Framingham, SCORE, and DECODE Risk Equations Do Not Provide Reliable Cardiovascular Risk Estimates in Type 2 Diabetes

RUTH L. COLEMAN, MSC
RICHARD J. STEVENS, PHD
RAVI RETNAKARAN, MD
RURY R. HOLMAN, FRCP

Accurate cardiovascular disease (CVD) risk estimates can inform choice of therapeutic strategies for individuals, provided they have been appropriately validated (1). Risk calculators are of particular relevance in diabetic patients given their 2–4 times higher CVD risk compared with the nondiabetic population (2). Framingham Study (3) risk equations for coronary heart disease (CHD) and CVD, based on age, sex, blood pressure, cholesterol (total and HDL), and smoking, with diabetes status as a categorical variable, have been validated prospectively in general populations (4,5) but not in diabetic subjects (6). The Systematic Coronary Risk Evaluation (SCORE) Project risk scores for fatal CHD and CVD (7) appear to overestimate risk in the general population (8,9) and have not been evaluated in diabetes. Following recognition of glycemia as a CVD risk factor (10), the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) Study Group developed a fatal CVD risk equation incorporating glucose tolerance status and fasting plasma glucose (11). We have evaluated these three risk equations in patients with type 2 diabetes using UK Prospective Diabetes Study (UKPDS) data (12).

RESEARCH DESIGN AND METHODS

— The UKPDS (12,13) recruited 5,102 of 7,616 people with newly diagnosed type 2 diabetes in 23 U.K. centers and followed them for median 10.4 years (range 6–20). Exclusion criteria included severe vascular disease, myocardial infarction, or stroke within 1 year and major systemic illness. The study received ethical committee approval, conformed to Declaration of Helsinki guidelines (1975 and 1983), and all patients gave informed consent. The 3,898 patients with complete baseline risk factor data—59% male, 30% current smokers, mean ± SD age 53 ± 9 years, systolic blood pressure 135 ± 19 mmHg, total cholesterol 5.4 ± 1.1 mmol/l, HDL cholesterol 1.07 ± 0.24 mmol/l, and A1C 7.2 ± 1.8%—reflected the whole cohort. Observed 10-year fatal CHD (myocardial infarction or sudden death) and fatal CVD (myocardial infarction, sudden death, stroke, or peripheral vascular disease) event rates were derived from Kaplan-Meier survival curves. Framingham, SCORE, and DECODE 10-year risk scores were calculated for fatal CVD and fatal CHD (except for DECODE) for each patient.

Estimated event rates were deemed acceptable if within 95% CIs of observed rates. Risk equations were also evaluated for different durations of diabetes by selecting patients for analysis at random times at 1–10 years after diagnosis of diabetes. This analysis excluded 779 patients because of a fatal CVD event or censoring before their chosen start time or missing risk factor data. Risk equation sensitivity and specificity were examined by comparing areas under the receiver-operating characteristic (ROC) curve using actual survival times where possible.

RESULTS

— The 10-year fatal CVD event rate (95% CI) observed in the UKPDS was 7.4% (6.5–8.3). The Framingham risk equation underestimated this rate by 32% with an absolute risk (AR) of 5.0% (Fig. 1*A*). The SCORE risk equation overestimated risk by 18% (AR 8.7%), whereas the DECODE risk equation (AR 6.6%) yielded an acceptable estimate. For male patients, only the SCORE risk equation provided a reasonable estimate. For female patients, only the Framingham risk equation performed well. For Caucasians (n = 3,207), the 7.9% (6.7–9.0) observed event rate was underestimated by 34% using the Framingham equation (AR 5.2%), overestimated by 19% using the SCORE equation (AR 9.4%), and estimated appropriately by the DECODE equation (AR 7.2%). The 5-year fatal CVD event rate (95% CI) observed in the UKPDS for those selected with known diabetes duration of median 5 years (interquartile range 3–7) was 4.5% (95% CI 3.7–5.3). The Framingham equation underestimated this rate by 56% (AR 2.0%), whereas both the SCORE (AR 5.6%) and DECODE (AR 15.6%) equations yielded overestimates (Fig. 1*B*). The SCORE and DECODE equations appropriately estimated fatal CVD in male patients but not female.

The 10-year fatal CHD event rate (95% CI) observed in the UKPDS was 6.3% (5.5–7.1). The Framingham risk equation underestimated this rate (AR 4.3%), while the SCORE equation provided a reasonable estimate (AR 5.7%). Both equations provided reliable estimates for female but not male patients.

From the Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology, and Metabolism, University of Oxford, Churchill Hospital, Oxford, U.K.

Address correspondence and reprint requests to Professor Rury Holman, Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology, and Metabolism, Churchill Hospital, Oxford, U.K. OX3 7LJ. E-mail: rury.holman@dtu.ox.ac.uk.

Received for publication 30 June 2006 and accepted in revised form 1 February 2007.

Published ahead of print at http://care.diabetesjournals.org on 8 February 2007. DOI: 10.2337/dc06-1358.

Abbreviations: AR, absolute risk; CHD, coronary heart disease; CVD, cardiovascular disease; DECODE, Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe; ROC, receiver-operating characteristic; SCORE, Systematic Coronary Risk Evaluation; UKPDS, UK Prospective Diabetes Study.

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

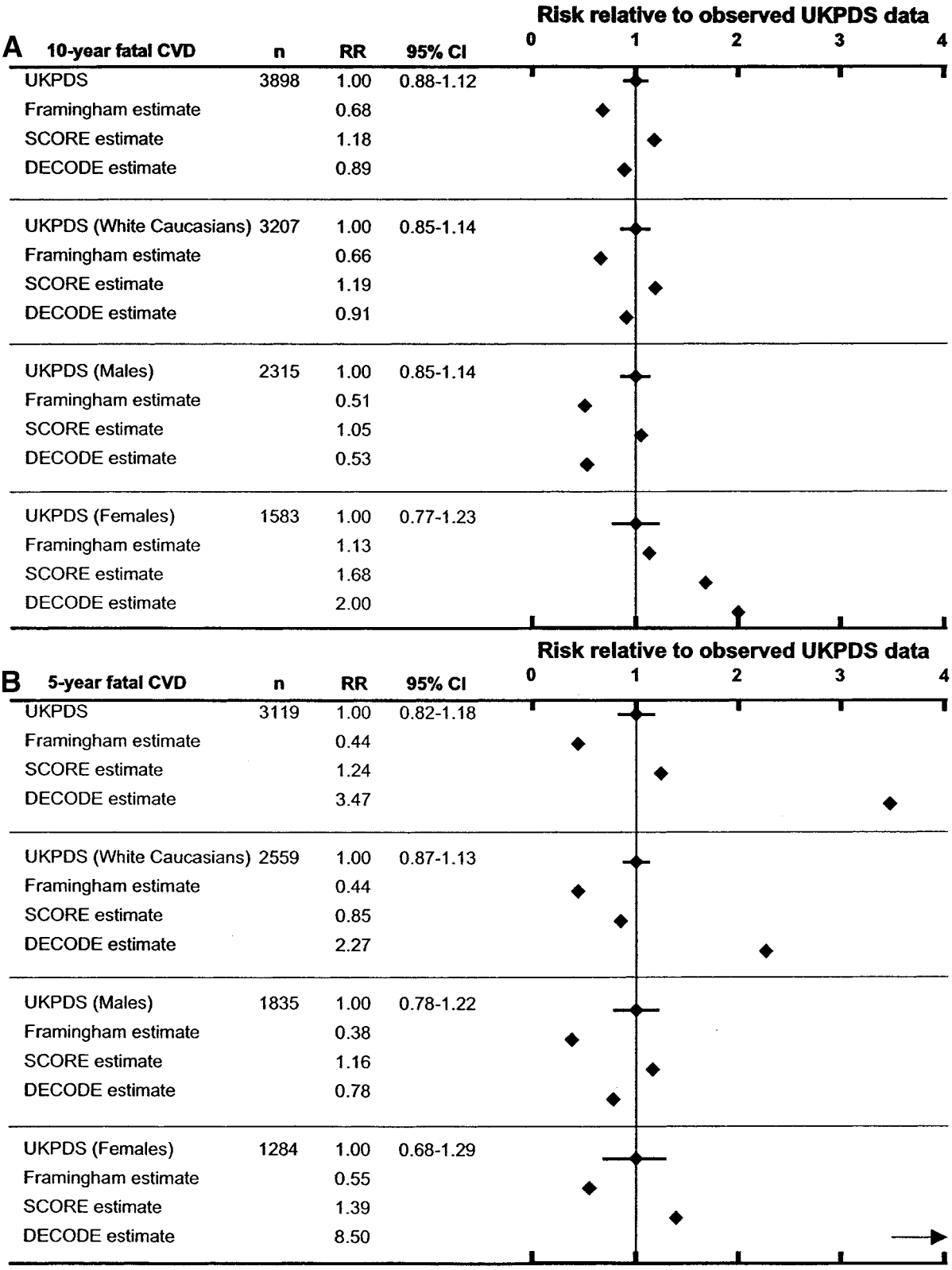

Figure 1—A: *Ten-year fatal CVD risks estimated using the Framingham, SCORE, and DECODE equations relative to those observed in UKPDS patients with newly diagnosed diabetes.* B: *Five-year fatal CVD risks estimated using Framingham, SCORE, and DECODE equations relative to those observed in UKPDS patients with diabetes diagnosed for 1–10 years.*

For Caucasians, the observed rate of 7.2% (6.3–8.1) was underestimated by both the Framingham (4.6%) and SCORE (6.2%) equations. The 5-year fatal CHD event rate (95% CI) observed in the UKPDS for those with a prior period of diabetes was 3.9% (3.1–4.6). The Framingham equation underestimated this rate (AR 2.0%) while the SCORE equation provided a reasonable estimate (AR 3.6%). Both models performed well in female patients, but only the SCORE equation provided a reasonable estimate in male patients.

The area under the ROC curve analysis for fatal CVD revealed similar discriminative capacity for the Framingham (c = 0.76) and SCORE (c = 0.77) equations while DECODE, which required times rounded to 5 or 10 years, did less well (c = 0.67).

To determine the degree to which absence of glycemia as a risk factor contributed to poor risk equation performance, we estimated CHD risk using the the UKPDS Risk Engine (14,15), a type 2 diabetes–specific model that has been validated in a diabetic cohort (16), with A1C values set to a nondiabetic value (5%). Under these artificial conditions, 10-year fatal CHD risks were underestimated to the same extent as the Framingham model (4.2%).

CONCLUSIONS — The Framingham, SCORE, and DECODE models do not provide reliable fatal CVD and CHD risk estimates in type 2 diabetes. The underestimate seen with Framingham is consistent with previous reports (16–18) and unsurprising given that there were only 337 diabetic individuals in the Framingham cohort. Also, incorporating diabetes as a categorical variable implies that diabetes increases risk similarly regardless of glycemic control or diabetes duration. This limitation pertains also to the SCORE equation, which simply doubles risk estimates for diabetic men and quadruples them for diabetic women. The DECODE equation, which included over 2,000 subjects with diabetes, incorporated fasting plasma glucose in a categorical fashion and thus does not adequately consider the effect of different levels of glycemia.

The area under the ROC curve analysis showed better discrimination for the Framingham equation than previously reported in diabetic cohorts (16). The DECODE value may be lower than might be expected given the limitation of only using 10-year or 5-year estimates.

The similar underestimation of CVD risk seen with the Framingham equations when using the UKPDS Risk Engine, with A1C levels set artificially to a nondiabetic value, highlights the importance of glycemia to CVD risk estimation in type 2 diabetes. This report emphasizes the need for validated diabetes-specific risk calculators that can estimate CVD risk reliably type 2 diabetic patients.

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