PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach
AUTHORS	Ni, Melody; Huddy, Jeremy; Priest, Oliver; Olsen, Sisse; Phillips, Lawrence; Bossuyt, Patrick; Hanna, George

VERSION 1 – REVIEW

REVIEWER	S. Y. Irving Univ of Pennsylvania, School of Nursing; Children's Hospital of Philadelphia, USA No Competing Interest
REVIEW RETURNED	10-Jul-2017

GENERAL COMMENTS	Thank you for this timely and well-done work to address the topic of pH for verification of NG tube placement as it continues to be in question across age groups and patient populations. Some clarity as to the audience this is intended to be of most interest to? The clinician placing the tube, and is that group primarily nurses? The extensive statistical design and granularity of analysis although very informative and clearly examines the question but may detract from your outcome message of using a pH of 5 as the safest cutoff to verify NG tube location in the stomach. A statement on how pH was measured in your dataset, specific paper/strip that was used, would be helpful – not brand, but if it were a strip vs paper and is the same paper/strip is used throughout. That said, the systematic approach in this work adds to the science and body of evidence on appropriate pH cutoff to use as safe level for identification of NG tube location. Overall comments: Thank you for this timely and well-done work to address the topic of pH for verification of NG tube placement as it continues to be in question across age groups and patient populations. Some clarity as to the audience this is intended to be of most interest to? The clinician placing the tube, and is that group primarily nurses? The extensive statistical design and granularity of analysis although very informative and clearly examines the question but may detract from your outcome message of using a pH of 5 as the safest cutoff to verify NG tube location in the stomach. A statement on how pH was measured in your dataset, specific paper/strip that was used, would be helpful – not brand, but if it were a strip vs paper and is the same paper/strip is used throughout. That said, the systematic approach in this work adds to the science and body of evidence on appropriate pH cutoff to use as safe level for identification of NG tube location. Please see attached for detailed brief review.

	Abstract Pg 3, lines 7 -9: Statement seems misplaced here, an assumption, does not add to the objective of the manuscript. Pg 3, lines 16-17:clarify what “the” existing safety guidelines Implies there is a national guideline, but for readers outside of the UK,who are not aware of this, it is unclear. Manuscript body Pg 5, line 5:Please provide reference for the numbers of NGT placed (1 million in UK; 1.5 billion worldwide) Pg 5, line 47 – 49: 1st mention of delay to initiation of feeding due to need for Chest x-ray; please give the mean (or range) duration of delay; Is it chest or abdominal x-ray for NG tube placement? Pg 7, lines 14-16:I interpret this as if the pH exceeded the cutoff, x-ray was done and tube was in gastric cavity, the x-ray was deemed unnecessary and gastric placement was determined solely by pH if this is true, it is not clear as written. Pg 9, lines 14-16: There are in fact reports of erroneous radiographic reports or incomplete reporting that could impact accuracy of x-rays; should add acknowledgement of this and why this assumption is made for the current study; particularly since stated below that misinterpretation of x-rays was a frequently cited reason for misfeeding. Pg 10, lines 50 – 55: Please describe length/extend of feeding delay related to use of x-ray for NG tube placement, particularly since the x-ray correctly identified 30% of misplaced tubes Pg 12, line 57: In implications for practice section, please explain statement that decreasing the pH cut-off will increase the number of requests for x-rays. Given data presented here, the case is strong for decreased cut-off increases likelihood of correct placement, please explain. References Many of the references are dated, please briefly explain in the body why these references are best to depict/support your research Pg 14, lines 16 – 17 no journal given. Appendices All very helpful, Tables A, A2 and B are most helpful and should be placed in the main manuscript and not only in the appendices.

REVIEWER	Agi McFarland Glasgow Caledonian University Scotland
REVIEW RETURNED	19-Jul-2017

GENERAL COMMENTS	Point 2, Abstract: In the Objectives it is stated that it is "unclear which pH cut off is the safest". It is not unclear as current guidelines clearly recommend a cut off value of 5.5. This is therefore misleading. Point 4, Methods: There are a number of assumptions and the justification for the study appears unclear. The recommendation to lower the pH limit to 4 is stated but it is unclear how the authors chose this limit (i.e. on what evidence this was based). The determination of what constitutes "sufficient detail" of the NRLS reports is not specified, nor details given of the review process and decisions. For example, did the independent reviewers always agree? How were disagreements handled? A further concern with the methodology lies with the structure of the tree itself. The pH test is reliant on the ability to obtain aspirate to test, and this has been reported to be as low as 20% of tubes (i.e. in 80%, practitioners are unable to obtain aspirate for testing). There should be an additional decision node and subsequent branch added which details the clinical pathway in cases where the pH test is unavailable (i.e. aspirate unable to be obtained) as this will alter the number of chest x-rays that will need to be completed. As such, the pathway is currently not representative. Point 5, Ethics: Only very briefly stated that it was obtained, no further information given. No information in the main body of the article. Point 6, Outcomes: Not stated. These would be a useful addition to the article text. The overall aim is stated but not specific outcomes. Point 8, References: Literature in relation to aspirate success is missing (see my comments in to Methods). Additionally, given the topic and methodology, I would expect McFarland (2017) DOI 10.1111/jan.13103 to be referenced in the section Comparison with existing literature. Point 12, Study limitations: The study has several limitations which are not addressed (see my comments above). The most important one is to acknowledge that the current analysis assumes that pH testing is always available. It is crucial to highlight the clinical impact of this underlying assumption to the results of the analysis. I think the paper is interesting and would be relevant but it needs further work in relation to my points outlined above. It is also a consideration as to what it is that is being proposed; if the national guidelines are already clear that the pH cutoff is 5.5, what is this work adding to the knowledge base? Why is this analysis necessary? I don't feel the case is made strongly enough in the current version of the paper and this would be a key area to work on for the revision.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: S. Y. Irving
Institution and Country: Univ of Pennsylvania, School of Nursing; Children's Hospital of Philadelphia, USA
Competing Interests: None

General Comment: Thank you for this timely and well-done work to address the topic of pH for verification of NG tube placement as it continues to be in question across age groups and patient populations. Some clarity as to the audience this is intended to be of most interest to? The clinician placing the tube, and is that group primarily nurses?

Comment: Thank you for the encouraging remarks. The main audience of this paper are policy makers and clinicians responsible for safety checks (e.g. nurses). This has been included in Introduction (p5 line 10-11).

Response: The extensive statistical design and granularity of analysis although very informative and clearly examines the question but may detract from your outcome message of using a pH of 5 as the safest cutoff to verify NG tube location in the stomach.

Comment: We have extensively amended the section titled 'Safety of the pH test under various cut-offs' (p13 line: 5 to p14 line 18)

Response: A statement on how pH was measured in your dataset, specific paper/strip that was used, would be helpful – not brand, but if it were a strip vs paper and is the same paper/strip is used throughout.

Comment: We have extensively amended the section titled 'Safety of the pH test under various cut-offs' (p10 line 3-4)

That said, the systematic approach in this work adds to the science and body of evidence on appropriate pH cutoff to use as safe level for identification of NG tube location.

Response: Thanks again for the encouraging comments on our work.

Abstract
Comment: Pg 3, lines 7 -9: Statement seems misplaced here, an assumption, does not add to the objective of the manuscript.

Response: Objectives has now been re-written accordingly (p2, line 2-6)

Comment: Pg 3, lines 16-17 clarify what "the" existing safety guidelines Implies there is a national guideline, but for readers outside of the UK, who are not aware of this, it is unclear.

Response: We have clarified this in Objectives (p2, line 2)

Manuscript body
Comment: Pg 5, line 5 Please provide reference for the numbers of NGT placed (1 million in UK; 1.5 billion worldwide)

Response: Reference has been added for the UK and justification has been made for the guesstimate made for the worldwide consumption (footnote 1, p5).

Comment: Pg 5, line 47 – 49 1st mention of delay to initiation of feeding due to need for Chest x-ray; please give the mean (or range) duration of delay; Is it chest or abdominal x-ray for NG tube placement?

Response: More details about chest x-ray related delays have now been added (p6, line 1, footnote 3).

Comment: Pg 7, lines 14-16 I interpret this as if the pH exceeded the cutoff, x-ray was done and tube was in gastric cavity, the x-ray was deemed unnecessary and gastric placement was determined solely by pH if this is true, it is not clear as written

Response: Thank you for pointing this out. We have now reworded accordingly (p8, line 7-11).

Comment: Pg 9, lines 14-16 There are in fact reports of erroneous radiographic reports or incomplete reporting that could impact accuracy of x-rays; should add acknowledgement of this and why this assumption is made for the current study; particularly since stated below that misinterpretation of x-rays was a frequently cited reason for misfeeding

Response: Thank you very much for pointing this out. We have now added additional reference (Ref 7) and included in the sensitivity analysis where the impact of chest x-ray was tested (p11, line 8-13). We added explanations as to why we assumed chest x-rays were accurate in the main body of analysis (p11, line 14-16)

Comment: Pg 10, lines 50 – 55 Please describe length/extend of feeding delay related to use of x-ray for NG tube placement, particularly since the x-ray correctly identified 30% of misplaced tubes

Response: Further details have been added (p14, line 17-18)

Comment: Pg 12, line 57 In implications for practice section, please explain statement that decreasing the pH cut-off will increase the number of requests for x-rays. Given data presented here, the case is strong for decreased cut-off increases likelihood of correct placement, please explain.

Response: We have explained why more x-rays will follow a lower pH cutoff (p17, line 6-9)

References
Comment: Many of the references are dated, please briefly explain in the body why these references are best to depict/support your research

Response: We have now included more recent references (Ref 1, 7, 9, 11, 21, 22). We also explained why dated references were important for the study (p15, line 22-25).

Comment: Pg 14, lines 16 – 17 no journal given.

Response: We apologize for this. This has now been corrected (Ref 8).

Appendices
Comment: All very helpful, Tables A, A2 and B are most helpful and should be placed in the main manuscript and not only in the appendices.

Response: Thank you for the suggestion. We have now added Tables A, A2 and B into the Results section of the main text as Table 1, 2 and 3.

Reviewer: 2
Reviewer Name: Agi McFarland
Institution and Country: Glasgow Caledonian University, Scotland
Competing Interests: None declared

Comment: Point 2, Abstract: In the Objectives it is stated that it is "unclear which pH cut off is the safest". It is not unclear as current guidelines clearly recommend a cut off value of 5.5. This is therefore misleading.

Response: Objectives section has now been reworded (p3 line 2-6)

Comment: Point 4, Methods: There are a number of assumptions and the justification for the study appears unclear. The recommendation to lower the pH limit to 4 is stated but it is unclear how the authors chose this limit (i.e. on what evidence this was based).

Response: We have clarified this point in Introduction (p5 line 17-22).

Comment: The determination of what constitutes "sufficient detail" of the NRLS reports is not specified, nor details given of the review process and decisions. For example, did the independent reviewers always agree? How were disagreements handled?

Response: We have added further details to the Methods section (p7 line 8-12).

Comment: A further concern with the methodology lies with the structure of the tree itself. The pH test is reliant on the ability to obtain aspirate to test, and this has been reported to be as low as 20% of tubes (i.e. in 80%, practitioners are unable to obtain aspirate for testing). There should be an additional decision node and subsequent branch added which details the clinical pathway in cases where the pH test is unavailable (i.e. aspirate unable to be obtained) as this will alter the number of chest x-rays that will need to be completed. As such, the pathway is currently not representative.

Response: Thank you for pointing this out. We have 1) added an explanation as to why we only considered successfully aspirated patients (p7 line 16-18) 2) carried out a sensitivity analysis to explore implications (p11 line 8-13 and p15 line 1-3) as well as 3) added this as a limitation of the study (p16, 5-12).

Comment: Point 5, Ethics: Only very briefly stated that it was obtained, no further information given. No information in the main body of the article.

Response: We have added a section on ETHICS (p6 line 12-16)

Comment: Point 6, Outcomes: Not stated. These would be a useful addition to the article text. The overall aim is stated but not specific outcomes.

Response: We have added clarification of outcomes (p6 line 6-8)

Comment: Point 8, References: Literature in relation to aspirate success is missing (see my comments in to Methods). Additionally, given the topic and methodology, I would expect McFarland (2017) DOI 10.1111/jan.13103 to be referenced in the section Comparison with existing literature.

Response: We have include the reference (Ref 22) as well as discussed its relevance to our study (p16 line 23-26)

Comment: Point 12, Study limitations: The study has several limitations which are not addressed (see my comments above). The most important one is to acknowledge that the current analysis assumes that pH testing is always available. It is crucial to highlight the clinical impact of this underlying assumption to the results of the analysis.

Response: We have rewritten the Strength and Limitations. This has been added as a limitation of the study (p16, 5-12).

Comment: I think the paper is interesting and would be relevant but it needs further work in relation to my points outlined above. It is also a consideration as to what it is that is being proposed; if the national guidelines are already clear that the pH cutoff is 5.5, what is this work adding to the knowledge base? Why is this analysis necessary? I don't feel the case is made strongly enough in the current version of the paper and this would be a key area to work on for the revision.

Response: We have added clarification in the Objectives (p3) and in the main text (please see INTRODUCTION, especially p5, 17-25 as well as Strengths and Limitations in p15-16).

VERSION 2 – REVIEW

REVIEWER	Agi McFarland Glasgow Caledonian University United Kingdom
REVIEW RETURNED	11-Sep-2017

GENERAL COMMENTS	On p5, line 53: it may be worth considering giving a brief indication of the cost difference to highlight to the reader the magnitude of the difference between the 2 tests. On p11: It is not clear where the 10% misinterpretation rate is obtained from, please clarify (line 25). It is misleading to assume a chest x-ray accuracy of 100% in the analysis and even given the data from this current study (e.g. Table 3, Mode of failure to identify tube placement) shows that chest x-rays are open to interpretation errors thereby rendering the 100% accuracy assumption incorrect. Assuming a 100% accuracy of chest x-ray will overestimate the usefulness of this method. Only direct visualisation of tube placement (e.g. via an endoscope) can be 100% accurate. This needs to be acknowledged and the analysis adjusted accordingly.

	Figure 2 is a useful diagram. It may be worth highlighting in the narrative that no trade off combination is entirely free from feeding incidents and delays. Sensitivity analysis: All of the ranges and subsequent model results should be reported in a table. Some minor recomended adjustments: P3 line 37: “Routine chest x-rays was less safe…”. Change to “were less safe” P15 line 28: “Routine chest x-rays was less safe…”. Change to “were less safe” P16 line 15: “is known to be less sensitive compared to pH meter”. Change to “is known to be less sensitive when compared to pH meter” P17 line 20: “{, #110}. Not sure what this is referring to? P17 line 24: “human errors in its applications”. Change to “human errors in their applications”.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Agi McFarland

Institution and Country: Glasgow Caledonian University, United Kingdom Competing Interests: None declared

Comment: On p5, line 53: it may be worth considering giving a brief indication of the cost difference to highlight to the reader the magnitude of the difference between the 2 tests.

Response: Costs of pH strips and chest x-rays have now been added (p5, line 25-p6, line 1; footnote 3, p6).

Comment: On p11: It is not clear where the 10% misinterpretation rate is obtained from, please clarify (line 25).

Response: We have added explanations as footnote 5, Page 11

Comment: It is misleading to assume a chest x-ray accuracy of 100% in the analysis and even given the data from this current study (e.g. Table 3, Mode of failure to identify tube placement) shows that chest x-rays are open to interpretation errors thereby rendering the 100% accuracy assumption incorrect. Assuming a 100% accuracy of chest x-ray will overestimate the usefulness of this method. Only direct visualisation of tube placement (e.g. via an endoscope) can be 100% accurate. This needs to be acknowledged and the analysis adjusted accordingly.

Response: We wish to thank the reviewer to point this out. We agree that the chest x-rays lacked accuracy. We have now discussed in detail the reasons such an assumption was made and its implications (p18, line 6-26).

Response: We have also acknowledged this assumption as a limitation of the present study. (p4, line 12-13)

Comment: Figure 2 is a useful diagram. It may be worth highlighting in the narrative that no trade off combination is entirely free from feeding incidents and delays.

Response: This is now been added in P13, line 7-8

Sensitivity analysis: All of the ranges and subsequent model results should be reported in a table.

Response: Table 4 has now been added to the main text (p15).

Some minor recomended adjustments:
• P3 line 37: “Routine chest x-rays was less safe…”. Change to “were less safe” – corrected
• P15 line 28: “Routine chest x-rays was less safe…”. Change to “were less safe” – corrected
• P16 line 15: “is known to be less sensitive compared to pH meter”. Change to “is known to be less sensitive when compared to pH meter” - corrected
• P17 line 20: “{, #110}. Not sure what this is referring to? –The missing reference has been corrected.
• P17 line 24: “human errors in its applications”. Change to “human errors in their applications”- corrected

Correction: *Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach*

Ni MZ, Huddy JR, Priest OH, *et al*. Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach. *BMJ Open* 2017;7:e018128. doi: 10.1136/bmjopen-2017-018128

In the 'Outcomes of feeding decisions' section, the sentence: "For the remaining outcomes, we applied the analytic hierarchy process,[14]…"
should read: "For the remaining outcomes, we applied the Measuring Attractiveness by a Categorical Based Evaluation Technique (MACBETH) approach.[14]…"
Reference 14 should be: Bana e Costa CA, De Corte JM, Vansnick JC. "MACBETH". *International Journal of Information Technology and Decision Making* 2012;11:359–387.
Reference 15 should be: Bana e Costa CA, Chagas MP. A career choice problem: an example of how to use MACBETH to build a quantitative value model based on qualitative value judgments. *Eur J Operational Res* 2004;153:323–331.

BMJ Open 2018;**8**:e018128corr1. doi:10.1136/bmjopen-2017-018128corr1