Mortality in a Large Population-Based Cohort of Patients with Drug-Treated Diabetes Mellitus

ABSTRACT

Objectives. This paper presents detailed cause-specific data about excess mortality among diabetic persons in Finland, by age and sex.

Methods. Five-year follow-up data on the Finnish population aged 30 through 74 years were analyzed. During these 5 years, 11 215 persons with diabetes and 102 843 persons without diabetes died. The diabetic population was defined as people who were entitled to free medication for diabetes at the beginning of the follow-up period, that is, at the end of 1980.

Results. The relative mortality of persons with drug-treated diabetes compared with nondiabetic persons was higher among women (3.4) than among men (2.4). Almost three quarters of the mortality excess was due to circulatory diseases. For most other causes of death, too, diabetic persons had higher than average mortality. The exceptions were lung cancer, chronic obstructive pulmonary disease, and alcohol poisoning.

Conclusions. Diabetes is a general risk factor for untimely death and makes a significant contribution to overall national death rates, particularly for circulatory diseases. Lower than average mortality from smoking-related diseases and alcohol poisoning, however, warrant optimism about the effects of health education among diabetic persons. (*Am J Public Health*. 1998;88:765–770)

Seppo V. P. Koskinen, MD, Antti R. S. Reunanen, MD, Tuija P. Martelin, PhD, and Tapani Valkonen, PhD

Introduction

The excess mortality of patients with diabetes mellitus, compared with people without diabetes, has been shown repeatedly. The relative and absolute mortality rates, however, have varied considerably. Part of this variation has been due to factors related to the selection of patients. In many studies the subjects have been drawn from patients attending specialized diabetes clinics.[1–6] The survival of diabetic patients has also been evaluated in some population-based prospective cohort studies, but the number of people with diabetes in these studies has usually been rather low.[7–15] By far the largest prospective study, although it was not population-based but comprised volunteers attending a health screening study, included up to 5000 diabetic men.[16] Few studies have drawn their study populations from the general population. However, the patients have usually been selected on the basis of type of therapy[17,18] or residence in a limited geographic area.[19–21] Only from the former German Democratic Republic has the mortality experience of diabetic patients been reported on a national basis.[22]

In connection with a large population study investigating the sociodemographic determinants of mortality by linking several national registers,[23–27] we had the opportunity to study survival of patients with diabetes. The particular aims of this study were to determine the age- and sex-specific excess mortality of diabetic patients compared with the population without diabetes, on a national basis, for all causes and the most important causes of death.

Methods

Compilation of the Data Set

All persons included in the 1980 Census of Finland constituted the study population. Information on age and sex was extracted from the census data files, which cover the total resident population.[25] For each person, the national drug register was consulted to establish whether that person was entitled to free medication for diabetes at the end of 1980. A 5-year mortality follow-up of each member of the study population was carried out by linking the cause-of-death registers for 1981 through 1985 with the census records. More than 99.8% of all deaths could be linked to the census records.[23] The linkage of the registers was carried out by Statistics Finland by means of the personal identification number, which was erased from the data before making them available to the researchers.

Each patient with diabetes mellitus needing drug treatment in Finland is entitled to drugs free of charge. The Social Insurance Institution of Finland is responsible for the drug reimbursement and maintains a national register of all persons entitled to reimbursed medication. Practically all patients with insulin-dependent diabetes mellitus and more than 90% of all patients

Seppo V. P. Koskinen and Antti R. S. Reunanen are with the Department of Health and Disability, National Public Health Institute, Helsinki, Finland. Dr. Koskinen is also with the Population Research Unit, Department of Sociology, University of Helsinki, as are Tuija P. Martelin and Tapani Valkonen.

Requests for reprints should be sent to Seppo V. P. Koskinen, MD, Department of Health and Disability, National Public Health Institute, Mannerheimintie 166, FIN-00300 Helsinki, Finland (e-mail: seppo.koskinen@ktl.fi).

This paper was accepted August 11, 1997.

with drug-treated non–insulin-dependent diabetes mellitus are included in the drug register. Laakso et al. have described the register in more detail.[28] They have also demonstrated that the national drug register data and analyses of representative population samples give very similar estimates of the prevalence of drug-treated diabetes in Finland. The register does not include information about type of diabetes, type of medication, time of onset of the disease, or time of initiation of the medication.

Our analysis is restricted to mortality in the age range 30 through 74 years. Older persons were not included in the data set because the coverage of the drug register and the information on cause of death may be less reliable for the oldest age group than for younger age groups. The mortality of young diabetic persons in Finland has been analyzed by Lounamaa.[29] At the beginning of the follow-up, 34 000 women (2.6% of the female population in this age group) and 24 000 men (2.1% of the male population in this age group) aged 30 through 74 years were entitled to free medication for diabetes.

Information on cause of death is restricted to the underlying cause. No other conditions mentioned in the death certificate have been included in the original data set. Causes of death have been classified into 18 categories according to the eighth revision of the *International Classification of Diseases, Injuries and Causes of Death* (ICD-8).

Statistical Analysis

An indicator of relative mortality differences was obtained by calculating the age-adjusted relative mortality rates of persons with drug-treated diabetes compared with the rest of the population (= 1.00). We also analyzed the absolute differences between the age-standardized death rates. In cause-specific analyses, the contribution of each cause of death to the total excess mortality of diabetic patients was computed.

The relative age-adjusted death rates were obtained by employing the Poisson regression model, with age, in 5-year groups, as a categorical variable.[30,31] The age-standardized cause-specific death rates needed to calculate the absolute mortality differences and the share of each cause of death in the total excess mortality of diabetics were derived by indirect age standardization, using 5-year age groups.

Results

Mortality from All Causes of Death

The data show a total of 11 215 deaths among persons with drug-treated diabetes (Table 1) and 102 843 deaths in the rest of the population. Deaths among diabetic patients thus constituted a significant proportion of all deaths in the age group 30 through 74 years. Even in the age groups younger than 50, almost 5% of the persons who died during the period 1981 through 1985 had received free medication for diabetes at the end of 1980. In the age group 65 through 74 years, almost 20% of women's deaths and almost 10% of men's deaths occurred among persons with drug-treated diabetes.

The mortality ratio between diabetic and nondiabetic persons was largest in the youngest age groups and declined rather steadily with increasing age. However, even in the age group 70 through 74 years, the death rate of persons with drug-treated diabetes was twice (men) or 3 times (women) as high as in the rest of the population. Within the whole age range 30 through 74 years, 10.1% of all deaths in the female population would have been

TABLE 1—Person-Years, Deaths, and Mortality among Persons with Drug-Treated Diabetes, by Sex and Age: Finland, 1981 through 1985

Age, y	Person-Years	Deaths No. (%)[a]	Mortality per 1000 person-years	Mortality Difference between Diabetic and Nondiabetic Populations: Absolute[b]	Mortality Difference between Diabetic and Nondiabetic Populations: Relative[c] (95% CI)
		Women			
30–34	4 244	31 (5.1)	7.3	6.7	12.8 (8.9, 18.5)
35–39	3 820	34 (4.2)	8.9	8.1	11.1 (7.8, 15.8)
40–44	3 260	34 (3.2)	10.4	9.0	7.5 (5.3, 10.7)
45–49	4 297	49 (3.4)	11.4	9.4	5.6 (4.2, 7.5)
50–54	7 041	96 (4.3)	13.6	10.5	4.3 (3.5, 5.3)
55–59	13 003	278 (7.4)	21.4	16.4	4.2 (3.7, 4.8)
60–64	22 218	686 (11.5)	30.9	22.6	3.7 (3.4, 4.0)
65–69	31 491	1 508 (16.1)	47.9	33.9	3.4 (3.2, 3.6)
70–74	41 157	3 156 (19.8)	76.7	52.1	3.1 (3.0, 3.2)
30–74	130 530	5 872 (14.3)	. . .	. . .	. . . . .
		Men			
30–34	6 353	70 (3.5)	11.0	9.2	6.1 (4.8, 7.7)
35–39	6 564	82 (3.4)	12.5	10.2	5.4 (4.3, 6.7)
40–44	5 714	115 (4.2)	20.1	16.6	5.7 (4.7, 6.9)
45–49	7 492	171 (4.3)	22.8	17.2	4.1 (3.5, 4.7)
50–54	10 945	371 (5.7)	33.9	24.5	3.6 (3.2, 4.0)
55–59	14 263	576 (5.9)	40.4	25.2	2.7 (2.4, 2.9)
60–64	16 252	919 (7.8)	56.5	33.0	2.4 (2.2, 2.6)
65–69	16 296	1 312 (9.1)	80.5	44.9	2.3 (2.1, 2.4)
70–74	15 591	1 727 (9.0)	110.8	55.6	2.0 (1.9, 2.1)
30–74	99 470	5 343 (7.3)	. . .	. . .	. . . . .

Note. CI = confidence interval.
[a]Percentage of all deaths in the Finnish population.
[b]Mortality in the nondiabetic population subtracted from mortality in the diabetic population.
[c]Mortality in the diabetic population divided by mortality in the nondiabetic population.

TABLE 2—Age-Standardized Relative Mortality of Persons with Diabetes[a] Compared with the Rest of the Population Aged 30 through 74 and Proportion of Total Excess Mortality, by Sex and Cause of Death: Finland, 1981 through 1985

	Women			Men		
Cause of Death (ICD-8 Codes)	No. Deaths among Diabetic Women	Relative Mortality (95% CI)	% of Total Excess Mortality	No. Deaths among Diabetic Men	Relative Mortality (95% CI)	% of Total Excess Mortality
Neoplasms (140–239)	733	1.40 (1.30, 1.51)	6	688	1.20 (1.11, 1.29)	4
Stomach cancer (151)	73	1.39 (1.09, 1.78)	1	79	1.40 (1.11, 1.77)	1
Colon cancer (153–154)	70	1.30 (1.02, 1.67)	0	46	1.26 (0.93, 1.71)	0
Lung cancer (162)	40	1.01 (0.73, 1.39)	0	193	0.81 (0.70, 0.93)	–1
Breast cancer (174)	120	1.58 (1.31, 1.91)	2	1	. . .	
Genital cancers (180–187)	94	1.38 (1.11, 1.71)	1	58	1.40 (1.07, 1.84)	0
Other	336	1.44 (1.28, 1.61)	3	311	1.55 (1.38, 1.74)	4
Circulatory diseases (390–458)	3984	4.51 (4.35, 4.68)	71	3553	2.97 (2.87, 3.08)	74
Ischemic heart disease (410–414)	2537	5.17 (4.94, 5.42)	46	2567	3.00 (2.87, 3.12)	54
Cerebrovascular diseases (430–439)	882	3.92 (3.63, 4.23)	16	599	3.46 (3.17, 3.77)	13
Other	565	3.36 (3.07, 3.69)	9	387	2.33 (2.10, 2.60)	7
Other diseases	1044	4.14 (3.86, 4.44)	21	904	3.23 (3.01, 3.47)	21
Diabetes (250)	530	195.00 (154, 248)	13	429	305.00 (238, 391)	14
Alcohol-related diseases[b] (291, 303, 571, 577)	43	2.56 (1.85, 3.55)	1	120	3.61 (2.98, 4.38)	4
Respiratory diseases (460–519)	171	2.28 (1.94, 2.69)	2	185	1.29 (1.11, 1.50)	1
COPD[c] (490–493)	26	1.08 (0.72, 1.62)	0	63	0.71 (0.55, 0.92)	–1
Other	145	2.86 (2.38, 3.43)	2	122	2.24 (1.85, 2.71)	2
Other	300	1.86 (1.65, 2.11)	4	170	1.60 (1.36, 1.87)	2
Accidents and violence (E800–E999)	111	1.68 (1.38, 2.05)	2	198	1.19 (1.03, 1.38)	2
Traffic accidents (E800–E845)	19	1.07 (0.67, 1.72)	0	40	1.30 (0.95, 1.77)	0
Alcohol poisoning (E860)	2	0.89 (0.29, 2.78)	0	17	0.96 (0.59, 1.54)	0
Suicide (E950–E959)	22	1.19 (0.78, 1.83)	0	55	1.04 (0.80, 1.37)	0
Other	68	2.49 (1.92, 3.23)	2	86	1.34 (1.07, 1.67)	1
All causes	5872	3.39 (3.30, 3.49)	100	5 343	2.41 (2.34, 2.48)	100

Note. ICD-8 = *International Classification of Diseases*, 8th revision; CI = confidence interval.
[a]Persons with diabetes are defined as persons provided with free medication for diabetes at the end of 1980.
[b]Alcoholic psychosis, alcoholism, cirrhosis of the liver, and diseases of the pancreas.
[c]Chronic obstructive pulmonary disease.

avoided had death rates for diabetic patients been the same as those in the nondiabetic population. In men, the corresponding proportion was 4.3%.

In every age group, the relative mortality excess associated with diabetes was larger for women than for men. The absolute difference in mortality rates between the diabetic and nondiabetic populations increased with age and was greater among men than among women in each age group.

In the diabetic population, the mortality of men exceeded that of women at all ages. The male-to-female mortality ratio was about 1.5 in both the youngest and the oldest age groups but peaked at 2.5 among those aged 50 through 54 years.

Cause-Specific Mortality

Ischemic heart disease was registered as the underlying cause in almost half of the deaths among diabetic patients (Table 2). Diabetes was the underlying cause of death in fewer than 9% of all deaths in the diabetic population.

The mortality of diabetic persons was higher than that of nondiabetic persons for nearly all of the 18 causes of death. In 13 causes among women and in 11 causes among men, the excess mortality of diabetic patients was statistically significant ($P < .05$). Deaths from circulatory diseases were much more common among persons with diabetes than in the rest of the population, particularly among women. Neoplasms, excluding lung cancer, were approximately 40% more frequent in the diabetic population than in nondiabetic persons. No statistically significant differences were observed in traffic accidents, alcohol poisoning, or suicide. Deaths from other nonnatural causes were significantly more frequent among diabetic than nondiabetic persons, particularly among women. A large proportion of deaths in this category were due to accidental falls.

In ischemic heart disease, the mortality ratio between diabetic and nondiabetic persons was clearly larger among women than among men. In most cancers, there was no gender difference in the relative risk associated with having diabetes. In other causes, the relative risk tended to be somewhat greater in women than in men.

There was only 1 cause among women and 3 causes among men for which mortality was lower among diabetic patients than in the rest of the population. Deaths from alcohol poisoning were slightly less common among diabetic patients of both sexes than among nondiabetic individuals. However, this difference was not statistically significant ($P > .1$). In 2 causes of death, lung cancer and chronic obstructive pulmonary disease, mortality was significantly ($P < .01$) lower in diabetic men than in other men. In women, mortality from these causes was at the same level among diabetic and nondiabetic persons.

Circulatory diseases were responsible for almost three quarters of the excess mortality among diabetic patients. Ischemic heart disease alone accounted for more than half of the excess deaths. Diabetes also made a significant contribution to the mortality from ischemic heart disease in the total Finnish population aged 30 through 74

TABLE 3—Age-Standardized Relative Mortality of Persons with Diabetes[a] Compared with the Rest of the Population and Proportion of Total Excess Mortality, by Sex, Cause of Death, and Broad Age Groups: Finland, 1981 through 1985

Cause of Death	Women		Men	
	Relative Mortality (95% CI)	% of Total Excess Mortality	Relative Mortality (95% CI)	% of Total Excess Mortality
	Age 30–49 y			
Neoplasms	1.13 (0.57, 2.24)	1	2.53 (1.74, 3.68)	5
Ischemic heart disease	33.8 (23.1, 49.7)	21	7.80 (6.61, 9.22)	35
Cerebrovascular diseases	4.76 (2.43, 9.33)	5	4.28 (2.77, 6.61)	5
Other circulatory diseases	5.73 (2.31, 14.2)	3	3.67 (2.21, 6.10)	3
Diabetes	1297 (797, 2111)	57	981 (637, 1510)	37
Other diseases	6.35 (3.98, 10.1)	12	4.32 (3.26, 5.73)	12
Accidents and violence	1.25 (0.57, 2.71)	1	1.28 (0.96, 1.72)	3
All causes	7.93 (6.71, 9.38)	100	4.93 (4.48, 5.43)	100
	Age 50–64 y			
Neoplasms	1.56 (1.34, 1.82)	8	1.27 (1.11, 1.45)	4
Ischemic heart disease	8.08 (7.26, 8.98)	45	3.38 (3.16, 3.61)	58
Cerebrovascular diseases	5.14 (4.29, 6.16)	14	4.66 (4.00, 5.44)	13
Other circulatory diseases	4.57 (3.65, 5.72)	9	2.63 (2.16, 3.19)	6
Diabetes	160 (107, 240)	17	291 (188, 451)	13
Other diseases	2.09 (1.66, 2.62)	5	1.81 (1.52, 2.15)	5
Accidents and violence	1.40 (0.94, 2.08)	1	1.21 (0.97, 1.51)	1
All causes	3.91 (3.67, 4.17)	100	2.67 (2.54, 2.80)	100
	Age 65–74 y			
Neoplasms	1.36 (1.24, 1.49)	5	1.12 (1.02, 1.24)	3
Ischemic heart disease	4.67 (4.43, 4.91)	51	2.60 (2.46, 2.75)	56
Cerebrovascular diseases	3.71 (3.42, 4.04)	17	3.01 (2.70, 3.35)	16
Other circulatory diseases	3.17 (2.86, 3.51)	10	2.17 (1.90, 2.47)	9
Diabetes	89.4 (67.0, 119)	11	92.2 (64.7, 131)	10
Other diseases	1.95 (1.76, 2.17)	6	1.46 (1.29, 1.65)	6
Accidents and violence	1.87 (1.47, 2.37)	1	1.12 (0.87, 1.44)	0
All causes	3.21 (3.11, 3.32)	100	2.11 (2.03, 2.19)	100

Note. CI = confidence interval.
[a]Persons with diabetes are defined as persons provided with free medication for diabetes at the end of 1980.

years. As many as 18.6% of all women's deaths and 6.3% of all men's deaths from ischemic heart disease would have been avoided had the death rates in diabetic patients been the same as those in the rest of the population. In deaths from all circulatory diseases, the corresponding proportions were 15.7% for women and 6.3% for men.

Diabetes, as the registered underlying cause of death, accounted for nearly 15% of the overall mortality difference between diabetic and nondiabetic individuals. Causes of death other than cardiovascular diseases and diabetes were responsible for only 16% of the excess deaths among diabetic women and 10% among diabetic men.

The mortality ratio between diabetic patients and others grew smaller from the youngest to the oldest age group for practically all causes of death, particularly for diabetes and ischemic heart disease, especially in women (Table 3). However, the differences remained considerable and statistically significant ($P < .001$) even in the oldest age group. The absolute mortality excess of diabetic patients tended to increase with age for most causes of death. Although the relative differences between diabetic and nondiabetic individuals in mortality from circulatory diseases declined rapidly from younger to older age groups, the contribution of this disease group to the excess mortality of diabetic patients increased with age. Excess mortality from ischemic heart disease among men was marked also in the diabetic population, but the relative gender difference was much smaller than in the rest of the population (2.9 vs 11.7 in the youngest, 2.6 vs 6.1 in the second, and 1.7 vs 3.0 in the oldest age group).

Discussion

This study comprised one of the largest population-based groups of diabetic patients ever followed up for mortality, and the number of deaths, 11 215, is an exceptionally large basis for mortality risk estimates. The national drug register has previously served as a reliable data set for studies on the occurrence of diabetes[28,32] and the mortality of diabetic individuals in Finland.[29,33] In these earlier studies, the coverage and validity of data in the drug register have been shown to be appropriate for epidemiological studies.

Our data set did not enable us to distinguish between patients with insulin-dependent disease and those with non–insulin-dependent disease. For practical purposes, however, it can be stated that the majority of patients aged 30 through 49 years had insulin-dependent diabetes, whereas the vast majority of older patients had non–insulin-dependent diabetes.

In each age group, the relative mortality of diabetic patients, compared with nondiabetic persons, was higher among women than among men. This is consistent with most earlier findings.[3,17,19,34,35] On the other hand, the absolute excess mortality due to diabetes in this study was greater among men than among women, and diabetic men had markedly higher mortality than diabetic women at all ages. An earlier study suggested that in some populations, diabetic women may have higher death rates than diabetic men,[36] but these differences were not statistically significant. The vast majority of studies have shown male excess mortality among diabetic patients as well, whereas varying results have been reported on gender differences in the absolute excess mortality of people with diabetes.

The mortality ratio between diabetic patients and the rest of the population was

largest in the youngest age group and declined rather sharply up to those in their 50s, particularly in women. Thereafter, the mortality ratio declined more slowly with age, remaining quite large even in the oldest group (70–74 years). The decline in the relative risk of death from younger to older age groups results partly from the increasing proportion of non–insulin-dependent diabetes, with shorter duration of the disease, but the convergence is also related to other changes associated with aging.[27,37]

Previous age-specific findings concerning the impact of diabetes on mortality have been based on small data sets. On average, the age-specific relative risks reported in many earlier studies have been somewhat lower than those obtained here.[3,12,35,38,39] These studies were based on a follow-up of all types of diabetic patients, including those not receiving drug treatment, whereas in our study only persons needing drug treatment were classified as diabetic patients. In our study, diabetic patients treated with diet alone were included in the large nondiabetic control group. The proportion of this patient group in the control group is so small, however—less than 5% even in the oldest age groups[28]—that it does not affect the mortality rates in the reference population. As diabetic patients treated with diet alone have lower mortality than persons treated with oral hypoglycemics,[10] exclusion of the former group (representing approximately one third of all diabetic persons[28]) from the diabetic population tends to increase the observed death rates among diabetic patients. Differences in case ascertainment may thus largely explain why the relative mortality of people with diabetes was higher in the present study than in most earlier reports.

The absolute difference between the death rates of diabetic and nondiabetic persons increased considerably with age. This is consistent with earlier results.[14,17,38]

The size of the data set allowed us to apply a more detailed cause-of-death classification than has been possible in previous studies. For obvious reasons, the largest relative mortality risks were found for diabetes as the underlying cause of death. The small number of decedents who died of diabetes in the group initially called nondiabetic persons includes diabetic patients treated with diet alone and patients treated with drugs but who received the reimbursement decision after the start of the follow-up period.

The relative mortality risks from cardiovascular causes in our study were slightly higher than those reported in many previous studies[5,10,12,14,21,35,38,40]; however, similar[16] and clearly higher rates[17,41,42] have been reported. The exclusion of diabetic patients treated with diet alone from the diabetic population obviously contributed to the relatively high cardiovascular mortality risk in our study. As in most earlier studies,[43] the relative increase in mortality from ischemic heart disease associated with diabetes was much larger among women than among men. However, male excess mortality was also evident in the diabetic population.

Some earlier reports have shown cancer incidence to be increased in diabetic patients, as found in our study,[15,44] but negative results have also been reported.[40,45] The modest increase in cancer mortality risk observed in our study may not be detected in studies with fewer diabetic patients. The excess cancer mortality may result partly from obesity, which is common in non–insulin-dependent diabetes and which increases the risk of some types of cancer.[46]

The mortality of women and men with diabetes was significantly increased for alcohol-related diseases, which included alcohol psychosis, alcoholism, liver cirrhosis, and pancreatitis. Relatively few earlier studies have noticed the association of diabetes with alcohol-related disease processes. Pancreatitis is a well-known factor causing secondary diabetes, and glucose intolerance is common in patients with liver cirrhosis, but otherwise the associations are not well recognized. According to recent studies from Japan, excess mortality from liver cirrhosis has been noticed in persons with diabetes,[47] and diabetes has been shown to markedly decrease survival of alcoholics.[48] In a French prospective population study, alcohol-related causes of death were particularly common in men with glucose intolerance but also in men with clinical diabetes.[49] Whatever the cause and effect may be, the observed association is important from the public health viewpoint and calls for more detailed studies.

Mortality from accidents and violence was slightly but significantly increased in diabetic patients in our study. The excess risk was mainly caused by various job-related and leisure-time accidents. In a previous Finnish prospective population study, diabetes was a significant determinant of hospitalization or death because of injurious falls.[50] Mortality from traffic accidents was only slightly and not significantly increased in diabetic patients, suggesting that diabetes is rarely a causal factor in fatal traffic accidents. We found no association between diabetes and suicide. Our study population was older than the population in the Danish study that found a small increase in suicide risk in persons with young-onset diabetes,[51] and this may explain the absence of association.

The only causes of death that were less frequent among diabetic patients than among nondiabetic persons were clearly smoking-related—lung cancer and chronic obstructive pulmonary disease. The risk was significantly decreased in males and close to unity in females. The proportion of smokers among diabetic patients has varied in earlier reports. Similar frequencies of smoking were found in diabetic and nondiabetic men in a large study from the United States,[16] and slightly lower frequencies in diabetic men in a study from France.[15] Diabetic nurses smoked significantly less frequently than nondiabetic nurses in the Nurses Health Study.[42] In Finland, smoking has been shown to be significantly less frequent among diabetic men than among men without diabetes.[14] Thus, our results on smoking-related pulmonary causes of death are probably attributable to the less frequent smoking in Finnish diabetic patients.

Conclusions

Circulatory diseases are the main source of the excess mortality in diabetic patients, because of the high relative mortality of diabetic patients from this group of diseases and because circulatory diseases are the most common cause of death even in the nondiabetic population. Diabetes is also a very important determinant of mortality from circulatory diseases in the whole population. In women, almost every sixth death from circulatory diseases in the age group 30 through 74 years was due to diabetes; in men, the corresponding proportion was more than 6%.

Our exceptionally large data set permitted more precise mortality risk estimates for drug-treated diabetic patients compared with the general population than could be derived from previous smaller studies. In addition to the well-known excess mortality from diabetes and cardiovascular diseases, we observed excess mortality from neoplasms, alcohol-related diseases, and accidents. These findings call for further studies.

There were only a few causes of death for which we found an average or even lower than average mortality among diabetic patients. Smoking-related diseases and alcohol poisoning were the most obvious of these. At least in some respects, it seems that in Finland diabetic patients have healthier habits than nondiabetics, perhaps in response to both the disease itself and the health education provided by health care personnel. Our results warrant optimism

with regard to the effects of health education among persons with diabetes. Further efforts to reduce smoking and other modifiable risk factors for circulatory disease among diabetic patients might well bring about a significant decrease in mortality. □

Acknowledgments

This study was funded by the Academy of Finland Medical Research Council.

We are grateful to Statistics Finland for permission (TK 53-69-87) to use the data files and to Jari Hellanto for his help with the construction of the data set.

References

1. Entmacher PS, Root HF, Marks HH. Longevity of diabetic patients in recent years. *Diabetes.* 1964;13:373–377.
2. Hayward RE, Lucena BC. An investigation into mortality of diabetics. *J Inst Actuarians.* 1965;91:286–337.
3. Marks HH. Longevity and mortality of diabetics. *Am J Public Health.* 1965;55:416–423.
4. Kessler II. Mortality experience of diabetic patients. A twenty-six-year follow-up study. *Am J Med.* 1971;51:715–724.
5. Królewski AS, Czyzyk A, Janeczko D, Kopczynski J. Mortality from cardiovascular diseases among diabetics. *Diabetologia.* 1977;13:345–350.
6. Green A, Borch-Johnsen K, Kragh Andersen P, et al. Relative mortality of type 1 (insulin-dependent) diabetes in Denmark: 1933–1981. *Diabetologia.* 1985;28:339–342.
7. Kannel WB, McGee DL. Diabetes and cardiovascular risk factors in the Framingham study. *Circulation.* 1979;59:8–13.
8. Barrett-Connor E, Wingard DL. Sex differential in ischemic heart disease mortality in diabetics: a prospective population based study. *Am J Epidemiol.* 1983;118:489–496.
9. Fuller JH, Shipley MJ, Rose J, Jarrett RJ, Keen H. Mortality from coronary heart disease and stroke in relation to degree of hyperglycemia: the Whitehall study. *BMJ.* 1983;287:867–870.
10. Reunanen A. Mortality in type 2 diabetes. *Ann Clin Res.* 1983;15(suppl 37):26–28.
11. Butler WJ, Ostrander LD Jr, Carman WJ, Lamphiear DE. Mortality from coronary heart disease in the Tecumseh study. Long-term effect of diabetes mellitus, glucose tolerance and other risk factors. *Am J Epidemiol.* 1985;121:541–547.
12. Kleinman JC, Donahue RP, Harris MI, Finucane FF, Madans JH, Brock DB. Mortality among diabetics in a national sample. *Am J Epidemiol.* 1988;128:389–401.
13. Rosengren A, Welin L, Tsipogianni A, Wilhelmsen L. Impact of cardiovascular risk factors on coronary heart disease and mortality among middle aged diabetic men: a general population study. *BMJ.* 1989;299:1127–1131.
14. Stengård JH, Tuomilehto J, Pekkanen J, et al. Diabetes mellitus, impaired glucose tolerance and mortality among elderly men: the Finnish cohorts of the Seven Countries Study. *Diabetologia.* 1992;35:760–765.
15. Balkau B, Eschwège E, Papoz L, et al. Risk factors for early death in non-insulin dependent diabetes and men with known glucose tolerance status. *BMJ.* 1993;307:295–299.
16. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors and 12-year cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care.* 1993;16:434–444.
17. Green A, Hougaard P. Epidemiological studies of diabetes mellitus in Denmark, 5: mortality and causes of death among insulin-treated diabetic patients. *Diabetologia.* 1984;26:190–194.
18. Raymond NT, Langley JD, Goyder E, Botha JL, Burden AC, Hearnshaw JR. Insulin treated diabetes mellitus: causes of death determined from record linkage of population based registers in Leicestershire, UK. *J Epidemiol Community Health.* 1995;49:570–574.
19. Panzram G, Zabel-Langhennig R. Prognosis of diabetes mellitus in a geographically defined population. *Diabetologia.* 1981;20:587–591.
20. Ochi JW, Melton LJ III, Palumbo PJ, Chu C-P. A population-based study of diabetes mortality. *Diabetes Care.* 1985;8:224–229.
21. Wong JSK, Pearson DWM, Murchison LE, Williams MJ, Narayan V. Mortality in diabetes mellitus: experience of a geographically defined population. *Diabetic Med.* 1991;8:135–139.
22. Michaelis D, Jutzi E. Trends in mortality rates in the diabetic population of the GDR. *Exp Clin Endocrinol.* 1990;95:83–90.
23. Valkonen T, Martelin T, Rimpelä A. *Socio-Economic Mortality Differences in Finland 1971–85.* Helsinki: Central Statistical Office of Finland; 1990. Study 176.
24. Valkonen T. Trends in regional and socioeconomic mortality differentials in Finland. *Int J Health Sci.* 1992;3:157–166.
25. Valkonen T, Martelin T, Rimpelä A, Notkola V, Savela S. *Socio-Economic Mortality Differences in Finland 1981–90.* Helsinki, Finland: Statistics Finland; Publication 1993:1.
26. Koskinen S, Martelin T. Why are socioeconomic mortality differences smaller among women than among men? *Soc Sci Med.* 1994;38:1385–1396.
27. Martelin T. *Differential Mortality at Older Ages: Sociodemographic Mortality Differences among the Finnish Elderly.* Helsinki: Finnish Demographic Society; 1994. Publication 16.
28. Laakso M, Reunanen A, Klaukka T, Aromaa A, Maatela J, Pyörälä K. Changes in the prevalence and incidence of diabetes mellitus in Finnish adults, 1970–1987. *Am J Epidemiol.* 1991;133:850–857.
29. Lounamaa R. *Mortality in Finnish Patients with Insulin-Dependent Diabetes Mellitus: A Follow-Up Study of Patients Diagnosed When under Twenty Years of Age.* Helsinki, Finland: Social Insurance Institution; 1993. Publication ML:126.
30. Aitkin M, Clayton D. The fitting of exponential, Weibull and extreme value distributions to complex censored survival data using GLIM. *Applied Stat.* 1980;29:156–163.
31. Payne C, ed. *The GLIM System. Release 3.77.* Oxford, England: The Numerical Algorithms Group, Royal Statistical Society; 1985.
32. Åkerblom HK, Reunanen A. The epidemiology of insulin-dependent diabetes mellitus (IDDM) in Finland and in Northern Europe. *Diabetes Care.* 1985;8(suppl 1):10–16.
33. Diabetes Epidemiology Research International Mortality Study Group. Major cross-country differences in risk of dying for people with IDDM. *Diabetes Care.* 1991;14:49–54.
34. Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia.* 1987;30:123–131.
35. Walters DP, Gatling W, Houston AC, Mullee MA, Julious SA, Hill RD. Mortality in diabetic subjects: an eleven-year follow-up of a community-based population. *Diabetic Med.* 1994;11:968–973.
36. Head J, Fuller JH. International variations in mortality among diabetic patients: the WHO Multinational Study of Vascular Disease in Diabetics. *Diabetologia.* 1990;33:477–481.
37. Manton KG, Stallard E. *Recent Trends in Mortality Analysis.* Orlando, Fla: Academic Press; 1984.
38. Waugh NR, Dallas JH, Jung RT, Newton RW. Mortality in a cohort of diabetic patients: causes and relative risks. *Diabetologia.* 1989;32:103–104.
39. Tuomilehto J, Schranz A, Aldana A, Pitkäniemi J. The effect of diabetes and impaired glucose tolerance on mortality in Malta. *Diabet Med.* 1994;11:170–176.
40. Jarret RJ, Shipley MJ. Mortality and associated risk factors in diabetics. *Acta Endocrinol.* 1985;110(suppl 272):21–26.
41. Moss SE, Klein R, Klein BEK. Cause-specific mortality in a population-based study of diabetes. *Am J Public Health.* 1991;81:1158–1162.
42. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med.* 1991;151:1141–1147.
43. Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. *Ann Med.* 1996;28:323–333.
44. Green A, Jensen OM. Frequency of cancer among insulin-treated diabetic patients in Denmark. *Diabetologia.* 1985;28:128–130.
45. Ragozzino M, Melton LJ III, Chu C-P, Palumbo PJ. Subsequent cancer risk in the incidence cohort of Rochester, Minnesota, residents with diabetes mellitus. *J Chronic Dis.* 1982;35:13–19.
46. Kissebach AH, Freedman DS, Peiris AN. Health risks of obesity. *Med Clin N Am.* 1989;73:111–138.
47. Sasaki A, Kamado K, Uehara M. Changes in causes of death in diabetic patients based on death certificates during a 30-year period in Osaka District, Japan, with special reference to cancer mortality. *Diabetes Res Clin Pract.* 1994;24:103–112.
48. Yokoyama A, Matshushita S, Ishii H, Takagi T, Maruyama K, Tsuchiya M. The impact of diabetes mellitus on the prognosis of alcoholics. *Alcohol Alcoholism.* 1994;29:181–186.
49. Balkau B, Eschwège E, Fontbonne A, Claude J-R, Warnet J-M. Cardiovascular and alcohol-related deaths in abnormal glucose tolerant and diabetic subjects. *Diabetologia.* 1992;35:39–44.
50. Malmivaara A, Heliövaara M, Knekt P, Reunanen A, Aromaa A. Risk factors for injurious falls leading to hospitalization or death in a cohort of 19,500 adults. *Am J Epidemiol.* 1993;138:384–394.
51. Kyvik KO, Stenager EN, Green A, Svendsen A. Suicides in men with IDDM. *Diabetes Care.* 1994;17:210–212.