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Mortality of Type 1 (insulin-dependent) diabetes mellitus in Denmark: a study of relative mortality in 2930 Danish Type 1 diabetic patients diagnosed from 1933 to 1972

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Summary. This study included 2930 (1642 male, 1288 female) Type 1 (insulin-dependent) diabetic patients diagnosed before the age of 31 years and between 1933 to 1972. The patients were followed from first admission to Steno Memorial Hospital until death, emigration, or until 1 January 1983. Relative mortality was studied, and the influence of calendar year of diagnosis, diabetes duration, age at diagnosis, current age and sex were studied. Relative mortality decreased continuously during the period, and patients diagnosed after 1956 had a relative mortality 30–40% lower than patients diagnosed from 1933 to 1946. Relative mortality increased with increasing diabetes duration until about 20 years of duration, after which it declined. It also increased with increasing age until 31–40 years. It decreased with increasing age at diabetes onset. Factors like calendar year of diabetes onset, age at diagnosis, current age and sex had no influence on relative mortality within the first 15 years of duration, although the relative mortality increased with diabetes duration. In the interval of 16 to 40 years of diabetes duration, the relative mortality decreased with increasing calendar year of diagnosis and age at diagnosis. In patients with a diabetes duration of more than 40 years, the relative mortality decreased with increasing age and diabetes duration. These results show that the prognosis of Type 1 diabetic patients has improved considerably during the last 40 years. Furthermore, they show that diabetes duration is the most important determinant of relative mortality.

Key words: Type 1 diabetes, relative mortality, prognosis, epidemiology.

Studies of absolute and relative mortality in diabetic populations have consistently shown increased but varying relative mortality. These variations may in part be explained by differences in the composition of the study populations (e.g. race, sex and type of diabetes), and in the sample procedures and statistical methods applied [1]. Relative mortality also depends on diabetes duration [2, 3], and thus differences in age and diabetes duration composition may have contributed to the variations in the relative mortality. Furthermore, improvement in the prognosis of Type 1 diabetes during the last decades might have contributed.

In a recent study we [2] found that the relative mortality of Type 1 diabetic patients in Denmark had decreased during the period from 1933 to 1981, and that it was highest after 15 to 25 years of diabetes duration. However, this study included two different populations, one collected from a specialized diabetes care center and the other population-based.

The first aim of the present study was to re-evaluate possible seqular trends in the relative mortality of Type 1 diabetes within a homogenous and representative sample.

Our second aim was to evaluate interactions between previously reported indicators of diabetes mortality and diabetes duration, since relative mortality shows substantial variations with increasing diabetes duration.

Subjects and methods

The study included 2930 (1642 male, 1288 female) Type 1 (insulin-dependent) diabetic patients. In all cases, diabetes was diagnosed before the age of 31 years and between 1933 and 1972. Of these patients, 1163 were diagnosed prior to 1953. Results on the relative mortality of these patients have been reported previously [2–4]. The remaining 1767 patients, diagnosed between 1953 and 1972, were identified from our hospital records, and data on these patients have *not* been reported previously. These patients were included to evaluate seqular changes in the relative mortality.

Continuous insulin treatment from diabetes onset was necessary in all cases (Fig. 1). The patients were admitted to Steno Memorial Hospital before 1972 and were followed from admission until death, emigration, or until 1 January 1983. The patients were referred to the Steno Memorial Hospital from all parts of Denmark, but predominantly from greater Copenhagen (39%) or larger cities (40%). They were always referred from a general practitioner or a hospital, and treatment was always given free of charge. Median diabetes duration

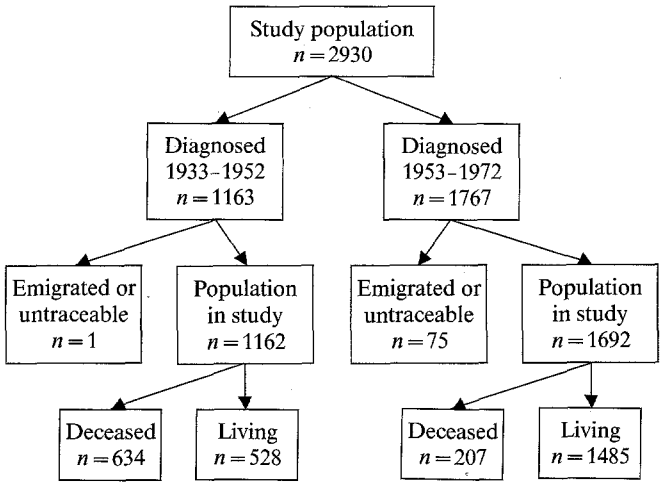

Fig. 1. The subdivision of the cohort of 2930 Type 1 diabetic patients

at referral was 4 years (range 0-39 years). After the first admission, 53% of patients were followed at the Steno Memorial Hospital, while 47% were followed by their general practitioner, often supported by local medical departments. All patients were identified through the central national register, using their name, address and personal identification number.

Assuming a constant age-specific incidence of Type 1 diabetes in Denmark, the present population represents 25-30% of all Danish Type 1 diabetic patients diagnosed from 1933 to 1972 [5]. The assumption of a constant incidence is supported by a recent Danish study (A. G. Mølbak, personal communication). If the incidence has increased over the observation period as suggested by Danish [6] and Swedish [7] studies, the present study population represents an even higher percentage of all Danish Type 1 diabetic patients. Distribution of age at diagnosis ($p = 0.15$) and sex ($p = 0.42$) did not differ between the present study and a population-based incidence study [5]. The impact of previously reported indicators of diabetes mortality was also shown to be the same in the first part of the present population and in a population-based sample of Type 1 diabetic patients [1, 2].

The hospital records allowed us to collect data concerning sex, age at diagnosis, year of diagnosis and diabetes duration at admission.

For analysis of relative mortality, the age, sex, and calendar year, specific death rates for the total Danish population were obtained from the statistical yearbook of the Department of Statistics.

Statistical model and analysis

Analysis of the relative mortality was performed using discrete logistic failure time models [8].

Let

T	= time from diagnosis to death measured in years
Y_d	= the calendar year of diagnosis
A_d	= the age at diagnosis
S	= sex
Y(t)	= $Y_d + t$ = the "current" year
A(t)	= $A_d + t$ = the "current" age
$X_1, \ldots, X_k$	= additional covariates or explanatory factors.

The hazard at a given number of years, t, since diagnosis is defined as the conditional probability of death at t,

$$P(T = t | T \geq t).$$

We will consider the hazard as dependent on the above mentioned covariates and factors and will therefore consider

$$P(T = t | T \geq t, Y_d, A_d, S, Y(t), A(t), X_1, \ldots, X_k)$$

Even if there were no excess mortality among diabetic patients, the hazard would be dependent on current age, sex and current calendar year reflecting the known age-, sex-, and calendar year-dependent death rates of the population at large.

To distinguish between the "normal" mortality and the excess or relative mortality characterizing the diabetic patients, the death rates have to be introduced in the formula for the hazard rate.

Let ¶ (y, a, s) = the probability of death in year, y, for a given age, a, and sex, s.

We will presume that the hazard may be described by some kind of general linear model, i.e. that a so-called link-function, l, exists for which

$$\begin{aligned} &P(T = t | T \geq t, Y_d, A_d, S, Y(t), A(t), X_1, \ldots, X_k) \\ &= l(\alpha(Y(t), A(t), S) + \beta_0 + \Sigma \beta_i (X_i) \\ &+ \beta_{k+1}(Y_d) + \beta_{k+2}(A_d) + \beta_{k+3}(S) \\ &+ \beta_{k+4}(Y(t)) + \beta_{k+5}(A(t)) + \beta_{k+6}(t)) \end{aligned}$$

The parameters, $\beta_1, \ldots, \beta_{k+6}$ describe the effect of factors and covariates on the relative mortality. Note that it is presumed that age, sex and calendar year may be of importance for relative mortality as well as for the population-specific normal mortality. β_0 is the general level of excess mortality among the diabetic patients. $\alpha(y,a,s)$ specifies the normal level of mortality within the framework given by the link-function of the general linear model. No excess mortality among diabetic patients corresponds to $\beta_0 = \beta_1 = \ldots = \beta_{k+6} = 0$, in which case the hazard rate equals the death rate of the population at large. It follows that

$$¶(y,a,s) = l(\alpha(y,a,s)).$$

With ¶ and l known, it follows that α may be determined as well. The β-parameters are therefore the only unknown parameters of the model.

Several different link functions for binary data (deceased/living) have been suggested. In the present sutdy a logistic link was applied, i.e.

$$P(T = t | T \geq t, Y_d, A_d, S, Y(t), A(t), X_1, \ldots, X_k) = \frac{\exp(\alpha(Y(t), A(t), S) + \beta_0 + \sum_1^i \beta_i(X_i) + \beta_{k+1}(Y_d) + \ldots + \beta_{k+6}(t))}{1 + \exp(\alpha(Y(t), A(t), S) + \ldots + \beta_{k+6}(t))}$$

The data was analysed according to this model and the following general considerations:

1) A backward variable-selection strategy was applied eliminating one factor/covariate at a time (a more demanding, but also a more reliable strategy than forward selection, where the initial calculations concern choices between equally unrealistic models).

2) No linear assumptions concerning the β-parameters were made (e.g. $\beta_i(X_i) = \beta_i \cdot X_i$), as non-linear and even non-monotonous effect of covariates on relative mortality were presumed possible.

3) The years of entry and the years in which censoring occurred were excluded from the analysis because the exact data of entry or censoring were not available. For these years the normal probability of death was not known. The number of years excluded from the study in this way were neglible compared to the total number of years at risk which were analyzed.

4) Standard likelihood ratio tests were used in the analysis.

5) Given the estimated parameters of the model, the expected numbers of deaths occurring under specified conditions may be calculated. In connection with the evaluation of the results of the analysis, specific care was taken to check the correspondence between observed and expected numbers of deaths in high risk years. No discrepancy was found.

6) To analyze the interaction of the effects of factors and the effect of diabetes duration on relative mortality the material was analyzed both as a whole and divided into submaterials defined by stratification according to 5-year intervals of diabetes duration.

The results may be easier to evaluate using a multiplicative formula for the hazard.

Set $\theta = \exp(\alpha)$

$\Phi = \exp(\beta)$

Table 1. Basic characteristics of the study population

Year of diagnosis	Percent males	Age at diagnosis (median + range)	Duration at admission to Steno Memorial Hospital (median + range)	Number of out-patient clinic visits during the first 20 years of diabetes duration (median/range)
1933–1952 ($n=1163$)	55.4	14 years (0–30)	5 years (0–36)	0 (0–193)
1953–1972 ($n=1767$)	56.5	15 years (0–30)	3 years (0–27)	16 (0–201)
p	0.55[a]	0.28[b]	<0.0001[b]	<0.0001[b]

[a] χ^2test; [b] Mann-Whitney test

Expressed in terms of the θ and Φ parameters, the hazard may be written

$$P(T=t|T\geq t_1,Y_d,\ldots,X_k) = \frac{\theta(Y(t),A(t),S)\cdot\Phi_o\cdot\prod_1^k\Phi_i(X_i)\cdot\Phi_{k+1}(Y_d)\cdot\ldots\cdot\Phi_{k+6}(t)}{1+\theta(Y(t),A(t),S)\ \Phi_o\cdot\ldots\cdot\Phi_{k+6}(t)}$$

when the hazard – normal and with diabetes – is low, the denominator will be close to 1, for which reason we have an approximatively multiplicative hazard rate. In this case it is reasonable to talk of the Φ-parameters as relative hazard factors.

The ratio between the parameters for men and women will correspond approximatively to the ratio between hazard rates for men and women, given that all other factors are the same.

All parameters reported later in this paper are parameters corresponding to the multiplicative version of the model.

The product of all Φ-parameters – including Φ_o – characterizing a given situation/year may be used as an approximative factor of excess mortality. Exact calculations will of course require knowledge of the normal death rate, but as long as this is small, the product of the Φ-parameters will provide an usable approximation.

Results

Basic characteristics of patients diagnosed from 1933 to 1952 and from 1953 to 1972

When comparing patients diagnosed from 1933 to 1952 [2–4] with patients diagnosed from 1953 to 1972 (Table 2), no difference in sex distribution or age at onset was found. Patients diagnosed from 1953 to 1972 had, however, shorter diabetes duration at admission to the Steno Memorial Hospital than patients diagnosed from 1933 to 1952 (median 3 years versus 5 years, range 0–27 years versus 0–36 years, $p<0.0001$). Also the number of out-patient clinic visits during the first 20 years of diabetes duration was significantly higher in patients diagnosed from 1953 to 1972 than in patients diagnosed from 1933 to 1952 ($p<0.001$).

Factors influencing relative mortality

Calendar year of diagnosis significantly influenced the relative mortality ($p<0.0005$), and a decrease in the relative mortality was found with increasing calendar year of diagnosis. During the observation period of 40 years, a 30–40% decrease in relative mortality was observed (Table 2).

Table 2. Hazard rate ("odds ratio") for relative mortality in the logistic model with diabetes duration as independent variable

Factor		"Odds ratio"	p
Diabetes duration (years)	1– 5	1	
	6–10	0.7	
	11–15	1.0	
	16–20	2.6	<0.00001
	21–25	2.3	
	26–30	2.1	
	31–39	1.4	
	40+	1.3	
Calendar year of diagnosis	1933–40	1.0	
	1941–45	1.1	
	1946–55	0.7	<0.0005
	1956–65	0.7	
	1966–72	0.6	
Age at diagnosis (years)	0– 5	1.0	
	6–10	1.0	
	11–15	0.8	<0.00001
	16–20	0.6	
	21–25	0.5	
	26–30	0.4	
Current age (years)	0–20	1.0	
	21–31	1.4	
	31–40	1.9	<0.00001
	41–50	1.2	
	51+	0.8	
Calendar year during follow-up	1940–45	–	
	1946–50	–	
	1951–55	–	
	1956–60	–	0.53
	1961–65	–	
	1966–70	–	
	1971–75	–	
	1976+	–	
Diabetes duration at admission (years)	0– 5	1.0	
	6–15	1.4	<0.00001
	16+	1.9	
Sex	M	–	1.0
	F	–	
Underlying hazard rate (Φ_o)		6.5	

– Means insignificant. The relative mortality of an individual with the characteristics i in the 7 parameters can be estimated in the multiplicative model by multiplying the "odds ratio" as described in the text

Diabetes duration also significantly influenced the relative mortality ($p<0.00001$), with the highest relative mortality after 15 to 30 years of duration, leading to a "bell-shaped" configuration of the relative mortality.

Low *age at diagnosis* significantly increased the relative mortality ($p<0.0001$). Furthermore, *current age* was of significant importance ($p<0.00001$), with the highest relative mortality in the age interval 31 to 40 years.

Table 3. Hazard rate ("odds ratio") for relative mortality in the logistic model after stratification according to diabetes duration

Diabetes duration (years)		1-5	6-10	11-15	16-20	21-25	26-30	31-39	40+
Calendar year of diagnosis	1933-40	–	–	–	–	–	1.0[c]	–	–
	1941-45	–	–	–	–	–	0.8	–	–
	1946-55	–	–	–	–	–	0.6	–	
	1956-65	–	–	–	–	–	–		
	1966-72	–	–	–			–		
Age at diagnosis (years)	0- 5	–	–	–	1.0[d]	1.0[d]	1.0[d]	1.0[d]	–
	6-10	–	–	–	1.3	1.9	0.9	0.8	–
	11-15	–	–	–	1.5	1.2	0.5	0.5	–
	16-20	–	–	–	1.2	0.8	0.18	0.4	–
	21-25	–	–	–	0.7	0.6	0.20	0.23	–
	25-30	–	–	–	0.4	0.2	0.12	0.20	–
Current Age (years)	0-20	–	–	–	–	–			
	21-30	–	–	–	–	–	–		
	31-40	–	–	–	–	–	–	–	
	41-50			–	–	–	–	–	1.0[b]
	51+				–	–	–	–	0.4
Calendar year during followup	1940-45	–	–						
	1946-50	–	–	1.0[a]					
	1951-55	–	–	3.1	–				
	1956-60	–	–	1.3	–	–			
	1961-65	–	–	0.7	–	–	–		
	1966-70	–	–	0.8	–	–	–	–	
	1971-75	–	–	1.3	–	–	–	–	–
	1976+	–	–	1.0	–	–	–	–	–
Duration at admission (years)	0- 5	–	–	–	1.0[d]	1.0[c]	–	1.0[a]	–
	6-15		–	–	1.7	1.3	–	1.3	–
	16+				3.3	2.3	–	1.7	–
Sex	M	–	–	–	–	–	–	–	–
	F	–	–	–	–	–	–	–	–
Diabetes duration	40-44								1.0[a]
	45+								0.6
Underlying hazard rate (Φ_0)		3.9	3.6	4.6	12.1	13.6	41.6	13.8	10.9

– Means insignificant ("odds ratio" = 1.0), [a] $p < 0.05$ [b] $p < 0.005$ [c] $p < 0.001$ [d] $p < 0.00001$. The relative mortality of an individual with the characteristics i in the 7 parameters can be estimated in the multiplicative model by multiplying the "odds ratio" as described in the text

Long *diabetes duration at admission* to hospital significantly ($p < 0.00001$) increased the relative mortality.

Neither *sex* nor *calendar year during follow-up* significantly influenced relative mortality.

Interaction between diabetes duration and factors influencing relative mortality

To disclose interactions between the effect of risk factors and diabetes duration, the data were reanalysed after stratifying diabetes duration into 5-year intervals (Table 3).

In the *first 3 intervals of duration* (0-15 years) neither calendar year of diagnosis, diabetes duration, age at diagnosis, current age, sex, nor diabetes duration at admission significantly influenced the relative mortality. The only significant factor was calendar year during follow-up; this was significant in the duration interval 11-15 years only, and was without any trend ($p < 0.05$).

In the *interval 16 to 40 years of duration* the pattern changed. Calendar year of diagnosis was now of significant importance, as shown in Table 3. Although this was significant in the duration interval 26 to 30 years only, identical but insignificant influences were found in all strata of diabetes duration. Age at diagnosis had a strong influence in relative mortality in this interval ($p < 0.00001$). Patients diagnosed after the age of 20 years constantly showed the lowest relative mortality. Although current age was not significantly correlated to the relative mortality, the highest relative mortality was constantly found in the age interval 30 to 35 years due to the interaction between age at diagnosis and diabetes duration. Long diabetes duration at admission significantly increased the relative mortality (p ranging from 0.00001 to 0.30).

In patients with a *diabetes duration of 40 years or more*, the pattern changed again. Calendar year of diagnosis, age at diagnosis and diabetes duration at admission were no longer significant, nor were sex or calen-

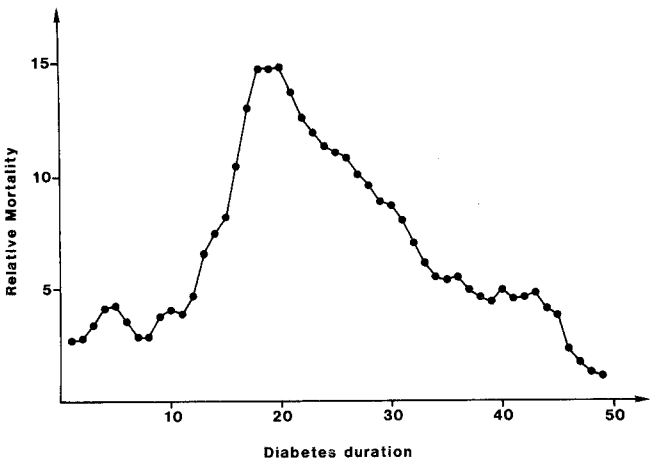

Fig. 2. Relative mortality as a function of diabetes duration independent of sex, age at diagnosis and calendar year of diagnosis

dar year during follow-up. Age exceeding 50 years ($p < 0.01$) and diabetes duration exceeding 45 years ($p < 0.05$) both resulted in decreasing relative mortality.

Discussion

The present study consisted of 2930 Type 1 diabetic patients diagnosed before the age of 31 years and between 1933 and 1972. The patients may be regarded as representative of Danish Type 1 diabetic patients with respect to sex, age at diagnosis and factors influencing relative mortality [2, 5]. As treatment at hospital has always been free of charge, and as patients have always been referred to the hospital by their general practitioner or a department of internal medicine/paediatric department, selection on the basis of socio-economic status is unlikely.

The observation that long diabetes duration at admission increased the relative mortality, however, indicates that patients admitted after ≥ 15 years in some cases are admitted because they already have complications, or that early treatment and instruction at a specialized diabetes care center is of prognostic benefit for the patient [9].

The analysis revealed that several interrelated variables had to be taken into account to describe the relative mortality of the population. This mutual relationship between the variables complicates the separate evaluation of each variable. The use of backward selection strategy and the classification of continuous variables in the statistical analysis diminish these problems, but the results still represent the "best fit" of the model to the observed data. However, when the combined effect of the variables was taken into consideration, several characteristics were revealed.

The relative mortality decreased considerably over the last 50 years, confirming observations from the USA [10, 11], as well as the results of our own previous studies (including the first part of the present study population) [2, 3]. The decrease in relative mortality may be due to the decreasing incidence of persistent proteinuria found in USA [12], as well as in Denmark [13], in combination with the very high relative mortality of patients with proteinuria [4].

The highest relative mortality was found after 16 to 30 years of diabetes duration, leading to a "bell-shaped" configuration of the relative mortality (Fig. 3). As shown previously [4], this peak represents patients developing persistent proteinuria, while patients not developing proteinuria had a low and constant relative mortality. The peak may thus be explained by a maximal incidence of proteinuria after 15–17 years [13, 14], and a median survival of 7 years after onset of proteinuria [14].

In concordance with previous studies [2, 15], low age at diagnosis resulted in a high relative mortality. The cause of this is unknown, but it may be due to the therapeutical problems of maintaining good metabolic regulation during childhood and puberty.

Some controversy exists on the question whether diabetes duration or age is the main predictor of high relative mortality. Dorman et al. [10] showed that attained age rather than diabetes duration and age at diagnosis was the main predictor. This result is in concordance with the study by Krolevski et al. [12], where the incidence of proteinuria in 292 Type 1 diabetic patients was related to attained age rather than diabetes duration. The present study suggests that age at diagnosis in combination with diabetes duration were the main predictors. However, the study by Dorman et al. [10], as well as the present study, indicates that the highest relative mortality is found in the age interval 30 to 40 years.

As shown previously [2], the relative mortality is generally low within the first 15 years and after more than 40 years of duration. To study this phenomenon in further detail and to evaluate the interaction between the potential predictors for increased relative mortality and diabetes duration, the data were reanalysed after subdividing the material according to short (≥ 15 years), median (16–39 years) and long (≥ 40 years) diabetes duration.

In patients with short diabetes duration none of the factors significantly influenced the relative mortality. Dorman et al. [10] demonstrated a decreasing mortality over the last 30 years. This was mainly due to a decreasing mortality at diagnosis due to ketoacidosis. In our population, patients with very severe ketoacidosis are initially admitted to intensive care units of other hospitals. Changes in the mortality at diagnosis would thus not be registered in the present study, and this may explain the difference between the two studies.

In patients with median diabetes duration, age at onset and diabetes duration at admission were the main predictors for increased relative mortality. This is concordant with the observation that both these factors influence the risk of developing persistent proteinuria [3, 12, 13].

The most interesting finding in this part of the study, however, was that after 40 years of duration, almost all the factors *lost* their significant effect. At this point, where 40% of the patients were still living, only age and diabetes duration influenced the relative mortality; relative mortality even decreased with increasing age and diabetes duration. This finding suggests that the population of Type 1 diabetic patients consists of two or more subpopulations with different survival characteristics.

In conclusion, the present study reveals (1) that the relative mortality of Type 1 diabetic patients has decreased 30–40% during the last 40 years; and (2) that diabetes duration has a strong but varying impact on relative mortality. These findings are in concordance with the presence of a subgroup of patients characterized by a highly increased mortality manifest after 15–40 years of diabetes duration.

Future studies, aiming at characterizing these subgroups in detail might reveal important differences between the groups.

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References

1. Andersen PK, Borch-Johnsen K, Deckert T, Green A, Hougaard P, Keiding N, Kreiner S (1985) A Cox regression model for the relative mortality and its application to diabetes mellitus survival data. Biometrics 41: 921–932
2. Green A, Borch-Johnsen K, Andersen PK, Hougaard P, Keiding N, Kreiner S, Deckert T (1985) Relative mortality of Type 1 (insulin-dependent) diabetes in Denmark (1933–1981). Diabetologia 28: 339–342
3. Borch-Johnsen K, Andersen PK, Deckert T (1985) The effect of proteinuria on relative mortality in type 1 (insulin-dependent) diabetes mellitus. Diabetologia 28: 590–596
4. Deckert T, Poulsen JE, Larsen H (1979) The prognosis of insulin dependent diabetes mellitus and the importance of supervision. Acta Med Scand [Suppl] 624: 48–53
5. Christau B, Kromann H, Christy M, Andersen OO & Nerup J (1979) Incidence of insulin-dependent diabetes mellitus (0–29 years at onset) in Denmark. Acta Med Scand [Suppl] 624: 54–60
6. Green A, Andersen PK (1983) Epidemiological studies of diabetes mellitus in Denmark: 3. Clinical characteristics and incidence of diabetes among males aged 0–19 years. Diabetologia 25: 226–230
7. Dahlquist G, Blom L, Holmgren G, Hägglöf B, Larsson Y, Sterky G, Wall S (1985) The epidemiology of diabetes in Swedish children 0–14 years – a sex year prospective study. Diabetologia 28: 802–808
8. Kalbfleisch and Prentice (1980) The statistical analysis of failure time data. Wiley, New York
9. Borch-Johnsen K, Kreiner S, Deckert T (1986) Diabetic Nephropathy – susceptible to care? Diabetes Research (in press)
10. Dorman JS, LaPorte RE, Kuller LH, Cruickshanks KJ, Orchard TJ, Wagener DK, Becker DJ, Cavender DE & Drash AL (1984) The Pittsburg insulin-dependent diabetes mellitus (IDDM) morbidity and mortality study: Mortality results. Diabetes 33: 271–276
11. Entmacher PS, Roos HF & Marks HH (1964) Longevity of diabetic patients in recent years. Diabetes 13: 373–377
12. Krolewski AS, Warram JH, Christlieb AR, Busick EJ & Kahn CR (1985) The changing natural history of nephropathy in type 1 diabetes. Am J Med 78: 785–794
13. Kofoed-Enevoldsen A, Borch-Johnsen K, Kreiner S, Nerup J & Deckert T (1987) Declining incidence of persistent proteinuria in Type 1 (insulin-dependent) diabetic patients in Denmark. Diabetes (in press)
14. Andersen AR, Christiansen JS, Andersen JK, Kreiner S & Deckert T (1983) Diabetic Nephropathy in Type 1 (insulin-dependent) diabetes. Diabetologia 25: 496–501
15. Goodkin G (1975) Mortality factors in diabetes. J Occup Med 17: 716–721

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