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## Comparison of the heart failure risk stratification performance of the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate in patients with Type 2 diabetes

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### Abstract

**Aims**—To investigate the risk prediction and the risk stratification performances of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and the Modification of Diet in Renal Disease (MDRD) equation for estimated glomerular filtration rate (eGFR<sub>CKD-EPI</sub> vs. eGFR<sub>MDRD</sub>) on heart failure in patients with Type 2 diabetes.

**Methods**—The study cohort included 12 258 White and 16 886 African American low-income patients with Type 2 diabetes who were 30–90 years old at baseline. Heart failure risk according to different eGFR<sub>CKD-EPI</sub> and eGFR<sub>MDRD</sub> categories was prospectively assessed.

**Results**—During a mean follow-up of 6.5 years, 5043 incident heart failure cases were identified. Multivariable-adjusted hazard ratios (HRs) of heart failure associated with the eGFR<sub>CKD-EPI</sub> categories [ > 90 (reference group), 75–89, 60–74, 30–59 and < 30 ml/min/1.73 m<sup>2</sup>] were 1.00, 1.11, 1.31, 1.75 and 2.93 ( $P_{\text{trend}} < 0.001$ ) for African American patients, and 1.00, 1.11, 1.08, 1.59 and 2.92 ( $P_{\text{trend}} < 0.001$ ) for White patients, respectively. The model with eGFR<sub>CKD-EPI</sub> and the other risk factors had significantly higher Harrell's C than the model with eGFR<sub>MDRD</sub> and other risk factors. Patients reclassified downward from eGFR<sub>MDRD</sub> 60–74 to eGFR<sub>CKD-EPI</sub> 30–59 and from eGFR<sub>MDRD</sub> 30–59 to eGFR<sub>CKD-EPI</sub> < 30 ml/min/1.73 m<sup>2</sup> showed higher heart failure risk than those who were not reclassified.

**Conclusions**—Impaired kidney function (i.e. GFR < 60 ml/min/1.73 m<sup>2</sup>), and even mildly decreased GFR (60–74 ml/min/1.73 m<sup>2</sup>) estimated by both equations is associated with an increased risk of heart failure. Compared with GFR estimated using the MDRD equation, GFR estimated using the CKD-EPI equation added more predictive power to the model with the other risk factors. Also, eGFR<sub>CKD-EPI</sub> provided more accurate heart failure risk stratification than eGFR<sub>MDRD</sub>.

## Introduction

Chronic kidney disease (CKD) has emerged as a major health concern worldwide with its high prevalence and heavy economic burdens exerted on society [1,2]. In addition to its risk of progression to end-stage renal disease, CKD is known to be associated with significantly increased risks of cardiovascular disease morbidity and mortality, even at its earliest stage [3,4]. Glomerular filtration rate (GFR) is the best overall index of kidney function and is widely used in the diagnosis, evaluation and management of CKD [5–7]. GFR is most often assessed using estimating equations from serum creatinine measurements [8]. The Modification of Diet in Renal Disease (MDRD) study equation, which was derived from 1628 subjects with CKD, is the most commonly used estimating equation [9]. However, the MDRD study equation, which incorporates age, sex, race and serum creatinine level, has been shown to systematically underestimate GFR in individuals with measured GFR  $\geq 60$  ml/min/1.73 m<sup>2</sup>, leading to over-diagnosis of CKD [10]. In 2009, a new estimating equation for GFR based on the same four variables used in the MDRD study equation was proposed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) [11]. The CKD-EPI equation, which was developed and internally validated in 10 studies (8254 patients), including the MDRD study, and externally validated in another 16 studies (3896 patients), has been shown to provide more accurate GFR estimates, lower CKD prevalence and better risk predictions [7,12–16]. However, most of these studies were conducted among the general population or among high-risk populations with existing cardiovascular disease and/or CKD [7,13,14,16]. The risk prediction performance of the CKD-EPI equation on cardiovascular disease in patients with diabetes, who are already at high risk of cardiovascular disease compared with people without diabetes [17] is largely unknown [15]. Moreover, no previous study has focused on heart failure as a major outcome. Therefore, this study aims to compare heart failure risk stratification performance of the CKD-EPI equation and the MDRD equation for eGFR in patients with Type 2 diabetes within the Louisiana State University Hospital-Based Longitudinal Study.

## Methods

### Study population

Between 1997 and 2012, the Louisiana State University Health Care Services Division (LSUHCS D) operated seven public hospitals and affiliated clinics in Louisiana, which provided quality medical care to the residents of Louisiana regardless of their income or insurance coverage [18–24]. Overall, LSUHCS D facilities have served about 1.6 million patients (35% of the Louisiana population) since 1997. Administrative, anthropometric, laboratory and clinical diagnosis data collected at these facilities have been available in electronic form since 1997 for both inpatients and outpatients. Using these data, we have established the Louisiana State University Hospital-Based Longitudinal Study. Since 1997, LSUHCS D's internal diabetes disease management guidelines have called for physician confirmation of diabetes diagnoses by applying the American Diabetes Association (ADA) criteria: a fasting plasma glucose level  $\geq 126$  mg/dl; 2-h glucose level  $\geq 200$  mg/dl after a 75 g 2-h oral glucose tolerance test (OGTT); one or more classic symptoms plus a random plasma glucose level  $\geq 200$  mg/dl [25]. A cohort of diabetic patients was identified through

the Louisiana State University Hospital-Based Longitudinal Study database between 1 January 1999 and 31 December 2009 by using the International Classification of Disease Code (ICD) 250 (ICD-9). The first record of diabetes diagnosis was used to establish the baseline for each patient our analyses due to the design of the cohort study. Before being diagnosed with diabetes, these patients had used our system for an average of 5.0 years. We have validated the diabetes diagnosis in LSUHCS hospitals. The agreement of diabetes diagnosis was 97%: 20 919 of a sample of 21 566 hospital discharge diagnoses based on ICD codes also had physician-confirmed diabetes by using the ADA diabetes diagnosis criteria [22].

This study included 29 144 patients with newly diagnosed diabetes (12 258 White and 16 886 African American) who were 30–90 years of age without a history of dialysis, heart failure or CHD, and with complete data on all risk factor variables. In these patients with Type 2 diabetes, ~ 78.9% qualify for free care (by virtue of being low income and uninsured – any individual or family unit whose income is at or below 200% of the Federal Poverty Level), ~ 5.0% of patients are self-pay (uninsured, but incomes not low enough to qualify for free care), ~ 5.0% of patients are covered by Medicaid, ~ 8.9% of patients have Medicare, and ~ 2.2% of patients are covered by commercial insurance. The study and analysis plan were approved by the Pennington Biomedical Research Center and the LSU Health Sciences Center Institutional Review Boards, LSU System. We did not obtain informed consent from patients involved in our study because we used anonymized data compiled from electronic medical records.

### Baseline measurements

The patient's characteristics, including age of diabetes diagnosis, sex, race/ethnicity, family income, smoking status, types of health insurance, body weight, height, BMI, blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, HbA<sub>1c</sub>, creatinine, history and incidence of heart failure, and CHD, and medication (anti-hypertensive drug, cholesterol-lowering drug and antidiabetic drug) within half year after the diabetes diagnosis (baseline) were extracted from the computerized hospitalization records. At each clinical visit, nurses measured height, weight and blood pressure. BMI was calculated by dividing weight in kilograms by the square of height in metres. Plasma total, LDL cholesterol, HDL cholesterol and triglycerides were measured by enzymatic colorimetric methods. Serum glucose was measured by the glucose-oxidase method. HbA<sub>1c</sub> was measured by immunoassay. Serum creatinine, which was measured using the modified kinetic Jaffe method, was standardized to isotope dilution mass spectrometry. Creatinine concentrations were reduced by 5%, the established calibration factor [26].

### GFR estimation

GFR was estimated using the MDRD study equation (eGFR<sub>MDRD</sub>) [8]:  $eGFR_{MDRD} = 186 \times \text{serum creatinine}^{-1.154} \times \text{Age}^{-0.203} \times 0.742$  (if female)  $\times 1.210$  (if African American) and the CKD-EPI equation (eGFR<sub>CKD-EPI</sub>) [11]:  $eGFR_{CKD-EPI} = 141 \times \min(\text{serum creatinine}/k, 1)^{\alpha} \times \max(\text{serum creatinine}/k, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$  (if female)  $\times 1.159$  (if African American), where  $k$  is 0.7 for females and 0.9 for males,  $\alpha$  is  $-0.329$  for females and  $-0.411$

for males, min indicates the minimum of serum creatinine/ $k$  or 1, and max indicates the maximum of serum creatinine/ $k$  or 1.

### Prospective follow-up

Follow-up information was obtained from the Louisiana State University Hospital-Based Longitudinal Study inpatient and outpatient database by using the unique number assigned to every patient who visited the LSUHCSH hospitals. Since 1997, diagnosis of heart failure in the LSUHCSH hospitals has been made by the treating physicians using the Framingham Criteria for Heart Failure diagnosis [27]. After clinical diagnosis of heart failure, an echocardiogram was used for each heart failure patient to support the clinical diagnosis, classify heart failure (ejection fraction  $\leq 40\%$  or  $> 40\%$ ), and guide the treatment according to the classification. The diagnosis of heart failure was the primary endpoint of interest of the study, and was defined according to the ICD-9: heart failure (ICD-9 codes 402.01, 402.11, 402.91 and 428). We conducted a validation study among 4380 heart failure patients (including patients with and without diabetes) in LSUHCSH hospitals from 2008: of the 4380 heart failure patients, 2353 had an ejection fraction  $\leq 40\%$ , and 2027 had an ejection fraction  $> 40\%$ ; 2246 (95%) of the 2353 heart failure patients were confirmed using both the Framingham Criteria for Heart Failure diagnosis [28] and ejection fraction ( $\leq 40\%$ ), and 1430 (71%) of the 2027 heart failure patients were confirmed by using both the Framingham Criteria for Heart Failure diagnosis and ejection fraction ( $> 40\%$ ). Follow-up of each cohort member continued until the date of the diagnosis of heart failure, the date of the last visit if the subject stopped use of LSUHCSH hospitals, death or 31 May 2012 [22].

### Statistical analyses

eGFR<sub>CKD-EPI</sub> and eGFR<sub>MDRD</sub> were categorized as  $\geq 90$ , 75–89, 60–74, 30–59 and  $< 30$  ml/min/1.73 m<sup>2</sup>. Cox proportional hazards regression models were used to estimate the association of eGFR with the risk of heart failure. We cross-tabulated eGFR using the above categories and evaluated the proportion of patients in each category of eGFR by the MDRD study equation that was reclassified by the CKD-EPI equation. The risk of heart failure in patients who were reclassified and patients who were not reclassified were assessed using Cox proportional hazards regression models. The analyses were stratified by race (White vs. African American patients) and age ( $\geq 60$  vs.  $< 60$  years). All of the above analyses were first carried out adjusting for age and sex (age- and sex-adjusted model) and further for smoking, income, type of insurance, BMI, systolic blood pressure, HbA<sub>1c</sub>, LDL cholesterol, triglycerides, myocardial infarction, use of anti-hypertensive drugs, use of diabetes medications and use of cholesterol-lowering agents (multivariate-adjusted model). We computed the Harrell's C for the model based on all the covariates listed above (model 1), the model based on a combination of the covariates and eGFR<sub>CKD-EPI</sub> (model 2), and the model based on a combination of the covariates and eGFR<sub>MDRD</sub> (model 3). The predictive values of these models were compared by using the Harrell's C associated with the models [29]. Statistical significance was considered to be  $P < 0.05$ . All statistical analyses were performed by using SAS for Windows, v. 9.3 (SAS Institute, Cary, NC, USA) and STATA for Windows, v. 13.1 (StataCorp LP, College Station, TX, USA).

## Results

The general characteristics of the study population at baseline are presented by race and eGFR<sub>CKD-EPI</sub> categories in Table 1. Both African American and White patients who had eGFR<sub>CKD-EPI</sub>  $\leq 60$  ml/min/1.73 m<sup>2</sup> had lower BMI, a lower proportion of current smokers, higher triglycerides and a higher proportion of cholesterol-lowering medication use, when compared with those who had eGFR<sub>CKD-EPI</sub>  $> 60$  ml/min/1.73 m<sup>2</sup>. The interaction of eGFR and race was significant on the risk of incident heart failure ( $P < 0.001$  for eGFR<sub>CKD-EPI</sub>  $\times$  race and  $P = 0.011$  for eGFR<sub>MDRD</sub>  $\times$  race).

During a mean follow-up of 6.5 years, 5043 patients developed heart failure. For African Americans, relative to patients who had eGFR<sub>CKD-EPI</sub>  $\geq 90$  ml/min/1.73 m<sup>2</sup>, patients who had eGFR<sub>CKD-EPI</sub> 75–89 ml/min/1.73 m<sup>2</sup> had a 11% [95% confidence interval (CI) 0–23%] increased risk for heart failure, those who had eGFR<sub>CKD-EPI</sub> 60–74 ml/min/1.73 m<sup>2</sup> had a 31% (95% CI 17–46%) increased risk for heart failure, those who had eGFR<sub>CKD-EPI</sub> 30–59 ml/min/1.73 m<sup>2</sup> had a 75% (95% CI 56–97%) increased risk for heart failure, and patients who had eGFR<sub>CKD-EPI</sub>  $< 30$  ml/min/1.73 m<sup>2</sup> had a 193% (95% CI 140–257%) increased risk for heart failure when adjusted for multiple covariates (Table 2). The pattern of the association between eGFR<sub>CKD-EPI</sub> and heart failure risk in White patients was similar to that found in African American patients.

Similarly, the multivariable-adjusted hazard ratios (HRs) of heart failure at five eGFR<sub>MDRD</sub> groups ( $\geq 90$ , 75–89, 60–74, 30–59 and  $< 30$  ml/min/1.73 m<sup>2</sup>) were 1.00, 1.08 (95% CI 0.98–1.20), 1.34 (95% CI 1.20–1.49), 1.77 (95% CI 1.57–1.99) and 3.17 (95% CI 2.57–3.92) among African American patients ( $P_{\text{trend}} < 0.001$ ), and 1.00, 1.08 (95% CI 0.96–1.21), 1.09 (95% CI 0.96–1.23), 1.59 (95% CI 1.40–1.80) and 3.06 (95% CI 2.39–3.92) among White patients ( $P_{\text{trend}} < 0.001$ ), respectively (Table 2). Harrell's C for the models without eGFR but all the other covariates (model 1) were 0.683 (95% CI 0.668–0.698) for African American patients and 0.710 (95% CI 0.694–0.727) for White patients. Harrell's C for the models with eGFR<sub>CKD-EPI</sub> and all the other covariates (model 2) were 0.697 (95% CI 0.682–0.711) for African American patients and 0.716 (95% CI 0.700–0.733) for White patients. Harrell's C for the models with eGFR<sub>MDRD</sub> and all the other covariates (model 3) were 0.694 (95% CI 0.680–0.710) for African American patients and 0.714 (95% CI 0.698–0.731) for White patients. Among African American patients, values of Harrell's C were statistically different between model 1 and model 2 ( $P < 0.001$ ), between model 1 and model 3 ( $P < 0.001$ ), and between model 2 and model 3 ( $P = 0.007$ ). Among White patients, values of Harrell's C were statistically different between model 1 and model 2 ( $P = 0.019$ ), between model 1 and model 3 ( $P = 0.108$ ), and between model 2 and model 3 ( $P = 0.035$ ).

The median value for eGFR<sub>CKD-EPI</sub> [90.0 (interquartile range, IQR, 33.6)] was higher than for eGFR<sub>MDRD</sub> [89.0 (IQR, 34.9)]. More patients (144) left the MDRD defined  $> 60$  category than the number of new patients that enter this category when using the CKD-EPI. As a result, using eGFR<sub>CKD-EPI</sub>, the overall prevalence of impaired eGFR (i.e.  $< 60$  ml/min/1.73 m<sup>2</sup>) was 12.5% compared with 12% using eGFR<sub>MDRD</sub> (Table 3).

Compared with African American patients with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} > 90$  ml/min/1.73 m<sup>2</sup>, the multivariable-adjusted HRs were: 1.34 (95% CI 1.18–1.50) for African American patients with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} 60–74$  ml/min/1.73 m<sup>2</sup>; 1.40 (95% CI 1.08–1.81) for those with  $eGFR_{CKD-EPI} 30–59$ , but  $eGFR_{MDRD} 60–74$  ml/min/1.73 m<sup>2</sup>; 1.79 (95% CI 1.58–2.02) for those with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} 30–59$  ml/min/1.73 m<sup>2</sup>; 1.90 (95% CI 1.17–3.08) for those with  $eGFR_{CKD-EPI} < 30$  but  $eGFR_{MDRD} 30–59$  ml/min/1.73 m<sup>2</sup>; and 3.18 (95% CI 2.57–3.94) for those with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} < 30$  ml/min/1.73 m<sup>2</sup> (Table 4). Compared with White patients with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} > 90$  ml/min/1.73 m<sup>2</sup>, the HRs were: 1.58 (95% CI 1.39–1.81) for White patients with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} 30–59$  ml/min/1.73 m<sup>2</sup>; 2.16 (95% CI 1.20–3.88) for those with  $eGFR_{CKD-EPI} < 30$ , but  $eGFR_{MDRD} 30–59$  ml/min/1.73 m<sup>2</sup>; and 3.05 (95% CI 2.38–3.91) for those with both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD} < 30$  ml/min/1.73 m<sup>2</sup> (Table 4). Stratification for age yielded similar results (Table 4).

## Discussion

This study demonstrated that both reduced  $eGFR_{CKD-EPI}$  and reduced  $eGFR_{MDRD} (< 75$  ml/min/1.73 m<sup>2</sup>) were significantly associated with an increased risk of incident heart failure among patients with Type 2 diabetes. However, compared with  $eGFR_{MDRD}$ ,  $eGFR_{CKD-EPI}$  adds more predictive power to a model with only conventional covariates. Also,  $eGFR_{CKD-EPI}$  provides better risk stratification when  $eGFR < 75$  ml/min/1.73 m<sup>2</sup>, because patients reclassified downward by the CKD-EPI equation showed higher heart failure risk than those who were not reclassified.

Although the association of  $eGFR$  with all-cause mortality, cardiovascular disease mortality or end-stage renal disease has been extensively studied in patients with and without diabetes [30] few studies have investigated the association between  $eGFR$  and incident cardiovascular disease risk in patients with diabetes [31,32]. This risk association may be of particular interest because, in patients with Type 2 diabetes, the additional development of diabetic kidney disease would markedly amplify their risk for cardiovascular disease [32,33]. Two studies assessed the association of  $eGFR_{MDRD}$  with composite cardiovascular disease end points including cardiovascular disease death and incident cardiovascular disease in patients with Type 2 diabetes [28,29]. Both studies found that risk of the composite cardiovascular disease end points increased at  $eGFR_{MDRD} < 60$  ml/min/1.73 m<sup>2</sup>, when compared with  $eGFR > 90$  ml/min/1.73 m<sup>2</sup>. In the current study, besides  $eGFR_{MDRD} < 60$  ml/min/1.73 m<sup>2</sup>, even mildly decreased  $eGFR_{MDRD}$  (60–74 ml/min/1.73 m<sup>2</sup>) predicts heart failure risk, which indicated that  $eGFR$  might be a more sensitive marker for incident cardiovascular disease than for cardiovascular disease mortality. In this study, for the first time,  $eGFR_{CKD-EPI} < 75$  ml/min/1.73 m<sup>2</sup> was also found to be associated with an increased risk of heart failure, which suggested that like  $eGFR_{MDRD}$ ,  $eGFR_{CKD-EPI}$  can be also used for cardiovascular disease risk stratification.

Moreover, the increment in prognostic utility of  $eGFR$  in heart failure was investigated. The result indicated that, among African American patients, both  $eGFR_{CKD-EPI}$  and  $eGFR_{MDRD}$  added more predictive value in heart failure risk beyond other heart failure risk factors, i.e. age, sex, smoking, income, type of insurance, BMI, systolic blood pressure, HbA<sub>1c</sub>, LDL



cholesterol, triglycerides, myocardial infarction, use of anti-hypertensive drugs, use of diabetes medications and use of cholesterol-lowering agents. However, among White patients, only  $eGFR_{CKD-EPI}$  added more predictive power to other covariates in predicting heart failure. Besides, we also compared the model with  $eGFR_{CKD-EPI}$  (model 2) with the model with  $eGFR_{MDRD}$  (model 3), the model with  $eGFR_{CKD-EPI}$  had significantly higher predictive power than the model with  $eGFR_{MDRD}$  (model 3), which indicated that  $eGFR_{CKD-EPI}$  was a better predictor for future heart failure than  $eGFR_{MDRD}$ .

By showing that, when  $eGFR$  below  $75 \text{ ml/min/1.73 m}^2$ , patients reclassified downward by the CKD-EPI equation showed higher risk than those who were not reclassified, our study demonstrated that  $eGFR_{CKD-EPI}$  may provide more accurate heart failure risk stratification than  $eGFR_{MDRD}$ . However, it is unclear whether our finding could be attributable to a higher accuracy of the CKD-EPI equation than the MDRD equation. Because the ‘gold’ standard – the direct measured GFR was not available, our study cannot verify whether the CKD-EPI equation provides a more accurate GFR estimate than the MDRD study equation in patients with Type 2 diabetes [12]. Actually, results regarding the performance of the CKD-EPI equation in estimating GFR in patients with diabetes were mixed [34–36]. Two studies [31,32] showed that the CKD-EPI equation did not exhibit better performance than the MDRD study equation in estimating GFR, whereas another study [36] demonstrated that the CKD-EPI equation is more accurate overall and across subgroup with diabetes. Because of the small sample size in these studies, it is crucial to test the performance of the CKD-EPI equation in a bigger diabetic cohort. Of note, our study did not find a lower prevalence of  $eGFR < 60 \text{ ml/min/1.73 m}^2$  using  $eGFR_{CKD-EPI}$  compared with when using  $eGFR_{MDRD}$ , which is inconsistent with previous studies [7,13,14]. Differences in the characteristics of the study populations may contribute to this inconsistency: compared with previous cohorts [7,13,14], the current Type 2 diabetes cohort had a higher proportion of African American patients, and patients were mainly from low income class. There are several strengths in our study, including the large sample size, high proportion of African American patients, long follow-up time, and the use of administrative databases to avoid the problem of differential recall bias. In addition, patients in this study used the same public healthcare system and have the same socio-economic status, which minimizes the influence from the accessibility of health care, particularly when comparing African American and White patients. One limitation of our study is that our analysis was not performed on a representative sample of the state of Louisiana’s population, which limits the generalizability of this study; however, LSUHCSD hospitals are public hospitals and cover over 1.6 million patients, most of whom are low-income persons in Louisiana. A second limitation is that even though our analyses were adjusted for an extensive set of confounding factors, residual confounding due to the measurement error in the assessment of confounding factors, unmeasured factors such as physical activity, education, dietary factors, and family history of diabetes and other chronic diseases cannot be excluded.

In conclusion, we found that impaired kidney function (i.e.  $GFR < 60 \text{ ml/min/1.73 m}^2$ ), even mildly decreased GFR ( $60\text{--}74 \text{ ml/min/1.73 m}^2$ ) estimated by both equations is associated with an increased risk of heart failure in low-income patients with Type 2 diabetes. Compared with GFR estimated using the MDRD study equation, GFR estimated using the CKD-EPI equation added more predictive power to the model with the other risk factors.

Also, eGFR<sub>CKD-EPI</sub> provided more accurate heart failure risk stratification than eGFR<sub>MDRD</sub> in this low-income cohort.

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### What's new?

- This is the first large prospective study to assess the risk prediction and risk stratification performances of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and the Modification of Diet in Renal Disease (MDRD) equation for estimated glomerular filtration rate ((eGFR<sub>CKD-EPI</sub> vs. eGFR<sub>MDRD</sub>) on heart failure in low-income patients with Type 2 diabetes.
- The study showed that impaired kidney function (i.e. GFR < 60 ml/min/1.73 m<sup>2</sup>), and even mildly decreased GFR (60–74 ml/min/1.73 m<sup>2</sup>) estimated by both equations is associated with an increased risk of heart failure.
- Compared with eGFR<sub>MDRD</sub>, eGFR<sub>CKD-EPI</sub> adds more predictive power to a model with only conventional covariates.
- Also, eGFR<sub>CKD-EPI</sub> may provide more accurate heart failure risk stratification than eGFR<sub>MDRD</sub>.

**Table 1**  
Baseline characteristics of African American and White patients with Type 2 diabetes

Characteristics	eGFR <sub>CKD-EPI</sub> categories at baseline (ml/min/1.73 m <sup>2</sup> )					P
	90	75–89	60–74	30–59	< 30	
<b>African American patients</b>						
No. patients	9 271	3 473	2 258	1 595	289	
Age, mean (SD), years	47.3 (8.8)	52.1 (9.2)	55.2 (9.5)	57.8 (10.5)	48.1 (9.0)	<0.001
Income, mean (SD), \$/family	11 971 (10 810)	12 151 (11 593)	12 181 (11 370)	11 663 (9 560)	12 160 (13 047)	<0.001
BMI, mean (SD), kg/m <sup>2</sup>	33.9 (8.7)	34.1 (8.2)	33.7 (7.9)	32.8 (7.7)	31.6 (8.2)	<0.001
Blood pressure, mean (SD), mmHg						
Systolic	145 (24)	147 (25)	148 (25)	150 (27)	154 (32)	<0.001
Diastolic	83 (13)	82 (16)	81 (14)	80 (15)	82 (18)	0.367
Total cholesterol, mean (SD), mmol/l	4.9 (1.3)	4.9 (1.2)	4.9 (1.2)	4.9 (1.3)	4.7 (1.5)	0.183
HDL cholesterol, mean (SD), mmol/l	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)	1.1 (0.4)	<0.001
LDL cholesterol, mean (SD), mmol/l	3.0 (1.0)	3.0 (1.0)	3.0 (1.1)	2.9 (1.1)	2.8 (1.3)	0.134
Triglycerides, mean (SD), mmol/l	1.4 (0.9)	1.4 (0.8)	1.4 (0.8)	1.5 (0.9)	1.6 (0.9)	<0.001
HbA <sub>1c</sub> , mean (SD), mmol/mol	68 (31)	62 (27)	61 (27)	6.1 (27)	58 (26)	<0.001
HbA <sub>1c</sub> , mean (SD), %	8.4 (2.8)	7.8 (2.5)	7.7 (2.5)	7.7 (2.5)	7.5 (2.4)	<0.001
Obesity status, %						
Normal weight (<25)	13.9	11.1	11.3	13.5	18.7	
Overweight (25–29.9)	23.5	22.0	23.9	26.3	30.5	
Obesity class I (30.0–34.9)	23.5	26.9	27.1	26.3	24.9	
Obesity class II (≥35.0)	39.1	40.1	37.8	33.9	26.0	
Current smoker (%)	35.3	32.9	27.5	25.9	23.2	<0.001
Medication use, %						
Blood pressure	92.0	94.6	96.5	97.1	96.4	<0.001
Diabetes	87.2	83.3	84.0	82.8	80.4	0.005
Cholesterol	67.0	71.7	74.3	78.4	75.0	<0.001
<b>White patients</b>						
No. patients	5 311	2 887	2 306	1 569	185	
Age, mean (SD), years	48.1 (9.0)	53.0 (9.2)	56.3 (9.1)	59.7 (9.6)	58.2 (11.7)	<0.001

Characteristics	eGFR <sub>CKD-EPI</sub> categories at baseline (ml/min/1.73 m <sup>2</sup> )					P
	90	75–89	60–74	30–59	< 30	
Income, mean (SD), \$/family	13 457 (11 890)	13 656 (12 569)	13 051 (10 263)	13 515 (11 576)	14 752 (16 286)	< 0.001
BMI, mean (SD), kg/m <sup>2</sup>	35.1 (9.0)	35.1 (8.8)	34.7 (8.2)	34.4 (8.6)	33.1 (8.9)	< 0.001
Blood pressure, mean (SD), mmHg						
Systolic	141 (21)	141 (21)	143 (22)	144 (24)	141 (26)	0.116
Diastolic	79 (12)	78 (12)	77 (13)	75 (14)	73 (15)	< 0.001
Total cholesterol, mean (SD), mmol/l	5.1 (1.4)	5.0 (1.3)	5.0 (1.3)	4.9 (1.4)	1.5 (57)	< 0.001
HDL cholesterol, mean (SD), mmol/l	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.0 (0.3)	< 0.001
LDL cholesterol, mean (SD), mmol/l	2.9 (1.1)	2.9 (1.0)	2.9 (1.0)	2.8 (1.1)	2.4 (1.2)	< 0.001
Triglycerides, mean (SD), mmol/l	1.9 (1.1)	2.0 (1.1)	2.0 (1.1)	2.0 (1.0)	2.1 (1.1)	< 0.001
HbA <sub>1c</sub> , mean (SD), mmol/mol	62 (25)	54 (22)	54 (22)	54 (21)	54 (21)	< 0.001
HbA <sub>1c</sub> , mean (SD), %	7.8 (2.3)	7.1 (2.0)	7.1 (2.0)	7.1 (1.9)	7.1 (1.9)	< 0.001
Obesity status, %						< 0.001
Normal weight (< 25)	11.2	9.9	8.7	9.9	15.1	
Overweight (25–29.9)	20.0	21.0	21.8	22.8	24.3	
Obesity class I (30.0–34.9)	23.5	24.9	26.1	27.9	21.1	
Obesity class II (≥ 35.0)	45.3	44.1	43.5	39.5	39.5	
Current smoker (%)	42.2	36.9	33.7	25.0	24.6	< 0.001
Medication use, %						
Blood pressure	89.2	92.6	94.4	96.6	96.2	< 0.001
Diabetes	86.7	83.7	82.6	83.6	90.8	0.013
Cholesterol	72.7	80.2	81.2	83.0	81.5	< 0.001

Values are adjusted for age.

Table 2

Hazard ratios for heart failure according to estimated glomerular filtration rate categories by the CKD-EPI equation and the MDRD study equation at baseline among African American and White patients with Type 2 diabetes

	eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )				P for trend
	90	75-89	60-74	30-59	
<b>African American patients</b>					
No. cases	1 266	546	448	158	111
Person-year	65 582	22 982	14 694	10 189	1 516
Age- and sex-adjusted HR (95% CI)	1.00	1.14 (1.02-1.26)	1.38 (1.23-1.55)	1.93 (1.72-2.17)	3.42 (2.81-4.16)
Multivariable adjustment HR (95% CI) *	1.00	1.11 (1.00-1.23)	1.31 (1.17-1.46)	1.75 (1.56-1.97)	2.93 (2.40-3.57)
<b>White patients</b>					
No. cases	719	498	429	484	84
Person-year	33 191	17 460	13 524	8 948	878
Age- and sex-adjusted HR (95% CI)	1.00	1.12 (1.00-1.26)	1.15 (1.02-1.31)	1.75 (1.54-1.98)	3.29 (2.61-4.14)
Multivariable adjustment HR (95% CI) *	1.00	1.11 (0.98-1.24)	1.08 (0.95-1.23)	1.59 (1.40-1.80)	2.92 (2.31-3.69)
<b>Both</b>					
No. cases	1 985	1 044	877	942	195
Person-year	98 773	40 442	28 218	19 138	2 395
Age- and sex-adjusted HR (95% CI) †	1.00	1.13 (1.05-1.22)	1.27 (1.16-1.38)	1.85 (1.70-2.02)	3.39 (2.92-3.94)
Multivariable adjustment HR (95% CI) †	1.00	1.11 (1.03-1.20)	1.19 (1.10-1.30)	1.68 (1.54-1.83)	2.94 (2.53-3.41)
<b>eGFR<sub>MDRD</sub> categories (ml/min/1.73 m<sup>2</sup>)</b>					
	eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )				P for trend
	90	75-89	60-74	30-59	
<b>African Americans</b>					
No. cases	1 325	541	461	408	94
Person-year	66 697	23 739	14 418	8 863	1 248
Age- and sex-adjusted HR (95% CI)	1.00	1.09 (0.98-1.20)	1.43 (1.28-1.60)	1.97 (1.75-2.21)	3.54 (2.87-4.37)
Multivariable adjustment HR (95% CI) *	1.00	1.08 (0.98-1.20)	1.34 (1.20-1.49)	1.77 (1.57-1.99)	3.17 (2.57-3.92)
<b>Whites</b>					
No. cases	667	519	450	506	72
Person-year	29 885	18 814	15 004	9 526	772



	eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )					P for trend
	90	75–89	60–74	30–59	< 30	
Age- and sex-adjusted HR (95% CI)	1.00	1.08 (0.96–1.21)	1.12 (0.99–1.27)	1.73 (1.52–1.96)	3.42 (2.68–4.37)	< 0.001
Multivariable adjustment HR (95% CI) <sup>*</sup>	1.00	1.08 (0.96–1.21)	1.09 (0.96–1.23)	1.59 (1.40–1.80)	3.06 (2.39–3.92)	< 0.001
Both						
No. cases	1 992	1 060	911	914	166	
Person-year	96 582	42 553	29 422	18 389	2 020	
Age- and sex-adjusted HR (95% CI) <sup>†</sup>	1.00	1.09 (1.01–1.18)	1.27 (1.17–1.38)	1.87 (1.72–2.04)	3.51 (3.00–4.12)	< 0.001
Multivariable adjustment HR (95% CI) <sup>‡</sup>	1.00	1.09 (1.01–1.18)	1.21 (1.11–1.31)	1.70 (1.57–1.85)	3.11 (2.65–3.65)	< 0.001

<sup>\*</sup>Adjusted for age, sex, smoking, income, type of insurance, BMI, systolic blood pressure, HbA1c, LDL cholesterol, triglycerides, myocardial infarction, use of antihypertensive drugs, use of diabetes medications, and use of cholesterol-lowering agents

<sup>†</sup>Adjusted also for race.

**Table 3**

Reclassification across estimated glomerular filtration rate categories by the CKD-EPI equation from estimated glomerular filtration rate categories based on the MDRD study equation

	eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )					eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )					Total
	90	75-89	60-74	30-59	< 30	90	75-89	60-74	30-59	< 30	
90	13 738 (47.1%)	413 (1.4%)	0 (0%)	0 (0%)	0 (0%)	14 151 (48.6%)					
75-89	844 (2.9%)	5 530 (19.0%)	325 (1.1%)	0 (0%)	0 (0%)	6 699 (23.0%)					
60-74	0 (0%)	417 (1.4%)	4 104 (14.1%)	279 (1.0%)	0 (0%)	4 800 (16.5%)					
30-59	0 (0%)	0 (0%)	135 (0.5%)	2 885 (9.9%)	72 (0.3%)	3 092 (10.6%)					
< 30	0 (0%)	0 (0%)	0 (0%)	0 (0%)	402 (1.4%)	402 (1.4%)					
Total	14 582 (50.0%)	6 360 (21.8%)	4 564 (15.7%)	3 164 (10.9%)	474 (1.6%)	29 144 (100.0%)					

**Table 4**  
Hazard ratios for heart failure according to classification to estimated glomerular filtration rate categories by the CKD-EPI equation and MDRD satudy equation at baseline among African American and White patients with diabetes

	eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )					eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )				
	90	75–89	60–74	30–59	< 30					
Both African American and White Patients										
90	No. cases	1 902	90	–	–	–	–	–	–	–
	Person-year	93 647	2 936	–	–	–	–	–	–	–
	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	1.00	1.03 (0.83–1.28)	–	–	–	–	–	–	–
	Multivariable adjustment HR (95% CI) <sup>‡</sup>	1.00	0.95 (0.77–1.18)	–	–	–	–	–	–	–
75–89	No. cases	83	901	76	–	–	–	–	–	–
	Person-year	5 126	35 142	2 284	–	–	–	–	–	–
	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	0.89 (0.72–1.11)	1.12 (1.04–1.22)	1.02 (0.80–1.29)	–	–	–	–	–	–
	Multivariable adjustment HR (95% CI) <sup>‡</sup>	0.94 (0.75–1.17)	1.11 (1.02–1.20)	1.01 (0.80–1.28)	–	–	–	–	–	–
60–74	No. cases	–	53	780	78	–	–	–	–	–
	Person-year	–	2 365	25 210	1 847	–	–	–	–	–
	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	1.20 (0.91–1.58)	1.28 (1.17–1.39)	1.34 (1.06–1.69)	–	–	–	–	–
	Multivariable adjustment HR (95% CI) <sup>‡</sup>	–	1.26 (0.96–1.66)	1.20 (1.10–1.30)	1.25 (0.99–1.58)	–	–	–	–	–
30–59	No. cases	–	–	21	864	29	–	–	–	–
	Person-year	–	–	723	17 291	375	–	–	–	–
	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	–	1.37 (0.89–2.11)	1.88 (1.73–2.06)	2.58 (1.38–3.73)	–	–	–	–
	Multivariable adjustment HR (95% CI) <sup>‡</sup>	–	–	1.38 (0.89–2.12)	1.70 (1.56–1.86)	2.08 (1.44–3.02)	–	–	–	–
< 30	No. cases	–	–	–	–	166	–	–	–	–
	Person-year	–	–	–	–	2 020	–	–	–	–
	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	–	–	–	3.53 (3.01–4.14)	–	–	–	–
	Multivariable adjustment HR (95% CI) <sup>‡</sup>	–	–	–	–	3.10 (2.64–3.65)	–	–	–	–
African American patients										
90	No. cases	1 248	77	–	–	–	–	–	–	–
	Person-year	64 032	2 665	–	–	–	–	–	–	–

		eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )					eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )				
		90	75-89	60-74	30-59	< 30	90	75-89	60-74	30-59	< 30
75-89	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	1.00	1.10 (0.87-1.40)	-	-	-	1.00	1.10 (0.87-1.40)	-	-	-
	Multivariable adjustment HR (95% CI) <sup>†</sup>	1.00	1.02 (0.81-1.30)	-	-	-	1.00	1.02 (0.81-1.30)	-	-	-
	No. cases	18	468	55	-	-	18	468	55	-	-
	Person-year	1 550	20 257	1 932	-	-	1 550	20 257	1 932	-	-
60-74	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	0.74 (0.47-1.18)	1.13 (1.01-1.25)	1.01 (0.76-1.33)	-	-	0.74 (0.47-1.18)	1.13 (1.01-1.25)	1.01 (0.76-1.33)	-	-
	Multivariable adjustment HR (95% CI) <sup>†</sup>	0.71 (0.45-1.14)	1.12 (1.00-1.24)	1.04 (0.79-1.38)	-	-	0.71 (0.45-1.14)	1.12 (1.00-1.24)	1.04 (0.79-1.38)	-	-
	No. cases	-	1	393	67	-	-	1	393	67	-
	Person-year	-	60	12 714	1 643	-	-	60	12 714	1 643	-
30-59	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	-	1.24 (0.18-8.84)	1.44 (1.28-1.61)	1.52 (1.18-1.96)	-	-	1.24 (0.18-8.84)	1.44 (1.28-1.61)	1.52 (1.18-1.96)	-
	Multivariable adjustment HR (95% CI) <sup>†</sup>	-	1.20 (0.16-8.56)	1.34 (1.18-1.50)	1.40 (1.08-1.81)	-	-	1.20 (0.16-8.56)	1.34 (1.18-1.50)	1.40 (1.08-1.81)	-
	No. cases	-	-	-	391	17	-	-	-	391	17
	Person-year	-	-	-	8 547	268	-	-	-	8 547	268
< 30	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	-	-	-	1.98 (1.75-2.23)	2.61 (1.61-4.22)	-	-	-	1.98 (1.75-2.23)	2.61 (1.61-4.22)
	Multivariable adjustment HR (95% CI) <sup>†</sup>	-	-	-	1.79 (1.58-2.02)	1.90 (1.17-3.08)	-	-	-	1.79 (1.58-2.02)	1.90 (1.17-3.08)
	No. cases	-	-	-	-	94	-	-	-	-	94
	Person-year	-	-	-	-	1 248	-	-	-	-	1 248
White patients	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	-	-	-	3.57 (2.89-4.41)	3.18 (2.57-3.94)	-	-	-	3.57 (2.89-4.41)	3.18 (2.57-3.94)
	Multivariable adjustment HR (95% CI) <sup>†</sup>	-	-	-	-	-	-	-	-	-	-
90	No. cases	654	13	-	-	-	654	13	-	-	-
	Person-year	29 615	271	-	-	-	29 615	271	-	-	-
75-89	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	1.00	1.05 (0.60-1.83)	-	-	-	1.00	1.05 (0.60-1.83)	-	-	-
	Multivariable adjustment HR (95% CI) <sup>†</sup>	1.00	0.95 (0.55-1.66)	-	-	-	1.00	0.95 (0.55-1.66)	-	-	-
	No. cases	65	433	21	-	-	65	433	21	-	-
	Person-year	3 576	14 885	353	-	-	3 576	14 885	353	-	-
60-74	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	0.94 (0.73-1.22)	1.09 (0.97-1.24)	1.36 (0.87-2.11)	-	-	0.94 (0.73-1.22)	1.09 (0.97-1.24)	1.36 (0.87-2.11)	-	-
	Multivariable adjustment HR (95% CI) <sup>†</sup>	1.02 (0.79-1.32)	1.08 (0.96-1.23)	1.14 (0.73-1.79)	-	-	1.02 (0.79-1.32)	1.08 (0.96-1.23)	1.14 (0.73-1.79)	-	-
	No. cases	-	52	387	11	-	-	52	387	11	-

		eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )					
		90	75–89	60–74	30–59	< 30	
eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )							
Person-year		–	2 304	12 496	204	–	
Age- and sex-adjusted HR (95% CI) †		–	1.25 (0.95–1.67)	1.11 (0.98–1.27)	0.95 (0.52–1.75)	–	
Multivariable adjustment HR (95% CI) †		–	1.33 (1.00–1.77)	1.06 (0.93–1.21)	1.07 (0.59–1.98)	–	
30–59	No. cases	–	–	21	473	12	
Person-year		–	–	675	8 744	106	
Age- and sex-adjusted HR (95% CI) †		–	–	1.40 (0.91–2.17)	1.74 (1.53–1.99)	2.35 (1.32–4.21)	
Multivariable adjustment HR (95% CI) †		–	–	1.38 (0.89–2.14)	1.58 (1.39–1.81)	2.16 (1.20–3.88)	
< 30	No. cases	–	–	–	–	72	
Person-year		–	–	–	–	772	
Age- and sex-adjusted HR (95% CI) †		–	–	–	–	3.44 (2.69–4.39)	
Multivariable adjustment HR (95% CI) †		–	–	–	–	3.05 (2.38–3.91)	
Age 60 years							
No. cases		184	66	–	–	–	
Person-year		6 412	2 028	–	–	–	
Age- and sex-adjusted HR (95% CI) †		1.00	1.08 (0.81–1.43)	–	–	–	
Multivariable adjustment HR (95% CI) †		1.00	0.95 (0.72–1.27)	–	–	–	
No. cases		19	215	62	–	–	
Person-year		642	6 139	1 669	–	–	
Age- and sex-adjusted HR (95% CI) †		0.97 (0.60–1.58)	1.11 (0.91–1.36)	1.10 (0.82–1.48)	–	–	
Multivariable adjustment HR (95% CI) †		0.98 (0.60–1.58)	1.08 (0.88–1.32)	1.06 (0.79–1.42)	–	–	
No. cases		–	–	245	54	–	
Person-year		–	–	5 906	1 203	–	
Age- and sex-adjusted HR (95% CI) †		–	–	1.28 (1.05–1.56)	1.29 (0.94–1.76)	–	
Multivariable adjustment HR (95% CI) †		–	–	1.15 (0.95–1.41)	1.17 (0.85–1.60)	–	
30–59	No. cases	–	–	6	366	17	
Person-year		–	–	179	6 929	187	
Age- and sex-adjusted HR (95% CI) †		–	–	1.18 (0.52–2.68)	1.57 (1.31–1.89)	2.31 (1.39–3.83)	
Multivariable adjustment HR (95% CI) †		–	–	1.19 (0.52–2.69)	1.43 (1.19–1.72)	1.82 (1.10–3.04)	

eGFR <sub>MDRD</sub> categories (ml/min/1.73 m <sup>2</sup> )		eGFR <sub>CKD-EPI</sub> categories (ml/min/1.73 m <sup>2</sup> )				
		90	75–89	60–74	30–59	< 30
< 30	No. cases	–	–	–	–	63
	Person-year	–	–	–	–	504
90	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	–	–	–	3.90 (2.92–5.20)
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	–	–	–	–	2.87 (2.14–3.86)
Age < 60 years						
90	No. cases	1 718	24	–	–	–
	Person-year	87 235	908	–	–	–
75–89	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	1.00	1.05 (0.70–1.57)	–	–	–
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	1.00	1.02 (0.68–1.53)	–	–	–
60–74	No. cases	64	686	14	–	–
	Person-year	4 484	29 003	615	–	–
30–59	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	0.90 (0.70–1.16)	1.12 (1.02–1.22)	0.86 (0.51–1.46)	–	–
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	0.93 (0.72–1.20)	1.10 (1.00–1.20)	0.89 (0.52–1.50)	–	–
60–74	No. cases	–	53	535	24	–
	Person-year	–	2 362	19 304	643	–
30–59	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	1.26 (0.95–1.66)	1.24 (1.12–1.37)	1.55 (1.04–2.33)	–
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	–	1.32 (1.00–1.75)	1.17 (1.06–1.30)	1.66 (1.10–2.49)	–
< 30	No. cases	–	–	15	498	12
	Person-year	–	–	544	10 362	187
60–74	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	–	1.41 (0.85–2.35)	2.13 (1.92–2.36)	2.64 (1.49–4.66)
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	–	–	1.41 (0.84–2.34)	1.86 (1.68–2.06)	2.01 (1.14–3.55)
< 30	No. cases	–	–	–	–	103
	Person-year	–	–	–	–	1 516
60–74	Age- and sex-adjusted HR (95% CI) <sup>†</sup>	–	–	–	–	3.28 (2.69–4.00)
	Multivariable adjustment HR (95% CI) <sup>†‡</sup>	–	–	–	–	3.11 (2.54–3.80)

<sup>†</sup>Adjusted for age, sex, smoking, income, type of insurance, BMI, systolic blood pressure, HbA1c, LDL cholesterol, triglycerides, myocardial infarction, use of antihypertensive drugs, use of diabetes medications, and use of cholesterol-lowering agents

<sup>‡</sup>Also adjusted for race.