Improvements in the Life Expectancy of Type 1 Diabetes

The Pittsburgh Epidemiology of Diabetes Complications Study Cohort

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Survival in type 1 diabetes has improved, but the impact on life expectancy in the U.S. type 1 diabetes population is not well established. Our objective was to estimate the life expectancy of the Pittsburgh Epidemiology of Diabetes Complications (EDC) study cohort and quantify improvements by comparing two subcohorts based on year of diabetes diagnosis (1950–1964 [n =390] vs. 1965–1980 [n=543]). The EDC study is a prospective cohort study of 933 participants with childhood-onset (aged <17 years) type 1 diabetes diagnosed at Children's Hospital of Pittsburgh from 1950 to 1980. Mortality ascertainment was censored 31 December 2009. Abridged cohort life tables were constructed to calculate life expectancy. Death occurred in 237 (60.8%) of the 1950–1964 subcohort compared with 88 (16.2%) of the 1965–1980 subcohort. The life expectancy at birth for those diagnosed 1965–1980 was ~15 years greater than participants diagnosed 1950-1964 (68.8 [95% CI $6\overline{4}.7-72.8$] vs. 53.4 [50.8–56.0] years, respectively) (P < 0.0001); this difference persisted regardless of sex or pubertal status at diagnosis. This improvement in life expectancy emphasizes the need for insurance companies to update analysis of the life expectancy of those with childhoodonset type 1 diabetes because weighting of insurance premiums is based on outdated estimates. Diabetes 61:2987-2992, 2012

everal worldwide studies have shown that survival in type 1 diabetes has improved over time (1-9). However, formal assessments of life expectancy of people with type 1 diabetes are relatively rare, and the most recent we found was published in 2001, where Brown et al. (10) reported a life expectancy at birth of 59.7 years in a subset of the Canterbury Diabetes Registry (New Zealand) cohort diagnosed with diabetes when aged younger than 30 years and that began insulin therapy within 12 months of diagnosis. In 1999, Borch-Johnsen (3) reported an increase in life expectancy of 15 years over a 50-year period up to 1982 in a Danish type 1 diabetes cohort. The life expectancy of individuals with type 1 diabetes in the U.S. seems to have been last formally assessed in 1975 by Goodkin (11), who reported that life expectancy in type 1 diabetes (diagnosis age <15 years) was reduced 27 years compared with individuals without diabetes in a life insurance cohort. Using National Health Interview Survey data from 1984 to 2000, however,

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Narayan et al. (12) estimated that U.S. children diagnosed with diabetes at age 10 years lose an average of \sim 19 lifeyears. Similarly, the estimated life expectancy for people with diabetes was 13 years less than people without diabetes in Ontario, Canada; however, this estimate included type 1 and type 2 diabetes (13).

The Pittsburgh Epidemiology of Diabetes Complications (EDC) study cohort provides a unique opportunity to examine mortality and life-expectancy changes over time in a U.S. cohort with long-term (>30 years) follow-up, because the participants were all diagnosed with childhood-onset type 1 diabetes between 1950 and 1980. To determine if, and to what degree, life expectancy has improved, this article compares two subcohorts based on year of type 1 diabetes diagnosis (1950–1964 vs. 1965–1980). We further assess the representativeness of the EDC cohort by comparing the 1965–1980 subcohort with the population-based Allegheny County Type 1 Diabetes Registry (ACR) of childhood-onset type 1 diabetes.

RESEARCH DESIGN AND METHODS

The Pittsburgh EDC study is a prospective cohort study of childhood-onset (age <17 years) type 1 diabetes. All participants were diagnosed or seen within 1 year of diagnosis at Children's Hospital of Pittsburgh between 1950 and 1980. Potential participants were identified using hospital records and were considered eligible for the study if the record noted a clinical diagnosis of type 1 diabetes. The cohort has been described in detail elsewhere (6). Briefly, 933 individuals were studied, with 658 participating in the EDC study baseline examination between 1986 and 1988 and 130 completing questionnaires only. The remaining 145 participants died before the baseline examination in 1986. A comparison of these 145 individuals and those who survived and participated in the study baseline assessment is provided in Table 1. Mortality status ascertainment was censored at 31 December 2009. As of that date, vital status was known for 878 individuals (>94%). The 55 individuals with unknown status were censored at the last date each was known to be living. Death certificates and hospital, autopsy, and coroner reports were obtained, as appropriate, to document mortality for all participants who died during the follow-up period, including the 145 who died before the EDC study baseline examination, and were reviewed by a physician mortality classification committee. The correlation between age and duration of type 1 diabetes at time of study baseline was assessed using Pearson correlation. The EDC study protocol was approved by the University of Pittsburgh institutional review board. Informed consent was obtained in writing from the participants.

To explore changes in survival, before analyses, the participants were divided into two groups by year of type 1 diabetes diagnosis: 1950–1964 and 1965–1980. This method of division was chosen because it divides the period into two equal halves, and data would become sparse if smaller time periods, such as by year, were used. The difference in observed survival between the two subcohorts was visually assessed using Kaplan-Meier curves and the log-rank statistic. Abridged life tables were constructed using the cohort approach, where individuals in a group, in this case, individuals diagnosed with type 1 diabetes during two specific periods of time, are followed up through their lifetime to describe the mortality experience of the group. Life-table intervals were defined as the age groups 0–1 year, 1–5 years, and by 5-year intervals thereafter. The information used to calculate the life-table statistics includes the total population alive at the beginning of each interval, the number of deaths occurring in each interval, and the number of persons censored within

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TABLE 1 Characteristics of the Pittsburgh EDC cohort by vital status at the 1986–1988 assessment (study baseline)

	Deceased $n = 145$	Living $n = 788$	P^{st}
Female (% [n])	44.8 (65)	50.5 (398)	0.21
Year of birth (range)	1950 (1935–1964)	1960 (1939–1979)	< 0.0001
Year of type 1 diabetes diagnosis (range)	1958 (1950–1970)	1969 (1950–1980)	< 0.0001
Age at onset (mean [SD] years)	8.7 (3.9)	8.2 (4.0)	0.24
Type 1 diabetes diagnosed 1965 or later (% $[n]$)	11.0 (16)	66.9 (527)	< 0.0001
Type 1 diabetes duration at last follow-up (mean [SD] years)†	18.7 (7.3)	34.8 (9.3)	< 0.0001

^{*}P value for difference by vital status. †Years of type 1 diabetes duration at death or censoring at most recent follow-up for surviving participants.

the interval. These values are then used to calculate the probability of death and survival by the end of each interval, conditional on being alive at the beginning of the interval. By definition, this cohort has survived to the age of type 1 diabetes diagnosis and, therefore, had no prior death. Therefore, a key assumption of this analysis is that the life tables and resulting life expectancy estimates are conditional on living to childhood-onset type 1 diabetes diagnosis.

Because the EDC study has a large proportion of individuals who are currently living, the true maximum life span of the cohort has not been observed. Therefore, before the life tables were constructed, the terminal age was estimated by extrapolation of Weibull accelerated-failure time curves based on observed mortality patterns to the age at which the probability of survival in this study cohort approximates zero. The Weibull distribution was chosen to estimate the terminal age because it is a flexible distribution used to model survival times and life-span data. The terminal age was estimated to be ${\sim}85$ years old for the total cohort. It is necessary to use the same terminal age for both subcohorts because setting this age at different values would lead to an overestimated difference in life expectancy.

Another consequence of having surviving study participants is that the entire survival curve has not been observed, and thus, the survival function for the age intervals with censored observations must be estimated. Therefore, the computation of these life tables was based on the methodology described by Chiang (14), using the maximum likelihood exponential adjustment of the probability of death for censored data (15). When this method is used, individuals are censored at the age they were last known to be living, and the event rates for incomplete segments (i.e., the age intervals with censored observations) are assumed to have an underlying exponential distribution, using Chiang's (14) maximum likelihood formula and including the information from the observed deaths within the interval (15).

Conditional life expectancy for each age interval (i.e., the average number of years of life remaining in participants who attained the age at the beginning of

the interval) was calculated and compared using a two-sided paired Z test across the diagnosis subcohorts. This report focuses on conditional life expectancy at birth because this is the most frequently cited statistic derived from life-table analysis due to its intuitive interpretation of mean age in years at death. In addition, life expectancy at various ages is presented in the tables. Comparisons of life expectancy were made across the two diagnosis subcohorts by sex and by puberty status at diagnosis because pubertal onset of type 1 diabetes has been shown to be associated with an increased risk of death compared with prepubertal onset (16). Pubertal onset of type 1 diabetes was defined as an age of diagnosis of ≥ 11 years for female and ≥ 12 years for male participants. A significance level of $\alpha = 0.05$ was used for all statistical tests. All life table and life expectancy calculations were performed using Survival 10.0 software (17).

For validation, data from the population-based ACR were used. The ACR (n=1,075), which has been described in detail (18), includes all individuals diagnosed with childhood-onset (aged <18 years) type 1 diabetes in Allegheny County (Pittsburgh, PA) between 1965 and 1979 and prescribed insulin at diagnosis. Individuals were identified via hospital record review and validated by contacting pediatricians throughout the county (ascertainment >95%) (19). Only individuals diagnosed at age <17 years were included in this analysis to match the inclusion criteria of the EDC study. Children who developed diabetes from a secondary cause (i.e., cystic fibrosis, Down syndrome, or steroid-induced diabetes) were excluded. Vital status has been determined as of 1 January 2008, when a search of the National Death Index was conducted, and total (8) and cause-specific mortality (20) have been reported. The ACR includes 271 participants who are also participants in the EDC 1965–1980 diagnosis cohort.

For a descriptive comparison of the improvement in life expectancy between the EDC and U.S. general population, U.S. life tables were used (21). To obtain estimates for the general U.S. population during the same intervals

TABLE 2 Characteristics of overall cohort and diagnosis year subcohorts for the Pittsburgh EDC and ACR cohorts

		ACR cohort				
		T1D dia	1D diagnosed		T1D diagnosed	
	Overall $n = 933$	$ \begin{array}{r} 1950 - 1964 \\ n = 390 \end{array} $	1965-1980 n = 543	P^*	$ \begin{array}{r} 1965 - 1979 \\ n = 1,018 \end{array} $	P^{\dagger}
Female (% [n])	49.6 (463)	46.2 (180)	52.1 (283)	0.07	48.7 (496)	0.20
Year of birth (range)	1958 (1935–1979)	1950 (1935–1963)	1964 (1950–1979)	< 0.0001	1961 (1949–1978)	< 0.0001
Year of T1D diagnosis						
(range)	1965 (1950–1980)	1959 (1950-1964)	1972 (1965–1980)	< 0.0001	1972 (1965–1979)	0.23
Age at onset						
(mean [SD] years)	8.31 (3.98)	7.93 (3.87)	8.58 (4.04)	0.01	10.52 (3.98)	< 0.0001
Pubertal diagnosis						
(% [n])	25.1 (234)	21.0 (82)	28.0 (152)	0.02	46.1 (469)	< 0.0001
Deceased (% $[n]$)	34.8 (325)	60.8 (237)	16.2 (88)	_	25.6 (261)	< 0.0001
Person-years						
of follow-up	30,127.61	13,555.75	16,571.86	_	32,674.59	_
Mortality incidence						
density (95% CI)‡	1,079 (961–1,196)	1,748 (1,525–1,971)	531 (420–642)	< 0.0001	799 (702–896)	0.001

T1D, type 1 diabetes. *Comparing the 1950–1964 subcohort with the 1965–1980 subcohort within Pittsburgh EDC. †Comparing the 1965–1980 Pittsburgh EDC subcohort with the 1965–1979 ACR cohort. ‡Mortality incidence density is calculated as standardized number of deaths per 100,000 person-years.

(1950–1964 and 1965–1980), the life expectancy at the midpoint year of each period was used (1957 and 1972, respectively). The life tables for Caucasians were used for comparability because the EDC cohort is 98% Caucasian. In addition, life expectancy at age 8 was used because this was approximately equivalent to the median year of type 1 diabetes diagnosis in the EDC cohort and the life-expectancy estimates are conditional on surviving to the age of diagnosis.

RESULTS

The characteristics of both EDC cohorts (overall and diagnosis years 1950–1964 and 1965–1980) and ACR (1965–1979) are presented in Table 2. The proportion of participants in the EDC who were female was slightly lower in the 1950-1964 subcohort, with 46.2% being female, compared with 52.1% in the 1965–1980 subcohort (P = 0.07). The mean age at onset was significantly vounger in the 1950–1964 subcohort compared with the 1965-80 subcohort (7.9 vs. 8.6 years, respectively, P =0.01). In the 1950–1964 subcohort, the distribution of the age at diagnosis was 26.4% at <5 years, 39.0% at 5-9 years, 32.3% at 10–14 years, and 2.3% at \geq 15 years old. The distribution of age at diagnosis in the 1965–1980 subcohort was 21.2% at <5 years, 36.7% at 5–9 years, 38.1% at 10–14 years, and 4.1% at \geq 15 years old. Likewise, the proportion of participants with pubertal onset of type 1 diabetes was lower in the 1950-1964 compared with the 1965–1980 subcohort (21 vs. 28%, respectively, P = 0.02). The overall EDC cohort was followed up for a total of 30,127.6 person-years, with 13,555.7 from the 1950–1964 subcohort and 16,571.9 person-years from the 1965–1980

subcohort. The mortality rate was three times greater in the 1950–1964 subcohort compared with the 1965–1980 subcohort (1,748 [95% CI 1,525–1,971] vs. 531 [420–642] per 100,000 person-years, respectively; P < 0.0001). The ACR showed a higher mean age at onset and death than the later EDC cohort.

As shown in the Kaplan-Meier curves in Fig. 1, crude survival was greater in the more recent (1965–1980) subcohort (log-rank test P < 0.0001) than in the earlier cohort. However, the later EDC and ACR cohorts had similar survival (log-rank test P = 0.10). Table 3 reports the observed probability of death and the life expectancy at various ages for the two EDC diagnosis subcohorts. The life expectancy at birth for the participants diagnosed with type 1 diabetes between 1950 and 1964 is 53.4 years compared with 68.8 years for participants diagnosed between 1965 and 1980, an increase of > 15 years (P < 0.0001). A similar increase in life expectancy between the two diagnosis subcohorts persisted, regardless of sex, age at diagnosis, and pubertal status at diagnosis (Table 4). Table 3 shows the observed probability of death and life expectancy at various ages for the 1965–1980 EDC cohort and the ACR, for individuals diagnosed at age <17 years, as in EDC, during the same period of time. The life expectancy at birth in the population-based ACR cohort is estimated to be 67.2 years, which is 1.6 years less than the estimated life expectancy of the comparable EDC cohort; this difference did not reach statistical significance (P = 0.49).

The estimated life expectancy for the comparable cohort of the general U.S. population in 1957 and 1972 (the

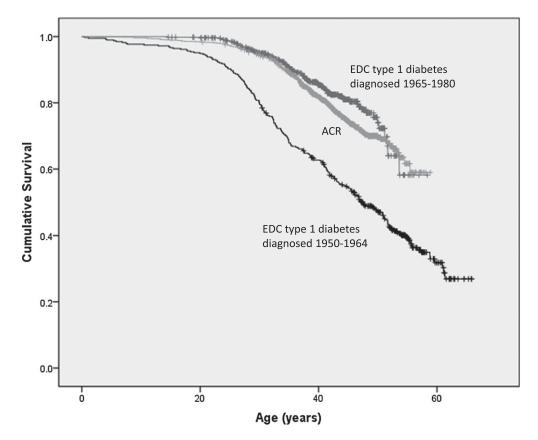


FIG. 1. Observed Kaplan-Meier survival function comparing EDC study type 1 diabetes diagnosis year subcohorts (1950–1964 vs. 1965–1980) and the ACR cohort. The small vertical lines represent censoring times of surviving individuals. EDC 1950–1964 vs. 1965–1980 \log -rank P < 0.0001; EDC 1965–1980 vs. ACR \log -rank P = 0.10. Remaining number at risk at each age: EDC 1950–1964: birth, 390; 20 years, 370; 40 years, 239; 60 years, 26; EDC 1965–1980: birth, 543; 20 years, 537; 40 years, 272; 60 years, 0; ACR: birth, 1,018; 20 years, 1,002; 40 years, 704; 60 years, 0.

TABLE 3
Probability of death and life expectancy by age in the Pittsburgh EDC study by year of type 1 diabetes diagnosis subcohort (1950–1964 and 1965–1980) and the ACR cohort (1965–1979)

	EDC diabetes diagnosed $1950-1964 (n = 390)$		EDC diabetes diagnosed $1965-1980 (n = 543)$		ACR 1965–1979 ($n = 1,018$)			
Age (years)	Probability of death before next age (Observed)	Estimated life expectancy (95% CI)	Probability of death before next age (Observed)	Estimated life expectancy (95% CI)	P^*	Probability of death before next age (Observed)	Estimated life expectancy (95% CI)	P^{\dagger}
Birth	0.003	53.4 (50.8–56.0)	0.000	68.8 (64.7–72.8)	< 0.0001	0.000	67.2 (65.2–69.1)	0.49
1	0.008	52.6 (50.0-55.2)	0.000	67.8 (63.7–71.8)	< 0.0001	0.001	66.2 (64.2–68.1)	0.49
5	0.013	49.0 (46.4–51.5)	0.000	63.8 (59.7–67.8)	< 0.0001	0.003	62.2 (60.3–64.2)	0.51
10	0.011	44.6 (42.0–47.1)	0.002	58.8 (54.7–62.8)	< 0.0001	0.007	57.4 (55.4–59.4)	0.56
15	0.019	40.0 (37.5-42.6)	0.000	53.9 (49.8–57.9)	< 0.0001	0.005	52.8 (50.8-54.7)	0.64
20	0.049	35.7 (33.2–38.3)	0.011	48.9 (44.8–52.9)	< 0.0001	0.011	48.0 (46.1–50.0)	0.72
25	0.114	32.4 (29.9–33.7)	0.039	44.4 (40.3–48.5)	< 0.0001	0.031	43.5 (41.6-45.5)	0.71
30	0.151	31.3 (28.7–33.8)	0.044	41.1 (36.9–45.2)	< 0.0001	0.582	39.8 (37.9-41.8)	0.60
35	0.077	31.4 (28.8–34.0)	0.059	37.9 (33.6–42.1)	0.01	0.081	37.1 (35.2–39.1)	0.77
40	0.132	28.8 (26.3–31.4)	0.052	35.1 (30.6–39.5)	0.02	0.096	35.2 (33.2–37.2)	0.97
45	0.133	27.8 (25.3–30.3)	0.073	31.9 (27.3–36.4)	0.13	0.072	33.7 (31.6–35.7)	0.48
50	0.185	26.7 (24.3–29.1)	0.179	29.2 (24.6–33.8)	0.35	0.101	31.1 (29.2–33.1)	0.45

The life expectancies presented are at the beginning of each age interval, the start of which is denoted in the age column. The final age interval is 50–85 years. *P for difference in life expectancy between the EDC 1950–1964 and 1965–1980 subcohorts. †P for difference in life expectancy between EDC 1965–1980 subcohort and the ACR cohort.

midpoint years for the two EDC subcohorts) was \sim 71.5 and 72.4 years, respectively, an increase of <1 year.

DISCUSSION

This report describes changes in the life expectancy of the Pittsburgh EDC study by year of type 1 diabetes diagnosis (1950–1964 vs. 1965–1980). Crude survival was significantly higher in the more recent (1965–1980) diagnosis subcohort, as previously reported (6), and likewise, life expectancy at birth is now shown to have significantly increased by \sim 15 years compared with the 1950–1964 subcohort. It should be noted that in the EDC study cohort, age is highly correlated with type 1 diabetes duration (r=0.85); thus, the observed mortality patterns would be similar if diabetes duration were used as the time scale. The most recent report of life expectancy in type 1 diabetes estimated the life expectancy at birth was 59.7 years in the

Canterbury Diabetes Registry's 1984 prevalence database (10), which approximates the 61-year midpoint life expectancy of the two EDC subcohorts. The improvement in the EDC 1965–1980 subcohort was apparent in both sexes and persisted regardless of pubertal status at type 1 diabetes diagnosis. In a Romanian type 1 diabetes cohort, the mean age at death increased by $\sim\!\!7$ years between two similar intervals of diabetes diagnosis (1946–1965 vs. 1966–1985), and this improvement also did not differ by sex (22).

Although absolute mortality, expressed as mortality frequency and incidence density, was higher, the estimated life expectancy in the 1965–1980 EDC subcohort was similar to that of the population-based ACR cohort diagnosed in 1965–1979. The higher mortality rate, but similar life expectancy, reflects the somewhat older age of the ACR cohort. Accounting for the difference in age distribution, survival was similar between the two groups (Fig. 1). These results suggest that the hospital-based EDC

TABLE 4
Life expectancy at birth by year of type 1 diabetes diagnosis subcohort stratified by sex, age at diabetes diagnosis, and pubertal status at diabetes diagnosis

	Year of type 1 diabetes diagnosis				
	$1950 - 1964 \ (n = 390)$				
	\overline{n}	Life expectancy (95% CI)	\overline{n}	Life expectancy (95% CI)	P^*
Sex					
Men	210	51.5 (48.1–54.9)	260	67.0 (61.2–72.9)	< 0.0001
Women	180	54.8 (50.9–58.8)	283	70.5 (65.3–76.0)	< 0.0001
Age at diagnosis					
<median age†<="" td=""><td>196</td><td>52.6 (48.9–55.9)</td><td>272</td><td>65.8 (54.7–76.9)</td><td>0.03</td></median>	196	52.6 (48.9–55.9)	272	65.8 (54.7–76.9)	0.03
≥Median age	194	54.2 (50.8–57.6)	271	69.2 (65.0–73.5)	< 0.0001
Prepubertal	308	54.9 (51.9–58.0)	391	70.8 (66.0–75.6)	< 0.0001
Pubertal‡	82	54.0 (48.9–59.1)	152	68.5 (63.3–73.7)	< 0.0001

^{*}P for difference in life expectancy between type 1 diabetes diagnosis year subcohorts. \dagger Cohort-specific median age at onset: 8.1 years (interquartile range 4.8–11.3, range 0.25–15.9) in the 1950–1964 cohort and 8.8 years (interquartile range 5.9–11.8, range 0.28–16.3) in 1965–1980 cohort. \ddagger Pubertal onset of type 1 diabetes was defined as diagnosis age \ge 11 years for female and \ge 12 years for male participants.

study cohort is representative of the local type 1 diabetes population in mortality in addition to sharing similar epidemiologic characteristics, as previously described (23). We thus believe the dramatic improvement in life expectancy is likely true for the general population with childhood-onset type 1 diabetes and not due to a preferential participation of healthier individuals in the EDC in later years. Furthermore, the improvement in life expectancy is far greater than that seen in the general population.

There are several potential explanations for the substantial increase in life expectancy between the two subcohorts. First, no early childhood deaths were observed in the more recent subcohort (1965–1980), with the first death occurring at age 12 years, compared with the first death occurring at age 6 months in the earlier cohort (1950–1964). The lack of early deaths in the 1965–1980 subcohort is likely related to the earlier recognition and improved treatment of type 1 diabetes in young children after the 1950s. Indeed, it has been reported that a large proportion of childhood deaths in type 1 diabetes were attributed to diabetic ketoacidosis or hypoglycemia (24,25).

A second potential explanation for the increase in life expectancy is that there was a general decline in the acute and long-term complications of type 1 diabetes in individuals diagnosed after 1965, because a greater proportion of their diabetes duration occurred during an era of better glucose monitoring and insulin administration (6,26).

The greater life expectancy may also be due specifically to the reduction of renal disease resulting from improved diabetes care. Several reports have demonstrated a decline in renal disease in type 1 diabetes (6,27,28). In addition, an increase in ACE inhibitor use within the Pittsburgh EDC cohort was associated with a decrease in death (29). In fact, the Finnish Diabetic Nephropathy (FinnDiane) study (30) and the Pittsburgh EDC study (31) have both recently shown that in the absence of renal disease and microalbuminuria, the long-term mortality risk in type 1 diabetes is not increased compared with the general population.

An increase in statin use is another possible contributor to increasing life expectancy in type 1 diabetes. Although historically, low rates of statin use in the EDC cohort have prevented detailed analysis of the effect of statins on mortality rates, the 2008 Cholesterol Treatment Trialists' Collaborators' meta-analysis reported a 9% reduction in mortality for each millimole per liter decrease in LDL cholesterol in people with diabetes (type 1 and type 2 combined) (32).

This report has several noted strengths. The Pittsburgh EDC study includes participants who were diagnosed during a 30-year period (1950-1980), allowing the study cohort to be divided into two subcohorts that likely experienced different natural histories of type 1 diabetes due to improvements in treatment. The EDC study has also obtained death certificates for all individuals, including those who were eligible to participate but died before the baseline examination, thus minimizing potential survival bias. Similarly, 130 individuals who were eligible, but declined examination, have provided survey and mortality follow-up. In addition, we were able to validate the lifeexpectancy estimates for the 1965–1980 subcohort by using the population-based ACR data collected during the same time period, which also had a very high 95% vital status ascertainment. It could be argued that it is not appropriate to include the 271 participants who are common to both the EDC 1965-1980 diagnosis subcohort and the ACR in this validation. However, if the rates of ACR are the

gold standard, and they are as a true population-based cohort, then the similarity with EDC is an important validation regardless of the amount of overlap. This validation is not of methodology, but rather of whether the estimated rates seen in the hospital-based EDC are representative of the local type 1 diabetes population. Because the overlapping segment of EDC is itself part of the population, a bias would be created if these individuals were excluded from the ACR for this comparison.

A key limitation to these analyses is that complete lifetime follow-up is not possible for currently surviving participants because the EDC study is ongoing. Although we have attempted to correct for this incomplete follow-up by using Chiang's maximum likelihood adjustment in our calculations of life expectancies, we note that these results are intended as a description of the particular cohort studied and may not be applicable to type 1 diabetes in general, particularly those diagnosed after adolescence. In addition, these findings may not be fully reflective of the life expectancy of a child diagnosed in 2012. Although a period or "current" life-table approach theoretically would address this issue, this is debatable because the "current" age-specific mortality rates that would be used would reflect, at older ages, a survival cohort of those diagnosed before improved care could contribute much to their prognosis.

We thus intend for these estimates to be used as relative comparisons of life expectancy between the two subcohorts being examined and to describe improvements in mortality and life expectancy over time. The EDC is a study of a hospital-based cohort and may not reflect the overall type 1 diabetes population; however, the ACR data presented clearly show that life expectancy is similar in the two cohorts, so these data likely present a reasonable estimate of the life expectancy of childhood-onset type 1 diabetes in this area.

In conclusion, life expectancy improved from the 1950– 1964 to 1965–1980 type 1 diabetes diagnosis subcohorts of the Pittsburgh EDC study, a hospital-based cohort of childhood-onset type 1 diabetes. A similar improvement between diagnosis subcohorts was observed regardless of sex or pubertal status at diagnosis. Further investigation shows this life expectancy is similar to community-based life expectancy, suggesting childhood-onset type 1 diabetes diagnosed in the late 1960s and 1970s is associated with only a 4- to 6-year loss-of-life expectancy compared with >17 years for those diagnosed in the 1950s and early 1960s. These results support the need for insurance companies to update their analysis of the life expectancy of those with childhood-onset type 1 diabetes, because the current weighting of insurance premiums is based on earlier, outdated estimates.

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R.G.M. contributed to the study concept and design, to acquisition, analysis, and interpretation of the data, to drafting the manuscript and critical review of the manuscript for important intellectual content, to statistical

analysis, and to administrative, technical, or material support. A.M.S. contributed to the study concept and design, to acquisition, analysis, and interpretation of the data, to critical review of the manuscript for important intellectual content, and to statistical analysis. R.K.S. contributed to the study concept and design, analysis and interpretation of the data, critical review of the manuscript for important intellectual content, and statistical analysis. T.J.S. contributed to the study concept and design, analysis and interpretation of the data, critical review of the manuscript for important intellectual content, statistical analysis, and to administrative, technical, or material support. T.J.O. supervised the study and contributed to study concept and design, analysis and interpretation of the data, critical review of the manuscript for important intellectual content, obtaining funding, and to administrative, technical, or material support. T.J.O. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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