

Peer Review File

Article information: <https://dx.doi.org/10.21037/aob-22-45>

Reviewer A

Abstract

Major issues: lacks clarity. ie. what is the aim of this article. This needs to be stated.

Reply 1: This has been added to the abstract.

Line 49 - 51: "This lead to a need for patient blood management (PBM) which is a natural continuation of the history of modern transfusion". PBM isn't simply a "natural continuation of the history of modern transfusion". In his article [Isbister et al. Anesthesia & Analgesia, 2002] Prof. Isbister, considered one of the fathers of Patient Blood Management, described virtually the opposite point. ie. that the principles of PBM pre-dated transfusion: "By the end of the 19th century, the groundwork was being laid for what is now defined as PBM. Surgeons had begun focusing attention on examining a patient's blood, minimizing hemorrhage, and tolerating anemia, as blood transfusion was not a therapeutic option"

Reply 2: Due to word limitations for the abstract this has been added to the Pre-1900 section.

Line 64 - 66: "Substituting legacy methods, the digital algorithms and artificial (AI) intelligence have reformed our world, however, challenges remain with providers overriding software alarms and alarm fatigue". This sentence is very confusing to this reviewer. For example digital algorithms and AI extend beyond alerts and early warning systems (assuming this is what the authors are referring to?). In addition Machine Learning, a subset of AI, is not mentioned which is more relevant to PBM and healthcare in general.

Reply 3: This section has been removed from the abstract per the other reviewer's comments.

Is the second sentence of the Abstract complete?

Reply 4: This has been corrected.

Main Text Comments

Line 178 - 187 The Jehovah's Witness Patients is problematic. The authors reference 3 articles (Ref 37, 38, 39) however much of the wording is very similar to reference 38. For example,

- Line 178 - 180: "The Jehovah's Witness (JW) religion was founded in Pittsburgh in 1872 by Charles Taze Russell during the Adventist movement based on a literal millennialist interpretation of the Bible."

- Ref 38: "The JW religion, founded in 1872, by Charles Taze Russell during the Adventist movement in Pittsburgh is an international organization, the followers of which believe that the Bible is the true word of God."

- Line 180 - 183: "In 1931, the organization officially became known as the 'Jehovah's witnesses.(37) They share some Christian beliefs but hold some unique views as being politically neutral, do not

salute flags, enlist in the military, or vote in public elections. They celebrate neither Christmas nor birthdays and must satisfy their ministry's minimum monthly time requirement.(38)"

- Ref 38: "In 1931, the organization officially became known as the 'Jehovah's witnesses'.[1] They are politically neutral, do not salute flags, enlist in the military nor vote in public elections. They celebrate neither Christmas nor birthdays, and must satisfy a minimum monthly time requirement to their ministry."

- Line 184 - 186: "It was not until 1945 that the governing body of the 'JW' The Watchtower Society (WTS) introduced the blood transfusion ban, based on the strict literal interpretation of several scriptural passages of the New World Translation of the Bible."

Ref 38: "In 1945, the governing body of the JW 'The Watchtower', introduced the blood ban, based on the strict literal interpretation of several scriptural passages of New world Translation of Bible such as..."

Have the authors taken any time to confirm whether the information used from the Indian J Anaesth (Ref 38) is accurate or relevant globally?

Reply 5: The original articles were reviewed and changes to the reference made as needed. Reference 38 has been removed from the manuscript. In some cases, more than one article corroborated the statements and multiple references were used. All three were peer-reviewed journal articles and accuracy should have been verified prior to publication.

The article published by Klein et al. [Anaesthesia 2018, <https://doi.org/10.1111/anae.14441>] included input from the "Hospital Information Services for Jehovah's Witnesses", did the authors of this study likewise seek any input for accuracy?

Reply 6: Changes were made to the manuscript after a review of the source peer-reviewed article whose accuracy should have been verified prior to publication. Thank you for the reference this has been added.

Line 220: check inverted commas

Reply 7: These have been corrected

Line 222: check inverted comma

Reply 8: We paraphrased the quote.

Line 224: Can the authors please confirm whether Ron Lapin was an orthopedic surgeon.

Reply 9: His obituary lists him as a surgeon and the designation has been removed from the manuscript.

Line 227: This reviewer has never heard of "surgical blood conservation" referred to as "perioperative autologous cell salvage" or grouped together with "preoperative autologous blood donation", "intraoperative acute normovolemic hemodilution", or "cell salvage". Please supply a reference for this statement or do not group these strategies together as it is likely confusing to the reader.

Reply 10: We rephrased the sentence and provided citations for perioperative autologous cell salvage (PACS) surgical blood conservation.

Line 249: Have the authors considered the National Blood Authority (Australia) guidelines and

evidence-based recommendations for ANH and ICS?

Reply 11: Additional citations have been provided.

Line 250 HIV in the blood supply. This section refers only to the US. There is no mention of other significant events that played a role in shaping PBM. For example in Canada in 1997 Justice Krever's Commission Report led to 50 recommendations and resulted in the implementation of blood conservation initiatives in Canada, including the well-known ONTraC program.

Reply 12: This has been added to the manuscript.

Line 271-280 is the same paragraph repeated twice

Reply 13: The duplicate paragraph has been deleted.

Line 310 -315 refers to the cost of processing transfusion, however makes no reference to the highly cited Transfusion activity-based costs of blood transfusions published by Shander et al. [Transfusion 2010]

Reply 14: This reference has been added.

Line 320: this reviewer does not agree with bundling PAD, ANH, and ISC into ABT. This can be confusing.

Reply 15: This paragraph has been removed.

Line 347: Steps to Prevent Hospital Acquired Anemia(?) An error?

Reply 16: This heading has been removed.

Line 366: In addition to SABM please refer to the history of NATA which is a European based society established before SABM. Also there is no mention of the National Blood Authority (Australia). A history of PBM cannot exclude the role this Blood Authority has played. It was established following the 2001 Stephen Review of the Australian Blood Banking and Plasma Product Sector following the infected blood scandals referred to by the authors of this manuscript. Today the National Blood Authority of Australia is considered a global leader in PBM.

Reply 17: The manuscript has been revised to reflect the role of NATA and National Blood Authority, Australia. The authors do not have access to the "2001 Stephen Review of the Australian Blood Banking and Plasma Product Sector" submitted in the Australian parliament. If the reviewers can kindly share access, we will be happy to incorporate.

The section on data mining is written poorly and needs a major revision.

Line 370-373: The first 2 sentences are unclear. What are the authors trying to say?

Reply 18: Revised to introduce statement that a high-quality data collection and analysis can further drive PBM.

Line 374: The authors say "The mortality rate of wounded men who reached hospitals alive in World War II was less than half compared with the great war (World War I) due to the availability and liberal use of blood and plasma". Is it possible to draw the conclusion the mortality rate halved "due to" blood? The reference reads "the liberal use of blood and plasma played a major role". Is it likely

there were other significant changes in medicine between the two time periods? In addition it appears the JAMA article referenced is referring to a book available at: <https://collections.nlm.nih.gov/catalog/nlm:nlmuid-0014773-bk>

Reply 19: This has been reworded. Thank you for the book reference.

Line 389-395. This paragraph appears to be summarising the points made by the researchers in the following manuscripts:

- Trentino et al., Systematic reviews and meta-analyses comparing mortality in restrictive and liberal hemoglobin thresholds for red cell transfusion: an overview of systematic reviews. BMC Medicine, 2020.
- Trentino, K., et al., Observational studies - should we simply ignore them in assessing transfusion outcomes? BMC Anesthesiology, 2016.
- Faraoni, D et al., Randomized controlled trials vs. observational studies: why not just live together? BMC Anesthesiol, 2016.
- Trentino, K.M., et al., Restrictive Versus Liberal Transfusion Trials: Are They Asking the Right Question? Anesth Analg, 2020.

Reply 20: Thank you, the references have been added.

Line 400-403: no mention of the studies that have actually demonstrated the linking of data from

- Mukhtar SA et al. Anaesth Intensive Care 2013;4(2):207-15.
- Norgaard A et al. Blood transfusion 2014;12(4):509-19.
- Cohn CS, et al. Transfusion 2014;54(2):316-22.

Reply 21: Thank you for the references, this has been added.

Line 427-428: "A next-generation benchmarking tool includes PBM real-time data visualization to guide individual-provided decisions.(Ref 85). What makes this a next-generation benchmarking tool? How does it differ to the visualizations of Wintermeyer et al. [Transfusion, 2016] and Trentino et al. [Transfusion, 2016]? Did the authors mean "individual-provided decisions"? In either case can a retrospective data capture be used to guide decisions?

Reply 22: The statement is revised inform of new generation data visualization tool.

Line 431: "AI intelligence", use of intelligence twice

Reply 23: This has been changed as requested.

Line 437: ANN is just one of many machine learning models that can be used to predict outcome. This reviewer would argue that it is not an ANN per se that predicts best, rather the quality and accuracy of the underlying data collected. Other statistical and machine learning methods perform as well if not better depending on the problem at hand.

Reply 24: This has been changed per the reviewer's suggestion and an example of AI in transfusion medicine has been provided.

Line 443-445: How the authors jump from machine learning algorithms to the need for cross validation to the issue of alarm fatigue is confusing. The point is unclear.

Reply 25: This has been deleted.

Line 466: Sentence incomplete, paragraph unclear.

Reply 26: This has been modified for clarity.

Line 501: Sentence incomplete

Reply 27: The sentence has been modified.

Reviewer B

Line 47: "lives" missing

Reply 1: This has been added.

Line 50: Please consider integrating, or commenting on, the SABM definition of PBM.

Reply 2: Due to space constraints in the abstract this was not included and will be covered in another manuscript of the PBM series of this journal.

Line 69/70: Worth noting that the burden for PBM (incl. avoiding transfusions) is higher than what led to the current standard of care (including giving transfusions).

Reply 3: This section was removed per the other reviewer's comments.

Line 129: Grammar/typo; please proofread throughout, there were a few more.

Reply 4: This change has been made.

Line 148: It's --> Its

Reply 5: This change has been made

Line 234: Cell Saver(R) is a brand name; should either use generic name, or mention the company (Haemonetics) owning the trademark (and mention other companies and their devices; good review here: PMID: 31468332)

Reply 6: Removed Cell Saver and consistently used cell salvage. Quoted the PMID source.

238-244: Would use AABB definitions for contraindications. Also, some leaders in the field like Jon Waters are challenging these relative contraindications. Not all of them are evidence-based.

Reply 7: This change has been made.

Line 341: typo/grammar?

Reply 8: This has been reworded.

Line 465: Grammar/typo?

Reply 9: Our apologies as we could not find this concern.

Line 804/805: Malignancy is not a contraindication.

Reply 10: This has been removed from the table.

Would include reference to: Mueller MM, Van Remoortel H, Meybohm P, Aranko K, Aubron C, Burger R, Carson JL, Cichutek K, De Buck E, Devine D, Fergusson D, Folléa G, French C, Frey KP, Gammon R, Levy JH, Murphy MF, Ozier Y, Pavenski K, So-Osman C, Tiberghien P, Volmink J, Waters JH, Wood EM, Seifried E; ICC PBM Frankfurt 2018 Group. Patient Blood Management: Recommendations From the 2018 Frankfurt Consensus Conference. JAMA. 2019 Mar 12;321(10):983-997. doi: 10.1001/jama.2019.0554. PMID: 30860564.

Reply 11: This has been added to the manuscript.

Would include some of the clinical downsides of transfusion and highlight the independent increase in morbidity and mortality with every transfused unit

Reply 12: This has been added to the manuscript.

Would further build on transfusion trends, numbers of units utilized etc.

Reply 13: The most recent NBCUS data has been added to the conclusion.

Section about WWII and early days of blood banking should include work of Charles Drew.

Reply 14: This has been added to the Entry into the Modern Era of Transfusion Medicine.

Section about new technology and LIS, could talk about electronic systems for inventory management and remote electronic dispensing etc.

Reply 15: I have included ANN as an example that can be incorporated LIS, I don't think remote dispensing is relevant to the topic

Could be interesting to highlight different cross match practices in US versus EU. E.g., bed-side test etc.

Reply 16: The authors feel that this is beyond the scope of the manuscript.

Would consider the title to include "transfusion management", either in addition to PBM or replacing it.

Reply 17: The authors have reviewed and as patient blood management includes transfusion management and as this manuscript is part of a patient blood management series do not want to change the title at this point. Thank you for the comment.