Practice Recommendations Based on Low, Very Low, and Missing Evidence

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Largely bypassing discussion of industry's influence, the chairs of the Kidney and Dialysis Outcomes Quality Initiative (KDOQI) advisory board and anemia work group and Dr. Uhlig review the structure and the process of guideline development that was used to write the opinion-based clinical practice recommendations (CPR) and evidence-based guidelines (EBG) (1). They propose that the CPR are more than mere opinion, even though they are based on a "quality of evidence (that) is low, very low, or missing" (2).

Despite their claims, it is obvious that no process or analysis can ever compensate for absent or low-value evidence. Less obvious, if work groups are partial to an industry's position, then overstating the validity of their CPR could provide great benefits to that industry. Indeed, that is precisely a criticism of the present bone guidelines that has appeared in the lay press (3).

There are reasons to be concerned that the KDOQI guideline process may include pro-industry leanings, faulty analysis of evidence, and lack sufficient protections against the introduction of bias. Here are three examples:

First, as I have outlined (4), the upper hemoglobin limit was increased to 13 g/dl, despite the lack of sufficient evidence that a hemoglobin target of 12 to 13 g/dl is as safe or results in a significant increase in quality of life compared with 11 to 12 g/dl. Second, the final draft that was released for public comment in October 2005 after review by the anemia and advisory chairs (5) had the EBG, "Efficacy favors SC (subcutaneous) rather than IV (intravenous) administration for short-acting ESA's (erythropoiesis-stimulating agents). Moderately strong recommendation." This was based on clinical trial data that subcutaneous administration of epoetin results in a significant reduction in required dosage to achieve the same hemoglobin (6). This EBG was removed in the final guidelines and replaced by the CPR, "In the opinion of the Work Group, convenience favors IV (intravenously) administration in HD-CKD [hemodialysis–chronic kidney disease] patients" (2). Therefore, the scientific evidence that subcutaneous administration is more efficacious was replaced by an opinion that favors the convenience (and higher dosage) of intravenous epoetin administration. Third, after review of the extracted ferritin data, the work group concluded, "Evidence in 6 functional iron studies- . . .demonstrates that as the baseline ferritin reaches 500 ng/ml, the likelihood of treating a patient (with iron) who will respond approaches nihil (zero). . ." (5). These studies had almost no patients with ferritin >500 ng/ml, so predictably few with high ferritin responded and no study found that ferritin was a good predictor of iron responsiveness (7–12). The "nihil" claim was removed, but the CPR continued to caution against routine administration of iron when ferritin is >500 ng/ml (2). The likely result of this CPR is a reduction in intravenous iron use and a reciprocal increase in erythropoiesis-stimulating agent administration (13,14).

We should be concerned that KDIGO, a private corporation that is run by a select group of individuals and funded by industry, has co-opted renal guideline development. In addition, nephrologists should expect pressure from these organizations to conform to the CPR.

Ideally, opinion-based recommendations should reflect the most recent available information that is interpreted by experts without conflicts of interest to optimize care for our patients. Other specialty societies develop their own guidelines, and the American Society of Nephrology should consider developing timely and frequently updated practice recommendations for the benefit of its members and our patients.

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