Dear Reviewers,

Re- Manuscript 34086: Colonoscopy quality with Entonox® versus intravenous conscious sedation: 18,608 colonoscopy retrospective study

Thank you for taking the time to review our manuscript.

I have endeavoured to address the comments of each of the reviewers as I understand them-

Reviewer 1- No corrections as I understand it.

Reviewer 2- No corrections as I understand it.

Reviewer 3- No corrections as I understand it.

Reviewer 4- Minor issues only which I feel we can effectively address.

Comment from reviewer 4	Suggested corrections
1. In 2nd paragraph of materials and methods, you excluded 234 patients receiving both Entonox and midazolam. But in the last sentence of that paragraph, you mentioned that patient with Endonox had the option of fentanyl plus or minus midazolam. There is little confusion for me, may be the other readers.	Paragraph 2 of 'materials and methods' has been restructured to make this more clear. It now reads- At each of these units, throughout this timeframe, patients were offered the choice of either: (1) Entonox, (2) intravenous conscious sedation (IVM) with midazolam plus or minus opioid, or (3) no sedation or analgesia (i.e. unmedicated), administered by the endoscopist. Patients offered Entonox had the option of fentanyl plus or minus midazolam as an adjunct if required and clinically appropriate. There were 234 individual cases of patients receiving both Entonox and midazolam sedation (1.26% of the total), and all these cases were all excluded from the analysis. This situation could have arisen in the case where the patient was not adequately responding to IVM and Entonox was then introduced as an adjunct or vice versa. Ninety-nine percent of patients receiving IVM had a combination of Fentanyl analgesia and midazolam sedation at the start of the procedure.
2. Who did the sedation in your study, gastroenterologist, nurse or anesthesiologist?	Again within paragraph 2 of 'materials and methods' this has been clarified. Reading- At each of these units, throughout this timeframe, patients were offered the choice of either: (1) Entonox, (2) intravenous

	conscious sedation (IVM) with midazolam plus or minus opioid, or (3) no sedation or analgesia (i.e. unmedicated), administered by the endoscopist. Patients offered Entonox had the option of fentanyl plus or minus midazolam as an adjunct if required and clinically appropriate. There were 234 individual cases of patients receiving both Entonox and midazolam sedation (1.26% of the total), and all these cases were all excluded from the analysis. This situation could have arisen in the case where the patient was not adequately responding to IVM and Entonox was then introduced as an adjunct or vice versa. Ninety-nine percent of patients receiving IVM had a combination of Fentanyl analgesia and midazolam sedation at the start of the procedure.
3. As you mentioned in your discussion, unmedicated patients had no or mild discomfort than sedated patients. It was conflict if you take cost-effectiveness into consideration. The reasons may contribute to doctors' skill, use of CO2 insufflation, water emersion or exchange, good bowel preparation and male gender. Of course, these confounders may be difficult to analysis in your data.	Although this does not ask for an alteration and seems more like a comment I do agree and comment on it within the discussion section. Further clarification on this has been added to the discussion section. Within this study there was no data collected on the individual endoscopists experience in relation to patient outcomes.

Thank you again for taking the time to review our manuscript and hope that these alterations are agreeable to you.

Sincerely yours,

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