# High Risk of Cardiovascular Disease in Patients With Type 1 Diabetes in the U.K.

## A cohort study using the General Practice Research Database

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**OBJECTIVE** — To estimate the absolute and relative risk of cardiovascular disease (CVD) in patients with type 1 diabetes in the U.K.

**RESEARCH DESIGN AND METHODS** — Subjects with type 1 diabetes ($n$ = 7,479) and five age- and sex-matched subjects without diabetes ($n$ = 38,116) and free of CVD at baseline were selected from the General Practice Research Database (GPRD), a large primary care database representative of the U.K. population. Incident major CVD events, comprising myocardial infarction, acute coronary heart disease death, coronary revascularizations, or stroke, were captured for the period 1992–1999.

**RESULTS** — The hazard ratio (HR) for major CVD was 3.6 (95% CI 2.9–4.5) in type 1 diabetic men compared with those without diabetes and 7.7 (5.5–10.7) in women. Increased HRs were found for acute coronary events (3.0 and 7.6 in type 1 diabetic men and women, respectively, versus nondiabetic subjects), coronary revascularizations (5.0 in men, 16.8 in women), and for stroke (3.7 in men, 4.8 in women). Type 1 diabetic men aged 45–55 years had an absolute CVD risk similar to that of men in the general population 10–15 years older, with an even greater difference in women.

**CONCLUSIONS** — Despite advances in care, these data show that absolute and relative risks of CVD remain extremely high in patients with type 1 diabetes. Women with type 1 diabetes continue to experience greater relative risks of CVD than men compared with those without diabetes.

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Type 1 diabetes is associated with cardiovascular disease (CVD) (1,2), but estimates of the increased risk are imprecise. It is important to have precise CVD risk estimates to inform guidelines for prevention of CVD in such patients and for evaluation of the impact of improvements in therapy over time. Precise CVD risk estimates also allow better design of clinical trials for this patient population.

Most of the large prospective cohort studies of patients with type 1 diabetes capturing CVD morbid events do not have nondiabetic comparison groups and cannot provide estimates of relative risk for CVD, though they do provide measures of absolute risk (3–7). Their crude coronary event rates (combining morbidity and mortality) have wide CIs, and there is wide variation between the cohorts in absolute rates of CVD, reflecting the different ages and populations and the small numbers of events. CVD mortality risks, on the other hand, have been estimated more accurately from population-based studies but do not capture morbidity (2,8–10). The large Diabetes U.K. cohort study of 23,751 patients <30 years of age with diabetes and treated with insulin showed standardized mortality ratios for ischemic heart disease of 8.8 (95% CI 7.4–10.3) in women and 4.5 (3.9–5.1) in men, compared with the U.K. general population (11).

The aim of this study is to generate recent and precise estimates of absolute and relative CVD mortality and morbidity risks in patients with type 1 diabetes from the General Practice Research Database (GPRD). This is a large primary care database from a network of 603 U.K. practices on which prescription data and diagnoses are recorded with standardized quality control methods. The GPRD provides a unique opportunity to estimate accurate CVD morbidity and mortality in a large type 1 diabetic cohort compared with a representative nondiabetic group.

## RESEARCH DESIGN AND METHODS

— This was a cohort study involving a study group of patients with type 1 diabetes and a nondiabetic comparison group selected from the GPRD. The GPRD methods have previously been described (12,13). The GPRD was set up in 1987 and contains data derived from computerized general practice records. Contributing practices agree to record all significant medical conditions, hospitalizations, pregnancies, births, deaths, and prescriptions issued. Prescriptions are directly issued from the database software and coded on the database with the Prescription Pricing Authority codes. Medical conditions are coded with a modification of the Oxford Medical Information System (OXMIS) classification and READ codes (adopted by the Department of Health for use in general practice). Several studies have confirmed the validity of the diagnostic and prescription data in the GPRD (>80% agreement) (12,14,15). Ethical approval for this

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**Abbreviations:** CHD, coronary heart disease, CVD, cardiovascular disease, GPRD, General Practice Research Database; OXMIS, Oxford Medical Information System.

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

study was given by the GPRD scientific and ethical advisory group.

### Diabetes population

At baseline (1 January 1992), the GPRD contained information on 3,595,966 patients from 603 general practices across the U.K., which accounts for 6% of the U.K. population. Age and sex distributions of the GPRD population have been shown to be similar to the Office for National Statistics estimates for the national population (13). The geographical distribution and practice size of the general practices were broadly representative of the U.K. While ethnicity and socioeconomic status is not recorded on the database, the representativeness of the practice sample in terms of age, sex, geography (including urban versus rural), and practice size means that the sample should also be representative for ethnicity and socioeconomic status since within any practice virtually all registered patients are included in the database. All subjects with ≥6 months' data before 1 January 1992 were considered eligible for inclusion. Diabetic patients were identified by searching for the relevant diagnostic codes and prescriptions. This extraction yielded 64,640 diabetic patients who were then classified into type 1 diabetes using the following algorithm: prescriptions of insulin and age <35 years at diagnosis of diabetes, plus if oral hypoglycaemic drugs were used the duration was restricted to ≤1.5 years, as some type 1 diabetic patients will have a honeymoon period during which their insulin requirement has not yet become clear. Of 7,713 type 1 diabetic subjects thus identified, only 3% (224) had a record of prescriptions for oral hypoglycemic drugs before starting insulin.

### Nondiabetic subjects

The nondiabetic comparison group was a random sample of those who neither had any OXMIS/READ code indicating diabetes nor had any diabetes-related drugs. Five age- and sex-matched control subjects per patient were selected. The matching variables were year of birth and sex.

### Cardiovascular events

To capture major incident CVD events between 1992 and 1999, a comprehensive list of CVD-related OXMIS/READ codes was defined. Records of myocardial infarction, coronary revascularizations, and stroke from the computerized general practice records were captured using these codes. Angina pectoris and silent myocardial infarctions were not included as major CVD events because our focus was on unequivocal CVD events. CVD deaths were captured by selecting the relevant cause of death entered on the date of death. Acute coronary heart disease (CHD) death was captured if cause of death was, for example, ischemic heart disease sudden death or coronary artery atheroma sudden death. Death was confirmed by checking that the patient had been deregistered from the GPRD due to death. Major incident CVD was defined as fatal and nonfatal acute myocardial infarction, fatal and nonfatal stroke, coronary revascularizations, and acute CHD death. Major CHD was defined as fatal and nonfatal acute myocardial infarction, coronary revascularizations, and acute CHD death. Fatal CVD was defined as fatal myocardial infarction, fatal stroke, and acute CHD death. Acute coronary events were defined as fatal and nonfatal myocardial infarction and acute CHD death. Coronary revascularizations were defined as coronary artery bypass graft, percutaneous transluminal coronary angioplasty, other angioplasty, or other coronary surgery.

Diagnoses of major CVD events were then captured from the computerized general practice records. Such diagnoses were usually based on a hospital discharge letter sent to the general practitioner with a confirmed diagnosis, which was then entered on the database by the general practitioner, but a diagnosis made directly by the general practitioner was also included. Additional confirmatory evidence was also sought on the general practitioner records, specifically, whether there was a concomitant record of relevant drug prescriptions (for example, nitrates, β-blockers, aspirin, etc.) and/or supporting diagnostic evidence (for example, a recorded electrocardiogram, cardiac enzyme, or computed tomography scan report) within 2 months of diagnosis. An algorithm to categorize an event as definite, probable, or possible myocardial infarction or stroke was used. Definite myocardial infarctions (78%) or strokes (85%) were patients who either died within 1 month of diagnosis or in whom a diagnostic code and relevant drug prescriptions and supporting hospital diagnostic test evidence were present on the computerized record. Probable myocardial infarctions (19%) or probable strokes (15%) included patients with a diagnostic code and either relevant drug prescriptions or supporting hospital evidence. Possible myocardial infarctions (3%) were those with a diagnostic code but no prescription or hospital data.

### Statistical analyses

The statistical package Stata 7.0 (Stata, College Station,TX) was used. A $P$ value of $<0.05$ was considered to be statistically significant. Subjects either contributed person-years of observation from 1 January 1992 until a major cardiovascular event, departure from the GPRD either because they left the practice or the practice left the database, or death from other causes ($n = 528$), or they continued to contribute up to the censoring date of 1 October 1999, whichever occurred first. The distribution of follow-up was similar between type 1 diabetic cases and nondiabetic subjects (median follow-up time was 4.7 [interquartile range 2.7–6.9] in type 1 diabetic cases and 4.6 [2.6–6.9] in nondiabetic subjects). Absolute CVD rates and 95% CIs were calculated per 1,000 person-years. Cox proportional hazards models were used to calculate hazard ratios (HRs) for CVD in patients with type 1 diabetes versus nondiabetic subjects. Since death due to other causes was used in the right censoring time, technically the Cox model provides descriptions of the CVD cause-specific risk or hazard function (16). Matching was taken into account in the Cox proportional hazards models by estimating HRs associated with diabetes in a model stratified by the matching variables (year of birth and sex). Likelihood ratio tests were used additionally to test for an interaction between diabetes and sex. For the analyses of incident major CVD, those type 1 diabetic and nondiabetic subjects with CVD pre-1992 ($n = 636$) were excluded, leaving 7,479 type 1 diabetic and 38,116 control patients. For the analyses of incident myocardial infarction and major CHD, those (including both type 1 diabetic and nondiabetic subjects) with prior myocardial infarction ($n = 291$) and CHD ($n = 485$) were excluded. Similarly, for the analyses of incident stroke, those with prior stroke ($n = 180$) were excluded. The Schoenfeld method (17) was used to test for departure from the assumption that for any group being compared, the HR was constant throughout the follow-up period. To estimate current age-specific rates from the Cox proportional hazards models, we took into account that people age as the follow-up in-

**Table 1—*Absolute and relative risk (HR) for first major CVD events in type 1 diabetic men and women and nondiabetic comparison group free of prior CVD***

| | | Men | | | Women | | |
|---|---|---|---|---|---|---|---|
| | | Type 1 diabetes | Without diabetes | Type 1 diabetes vs. comparison group | Type 1 diabetes | Without diabetes | Type 1 diabetes vs. comparison group |
| | *n* | Absolute risk per 1,000 person-years | Absolute risk per 1,000 person-years | HR | Absolute risk per 1,000 person-years | Absolute risk per 1,000 person-years | HR |
| Acute coronary events | 269 | 3.5 (2.7–4.4) | 1.3 (1.1–1.5) | 3.0 (2.2–4.1) | 2.9 (2.2–3.9) | 0.5 (0.3–0.7) | 7.6 (4.9–12.0) |
| Coronary revascularisations | 113 | 2.0 (1.5–2.8) | 0.4 (0.3–0.6) | 5.0 (3.2–7.8) | 1.5 (1.0–2.3) | 0.1 (0.06–0.2) | 16.8 (7.5–37.5) |
| Stroke (fatal + nonfatal) | 199 | 2.7 (2.1–3.6) | 0.8 (0.7–1.0) | 3.7 (2.6–5.3) | 2.0 (1.4–2.8) | 0.5 (0.3–0.7) | 4.8 (3.0–7.9) |
| Major CHD | 352 | 5.1 (4.2–6.3) | 1.6 (1.4–1.9) | 3.6 (2.8–4.6) | 4.1 (3.2–5.2) | 0.5 (0.4–0.7) | 9.6 (6.4–14.5) |
| Fatal CVD | 167 | 2.8 (2.1–3.7) | 0.5 (0.4–0.7) | 5.8 (3.9–8.6) | 2.5 (1.9–3.5) | 0.3 (0.2–0.4) | 11.6 (6.7–20.1) |
| Major CVD | 508 | 7.3 (6.1–8.6) | 2.3 (2.0–2.6) | 3.6 (2.9–4.5) | 5.5 (4.4–6.8) | 0.9 (0.7–1.2) | 7.7 (5.5–10.7) |

Data are risk (95% CI). Absolute risk is the absolute major CVD event rate expressed in person-years at risk. Acute coronary events defined as fatal and nonfatal myocardial infarction and acute CHD death. Coronary revascularizations defined as coronary artery bypass graft, percutaneous transluminal coronary angioplasty, other angioplasty, or other coronary surgery. Major CHD defined as fatal and nonfatal myocardial infarction, coronary revascularizations, and acute CHD death. Major CVD defined as fatal and nonfatal myocardial infarction, coronary revascularizations, acute CHD death, and fatal and nonfatal stroke. Fatal CVD defined as death due to myocardial infarction, acute CHD, or stroke. All HRs are stratified for the matching variables (year of birth and sex).

creases by splitting the observed individual follow-up times into periods (split Stata command) that correspond to different current-age (or attained-age) groups with a procedure called Lexis expansion (18). In other words, each subject's person-years of observation from study entry until first CVD event or censoring were split into several observations by expanding data by 10-year age bands using a Lexis program. Before a Lexis expansion, the models were (st)set using start and exit time of the study as well as setting date of birth in the origin. For major CVD, absolute and relative event rates were estimated by sex and 10-year current age bands. The effect of duration of diabetes on major CVD risk among those with type 1 diabetes was also assessed from these Cox proportional hazards models.

**RESULTS** — The prevalence of type 1 diabetes in 1992 was 2.15/1,000. The baseline CVD prevalence was 3% (234) in type 1 diabetic patients and 1% (402) in the nondiabetic group (risk ratio [RR] 3.0 [95% CI 2.5–3.5]). This RR was 3.8 (2.9–5.0) for women and 2.6 (2.1–3.2) for men. The study population contained 7,479 patients with type 1 diabetes and 38,116 subjects without diabetes, 55% were males, and the mean ± SD age was 33 years (±14.5) in both groups. The average duration of diabetes was 15 years (±12).

### Risk of major CVD with diabetes

During the period of follow-up, we ascertained 219 first major incident CVD events in 7,479 type 1 diabetic patients (cumulative incidence of 3%) and 289 events in 38,116 age- and sex-matched nondiabetic patients (cumulative incidence of 0.76%). Table 1 shows the incidence data for first major CVD, split by type of event. Type 1 diabetes was associated with a fourfold risk of major CVD in men and an eightfold risk in women and an HR of 4.5 (95% CI 3.8–5.4) in all those with type 1 diabetes compared with those without after stratification for year of birth and sex. Type 1 diabetic patients also had greatly elevated HRs for acute coronary events, coronary revascularizations, stroke, major CHD, and fatal CVD. A much greater HR in women was observed particularly for coronary revascularizations but was also evident for each CVD component and for fatal CVD so that the greater elevation in risk in women cannot be attributable to a greater propensity for diagnosis or treatment of CVD in diabetic women.

### Risk of major CVD by age

The increased absolute risk for CVD in men and women with type 1 diabetes compared with control subjects was apparent across all current age bands (Table 2). HR for CVD was higher in younger women. Type 1 diabetic men aged 45–55 years experienced absolute risks of CVD akin to nondiabetic men ~10–15 years older. In women this difference was even greater.

### Fatal CVD risk

As the European Guidelines on cardiovascular disease prevention are couched in terms of fatal CVD events only, with 10-year fatal CVD risks of 5% being considered high, we report these risks here also (Fig. 1) (19). Typically, type 1 diabetic patients reach a 10-year risk of fatal CVD of ≥5% near 50 years of age, ~10–15 years before the general population typical risk reaches this level, a risk that is typically reached at age 60 in a nondiabetic population.

### Sex difference

The greater HR for all CVD events associated with diabetes in women than in men as shown in Table 1 was further explored. The HR of major CVD events for men compared with women was 1.3 (95% CI 1.0–1.7; $P = 0.07$) in type 1 diabetic patients and 2.6 (2.0–3.4; $P < 0.0001$) in nondiabetic subjects. The likelihood ratio test for the sex by diabetes interaction was statistically significant ($P = 0.0007$), reinforcing that the HR of 7.7 for diabetes compared with those without among women was significantly greater than the HR of 3.6 among men (Table 1). Similarly for major coronary events, HRs of 1.3 (0.9–1.7; $P = 0.2$) and 3.0 (2.1–4.2; $P < 0.0001$), respectively, were found in men compared with women with type 1 diabetes and those without (likelihood ratio test $P$ value for the diabetes by sex inter-

action = 0.0001). In summary, a lack of sex difference in CVD risk was found in those subjects with diabetes, whereas there was a significant sex difference in CVD risk in those without diabetes, with men being at higher CVD risk than women.

### Duration of diabetes

Among those with diabetes, diabetes duration was not significantly related to major CVD risk independently of current age, with which it was highly correlated (HR 1.00 [95% CI 0.99–1.02]) for every 1-year increment in duration.

**CONCLUSIONS** — Dramatically increased absolute and relative risks of CVD morbidity and mortality were found in patients with type 1 diabetes compared with those without diabetes in the U.K. in the most recently available data. These high risks were seen for strokes, acute coronary events, and for coronary revascularizations. High CVD incidence rates were reached in patients with type 1 diabetes at a much younger age compared with the general population, with large differences especially in women. Thus, CVD rates remain greatly elevated, despite improvements in treatment, notably since the St. Vincent Declaration (20) and landmark findings of the Diabetes Control and Complications Trial that emphasized the need for intensive glycemic control based on efficacy in prevention of microvascular type 1 diabetes complications (21).

It is difficult to make any useful comparison with absolute risks of CVD morbidity in other cohorts of patients with type 1 diabetes, as these have not reported absolute risks by age bands and have widely varying estimates of overall risk, reflecting the small sample sizes in these cohorts and the differing age composition (3–5).

Estimates of coronary and cerebrovascular mortality (but not morbidity) reported by the large Diabetes U.K. cohort study (11) are consistent with our study. Relative risks for CHD mortality were reported of 8.8 (95% CI 7.4–10.3) in women and 4.5 (3.9–5.1) in men with type 1 diabetes, which compared with our RRs of 9.6 (6.4–14.5) and 3.6 (2.8–4.6), respectively (11). For stroke, the RRs were almost identical to Diabetes U.K. cohort data with 3.1 (2.2–4.3) in men and 4.4 (3.1–6.0) in women (22) compared with the GPRD with 3.7 (2.6–5.3) in men and 4.8 (3.0–7.9) in women. Comparable

**Table 2—*Absolute and relative risk (HR) for major CVD in type 1 diabetic men and women compared with the nondiabetic comparison group stratified by (current) age bands***

| | Men | | | | | | Women | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Type 1 diabetes | | | | Type 1 diabetes vs. comparison group | | Type 1 diabetes | | | | Type 1 diabetes vs. comparison group |
| | Person-years | CVD | Absolute risk per 1,000 person-years | Absolute risk per 1,000 person-years | HR | | Person-years | CVD | Absolute risk per 1,000 person-years | Absolute risk per 1,000 person-years | HR | |
| ≤35 years | 52,985 | 10 | 0.8 (0.4–1.6) | 0.07 (0.02–0.2) | 11.3 (2.9–43.8) | | 47,416 | 6 | 0.5 (0.2–1.3) | 0.05 (0.01–0.2) | 9.8 (1.8–53.6) | |
| 35–45 years | 29,715 | 51 | 4.8 (3.2–7.1) | 1.1 (0.8–1.6) | 4.4 (2.5–7.6) | | 21,323 | 17 | 3.5 (2.1–6.1) | 0.2 (0.09–0.6) | 15.4 (5.0–47.3) | |
| 45–55 years | 17,143 | 81 | 10.6 (7.3–15.2) | 3.6 (2.8–4.7) | 3.0 (1.9–4.8) | | 13,390 | 34 | 10.2 (6.7–15.5) | 1.1 (0.6–1.9) | 10.1 (5.0–20.4) | |
| 55–65 years | 8,166 | 114 | 39.4 (29.5–52.6) | 9.7 (7.7–12.3) | 4.1 (2.8–6.0) | | 6,535 | 44 | 22.8 (15.0–34.7) | 3.9 (2.6–6.0) | 5.7 (3.2–10.4) | |
| 65–75 years | 3,128 | 57 | 35.2 (21.6–57.5) | 15.3 (11.3–20.8) | 2.3 (1.3–4.1) | | 3,111 | 30 | 38.7 (24.1–62.3) | 4.9 (2.8–8.4) | 8.3 (4.0–17.2) | |
| >75 years | 830 | 37 | 122.2 (69.4–215.2) | 34.2 (23.1–50.6) | 3.5 (1.6–7.3) | | 743 | 25 | 87.3 (39.2–194.3) | 28.2 (18.0–44.2) | 4.0 (1.4–11.2) | |
| Total | | 350 | | | | | | 156 | | | | |

Data are risk (95% CI). Absolute risk is the absolute major CVD event rate expressed in person-years at risk. All HRs are stratified by year of birth and sex.

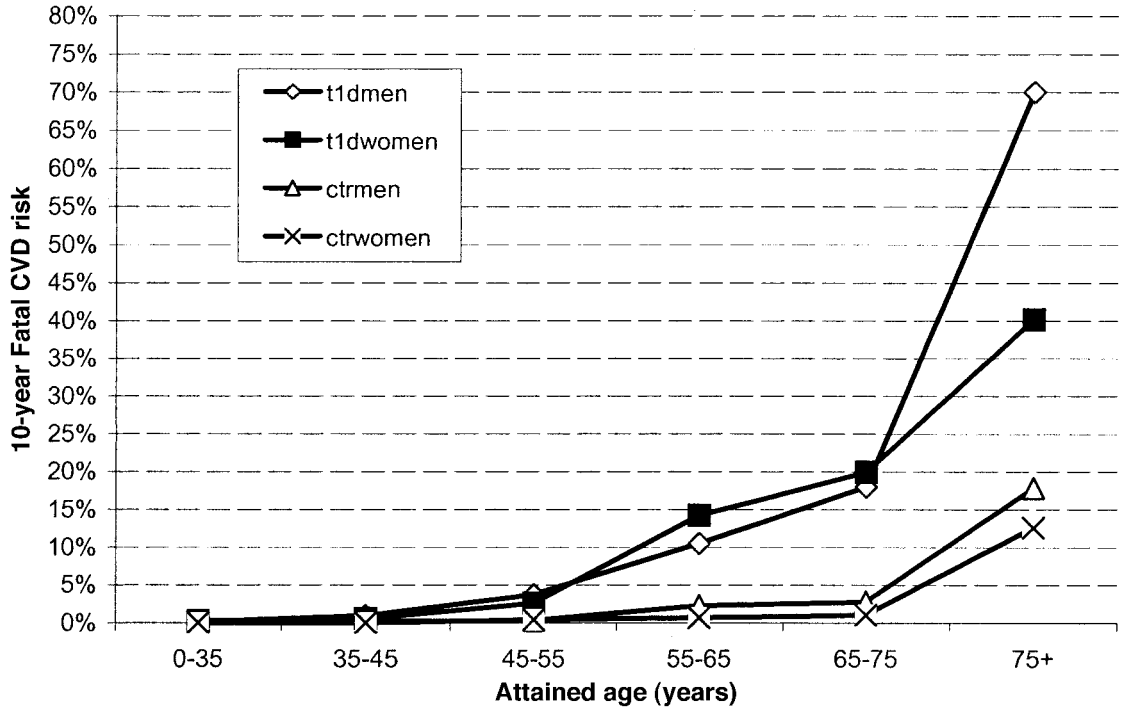


**Figure 1—***Estimated 10-year fatal CVD risk by current (or attained) age in type 1 diabetic (t1d) men and women compared with nondiabetic comparison group (ctr).*

results were also found for absolute CHD rates, even though only CHD mortality was collected in the Diabetes U.K. cohort study (11), whereas we also examined morbidity.

The main strengths of the GPRD are the large sample size, the longitudinal design, the use of unselected diabetes encountered in general practice, the excellent prescribing data, and the precise estimates of mortality and major clinical events. A matched nondiabetic comparison group provides an ongoing direct comparison group from the same source as the diabetic population, which has not been done previously (2,11). In terms of limitations, RRs are highest for event types (deaths and cardiac surgery) that are least susceptible to overreporting. Thus, there is no evidence for ascertainment bias in terms of picking up "softer" events in patients with type 1 diabetes, due to more frequent visits to their general practitioners. Cardiovascular risk factors are captured but are not comprehensive. As in all cohorts without immunological data on which to base diabetes classification, it is possible that a small proportion of patients defined here could have type 2 diabetes. However, we note that only 3% of those defined as having type 1 diabetes in this dataset had received oral hypoglycaemic drugs before insulin therapy. With regard to follow-up, although we captured all available data up to 1999, many patients have not contributed a full period of 7 years of follow-up, as some patients move from practices contributing to the database and some practices stopped contributing during this period. Absolute risks in both groups could be over- or underestimated if those leaving the database were systematically less or more ill, respectively, than those contributing longer follow-up, but we have no reason to believe this is the case. More importantly, incomplete follow-up will not introduce any bias in estimates of relative risk, as such losses to follow-up were the same in those with and without diabetes.

The European Guidelines view a 10-year risk of ≥5% for developing a fatal CVD event as "high risk" (19). Our data show that type 1 diabetic patients are at this risk by ~50 years of age compared with at least 10–15 years later in the nondiabetic population.

It remains unclear to what extent the very high risks of CVD in type 1 diabetes can be explained solely by the long duration of glycemic exposure. A recent meta-analysis in type 1 diabetic patients suggested an RR of 1.15 (95% CI 0.92–1.43) for CVD with every 1% increase in $HbA_{1c}$ levels (23). At the June 2005 American Diabetes Association Annual Meeting, 17-year follow-up results from the Diabetes Control and Complications/Epidemiology of Diabetes Interventions and Complications Trial were presented, finding a 57% significant risk reduction in nonfatal myocardial infarction, stroke, and CVD death ($P = 0.018$) in those originally assigned to intensive glucose control despite convergence of glycemic control since Diabetes Control and Complications Trial cessation. These data emphasize the importance of glycemic control for preventing CVD in type 1 diabetes. It is clear that other CVD risk factors such as hypertension and renal disease are also important among patients with type 1 diabetes (3–5). However, these risk factors do not completely explain the increased risk of CVD in type 1 diabetes compared with those without diabetes (24). Notably, in the absence of renal disease, type 1 diabetes is associated with a more favorable lipid pattern compared with the general population (25). However, other, more subtle derangements of lipoproteins may be present (26,27).

Our data also emphasize that the particularly high relative risk of CVD in women with type 1 diabetes as found in earlier studies has not been abolished by recent changes in clinical care of patients with diabetes (2,11). The causes of these

higher risks in women also remain unclear. Whatever its basis, the ongoing dramatic elevation in CVD risk in type 1 diabetic patients, especially diabetic women, needs to be emphasized to clinicians, as the relatively good lipid profile of type 1 diabetic patients without renal disease could lead to their CVD risk being underappreciated.

The age-group–specific estimates for CVD risks presented here reflect the group risk for a mix of individuals at high to low risk, and the challenge is how to differentiate these. However, our data emphasize that certainly, at least from 45 years of age, type 1 diabetic patients should be evaluated for potential preventive interventions, such as statin therapy. Some patients will warrant intervention even earlier than this. While measurement of established risk factors is of use, in type 1 diabetic patients the ability to accurately predict those at risk of CVD is limited. In the absence of valid risk engines in this group, there may be an argument for using other imaging modalities to ascertain early disease in addition to risk factor measurement.

There is a lack of clinical trial evidence for specific interventions (cholesterol lowering, blood pressure lowering) in type 1 diabetic patients. For some interventions efficacy data will have to be generalized from studies in type 2 diabetic patients (28), because type 1 diabetes is rarer and specific trials in this group of patients will logistically be difficult. On the other hand, the availability of accurate data on absolute and relative CVD risks as obtained with the GPRD could help to calculate sample sizes to make a better decision on whether to conduct clinical trials in type 1 diabetic patients. Combined with good risk stratification data from prospective cohort studies, these more precise estimates on absolute and relative risk of CVD could be useful for more targeted guidelines for type 1 diabetes, as well as risk equations and future clinical trials.

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