

Supplementary Online Content

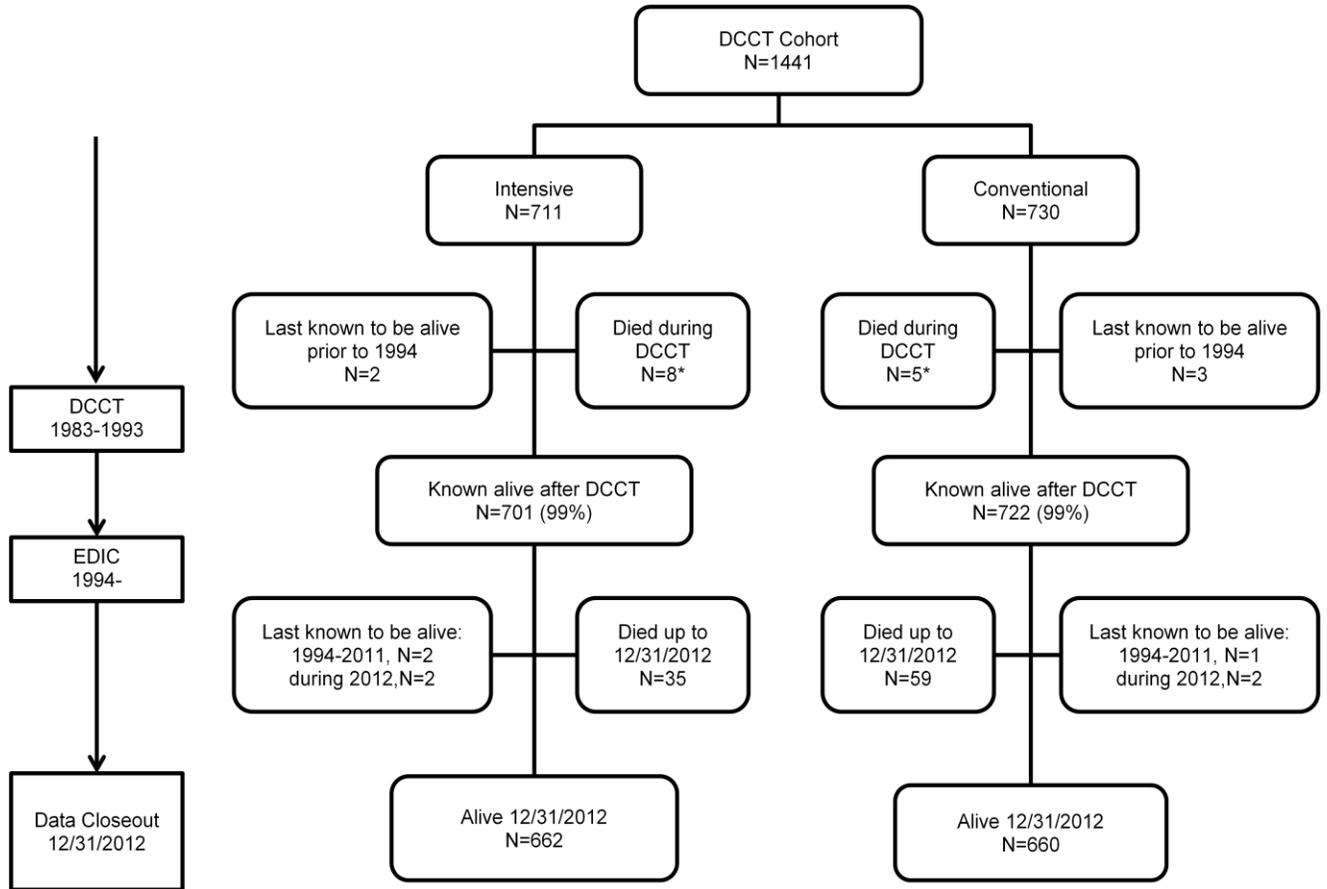
Writing Group for the DCCT/EDIC Research Group; Orchard TJ, Nathan DM, Zinman B; et al. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *JAMA*. doi: 10.1001/jama.2014.16107

eFigure. Patient Disposition Since the Start of Randomization Into the EDDT in 1983 Through December 31, 2012

eTable. Differences in Time-Dependent Covariates During DCCT and EDIC Between the Original DCCT Intensive vs Conventional Groups up to the Time of Death or Right Censoring

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Patient Disposition Since the Start of Randomization Into The DCCT in 1983 Through December 31, 2012



* One patient in each group died between the closeout of the DCCT in 1993 and the launch of EDIC in April, 1994.

Consort Figure

The eFigure presents the patient disposition since randomization into the DCCT starting in 1983. Patients were enrolled into the DCCT during 1983-1989 and follow-up ended in 1993 so that the period of follow-up ranged from 4 to almost 10 years, with a mean of 6.5 years. During the DCCT 11 patients died and 2 more died during the intervening year before the start of EDIC. The date last known to be alive is the date of last contact during the DCCT or EDIC at which the survival time (measured since the day of randomization) was right censored in the survival analysis. For 5 subjects the right censoring date occurred during DCCT, for 7 it occurred during EDIC and for 1322 (99.1% of the 1334 survivors) vital status was known as of the time of data closeout, i.e. were administratively censored (12/31/2012).

There were no eligibility or exclusion criteria for entry into EDIC other than the requirement that they had participated in DCCT and provided consent to enroll in EDIC. So those who did not enter EDIC had either died or had refused consent to enroll. However, for many of those who did not enroll, we were still able to assess vital status as shown in the Figure.

eTable. Differences in Time-Dependent Covariates During DCCT and EDIC Between the Original DCCT Intensive vs Conventional Groups up to the Time of Death or Right Censoring

Time-Dependent Covariate	Intensive (N=711)	Conventional (N=730)	INTENSIVE:CONVENTIONAL	
			Hazard Ratio ^a (95% CI)	P-value
<u>Renal Disease^c</u>	N (Percent^b)			
A. AER ^d ≥ 40 mg/24 h, %	227 (33.8) ^d	334 (48.1) ^d	0.63 (0.53, 0.75)	<0.001
B. AER ≥ 300 mg/24 h, %	49 (6.9)	122 (16.7)	0.39 (0.28, 0.54)	<0.001
C. Renal Insufficiency (% yes)	18 (2.5)	26 (3.6)	0.69 (0.38, 1.26)	0.23
<u>Hypoglycemia</u>				
A. Coma/Seizure (% yes)	376 (52.9)	292 (40.0)	1.57 (1.35, 1.83)	<0.001
B. All Severe Episodes (%yes) [‡]	534 (75.1)	463 (63.4)	1.40 (1.23, 1.58)	<0.001
<u>Mean HbA1c during DCCT/EDIC</u>	Mean ± SD		Mean Difference^f (95% CI)	
A. HbA1c (%) ^e	7.8 ± 1.0	8.4 ± 1.0	-0.57 (-0.67, -0.46)	<0.001

CI = 95% Confidence Interval, AER = Albumin Excretion Rate, HbA1c = glycated hemoglobin

Time-Dependent Covariates: The eTable presents the differences between the treatment groups for the time-dependent-covariates that are employed in Tables 4 and 5 to describe covariate effects on mortality and the extent to which group differences in covariates explain the group effect on mortality.

- a. Hazard ratio for intensive versus conventional from an unadjusted Cox PH model.
- b. Simple percentage of subjects in each group with the covariate event up to the time of death, last known date to be alive, or 12/31/12.
- c. Microalbuminuria/albuminuria included subjects who progressed to ESRD that was not preceded by a timed renal collection to measure the albumin excretion rate. Renal insufficiency was defined by a history of an eGFR < 30 ml/min/1.73m² using the CKD-EPI equation [22], of kidney transplantation, or the implementation of dialysis.
- d. 74 subjects who entered the DCCT with an AER ≥ 40 mg/24 h were excluded from the analysis of incident microalbuminuria during follow-up. Thus, the denominators for the percent with microalbuminuria during the study are 672 and 695 in the intensive and conventional groups, rather than the total group sizes of 711 and 730 that apply to the other outcomes in the table.
- e. For each subject the mean of all HbA1c values during DCCT and EDIC up to the time of death, last known date to be alive, or 12/31/12 was computed. Then the simple mean and SD of the values for each group were computed.
- f. Simple mean difference used to compute a t-test and p-value.