Reviewer’s report

Title: Optimal and continuous anaemia control in a cohort of dialysis patients in Switzerland

Version: 4 Date: 3 October 2008

Reviewer: Dorothea Nitsch

Reviewer’s report:

Major points:
I am not sure that I have understood the feedback to the first point I raised with regards to correlated/clustered data. I guess that the authors have thought about these issues, but their thoughts are not clearly expressed in the manuscript, and as such there are still concerns with regards to the validity of their analysis. I guess they did the right thing, but I can’t guesswork when doing a statistical review, unfortunately.

My problems have to do with counting of people - standard statistical approaches, as used by the authors assume that only one measurement was done per person - here however we have in total up to 12 measurements over time.

Conventional calculations of Means/SEMs across the whole sample of HB measurements would therefore count one patients 12 times - and such an explosion in sample size would invalidate the measure of variation/uncertainty (the standard error) with regards to the calculated mean.

This problem applies to Figure 3 and the corresponding text on page 7: which mean Hb do the authors mean - did they first calculate the mean Hb per patient and then from that the mean Hb in the population? Or did they calculate the mean of 12 time 350 Hb measurements?

Given that in an individual patient the Hb might have varied - at which time point over the 12 months did they establish the effect of age, gender and co-morbidities (text page 7 and figure 4)? Did they count 12 times as much men and women than there were in the sample, or do they talk about the mean of individual patient-means?

With regards to the reported effects of EPo administration and dose on page 8: at which time point are they carrying out their statistical tests? At start or end of the observation period? They say themselves that the proportion of iv vs po Epo administration changes - and they know themselves that the route of administration may well have a differing effect on achieved Hb level.

On page 9, the analysis of mortality: which Hb did they use to predict mortality? There has been an excellent paper by Dekker in KI recently discussing methodology and pitfalls in time-dependent variables - might be worth reading.
Lastly - I do not understand why in table 2 there are in total 360 patients and 102.6% total percent - I thought they included 350 patients (according to table 1). This needs clarification.

Minor points:
on page 15 line three from the bottom:
replace "randomization" with "random selection into the study". Randomization refers to randomising a treatment, and not to random sampling of patients into a study.

Figure 1: legend: replace "non-randomized" with "in selected patients".

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.