Lifetime risk and years lost to type 1 and type 2 diabetes in Denmark 1996–2016

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Abbreviations

APC — Age-Period-Cohort
CI — Confidence interval
DM — Diabetes mellitus
ESM — Electronic supplementary material
ICD — International classification of disease
M — Men
PY — Person-years
T1D — Type 1 diabetes
T2D — Type 2 diabetes
W — Women
YLL — Years of life lost

1 Abstract

Objective Lifetime risk and life time lost to diabetes are measures of current diabetes burden in a population. We aimed at quantifying these measures in the Danish population.

Research Design and Methods We modeled incidence and mortality of type 1 and type 2 diabetes and non-diabetes mortality based on complete follow-up of the entire population of Denmark 1996-2016. A multistate model with these transition rates wer used to assess the lifetime risk of diabetes as well as the difference in expected life time betewen persons with type 1 and type 2 diabetes and persons without.

Results In 2016 the life time risk of type 1 diabetes was 1.1% and for type 2 diabetes 24%, the latter a 50% increase from 1996.

For 50 year old persons the lifetime lost was 6.6 years for type 1 diabetes and 4.8 years for type 2 diabetes. These figures have been declining over the study period.

At 2016, the total foreseeable life lost in Denmark among type 1 diabetes patients was 182,000 years and among type 2 diabetes patients 766,000 years, corresponding to 6.6 years and 3.0 years per person, respectively.

Conclusion At the individual level, improvement in the disease burden both for type 1 diabetes and type 2 diabetes have occurred. At the population level the increasing number of type 2 diabetes patients has contributed to a large increase in the total loss of life time.

2 Introduction

Relatively few studies have looked at lifetime lost to diabetes [1, 2, 3, 4, 5] and even fewer have provided figures of the lifetime risk of diabetes [1, 6, 7, 2]. The lifetime lost or years of life lost to a disease have been given many interpretations in the literature (for an overview see [8]). In this study we used the standard definition from demography, namely as the difference in expected lifetime between persons with and without diabetes at a given age. We base our calculations of lifetime risk and of life time lost to diabetes on a proper multistate model taking both type 1 diabetes and type 2 diabetes into account.

3 Reseach Design and Material

3.1 Data

We used a Danish Diabetes Register [9] linked to the total population of Denmark, including the causes of death register. We constructed tables of person-years, incident cases of type 1 diabetes, type 2 diabetes and deaths by cause for the entire Danish population subdivided by current diabetes status (no diabetes, type 1 diabetes, type 2 diabetes). The causes of death used were Cardiovascular disease (ICD10: I00–I999), Cancer (ICD10: C00–D099, so carcinoma *in situ* are *in*cluded, benign and unspecified tumours *ex*cluded), Respiratory (ICD10: J00–J999) and other causes. These tables were classified by sex, age and date of follow-up and date of birth in 1-year intervals, so called Lexis triangles, [10], further details are given in the electronic supplementary material (ESM).

3.2 Statistical methods

We fitted models for incidence rates of type 1 diabetes and type 2 diabetes, and cause-specific mortality rates for persons without diabetes and with type 1 diabetes and type 2 diabetes separately. All models were age-period-cohort (APC) models with smooth effects of current age, date of follow-up (period) and date of birth (cohort), providing estimated age-specific rates at each 1 January 1996–2017. Analyses were done separately for men and women — for further details, see the ESM.

Estimated rates were used in a multistate model with states no diabtes, type 1 diabetes, type 2 diabetes and the four causes of death.

3.3 Measures

The lifetime risk of diabetes is the probability of getting diabetes before death. The expected lifetime (at birth) is the area under the survival curve, so the lifetime lost to diabetes is the difference in the area *between* the survival curves for a person with and a person without diabetes. If we condition on being alive at a given age, we used the *conditional* survival curves for that age. We subdivided the years of life lost by cause of death [8].

We used the age-specific rates at each 1 January to compute the lifetime risk of type 1 diabetes and type 2 diabetes and the years of life lost to different causes of death. We also computed the *population* burden as the future years of life lost, both among prevalent cases of diabetes at a given date and among persons diagnosed with diabetes during a given year. A detailed account of methods used for computation of these measures is in the ESM.

4 Results

In the study period 1996–2016 incl. there were 19,712 type 1 diabetes diagnoses and 343,952 type 2 diabetes diagnoses, while there was 12,762 deaths among type 1 diabetes patients, 149,000 among type 2 diabetes patients and 988,569 among persons without diabetes (table ESM 1). The dominant single cause of death was CVD except for type 1 diabetes where the dominant cause of death was other causes.

Lifetime risk of diabetes The lifetime risk of type 1 diabetes declined from 2.0 to 1.2% for men and from 1.5 to 1.0% for women over the study period, while lifetime risk for type 2 diabetes showed a peak around 2011 of more than 30% for men and 25% for women. (driven by the very high recorded incidences that year [9]). The lifetime risk of type 2 diabetes was 26% for men and 21% for women at 2017; corresponding to increases of 51 and 36% since 1996 (figure 1, table 1).

Expected life time In the study period, the expected lifetime (at birth) without diabetes increased from 70.2 to 74.4 for men and from 75.5 to 78.8 years for women. At the population level, the expected life time spent (sojourn time) with type 1 diabetes was 0.6 years for men and 0.5 years for women, unchanged over the study period; while the expected life time with type 2 diabetes increased from 2 to 4.6 years, similar for men and women, table 1. Thus, of the increase in expected lifetime in the period more than half were expected to be years with type 2 diabetes (table 1).

Years of life lost to diabetes In 2017, the lifetime lost to type 1 diabetes was 8.7 years at age 20, and about 5.5 years at age 60 (table ESM 4). Life time lost to type 2 diabetes at age 60 was 3.8 years (table ESM 5), so type 1 diabetes carries about 30% higher life time loss compared to type 2 diabetes (figure 2, ESM tables 4–5), reflecting the earlier diagnosis and hence longer duration of diabetes at a given age for type 1 diabetes as compared to type 2 diabetes. We also found that the years lost to diabetes have been diminishing over the study period, at age 50 from about 9 to 7 years for type 1 diabetes and from 8 to 5 years for type 2 diabetes.

Future years of life lost The future years of life lost among the *prevalent diabetes patients* — the currently accumulated future population burden in Denmark — was 947,600 years in 2017 (table ESM 2), 19% of which were among persons with type 1 diabetes, despite only 10% of Danish diabetes patients are type 1 diabetes [9]. The average future lifetime lost was 6.6 years for type 1 diabetes and 3.0 years for type 2 diabetes, partly attributable to different age-distribution.

The *extra* future lifetime lost among *newly diagnosed diabetes patients* in a single year was around 70,000 years during 2016, some 10% of these from type 1 diabetes, even if only 5% of newly diagnosed cases are type 1 diabetes (table ESM 3). The average lifetime lost for persons diagnosed in 2016 were 8.2 for type 1 diabetes and 3.6 for type 2 diabetes (figure ESM 2)

For both these measures we found an increase at the population level over time, but at the *individual* level we found that the *average* lifetime lost among patients were decreasing over the study period, over the last 10 years some 35% for type 1 diabetes, but less than 10% for type 1 diabetes (ESM tables 2 & 3).

Years of life lost by cause of death We found that the major contributor to years of life lost in type 1 diabetes (ESM table 4, figure ESM 4–7) was other causes of death (4.1 years at age 50) and only second CVD (2 years at age 50), whereas respiratory causes contribute slightly less than 1 year throughout the age range. Cancer contributes almost nothing in type 1 diabetes women and a negative 1 year among type 1 diabetes men. In type 2 diabetes (table ESM 5, figure ESM 4–7) other causes and CVD contribute similar amounts of life lost—about 1.5 years each at age 50, and respiratory causes less than 0.5 years.

5 Conclusion

Our study is the first to simultaneously evaluate the life time risk as well as the life time lost to type 1 diabetes and type 2 diabetes in an entire population using a proper multistate methodology. We evaluated both the individual and the population level of years of life lost to diabetes.

We found the life time risk of type 1 diabetes to be just over 1% and that of type 2 diabetes to be about 25% — both of these figures properly account for the competing type of diabetes as well as death, and the lifetime risk of any type of diabetes is therefore 26%.

Whichever way the life time lost to diabetes is illustrated, there has been a very clear improvement over the last two decades at the individual patient level, but the overall population burden, particularly for type 2 diabetes, has been massively increasing.

Life years lost to type 1 diabetes are some 30% higher than to type 2 diabetes at any given age. This may be due to longer exposure to risk factors for acute and chronic micro- and macrovascular complications to diabetes with earlier onset. Furthermore, the aggressive approach to manage cardiometabolic risk factors in type 2 diabetes is less well documented in type 1 diabetes, and quality registers have proven less favorable blood pressure- and lipid levels in type 1 diabetes compared to type 2 diabetes as well as some renal- and cardio-protective under-treatment [11].

A number of studies [4, 12, 5] have used sub-optimal methods for calculations or very crude model assumptions, and are therefore not directly comparable to ours. The studies by Narayan *et al.* [1] and Gregg *et al.* [2] use similar methodology as we, comparing the mortality among persons with and without diabetes at a given survey date (ignoring subsequent diabetes development — not explicitly mentioned in any of the papers) which gives a more valid picture of the life time lost to diabetes. The most recent study by Gregg *et al.* arrived at years of life lost to diabetes at age 40 for white men of 5.8 and white women 6.8 years in the period 2000–11, where we found 7.3 years and 7.0 years in 2005.

Livingstone *et al.* [3] provided estimates of lifetime lost to type 1 diabetes in Scotland for the period 2008–10 of 9.2 years for men and 10.8 years for women aged 40. Hou *et al.* [13] estimated the lifetime lost to type 1 diabetes in Australia for the period 1997–2010 to 10.0 years for men and 11.2 years for women aged 40. For 2008 we found 6.4 years for men 6.2 years for women at age 40, somewhat smaller than the American and Australian studies.

Strengths and weaknesses A major strength of our study is the total population coverage which eliminates sampling biases, and the use of a multistate model to compute realistic survival curves for persons without diabetes, taking the future possibility of both type 1 diabetes and type 2 diabetes into account. Moreover, we used 1 month updating intervals in model updating, minimizing the approximation bias, and we took calendar time

and cohort trends in rates into account, enabling us to derive these measures for successive years, and thus realistically account for trends.

One study weakness is potential misclassification of insulin treated type 2 diabetes as type 1 diabetes in the early years of the diabetes register (before 2005). Thus years of life lost to type 1 diabetes may be underestimated before 2005 due to contamination with type 2 diabetes patients.

5.1 Conclusion

Our study shows that there has been a decrease in lifetime risk of T1d to slightly over 1% and an increase in type 2 diabetes risk to 25%

Further, we demonstrated a decline in the individual burden of type 2 diabetes over the last two decades, but also clearly demonstrates that the population burden is increasing, indicating that preventive measures have not had the desired effect yet, and in particular that the burden of type 1 diabetes still is quite high, despite decreasing life time risk.

6 Paraphernalia

Data availability

The data base for this study are population wide registers, placed at our disposal on the servers of Statistics Denmark. They are barred from release to the public on grounds of confidentiality.

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Duality of interest

BC and MEJ own shares in NovoNordisk. BC has received lecture and consultancy fees from NovoNordisk and LeoPharma. MEJ is PI on a trial sponsored by AstraZeneca, and received research grants from AMGEN AB, Astra Zeneca and Sanofi Avensis,

Contribution statement

BC and MEJ conceived the structure of the underlying register. PFR provided support for obtaining data access and contributed to data definition. BC detailed and developed the study and the statistical methods needed, performed all data analysis, and wrote a first draft of the manuscript. MEJ and PFR contributed substantially to the writing of the manuscript. All authors contributed to critical revision and take responsibility for the content.

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Table 1: *Life time risk, expected lifetime spent with diabetes and life time lost by type of diabetes, sex and date (1 January each year). Note the different ages at calculation of life lost for T1D and T2D, accommodating the different age-distributions of T1D and T2D.*

	Lifetime risk (%)		Expected lifetime (years) spent with			Life time lost (years) to T1D, at ages				T2D, at ages			
Date	T1D	T2D	no DM	T1D	T2D	25	40	50	60	40	50	60	75
Men													
1996	2.0	17.5	70.2	0.6	2.1	9.6	8.3	6.6	4.7	9.5	7.7	5.7	2.9
1999	1.7	19.0	70.9	0.5	2.4	11.4	10.0	8.2	6.1	8.7	7.1	5.2	2.7
2002	1.6	20.6	71.5	0.5	2.8	12.7	11.1	9.3	6.9	8.1	6.5	4.9	2.4
2005	1.5	23.3	71.8	0.5	3.4	13.2	11.6	9.7	7.3	7.3	5.9	4.4	2.2
2008	1.5	28.1	71.4	0.5	4.4	13.6	12.0	10.1	7.8	6.4	5.1	3.9	2.0
2011	1.4	31.5	71.4	0.6	5.2	12.4	11.0	9.4	7.5	5.7	4.6	3.5	1.9
2014	1.3	29.7	72.7	0.6	5.1	10.2	9.1	7.9	6.4	5.6	4.6	3.6	2.0
2017	1.2	26.4	74.4	0.6	4.6	8.1	7.3	6.3	5.2	5.7	4.7	3.7	2.1
Women													
1996	1.5	15.5	75.5	0.5	2.0	10.9	9.7	8.3	6.4	9.5	8.1	6.3	3.5
1999	1.3	16.5	75.9	0.4	2.3	11.5	10.3	9.1	7.1	8.6	7.3	5.7	3.2
2002	1.1	17.7	76.3	0.4	2.6	11.9	10.8	9.5	7.7	7.8	6.6	5.1	2.9
2005	1.1	19.8	76.5	0.4	3.2	12.4	11.2	9.9	8.1	7.0	5.9	4.6	2.5
2008	1.1	23.4	76.2	0.4	4.0	12.6	11.4	10.2	8.4	6.2	5.2	4.0	2.1
2011	1.0	25.7	76.3	0.5	4.7	11.4	10.4	9.4	7.9	5.7	4.8	3.7	2.0
2014	1.0	23.9	77.4	0.5	4.5	9.8	9.0	8.1	6.9	5.6	4.8	3.7	2.0
2017	1.0	21.1	78.8	0.5	4.1	8.2	7.6	6.9	6.0	5.7	4.9	3.8	2.1

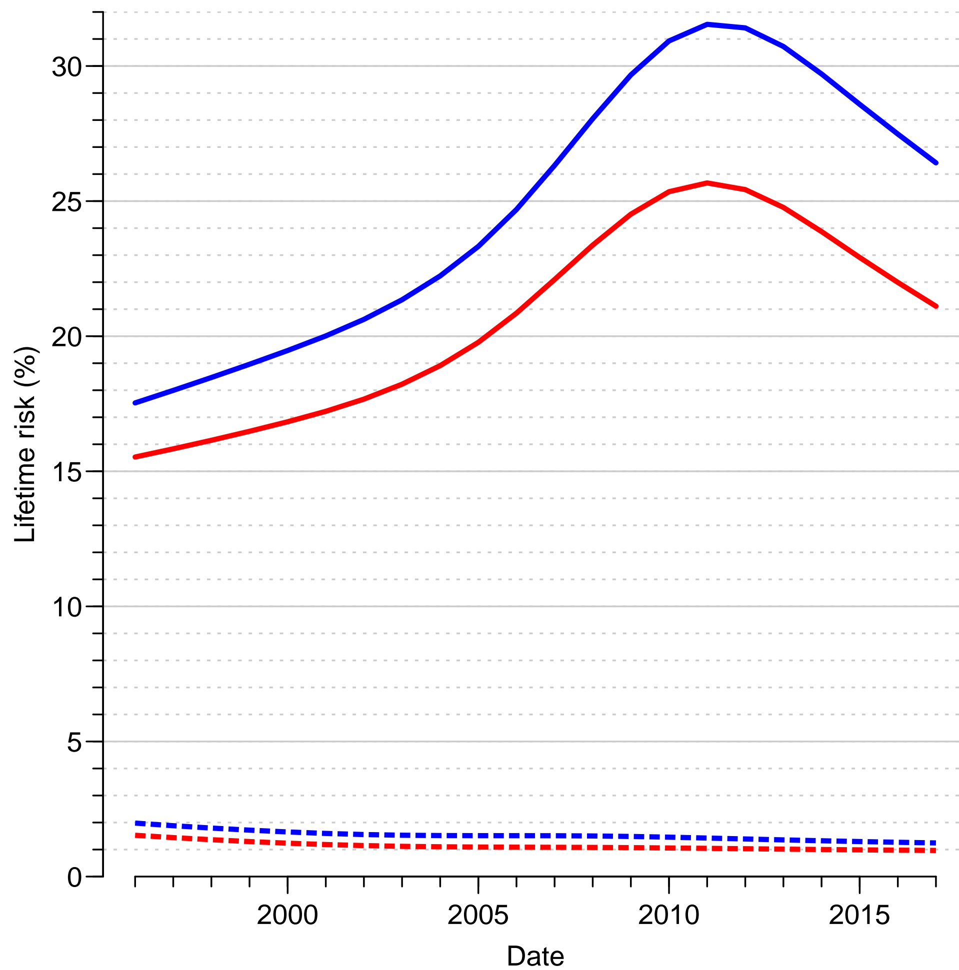

Figure 1: *Lifetime risk of T1D and T2D by sex and date of reference. The calculations are based on annual estimated cross-sectional incidence and mortality rates from age-period-cohort models for incidence and mortality.*

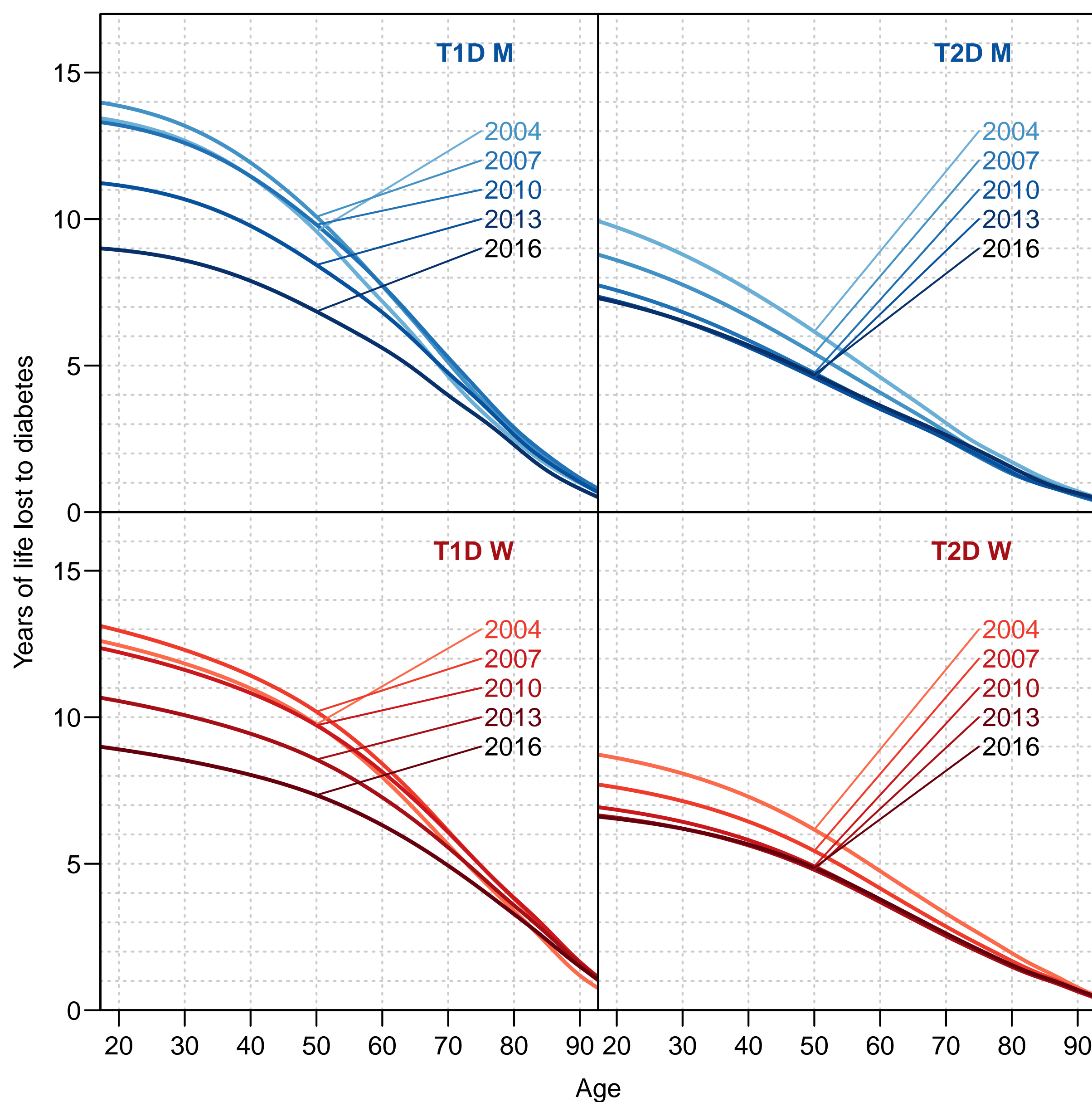

Figure 2: *Years of life lost to T1D and T2D at 1 January 2004,2007,...,2017 by sex and type of diabetes. The calculations are based on annual estimated cross-sectional incidence and mortality rates from age-period-cohort models for incidence and mortality.*

Lifetime risk and years lost to type 1 and type 2 diabetes in Denmark 1996–2016

Electronic Supplementary Material

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1 Calculation of life expectancy and lifetime lost

As it is common, we derived this measure for persons at different ages, for example the difference in expected residual lifetime for a person aged, say, 64 with diabetes and a person aged 64 without diabetes. This is a measure of the *individual* (age-specific) burden (at a given date).

1.1 Definition and tradition

The life expectancy as reported by most statistics bureaux is the area under the survival curve constructed from cross-sectional age-specific mortality rates[1]. It represents the expected lifetime of a person at birth under the assumption that the age-specific mortality rates remain constant during the person's life. This measure may also be reported for persons that have attained a certain age, a; the expected *residual* life time at age a. This will typically appear as a column in life tables, see *e.g.* https://dst.dk/Site/Dst/Udgivelser/GetPubFile.aspx?id=29442&sid=befudv2017, table 4.7, p. 45. The expected residual life time at age a is derived as the area under the *conditional* survival curve given survival till age a.

1.2 Lifetime lost

Lifetime lost to a disease comes in many guises, see for example [2], but here we shall use the standard definition as the difference between the expected residual lifetimes of a diseased person and a person of the same age without the disease. This is the area between the survival curves for persons with and without the disease ('years of life lost', YLL), formally:

$$\text{YLL}(a) = \int_a^\infty S_{\text{pop}}(u|a) - S_{\text{dis}}(u|a)\,\text{d}u$$

where $S(u|a)$ is the probability of surviving till age u, given attained age a. In simple cases with only one time scale and only transition from alive to dead, $S(u|a) = S(u)/S(a)$, but in more realistic situations this is not the case.

Andersen [1] also introduced the "τ-restricted" life expectancy and the corresponding lifetime lost by considering only a time span of τ after the age we refer to; formally we compare the area between the *conditional* survival curves in the interval $[a, a+\tau]$:

$$\text{YLL}_\tau(a) = \int_a^{a+\tau} S_{\text{pop}}(u|a) - S_{\text{dis}}(u|)\,\text{d}u$$

Thus, the prerequisite for calculation of life lost to a disease is the availability of survival curves for diseased and non-diseased persons. Or more specifically, *conditional* survival curves given survival to a given (set of) age(s), $S_{\text{pop}}(u|a)$. Such survival curves can be derived from the age-specific mortality rates; in some cases disease incidence rates are needed too — see below.

We may compare population survival with either patients alive at a given age (prevalent cases) or patients diagnosed at a given age (incident cases). If we assume that mortality

[1] A short mathematical derivation of this can be found in https://bendixcarstensen.com/AdvCoh/relations.pdf.

rates depend on disease duration these two will be different. In our data we only have observed diabetes duration up to 20 years, and the calculations would need duration effects till at least 50 years, so we do not have the data basis for calculating life lost at a given age at diagnosis.

1.3 Constructing survival curves

The survival curve for persons with diabetes (or newly diagnosed with diabetes) at a given age is a simple transformation of the age-specific mortalities, μ_{DM} (with or without duration included):

$$S_{\mathrm{DM}}(t|a) = \exp\left(-\int_a^t \mu_{\mathrm{DM}}(u)\,\mathrm{d}u\right)$$

On the other hand, a comparison survival curve for persons without disease can be computed in three different ways:

1. use mortality rates among non-diseased persons (μ_{noDM}), transform these to a survival curve by $S_a(t|a) = \exp(-\int_a^t \mu_{\mathrm{noDM}}(u)\,\mathrm{d}u)$, and compute the integral under this curve. This will *over*-estimate the survival among persons without diabetes and hence the expected lifetime among persons without disease, because it ignores the possibility that a non-diseased person later falls ill from diabetes and thus moves to a state with higher mortality.

2. use a multistate model with *both* incidence rates of disease and mortality rates of persons with and without disease to compute a survival function for a person that is non-diseased at a given age. The survival function is computed as the probability of being alive (diseased or non-diseased) at any given age. This is the correct way of computing the expected residual life time among persons without disease at a given time, because it refers to a real-world scenario of persons alive at a given age, with no assumptions about their future life-course.

3. use mortality rates for the *entire* population. This will (slightly) *under*-estimate the survival, because the mortality rates also include persons who already has the disease at age a. If the the disease is not too prevalent or does not carry too high excess mortality this approach may be a reasonable alternative to the correct.

In our calculations we used a more elaborate version of option 2 above, using a multistate model with separate incidence rates of T1D and T2D, as indicated in figure 1 using different rates for causes of death.

1.4 Models for rates

We used transitions and person years tabulated by current age, date of follow up (period) and date of birth (cohort) in 1-year classes (Lexis triangles). We fitted age-period-cohort models for all transition rates illustrated in figure 1, using a Poisson likelihood with log person years as offset, separately for men and women.

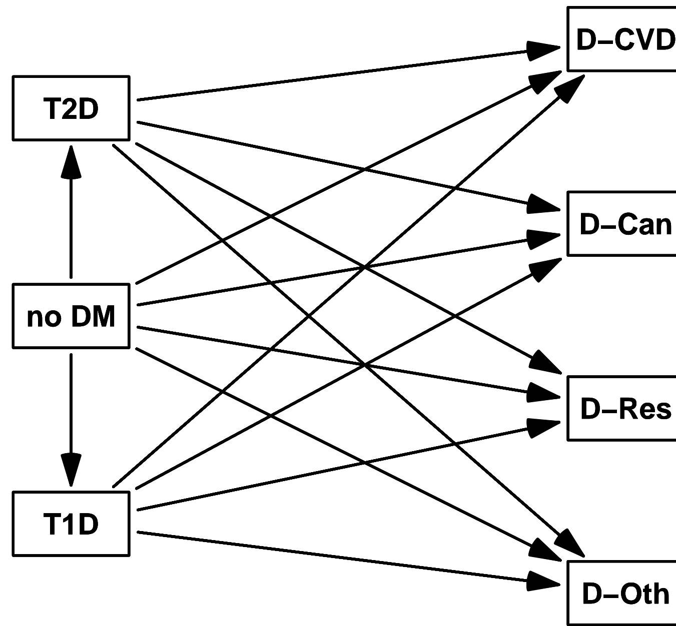

Figure ESM 1: *Multistate model used to compute the survival probabilities of persons in each of the states "no DM", "T1D" and "T2D". The right hand states refer to death from cardiovascular disease ("D-CVD"), cancer ("D-Can"), respiratory causes ("D-Res") and other causes ("D-Oth"). For persons in "T1D" and "T2D" the survival is just the probability of remaining in the state. For persons in state "no DM" at a given age the survival is the probability of being in either of the states "no DM", "T1D" and "T2D"*

1.5 Multistate-model based survival curves

We estimated a parametric model for each of the 14 transitions (age-period-cohort models with smooth effects) for each sex, and from these derived the estimated cross-sectional age-specific rates at 1996-01-01, 1997-01-01,. . . , 2017-01-01, in ages 0–1200 months. Thus, in line with the normal demographic practice we used cross-sectional rates to compute measures relating to lifetime experience.

The cross-sectional rates were used to construct 1-month transition probabilities between the states, one per transition illustrated in figure 1. We used three different initial state occupancy vectors; one with probability 1 in state "no DM", one in state "T1D" and one in state "T2D". These were then successively multiplied by the transition probability matrices, yielding the state probabilities at all ages.

The sum of the probabilities of being in any of the alive states at a given time were taken as the survival function for persons starting in each of the three transient states ("no DM", "T1D" and "T2D"). This calculation was repeated for persons starting at ages 0, 1, 2 etc.

Following Andersen [1] we used the differences in cumulative risks of each cause of death to decompose the total lifetime lost to each of the causes of death to T1D, resp. T2D.

1.6 Population related measures

The years of life lost to T1D resp. T1D are in principle unrelated to the Danish population in the sense that the measures applies to any population with incidence and mortality rates as the Danish, regardless of the age-composition of the population and patients.

But we also want to compute the population burden of diabetes in terms of the total number of years lost to diabetes in the population. This can be done in (at least) two different ways:

1. the total future lifetime lost for persons alive with diabetes at a given time (the beginning of a given calendar year, say).

2. the total future lifetime lost among those diagnosed with diabetes during a given period (a calendar year, say).

The first measure shows the annual burden of diabetes in the *current* population, but it will be very small because it conditions on diseased and non-diseased being a live at a given date

The second shows *extra future* burden incurred in those diagnosed in a *period* of one year, and as such is a more relevant measure.

2 Methodological issues

Most studies use the overall population mortality as basis for comparison (which is a reasonable approximation), and some use the non-diabetes mortality rates (which result in an over-estimate of life time lost). Incidentally, the studies based on the NHIS [6, 3] by virtue of the data available use an empirical approximation to the correct survival probabilities for persons alive without diabetes at a given time – only mortality among persons surveyed is available, not the future diabetes occurrence.

Some studies [5, 4] indicate they used Chiang's method for calculation of the life table probabilities. This method dates back to 1968 and is aimed at compensating for irregular distribution of deaths across wide age-intervals, a natural consequence of the absence of computers in 1968. Notably it requires input of the average time lived in the interval before death for those who die in an interval, but none of the studies detail how they estimated this quantity. This will in most cases give results indistinguishable from just using the standard mathematical relationship of cumulative risk (= life table probability) as the exponential of minus the cumulative rate. These studies have used 5-year intervals which induce an extra inaccuracy relative to 1-year intervals, or as we have done in our study 1 month intervals of age for calculation of transition probabilities.

The papers by Gregg *et al.* [3] and Narayan *et al.* [6] among others use an approach similar to ours by estimating rates in a multistate model and a Markov-chain approach to estimation of survival probabilities in different scenarios, the latter using a 1-year updating intervals. However, the updating interval should be chosen so small that the probability of transition from no diabetes to diabetes and further to death within a single interval is negligible. Which is not the cases in older ages in a 1-year interval, so these studies are likely to have a small extra bias from this.

Unlike the papers mentioned above, our study exploits the possibility from register data to build results on credible models for incidence and mortality rates (namely as smooth

continuous functions of age and calendar time) as well as using modern computing to arrive at results based on continuous time models, through using 1-month updating intervals for the Markov chain. This is a major strength of our study and can be implemented in any study — using 100 1-year age classes or 1200 1-month age classes makes little difference on a modern computer. The hurdle for many may be lack of experience with handling models with smooth continuous effects of time scales.

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Table ESM 1: *Events (diabetes diagnoses and deaths) and person-years (in 1000s) in the Danish population in the 21 year study period 1996–2016, subdivided by current diabetes status.*
The three parts of the P-years column correspond to the person-years in the three leftmost boxes (noDM, T1D, T2D) in figure 1. The 14 combinations of type of diabetes (2) and cause of death (4) on one hand and status (3) on the other hand correspond to the events (arrows) in 1. Of course there are no diabetes events among persons with diabetes.

Status	Diabetes cases		Deaths by cause					
Period	T1D	T2D	CVD	Cancer	Respir	Other	All	P-years
No diabetes								
1996-1998	3,478	33,986	58,088	42,494	15,170	43,916	159,668	15,623.6
1999-2001	2,994	36,887	55,457	42,406	14,917	41,430	154,210	15,726.0
2002-2004	2,816	49,185	50,897	40,506	15,295	41,733	148,431	15,808.1
2005-2007	2,780	44,326	42,956	40,444	14,122	42,943	140,465	15,872.1
2008-2010	2,734	56,453	36,812	39,304	15,031	44,762	135,909	16,019.6
2011-2013	2,477	69,728	31,855	39,093	14,811	40,947	126,706	16,105.7
2014-2016	2,433	53,387	29,588	38,229	14,137	41,226	123,180	16,301.0
1996-2016	19,712	343,952	305,653	282,476	103,483	296,957	988,569	111,456.1
T1D								
1996-1998	.	.	868	290	137	671	1,966	68.1
1999-2001	.	.	997	365	130	643	2,135	71.2
2002-2004	.	.	835	333	175	860	2,203	73.1
2005-2007	.	.	610	397	137	950	2,094	74.4
2008-2010	.	.	501	402	183	803	1,889	73.3
2011-2013	.	.	348	284	157	643	1,432	71.0
2014-2016	.	.	243	237	113	450	1,043	70.0
1996-2016	.	.	4,402	2,308	1,032	5,020	12,762	501.1
T2D								
1996-2016	.	.	4,402	2,308	1,032	5,020	12,762	501.1
1996-1998	.	.	8,133	2,788	1,114	3,564	15,599	212.6
1999-2001	.	.	8,559	3,556	1,294	4,005	17,414	269.6
2002-2004	.	.	8,084	4,025	1,860	5,199	19,168	341.0
2005-2007	.	.	7,485	4,760	1,973	6,414	20,632	421.0
2008-2010	.	.	7,080	5,508	2,562	7,416	22,566	502.6
2011-2013	.	.	7,546	6,704	3,013	7,907	25,170	631.1
2014-2016	.	.	7,850	7,965	3,584	9,052	28,451	718.1
1996-2016	.	.	54,737	35,306	15,400	43,557	149,000	3,096.0

Table ESM 2: *Future years of life lost (1000s) among* currently prevalent diabetes patients *each 1 January, and average years of life lost* per person *among these. Note that only every 3rd year is shown.*

		Total YLL (1000s)			Average YLL	
	Date	T1D	T2D	DM	T1D	T2D
Men	1996	85.1	149.4	234.4	6.9	4.9
	1999	110.9	188.2	299.2	8.4	4.6
	2002	129.8	222.8	352.6	9.5	4.3
	2005	138.8	266.8	405.6	9.9	3.9
	2008	148.1	276.8	424.9	10.3	3.4
	2011	141.4	310.5	451.8	9.6	3.1
	2014	121.2	377.9	499.1	8.0	3.0
	2017	99.9	428.5	528.4	6.4	3.1
Women	1996	74.7	150.6	225.3	7.8	4.8
	1999	86.6	173.5	260.2	8.6	4.4
	2002	94.8	192.6	287.3	9.1	4.1
	2005	102.2	223.3	325.5	9.7	3.7
	2008	108.5	225.4	334.0	10.0	3.2
	2011	103.2	248.4	351.7	9.3	3.0
	2014	92.7	303.7	396.3	8.1	2.9
	2017	81.9	337.3	419.2	6.9	3.0
M+W	1996	159.8	300.0	459.7	7.3	4.9
	1999	197.6	361.8	559.3	8.5	4.5
	2002	224.6	415.4	639.9	9.3	4.2
	2005	241.0	490.1	731.1	9.8	3.8
	2008	256.7	502.2	758.8	10.2	3.3
	2011	244.6	558.9	803.5	9.5	3.0
	2014	213.9	681.5	895.4	8.0	3.0
	2017	181.8	765.8	947.6	6.6	3.0

Table ESM 3: *Future years of life lost among* persons diagnosed each year *and average future years of life lost* per person *among these. Note that only every 3rd year is shown.*

		Total YLL			Average YLL	
	Year	T1D	T2D	DM	T1D	T2D
Men	1998	5,757	33,376	39,134	8.8	5.1
	2001	6,096	32,815	38,912	10.4	4.8
	2004	5,749	40,636	46,385	11.3	4.4
	2007	6,652	34,104	40,757	11.8	3.9
	2010	6,079	41,343	47,422	11.5	3.5
	2013	4,703	34,857	39,560	10.0	3.4
	2016	3,748	38,619	42,367	8.1	3.6
Women	1998	4,335	26,082	30,418	9.5	4.9
	2001	4,334	24,678	29,012	10.4	4.5
	2004	4,180	32,055	36,236	10.8	4.1
	2007	4,419	25,293	29,712	11.5	3.7
	2010	4,090	29,556	33,647	11.1	3.4
	2013	3,421	26,917	30,339	9.7	3.4
	2016	2,652	28,177	30,830	8.4	3.6
M+W	1998	10,093	59,460	69,553	9.1	5.0
	2001	10,431	57,494	67,925	10.4	4.7
	2004	9,929	72,693	82,622	11.1	4.3
	2007	11,072	59,397	70,470	11.7	3.8
	2010	10,170	70,900	81,070	11.4	3.4
	2013	8,125	61,775	69,900	9.9	3.4
	2016	6,401	66,797	73,198	8.2	3.6

Table ESM 4: *Years of life lost to T1D in the entire Danish population by cause of death. Note that only every 3rd year is shown.*

		CVD		Cancer		Respir.		Other		All causes	
Date	Age	M	W	M	W	M	W	M	W	M	W
1996	20	3.4	6.2	−2.0	−1.3	0.4	−0.1	7.9	6.4	9.7	11.2
	30	3.5	6.2	−2.0	−1.1	0.4	−0.1	7.3	5.7	9.3	10.6
	40	3.7	6.1	−1.9	−1.0	0.4	−0.1	6.1	4.7	8.3	9.7
	50	4.0	5.7	−1.6	−0.8	0.5	−0.2	3.6	3.6	6.6	8.3
	60	4.2	5.0	−1.3	−0.7	0.4	−0.4	1.4	2.3	4.7	6.4
	70	3.4	3.7	−1.2	−0.4	0.1	−0.5	0.4	1.3	2.7	4.1
	80	1.7	1.8	−0.8	0.0	0.2	−0.4	−0.1	0.6	1.1	2.0
1999	20	4.4	6.2	−2.2	−1.0	0.0	0.0	9.4	6.5	11.6	11.8
	30	4.5	6.3	−2.1	−0.9	0.0	0.0	8.7	5.8	11.1	11.2
	40	4.6	6.2	−2.0	−0.7	0.0	0.0	7.4	4.9	10.0	10.3
	50	4.9	5.8	−1.7	−0.5	0.1	−0.1	4.9	3.8	8.2	9.1
	60	5.1	5.2	−1.4	−0.5	0.0	−0.2	2.3	2.6	6.1	7.1
	70	4.2	4.1	−1.2	−0.5	−0.2	−0.3	1.0	1.6	3.7	4.9
	80	2.3	2.2	−0.8	−0.1	0.0	−0.3	0.3	0.8	1.8	2.6
2002	20	4.3	5.7	−2.1	−0.6	−0.3	0.2	11.0	6.9	12.9	12.2
	30	4.4	5.7	−2.0	−0.4	−0.3	0.2	10.2	6.1	12.3	11.6
	40	4.6	5.7	−1.9	−0.3	−0.3	0.1	8.7	5.2	11.1	10.8
	50	4.8	5.4	−1.6	−0.1	−0.2	0.1	6.3	4.1	9.3	9.5
	60	4.9	4.9	−1.2	−0.2	−0.2	0.0	3.4	3.0	6.9	7.7
	70	4.1	4.0	−1.1	−0.5	−0.4	−0.1	1.8	2.0	4.4	5.4
	80	2.3	2.3	−0.8	−0.1	−0.1	−0.2	0.9	1.1	2.3	3.1
2005	20	2.5	4.2	−1.4	0.1	−0.2	0.3	12.6	8.0	13.5	12.7
	30	2.6	4.3	−1.3	0.2	−0.2	0.3	11.8	7.2	12.9	12.0
	40	2.7	4.2	−1.1	0.4	−0.2	0.3	10.2	6.2	11.6	11.2
	50	2.8	4.1	−0.8	0.6	−0.1	0.3	7.8	5.1	9.7	9.9
	60	3.0	3.7	−0.4	0.4	0.0	0.2	4.8	3.8	7.3	8.1
	70	2.4	3.2	−0.5	−0.2	−0.1	0.1	2.9	2.8	4.8	5.8
	80	1.3	1.9	−0.5	−0.1	0.1	0.0	1.6	1.7	2.6	3.5

Table ESM 4: *(cont.) Years of life lost to T1D in the entire Danish population by cause of death. Note that only every 3rd year is shown.*

		CVD		Cancer		Respir.		Other		All causes	
Date	Age	M	W	M	W	M	W	M	W	M	W
2008	20	1.3	3.0	−0.3	0.5	0.1	0.5	12.8	8.9	13.9	12.9
	30	1.3	3.0	−0.2	0.7	0.1	0.5	12.0	8.1	13.2	12.2
	40	1.4	3.0	0.0	0.9	0.1	0.5	10.4	7.0	12.0	11.4
	50	1.5	2.9	0.3	1.0	0.2	0.4	8.1	5.8	10.1	10.2
	60	1.5	2.7	0.6	0.9	0.2	0.4	5.5	4.5	7.8	8.4
	70	1.2	2.3	0.4	0.1	0.3	0.3	3.4	3.5	5.3	6.2
	80	0.5	1.5	0.0	−0.1	0.4	0.2	2.0	2.3	2.9	3.9
2011	20	1.3	2.4	0.1	0.6	0.4	0.7	10.9	8.0	12.6	11.7
	30	1.3	2.5	0.2	0.7	0.4	0.7	10.2	7.3	12.0	11.1
	40	1.4	2.5	0.3	0.9	0.4	0.7	8.9	6.4	11.0	10.4
	50	1.4	2.4	0.6	1.0	0.4	0.6	7.0	5.3	9.4	9.4
	60	1.3	2.2	0.8	0.9	0.4	0.6	5.1	4.2	7.5	7.9
	70	0.9	1.9	0.5	0.1	0.5	0.5	3.3	3.3	5.2	5.9
	80	0.3	1.3	0.1	−0.2	0.6	0.5	1.9	2.2	2.8	3.8
2014	20	1.8	2.2	−0.4	0.4	0.6	0.9	8.4	6.6	10.4	10.0
	30	1.8	2.2	−0.3	0.4	0.6	0.9	7.9	6.0	10.0	9.5
	40	1.8	2.2	−0.2	0.6	0.6	0.8	7.0	5.3	9.1	9.0
	50	1.8	2.1	0.0	0.7	0.6	0.8	5.6	4.5	7.9	8.1
	60	1.5	2.0	0.0	0.6	0.5	0.7	4.3	3.6	6.4	6.9
	70	1.0	1.7	−0.1	0.1	0.6	0.7	3.0	2.9	4.5	5.4
	80	0.4	1.2	−0.3	−0.3	0.7	0.7	1.8	1.9	2.5	3.5
2017	20	2.1	1.9	−1.0	0.1	0.7	1.0	6.4	5.4	8.2	8.4
	30	2.1	1.9	−1.0	0.1	0.7	1.0	6.1	5.0	7.9	8.0
	40	2.1	1.9	−0.9	0.2	0.7	1.0	5.4	4.4	7.3	7.6
	50	2.0	1.9	−0.8	0.3	0.7	1.0	4.4	3.8	6.3	6.9
	60	1.7	1.7	−0.7	0.3	0.6	0.9	3.5	3.1	5.2	6.0
	70	1.2	1.5	−0.8	−0.1	0.6	0.8	2.7	2.5	3.7	4.7
	80	0.5	1.1	−0.6	−0.4	0.7	0.8	1.6	1.6	2.2	3.2

Table ESM 5: *Years of life lost to T2D in the entire Danish population by cause of death. Note that only every 3rd year is shown.*

		CVD		Cancer		Respir.		Other		All causes	
Date	Age	M	W	M	W	M	W	M	W	M	W
1996	20	6.8	6.6	−0.6	1.0	−0.7	−0.1	6.4	3.8	11.9	11.3
	30	6.8	6.4	−0.4	1.0	−0.6	−0.1	5.2	3.3	10.9	10.6
	40	6.6	6.1	−0.3	1.0	−0.6	−0.2	3.8	2.6	9.5	9.5
	50	6.3	5.9	−0.2	0.7	−0.6	−0.2	2.2	1.7	7.7	8.1
	60	5.8	5.6	−0.3	0.2	−0.6	−0.3	0.8	0.8	5.7	6.3
	70	4.7	4.9	−0.3	0.0	−0.5	−0.3	−0.1	−0.1	3.8	4.5
	80	2.9	3.0	−0.3	0.0	−0.3	−0.1	−0.3	−0.3	2.0	2.5
1999	20	5.2	5.1	−0.3	1.1	−0.5	0.0	6.6	3.9	11.1	10.2
	30	5.2	4.9	−0.2	1.2	−0.5	0.0	5.5	3.5	10.0	9.6
	40	5.0	4.7	0.0	1.1	−0.4	0.0	4.1	2.8	8.7	8.6
	50	4.8	4.5	0.0	0.8	−0.4	0.0	2.7	2.0	7.1	7.3
	60	4.5	4.3	−0.1	0.4	−0.4	−0.1	1.3	1.2	5.2	5.7
	70	3.6	3.9	−0.2	0.0	−0.4	−0.2	0.4	0.3	3.4	4.0
	80	2.3	2.4	−0.2	0.0	−0.2	−0.1	0.0	0.0	1.9	2.3
2002	20	4.0	3.8	−0.1	1.2	−0.3	0.2	6.8	4.0	10.3	9.3
	30	3.9	3.7	0.0	1.2	−0.3	0.2	5.7	3.6	9.3	8.7
	40	3.8	3.5	0.2	1.2	−0.3	0.2	4.3	3.0	8.1	7.8
	50	3.6	3.4	0.2	0.9	−0.2	0.1	2.9	2.2	6.5	6.6
	60	3.3	3.2	0.1	0.5	−0.2	0.0	1.7	1.4	4.9	5.1
	70	2.6	2.9	−0.1	0.1	−0.2	−0.1	0.8	0.7	3.2	3.6
	80	1.7	1.9	−0.2	0.0	−0.1	0.0	0.4	0.3	1.8	2.1
2005	20	3.0	2.7	0.1	1.3	−0.2	0.3	6.4	3.9	9.4	8.3
	30	3.0	2.6	0.2	1.3	−0.1	0.3	5.4	3.5	8.5	7.8
	40	2.9	2.5	0.4	1.3	−0.1	0.3	4.1	2.9	7.3	7.0
	50	2.8	2.4	0.4	1.0	−0.1	0.3	2.8	2.3	5.9	5.9
	60	2.5	2.3	0.2	0.6	0.0	0.2	1.8	1.5	4.4	4.6
	70	2.0	2.0	0.0	0.2	0.0	0.1	1.0	0.9	3.0	3.2
	80	1.3	1.4	−0.2	0.0	0.0	0.0	0.5	0.5	1.7	1.9

Table ESM 5: *(cont.) Years of life lost to T2D in the entire Danish population by cause of death. Note that only every 3rd year is shown.*

		CVD		Cancer		Respir.		Other		All causes	
Date	Age	M	W	M	W	M	W	M	W	M	W
2008	20	2.3	1.8	0.3	1.4	0.0	0.5	5.6	3.6	8.2	7.3
	30	2.3	1.8	0.5	1.4	0.0	0.5	4.6	3.2	7.4	6.9
	40	2.2	1.7	0.6	1.4	0.1	0.4	3.5	2.7	6.4	6.2
	50	2.1	1.6	0.6	1.1	0.1	0.4	2.4	2.1	5.1	5.2
	60	1.9	1.6	0.4	0.7	0.1	0.3	1.5	1.5	3.9	4.0
	70	1.5	1.4	0.1	0.2	0.1	0.2	0.9	0.9	2.6	2.7
	80	0.9	1.0	−0.1	0.0	0.1	0.1	0.5	0.6	1.4	1.6
2011	20	1.9	1.4	0.5	1.5	0.1	0.6	4.8	3.2	7.4	6.7
	30	1.9	1.4	0.6	1.5	0.1	0.6	4.0	2.8	6.7	6.3
	40	1.8	1.3	0.7	1.4	0.2	0.6	3.0	2.4	5.7	5.7
	50	1.7	1.3	0.7	1.2	0.2	0.5	2.0	1.9	4.6	4.8
	60	1.6	1.2	0.5	0.8	0.2	0.4	1.3	1.3	3.5	3.7
	70	1.2	1.1	0.2	0.3	0.2	0.3	0.8	0.8	2.5	2.5
	80	0.7	0.7	−0.1	0.0	0.2	0.2	0.5	0.6	1.3	1.5
2014	20	1.9	1.3	0.7	1.8	0.2	0.7	4.4	2.8	7.2	6.6
	30	1.9	1.2	0.8	1.7	0.2	0.7	3.6	2.5	6.5	6.2
	40	1.8	1.2	0.9	1.7	0.2	0.7	2.7	2.1	5.6	5.6
	50	1.7	1.1	0.9	1.4	0.2	0.6	1.8	1.7	4.6	4.8
	60	1.5	1.1	0.6	0.9	0.2	0.6	1.1	1.2	3.6	3.7
	70	1.2	0.9	0.3	0.5	0.2	0.4	0.8	0.7	2.5	2.6
	80	0.7	0.6	0.0	0.0	0.2	0.3	0.5	0.6	1.4	1.5
2017	20	1.9	1.2	1.0	2.1	0.2	0.8	4.1	2.5	7.2	6.5
	30	1.9	1.1	1.1	2.1	0.2	0.8	3.4	2.2	6.5	6.2
	40	1.8	1.1	1.1	2.0	0.2	0.8	2.6	1.9	5.7	5.7
	50	1.7	1.0	1.1	1.7	0.2	0.7	1.7	1.5	4.7	4.9
	60	1.6	1.0	0.8	1.2	0.2	0.7	1.1	1.0	3.7	3.8
	70	1.2	0.8	0.4	0.7	0.2	0.5	0.8	0.6	2.7	2.7
	80	0.8	0.6	0.0	0.2	0.2	0.3	0.6	0.5	1.6	1.6

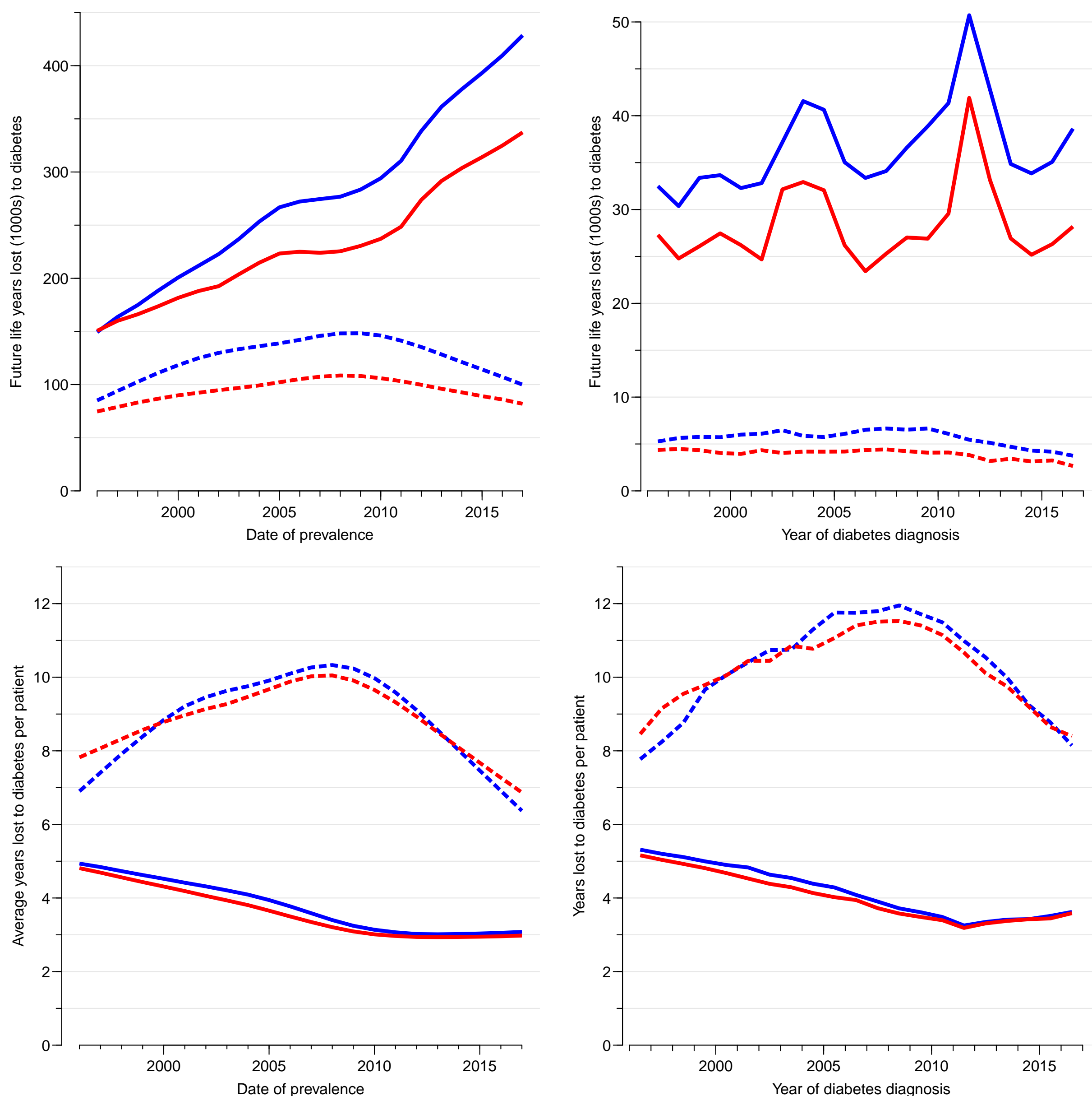

Figure ESM 2: *Upper panels: Total future years of life lost among all* currently prevalent *diabetes patients each 1 January (left) and among* newly diagnosed *patients each year (right). Lower panels:* Average *future years of life lost among all currently prevalent diabetes patients each 1 January (left) and among all diagnosed patients each year (right).*
Red lines are women, blue lines are men, broken lines are T1D and full lines are T2D.

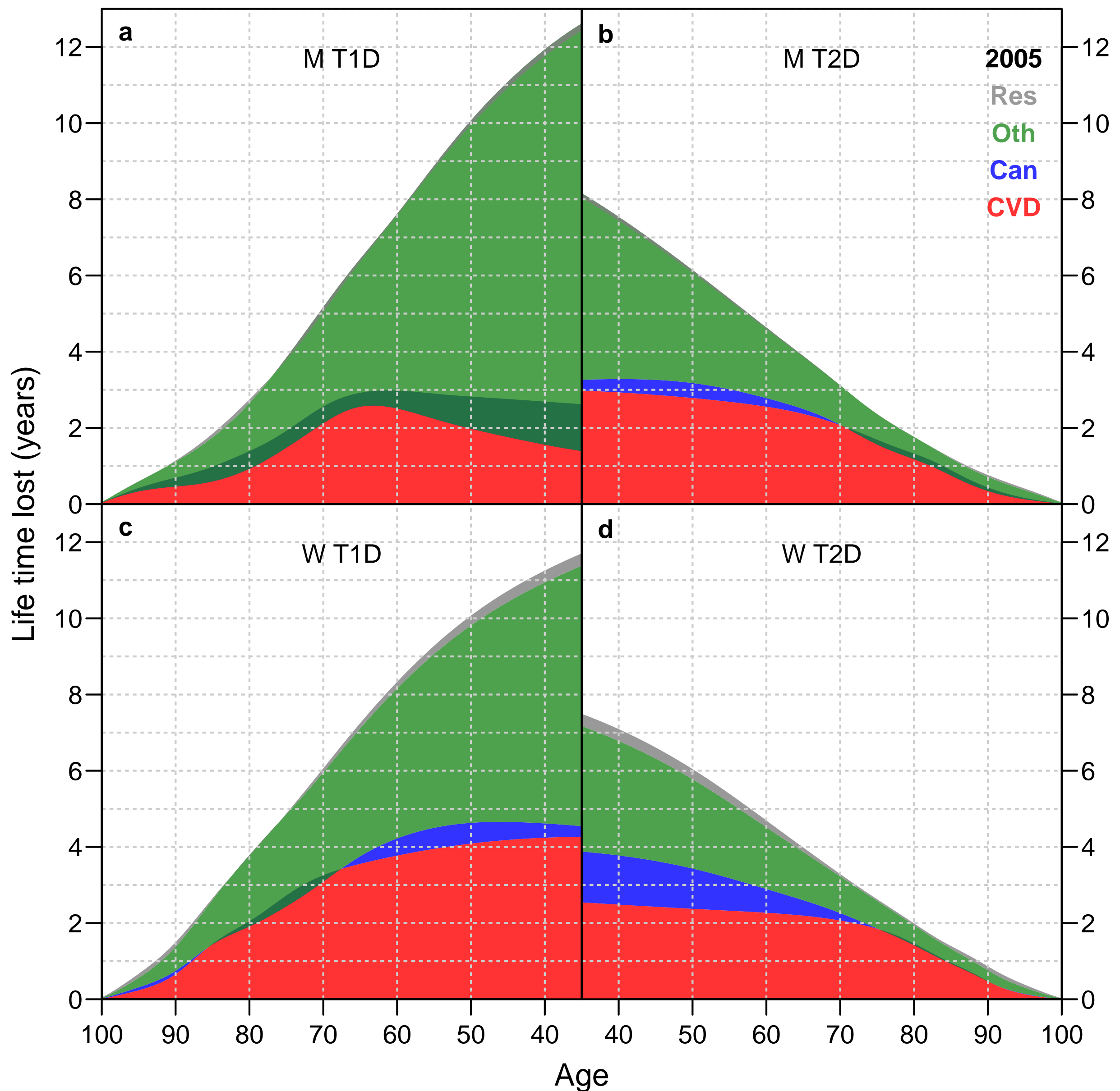

Figure ESM 3: *Years of life lost to different causes of death 2005 by sex, type of diabetes and age.*
The dark green areas in panels a and c is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue and green areas). This area is therefore part of both the CVD and the Other component.*
a: Men, T1D; b: Men, T2D; c: Women, T1D; d: Women, T2D. Colors: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD.

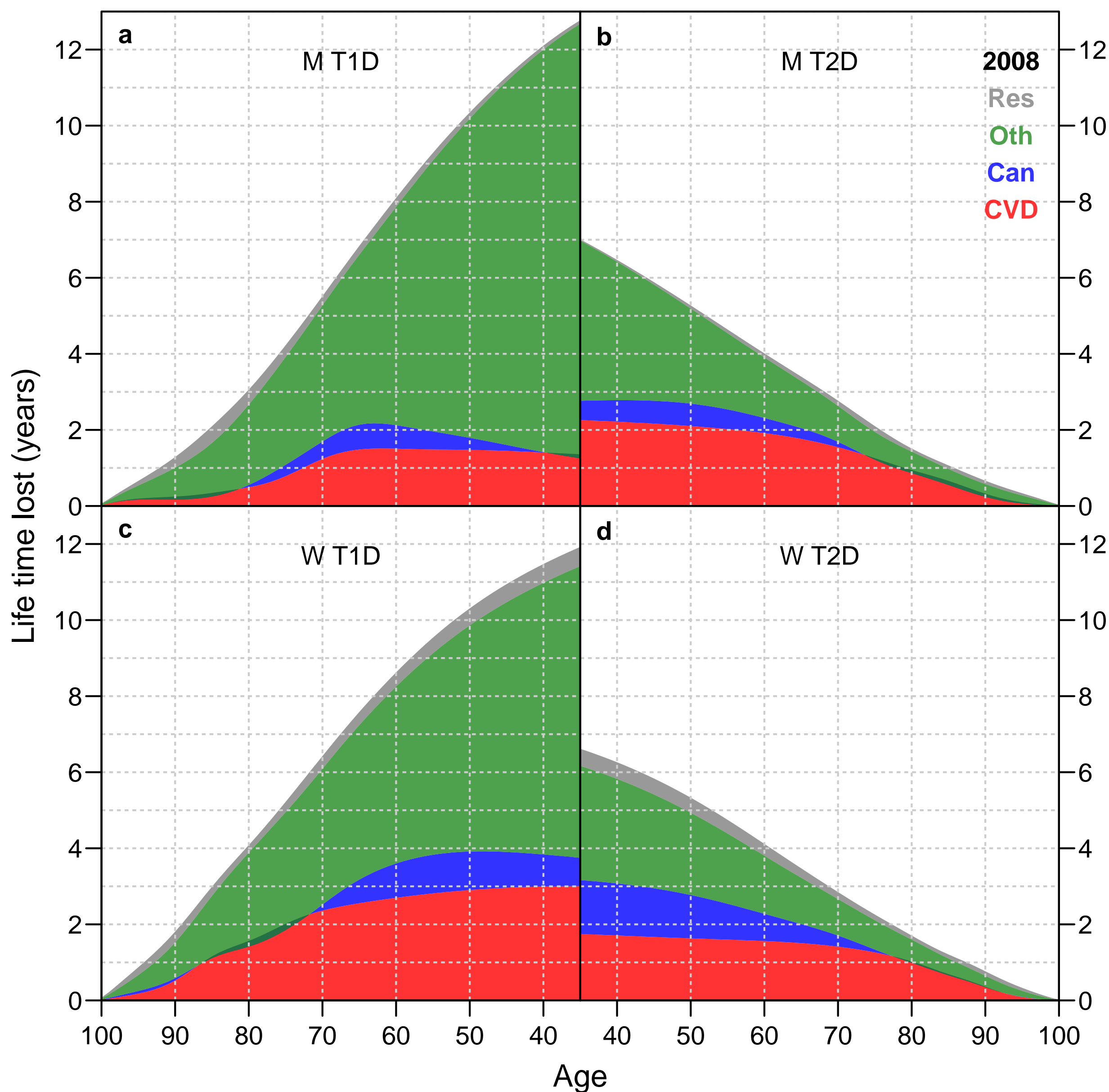

Figure ESM 4: *Years of life lost to different causes of death 2008 by sex, type of diabetes and age.*
The dark green areas in panels a and c is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue and green areas). This area is therefore part of both the CVD and the Other component.*
a: Men, T1D; b: Men, T2D; c: Women, T1D; d: Women, T2D. Colors: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD.

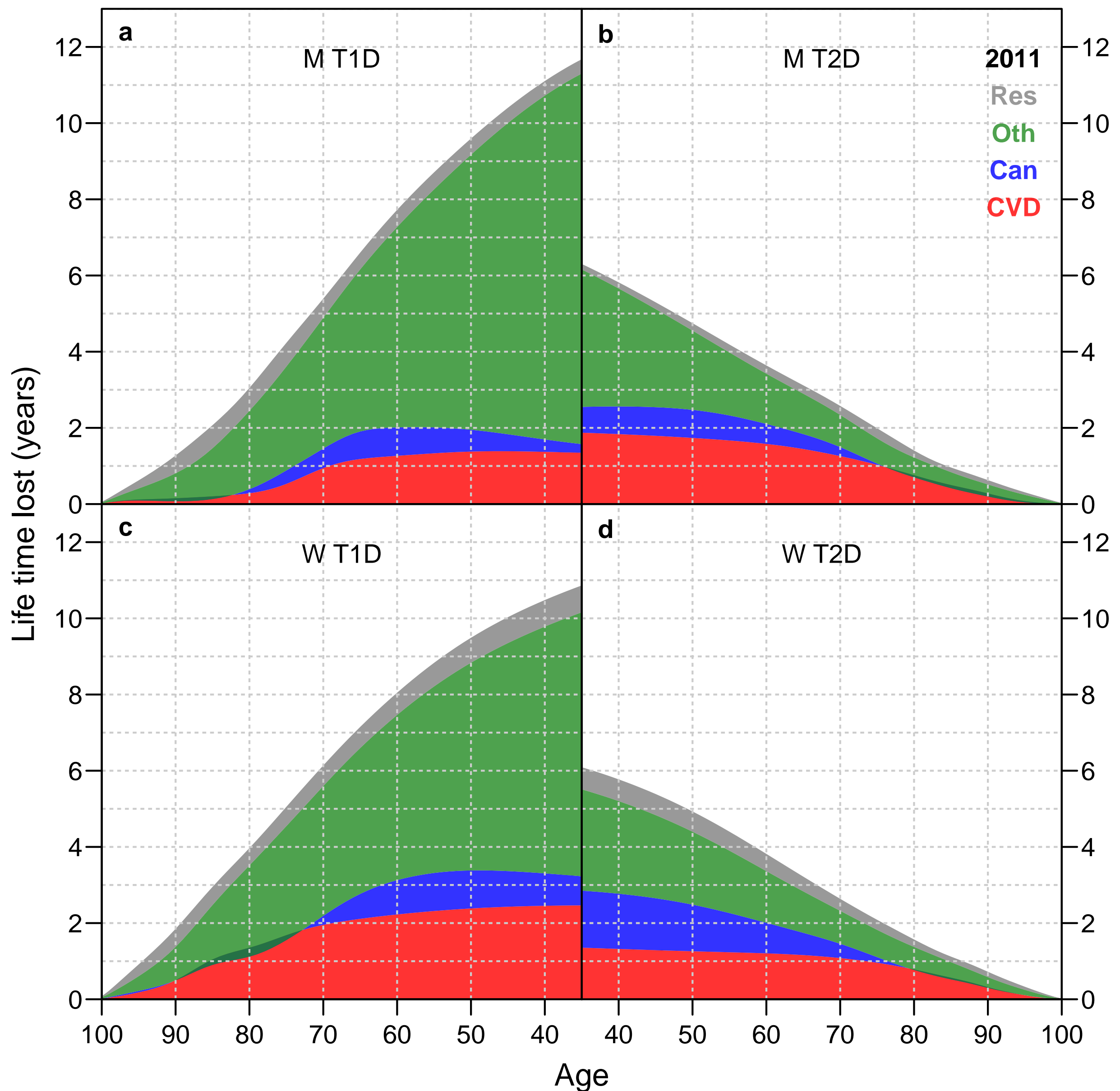

Figure ESM 5: *Years of life lost to different causes of death 2011 by sex, type of diabetes and age.*
The dark green areas in panels a and c is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue and green areas). This area is therefore part of both the CVD and the Other component.*
a: Men, T1D; b: Men, T2D; c: Women, T1D; d: Women, T2D. Colors: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD.

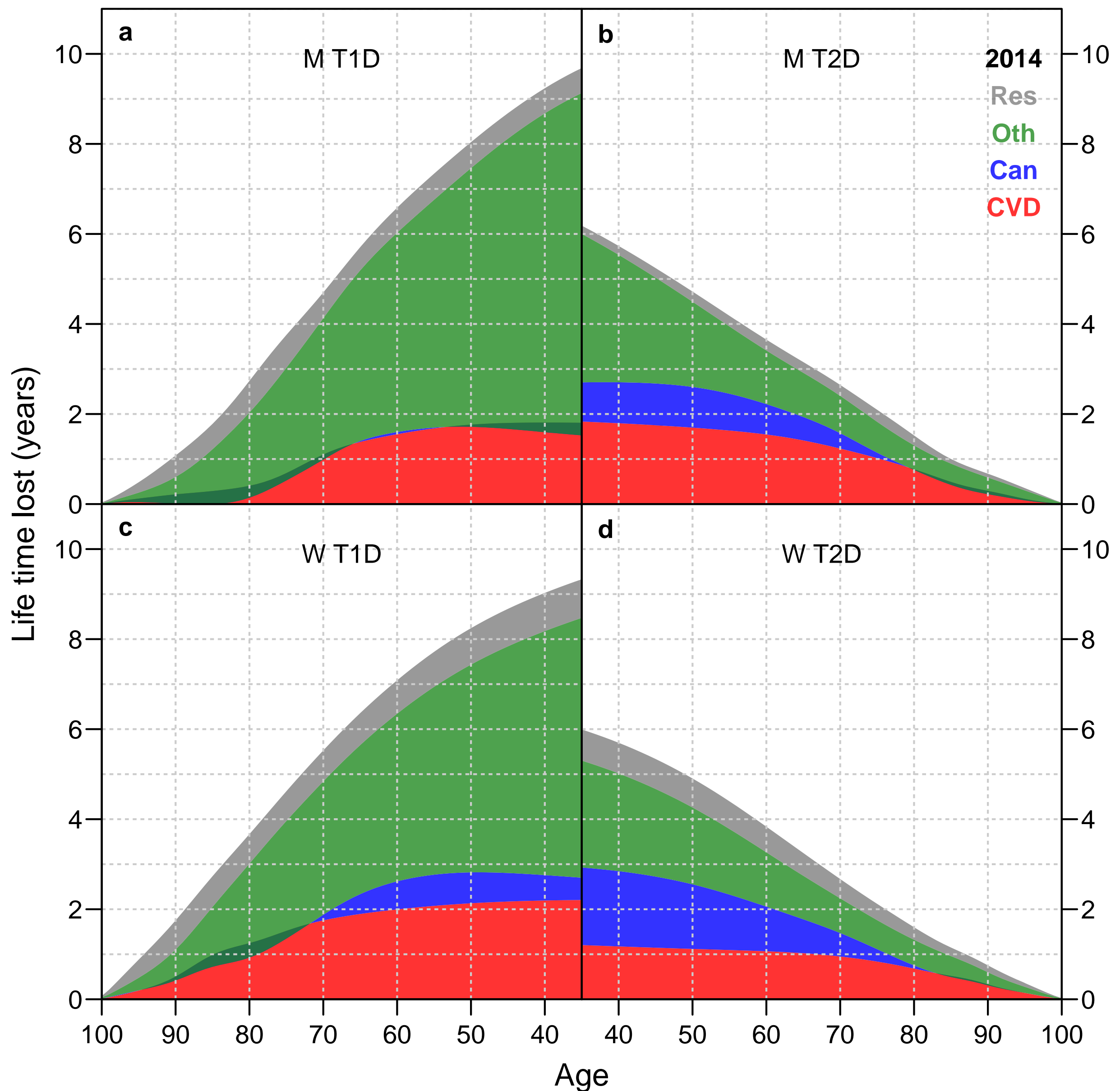

Figure ESM 6: *Years of life lost to different causes of death 2014 by sex, type of diabetes and age.*
The dark green areas in panels a and c is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue and green areas). This area is therefore part of both the CVD and the Other component.*
a: Men, T1D; b: Men, T2D; c: Women, T1D; d: Women, T2D. Colors: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD.

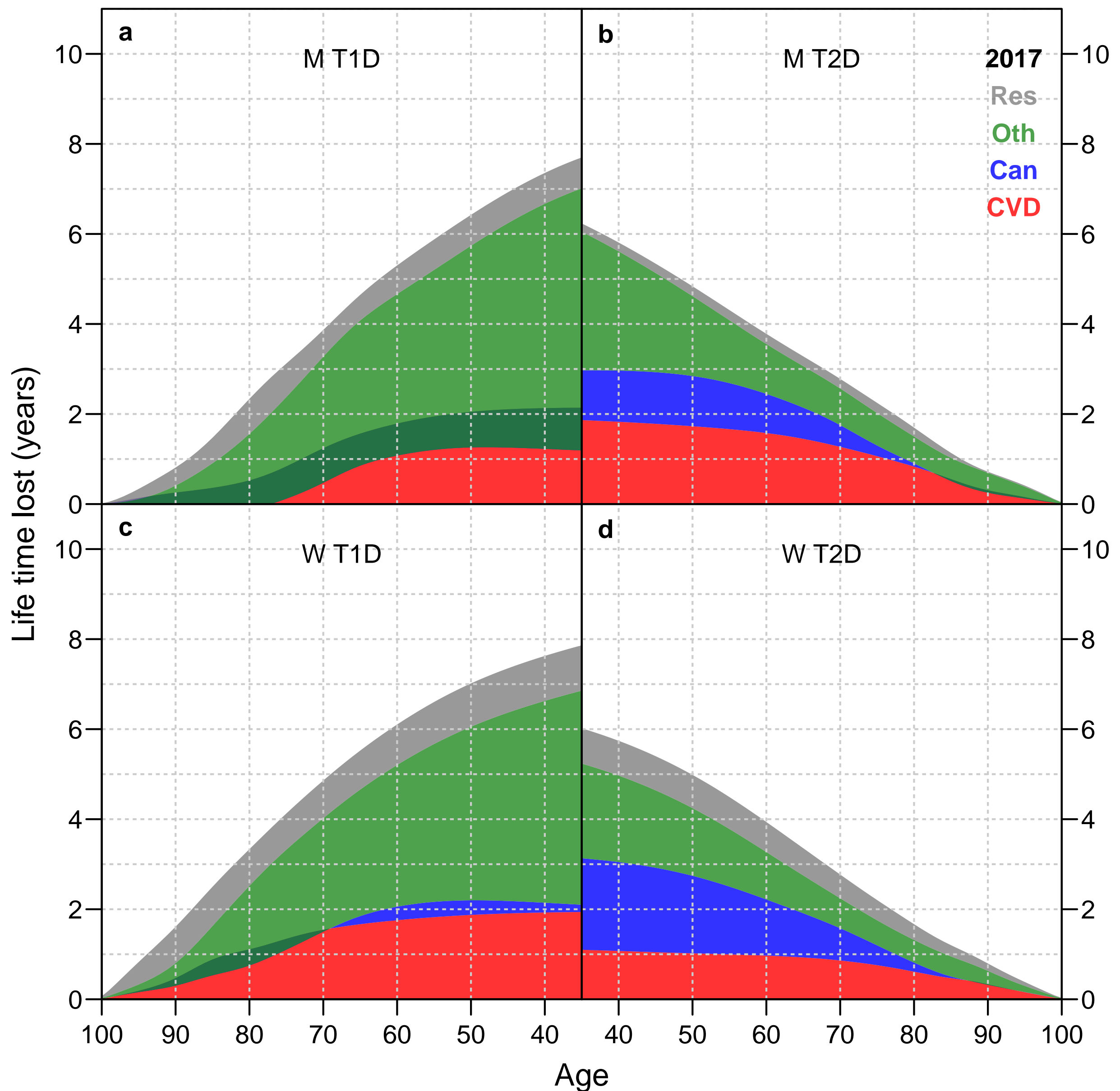

Figure ESM 7: *Years of life lost to different causes of death 2017 by sex, type of diabetes and age.*
The dark green areas in panels a and c is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue and green areas). This area is therefore part of both the CVD and the Other component.*
a: Men, T1D; b: Men, T2D; c: Women, T1D; d: Women, T2D. Colors: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD.

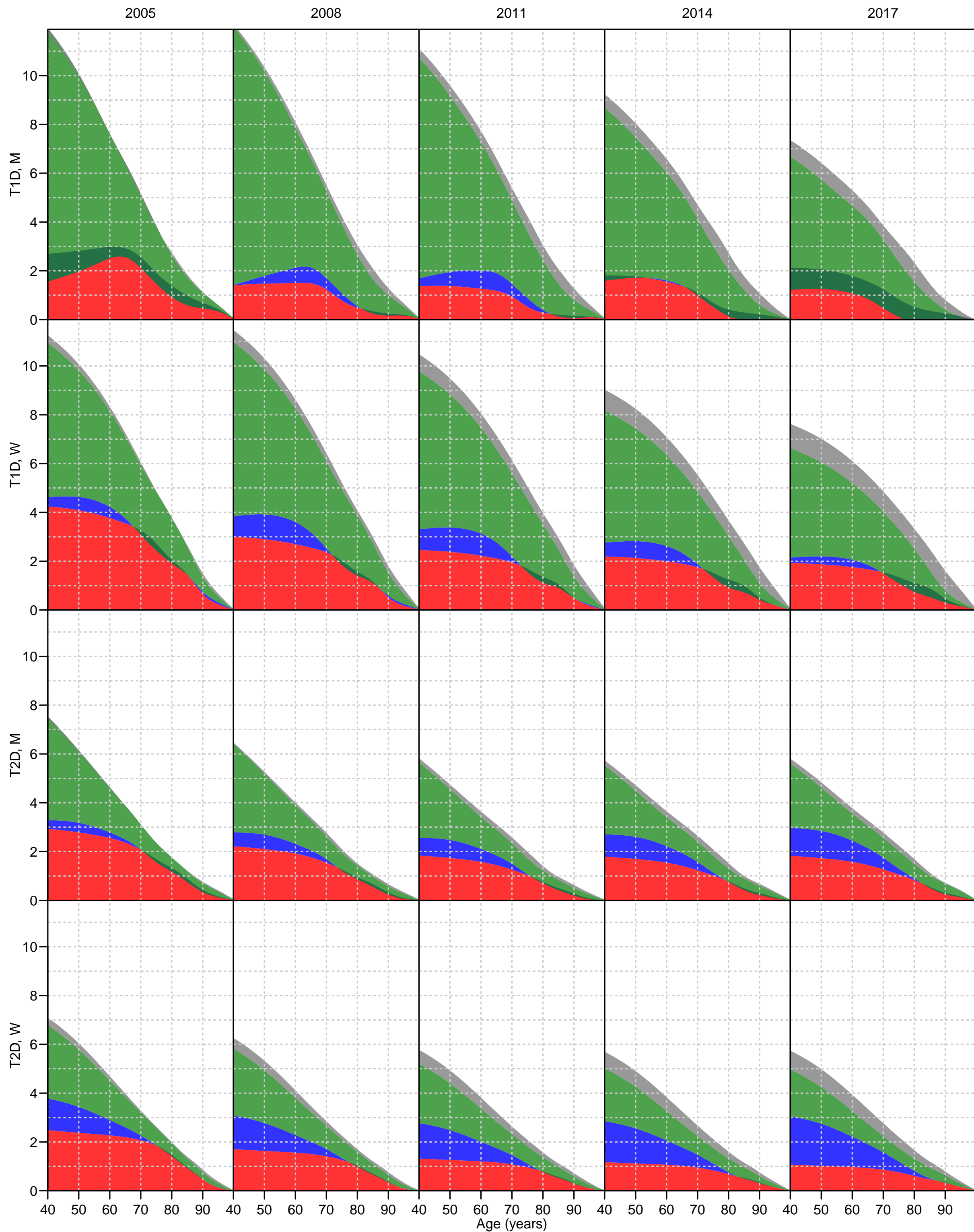

Figure ESM 8: *Years of life lost to different causes of death by date, sex, type of diabetes and age.*
Colors indicate cause of death: gray: Respiratory causes; green: other causes; blue: cancer; red: CVD. The dark green areas is equal to the negative *years of life lost to cancer for T1D patients (it is the overlap of red, blue(negative) and green areas). This area is therefore part of both the CVD and the Other component.*