Given that trials of lipid lowering in patients with chronic kidney disease (CKD) requiring dialysis have been neutral (1), and the only evidence for lipid-lowering therapy in patients with CKD not requiring dialysis is based on secondary analyses, such as the Pravastatin Pooling Project (2), it is commendable that a subgroup defined by kidney function was examined in JUPITER (Justification for the Use of Statins in Prevention—an Intervention Trial Evaluating Rosuvastatin), as reported recently in this journal (3). However, we do not believe that it is appropriate to call this a subgroup with “moderate CKD.”

The JUPITER CKD subgroup is influenced by the limitations of the Modified Diet in Renal Disease (MDRD) equation for estimating glomerular filtration rate (GFR) and the study inclusion criteria. Moderate CKD is defined by a GFR of 30 to 59 ml/min, with or without other evidence of kidney damage, but should be present for 3 months to be truly “chronic” kidney disease (4). The MDRD GFR equation uses the serum creatinine, age, sex, and African American ethnicity to estimate GFR but underestimates GFR at higher levels (5). The characteristics of this JUPITER subgroup that suggest the term “moderate CKD” is inappropriate are as follows:

1. In the CKD subgroup, 50% of participants had a GFR between 51 and 58 ml/min, and 25% had a GFR between 58 and 60 ml/min (Table 1 [3]). At least one-fourth of patients could have been misclassified simply due to variability in the creatinine assay (6). The authors do not report whether creatinine was measured centrally or what calibration procedures were used.
2. Female participants were substantially over-represented in the CKD subgroup, whereas African-American participants were substantially under-represented (Table 1 [3]). The multipliers in the MDRD equation result in lower GFRs for women and higher GFRs for African Americans with the same serum creatinine, and the problem of a universal cutoff of 60 ml/min causing 50% more women than men to be classified as having CKD has been described (7).
3. The 10-year age difference between women and men in the inclusion criteria may result in more females having a GFR <60 ml/min. In an age-specific MDRD GFR “reference range” in a population free of vascular disease, hypertension, diabetes, or kidney disease, the median GFR in women age 60 to 64 years was 10 ml/min lower compared with men age 50 to 54 years (7).

The results were described as similar with the Cockroft-Gault equation, but it would be interesting to see how the characteristics, or indeed the classification, of the patients was altered.

We do not question the effect of the intervention in the patients described or the use of the MDRD equation for this purpose. However, patients seen by nephrologists and cardiologists with a GFR between 30 and 59 ml/min (“moderate” CKD by the K/DOQI [Kidney Disease Outcomes Quality Initiative] classification) have a high prevalence of diabetes and cardiovascular disease (excluded by design in the JUPITER trial) and higher, rather than lower, systolic blood pressure than people with normal kidney function. We suggest that this JUPITER subgroup is better described as “patients with an MDRD GFR <60 ml/min on 1 occasion” to avoid inappropriate extrapolation of these results.

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