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The authors appreciate the insightful comments by both reviewers and appreciate the opportunity of offering the following rebuttal for the comments by the second reviewer.

1. *The reviewer has a problem combining UGI bleeding with GIB from an undefined source. Please comment to include whether removing the latter group from analysis changes the conclusions of the study.*

The authors determined, a priori, that limiting the cohort to be studied to that wherein an exact source of bleeding was defined (peptic ulcer – gastric / duodenal, varices, esophagitis) would introduce bias in the extent of diagnostic work up in the cohort. Therefore inclusion of GIB from unspecified sources better reflected the overall outcome of patients experiencing predominantly upper GI bleeds.

Hemorrhage of the GI tract unspecified (578.9) was reported 1,028 of the 19,528 patients as the principal diagnosis;2.97% of the mortality and 5.31% of the non-mortality associated GI bleeding cases. The exclusion of Hemorrhage of GI tract unspecified does not change the conclusions of the study with respect to the protective effect of endoscopy, the impact of other therapeutic modalities and patient characteristics. The final model was re-examined in a reduced cohort that excluded the patients with 578.9 as the principal diagnosis (N=18,500). All factors found to be significant in the original model remained significant in the sensitivity analysis. While estimates and effect sizes changed somewhat, the inferences did not.

2. *Please comment on the absence of endoscopic therapy in the database related to outcomes. In the adult literature, there is a clear relationship to endoscopic therapy and outcomes.*

As an observational database comprised of billing and discharge data, procedures are coded using either ICD-9 or CPT coding systems. CPT is an optional coding system in PHIS data

reporting and is missing for over 90% of hospitals in most years. ICD-9 was mandatory until the adoption of ICD-10 in October of 2015 (just after the end dates of our study population encounters). We queried the PHIS data for ICD-9 code 39.92 - Injections with sclerosing agent into vein. In the 19,528 cases involving GIB queried, only 4 of those cases had ICD-9 procedure codes for 39.92. This procedure additionally falls under "operations on vessels" and is not specifically a GI procedure according to the coding scheme. Thus, there is no way to determine for certain if the procedure was performed for GI conditions. We posit that the low numbers found in the PHIS database for sclerotherapy are due to coding limitations and practices, or other more generic codes being used for this procedure.

Other endoscopic therapy codes include: 42.33 - Endoscopic excision or destruction of lesion or tissue of esophagus; 43.41 - Endoscopic excision or destruction of lesion or tissue of stomach; 45.30 - Endoscopic excision or destruction of lesion of duodenum; and 44.43 - Endoscopic control of gastric or duodenal bleeding. Since method of excision, destruction, or control is not specified by these procedures, we combine the endoscopic procedures into a single variable. Of the 5,939 patients undergoing endoscopic procedures reported in this cohort, 743 (12.51%) were coded with at least one of the four endoscopic therapy procedures above.

3. *What does vasopressin have to do with GIB except with varices? It has been abandoned as "blind Rx" in the adult population.*

The use of vasopressin in patients with GIB relates to its use in hemodynamic instability in the context of ICU use; its use in variceal bleed therapy is limited and the authors consider it a surrogate marker of extraordinary measures used to treat hemodynamically unstable patients and therefore our reported observation on the association with mortality.

We appreciate the reviewer's observation and have amended the text to reflect the use of vasopressin for hemodynamic support rather than specific treatment of GI bleeding (Page 20: Para 2, Line 3 - 5)

4. *There are multiple variables used to potentially Rx upper GIB that are associated with an increase in mortality in this series to increase proton pump inhibitors. Please elaborate that these are only markers for more severe GIB. Can you comment on whether these drugs were used only in patients in whom acid suppression was potentially therapeutic vs. in those without a definite diagnosis?*

We appreciate this comment and have amended the discussion as suggested. The authors respectfully submit that in all major categories of diagnoses; variceal hemorrhage, esophagitis, gastroduodenal inflammatory or ulcerative processes PPI treatment constitutes

an established therapeutic measure; the potential for clinical benefit includes those patients wherein the bleeding (source) was not specified or blood was noted in the stool.

The receipt of PPI was significantly associated with the lack of a definite diagnosis (562.02, 562.03, 578.1, or 578.9) ($\chi 2(1)=881.1$; $P<0.0001$). 5,401 of the 10,524 patients receiving PPI (51.32%) had a diagnosis for which PPI would have been therapeutic, whereas 6,494 of the 9,004 (72.12%) of patients not having a definite diagnosis received a PPI. It would seem, therefore, that PPI was administered in more cases than when it would have been traditionally therapeutic.

5. *It is not unexpected that sick patients/children die with or without a primary diagnosis of GI bleeding. The reviewer had difficulty defining whether the GIB had any role in the mortality of those who died in the setting of one or multiple CCCs. Please elaborate.*

The study, as performed cannot purport to derive a causal relationship but only association, and in this regard mortality was noted as significantly higher in patients with multiple chronic comorbidities over those with less. It is methodologically impossible for the authors to define the intrinsic mortality of multiple comorbidities compared with the same comorbidity profile with GI bleeding whilst adjusting to the severity of the same comorbidities and other recognized confounders. This is reflected in the discussion (Pg 18, Para 3, Line 3)

6. *Please define the rationale for random octreotide therapy in GIB (19.8% of patients who died vs. 4.04%). Approaching this from an adult with an unknown source of GIB, it is unusual to RX with random octreotide or vasopressin. What percent of patients treated with these drugs had documented portal hypertension/varices?*

255 of the 1004 patients receiving octreotide or vasopressin had a diagnosis of varices with bleeding: 253 of 879 (28.8%) of patients receiving octreotide had a diagnosis of varices with bleeding, and 8 of 183 (4.57%) patients receiving vasopressin had a diagnosis of varices with bleeding.

420 (41.8%) of the 1,004 patients receiving octreotide or vasopressin had a diagnosis of portal hypertension: 417 of 879 (47.4%) patients receiving octreotide had a portal hypertension diagnosis, whereas 18/183 (9.8%) receiving vasopressin had a portal hypertension diagnosis.

Receiving octreotide or vasopressin was significantly associated with having a portal hypertension diagnosis (χ^2 (1) =3261.5, $p<0.0001$), and with having varices with bleeding (χ^2 (1) =2477.2, $p<0.0001$). This suggests that it is not random, but would have been more likely received in a patient who had one of those diagnoses

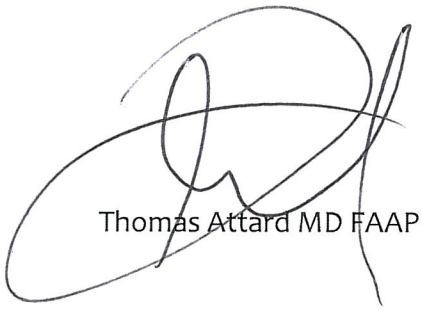
It is not unusual for pediatric patients with GI bleeding to be empirically treated with octreotide before a definitive endoscopic diagnosis is established, the authors speculate that the increased likelihood of octreotide (and vasopressin) use in the mortality cases was a consequence of the severity of the bleed or the degree of hemodynamic compromise (Page 16, Para 3, Line 7 - 9)

7. *In Table S2, you define codes for endoscopic, radiologic, and surgical procedures that potentially treat GIB to include codes for laparoscopy, exploratory laparotomy, and "other" laparotomy. However, the reviewer finds it difficult to do a crosswalk to Table 2 where only a very small subset of individuals had these procedures. Likewise, 12.87% – 23.89% had endoscopy for presumptive UGI bleeding, but I am unable to define how many actually had therapeutic codes as defined in Table S2 applied. Please comment.*

We have amended Table S2 to reflect the requested data on diagnostic/therapeutic codes on endoscopy and relationship with mortality. As noted the laparoscopy, exploratory laparotomy and laparotomy are a very small proportion and were disregarded. A total of 5,939 patients received endoscopy. The table stratifies therapeutic endoscopy type. The vast majority of endoscopic procedures were EGD.

We look forward to your favorable review of our revised submission and welcome any further edits you may require.

With Best regards,



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