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Reply

Sir,

I am grateful to Professor Wizemann for reading my article [1] and am pleased that he enjoyed it. I agree with him that if we go down the road of linking remuneration with outcomes, potentially a powerful ‘driver’ mechanism to alter health care, we need first to be sure we can properly measure and understand the quality, and the quantity, of the outcomes and the independent value that interventions used to change the outcomes may have. Like him, I am sceptical that for dialysis patients, we can be confident enough about the relationships between clinical practice and outcomes to attempt to link clinical practice to remuneration just yet.

I am, though, not knowledgeable about the German system he describes. One could equally say that, aspirationally, 85% of patients should have a plasma albumin >40 g/L— as albumin is associated with survival in dialysis patients [2]— but it would be an optimist, or a fool, who would infuse albumin with each dialysis session purely to achieve the desired threshold (in the absence of RCT data to support this and to remove doubt that such a practice, with a costly intervention, did not cause more harm than good).

As for the Order of the Garter [3], this is a matter entirely in the gift of my Gracious Sovereign, Queen Elizabeth II, and while I hope to enjoy St George’s Day this year (23 April), I think it sadly rather unlikely that my equilibrium would be disturbed by her choosing, on that day, to take the opportunity to bestow upon me one of the two vacant places in the Order.

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The impact of stopping inhibitors of the renin-angiotensin system in patients with advanced chronic kidney disease

Sir,

We read with interest the findings of Ahmed et al. [1] in relation to the effects of cessation of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB) in chronic kidney disease (CKD). The improvement in eGFR after discontinuation of ACEi/ARB, without a significant increase in proteinuria, suggested that a subgroup of patients may not benefit from continued use of ACEi/ARB. While we agree with the authors that there are patients who do not benefit from such therapy, we feel there are several important caveats to this report.

Firstly, the report points to the elderly and comorbid nature of the cohort (mean age was 73.3 years and 46% diabetic). Ageing is associated with increasing vascular stiffness and altered activity and responsiveness to vaso-active stimuli, making ‘white coat hypertension’ more prevalent and the older kidney more susceptible to insults, particularly for those with progressive CKD. Since antihypertensive treatment initiation was based on clinic blood pressure (BP) recordings, there might be a risk that some treated patients may have had significant episodes of hypotension out of hospital, which has been shown previously [2]. Since BP increased significantly on switching antihypertensive agents, it is possible that the reduction in serum creatinine was related to improved renal perfusion as the BP increased rather than an inherent property of the medication.

Secondly, although only 5 of 52 patients had ‘presumed’ renovascular disease, it would be surprising if more patients did not have had significant small or large vessel renal atherosclerotic disease, making the decision to try ACEi/ARB withdrawal logical, and a commonly practised intervention. The authors point to disparity in renal size as evidence of renovascular disease, but this has been shown to be a poor marker of renal vascular disease which is often bilateral [3], and we feel that the contribution of large vessel disease has been inadequately explored in this report. Additionally, the increase in proteinuria after cessation of ACEi/ARB, although not statistically significant, should be interpreted with caution due to small numbers, as there is a significant risk of a type II statistical error. As the authors point out, there remains good reason to attempt to reduce proteinuria in patients with a urinary protein leak >500 mg/day with these agents [4].

Finally, of seven patients with severe congestive cardiac failure, four experienced worsening of their condition, with two deaths. These patients were managed with diuretics...
and nitrates alone and not by the reintroduction of ACEi/ARB, and while these deaths could have been due to the burden of co-morbidities, such findings nonetheless emphasize the potential systemic benefits of ACEi/ARB in patients with cardiovascular disease, even if it is at the expense of renal dysfunction.

Conflict of interest statement. None declared.

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Reply

Sir,

We appreciate the comments made by Dr Baweja et al. to our study on the discontinuation of angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptors blockers (ARBs) in advanced stages of chronic kidney disease (CKD). These are most astute and appropriate remarks that we overall agree with. The ageing nature of the CKD population means that an increasing number of those who reach Stages 4 and 5 have extensive atherosclerosis and vascular disease involving extra- but also intra-renal vasculature, thus putting them at increased risk of accelerated decline in renal function on these agents secondary to ischaemic nephropathy.

We have to acknowledge the fact that in despite the very widespread use of ACEIs and ARBs for renoprotection, we continue to experience an ever-increasing end-stage renal disease epidemic and increasing evidence of both iatrogenic reversible and irreversible acute kidney injury in addition to the ongoing CKD from the use of these agents in elderly patients [1,2].

We particularly appreciate the comment on increasing blood pressure and its possible impact on ischaemic kidneys’ perfusion pressure and function. They are most pertinent and supported by a preliminary analysis we are undertaking to determine who is most likely to respond to stoppage of ACEIs. This is all the most relevant, since it is becoming apparent that target blood pressure levels for different age groups of CKD patients may warrant serious reconsideration [3] and that low systolic blood pressure levels may be associated with accelerated decline in kidney function [4]. In our study, although the blood pressure increase was statistically significant, 53% of patients had blood pressure levels within the recommended targets before and after stopping ACEIs/ARBs. The authors therefore rightly state that the increase in blood pressure should be interpreted with caution due to the small numbers of subjects in this study.

Finally, the mortality associated with CKD Stages 4 and 5 in the elderly is high and the effect of stopping ACEIs on mortality cannot be determined from our pilot study. In order to address many of these questions, we are planning in the UK a prospective randomized controlled trial of stopping ACEIs/ARBs in advanced stages of CKD.

In the meanwhile, our study prompts nephrologists to use ACEIs/ARBs cautiously and critically in advanced stages of CKD especially in older patients. Blood pressure levels in CKD patients and CKD parameters and recommendations, including the use of ACEIs/ARBs, have to be tailored to patients’ age, underlying disease and stage rather than be indiscriminated of all these important confounders.

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