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Conflicts of interest and viewpoint bias in KDOQI and KDIGO workgroups

Sir,

I read with interest Dr Shaldon’s letter [1] on anemia guidelines and workgroups’ conflicts of interest, and the original commentary [2] and response letter [1] by Drs Macdougall, Eckardt and Locatelli. Macdougall et al. refer to the KDOQI (and KDIGO) workgroup members as having ‘potential conflicts of interest’ [1]. These are actual, not potential, conflicts of interest. Exposure of those conflicts in disclaimers does not neutralize them nor render the opinions necessarily balanced.

Lost in the discussion of conflicts of interest is workgroup viewpoint bias. In my opinion, the KDOQI anemia workgroup focused on the value of ESA and higher hemoglobin and failed to adequately weigh existing and emerging evidence of harm against meager evidence of benefits. This led to the unsupported ‘evidence-based’ claim that all CKD patients should have hemoglobin >11 g/dl [3], thus labeling deviations from this recommendation substandard care. This ‘evidence-based guideline’ was later withdrawn. I believe that a workgroup of experts without pharmaceutical or dialysis corporate conflicts of interest would have been more circumspect. Regardless, guideline groups must reflect a balance of viewpoints to avoid skewed recommendations [4].

Macdougall et al. state in their reply to Shaldon that ‘there is no evidence that “over-swings” of haemoglobin levels...increased risk’ [1], referring to an evaluation of observational data generated within a randomized trial not designed to answer such a question. They fail to note that observational data in 58 000 US dialysis patients showed that those with time-averaged hemoglobin ≥13 g/dl had an increased risk of death [5]. These patients most certainly were not targeted to ≥13 g/dl—which would be Medicare fraud and deviate from the KDOQI and the dialysis chain’s guidelines—but they undoubtedly had frequent ‘over-swings’ leading to a high time-averaged hemoglobin [5]. In 2006, KDOQI promoted persistently higher hemoglobin for all patients despite contrary evidence. KDOQI and KDIGO leaders should not now promote hemoglobin ‘over-swings’ as safe without definitive evidence of safety.

Lastly, Macdougall and colleagues claim that the US physician can follow ‘...evidence-based clinical practice guidelines (that’s KDOQI) or alternatively obey the FDA label’ [2]. Unlike KDOQI and KDIGO, the FDA reviews all data, including unpublished data. FDA recommendations are evidence based.

Elimination of conflicts of interest, broad representation of viewpoints and circumspect guideline recommendations would go far to instill confidence in this system.

Conflict of interest statement. Dr Coyne has received consulting fees, honoraria and lecture fees from Abbott, Amgen and Watson; has consulted for AMAG, INEOS and Roche; and participates in trials funded by all the above companies and Genentech.

Division of Renal Diseases Daniel W. Coyne Washington University, St Louis MO, USA
E-mail: DCoyne@wustl.edu

1. Shaldon S. Conflict of interest in clinical guidelines should be avoided. Nephrol Dial Transplant 2008; 23: 1771; author reply 1772


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Reply

Sir,

Dr Coyne comments on our recent Editorial Comment [1], and the subsequent correspondence from Dr Shaldon [2,3]. He reiterates a position about the guideline process that he previously voiced in commentaries published in the Clinical Journal of the American Society of Nephrology [4,5] and to which an extensive reply has already been provided [6,7]. Repeating his comments, in our opinion, does not make them more valid.

With respect to the question of optimal haemoglobin levels and potential risks, Dr Coyne unfortunately does not distinguish between targeted and achieved Hb levels. This distinction, however, is crucial for the correct interpretation of the evidence base, as outlined in detail in the KDOQI guideline document [8]. The study by Regidor et al. [9] reports data on the relationship between achieved Hb values and mortality. Compared to Hb levels between 11.5 and <12 g/dl, all Hb ranges <11.5 g/dl were associated with increased hazard ratios of all-cause mortality. In contrast, Hb levels of ≥12.5 and ≥13 were associated with decreased hazard ratios of death, while Hb levels between 13.5 to <14 and ≥14 g/dl were associated with increased risks of death. Dr Coyne misquotes this study when writing that those patients with time-averaged Hb levels ≥13 g/dl had an increased risk of death.

A post hoc analysis of the CHOIR data has suggested that the increased cardiovascular event rate in the group...