Letters and Replies

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CKD—fiction not fact

Sir,


The central question of this debate is: ‘Should the diagnosis of chronic kidney disease be based on thresholds of estimated GFR (eGFR) that do not take into account the decline in actual GFR with ageing and the effects of gender on the normal levels of both actual and estimated GFR?’ Our answer is an unequivocal ‘No’.

A subsidiary and related question addressed by de Jong and Gansevoort concerns the role of assessing abnormal albuminuria in identifying patients with true ‘chronic kidney disease’. We acknowledge this opinion and agree that such measurements do have a role, but we suggest that further research is needed to establish whether the patho-physiological connection of albuminuria is with ‘kidney’ or with ‘vascular’ disease. These are serious questions and the debate is not a ‘squabble’ (a petty, noisy discussion of a trivial issue). The outcome of this debate will affect millions of individuals throughout the world and directly impinges on our ability to quantify accurately the overall global burden of ‘chronic kidney disease’. The public health implications of this debate are enormous. We submit that without any correction for the effects of age and gender on eGFR thresholds for defining ‘chronic kidney disease’, this burden will be grossly overestimated, particularly among the elderly and among females with what is currently defined as ‘Stage 3 Chronic Kidney Disease’ by both KDOQI and KDIGO criteria. We applaud the comment of de Jong and Gansevoort focusing primarily on albuminuria rather than eGFR. We would question whether ‘micro-albuminuria’ in the absence of a decline in eGFR to abnormal levels (e.g. Stage 1 and 2 CKD by current criteria) should be regarded as a manifestation of ‘chronic kidney disease’ rather than a reflection of a generalized vascular disorder (‘chronic vascular disease’) in which the kidneys, along with other organs, are the victim rather than the culprit. Further, the hypothesis that ‘microalbuminuria’ is a ‘window into the vascular system’ is not proven, as has been pointed out by Couser [6]. It is our duty to stay our hand in promoting public health initiatives (such as population-wide screening for CKD using eGFR and/or measurements of urinary albumin excretion) until there is a sound patho-physiological justification for proceeding with such a massive undertaking.

The issue of whether CKD constitutes an independent ‘risk’ factor for cardiovascular disease (CVD) or vice versa remains unresolved. The epidemiological associations do not thus far define what is cause and what is effect. Furthermore, individuals with eGFR <60 ml/min/1.73 m² without any abnormal albuminuria (currently also defined as Stage 3 CKD), but who still have eGFR values above the 5th percentile adjusted for age and gender, have not clearly been shown to have any greatly increased risk of fatal and non-fatal cardiovascular events (i.e. >20% above the rate observed in those with eGFR ≥60 ml/min/1.73 m² [7]). Adjustment for all of the traditional cardiovascular risk factors, such as those included in the Framingham Risk score, attenuates the risk relationship of CKD with CVD, although such
scoring systems do still tend to underestimate the risk of events in subjects with CKD Stage 3, at least as currently defined [8]. It has also been shown that traditional risk factors have a more powerful influence on CVD risk than non-traditional risk factors in those subjects with an eGFR of <60 ml/min/1.73 m² [9], but the effect of the presence or absence of proteinuria has not been examined.

The current classification schema also raises ethical issue in transplantation, since an otherwise healthy 60-year-old donor of a kidney would almost certainly be classified as having Stage 3 CKD post-donation [10]. According to current views, one would need to inform the donor that by allowing his or her eGFR to be surgically reduced, to levels currently defined as CKD Stage 3, he or she will be exposed to an additional risk of developing CVD later in life. This is unproven and unlikely.

Finally, the current classification system leads to absurdities in the recommended approach to patients thought to have CKD. Is it appropriate to label both a 30-year-old man with an eGFR of 55 ml/min/1.73 m² and 3+ proteinuria and a 60-year-old woman with an identical eGFR but no proteinuria as having the same ‘Stage’ of a postulated ‘disease’? We think not.

Classifying patients inappropriately as having CKD when they do not has many implications. Evaluation, testing and referral should be based on conventional criteria for CKD, and we should desist from relying on eGFR alone. Until the methods of assessing eGFR are prospectively verified in diverse populations (e.g. varying in ancestry, body habitus, diet), we should restrain efforts to mandate reporting of calculated eGFR routinely whenever a serum creatinine level is randomly assessed, but encourage cognitive evaluation of the serum creatinine concentrations (and calculated eGFR) within the clinical context of individual subjects. At present we would not describe subjects with a reduced eGFR as ‘healthy’ nor would we describe them as necessarily ‘diseased’.

We are certain that the purported ‘epidemic’ of CKD, as currently defined, is a fiction not a fact.

Conflict of interest statement. None declared.

2. De Jong PE, Gansevoort RT. Fact or fiction of the epidemic of chronic kidney disease—let us not squabble about estimated GFR only, but also focus on albuminuria. Nephrol Dial Transplant 2008; 23: 1092–1095

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Reply

Sir,

We write in response to the reply by Glassock and Winearls to our editorial ‘Chronic Kidney Disease is Common: What Do We Do Next?’ and commentary by De Jong and Gansevoort published simultaneously [1–3]. We also respond to the debate on the definition and classification of chronic kidney disease (CKD) and the interpretation of estimates of the prevalence for CKD that is occurring in the editorial pages of other nephrology subspecialty journals [4–6]. Each of these editorials notes shortcomings in the currently accepted definition and classification of CKD [7, 8]. We acknowledge that the simplicity of the current stages has some shortcomings. While most suggestions would reduce the number of people classified as having CKD, this alone does not clearly improve on or justify a change in the definition.

CKD is a heterogeneous condition, with many different causes, manifestations, comorbid conditions and factors affecting prognosis. Estimated glomerular filtration rate (GFR) is one way to classify patients but not the only way. For example, we would all agree that a child with focal and segmental glomerulosclerosis requires the nephrologist’s more urgent attention than an elderly patient with CKD Stage 3 due to hypertensive nephrosclerosis with well-controlled blood pressure. Within CKD Stages 1–3, nephrologists should focus on those at greatest risk for progressive GFR decline. At present, we lack sufficient data to quantify this risk. At the 2004 KDIGO Controversies Conference, modification of the classification system to incorporate risk for progression was thought to be too complex [8]. We think that adding a second dimension to CKD classification that summarizes the risk of kidney disease progression has merit. Going forward, our goal should be to articulate this differential risk while maintaining the appropriateness of the CKD classification system for use by all healthcare professionals.

Progressive GFR decline is not the only outcome of CKD and focusing only on this outcome may lead to missed opportunities to improve other health care outcomes, as suggested by a recent article showing reduced all-cause mortality among US veterans with CKD Stages 3 and 4 receiving care by nephrologists [9]. Similarly, focusing only on what nephrologists should do misses the point that CKD is common, especially in the elderly, and affects the management