Supplementary Material

Additional Methods

1. Derivation of the final analytic sample and classification of diabetes type
The NDSS included 1,581,024 individuals with all types of diabetes registered during the period 2002-2014. After excluding individuals with missing key variables or evidence of internal data inconsistencies/linkage error relating to these variables (i.e. date of birth, sex, registration date, or date of death; n=45,413), or who were aged >100 years (n=125; trimmed due to the possibility of old age reflecting linkage failure to a death record), 1,535,486 individuals remained. Of this group, 186,876 registrants' diabetes type was gestational or other/unknown, leaving 1,348,610 individuals whose diabetes type was nominated by their registering practitioner as type 1 or type 2.

Given known uncertainty in the classification of diabetes type (particularly early after diagnosis when registration is typically completed), we applied insulin prescription and other clinical criteria to better differentiate type 2 from type 1 diabetes. These criteria broadly align with our previous work,[1] albeit with some modifications to reflect the improved phenotyping enabled by our linkage to the Pharmaceutical Benefits Scheme (PBS) – an Australian government program designed to subsidise the cost of prescription medications. With all forms of insulin therapy eligible for a PBS benefit throughout the period 2002-2014, relevant treatment characteristics (i.e. initiation and longevity of insulin use) were able to be leveraged.

Although the current study was restricted to individuals with type 2 diabetes only, the criteria for both type 1 and type 2 are outlined below, given classification of type 2 was partly dependent on exclusion of the other.

Type 1 diabetes
NDSS registrants were classified as having type 1 diabetes if they were registered as type 1 diabetes on the NDSS, had evidence of ongoing treatment with insulin ($\geq$2 prescriptions on the PBS, except where time to census date/death was <2 years), and met one of the following additional criteria:

1) time between diagnosis date and first insulin prescription was less than one year, **or**
2) registered before 45 years of age and showing evidence of insulin therapy at the time of registration (only applied to individuals with missing diagnosis date [31%]); **or**
3) registered before 2002 with an age at diagnosis <30 years (or age at registration <45 years if missing diagnosis date) and treatment with insulin evident from 2002; i.e. when PBS data became available (only applied to individuals with missing insulin initiation date in the NDSS database).

In addition, registrants who were originally classified as type 2 on the NDSS, but whose age at diagnosis was <30 years and time to insulin was <1 year, were reclassified as type 1 diabetes.

Type 2 diabetes
Individuals satisfying none of the above requirements for type 1 diabetes (nor registered as gestational or other/unknown type) were classified as having type 2 diabetes and therefore included in the study, with the following exceptions:
- Age at diagnosis or registration was <10 years (given the recognised difficulties of differentially diagnosing type 2 diabetes in children)
- Follow-up time in the study was insufficient to apply insulin prescription criteria

Of the 1,348,610 individuals registered with type 1 or type 2 diabetes, 79,085 individuals who met the criteria for type 1 diabetes were excluded, as well as 1,507 who were unclassifiable (the latter including children [<10 years] with possible type 2 diabetes and those whose follow-up time was insufficient to apply insulin prescription criteria). Thus, the final analytic sample included 1,268,018 individuals with type 2 diabetes.

2. Cause of death (COD) coding

ICD-10 code groupings for all-cause mortality and the specific CODs investigated within each of the CVD, cancer, and non-CVD/non-cancer categories are displayed in the table below. References to corresponding GRIM and ACIM data (i.e. source of all-cause and cause-specific mortality rates in the general population) are also shown. The code groupings were selected for concordance with World Health Organization recommendations,[2] excepting minor modifications made by the publisher of the GRIM and ACIM data (i.e. Australian Institute of Health and Welfare [AIHW]) to ensure relevance to the Australian setting.[3]

ICD-10 Code Groupings	Citation(s) for general population mortality rate data
All-cause (ICD-10 all)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All causes combined. Canberra: AIHW.
CVD (I00–I99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All diseases of the circulatory system. Canberra: AIHW.
Hypertensive disease (I10–I15)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Hypertensive disease. Canberra: AIHW.
Coronary heart disease (I20–I25)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Coronary heart disease. Canberra: AIHW.
Heart failure (I50)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Heart failure. Canberra: AIHW.
Cerebrovascular disease (I60–I69)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Cerebrovascular disease. Canberra: AIHW.
Cancer (C00–D48)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All neoplasms. Canberra: AIHW.
Oesophageal cancer (C15)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: oesophageal cancer Canberra: AIHW.
Stomach cancer (C16)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: stomach cancer Canberra: AIHW.
Colorectal cancer (C18–C21)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Colorectal cancer. Canberra: AIHW.
Liver cancer (C22)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: liver cancer Canberra: AIHW.
Gallbladder cancer (C23–C24)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: gallbladder and extrahepatic bile duct cancer Canberra: AIHW.
Pancreatic cancer (C25)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Pancreatic cancer. Canberra: AIHW.
Laryngeal cancer (C32)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: laryngeal cancer Canberra: AIHW.

ICD-10 Code Groupings	Citation(s) for general population mortality rate data
Lung cancer (C33–C34)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Lung cancer. Canberra: AIHW.
Skin cancer (C43–C44)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Skin cancer. Canberra: AIHW.
Breast cancer (C50)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Breast cancer. Canberra: AIHW.
Uterine cancer (C54–C55)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: uterine cancer Canberra: AIHW.
Ovarian cancer (C56)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: ovarian cancer Canberra: AIHW.
Prostate cancer (C61)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Prostate cancer. Canberra: AIHW.
Kidney cancer (C64)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: kidney cancer Canberra: AIHW.
Bladder cancer (C67)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: bladder cancer Canberra: AIHW.
Brain cancer (C71)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: brain cancer Canberra: AIHW.
Lymphoid/ haematopoietic cancers * (C81–C86, C90.0, C91–C95)	Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: lymphoma (all types) Canberra: AIHW. Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: multiple myeloma Canberra: AIHW. Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: leukaemia (all types) Canberra: AIHW.
Diabetes (E10–E14)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Diabetes. Canberra: AIHW.
Non-CVD/non-cancer †	
Infectious diseases (A00–B99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All certain infectious and parasitic diseases. Canberra: AIHW.
Dementia (F01, F03, G30)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Dementia and Alzheimer disease. Canberra: AIHW.
Influenza and pneumonia (J09–J18)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Influenza and pneumonia. Canberra: AIHW.
Chronic obstructive pulmonary disease (J40–J44)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Chronic obstructive pulmonary disease (COPD). Canberra: AIHW.

ICD-10 Code Groupings	Citation(s) for general population mortality rate data
Liver disease (K70–K76)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Liver disease. Canberra: AIHW.
Musculoskeletal system (M00–M99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All diseases of the musculoskeletal system and connective tissue. Canberra: AIHW.
Kidney failure (N17–N19)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: Kidney failure. Canberra: AIHW.
All pregnancy, childbirth and the puerperium (O00–O99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All pregnancy, childbirth and the puerperium. Canberra: AIHW.
Congenital conditions (Q00–Q99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All congenital malformations, deformations and chromosomal abnormalities. Canberra: AIHW.
Signs/symptoms not elsewhere classified (R00–R99)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified. Canberra: AIHW.
External causes of death (V01–Y98)	Australian Institute of Health and Welfare (AIHW) 2018. GRIM (General Record of Incidence of Mortality) books 2016: All external causes of morbidity and mortality. Canberra: AIHW.

* Data from the three listed General Record of Incidence of Mortality (GRIM) books were compiled to calculate general population mortality rates for the 'lymphoid/ haematopoietic cancer' COD category.

† General population mortality rates for 'non-CVD/non-cancer' deaths were calculated *de novo* using data from the all-cause, CVD (I00–I99), cancer (C00–D48) and diabetes (E10–E14) GRIM books (i.e. CVD, cancer, and diabetes deaths were subtracted from all-cause deaths, with the resultant numerator divided by the relevant population size to generate annual rates per 100,000).

Table S1. Clinical characteristics of NDSS registrants by calendar year

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
n	471,906	519,354	564,652	607,261	650,388	694,798	742,502	791,777	843,893	899,986	948,977	994,369	1,033,369
Current age, y	62 ± 14	62 ± 14	63 ± 14	63 ± 14	63 ± 13	64 ± 13	64 ± 13	64 ± 13	64 ± 13	64 ± 13	65 ± 13	65 ± 13	65 ± 13
Age at diagnosis, y	56 ± 14	57 ± 14	57 ± 14	56 ± 13	56 ± 13	56 ± 13	57 ± 13	56 ± 13	56 ± 13	56 ± 13	56 ± 13	56 ± 13	56 ± 13
Age at registration, y	58 ± 14	58 ± 14	58 ± 14	58 ± 14	58 ± 13	58 ± 13	58 ± 13	58 ± 13	58 ± 13	57 ± 13	57 ± 13	57 ± 13	57 ± 13
Sex, % male	51.6	51.6	51.7	51.8	52.0	52.2	52.4	52.6	52.9	53.1	53.3	53.6	53.7
Medications [*]													
Insulin, %	14.9	17.7	18.5	18.9	19.2	20.0	21.2	22.3	23.0	23.6	24.1	24.7	25.3
Metformin, %	-	-	-	-	-	-	-	-	-	-	69.3	71.2	72.9
Sulfonylurea, %	-	-	-	-	-	-	-	-	-	-	41.3	40.9	40.6
AGI, %	1.1	1.4	1.5	1.6	1.7	1.7	1.7	1.7	1.6	1.6	1.7	1.6	1.6
Thiazolidinedione, %		0.9	3.7	6.3	9.0	11.1	12.0	12.3	12.3	11.9	11.4	10.8	10.3
DPP-4 inhibitor, %							1.2	3.2	5.9	9.7	13.5	16.7	20.1
GLP-1 RA, %									0.3	0.9	1.6	2.3	2.9
SGLT2 inhibitor, %												0.1	1.0
Deaths, n	12,685	13,931	14,966	15,987	17,307	18,622	20,414	21,340	22,426	24,129	25,478	26,869	28,749
CVD (I00-I99)	4,671	4,958	5,155	5,442	5,693	6,052	6,651	6,803	6,940	7,322	7,548	7,856	8,492
Cancer (C00-D48)	3,339	3,769	4,153	4,518	4,915	5,265	5,761	6,133	6,395	6,844	7,146	7,622	7,866
Diabetes (E10-E14)	1,859	2,109	2,247	2,319	2,393	2,624	2,873	2,976	2,836	3,000	3,146	3,310	3,419
Non-CVD/non-cancer [†]	2,816	3,095	3,411	3,708	4,306	4,681	5,129	5,428	6,255	6,963	7,638	8,081	8,972
Age at death, y	76 ± 11	76 ± 11	76 ± 11	77 ± 11	77 ± 11	77 ± 11	78 ± 11	78 ± 11	78 ± 11	78 ± 11	78 ± 11	78 ± 11	79 ± 11

Counts/summary data for individual calendar years are derived from all individuals who were registered at any time during the calendar year.

Data are mean ± standard deviation except where indicated. 'Current' age refers to age at the beginning of the relevant calendar year.

[*] Percentages indicate proportions of individuals who received at least two prescriptions for a medication in the relevant drug class (except where duration to end of follow-up was <1 year from the date of first prescription, in which case the one prescription was accepted) and who initiated treatment before the end of the relevant calendar year. Data for metformin and sulfonylureas are not reported prior to 2012 due to some medications in this class not being eligible for Pharmaceutical Benefits Scheme (PBS) subsidies, leading to under-estimation of proportions treated in earlier years.

[†] The non-CVD/non-cancer category included all deaths where the underlying cause of death fell outside the ICD-10 code groupings for CVD, cancer and diabetes.

AGI, α-Glucosidase inhibitor; CVD, cardiovascular disease; DPP-4, dipeptidyl peptidase 4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium-glucose cotransporter 2.
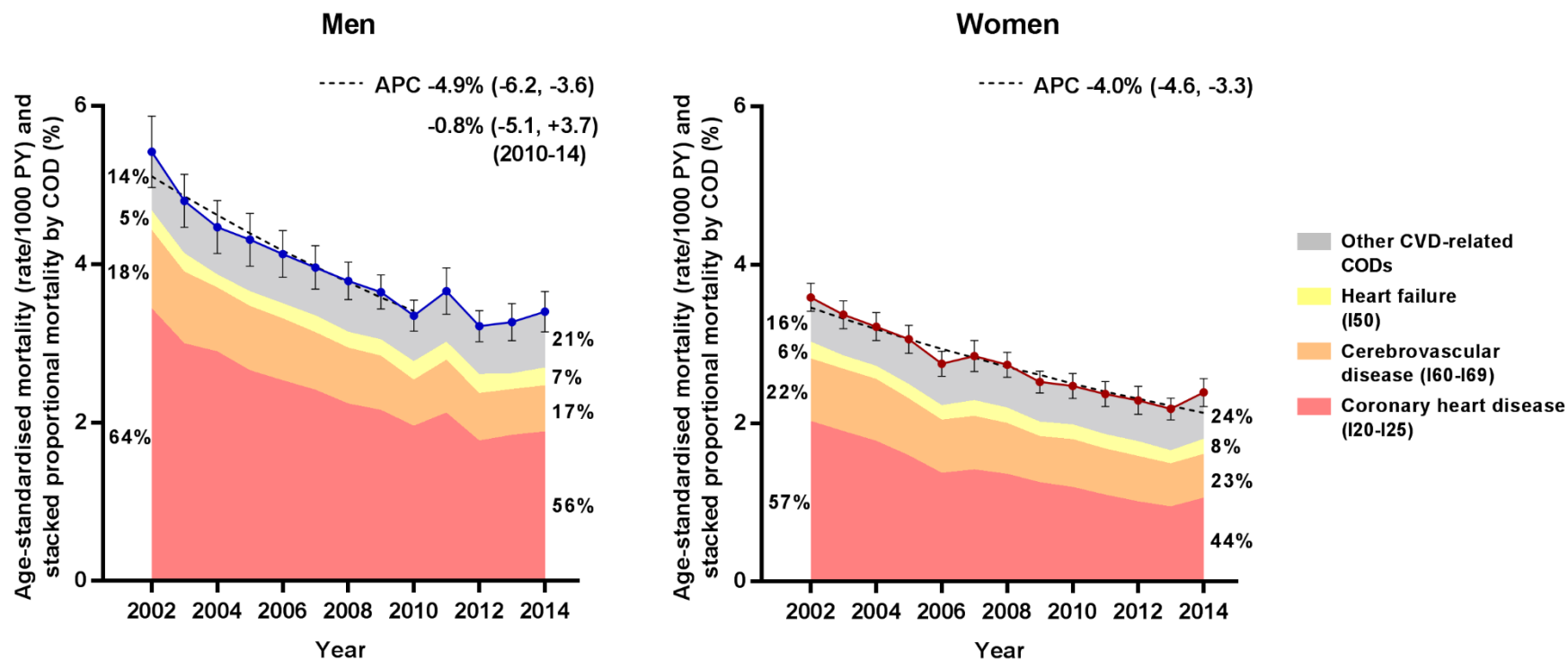
Figure S1. Age-standardised CVD mortality rate per 1000 person-years (PY) in men (left panel) and women (right panel) with type 2 diabetes, by calendar year. Stacked shadings represent proportions of deaths attributable to specific causes of death that each contributed ≥5% of total CVD mortality (data labels displayed for 2002 and 2014 only). Error bars represent 95% confidence intervals. Regression lines (dashed) are displayed for time periods over which the annual percentage change (APC) in age-standardised mortality was significantly different from zero at $P<0.05$.
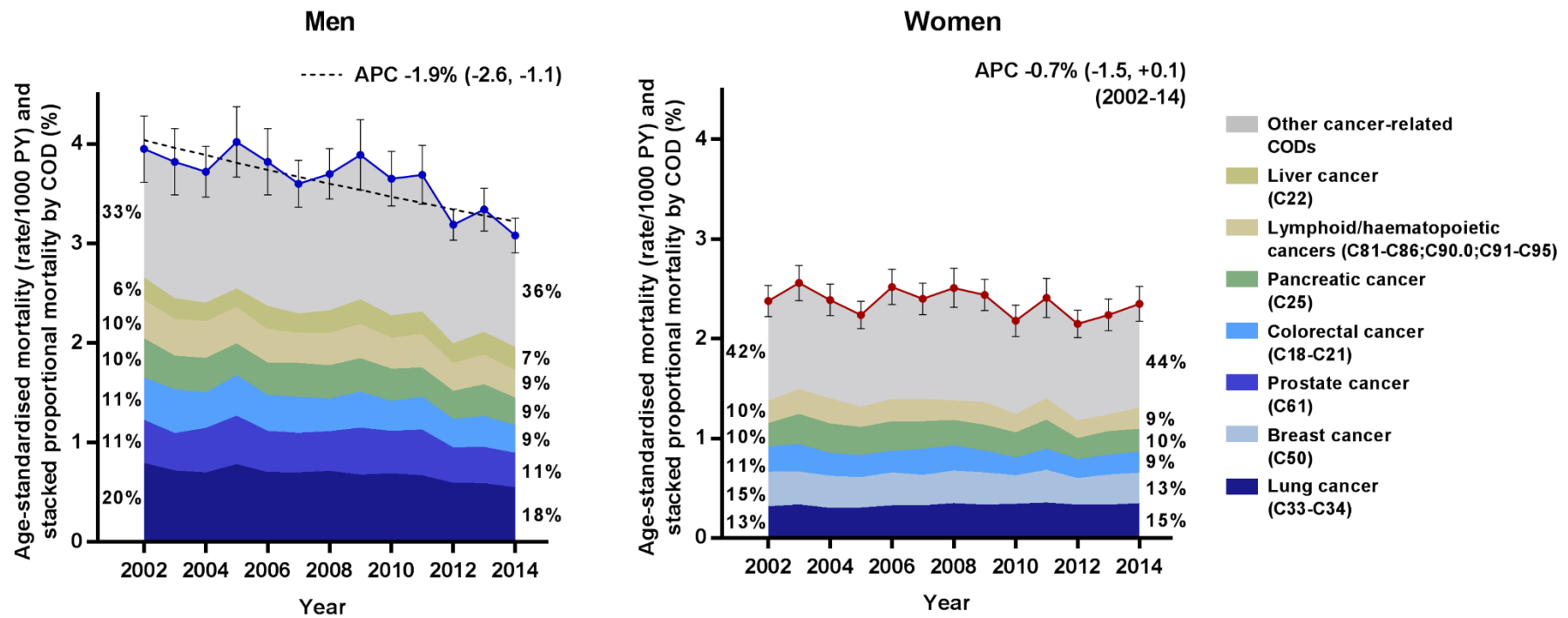
Figure S2. Age-standardised cancer mortality rate per 1000 person-years (PY) in men (left panel) and women (right panel) with type 2 diabetes, by calendar year. Stacked shadings represent proportions of deaths attributable to specific causes of death that each contributed ≥5% of total cancer mortality (data labels displayed for 2002 and 2014 only). Error bars represent 95% confidence intervals. Regression lines (dashed) are displayed for time periods over which the annual percentage change (APC) in age-standardised mortality was significantly different from zero at $P<0.05$.
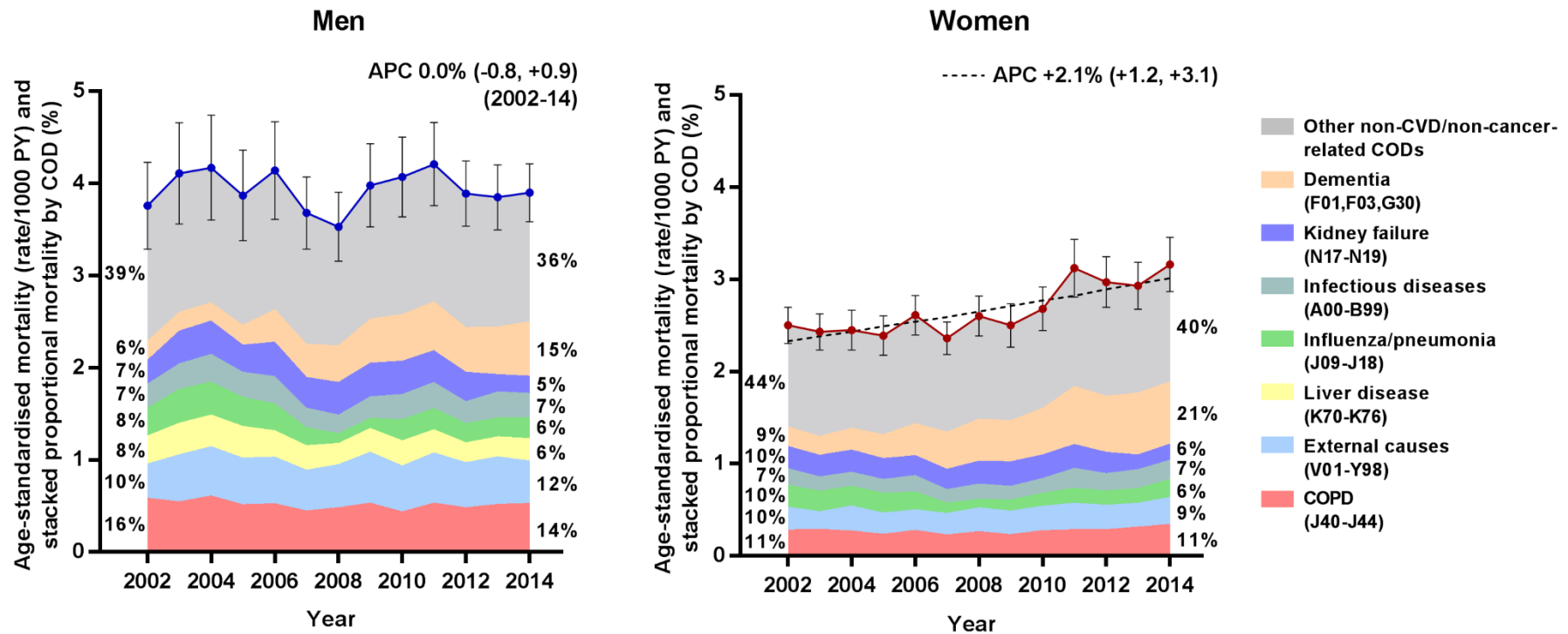
Figure S3. Age-standardised non-CVD/non-cancer mortality rate per 1000 person-years (PY) in men (left panel) and women (right panel) with type 2 diabetes, by calendar year. Stacked shadings represent proportions of deaths attributable to specific causes of death that each contributed ≥5% of total non-CVD/non-cancer mortality (data labels displayed for 2002 and 2014 only). Error bars represent 95% confidence intervals. Regression lines (dashed) are displayed for time periods over which the annual percentage change (APC) in age-standardised mortality was significantly different from zero at *P*<0.05.

NB: the marked change in proportional mortality due to dementia should be viewed in the context of known changes in coding practices from the mid-2000s, which also influenced mortality from dementia at a population level.[4]

Table S2: Mortality rates and MRRs over time in the youngest (10-39 years) men and women with type 2 diabetes

	2002-2005	2006-2010	2011-2014	P_{trend}
Men				
All-cause				
Mortality rate per 1000 PY	4.3 (3.6 – 5.0)	3.6 (3.1 – 4.1)	3.4 (2.9 – 3.9)	0.17
MRR	3.8 (3.2 – 4.4)	3.4 (2.9 – 3.9)	3.6 (3.1 – 4.2)	0.79
CVD				
Mortality rate per 1000 PY	0.8 (0.6 – 1.2)	0.5 (0.3 – 0.7)	0.7 (0.5 – 1.0)	0.88
MRR	5.9 (4.1 – 8.5)	3.3 (2.2 – 5.0)	6.5 (4.8 – 8.8)	0.85
Cancer				
Mortality rate per 1000 PY	0.7 (0.5 – 1.0)	0.8 (0.6 – 1.0)	0.5 (0.4 – 0.7)	0.53
MRR	4.8 (3.2 – 7.2)	5.7 (4.2 – 7.8)	4.2 (2.9 – 6.1)	0.73
Non-CVD/non-cancer				
Mortality rate per 1000 PY	2.2 (1.7 – 2.7)	1.9 (1.6 – 2.3)	1.8 (1.5 – 2.2)	0.12
MRR	2.5 (2.0 – 3.2)	2.4 (2.0 – 3.0)	2.6 (2.1 – 3.2)	0.77
Women				
All-cause				
Mortality rate per 1000 PY	1.2 (1.0 – 1.4)	1.5 (1.3 – 1.8)	2.2 (1.9 – 2.5)	0.060
MRR	2.2 (1.8 – 2.7)	3.0 (2.6 – 3.5)	4.6 (3.9 – 5.4)	0.055
CVD				
Mortality rate per 1000 PY	0.3 (0.2 – 0.4)	0.3 (0.2 – 0.5)	0.4 (0.3 – 0.6)	0.059
MRR	4.6 (3.1 – 6.8)	5.9 (4.2 – 8.3)	7.8 (5.4 – 11.3)	0.018
Cancer				
Mortality rate per 1000 PY	0.2 (0.1 – 0.3)	0.4 (0.3 – 0.5)	0.3 (0.2 – 0.5)	0.46
MRR	0.9 (0.6 – 1.6)	2.2 (1.6 – 3.1)	2.4 (1.6 – 3.5)	0.37
Non-CVD/non-cancer				
Mortality rate per 1000 PY	0.6 (0.4 – 0.8)	0.7 (0.5 – 0.9)	1.3 (1.1 – 1.6)	0.20
MRR	1.9 (1.5 – 2.5)	2.4 (1.9 – 3.1)	4.8 (3.9 – 5.8)	0.17

Data are mortality rates per 1000 person-years (PY), or mortality rate ratios (MRRs) with 95% confidence intervals. P_{trend} <0.05 indicates a significant change over time.
CVD, cardiovascular disease.

References

1.	Koye DN, Magliano DJ, Reid CM, et al. Trends in Incidence of ESKD in People With Type 1 and Type 2 Diabetes in Australia, 2002-2013. *Am J Kidney Dis* 2019; **73**: 300-8.
2.	Becker R, Silvi J, Ma Fat D, L'Hours A, Laurenti R. A method for deriving leading causes of death. *Bull World Health Organ* 2006; **84**: 297-304.
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