consistently seen across the age spectrum, with younger ages (<40 years) not experiencing the same declines in mortality as older populations, and even more concerning, for type 2 diabetes, increases in all-cause and cancer mortality rates were noted

Table 1—All-cause, CVD, diabetes, and cancer mortality rates between 2000 and 2011, by age-group, among the total number of subjects with type 1 diabetes and in men and women separately

		Year												Annual change in rate (95% CI)	% change 2000–2011†	P_{trend}
	Age-group (years)	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011			
Men and women combined																
All-cause	0–40	2.48	2.71	2.54	2.15	2.52	2.11	2.30	1.85	2.33	2.36	1.88	1.96	−0.03 (−0.04, −0.01)	−21.00	0.006
	40–60	10.00	10.94	10.21	10.41	9.79	10.03	9.55	9.36	10.16	9.24	8.73	7.41	−0.02 (−0.09, −0.06)	−25.90	<0.001
	60–85	61.43	46.96	52.23	51.18	42.34	33.71	31.49	28.82	27.75	24.35	25.95	26.31	−0.08 (−0.09, −0.06)	−57.20	<0.001
CVD	0–40	0.42	0.48	0.27	0.29	0.37	0.23	0.36	0.14	0.27	0.23	0.10	0.25	−0.08 (−0.13, −0.03)	−40.10	0.003
	40–60	3.50	3.82	3.17	3.31	3.02	3.28	2.35	2.94	2.75	3.29	2.32	1.77	−0.04 (−0.06, −0.02)	−49.40	<0.001
	60–85	25.29	26.41	26.12	20.47	16.02	12.48	12.85	9.77	11.42	8.06	7.81	9.09	−0.11 (−0.14, −0.08)	−64.10	<0.001
Diabetes	0–40	0.66	0.69	0.77	0.64	0.57	0.51	0.55	0.68	0.64	0.75	0.69	0.55	−0.01 (−0.04, 0.03)	−16.70	0.691
	40–60	2.26	2.55	2.12	2.31	2.23	2.11	2.06	1.74	2.27	2.15	1.73	1.65	−0.02 (−0.05, −0.00)	−27.00	0.022
	60–85	14.45	11.74	9.95	8.53	10.30	5.83	4.50	5.37	4.72	5.10	4.88	4.24	−0.10 (−0.14, −0.05)	−70.70	<0.001
Cancer	0–40	0.18	0.24	0.41	0.29	0.11	0.23	0.17	0.14	0.21	0.13	0.25	0.13	−0.05 (−0.11, 0.01)	−27.80	0.116
	40–60	1.45	1.43	1.56	1.42	1.17	1.27	1.63	1.23	1.47	1.23	1.51	1.21	−0.01 (−0.03, 0.02)	−16.60	0.541
	60–85	7.23	1.47	4.97	3.41	5.15	7.49	5.14	7.33	5.12	5.92	4.46	3.76	−0.03 (−0.08, 0.02)	−48.00	0.247
Men																
All-cause	0–40	2.65	3.89	3.21	2.25	3.28	2.47	2.69	2.08	2.68	2.90	2.29	2.43	−0.03 (−0.05, −0.02)	−8.30	0.032
	40–60	11.86	13.67	12.02	12.25	11.03	12.66	11.98	11.75	12.45	10.61	11.22	9.30	−0.02(−0.03, −0.01)	−21.60	0.006
	60–85	75.91	40.79	55.37	64.10	44.07	38.23	32.90	29.19	31.44	24.95	27.95	29.07	−0.08 (−0.10, −0.05)	−61.80	<0.001
CVD	0–40	0.44	0.56	0.36	0.36	0.46	0.22	0.49	0.11	0.21	0.40	0.15	0.38	−0.06 (−0.12, 0.01)	−13.60	0.098
	40–60	4.32	5.17	4.05	4.04	3.55	4.46	3.38	4.19	3.94	4.11	3.21	2.45	−0.03 (−0.06, −0.01)	−43.30	0.002
	60–85	25.30	22.94	27.69	25.34	18.03	12.98	12.83	8.46	14.01	8.60	9.72	10.19	−0.10 (−0.14, −0.06)	−59.70	<0.001
Diabetes	0–40	0.69	0.99	0.91	0.77	0.69	0.62	0.55	0.90	0.88	0.95	0.88	0.62	−0.00 (−0.04, 0.04)	−10.10	0.948
	40–60	2.59	2.66	2.59	2.76	2.43	2.84	2.55	1.65	2.79	2.46	1.95	2.14	−0.02 (−0.05, 0.01)	−17.40	0.124
	60–85	22.14	10.20	10.65	11.93	9.02	6.49	4.46	6.77	5.81	5.45	4.86	4.03	−0.11 (−0.17, −0.06)	−8.20	<0.001
Cancer	0–40	0.19	0.25	0.48	0.24	0.17	0.28	0.22	0.11	0.21	0.05	0.24	0.14	−0.07 (−0.15, 0.02)	−26.30	0.121
	40–60	1.49	1.77	0.98	1.41	1.38	1.36	1.72	1.33	1.52	1.07	1.95	1.26	0.00 (−0.03, 0.04)	−15.40	0.918
	60–85	9.49	2.55	6.39	4.47	6.01	8.66	5.58	7.62	5.13	6.31	5.35	4.88	−0.03 (−0.09, 0.03)	−48.60	0.366
Women																
All-cause	0–40	2.32	1.61	1.90	2.06	1.76	1.75	1.90	1.61	1.97	1.78	1.44	1.43	−0.03 (−0.05, 0.00)	−39.70	0.085
	40–60	7.77	7.75	8.13	8.36	8.42	7.21	6.98	6.89	7.85	7.86	6.26	5.55	−0.02 (−0.04, −0.01)	−28.80	0.004
	60–85	42.13	55.33	47.83	33.89	40.02	27.54	29.56	28.31	22.75	23.55	23.25	22.64	−0.07 (−0.10, −0.04)	−46.30	<0.001
CVD	0–40	0.41	0.40	0.17	0.23	0.28	0.23	0.22	0.17	0.33	0.05	0.05	0.11	−0.12 (−0.20, −0.03)	−73.20	0.008
	40–60	2.53	2.24	2.15	2.48	2.45	2.01	1.28	1.64	1.54	2.47	1.44	1.11	−0.05 (−0.08, −0.02)	−56.10	0.001
	60–85	25.28	31.12	23.91	13.95	13.34	11.80	12.89	11.55	7.89	7.34	5.24	7.64	−0.14 (−0.18, −0.09)	−69.80	<0.001
Diabetes	0–40	0.64	0.40	0.63	0.52	0.45	0.40	0.56	0.44	0.38	0.54	0.48	0.48	−0.02 (−0.07, 0.04)	−25.00	0.576
	40–60	1.87	2.41	1.60	1.81	2.01	1.32	1.54	1.84	1.74	1.84	1.50	1.17	−0.03 (−0.06, 0.00)	−37.40	0.081
	60–85	4.21	13.83	8.97	3.99	12.01	4.92	4.55	3.47	3.25	4.63	4.91	4.53	−0.07 (−0.14, 0.01)	7.60*	0.073
Cancer	0–40	0.17	0.23	0.35	0.34	0.06	0.17	0.11	0.17	0.22	0.22	0.27	0.11	−0.03 (−0.12, 0.06)	−78.70	0.511
	40–60	1.41	1.03	2.23	1.43	0.94	1.18	1.54	1.12	1.42	1.39	1.06	1.17	−0.02 (−0.06, 0.02)	−17.00	0.311
	60–85	4.21	0.00	2.99	1.99	4.00	5.90	4.55	6.93	5.11	5.41	3.27	2.26	−0.03 (−0.11, 0.05)	−46.30	0.467

†% change is calculated as follows: (2000 rate − 2011 rate)/2000 rate * 100. A negative percent change indicates a decline in rate between 2000 and 2011. *Increase in mortality rate between 2000 and 2011.

Table 2—All-cause, CVD, diabetes, and cancer mortality rates between 2000 and 2011 among subjects with type 1 diabetes in smaller age-groups

	Age-group (years)	Year											Annual change in rate (95% CI)	% change 2000–2011†	P_{trend}
		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011			
All-cause	0–40	2.48	2.71	2.54	2.15	2.52	2.11	2.30	1.85	2.33	2.36	1.88	1.96	−0.03 (−0.04, −0.01)	−20.97	0.006
	40–50	7.69	7.94	7.51	7.76	7.19	7.56	6.95	7.04	6.57	6.27	6.17	5.33	−0.03 (−0.04, −0.01)	−30.72	0.001
	50–60	14.60	16.18	14.44	14.23	13.34	13.25	12.79	12.19	14.46	12.71	11.68	9.77	−0.03 (−0.04, −0.01)	−33.10	<0.001
	60–70	53.41	28.04	23.81	29.23	31.70	21.95	25.07	23.41	24.10	20.46	22.39	24.00	−0.05 (−0.07, −0.03)	−55.05	<0.001
	70–85	78.20	87.25	112.3	120.1	94.37	113.9	87.48	89.56	77.29	86.22	89.32	69.96	−0.03 (−0.06, 0.00)	−10.54	0.098
CVD	0–40	0.42	0.48	0.27	0.29	0.37	0.23	0.36	0.14	0.27	0.23	0.10	0.25	−0.08 (−0.13, −0.03)	−40.48	0.003
	40–50	2.18	2.56	2.50	2.05	1.78	2.01	1.30	2.00	1.58	2.23	1.29	1.00	−0.05 (−0.08, −0.03)	−54.32	0.001
	50–60	6.15	6.01	4.21	5.12	4.72	4.93	3.67	4.09	4.14	4.53	3.51	2.66	−0.05 (−0.07, −0.02)	−56.77	<0.001
	60–70	18.69	17.25	10.99	12.37	12.40	9.07	8.95	7.71	10.15	6.65	6.33	8.30	−0.09 (−0.12, −0.06)	−55.60	<0.001
	70–85	39.10	45.92	58.12	45.96	33.70	35.81	46.86	32.84	28.63	30.59	34.15	24.12	−0.06 (−0.10, −0.01)	−38.31	0.03
Diabetes	0–40	0.66	0.69	0.77	0.64	0.57	0.51	0.55	0.68	0.64	0.75	0.69	0.55	−0.01 (−0.04, 0.03)	−16.67	0.691
	40–50	1.73	1.75	1.65	1.99	1.54	2.18	1.83	1.35	1.58	1.58	1.70	1.23	−0.02 (−0.05, 0.01)	−28.94	0.252
	50–60	3.33	3.94	2.87	2.78	3.17	2.00	2.35	2.22	3.09	2.82	1.76	2.13	−0.04 (−0.08, −0.01)	−36.15	0.006
	60–70	16.02	6.47	7.33	4.50	8.96	3.34	3.58	4.26	3.38	4.02	4.12	3.32	−0.08 (−0.13, −0.03)	−79.28	0.003
	70–85	11.17	22.96	15.50	21.21	16.85	22.79	12.50	17.91	22.90	22.25	18.39	21.71	0.02 (−0.05, 0.09)	94.33*	0.576
Cancer	0–40	0.18	0.24	0.41	0.29	0.11	0.23	0.17	0.14	0.21	0.13	0.25	0.13	−0.05 (−0.11, 0.01)	−27.78	0.116
	40–50	1.47	1.12	0.79	1.14	0.95	0.71	1.00	0.76	0.76	0.94	0.88	0.59	−0.05 (−0.09, −0.01)	−60.28	0.023
	50–60	1.41	1.97	2.77	1.82	1.46	2.00	2.43	1.79	2.32	1.58	2.23	1.93	0.00 (−0.03, 0.04)	36.78*	0.818
	60–70	10.68	0.00	3.66	3.37	2.76	5.73	5.01	6.65	4.23	4.90	4.42	3.83	−0.01 (−0.07, 0.04)	−64.14	0.646
	70–85	0.00	4.59	7.75	3.54	16.85	19.53	6.25	14.93	17.18	22.25	5.25	2.41	0.03 (−0.06, 0.13)	0.00	0.511

†% change is calculated as follows: (2000 rate − 2011 rate)/2000 rate * 100. A negative percent change indicates a decline in rate between 2000 and 2011. *Increase in mortality rate between 2000 and 2011.

in age-groups 0–40 years. Last, declines in cancer mortality rates were observed for older age-groups in type 2 but not in type 1 diabetes.

Comparison With the Literature

Our observation of declines in all-cause and CVD mortality are consistent with trends in other developed nations. For example, in a population of U.S. adults with diabetes, Gregg et al. (13) showed that between 1997 and 2006, all-cause and CVD death rates declined by 23% and 40%, respectively, which is comparable with our observed declines of 17.9% and 51.7% in type 2 diabetes, respectively. Declines in all-cause and CVD mortality have also been noted in populations without diabetes, with declines of 40% and 62% between 1950 and 2005, respectively, though evidence suggests the rate of decline is greater in diabetes, with declines of 48% and 69%, respectively, for the same time period (4). These declines in mortality may be explained, at least in part, by earlier detection and by improvements in diabetes care and in CVD treatments and risk factors (19–21). However, previous work by our group using the NDSS data has shown that people with type 1 and type 2 diabetes still experience a 200% and 20% increased risk of excess all-cause mortality, respectively, compared with the general population (8), similar to findings in the U.K. and Canada (2,22). Excess CVD mortality is in the realm of 50–110% and 300–400% for type 2 (23,24) and type 1 (22) diabetes, respectively, compared with populations without diabetes. Therefore, while data presented here suggest improvements in mortality rates among those with diabetes, much room exists for additional improvements.

Previous studies on mortality from diabetes and cancer are conflicting. For diabetes, we report overall declines of 18.5% and 38.5% in type 1 and 2 diabetes, respectively. National data from the U.S. recently reported relative declines of 64% between 1990 and 2010 for mortality due to hyperglycemic crisis among people with type 2 diabetes (25). These estimates are higher than those reported here, most likely due to the longer time frame of the U.S. study and the specific exploration of hyperglycemic crisis. For type 1 diabetes, a Finnish study found increases in mortality due

Table 3—All-cause, CVD, diabetes, and cancer mortality rates between 2000 and 2011, by age-group, among the total subjects with type 2 diabetes and in men and women separately

	Age-group (years)	Year												Annual change in rate (95% CI)	% change 2000 and 2011†	P_{trend}
		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011			
Men and women combined																
All-cause	0–40	1.49	1.19	1.72	2.20	1.83	2.09	2.48	1.90	2.13	2.48	2.48	3.50	0.05 (0.02, 0.07)	134.40*	<0.001
	40–60	8.25	7.73	7.20	7.20	6.90	6.67	6.53	6.79	6.51	6.54	6.50	6.08	−0.02 (−0.02, −0.01)	−26.29	<0.001
	60–85	44.29	43.00	42.20	41.58	41.00	39.84	40.09	40.02	40.82	39.34	38.66	35.31	−0.01 (−0.02, −0.01)	−20.27	<0.001
CVD	0–40	0.17	0.21	0.40	0.31	0.16	0.23	0.27	0.35	0.31	0.19	0.23	0.23	−0.02 (−0.08, 0.05)	32.34*	0.558
	40–60	2.38	2.28	1.84	1.86	1.65	1.63	1.49	1.36	1.42	1.38	1.43	1.16	−0.05 (−0.06, −0.04)	−51.28	<0.001
	60–85	16.72	16.36	15.14	14.90	14.26	13.09	12.43	12.00	12.14	11.57	10.83	9.17	−0.05 (−0.05, −0.05)	−45.13	<0.001
Diabetes	0–40	0.04	0.04	0.08	0.35	0.19	0.27	0.31	0.19	0.16	0.27	0.08	0.15	0.00 (−0.07, 0.08)	252.82*	0.922
	40–60	0.75	0.71	0.42	0.37	0.41	0.40	0.41	0.46	0.42	0.40	0.42	0.31	−0.05 (−0.07, −0.03)	−58.51	<0.001
	60–85	4.35	4.09	4.01	3.82	3.92	3.72	3.70	3.75	3.89	3.60	3.09	2.78	−0.03 (−0.03, −0.03)	−36.21	<0.001
Cancer	0–40	0.26	0.25	0.24	0.47	0.12	0.19	0.50	0.19	0.54	0.58	0.46	0.71	0.08 (0.03, 0.14)	179.38*	0.004
	40–60	2.65	2.70	2.82	2.76	2.72	2.53	2.41	2.49	2.36	2.34	2.08	2.02	−0.03 (−0.04, −0.02)	−23.62	<0.001
	60–85	10.44	10.56	10.37	10.55	10.52	10.52	10.71	10.59	10.61	10.57	10.44	9.03	−0.01 (−0.01, −0.00)	−13.53	<0.001
Men																
All-cause	0–40	2.66	2.72	3.98	5.03	3.28	3.59	3.99	3.10	2.49	4.07	2.89	4.87	0.01 (−0.02, 0.04)	82.96*	0.425
	40–60	9.57	8.83	8.55	8.59	8.53	8.17	7.54	8.14	7.92	7.76	8.02	7.17	−0.02 (−0.02, −0.01)	−25.07	<0.001
	60–85	48.18	46.49	45.77	44.57	43.78	42.84	42.30	42.21	42.45	41.52	39.97	37.07	−0.02 (−0.02, −0.02)	−23.06	<0.001
CVD	0–40	0.57	0.68	1.07	0.42	0.26	0.37	0.23	0.44	0.31	0.19	0.27	0.43	−0.09 (−0.018, 0.00)	−25.09	0.058
	40–60	3.15	2.86	2.59	2.46	2.29	2.16	2.01	1.96	2.04	1.84	1.97	1.61	−0.05 (−0.06, −0.04)	−48.93	<0.001
	60–85	17.91	16.85	16.07	15.78	14.93	13.92	13.17	12.60	12.64	12.13	10.90	9.47	−0.05 (−0.05, −0.05)	−47.10	<0.001
Diabetes	0–40	0.00	0.17	0.31	0.98	0.39	0.37	0.35	0.55	0.21	0.49	0.09	0.34	−0.01 (−0.11, 0.08)	n/a	0.775
	40–60	0.90	0.81	0.46	0.49	0.50	0.43	0.47	0.48	0.43	0.49	0.44	0.31	−0.06 (−0.09, −0.04)	−65.90	<0.001
	60–85	4.33	4.37	4.17	3.95	3.88	3.55	3.60	3.65	3.66	3.46	2.86	2.71	−0.04 (−0.04, −0.03)	−37.41	<0.001
Cancer	0–40	0.38	0.34	0.61	0.84	0.13	0.37	0.82	0.22	0.41	1.07	0.63	1.03	0.08 (−0.00, 0.16)	169.65*	0.051
	40–60	2.95	2.78	3.10	2.98	3.08	2.89	2.51	2.75	2.69	2.46	2.31	2.21	−0.03 (−0.04, −0.02)	−24.82	<0.001
	60–85	12.61	12.81	12.54	12.30	12.44	12.69	12.40	12.46	12.42	12.42	12.36	10.68	−0.01 (0.01, −0.01)	−15.33	<0.001
Women																
All-cause	0–40	1.15	0.71	0.92	1.09	1.22	1.41	1.73	1.25	1.92	1.42	2.18	2.42	0.09 (0.05, 0.12)	109.49*	<0.001
	40–60	6.57	6.35	5.52	5.52	4.95	4.88	5.36	5.23	4.90	5.13	4.76	4.82	−0.02 (−0.03, −0.01)	−26.68	<0.001
	60–85	40.08	39.22	38.31	38.33	37.97	36.55	37.66	37.58	38.99	36.87	37.18	33.29	−0.01 (−0.01,-0.01)	−16.95	<0.001
CVD	0–40	0.05	0.05	0.16	0.27	0.11	0.17	0.29	0.30	0.31	0.19	0.20	0.07	0.06 (−0.04, 0.15)	22.22*	0.254
	40–60	1.40	1.56	0.92	1.13	0.89	1.01	0.87	0.66	0.71	0.85	0.82	0.64	−0.06 (−0.08, −0.04)	−54.42	<0.001
	60–85	15.43	15.84	14.13	13.95	13.53	12.18	11.61	11.33	11.58	10.93	10.74	8.82	−0.05 (−0.05, −0.04)	−42.80	<0.001
Diabetes	0–40	0.05	0.00	0.00	0.11	0.11	0.23	0.29	0.00	0.12	0.13	0.07	0.00	0.03 (−0.09, 0.17)	−100.00	0.580
	40–60	0.57	0.57	0.36	0.24	0.30	0.37	0.34	0.45	0.40	0.31	0.40	0.32	−0.02 (−0.05, 0.01)	−43.85	0.129
	60–85	4.38	3.80	3.83	3.68	3.96	3.92	3.81	3.87	4.14	3.75	3.36	2.86	−0.02 (−0.03, −0.01)	−34.82	<0.001
Cancer	0–40	0.22	0.22	0.11	0.33	0.11	0.11	0.35	0.18	0.62	0.26	0.33	0.47	0.09 (0.01, 0.16)	113.89*	0.030
	40–60	2.27	2.59	2.46	2.49	2.30	2.10	2.29	2.19	1.99	2.21	1.80	1.80	−0.03 (−0.04, −0.02)	−20.69	<0.001
	60–85	8.09	8.12	8.02	8.63	8.43	8.13	8.86	8.51	8.57	8.49	8.24	7.13	−0.01 (−0.01, −0.00)	−11.92	0.018

n/a, % change cannot be estimated. †% change is calculated as follows: (2000 rate − 2011 rate)/2000 rate * 100. A negative percent change indicates a decline in rate between 2000 and 2011. *Increase in mortality rate between 2000 and 2011.

Table 4—All-cause, CVD, diabetes, and cancer mortality rates between 2000 and 2011 among subjects with type 2 diabetes in smaller age-groups

		Year											Annual change in rate (95% CI)	% change 2000–2011†	P_{trend}
	Age-group (years)	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011			
All-cause	0–40	1.49	1.19	1.72	2.20	1.83	2.09	2.48	1.90	2.13	2.48	2.48	3.50	0.05 (0.02, 0.07)	134.40*	<0.001
	40–50	3.89	3.94	4.04	4.54	4.46	4.16	4.90	4.31	4.14	4.29	4.18	3.79	−0.00 (−0.01, 0.01)	−2.58	0.64
	50–60	10.29	9.55	8.74	8.51	8.10	7.89	7.33	8.02	7.68	7.64	7.64	7.18	−0.02 (−0.03, −0.02)	−30.19	<0.001
	60–70	21.28	19.38	18.46	18.44	17.59	16.62	15.99	16.53	15.70	15.14	14.22	13.37	−0.04 (−0.04, −0.04)	−37.18	<0.001
	70–85	62.76	61.49	60.43	59.07	58.48	56.96	57.62	57.13	59.09	56.93	56.33	51.09	−0.01 (−0.01, −0.01)	−18.61	<0.001
CVD	0–40	0.17	0.21	0.40	0.31	0.16	0.23	0.27	0.35	0.31	0.19	0.23	0.23	−0.02 (−0.08, 0.05)	32.34*	0.558
	40–50	1.06	0.78	0.86	1.06	1.01	1.06	1.10	0.82	0.79	0.78	0.72	0.58	−0.04 (−0.06, −0.02)	−45.80	0.001
	50–60	3.00	3.00	2.32	2.25	1.97	1.91	1.68	1.62	1.73	1.67	1.78	1.44	−0.06 (−0.07, −0.05)	−51.93	<0.001
	60–70	7.10	6.33	5.74	5.59	5.05	4.71	4.02	4.10	3.89	3.63	3.35	2.84	−0.08 (−0.09, −0.08)	−60.07	<0.001
	70–85	24.43	24.22	22.37	21.95	21.14	19.27	18.54	17.75	18.14	17.34	16.22	13.72	−0.05 (−0.05, −0.04)	−43.83	<0.001
Diabetes	0–40	0.04	0.04	0.08	0.35	0.19	0.27	0.31	0.19	0.16	0.27	0.08	0.15	0.00 (−0.07, 0.08)	252.82*	0.922
	40–50	0.25	0.24	0.21	0.19	0.28	0.23	0.30	0.30	0.31	0.28	0.27	0.25	0.02 (−0.03, 0.06)	−2.58	0.461
	50–60	0.99	0.93	0.51	0.46	0.47	0.49	0.46	0.54	0.47	0.46	0.50	0.34	−0.06 (−0.08, −0.04)	−65.12	<0.001
	60–70	2.21	1.74	1.63	1.48	1.41	1.23	1.24	1.27	1.13	1.19	0.77	0.78	−0.08 (−0.08, −0.07)	−64.70	<0.001
	70–85	6.07	5.93	5.83	5.59	5.80	5.56	5.49	5.56	5.89	5.35	4.77	4.21	−0.02 (−0.03, −0.02)	−30.67	<0.001
Cancer	0–40	0.26	0.25	0.24	0.47	0.12	0.19	0.50	0.19	0.54	0.58	0.46	0.71	0.08 (0.03, 0.14)	179.38*	0.004
	40–50	0.98	1.49	1.35	1.47	1.44	1.19	1.42	1.35	1.15	1.07	1.08	1.09	−0.02 (−0.04, −0.00)	−11.43*	0.023
	50–60	3.43	3.27	3.53	3.39	3.35	3.18	2.89	3.05	2.96	2.97	2.56	2.47	−0.03 (−0.04, −0.02)	−27.94	<0.001
	60–70	6.98	6.59	6.46	6.79	6.64	6.36	6.18	6.45	6.24	6.00	5.76	5.31	−0.02 (−0.02, −0.02)	−23.98	<0.001
	70–85	13.21	13.67	13.38	13.39	13.42	13.58	14.01	13.61	13.79	13.90	13.81	11.70	−0.00 (−0.01, −0.00)	−11.47	0.001

†% change is calculated as follows: (2000 rate – 2011 rate)/2000 rate * 100. A negative percent change indicates a decline in rate between 2000 and 2011. *Increase in mortality rate between 2000 and 2011.

to (all) acute complications of diabetes between 1970–1989 (14), while a Japanese study of patients with diabetes diagnosed before 18 years of age observed an 80% decrease (from 421 to 83 deaths per 100,000 persons) between 1965 and 1980 (26), though more contemporary estimates for type 1 diabetes are lacking. Improvements in mortality from diabetes may be attributed to changes to practice guidelines for diabetes management over the last decade, which have emphasized the need for aggressive control of blood pressure, lipid levels, and hyperglycemia in patients with diabetes (27).

For cancer, we observed no change in ASMRs between 2000 and 2011 among people with type 1 and type 2 diabetes. However, among those with type 2 diabetes, we did observe significant decreases in cancer mortality among 40–60 and 60–85 year age-groups, though these improvements were not noted for younger age-groups, and in fact, we noted an increase in cancer mortality in those aged 0–40 years. One of the key reasons for our findings is likely to be competing mortality. We have previously reported that the proportion of deaths attributed to cancer is increasing over time, in part due to improvements in treatment of CVD. Thus, people with diabetes are surviving longer and not dying from diseases such as CVD and then develop other outcomes such as cancer (28). Cancer is now a leading COD in diabetes, accounting for 27 and 33% of all deaths in people with type 1 and type 2 diabetes, respectively (28). Only one other study that we are aware of has also shown that the proportion of deaths attributed to cancer among people with type 2 diabetes has increased from 23% in 1970 to 27% in 1990 (3). This increase in the proportion of deaths attributed to cancer is similar to what is being observed in the general population (29). However, the increase in the proportion of deaths attributed to cancer among the general population coincides with decreases in absolute mortality rates from cancer (30,31). Declines in cancer mortality rates among the general population may be attributed to increased uptake of screening and improved treatments. The absence of a decline in cancer mortality rates among those with diabetes may to be due to a range of factors including a

rise in cancer incidence, later presentations and diagnosis, and poorer responses to therapy (32).

To our knowledge, this is the first time that trends in absolute cause-specific mortality rates in diabetes have been explored by age-group. This is possibly because large study sizes are needed to obtain precise estimates, especially among younger age-groups, in which fewer deaths occur. We show significant declines in mortality from all causes, CVD, and diabetes in older age-groups, but this is not seen in those age <40 years old. In fact, significant increases in mortality were observed for all causes and cancer among younger people with type 2 diabetes and no change was observed for CVD or diabetes mortality. There are several potential explanations for no improvement and an increase in mortality rates among younger age-groups. These include a low number of CVD and diabetes events in these age-groups, which may result in a type II error, the worsening or lack of improvement in risk factors, and possible misclassification of type 1 and type 2 diabetes, which may differ over time. For example, the incidence of young-onset type 2 diabetes is increasing, and it is possible that young people with type 2 diabetes are being incorrectly misclassified as having type 1 diabetes, and this may drive the higher mortality rates in this age-group. However, in those with type 1 diabetes, we show that mortality is decreasing. Therefore, we believe that the more likely explanation is that young-onset type 2 diabetes represents a more severe form of diabetes. Our data support recently published studies suggesting that young-onset type 2 diabetes is the more lethal phenotype of diabetes and is associated with a greater mortality, more diabetes complications, unfavorable CVD risk factors, and greater difficulty in achieving glycemic control, even compared with type 1 diabetes (33–36). Given the increasing incidence of young-onset type 2 diabetes and its severity, there is an urgent need for diabetes prevention efforts to be targeted toward youth.

Strengths and Limitations

The main strength of this study is that it is disease registry–based with a large sample size, with a long follow-up time and the ability to distinguish between type 1 and type 2 diabetes. There are several limitations, however, that should be acknowledged. First, the NDSS is an administrative database, and there are inherent limitations with using administrative databases for research purposes (37). Namely, for our study, precise information about type of diabetes for all registrants was not available. The classification of diabetes, particularly in young patients, is challenging, and misclassification can occur. However, the proportions of people with type 1 and type 2 diabetes in this study (7.3% vs. 92.7%) are similar in other Australian data (38). Further, the proportion of people with type 2 diabetes who were also on insulin is consistent with other studies (39). Given these well-known demographics and our very large sample size, we believe that any misclassification in this study will not alter our results.

Second, the NDSS is considered among the best available national data sources for estimating overall prevalence of diagnosed diabetes in Australia (15). However, the NDSS does not capture those with undiagnosed diabetes. Recent Australian data show that for every five cases of known diabetes, there are four undiagnosed cases (40). The NDSS also may underestimate the total number of people with diet-controlled diabetes, as the diabetes-related products provided through the scheme may not be needed (40). In Australia, the proportion of known diabetes controlled by diet only was estimated to be 28% in 2000 (41). It is possible, therefore, that using the NDSS is reflective of the more serious diabetes cases. However, the NDSS coverage of type 1 diabetes is known to be very high, as access to insulin-related products is through the NDSS scheme (15). Further, we believe the coverage of type 2 diabetes is adequately reflective of people with type 2 diabetes in Australia given that the age distribution and median age at diagnosis are similar to those seen in other populations (39). We therefore do not believe this potential source of bias will significantly impact our findings.

Last, although the NDSS provides the largest data set for people with diagnosed diabetes, our findings are limited by a lack of covariates in the data set. Therefore, we were unable to explore the extent to which improvements in quality of care, medical treatments, and/or self-management behaviors contributed to the reductions in mortality over time.

Conclusion

We have shown that ASMRs from all causes, CVD, and diabetes in type 1 and type 2 diabetes have decreased over the last decade in Australia, while cancer ASMRs remain unchanged. These trends suggest continued success in the treatment of diabetes and its complications. However, these improvements are not seen across the entire age spectrum, with younger populations not benefiting from the same improvements as older populations, and continued efforts to rectify this disparity are needed. In addition, the absence of a decline in cancer mortality rates in diabetes is likely to lead to a higher burden of cancer among people with diabetes. This warrants urgent attention.

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