Comparison of Urinary Albumin-Creatinine Ratio and Albumin Excretion Rate in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study

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Background and objectives: The objective of this study was to compare random urine albumin-creatinine ratio (ACR) with timed urine albumin excretion rate (AER) in patients with type 1 diabetes.

Design, setting, participants, & measurements: A total of 1186 participants in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study provided spot urine specimens concurrent with 4-hour timed urine collections. ACR and AER were compared using Bland-Altman plots, cross-classification of albuminuria status and its change over time, and within-person variability.

Results: Despite moderate correlation (r = 0.62), ACR levels (mg/g) were lower than AER levels (mg/24 hr). This difference was greatest for men. Gender-specific estimated AER (eAER) values were empirically derived from ACR. Comparing the eAER with measured AER, agreement of prevalent microalbuminuria and macroalbuminuria classification was fair to moderate, and classification of change in albuminuria status over time was different. Intraclass correlations were 0.697 for ACR and 0.803 for AER. Effects of DCCT intensive versus conventional diabetes therapy on urine albumin excretion or classification of albuminuria were similar using the eAER versus measured AER, as were the effects of the previous glycosylated hemoglobin.

Conclusions: Systematic differences exist between urine ACR and AER, related to gender and other determinants of muscle mass. Use of ACR (or eAER) versus AER yields differences in classification of prevalent albuminuria states and changes in albuminuria states over time. These findings support the use of consistent ascertainment methods over time and further efforts to standardize and optimally interpret measurement of urine albumin excretion.


The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group has measured albumin excretion rate (AER) and creatinine clearance using a 4-hour timed urine collection and extrapolating results to a 24-hour excretion rate since its inception in 1983 (1). After 8 years in the EDIC follow-up study and after a mean study period of 14.5 years since DCCT baseline, we demonstrated an 87% reduction (95% confidence interval [CI] 65–95%; P < 0.001) in the risk for macroalbuminuria (AER >300 mg/24 h) in the intensive treatment group versus the conventional treatment group.

In 2004, 21 years after the randomization of the first patient, DCCT/EDIC decided to evaluate use of the ratio of concentrations of albumin and creatinine (ACR) measured in untimed “spot” specimens. Measurement of urine ACR represents a less complex and time-consuming alternative to the 4-hour timed collection, which may also be less susceptible to imprecision due to incomplete or inaccurate collection (2–8). Herein, we describe the relationship between the ACR and AER as measures of albumin excretion and derive functions to estimate AER from ACR. We then evaluate the relative sensitivity and specificity of the estimated AER (eAER) relative to the timed collection for determination of microalbuminuria and macroalbuminuria and the degree of variation over time. We also assess the effects of initial DCCT treatment group (intensive versus conventional) and glycosylated hemoglobin (HbA1c) on the eAER compared with those of the timed AER to assess the potential sensitivity of the untimed “spot” collection to detect treatment or covariate effects.

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aDeceased.

This trial has been registered at http://www.clinicaltrials.gov (identifiers NCT00360815 and NCT00360893).

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Materials and Methods

Participants

Of the 1297 active DCCT/EDIC participants, 1186 participated in this study between July 26, 2004, and September 9, 2008. Detailed descriptions of the eligibility criteria and intensive and conventional treatment procedures for participants who entered the DCCT, including baseline kidney function, and measures of kidney function during the DCCT have been published (9,10). In brief, at DCCT baseline, all participants were aged 13 through 39 years and had a duration of type 1 diabetes of 1 to 15 years. They were free of advanced microvascular or macrovascular complications of diabetes, had normal estimates of GFR (defined as serum creatinine levels ≤1.2 mg/dl [106.1 μmol/L] and/or creatinine clearance ≥100 ml/min per 1.73 m² [1.7 ml/s per 1.73 m³]) and normotension (BP ≤140/90 mmHg). At DCCT baseline, AER was ≤21 μg/min (30 mg/24 h) for the primary prevention cohort (1 to 5 years’ duration and no retinopathy) and ≤140 μg/min (200 mg/24 h) for the secondary intervention cohort (1 to 15 years’ duration and at least one microaneurysm). In addition, all participants were free of neuropathy that required treatment and had calculated LDL cholesterol levels (57). In addition, all participants were free of neuropathy that required treatment and had calculated LDL cholesterol levels (4.9 mmol/L). After DCCT closeout in 1994, 1375 (96%) of the patients in the former conventional treatment group and 687 in the secondary intervention cohort (1 to 15 years) were aged 13 through 39 years and had a duration of type 1 diabetes of 1 to 15 years. They were free of advanced microvascular or macrovascular complications of diabetes, had normal estimates of GFR (defined as serum creatinine levels <190 mg/dl [4.9 mmol/L]). After DCCT closeout in 1994, 1375 (96%) of the 1428 surviving members of the original DCCT cohort, including 688 patients in the former conventional treatment group and 687 in the former intensive treatment group, volunteered to participate in the EDIC study in 1994. A detailed description of the EDIC study procedures and baseline characteristics has been published (11).

Measurement of Albuminuria

In both DCCT and EDIC, AER was determined from a 4-hour urine collection and expressed as mg/24 h. The 4-hour collection took place in a monitored research environment; 91% began between 6 am and 12 pm and did not necessarily contain the first void of the day. For this study, a single void before the 4-hour collection was used to calculate the ACR. This void may have been a first or second morning void, but this was not required. Creatinine concentrations in serum and urine were measured by a variation of the Jaffe method on the Beckman CX3. Urine albumin concentration was measured by a fluorimunnoassay (1). The pooled within-subject coefficient of variation and coefficient of reliability assessed from split duplicate samples were 13.00% and 0.973, respectively, for ACR; 2.51% and 0.917 for serum creatinine concentration; 2.80% and 0.965 for urine creatinine concentration; 9.50% and 0.964 for urine albumin concentration; and 12.40% and 0.962 for the 4-hour excretion rate of albumin.

Assessment of Glycemic Control, Renal Function, and BP

Details regarding BP measurement and assays for levels of HbA₁c, creatinine, and albumin have been reported for the DCCT (1), and the procedures remained identical during the EDIC study. HbA₁c was measured quarterly during the DCCT and annually during EDIC. Thus, the average level of glycemia was computed as a weighted mean of values from DCCT and EDIC, whereby each quarterly measure during DCCT was weighted by one quarter relative to a weight of 1 for the annual EDIC measurements. Measurements of BP by sphygmomanometer and of HbA₁c level by ion-exchange HPLC were performed annually in the EDIC study. Approximately one half of the EDIC participants were evaluated with a 4-hour urine collection for albuminuria and creatinine clearance every other year. Participants were not asked to discontinue any medications, including angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or other antihypertensive medications, at the time of their annual assessments.

Statistical Analysis

The relationship between log(ACR) and log(AER) was examined using a Bland-Altman (12) plot that displays the log of the ratio AER/ACR on the vertical axis against the geometric mean of the two measures on the horizontal axis using a log scale. A Lowess (13) smoothed nonparametric regression line was superimposed on plots where appropriate. A simple estimate of the ratio α = AER/ACR was obtained from an intercept-only normal repeated measures regression model of the log(ACR/ACR). Gender-specific estimates of α were obtained by fitting the model with an indicator for gender. A further estimate of α was obtained by backward elimination with a P < 0.01 cutoff from an initial full model containing gender, weight, height, body mass index, body surface area (BSA), diastolic and systolic BP, current age, serum creatinine, GFR estimated by the Modification of Diet in Renal Disease (MDRD) formula (14), and log(ACR). Models for the probabilities of AER ≥30 mg/24 h and AER ≥300 mg/24 h were obtained from generalized estimating equation logistic regression models using a backward elimination from the same full model and a P < 0.01 cutoff.

The agreement between AER ≥30 mg/24 h or AER ≥300 mg/24 h and their estimates was summarized by Cohen’s k (15). Sensitivity, specificity, positive and negative predictive value, and proportion correctly classified were calculated. These statistics were estimated by bootstrap resampling (16). The number of bootstrap samples required ranged between 100 and 13000 and was obtained adaptively for each statistic to yield an asymptotic 95% CI with a half width of 0.01. Intraclass correlations for log(AER) and log(ACR) were calculated from a normal repeated measures regression model with a main effect for visit, under the assumption of compound symmetry. Statistical analyses were carried out using SAS 8.2 (SAS Institute, Cary, NC) and R 2.7.0 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

General Characteristics

Over 4 years, the 1186 participants completed 1836 visits, 2 years apart, at which time both an ACR and AER were measured. Table 1 summarizes the characteristics of the 1186 participants. The average age was 45.4 years with an average duration of diabetes of 24.5 years. Male participants constituted 51.6% of the sample and had significantly more hypertension (17.5 versus 10.5% >140/90) and higher body mass index (28.4 versus 27.9 kg/m²); serum creatinine levels (1.03 versus 0.86 mg/dl); estimated GFR (87.2 versus 81.6 ml/min); urine creatine excretion (1916 versus 1233 mg/d); and prevalences of microalbuminuria and macroalbuminuria, defined as AER ≥30 mg/24 h and ≥300 mg/24 h, respectively. Female participants had higher HbA₁c levels (7.9 versus 7.7%). During the period of this study, 578 (48%) of the subjects had a single visit, 566 (47%) had two visits, and 42 (5%) had three visits.

Estimated AER

Simple Estimate of AER. The scatterplot of AER against ACR showed an approximately linear relationship between the two quantities, with most participants having low values of ACR and AER (Figure 1A). Spearman correlation of ACR and AER was 0.62. In the Bland-Altman plot (Figure 1B), the smoothed loesses estimates of the mean difference log(AER) − log(ACR) for each gender and for both genders combined were >0, indicating that random ACR values (expressed in mg/g) were systematically lower than AER values (expressed in...
Table 1. Characteristics of participants by gender at initial visit

| Characteristic | All (N = 1186) | Male (n = 612) | Female (n = 574) | p
|---------------|---------------|---------------|---------------|---
| Age (years; mean ± SD)b | 45.4 ± 7.0 | 45.9 ± 6.7 | 44.8 ± 7.3 | 0.009 |
| DCCT intensive treatment group (n [%]) | 604 (50.9) | 304 (49.7) | 300 (52.3) | 0.372 |
| White race (n [%]) | 1145 (95.6) | 592 (96.7) | 553 (96.3) | 0.713 |
| Diabetes duration (years; mean ± SD) | 24.5 ± 4.9 | 24.3 ± 4.7 | 24.8 ± 5.0 | 0.151 |
| HbA1c (%; mean ± SD) | 7.79 ± 1.22 | 7.68 ± 1.14 | 7.90 ± 1.29 | 0.004 |
| BMI (kg/m²; mean ± SD) | 28.2 ± 4.9 | 28.4 ± 4.3 | 27.9 ± 5.4 | 0.001 |
| BSA (m²; mean ± SD) | 1.99 ± 0.24 | 2.11 ± 0.20 | 1.86 ± 0.20 | <0.001 |
| AER (mg/24 h; median [IQR])b | 10.1 (7.2 to 20.2) | 11.5 (7.2 to 25.9) | 8.6 (5.8 to 15.8) | <0.001 |
| AER ≥30 mg/24 h (n [%])b | 212 (17.9) | 145 (23.7) | 67 (11.7) | <0.001 |
| AER ≥300 mg/24 h (n [%])b | 56 (4.7) | 40 (6.5) | 16 (2.8) | 0.002 |
| Creatinine excretion rate (mg/24 h; median [IQR])b | 1553 (1209 to 1947) | 1916 (1647 to 2170) | 1233 (1058 to 1428) | <0.001 |

The initial visit is the first renal visit between July 26, 2004, and September 9, 2008, at which an ACR and AER were obtained. BMI, body mass index; IQR, interquartile range. To convert serum creatinine to μmol/L, multiply mg/dl values by 88.4; to convert standard creatinine clearance to ml/s, multiply ml/min values by 0.0167.

aFrom Wilcoxon rank-sum test (continuous variables) and Pearson χ² test (categorical variables).
bBased on 4-hour collection of urine.

mg/24 h) over the complete range of values. The mean difference between ACR (mg/g) and AER (mg/24 h) was greater for male compared with female participants (P < 0.0001).

**Gender-Adjusted Estimate of AER.** Gender-specific equations estimating AER from ACR (eAERgender) were eAERmale = 2.09 × ACR (95% CI 1.99 to 2.20) and eAERfemale = 1.38 × ACR (95% CI 1.32 to 1.46). The resulting ACR cutoffs for microalbuminuria and macroalbuminuria were, respectively, 19.1 and 143.5 for male participants and 29.0 and 217.4 for female participants.

**Covariate-Adjusted Estimate of AER.** A model with additional covariates (eAERcov) was also obtained by backward elimination from the initial full model. The final model yielded eAERcov = α × ACR where α = exp(−0.13 − 0.27(1f female) − 0.012 × age + 0.31 × BSA − 0.25 × log(ACR) + 0.34 × serum creatinine + 0.0072 × systolic BP + 0.13 (if the participant received an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker).

**Performance of eAER, eAERgender and eAERcov.** Table 2 describes the relationship between AER ≥30 or AER ≥300 relative to the levels provided by the three sets of estimating equations (eAER, eAERgender and eAERcov). All estimates were obtained via bootstrap resampling. For microalbuminuria (AER ≥30), eAERgender consistently performed better than the simple eAER, and the eAERcov, on the basis of the more extensive model, yielded better specificity and positive predictive value but at the cost of poorer performance for the remaining statistics. Analyses of macroalbuminuria (AER ≥300) provided similar results: eAERgender outperformed eAER for all measures except positive predictive value and outperformed eAERcov, except for specificity and positive predictive value. Thus, the eAERgender values performed best.

**Within-Individual Variation in AER and ACR**

The variability of the ACR and AER measurements over time was evaluated from the 621 participants who had two or more renal visits during the study period. The intraclass correlation among the quantitative values was 0.803 for log(AER), 0.685 for log(ACR), and 0.697 for log(eAERgender).
Table 3 presents the fractions of patients who were consistent across the two successive visits with respect to the categorization of microalbuminuria (≥30) versus not and of macroalbuminuria (≥300) versus not along with the index of agreement (the fraction greater than chance) and the fractions of patients who progressed or regressed at the second visit separately for the AER and eAERgender. Classifications were more variable using eAERgender than AER.

Table 4 presents the numbers of participants who changed classifications (progressors or regressors) or who remained unchanged on the basis of the AER versus eAERgender. Classifications were more variable using eAERgender than AER.

Figure 1. Scatterplots of the AER from the timed collection versus the ACR. (A) Scatterplot of log(AER) against log(ACR), with marginal box plots and histograms for each variable. Horizontal lines at AER = 30 and 300 mg/24 h are added for reference. (B) Bland-Altman plot of the log(AER) − log(ACR) on the vertical scale and the geometric mean of the AER and ACR on the horizontal scale, using a log scale, with horizontal reference lines for a geometric mean of 0, 30, and 300. Three smoothed nonparametric regression lines are superimposed: One for all participants, one for male participants, and one for female participants.

Use of eAER Instead of AER as an Outcome in the DCCT/EDIC

The AER has been used as an outcome in analyses in DCCT/EDIC, either as a continuous measure or as a categorical indicator of microalbuminuria or macroalbuminuria. On the basis of the paired AER and ACR values used herein, we assessed the differences between the original DCCT intensive versus conventional treatment groups on the levels of the eAER and the measured AER and on the prevalences of micro- and of macroalbuminuria using each measure using longitudinal regression models (Table 5). The results were markedly similar, with the group differences in the eAER being slightly more significant than for the measured AER in the analysis of the actual values and for microalbuminuria but not for macroalbuminuria.

The mechanism by which intensive therapy produced beneficial effects on microvascular outcomes is measured by the updated mean HbA1c reflecting the history of glycemia since entry into the DCCT. Thus, we also assessed the effect of the updated mean HbA1c on the level of albumin excretion and the prevalences of micro- and macroalbuminuria using the eAER and measured AER. In this case, the opposite pattern was observed, with the HbA1c having a greater effect on the measured AER than on the eAER for the actual values and for microalbuminuria but not for macroalbuminuria.

Discussion

We compared random urine ACR with 4-hour AER in a large, well-characterized population with type 1 diabetes. Despite moderate correlation between ACR and AER, there were systematic differences in these measurements, altered classification of prevalent albuminuria states and changes in albuminuria states over time, and differences in within-individual variability. These findings have important implications for clinical practice and research, supporting the use of consistent ascertainment methods over time and further efforts to standardize and optimally interpret measurement of urine albumin excretion.

It has previously been recognized that ACR values are biased in relation to AER by determinants of urine creatinine excretion, particularly gender (2). Creatinine is generated in muscle, and urinary excretion is the main disposition for generated creatinine, so muscle mass is a major determinant of urine creatinine excretion (17–20). Because men have greater muscle mass than women, men have greater urine creatinine excretion than women, and, on average, men have lower ACR values than women for a given AER (2). As a result, gender-specific thresholds have been developed, recommended, and used for the classification of urine ACR, with lower threshold levels used for men than women (15,21–24).

Similar gender relationships were observed in our population with type 1 diabetes. Specifically, male participants had greater urine creatinine excretion and lower ACR values for a given AER. We have also shown that the proportionate differ-
ence between ACR and AER was approximately constant over the complete range of albumin excretion, the difference among male participants being greater than that among female participants. This allowed us to derive separate gender-specific simple equations to obtain an eAER from the ACR. The specific gender-specific thresholds that we empirically derived to classify microalbuminuria are remarkably similar to those previously developed: 19 and 29 mg/g for male and female participants in our study, respectively, compared with 17 and 25 mg/g (2). If it is assumed that AER is the best estimate of kidney disease, then our results support the use of such gender-specific ACR thresholds.

In our study, the relationship of ACR with AER was influenced by additional covariates (other than gender) that also relate to muscle mass: Age, BSA, and serum creatinine concentration. This further reinforces the potential confounding influence of muscle mass in the interpretation of urine ACR. It is not immediately evident to us why BP and use of renin-aldosterone system antagonists influenced the ACR–AER relationship in our study.

Differences in ACR versus AER have important implications for clinical care and research. In clinical care, use of ACR versus AER may lead to differential estimates of disease prevalence, severity, and response to therapy. In research, associations of ACR with clinical outcomes may be influenced by nonalbuminuric covariates related to muscle mass, allowing possible introduction of confounding. We agree with previous recommendations to evaluate further and standardize the measurement and reporting of urine albumin excretion, taking these factors into account (25). Specifically, we recommend evaluation of the relationship of ACR with AER across diverse, widely representative populations. In particular, such evaluation should determine which clinical characteristics most strongly affect the ACR–AER relationships (e.g., age, gender, race) and test whether AER estimating equations that incorporate these characteristics improve the clinical classification of micro- and macroalbuminuria. Such work first requires standardization of urine albumin collection and assay methods.

Use of ACR versus AER yielded substantial differences in the classification of microalbuminuria (≥30) or albuminuria (≥300) from eAER versus AER

### Table 2. Classification of microalbuminuria (≥30) or albuminuria (≥300) from eAER versus AER

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>% Correct</th>
<th>( \kappa )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria (≥30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eAER</td>
<td>74.1</td>
<td>93.5</td>
<td>71.6</td>
<td>94.2</td>
<td>90.0</td>
<td>0.667</td>
</tr>
<tr>
<td>eAER(_{gender})</td>
<td>75.1</td>
<td>94.6</td>
<td>75.3</td>
<td>94.5</td>
<td>91.0</td>
<td>0.697</td>
</tr>
<tr>
<td>eAER(_{cov})</td>
<td>68.1</td>
<td>96.6</td>
<td>81.7</td>
<td>93.2</td>
<td>91.5</td>
<td>0.692</td>
</tr>
<tr>
<td>Albuminuria (≥300)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eAER</td>
<td>76.1</td>
<td>99.5</td>
<td>88.1</td>
<td>98.8</td>
<td>98.4</td>
<td>0.808</td>
</tr>
<tr>
<td>eAER(_{gender})</td>
<td>79.1</td>
<td>99.4</td>
<td>87.7</td>
<td>99.0</td>
<td>98.5</td>
<td>0.823</td>
</tr>
<tr>
<td>eAER(_{cov})</td>
<td>52.7</td>
<td>99.9</td>
<td>95.2</td>
<td>97.7</td>
<td>97.6</td>
<td>0.665</td>
</tr>
</tbody>
</table>

NPV, negative predictive value; PPV, positive predictive value.

### Table 3. Stability of AER and eAER between two successive visits

<table>
<thead>
<tr>
<th>Parameter</th>
<th>% Consistent</th>
<th>( \kappa )</th>
<th>Progressed (n [%])(^a)</th>
<th>Regressed (n [%])(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AER ≥30</td>
<td>90.5</td>
<td>0.669</td>
<td>39 (6.3)</td>
<td>20 (3.2)</td>
</tr>
<tr>
<td>eAER(_{gender}) ≥30</td>
<td>87.3</td>
<td>0.556</td>
<td>44 (7.1)</td>
<td>35 (5.6)</td>
</tr>
<tr>
<td>AER ≥300</td>
<td>97.7</td>
<td>0.738</td>
<td>9 (1.4)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>eAER(_{gender}) ≥300</td>
<td>97.3</td>
<td>0.639</td>
<td>12 (1.9)</td>
<td>5 (0.8)</td>
</tr>
</tbody>
</table>

\(^a\)Participants below the cutoff at the first visit and at or above it at the second visit.

\(^b\)Participants at or above the cutoff at the first visit and below it at the second visit.

### Table 4. Concordance between AER and eAER

<table>
<thead>
<tr>
<th>AER ≥30</th>
<th>Regressed(^a)</th>
<th>Unchanged</th>
<th>Progressed(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eAER(_{gender}) ≥30</td>
<td>9</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>512</td>
<td>27</td>
</tr>
<tr>
<td>eAER(_{gender}) ≥300</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>598</td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\)Participants below the cutoff at the first visit and at or above it at the second visit.

\(^b\)Participants at or above the cutoff at the first visit and below it at the second visit.
not increase agreement with AER. One important implication of our observed differences in classification is that studies should use consistent methods to ascertain urine albumin excretion over time. The EDIC Study has decided to continue its use of 4-hour AER, which has been used since DCCT inception in 1983.

This study cannot determine whether ACR, AER, or eAER derived from ACR is the “correct” method of measuring urine albumin excretion, because a true gold standard is not available. Ideally, 24-hour AER collected under stringent conditions could be used for comparison, or each measurement method could be compared in association with relevant clinical outcomes. However, we observed that within-individual variability was smaller for AER than for ACR (or eAER), suggesting that AER may be more reliable as a result of decreased measurement “noise.” This is in agreement with other studies that compared timed AER with random ACR (26–28). However, our ACR–AER comparison is unique in that AER performance may have been maximized by collection in a monitored research environment, whereas ACR performance was evaluated on suboptimal random urine samples. Other studies have reported less variability for first morning void ACR, which was not evaluated in this study (27,28). Moreover, urine ACR has important advantages in both clinical and research settings as a result of ease of collection and reduced impact of incomplete or inconsistent collection, compared with AER.

Effects of DCCT intensive diabetes therapy on urine albumin excretion were similar whether urine albumin excretion was measured by the eAER (from ACR) or the AER, as were associations of HbA1c with urine albumin excretion. Thus, it is

<table>
<thead>
<tr>
<th>Model</th>
<th>AER</th>
<th>eAERgender</th>
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<tbody>
<tr>
<td>% difference in geometric means</td>
<td>−12.8</td>
<td>−15.9</td>
</tr>
<tr>
<td>geometric mean value in conventional group</td>
<td>15.43</td>
<td>15.68</td>
</tr>
<tr>
<td>root mse</td>
<td>1.324</td>
<td>1.351</td>
</tr>
<tr>
<td>% difference in odds</td>
<td>−32.5</td>
<td>−40.3</td>
</tr>
<tr>
<td>prevalence (%)</td>
<td>16.2</td>
<td>16.9</td>
</tr>
<tr>
<td>% difference in odds</td>
<td>−46.3</td>
<td>−45.8</td>
</tr>
<tr>
<td>prevalence (%)</td>
<td>5.6</td>
<td>5.2</td>
</tr>
</tbody>
</table>

A generalized estimating equation (GEE) model with treatment group as the independent variable and the log of the AER or eAER as the dependent variable with an identity link and unstructured normal error specification. Percentage difference computed for the intensive group minus the conventional group. For the analysis of microalbuminuria (value ≥30) and macroalbuminuria (value ≥300), the GEE model used a logit link with unstructured binomial errors. For the latter, the overall prevalence of micro- and macroalbuminuria is shown.

A like analysis using the log of the updated weighted DCCT/EDIC mean HbA1c as the independent variable. The percentage change in the outcome is shown for a 1.05-fold (5%) increase in HbA1c such as an increase from 8.0 to 8.4% HbA1c.
reassuring that the effects of the DCCT interventions and the association with DCCT/EDIC glycemia are unaffected by measurements method.

This study has a number of limitations. First, we evaluated only random ACR and 4-hour timed AER, rather than a first morning void ACR or 24-hour timed AER. Second, we were unable to compare ACR and AER in relation to long-term clinical disease outcomes. Third, our results may not directly apply to populations with type 2 diabetes or without diabetes, because differences in age and body composition could alter relationships of ACR with AER in unpredictable ways. The main strengths of this study include excellent characterization of study participants, including standardized assessment of AER in a tightly controlled and directly observed setting; large sample size; and longitudinal ACR and AER measurements. As a result, our data clearly emphasize a number of limitations in the current assessment of urine albumin excretion and the need for more work to allow accurate evaluation of this key manifestation of diabetic kidney disease.

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Disclosures

None.

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