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Long-term and recent trends in survival and life expectancy for people with type 1 diabetes in Finland

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ABSTRACT

Aims: Type 1 diabetes has been associated with a significant reduction in life expectancy. Major advances in treatment of type 1 diabetes have been associated with improved survival. However, life expectancy for type 1 diabetes under contemporary care is not known.

Methods: Health care registers were used to obtain data on all people with type 1 diabetes in Finland in 1964–2017 and their mortality in 1972–2017. Survival analyses were used to study long-term trends in survival and abridged period life table methods to calculate life expectancy estimates. Causes of death were examined to consider development.

Results: Study data included 42,936 persons with type 1 diabetes and 6,771 deaths. Kaplan-Meier curves showed improved survival during the study period. In 2017, the remaining life expectancy at the age of 20 for a person diagnosed for type 1 diabetes was estimated to be 51.64 (95% CI: 51.51, 51.78) years which was 9.88 (9.74, 10.01) years lower than for the general Finnish population.

Conclusions: We found improved survival among persons with type 1 diabetes during the last decades. However, their life expectancy remained significantly below that of the general Finnish population. Our results call for further innovations and improvements in diabetes care.

1. Introduction

The epidemiology of type 1 diabetes (T1D) is well established with an estimated 9 million prevalent cases worldwide in 2021 [1]. Excess mortality in T1D compared to general population is apparent across countries worldwide [2]. A recent analysis of the global trends of diabetes in 195 countries reported slight increase in the age-standardised incidence and prevalence rates of T1D while age-standardised rates for mortality and disability-adjusted life years (DALYs) have decreased [3]. The increasing trend in the incidence of T1D has mainly occurred in high income regions including Europe and the United States, in which there has been a reported 2.7–4.0 % annual increase in type 1 diabetes recently [4]. The highest incidence of T1D globally has been reported in Finland [5] even though the incidence has decreased in the 2000s [6]. Also, worryingly, the prevalence of T1D among children and adolescents has increased, and for example in the US the estimates of children and adolescents below age 20 with T1D now exceed three million [7].

Major advances in the treatment of T1D have occurred in the past three decades followed by favorable changes in the age-standardized mortality and DALYs rates in type 1 diabetes over the past 28 years [3]. Moreover, life expectancy (LE) may no more be dependent on age at onset, but rather on the long-term progress in diabetes self-management education including continuous monitoring of blood sugar, the widespread use of insulin and insulin analogues, and sensor-augmented pump therapy [8].

T1D has traditionally been associated with a significant reduction in LE. Recent studies in Australia, Sweden, Scotland, and Taiwan have demonstrated that having type 1 diabetes results in a loss of 10.2–17.7 life-years [9–12]. A cohort study from the US reported an improvement in the LE of 15.4 years between persons diagnosed with T1D in 1950–1964 and 1965–1980 [13]. However, only few studies have focused on LE in a representative T1D population and contemporary estimates in LE. Further, most studies lack long follow-up since the onset of T1D, long-term trends in mortality and distributions of causes of

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death. One challenge has been to find appropriate methods to calculate LE for data with sparse cases in certain age groups. Thus, however, life expectancy for type 1 diabetes under contemporary care is not known.

Therefore, we examined life expectancy using large multi-cohort register data from Finland, which has the highest incidence of childhood type 1 diabetes in the world [5]. We examined whether there are cohort-based differences between the last six decades in mortality and provide results on the changes in the causes of death during the study period. Further, we estimated the life expectancy among the most recent cohort living with T1D under contemporary care. This study additionally provides new evidence of the impact of current diabetes care.

2. Materials and methods

2.1. Study population

Our study data was based on the Diabetes in Finland (FinDM) database, which has been gathered using several administrative registers and aims to cover all persons with diabetes in Finland from 1964 with extensive follow-up data. Currently data are available until 2017. Patients were classified into type 1 and type 2 diabetes according to information of the first year following the recorded onset of diabetes using primarily diagnosis codes for the special reimbursement codes for antidiabetic medication, secondarily diagnoses codes in the care periods and visits in health care, thirdly purchased antidiabetic medications, and lastly, causes of death and age at the onset of diabetes.[14] Causes and dates of death from the Causes of Death statistics of Statistics Finland were linked to persons with diabetes from 1972. The cause of death used in statistics is determined according to the selection and application rules of the International Classification of Diseases (ICD-8 to ICD-10)[15]. We selected people with T1D with diabetes onset at age of 29 years or younger. Those with older onset age of T1D were excluded because their diabetes type is more difficult to determine. To determine the relative importance of survival and LE in T1D, we used people with type 2 diabetes (T2D) and the general population as reference populations. The population and mortality tables for people with diabetes were aggregated from the FinDM database and for the general Finnish population from the public population database of Statistics Finland [16,17].

We divided our data into six cohorts according to the decade of the onset of diabetes, the first cohort being from 1964 until 1971, and the last from 2010 to 2017. In this study, people with diabetes were followed from diabetes onset until death, or, if no data on death was found, censored at the last observed event in any registers included in the data (i.e., care episode, prescription date of medicines, census information), at 100th birthday or eventual end of the follow-up at the final day of 2017, which ever came first. Due to the lack of data on dates and causes of death from the first eight years of follow-up, the oldest cohort is only followed from 1989 onward regarding those with no date of death or death in 1989 or later.

Further, we classified persons with T1D into six age groups (0–4, 5–9, 10–14, 15–19, 20–24, and 25–29 years) according to age at onset of T1D. Causes of death were classified into five categories according to underlying causes of death: 1) circulatory causes, 2) diabetes, 3) neoplasms, 4) external causes, and 5) other diseases.

2.2. Statistical methods

Study data was cross-tabulated to describe cohort characteristics. Age-standardised incidence rates of T1D per 100,000 person years among those under 30 years in Finland in diabetes onset cohorts were calculated using the direct standardisation method with the age structure of the newest onset cohort as the standard population. We calculated Kaplan-Meier estimates to describe changes in survival differences in six diabetes onset cohorts from diabetes onset until the end of follow-up. Kaplan-Meier curves were presented at chronological time scale and drawn starting from the midpoints of each diabetes onset cohort. For the first diabetes onset cohort of 1964–1971, first four years of survival were extrapolated from the survival of the subsequent cohort to compensate for lacking data of deaths for the first years and curve drawn with a dashed line to emphasize the elevated uncertainty among the first cohort. Global and pairwise log-rank tests with Benjamini-Hochberg adjustment were conducted to compare survival differences between the diabetes onset cohorts. Cumulative incidence of death with 95 % confidence interval (CI) was calculated for persons with type 1 and type 2 diabetes from birth until the end of follow-up.

In this study, LE was defined as the average number of years persons aged 20 with T1D are expected to live. LE was examined using Chiang's method of abridged period life tables (Supplementary Table 1) for five-year age intervals with last open-ended interval for those over 85 years old [18]. In this method, simultaneous mortality of older age groups is used as a measure of risk of death. We formed abridged period life tables for persons with T1D, T2D and the general Finnish populations for the last available year of the FinDM database, 2017. Results were presented as LE estimates at the beginning of each age interval and differences at them between populations with 95 % CI.

As the data concerning people with T1D in old age groups (earliest T1D cases were from the 1960s and not many of them reached the old age during the study period) as well as T2D in young age groups were sparse with only small amount of follow-up and few deaths for the yearly age-group cells, we used an imputation method that borrowed strength from the "nearby" cells: First the sufficient amount of follow-up was fixed for certain reference age-group (e.g. to be the observed follow-up time in the age-group that was least affected by the data constraints) and the required amount of follow-up time in other age-groups were then determined in relation to the corresponding age-group specific populations in general population. After determining the required follow-up time for each age-group, the follow-up and the number of deaths was gathered by borrowing data first from the most recent year and, if that was less than required follow-up time, follow-up from the year before was added. If there were not enough follow-up time within T1D (or T2D) in the whole follow-up period (e.g., the (observed) number of people with T1D aged 85 + was small in the most recent years and non-existing for the earlier), the collection of follow-up time and the number of deaths continued at the most recent year of data from the other type of diabetes (i.e., T2D for T1D) until the required amount of follow-up time was reached. In other words, we assumed in the imputation scheme that 1) the most recent years correspond to each other to such large degree that it is reasonable to combine them if necessary, and 2) that mortality of the other diabetes type approximates the mortality of the other type.

Sensitivity analyses were conducted with those persons who had survived at least 18 years after the onset of T1D to assess the comparability of diabetes onset cohorts.

All statistical analyses were conducted using the R statistical software, version 4.0.5 [19].

3. Results

Our study data consisted of 42,936 persons with T1D, of whom 48 % were male. 6,771 deaths occurred during the follow-up and mean age at T1D onset was 14.6 years (interquartile range (IQR) 7.7 and 21.7). The age at onset decreased markedly in later cohorts. Total follow-up time was 879,755 person years with mean follow-up time of 20.5 years and median of 19.7 years. Cohorts of diabetes onset were roughly the same size but varied by follow-up time and risk of death. (Table 1).

Kaplan-Meier curves (Fig. 1) showed survival differences in six diabetes onset cohorts with steeper slopes in older diabetes onset cohorts reflecting improved survival in persons with T1D. Global log-rank test showed differences to be statistically significant ($p < 0.001$) with pairwise tests being statistically significant as well ($p < 0.001$ to 0.026). The cumulative risk of death for persons with T1D was 3.1 % (95 % CI: 2.9 %, 3.3 %) at 30 years; 17.3 % (16.7 %, 17.8 %) at 50 years; 47.5 % (46.3 %,

Table 1
Basic characteristics of study data of persons with type 1 diabetes by diabetes onset cohort.

		Diabetes onset cohort					
		1964–1971	1972–1979	1980–1989	1990–1999	2000–2009	2010–2017
N		6658	6462	6655	6885	9179	7097
Incidence*		35	35	32	35	48	47
Deaths during follow-up		3184	2104	887	375	186	35
Sex (%)	male	42	36	40	47	53	54
	female	58	64	60	53	47	46
Age at onset	0–4	7	8	12	18	20	19
(%)	5–9	16	14	19	23	24	24
	10–14	24	19	20	23	22	24
	15–19	23	15	13	12	12	12
	20–24	16	18	15	10	10	10
	25–29	15	26	21	14	13	12
Median age at onset		15.7	18.1	14.6	11.9	11.3	11.4
(IQR)		(10.5–21.6)	(11.0–25.2)	(8.4–23.8)	(6.5–19.6)	(6.2–18.6)	(6.2–18.5)
Median follow-up time		29.0	40.1	32.4	22.1	12.6	4.0
Person years		145,439	229,019	207,995	152,216	116,530	28,556

IQR = interquartile range.
* Age-standardised incidence rate per 100,000 person years.

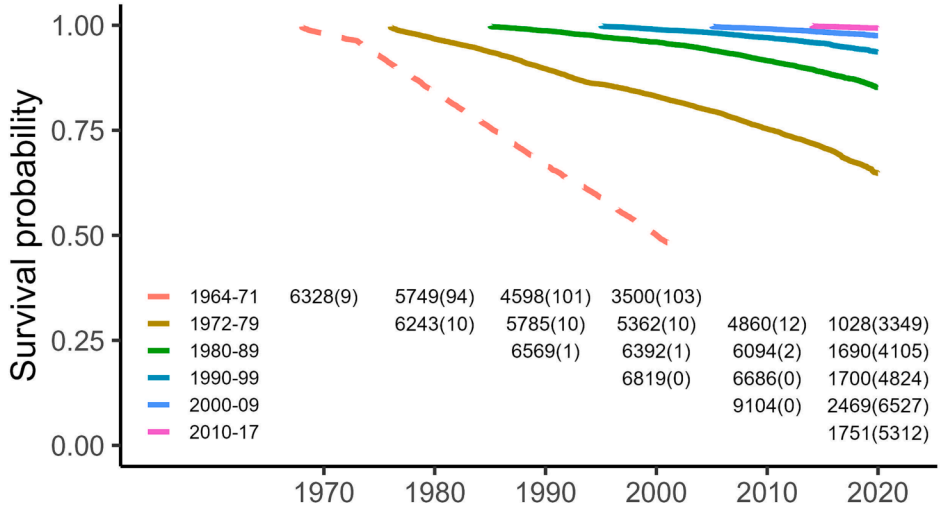

Fig. 1. Kaplan-Meier curves for the distribution of survival in diabetes onset cohorts among persons with type 1 diabetes including numbers at risk (censored).

48.6 %) at 70 years; and 85.2 % (79.4 %, 91.0 %) at 85 years of age (Fig. 2). Cumulative risk of death among persons with T1D remained consistently higher compared to persons with T2D until the age of over 90 years.

Distributions of the causes of death categories of persons with T1D have changed markedly between 1972 and 2017 (Fig. 3). Early in the period, diabetes as the cause of death dominated with over 60 % of deaths. Later, especially proportions of circulatory diseases and neoplasms have increased, covering over 50 % of deaths during the last years. During the study period, average age at death increased markedly in the study population. Meanwhile, in the general Finnish population, increase in the proportions of neoplasms and other diseases was observed with the proportion of diabetes decreasing by almost 30 % (Supplementary Fig. 1).

In 2017, the remaining life expectancy for persons with T1D at 20 years of age was estimated at 51.64 (95 % CI: 51.51, 51.78) years (Fig. 4). For people with T2D, corresponding figure was estimated at 54.87 (54.82, 54.91) years, and for general Finnish population 61.52 (61.50, 61.54) years. Thus, LE for persons with T1D was 9.88 (9.74, 10.01) years lower than for the general Finnish population at 20 years of age, and 3.22 (3.08, 3.37) years lower than for persons with T2D. Differences in LE were somewhat smaller at more advanced age with LEs for persons with T1D remaining lower than LE for persons with T2D until 75 years of age. At 80 years of age, LE for the general Finnish population was still 1.98 (1.91, 2.05) years higher that of persons with T1D.

Sensitivity analyses examining survival among those persons with T1D who had survived with T1D at least 18 years, provided largely similar results of survival in diabetes onset cohorts than of those with the whole data (Supplementary Fig. 2).

4. Discussion

In this large Finnish multi-cohort study among more than 40 000 individuals with type 1 diabetes, we found that survival has significantly improved during the study period between 1972 and 2017. Still, in 2017, the life expectancy at age 20 for individuals with T1D was 3.2 years lower that those with T2D and 9.9 years lower than for the general population. Our results of development in the proportions of causes of death also showed that they have markedly changed between 1972 and 2017. These results highlight the importance of the improved management and treatment of T1D and comorbidities.

Our results of the long-term trends in the survival of individuals with T1D are in line with previous studies that have shown on average of 15 years increase in life expectancy in individuals diagnosed during the 1980s or later compared to those diagnosed in the 1960s or before [13]. However, our recent trends showed that life expectancy of individuals

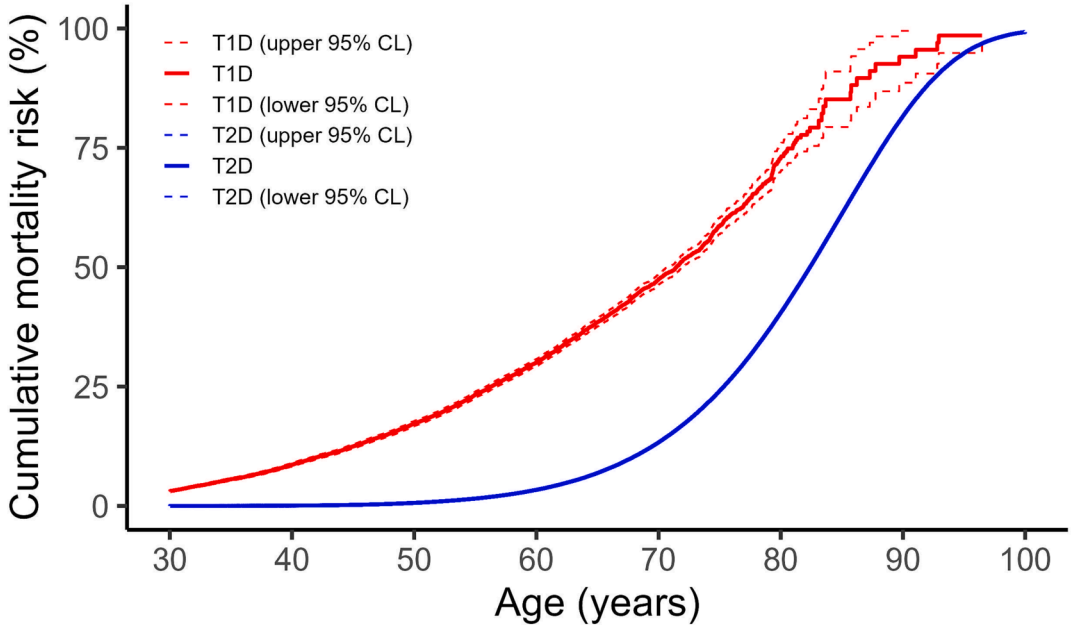

Fig. 2. Cumulative mortality risk among persons with type 1 and type 2 diabetes with 95% confidence intervals.

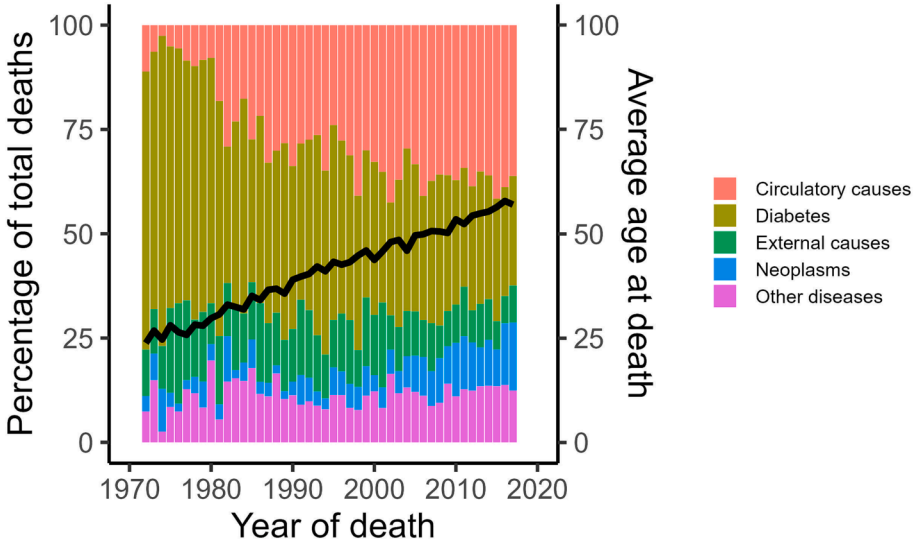

Fig. 3. Annual proportions of causes of death categories by year of death and average age at death among dead persons with type 1 diabetes in 1972–2017.

with T1D is still almost 10 years lower than that of the general population. While mortality has decreased in general populations, excess mortality in T1D populations compared to general populations remains apparent worldwide, albeit less marked in recent studies [2]. A Norwegian study reported a decrease of 3.8-fold excess mortality in those diagnosed with T1D in 1973–1982 to that of 2.2 in those diagnosed in 1999–2012 [20]. In Finland, some or no decrease in excess mortality of the T1D onset cohorts from 1960s to 1990s have been reported [21,22]. A study using the same database found three to fourfold excess mortality among 30–79 years old persons with insulin-treated diabetes in 2003–2007 compared to general Finnish population. However, relative excess mortality in 1998–2007 remained unchanged while that of non-insulin-treated people with diabetes declined.[23] A recent cohort study found a 3.2-fold excess mortality among those having survived 50 years or more with T1D compared to Finnish background population [24]. Thus, people with T1D have benefited from the improvement of life expectancy in the general Finnish population, but the decrease in excess mortality has been relatively slow.

It is likely that part of the decrease in mortality among persons with T1D is based on the changes in the care of diabetes and comorbidities. There are several potential explanations affecting the improvement in survival in recent decades. In the 1960s and before that, treatment for diabetes was demanding; the bodýs blood glucose levels were measured in urine, calories in the food were calculated and meals were weighed in grams, in addition insulin was dosed with long thick needles. The first major step in developing diabetes treatment in Finland, was the 1963 Health Insurance Act [25] that secured free insulin for individuals with diabetes followed by the 1972 Health Care Act [26] which guaranteed free treatment equipment for individuals with T1D. In the 1970s, plastic disposable syringes and smaller needles attached to them were introduced with advances in insulin administration and glucose measurement. The 1980s and 1990s saw the introduction and development of individual blood glucose meters and insulin pens as well as evolution of insulin treatment [27,28]. From the 1990s onwards, a shift to intensive

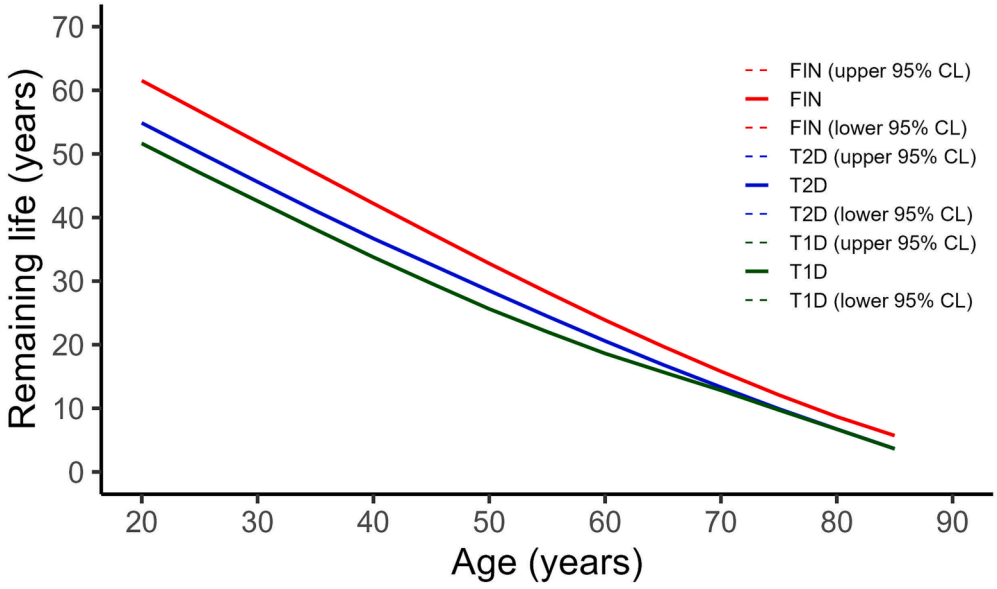

Fig. 4. Remaining life expectancy with 95% confidence interval for those with type 1 diabetes, type 2 diabetes, and general Finnish population in 2017.

diabetes therapy occurred after its effectiveness on decreasing the onset and severity of diabetic complications was shown [29]. Fast development of diabetes care has continued in the 2000s: there are various blood glucose meters and continuous glucose monitors available and insulin pumps have become more common [30]. In Finland, a key development was the national Development Programme for the Prevention and Care of Diabetes (DEHKO) during 2000–2010 which, in addition to prevention of type 2 diabetes and comorbidities, focused on developing diabetes care and its quality, as well as supporting self-care of individuals with diabetes [31]. In 2007, the first national clinical guideline for diabetes was published providing advice about the diagnosis, screening, prevention and treatment of diabetes and its complications. Today, the objectives of treatment and guidance are defined as good life of normal length as possible, avoidance of complications and fluent everyday life without unreasonable limitations [32].

By the end of the study period, the proportions of circulatory causes and neoplasms dominated the causes of deaths in persons with T1D. In a Finnish study, excess mortality was especially high in coronary heart disease with increased excess mortality from neoplasms among women [23].Even those with T1D of very long duration have been reported to remain at a high risk of cardiovascular disease [24]. As our results showed, proportion of diabetes as a cause of death has declined. Thus, the focus on causes of death which might be preventable with timely and adequate health care has shifted to complications of diabetes and other comorbidities. A recent Swedish study found younger age at onset of T1D to be associated with excess mortality and cardiovascular outcomes [33]. A Finnish study, however, found improved survival with early onset of T1D over, whereas survival of those with late onset of T1D had deteriorated since the 1980s [34]. Our results showed declining age at onset of T1D and increasing proportion of circulatory causes of death, which suggest need to emphasize prevention and care of cardiovascular disease among persons with T1D.

4.1. Strengths and limitations

This study was based on national register data with high validity and covering virtually all persons with diabetes in Finland with a time span of more than 50 years [14]. Further, we were able to follow individuals since the onset of T1D. The Finnish Causes of Death statistics has been considered reliable and valid by international standards [15]. However, results from the oldest diabetes onset cohort (1964–1971) should be interpreted with caution due to lacking dates of death until 1972. Also, changes in coding practices of the underlying causes of death may have affected to proportions of causes of death during the study period. Further, proportions of the causes of death cannot be directly compared as, due to age structure of our T1D data, the earlier years consist of those having died at younger age. We were able to compare results for T1D to those for T2D and general Finnish population. Also, this study did not include separate analysis by sex. Numbers for follow-up and deaths in analyses by sex would be even more sparse and would require even more elaborated imputation methods with increased uncertainty in results.

It is a fact that even with a large nationwide data with a long follow-up of persons with T1D such as we used, certain age groups lack sufficient numbers for follow-up and deaths to use conventional estimation methods for LE. Combining years is not enough, as the data lack enough persons with T1D in older age groups. Instead, we considered reasonable to assume that mortality in T2D approximates that of T1D. A Finnish study reported largely similar all-cause mortality in insulin-treated and non-insulin-treated people with diabetes with slightly higher mortality in the latter in younger age groups and in the former in older age groups [23]. Consequently, our estimate of LE for person with T1D is obviously conservative and may give too high LE results. While the imputation scheme used in this study combines two simple weighting corrections in an expedient way affecting only those age groups where imputation is needed, we consider that we have reached improved validity compared to alternative approaches. However, the use of imputation is to be noted as a limitation of this study, as the under- or overestimating true mortality in T1D cannot be excluded.

4.2. Conclusion

With this large data of six diabetes onset cohorts, we showed that the survival among persons diagnosed for type 1 diabetes has significantly improved during the recent decades. Based on these results, we might project that the individuals diagnosed with T1D during the 2020s have a mean life expectancy of 55–60 years at the age of 20 years. That is still below the life expectancy estimate of the general population and calls for further innovations and improvements in diabetes care. Also, prevention and care of complications of diabetes and comorbidities provide potential to improve life expectancy of persons with type 1 diabetes.

Role of the Funding Source

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Data statement

Due to data protection legislation in Finland individual-level data on the study subjects cannot be released.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2023.110580.

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