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See related article, “Podocyte Injury Damages Other Podocytes,” on pages 1275–1285.

## Declining Renal Function in Persons of Different Race without Chronic Kidney Disease

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*J Am Soc Nephrol* 22: 1183–1184, 2011.  
doi: 10.1681/ASN.2011050521

“Plus ça change, plus c’est la même chose”—the more things change, the more they stay the same. Although this epigram is generally attributed to a 19th-century man of letters from France,<sup>1</sup> it could easily have been coined by nephrologists in the United States with an interest in racial disparities in the burden of ESRD. Thus, two articles reporting outcomes seen in the initial years of ESRD coverage by Medicare note that hypertension and diabetes are the two most common causes, incidence rates are almost 3 times higher in African Americans, and survival was longer in African Americans than in Caucasians.

This ESRD paradox of higher incidence rates and longer survival remains unresolved to this day. Surprisingly, the recent explosion of research into quantifying the burden and risk factors of chronic kidney disease (CKD) has failed, so far, to cut the Gordian knot. Despite greater burdens of modifiable risk factors such as obesity, hypertension, and diabetes, creatinine-based GFR (GFR<sub>creatinine</sub>) values are typically higher among minority populations. Of note, abnormal albuminuria is also overrepresented. This scenario of higher GFR and abnormal albuminuria finds an obvious parallel in classic type 1 diabetic nephropathy. Sadly, this parallel does not seem to apply: Racial disparities are not mitigated—if anything, they widen when levels of albuminuria are accounted for.

Most recent CKD models assume that loss of GFR proceeds in an orderly, linear fashion. In this model, GFR levels in two populations could reach a single (low) GFR level in different ways as follows: one subgroup starts at a higher GFR but loses GFR more quickly; the other starts at a lower level but loses GFR more slowly. All things being equal, if this model of different lines converging on a single point is valid, two things should follow: GFR levels are never the same in the two populations until the point of convergence is reached, and the disparity should be narrower at lower GFR levels. In this regard, it is instructive that the National Health and Nutrition Examination Survey III dataset shows the odds of having GFR <60 and <30 ml/min per 1.73 m<sup>2</sup> with the Modification of Diet in Renal Disease equation are 0.57 and 0.54, respectively, when African Americans were compared with Caucasians. In other words, the disparity, if anything, widened as GFR levels fell.

As the paradoxes have accumulated, so has concern that reliance on GFR<sub>creatinine</sub> estimating equations may underlie these disparate findings.<sup>4</sup> Hence, the findings of Peralta and colleagues in this issue of *JASN* are highly germane.<sup>5</sup> Using the community-based Multi-Ethnic Study of Atherosclerosis da-

Published online ahead of print. Publication date available at www.jasn.org.

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tabase, GFR levels were measured longitudinally using creatinine- and cystatin-C-based methods. If cystatin-C is truly a more accurate marker of GFR than serum creatinine,<sup>6</sup> then this design is very attractive because it should give a truer measure of GFR trajectories.

The Peralta *et al.* study had all of the inherently attractive features of all prospective studies that incorporate regularly scheduled assessments of analytes such as kidney function. This being said, some of the design features demand reflection. Despite careful follow-up, the available follow-up time is comparatively small, and the average number of GFR assessments per study subject is modest at approximately 2.8. The study excluded 11% of subjects because creatinine-based estimated GFR (eGFR<sub>creatinine</sub>) was <60 ml/min per 1.73 m<sup>2</sup>, and GFR trajectories in the excluded population might be very informative. A unique feature of this study was the diversity of race and ethnicity in the study population. On a cautionary note, GFR estimating equations probably need to be validated in each separate ethnic group. Death also has potential to be a competing event, and comparative death rates were not reported in the study. If, as seems plausible, GFR loss was accelerating between the last available GFR test and death, GFR declines might be underestimated in the subgroup with the highest mortality rate. Incident cases are classically defined with a denominator consisting of the population without the condition of interest. Because subjects with a cystatin-C-based estimated GFR (eGFR<sub>cystatin C</sub>) < 60 at baseline were not formally excluded, the proportion of subjects with eGFR<sub>creatinine</sub> ≥ 60 and eGFR<sub>cystatin C</sub> < 60 may not have been trivial. In addition, the modest numbers of incident cases available probably prevent definitive quantification of racial disparities at this point.

Regarding cystatin-C-based GFR (GFR<sub>cystatin C</sub>), an important finding of this study was a more rapid rate of decline in kidney function in African American participants, a disparity that could not be explained by participant characteristics at study inception. Returning to the previously mentioned hypothesis of linear convergence at ESRD from different starting GFRs, it is noteworthy that baseline GFR<sub>cystatin C</sub> levels are identical in African American and Caucasian subgroups at 94 ml/min per 1.73 m<sup>2</sup>. The situation for eGFR<sub>creatinine</sub> could be described as “the same but different”: Although GFR loss patterns appear similar when based on serum creatinine, baseline GFR values are clearly lower in Caucasian participants.

Although this paper provides important insights, it appears that we still have a pattern of observations that amounts to “a riddle wrapped in a mystery inside an enigma, but perhaps there is a key.”<sup>7</sup> Regarding racial disparities in CKD and trajectories of GFR, this study suggests that models other than linear convergence should be considered.

## DISCLOSURES

None.

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See related article, “Racial and Ethnic Differences in Kidney Function Decline among Persons without Chronic Kidney Disease,” on pages 1327–1334.

## Sunrise of Statins after AURORA and 4D?

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*J Am Soc Nephrol* 22: 1184–1186, 2011.  
doi: 10.1681/ASN.2011050504

Ten years ago, a placebo-controlled trial of statin treatment for hemodialysis patients was considered unethical by many nephrologists. In 2005, to the surprise of many, the results of the 4D study (the German Diabetes and Dialysis Study)<sup>1</sup> demonstrated that lowering LDL cholesterol with atorvastatin (20 mg/d) in 1255 hemodialysis patients with type 2 diabetes did not produce statistically significant reductions in the primary outcome measure. Four years later, AURORA (A Study to Evaluate the Use of Rosuvastatin in Subjects on Regular Hemodialysis: An Assessment of Survival and Cardiovascular Events)<sup>2</sup> was hoped to provide clarification of whether LDL

Published online ahead of print. Publication date available at [www.jasn.org](http://www.jasn.org).

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