Reviewer's report

Title: The risk of upper gastrointestinal bleeding in patients treated with hemodialysis: A population-based cohort study

Version: 1 Date: 3 August 2012

Reviewer: Eric Weinhandl

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>>> All comments reflect major compulsory revisions.

1046 patients - 9 pediatrics - 166 with UGIB in "baseline" - 3 transplant - 57 PD = 811 patients. However, the authors report a final sample size of 808 patients. Please resolve this discrepancy.

Please list the caliper/criterion for a match according to age.

I am dubious about ascertainment of hypertension. In the HD population, I highly doubt that prevalence of hypertension is ONLY 71.1%. Hyperlipidemia is a difficult factor to address, as well, because we do not have compelling evidence that the relationship between lipid levels of CVD risk is homogeneous in ESRD and non-CKD. Do the authors have any access in this database to biochemical measures?

This analysis involves a pretty serious competing risk: death. Use of Kaplan-Meier curves is entirely inappropriate. Please use proper cumulative incidence estimators.

The authors write that they used a frailty model, but I can only assume that they included a random effect for each matched cluster. Is that true? Please make this explicit.

Upon revision, please report a log-rank test the corresponds to the correct cumulative incidence estimate comparison.

I would like for Tables 1 and 2 to have similarly order columns (i.e., HD on the left, non-CKD on the right).

Why does the adjusted model in Table 2 not include all of the covariates listed in Table 1? (I understand that the authors do not need to adjust for gender and age, as these factors have been used as matching factors.)

In P1 of the Discussion, the speculation about the difference in rates is unfounded. Reference 10 was a study of the DMMS Waves, which included only dialysis patients. There were no transplant patients in that study. Moreover, the % of PD patients in that study was low, as in most US studies of all dialysis patients. So the exclusion of PD patients from the current study cannot explain the almost 2-fold difference in UGIB rates. The authors should consider other
possibilities, including whether general population rates in Taiwan are higher or whether aspects of the HD population are substantially different.

This is NOT a prospective cohort study. The data were collected for claims.

"We found that HD patients were more likely to have... This findings are consistent with previous studies, which reported that [a] [b] [c] may be risk factors for UGIB." This makes no sense at all. Establishing a difference in prevalence of comorbidity does not confirm or refute whether these conditions are risk factors for UGIB in dialysis. Moreover, if the authors want to establish these conditions as risk factors, they will need to conduct a Cox model analysis in ONLY HD patients, b/c the confounder associations are predominantly informed by non-CKD controls in this analysis (as there are 4 such patients for each HD patient).

Why is misclassification likely to be nondifferential? I would challenge the authors not to write this, because I argue that they have no evidence to support this claim. Pure speculation.

The discussion of provider audits is interesting, but my educated guess (based on American experience) is that auditors are concerned about procedures and money, not about accuracy of diagnosis codes for comorbid conditions.

"However, there is no reason to assume that this [overestimation of medication use] would be different for case cohort and control cohort." There is plenty of reason to suspect differential inaccuracy. HD patients take many more medications than non-CKD patients and adherence to oral medication is documented to be low to very low.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.