Reviewer’s report

Title: Impact of Bleeding-related Complications and Blood Product Transfusions on Hospital Costs in Inpatient Surgical Patients

Version: 2 Date: 12 August 2010

Reviewer: Darryl T Gray

Reviewer’s report:

This study of hospital costs associated with post-operative bleeding complications/interventions is generally well-written, addresses an important issue and provides useful and interesting new data. However, the analysis and presentation raise some (generally addressable) issues. Specific comments follow:

Under the journal’s review criteria, it would appear mandatory that a revised manuscript would, at a minimum, explicitly address or comment on the issues raised below. This does not necessarily require that the analysis be redone.

ABSTRACT:

Assuming this is true, Results here and in the text should clarify that incremental LOS differences were unadjusted for covariates, while incremental “cost” differences were adjusted for covariates,

TEXT:

Introduction:

1st paragraph (and elsewhere): For surgical patients who *present* with bleeding, transfusion, death or other outcomes from hemorrhage may represent a consequence of the underlying condition (e.g., vascular trauma, hemorrhagic stroke [not applicable to this study], ruptured aortic aneurysm) rather than a complication caused by the surgical intervention itself. The abstract and paper should make clear the degree to which the authors are distinguishing between these two phenomena.

Materials and Methods:

1st paragraph: The authors should briefly describe the PCD (inclusion criteria for patient and provider populations, how hospitals are chosen, etc.). Is this a claims-based administrative database of ICD-9-CM diagnosis and procedure codes (with some limits on numbers of possible diagnosis vs procedure code fields), augmented by demographic data, a database with other additional lab or imaging test data, a database that captures electronic health record text, or something else? Criteria and data sources for variables such as race, geographic region, urban/rural status, etc. should be included and/or referenced. Presumably
the PCD has encrypted patient identifiers that allow multiple admissions for individual patients or admissions of different patients to the same hospital to be linked. It would appear that this study was eligible for expedited IRB review with a waiver of requirements for informed consent. It is not clear that it was exempt from a requirement for any (expedited) IRB review at all.

2nd paragraph: The 1/106-12/31/07 date range refers to the date of the first (or only) relevant surgical procedure, rather than to the date of admission or the date of discharge for the index admission, right? It would appear that use of the most recent admission would capture re-admission to manage bleeding from a prior surgical admission, rather than the original admission itself. Please comment. Also, would cases transferred from one hospital to another for surgical management of bleeding form a prior operation therefore be excluded entirely, or would the first or second hospital stay (but not both) be included? It would appear that each admission should be categorized by the single most relevant procedure (based on some specified criteria) and then counted just once in the analysis.

How were patients with Medicare managed care classified? This reviewer is unclear as to the meaning of the last sentence in this paragraph.

What was the age range for included patients? It would appear that the different spectra of ages, procedures and co-variates seen in pediatric surgical cases would argue for separate analyses of such cases if they were included in the study at all.

3rd paragraph: Pursuant to a more complete description of the PCD, was capture of cases with relevant ICD-9-CM diagnosis and procedure codes based solely on claims data, on automated review of electronic medical health record text, or something else? Presumably this was not manual data abstraction from the medical record. Per above, it would appear important to note, if true, that this study classified patients on the basis of bleeding only occurring as a complication caused by the surgical intervention itself (ICD-9-CM Dx codes 998.11 and 998.12) rather bleeding occurring as a consequence of the underlying or presenting condition (e.g., vascular trauma, ruptured aortic aneurysm, GI bleeding, bleeding into a tumor) from that or transfusion. Unless there was a time stamp as well as a date stamp, knowing the date of transfusion would not necessarily distinguish pre-op from post-op transfusion on the date of surgery. Did the authors consider excluding vascular trauma, ruptured aortic aneurysm, GI bleeding, etc., from the study to facilitate excluding bleeding occurring as a consequence of the underlying or presenting condition?

4th paragraph: How were costs captured? Is this a) billed charges; b) societal-perspective medical care costs based on actual re-imbursement (reflecting insurer payment with or without patient co-payment and/or deductibles) or standardized allowable (e.g. Medicare-allowable re-imbursement); c) estimated provider-perspective costs based on hospital-wide or procedure group-specific cost-to-charge ratios or on activity-based cost analysis; or d) something else? Costs of physician services are mentioned. These costs would generally be borne by the patient and/or insurer and not
captured as hospital costs per se. Also, physician services (e.g., of surgeons, anesthesiologists, radiologists and others providing care to surgical inpatients) would generally be captured using CPT-4 procedure codes rather than by ICD-9-CM procedure codes. Estimation of the costs of such physician services would differ from that of hospital costs. Please comment. Were “costs” from other years converted to 2007 dollars using relevant ratios of the Producer Price Index, the Consumer Price Index or some other approach?

5th paragraph: This reviewer is unclear as to the meaning of the 2nd sentence in this paragraph. It would appear that the analysis of resource use (days, costs as defined) associated with the presence or absence of bleeding complications/procedures is a cohort study, while the analysis of (pre-) existing risk factors associated with the presence or absence of bleeding complications/procedures is actually a (potentially nested) case-control study calling for separate analytical runs. Please comment.

6th paragraph: Re-transformation of natural log-transformed costs from OLS models may be associated with bias, especially if heteroskedasticity was present. Regression models using maximum likelihood for the generalized Gamma distribution have been described as a better alternative. Was this approach considered? How was “admitted surgical diagnosis” coded for inclusion in the model as constructed? How far before the operative date did the authors look for “prior hospitalizations”? Truncation at some pre-operative interval (e.g. 6 mos. or 1 year) would avoid bias if durations of patient or hospital inclusion in the PCD was related to variables of interest in this study). Were hospitalizations for any related or unrelated cause included and how were they coded? How were prior admissions with direct transfers from other hospitals to the hospital o the index admission handled? Were all co-morbidities listed modeled as separate covariates? Were coagulopathies, pre-op anemia or the use of drugs such as bone marrow suppressants, considered as possible covariates? How were co-morbid conditions occurring as post-op complications (e.g., MI or renal failure) distinguished from those present pre-operatively?

Obesity (and smoking status) are potentially relevant co-variates that are poorly captured by administrative data. Were existing algorithms (e.g., of Brixer and of Kahende, Fu or Mapel respectively) for trying to capture these risk factors using diagnosis data considered?

Did the authors consider propensity scoring as an approach to adjust for possible confounders of the comparison between cases with vs without bleeding complications/interventions in terms of resource use outcomes?

Was hierarchical modeling using generalized estimating equations or other approaches considered as a way to adjust for clustering of cases within hospitals? If a given hospital had generally higher costs, and, as an independent issue, had more bleeding complications, then some of the cost difference attributable to bleeding would actually be due to the hospitalsl higher costsin

Results
2nd paragraph: It would help to clarify that “differences in baseline demographic and clinical measures were highly STATISTICALLY significant across study groups due to the large sample size” Please comment here and/or elsewhere on differences that the authors interpreted as important vs unimportant.

3rd paragraph: Please clarify the purpose, and definition of the “prior hemostat exposure” co-variate under Methods. Interpretation of the result can be commented on here and/or elsewhere. Were there many Medicare patients under 65 years old (due to disability and/or ESRD)? If not, differences in the distribution of Medicare patients would be driven by the older age distribution of patients with bleeding complications and is not really an independent covariate.

6th paragraph: If “costs” were based on observed re-imbursement for individual patients, then the distribution of Medicare patients could have affected cost results independent of the effect of the presence or absence of bleeding complications/interventions. If post-op transfers TO other acute care hospitals were not included, then listed estimates would underestimate costs of the total inpatient episode of care. Please comment.

Discussion
The discussion should reflect consideration of issues such as those raised above as they pertain to Methods and Results.

Competing Interests
As this study was entirely industry-funded, the companies involved (United BioSource, Ethicon and Excenda) should be briefly described, and the existence of any products potentially relevant to the study should be briefly noted. For example, it would be useful for readers to if any of these companies makes products that prevent or reduce bleeding complications, since they could benefit directly or indirectly from results showing larger costs attributable to such complications.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.