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

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ABSTRACT

Introduction Lifetime risk and lifetime 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 diabetes (T1D) and type 2 diabetes (T2D) and non-diabetes mortality based on complete follow-up of the entire population of Denmark in 1996–2016. A multistate model with these transition rates was used to assess the lifetime risk of diabetes, as well as the difference in expected lifetime between persons with type 1 and T2D and persons without.

Results In 2016, the lifetime risk of T1D was 1.1% and that for T2D 24%, the latter a 50% increase from 1996. For 50-year-old persons, the lifetime lost was 6.6 years for T1D and 4.8 years for T2D. These figures have been declining over the study period.

At 2016, the total foreseeable lives lost in Denmark among patients with T1D were 182 000 years, and those among patients with T2D were 766 000 years, corresponding to 6.6 and 3.0 years per person, respectively.

Conclusion At the individual level, improvements in the disease burden for both T1D and T2D have occurred. At the population level, the increasing number of patients with T2D has contributed to a large increase in the total loss of lifetime.

Significance of this study

What is already known about this subject?
► Studies from the Western world have shown that the years of life lost to diabetes in mid-life (around 50 years) is between 5 and 10 years, with large difference between countries.
► Studies have focused on either type 1 diabetes (T1D) or type 2 diabetes (T2D) or have not distinguished between types of diabetes.

What are the new findings?
► In similar ages, the years of life lost to T1D are about twice as high as for T1D; for 50-year-old persons the lifetime lost was 6.6 years for T1D and 4.8 years for T2D. This has been decreasing over the last decades.
► The lifetime risk of T1D is currently 1.1%, and that for for T2D is 24%. At 2016, the total foreseeable life lost in Denmark among patients with T1D was 182 000 years, and that among patients with T2D was 766 000 years.

How might these results change the focus of research or clinical practice?
► There is a clear indication that the *individual* outlook for a person with diabetes is improving, whereas the *population* burden is increasing, indicating the prevention is an important focus area.

INTRODUCTION

Relatively few studies have looked at lifetime lost to diabetes,[1–5] and even fewer have provided figures of the lifetime risk of diabetes.[1 2 6 7] The lifetime lost or years of life lost to a disease have been given many interpretations in the literature (for an overview, see Andersen[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 lifetime lost to diabetes on a proper multistate model, taking both type 1 diabetes (T1D) and type 2 diabetes (T2D) into account.

RESEARCH DESIGN AND MATERIAL
Data

We used a newly established Danish Diabetes Register[9 10] linked to the total population of Denmark, including the causes of death register. Detailed information on diabetes incidence, prevalence, mortality, and current and predicted future numbers with diabetes is given in previous publications.[9 10] We constructed tables of person-years, incident cases of T1D, T2D and deaths by cause for the entire Danish population subdivided by current diabetes status (no diabetes, T1D and T2D). The causes of death used were cardiovascular disease (International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10): I00–I999), cancer (ICD-10: C00–D099, so carcinoma in situ are included, benign and unspecified tumors *ex*cluded), respiratory (ICD-10: J00–J999) and other causes. These tables were classified by sex, age and date of follow-up and
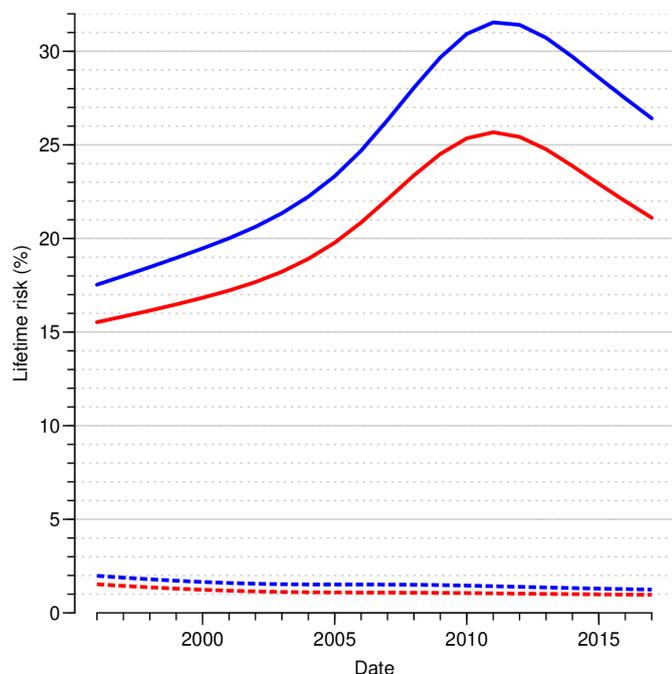
Figure 1 Lifetime risk of T1D and T2D by sex and date of reference. The calculations are based on annual estimated cross-sectional incidence and mortality rates from age–period–cohort models for incidence and mortality. Blue curves are men, red curves women; dotted lines T1D, full lines T2D. T1D, type 1 diabetes; T2D, type 2 diabetes.

date of birth in 1-year intervals, so called Lexis triangles[11]; further details are given in the electronic online supplemental material 1 (ESM), including a detailed overview of causes of death (online supplemental table 2)

Statistical methods

We fitted models for incidence rates of T1D and T2D, and cause-specific mortality rates for persons without diabetes and with T1D and T2D 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 January 1, 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 diabetes', 'T1D', 'T2D' and the four causes of death.

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 January 1 to compute the lifetime risk of T1D and T2D 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.

RESULTS

In the study period 1996–2016 inclusive, there were 19 712 T1D diagnoses and 343 952 T2D diagnoses, while there was 12 762 deaths among patients with T1D, 149 000 among patients with T2D and 988 569 among persons without diabetes (online supplemental table 1). The dominant single cause of death was CVD except for T1D, where the dominant cause of death was other causes.

Lifetime risk of diabetes

The lifetime risk of T1D 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 T2D 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 T2D was 26% for men and 21% for women on January 1, 2017, corresponding to increases of 51% and 36% since 1996 (figure 1 and table 1).

EXPECTED LIFETIME

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 lifetime spent (sojourn time) with T1D was 0.6 years for men and 0.5 years for women, unchanged over the study period, while the expected lifetime with T2D increased from 2.0 to 4.6 years, similar for men and women (table 1). Thus, of the increase in expected lifetime in the period, more than half was expected to be years with T2D (table 1).

Years of life lost to diabetes

At the beginning of 2017, the lifetime lost to T1D was 8.3 years at age 20 years and about 5.6 years at age 60 years (online supplemental table 5). Lifetime lost to T2D at age 60 years was 3.8 years (online supplemental table 6), so T1D carries about 30% higher lifetime loss compared with T2D (figure 2 and online supplemental tables 5 and 6), reflecting the earlier diagnosis and hence longer duration of diabetes at a given age for T1D as compared with T2D. We also found that the years lost to diabetes have been diminishing over the study period, at age 50 years from about 9 to 7 years for T1D and from 8 to 5 years for T2D.

Future years of life lost

The future years of life lost among *patients with prevalent diabetes*—the currently accumulated future population burden in Denmark—was 9 47 600 years on January 1, 2017 (online supplemental table 3), 19% of which were among persons with T1D, despite only 10% of Danish

Table 1 Lifetime risk, expected lifetime spent with diabetes and lifetime lost by type of diabetes, sex and date (January 1 each year)

Date	Lifetime risk (%)		Expected lifetime (years) spent with			Lifetime lost (years) to							
						T1D, at ages				T2D, at ages			
	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

Note the different ages at calculation of life lost for T1D and T2D, accommodating the different age distributions of T1D and T2D.
DM, diabetes mellitus; T1D, type 1 diabetes; T2D, type 2 diabetes.

patients with diabetes are T1D.[9] The average future lifetime lost was 6.6 years for T1D and 3.0 years for T2D, partly attributable to different age distributions.

The *extra* future lifetime lost among *newly diagnosed patients with diabetes* in a single year was around 70 000 years during 2016, some 10% of these from T1D, even if only 5% of newly diagnosed cases are T1D (online supplemental table 3). The average lifetime lost for persons diagnosed in 2016 were 8.2 years for T1D and 3.6 years for T2D (online supplemental figure 2).

For both of 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 was decreasing over the study period, over the last 10 years, some 35% for T1D, but less than 10% for T2D (online supplemental tables 3 and 4).

Years of life lost by cause of death
We found that the major contributor to years of life lost in T1D (online supplemental table 5 and online supplemental figures 4–7) was other causes of death (4.1 years at age 50) and only second was CVD (2 years at age 50), whereas respiratory causes contribute slightly less than 1 year throughout the age range. Cancer contributes almost nothing in women with T1D and a negative 1 year among men with T1D. In T2D (online supplemental table 6 and online supplemental figures 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.

DISCUSSION
Our study is the first to simultaneously evaluate the lifetime risk as well as the lifetime lost to T1D and T2D in an entire population using a proper multistate methodology. We evaluated both the individual and the population levels of years of life lost to diabetes.

We found the lifetime risk of T1D to be just over 1% and that of T2D 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 lifetime 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 T2D, has been massively increasing.

Life years lost to T1D are some 30% higher than those lost to T2D at any given age. That may be due to longer exposure to risk factors for acute and chronic microvascular and macrovascular complications to diabetes with earlier onset. Furthermore, the aggressive approach to manage cardiometabolic risk factors in T2D is less well
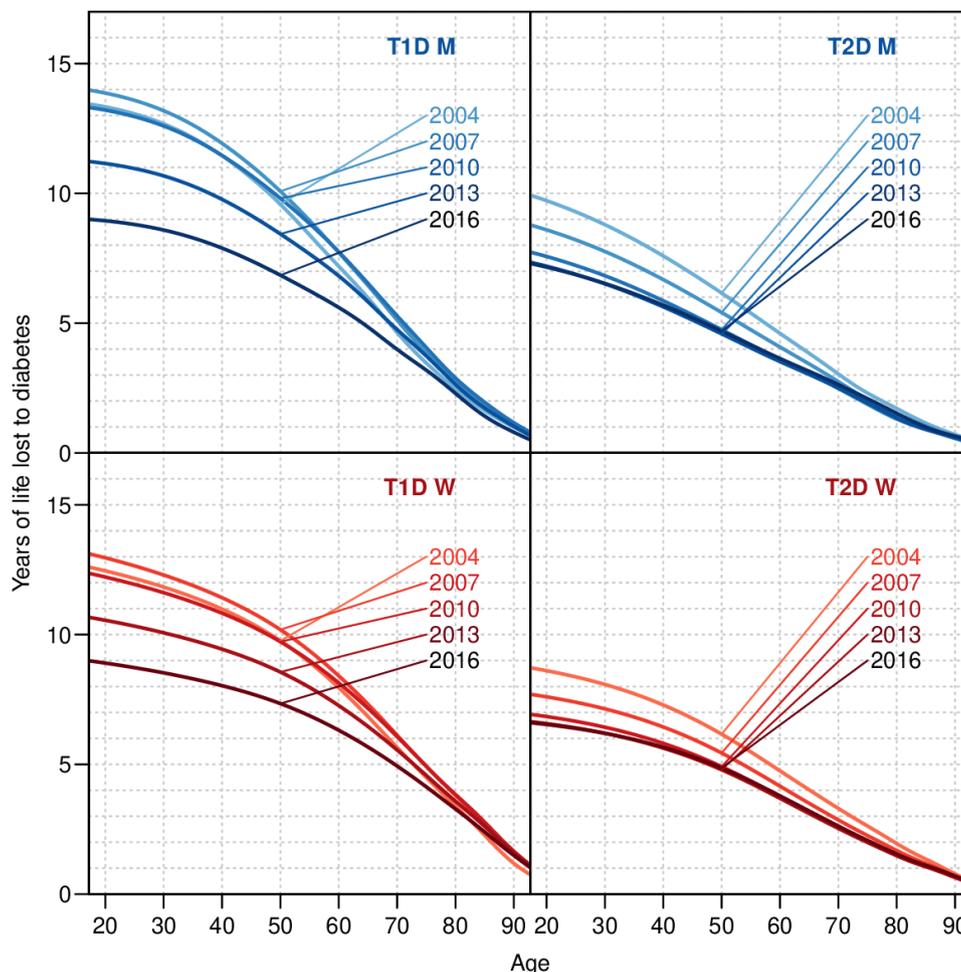
Figure 2 Years of life lost to T1D and T2D in January 1, 2004, 2007, …, 2016, by sex. The calculations are based on annual estimated cross-sectional incidence and mortality rates from age–period–cohort models for incidence and mortality. M, men; T1D, type 1 diabetes; T2D, type 2 diabetes; W, women.

documented in T1D, and quality registers have proven less favorable blood pressure and lipid levels in T1D compared with T2D, as well as some renal-protective and cardioprotective undertreatment.[12]

A number of studies modeling life years lost to diabetes[4 5 13–16] are old or have used suboptimal 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 do, 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 lifetime lost to diabetes. The most recent study by Gregg et al arrived at years of life lost to diabetes at age 40 years for white men of 5.8 and 6.8 years for white women in the period 2000–2011, where we found 7.3 and 7.0 years in 2005. The validity of this study, however, is limited by the fact that the diagnosis of diabetes is derived from a telephone survey.

Livingstone et al[3] provided estimates of lifetime lost to T1D in Scotland for the period 2008–2010 of 9.2 years for men and 10.8 years for women aged 40 years. Huo et

al[17] estimated the lifetime lost to T1D in Australia for the period 1997–2010 to 10.0 years for men and 11.2 years for women aged 40 years. For 2008, we found 6.4 years for men and 6.2 years for women at age 40 years somewhat smaller than the Scottish 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 T1D and T2D 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 T2D as T1D in the early years of the diabetes register (before 2005). Thus, years of life lost to T1D may be underestimated before 2005 due to contamination with patients with T2D.

SUMMARY

Our study shows that there has been a decrease in lifetime risk of T1D to slightly over 1% and an increase in T2D risk to 25%.

Further, we demonstrated a decline in the individual burden of T2D over the last two decades, but also clearly demonstrated that the population burden is increasing, indicating that preventive measures have not had the desired effect yet, and in particular, that the burden of T1D still is quite high, despite decreasing lifetime risk.

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