Type 2 Diabetes as a "Coronary Heart Disease Equivalent"

An 18-year prospective population-based study in Finnish subjects

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OBJECTIVE — The purpose of this study was to investigate the hypothesis that coronary heart disease (CHD) mortality in diabetic subjects without prior evidence of CHD is equal to that in nondiabetic subjects with prior myocardial infarction or any prior evidence of CHD.

RESEARCH DESIGN AND METHODS — During an 18-year follow-up total, cardiovascular disease (CVD) and CHD deaths were registered in a Finnish population-based study of 1,373 nondiabetic and 1,059 diabetic subjects.

RESULTS — Adjusted multivariate Cox hazard models indicated that diabetic subjects without prior myocardial infarction, compared with nondiabetic subjects with prior myocardial infarction, had a hazard ratio (HR) of 0.9 (95% CI 0.6–1.5) for the risk of CHD death. The corresponding HR was 0.9 (0.5–1.4) in men and 1.9 (0.6 –6.1) in women. Diabetic subjects without any prior evidence of CHD (myocardial infarction or ischemic electrocardiogram [ECG] changes or angina pectoris), compared with nondiabetic subjects with prior evidence of CHD, had an HR of 1.9 (1.4–2.6) for CHD death (men 1.5 [1.0–2.2]; women 3.5 [1.8–6.8]). The results for CVD and total mortality were quite similar to those for CHD mortality.

CONCLUSIONS — Diabetes without prior myocardial infarction and prior myocardial infarction without diabetes indicate similar risk for CHD death in men and women. However, diabetes without any prior evidence of CHD (myocardial infarction or angina pectoris or ischemic ECG changes) indicates a higher risk than prior evidence of CHD in nondiabetic subjects, especially in women.

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Type 2 diabetes increases the risk of coronary heart disease (CHD) events at least by two- to threefold in type 2 diabetic subjects compared with nondiabetic subjects (1). In type 2 diabetic women the relative risk is even greater (2). The reasons for this increased risk are largely unknown but could be related at least in part to more adverse changes in cardiovascular risk factors among diabetic women compared with diabetic men. Although the incidence of CHD events in nondiabetic subjects has considerably decreased during the last decades, this is not true for type 2 diabetic patients, particularly for women (3).

We previously reported that type 2 diabetic patients without a history of prior myocardial infarction have the same risk of CHD death as nondiabetic subjects with a history of prior myocardial infarction (4). This observation has led to the conclusion that type 2 diabetes is a CHD equivalent and has had a profound effect, particularly on the recommendations for treatment of dyslipidemia (5).

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Abbreviations: CHD, coronary heart disease; CVD, cardiovascular disease; ECG, electrocardiogram; WHO, World Health Organization

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

During recent years other studies have investigated the same question in different populations and study settings. Contradictory results have been obtained, with some studies confirming our original findings (6–10) and some studies reporting opposite results, especially among men (11–18). The conclusion of these studies is that type 2 diabetes might be a CHD equivalent, but only among women.

Our original study population included 1,059 patients with type 2 diabetes and 1,373 nondiabetic subjects, who were followed for up to 7 years (4). The limitation of our original study was that the number of CHD deaths during the follow-up was relatively low. Furthermore, data analysis was not done separately for men and women, and myocardial infarction was the only criterion used for CHD.

Because of contradictory data from other studies, we have prolonged the follow-up of our cohort to up to 18 years using mortality from CHD, cardiovascular disease (CVD), and all causes as end points. Furthermore, we have analyzed the results separately for men and women, and, in addition to a prior history of myocardial infarction, we have applied other criteria for the presence of CHD at baseline.

RESEARCH DESIGN AND METHODS

— A detailed description of study participants has been published previously (4). A random sample of 1,373 nondiabetic subjects (638 men and 735 women) and 1,059 type 2 diabetic subjects (581 men and 478 women) participated in the baseline study carried out in 1982–1984. All subjects were aged 45–64 years, and they were born and living in the Turku University Hospital district in West Finland and in the Kuopio University Hospital district in East Finland. The random sample of nondiabetic subjects was taken from the population register, and type 2 diabetic subjects were identified through a national drug reimbursement register. The mean age was 54.6 years in nondiabetic men, 54.8 years in nondiabetic women, 57.3 years in dia-

Table 1—*Subjects with prior evidence of CHD at baseline, and total, CVD, CHD, and non-CVD mortality in 2,432 subjects during 18 years of follow-up*

	Nondiabetic		Diabetic			
	Men	Women	Men	Women	Nondiabetic	Diabetic
n	638	735	581	478	1,373	1,059
Baseline						
Prior myocardial infarction	51 (8.0)	18 (2.4)	115 (19.8)	54 (11.3)	69 (5.0)	169 (16.0)
Angina pectoris	87 (13.7)	100 (13.6)	161 (28.0)	160 (33.7)	187 (13.6)	321 (30.6)
Ischemic ECG changes	137 (21.5)	171 (23.3)	251 (43.2)	241 (50.4)	302 (22.4)	492 (46.5)
Any of the above	194 (30.4)	236 (32.1)	318 (54.7)	309 (64.6)	430 (31.3)	627 (59.2)
Follow-up						
All-cause mortality	199 (31.2)	98 (13.3)	423 (72.8)	345 (72.2)	297 (21.6)	768 (72.5)
CVD deaths	104 (16.3)	26 (3.5)	285 (49.1)	236 (49.4)	130 (9.5)	521 (49.2)
CHD deaths	76 (11.9)	17 (2.3)	221 (38.0)	156 (32.6)	93 (6.8)	377 (35.6)
Non-CVD deaths	95 (14.9)	72 (9.8)	138 (23.8)	109 (22.8)	167 (12.2)	247 (23.3)

Data are *n* (%).

betic men, and 59.1 year in diabetic women.

Baseline study

The study program was carried out during one outpatient visit at the Clinical Research Unit of the University of Kuopio or the Rehabilitation Research Centre of the Social Insurance Institution in Turku as previously described (19). The visit included an interview on the history of chest pain suggestive of CHD, smoking, alcohol intake, physical activity, and the use of drugs. All medical records of subjects who reported in an interview that they had been admitted to the hospital for chest pain symptoms were reviewed. Review of the medical records was performed by two of us (M.L. in Kuopio and T.R. in Turku) after a careful standardization of the methods between the reviewers. Hospital records of those participants who reported that they had been hospitalized for CVD were reviewed. Modified World Health Organization (WHO) criteria for definite or possible myocardial infarction, based on chest pain symptoms, electrocardiogram (ECG) changes, and cardiac enzymes were used to verify the diagnosis of previous myocardial infarction (20). Subjects were classified as having hypertension if they were receiving drug treatment for hypertension or if systolic blood pressure was ≥160 mmHg or diastolic blood pressure was ≥95 mmHg in the sitting position after a 5-min rest. Standing height and body weight were measured. In all statistical analyses, subjects were classified as nonsmokers or current smokers. At baseline 86 (13.5%) of the nondiabetic men, 113 (15.4%) of the nondiabetic women, 250 (43.0%) of the diabetic men, and 271 (56.7%) of the diabetic women were receiving drug treatment for hypertension. Only 7 diabetic men, 2 diabetic women, and 2 nondiabetic subjects were receiving drug treatment for hyperlipidemia. Of the diabetic subjects, 92 (15.8%) men and 55 (11.5%) women were treated with diet only, 410 (70.6%) men and 352 (73.6%) women with oral hypoglycemic drugs but not with insulin, and 79 (13.6%) men and 70 (14.6%) women with insulin. The Rose classification was used to evaluate the presence of typical angina pectoris, and Whitehall changes according to Minnesota coding were used to identify ischemic changes on the ECG (21).

Classification of prior evidence of CHD

Four categories of prior evidence of CHD were defined: *1*) prior myocardial infarction verified at the hospital, *2*) angina pectoris, *3*) ischemic ECG changes, and *4*) any prior evidence of CHD (myocardial infarction or angina pectoris or ischemic ECG changes).

Biochemical methods

All laboratory specimens were taken after a 12-h fast at 0800. The methods for the determination of HbA_1, serum total cholesterol, triglycerides, HDL cholesterol, and plasma glucose have been previously reported (19).

Follow-up study

The follow-up period lasted until 1 January 2001. Information on the vital status of the participants and copies of death certificates of all deceased subjects were obtained from the Cause-of-Death Register (Statistics Finland). In the final classification of causes of death, hospital records and autopsy records, if available, also were used. The causes of death were reviewed by A.J. and S.L. The end points used in this study were total, cardiovascular (codes 390–459), and CHD death (codes 410–414) according to the ICD-8.

Statistical methods

Data analyses were conducted with the SPSS 11.5.1 programs (SPSS, Chicago, IL). The results for continuous variables are given as means ± SD and for categorical variables as percentages. Logarithmic transformation was used for triglycerides. The differences in the cumulative survival between the groups were studied by Kaplan-Meier estimates, with log-rank test statistics. Multivariate Cox regression models were used to examine the association of cardiovascular risk factors with the end points. The Mantel-Haenszel test was applied to evaluate homogeneity between nondiabetic and diabetic subjects in the association of a prior history of CHD with CHD mortality, when different definitions of prior CHD were used.

Approval of the ethics committees

The Ethics Committees of the Kuopio University Hospital and the Turku University Central Hospital approved the study. All study subjects gave informed consent.

RESULTS — Table 1 shows the number of subjects (with the percentage in parentheses) who had prior evidence of CHD and who died during the follow-up by sex for nondiabetic and diabetic subjects. The median follow-up was 17.5

Table 2—*Incidence per 1,000 person-years and Cox model HR for CHD death (adjusted for age, area of residence, and sex) during the 18-year follow-up according to the presence of diabetes and prior evidence of CHD disease in 1,373 nondiabetic and 1,059 diabetic subjects*

	Nondiabetic subjects				Diabetic subjects				Subjects with prior CHD: diabetic vs. nondiabetic		Subjects without prior CHD: diabetic vs. nondiabetic	
Prior evidence of CHD	Prior CHD	No prior CHD	HR (95% CI)	*P*	Prior CHD	No prior CHD	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
All												
Prior MI	26.8	3.2	5.4 (3.4–8.7)	<0.001	71.4	26.0	2.7 (2.1–3.4)	<0.001	2.3 (1.5–3.7)	<0.001	7.0 (5.4–9.2)	<0.001
Angina pectoris at baseline	9.8	3.3	2.9 (1.9–4.6)	<0.001	47.3	24.9	1.9 (1.5–2.4)	<0.001	4.0 (2.6–6.0)	<0.001	6.4 (4.8–8.4)	<0.001
ECG changes at baseline	8.8	3.0	2.8 (1.9–4.3)	<0.001	43.3	23.0	1.9 (1.5–2.3)	<0.001	4.1 (2.9–5.9)	<0.001	6.6 (4.8–9.1)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	8.1	2.4	3.4 (2.2–5.1)	<0.001	41.1	19.9	2.0 (1.6–2.6)	<0.001	4.2 (3.1–5.7)	<0.001	7.0 (4.8–10.1)	<0.001
Men												
Prior MI	34.1	5.8	5.1 (3.1–8.5)	<0.001	72.8	26.9	2.7 (2.0–3.6)	<0.001	2.0 (1.2–3.3)	0.005	4.3 (3.2–5.9)	<0.001
Angina pectoris at baseline	18.4	6.1	3.0 (1.8–5.0)	<0.001	55.5	26.1	2.0 (1.5–2.7)	<0.001	2.6 (1.6–4.2)	<0.001	4.0 (2.9–5.5)	<0.001
ECG changes at baseline	16.0	5.6	2.6 (1.7–4.2)	<0.001	48.3	25.1	1.9 (1.5–2.5)	<0.001	2.7 (1.8–4.0)	<0.001	4.3 (3.0–6.1)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	15.1	4.7	3.0 (1.9–4.7)	<0.001	46.6	21.6	2.1 (1.6–2.7)	<0.001	2.8 (2.0–4.0)	<0.001	4.2 (2.8–6.4)	<0.001
Women												
Prior MI	10.8	1.1	7.3 (2.0–26.1)	0.002	67.7	25.2	2.5 (1.6–3.9)	<0.001	5.4 (1.4–20.1)	0.012	18.7 (10.6–32.7)	<0.001
Angina pectoris at baseline	3.6	1.0	2.5 (0.9–7.0)	0.079	39.3	23.2	1.7 (1.2–2.4)	0.001	9.4 (4.0–22.0)	<0.001	19.2 (10.2–36.3)	<0.001
ECG changes at baseline	3.1	0.8	3.7 (1.4–9.6)	0.007	38.3	20.2	1.7 (1.3–2.4)	0.001	9.6 (4.8–19.5)	<0.001	21.6 (10.2–45.5)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	3.3	0.5	6.2 (2.0–19.2)	0.001	35.7	17.4	1.9 (1.3–2.7)	0.001	8.9 (4.9–16.0)	<0.001	34.4 (12.2–97.0)	<0.001

MI, myocardial infarction.

years with a total of 34,753 patient-years. During this period, 199 (31.2%) nondiabetic men, 98 (13.3%) nondiabetic women, 423 (72.8%) diabetic men, and 345 (72.2%) diabetic women died. Altogether 76 (11.9%) nondiabetic men, 17 (2.3%) nondiabetic women, 221 (38.0%) diabetic men, and 156 (32.6%) diabetic women died of CHD.

Table 2 shows the incidence of CHD death during the 18 years of follow-up per 1,000 person-years according to the status of diabetes and the presence of prior evidence of CHD at baseline. Hazard ratios (HRs) for CHD death derived from Cox models are given separately for men and women and for both sexes combined (adjustment for age, area of residence, and additionally for sex in analyses for which sexes were pooled). The incidence of CHD death was 3.2 per 1,000 person-years in nondiabetic subjects without prior myocardial infarction, 26.8 in nondiabetic subjects with prior myocardial infarction, 26.0 in diabetic subjects without prior myocardial infarction, and 71.4 in diabetic subjects with prior myocardial infarction. When the sexes were analyzed separately, the incidence of CHD death in diabetic subjects without prior myocardial infarction versus that in nondiabetic subjects with prior myocardial infarction was relatively higher in women than in men (incidence of CHD death per 1,000 person-years was 26.9 in diabetic men without prior myocardial infarction, 34.1 in nondiabetic men with prior myocardial infarction, 25.2 in diabetic women without prior myocardial infarction, and 10.8 in nondiabetic women with prior myocardial infarction).

Other definitions for prior evidence of CHD (angina pectoris, ischemic changes on an ECG, and any prior evidence of CHD [myocardial infarction or angina pectoris or ischemic changes on an ECG]) were also applied (Table 2). The lowest incidence of CHD death per 1,000 person-years was 0.5 in nondiabetic women without any prior evidence of CHD, whereas the incidence was 4.7 in nondiabetic men, 21.6 in diabetic men, and 17.4 in diabetic women. The diabetes-related risk was 2.0- to 2.8-fold in men with any prior evidence of CHD, 4.0- to 4.3-fold in men without prior evidence of CHD, 5.4- to 9.6-fold in women with prior evidence of CHD, and 18.7- to 34.4-fold in women without prior evidence of CHD.

Figure 1 shows Kaplan-Meier curves for CHD death during the 18-year fol-

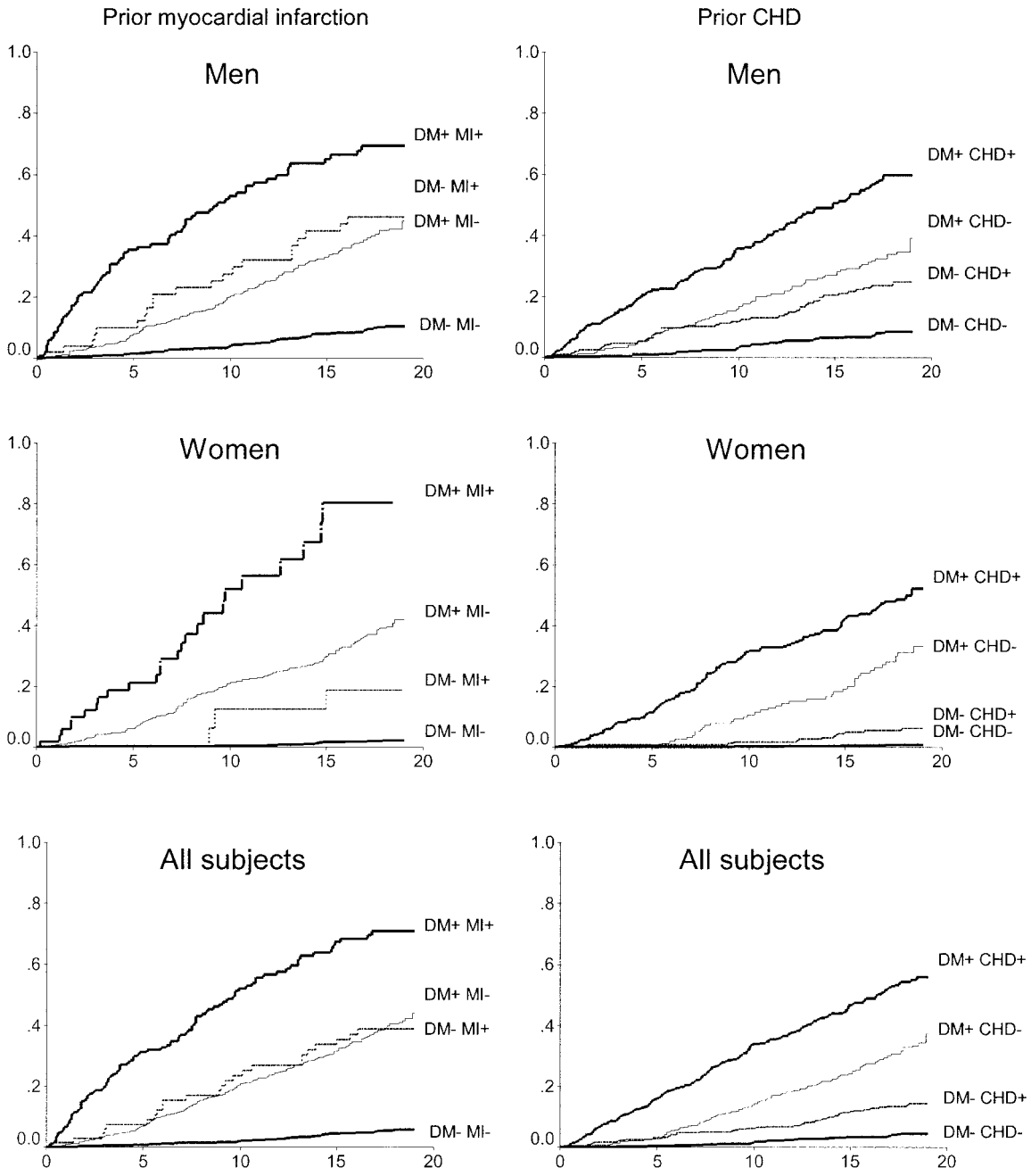

Figure 1—*CHD mortality. Kaplan-Meier estimates of CHD death during an 18-year follow-up according to the status of diabetes (DM) and prior evidence of CHD. Prior myocardial infarction (MI) is presented in the* left-hand panel *and prior CHD, defined as Whitehall changes of ECG, typical angina pectoris by the Rose classification, or prior myocardial infarction, in the* right-hand panel *in combination with the status of diabetes in men* (n = *1,219), in women* (n = *1,213), and in all* (n = *2,432).*

low-up in nondiabetic subjects and diabetic subjects with and without prior myocardial infarction or CHD. Diabetic subjects without prior myocardial infarction had a similar risk for CHD death as nondiabetic subjects with prior myocardial infarction when the sexes were analyzed together. However, when sexes were analyzed separately, the relative risk of CHD death for diabetic subjects without myocardial infarction, compared with that for nondiabetic subjects with myocardial infarction, was somewhat higher in women than in men. When the criteria were any prior evidence of CHD, diabetes was a stronger risk factor for CHD death when the sexes were analyzed together (Fig. 1). The presence of diabetes had a larger effect on CHD mortality in both men and women compared with that in nondiabetic subjects with any prior evidence of CHD.

Table 3 shows the risk for CHD, CVD, non-CVD, and total mortality in diabetic subjects without prior CHD compared with that for nondiabetic subjects with prior CHD. No statistically significant differences in multivariate HRs were found with respect to prior myocardial infarction either in pooled or sex-specific analyses (adjustment for age, area of residence, sex [in the pooled analyses], current smoking, hypertension, total cho-

Table 3—*HRs from Cox hazards models for all-cause, CVD, CHD, and non-CVD death during the 18-year follow-up in diabetic subjects without prior evidence of CHD compared with nondiabetic subjects with prior evidence of CHD*

	All subjects		Men		Women	
Prior evidence of CHD	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
CHD death						
Prior MI	0.95 (0.62–1.46)	0.809	0.85 (0.53–1.37)	0.507	1.91 (0.60–6.08)	0.273
Angina pectoris at baseline	2.14 (1.42–3.22)	<0.001	1.45 (0.90–2.34)	0.126	4.86 (2.08–11.33)	<0.001
ECG changes at baseline	2.11 (1.48–3.01)	<0.001	1.54 (1.02–2.33)	0.040	4.27 (2.08–8.79)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	1.89 (1.36–2.64)	<0.001	1.50 (1.01–2.22)	0.045	3.52 (1.83–6.79)	<0.001
CVD death						
Prior MI	1.19 (0.79–1.79)	0.396	1.00 (0.64–1.58)	0.985	2.89 (0.92–9.11)	0.070
Angina pectoris at baseline	2.35 (1.64–3.37)	<0.001	1.44 (0.94–2.19)	0.091	5.76 (2.78–11.94)	<0.001
ECG changes at baseline	2.30 (1.69–3.12)	<0.001	1.49 (1.04–2.13)	0.030	5.13 (2.81–9.35)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	2.03 (1.52–2.72)	<0.001	1.40 (0.99–1.99)	0.056	4.43 (2.56–7.68)	<0.001
Non-CVD death						
Prior MI	1.41 (0.78–2.55)	0.258	1.70 (0.78–3.71)	0.184	0.90 (0.36–2.26)	0.820
Angina pectoris at baseline	1.92 (1.26–2.93)	0.003	2.18 (1.17–4.06)	0.014	1.68 (0.93–3.03)	0.085
ECG changes at baseline	1.71 (1.21–2.43)	0.002	1.83 (1.12–2.99)	0.016	1.53 (0.91–2.57)	0.109
Any prior sign (MI, angina pectoris, or ECG change)	1.82 (1.31–2.53)	<0.001	1.83 (1.18–2.85)	0.007	1.69 (1.00–2.86)	0.049
All-cause death						
Prior MI	1.27 (0.91–1.77)	0.169	1.19 (0.80–1.75)	0.389	1.64 (0.81–3.35)	0.171
Angina pectoris at baseline	2.17 (1.65–2.86)	<0.001	1.67 (1.18–2.37)	0.004	3.12 (2.00–4.87)	<0.001
ECG changes at baseline	2.03 (1.62–2.56)	<0.001	1.61 (1.21–2.16)	0.001	2.75 (1.89–4.01)	<0.001
Any prior sign (MI, angina pectoris, or ECG change)	1.94 (1.56–2.41)	<0.001	1.56 (1.19–2.05)	0.001	2.72 (1.89–3.92)	<0.001

*HRs are adjusted for age, sex, area of residence, smoking status, hypertension, total cholesterol, HDL cholesterol, and logarithm of triglycerides. MI, myocardial infarction.

lesterol, HDL cholesterol, and triglycerides [logarithm]). However, when less specific criteria for prior evidence of CHD were used (myocardial infarction or angina pectoris or ischemic ECG changes), the presence of diabetes had a greater effect on CHD mortality than prior evidence of CHD in nondiabetic subjects. HRs were substantially larger in women than in men. HRs for CHD death, depending on the definition of prior CHD, varied from 0.85 to 1.54 in men and from 1.91 to 4.86 in women.

Age, duration of diabetes, and the presence of the metabolic syndrome (22) (using a modified WHO definition similar to that in the Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe [DECODE] study [23]) did not significantly affect the HRs of diabetic subjects without prior myocardial infarction compared with those for nondiabetic subjects with prior myocardial infarction (see APPENDIX Table 1).

The results for CVD and total mortality were quite similar to those for CHD mortality. In contrast, diabetes status was a stronger predictor for non-CVD mortality compared with prior CHD in men but not in women.

The interaction "diabetes status × previous myocardial infarction" was studied in Cox models after adjustment for age, sex, area of residence, current smoking, and total cholesterol. A significant interaction was observed with $P = 0.001$ for CHD death and 0.004 for CVD death. The Mantel-Haenszel test was applied to evaluate subgroup homogeneity between nondiabetic and diabetic subgroups. The results were significant ($P < 0.01$) in all subjects and in men and women, regardless of the definition used for prior CHD, demonstrating heterogeneity in the association of prior CHD with CHD mortality among nondiabetic and diabetic subjects.

CONCLUSIONS — Our study indicates that type 2 diabetes is a CHD equivalent during an 18-year follow-up, when the criterion for CHD is prior myocardial infarction. However, with respect to other definitions of CHD, including angina pectoris, ischemic ECG changes, or any evidence of prior CHD (myocardial infarction or angina pectoris or ECG changes), the prognosis for subjects with type 2 diabetes without prior CHD was worse than that for nondiabetic subjects with prior CHD, particularly for women. This indicates that the use of a prior myocardial infarction as a criterion for CHD underestimates the significance of diabetes status with respect to mortality from CHD. The relative effect of the simultaneous presence of diabetes and prior CHD was particularly detrimental among women. Finally, in men but not women, diabetic subjects without prior evidence of CHD (with the exception of prior myocardial infarction) had significantly higher non-CVD mortality compared with that in nondiabetic subjects with prior evidence for CHD.

Contradictory findings have been reported in studies investigating the predictive value of prior myocardial infarction or diabetes on the risk of subsequent CHD events. Previous studies have been very heterogeneous, particularly with respect to sex, and have included men only (11,13,17), women only (10), or both sexes (4,8,9,12,14–16,18). Because there is a sex difference in diabetic subjects in

the risk of CHD, it is important that the results are analyzed separately for both sexes. Furthermore, the age range has been variable, including relatively young (25–44 years) and old (65–85 years) subjects, making the comparison between the studies difficult, because diabetes is a considerably weaker risk factor for CHD death in elderly individuals (11,17).

In several studies in which CHD mortality has been analyzed separately in men and women, the effect of diabetes status, compared with the effect of prior CHD, has been greater in women than in men (8,9,14,15,18). This is not surprising because women with diabetes lose their relative protection against cardiovascular complications (2,24,25). A high relative risk of CHD mortality among type 2 diabetic women could be also due to the superior survival of women without diabetes (26). Finally, some studies have reported that a long duration of diabetes increases further the risk of CHD death (9,10,13,17).

Our original observation that type 2 diabetes is a "CHD equivalent" was based on a 7-year follow-up of nondiabetic and diabetic subjects (4). The baseline study was conducted in 1982–1984, and there is a possibility that drug treatments started during the follow-up could have modified the prognosis of these patients. In the beginning of 1990s effective cardiovascular drug treatments, including the use of statins and ACE inhibitors, were introduced, as well as β-blocker treatment and thrombolysis for patients suffering from an acute myocardial infarction. However, these treatment modalities are not likely to have a substantial effect on the prognosis of subjects included in this follow-up study, given the shape of the mortality curves reported in Fig. 1. Although there is some "leveling off effect" of the mortality curves in diabetic patients, the effects of these new treatment modalities to improve prognosis of the patients, if any, is very hard to demonstrate. This may indicate that the treatment of diabetic patients, being relatively unchanged during the first 10 years of the follow-up, has not changed the prognosis during the longer follow-up.

Our study has several strengths. The numbers of diabetic and nondiabetic subjects were large, and the follow-up period was long. The diagnosis of type 2 diabetes was based on a previous history of diabetes, laboratory examinations at the baseline study, and C-peptide measurement among insulin-treated diabetic patients. Therefore, it is highly unlikely that our study cohort included patients with type 1 diabetes. This careful differentiation of the types of diabetes has not been performed in any of the other studies (6–18). In contrast, the diagnosis of type 2 diabetes has been based on a reported history of diabetes in most of the studies (8–11,13,17). Furthermore, we evaluated CHD at baseline according to the WHO criteria, but this has not been systematically done in any of the other studies (8–18). Therefore, it is possible that classification errors have occurred in other studies with respect to the diagnosis of type 2 diabetes and CHD events. These possible errors may in part explain the discrepant findings.

In summary, we have demonstrated that type 2 diabetes is a "CHD equivalent" in an 18-year follow-up study of Finnish subjects, if prior myocardial infarction was used to define CHD. When less stringent criteria for prior CHD were used (myocardial infarction or ischemic ECG changes or angina pectoris), type 2 diabetes carried a larger risk than prior CHD, especially in women. These findings emphasize the need for active management of cardiovascular risk factors in the pre-

APPENDIX

Appendix Table 1—*The effect of age, duration of diabetes, and the metabolic syndrome on the equivalence of risks associated with type 2 diabetes and prior myocardial infarction*

	All subjects		Men		Women	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
CHD death						
Age below median (<56.9 years)	0.96 (0.47–1.96)	0.905	0.86 (0.39–1.89)	0.700	1.67 (0.21–13.24)	0.627
Age above median (≥56.9 years)	1.00 (0.57–1.72)	0.988	0.81 (0.43–1.52)	0.511	2.14 (0.52–8.85)	0.294
Diabetes duration below median (<8 years)	1.00 (0.63–1.60)	0.990	0.96 (0.56–1.63)	0.880	1.78 (0.53–5.94)	0.352
Diabetes duration above median (≥8 years)	0.91 (0.58–1.43)	0.674	0.71 (0.42–1.19)	0.193	2.06 (0.64–6.66)	0.228
No metabolic syndrome	0.99 (0.55–1.77)	0.968	0.83 (0.44–156)	0.559	3.52 (0.47–26.16)	0.220
Metabolic syndrome	0.67 (0.34–1.30)	0.233	0.71 (0.32–1.56)	0.392	0.73 (0.17–3.11)	0.667
CVD death						
Age below median (<56.9 years)	1.17 (0.60–2.28)	0.638	0.91 (0.44–1.89)	0.797	2.98 (0.40–22.45)	0.290
Age above median (≥56.9 years)	1.24 (0.73–2.09)	0.421	1.06 (0.59–1.91)	0.845	2.85 (0.70–11.67)	0.146
Diabetes duration below median (<8 years)	1.24 (0.80–1.92)	0.327	1.08 (0.66–1.77)	0.765	2.73 (0.84–8.84)	0.094
Diabetes duration above median (≥8 years)	1.17 (0.76–1.78)	0.479	0.88 (0.54–1.42)	0.593	2.96 (0.93–9.49)	0.067
No metabolic syndrome	1.33 (0.75–2.34)	0.330	1.10 (0.59–2.05)	0.759	5.34 (0.73–38.92)	0.098
Metabolic syndrome	0.79 (0.43–1.45)	0.449	0.69 (0.34–1.38)	0.295	1.25 (0.30–5.19)	0.758

HRs comparing diabetic subjects without prior myocardial infarction with nondiabetic subjects with prior myocardial infarction were calculated from Cox models for CHD mortality and CVD mortality, adjusted for age, sex (all subjects), area of residence, smoking status, hypertension, total cholesterol, HDL cholesterol, and logarithm of triglycerides.

vention of CHD in type 2 diabetic subjects, particularly in women.

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