

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The use of preoperative haemostasis and ABO blood typing tests in children: A retrospective observational study using a nationwide claims database in Japan
AUTHORS	Yonekura, Hiroshi; Ide, Kazuki; Kanazawa, Yuji; Takeda, Chikashi; Nakamori, Yuki; Matsunari, Yasunori; Sakai, Michihiro; Kawakami, Koji; Kamei, Masataka

VERSION 1 – REVIEW

REVIEWER	Aryeh Shander EHMC, USA
REVIEW RETURNED	18-Jun-2019

GENERAL COMMENTS	Interesting study corroborating adult data. Well done and needs just few minor adjustments. 1. "Medical Claim" should be changed to "medical billing". It might confused some readers. If possible, adding the burden (I am certain there are publications) of phlebotomy in children can be better described than "discomfort".
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REVIEWER	Ehrenfried Schindler Asklepios Klinik Sankt Augustin, Germany
REVIEW RETURNED	11-Jul-2019

GENERAL COMMENTS	<p>The enclosed study: „The use of preoperative hemostasis and ABO blood typing tests in children: A retrospective observational study using a nationwide claims database” is evaluating retrospectively the efficacy of preoperative coagulation screening in preventing bleeding complications in children. As a mJOR result the authors concluded that that the predictive value of preoperative hemostasis tests was poor.</p> <p>Comments: The study follows a retrospective, database review, observational, epidemiologic design. The study design is well described and without criticism. I congratulate the authors for this important work. Medical overuse especially in children should be avoided. The results of this study are in line with the results of many other studies in different countries according to the same topic. In the discussion the authors pointed out that outpatient surgery is not common in Japan. Nevertheless of the significance of this information for the reader this has nothing to do with prevalence of bleeding disorders and lab testing.</p> <p>Another small comment. On page 19 ff the authors are discussing the importance of “standard” coagulation system parameters like PT and PTT and its significance to identify preoperatively bleeding disorders. It might be worth to discuss a little bit more detailed that</p>
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	the most common congenital bleeding disorders like vWillebrands disease or F VIII deficiency are not detected by this parameters. IN older children a standardized questionnaire is superior or equal to lab parameters like some investigations have found. I have no further comments
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REVIEWER	Harriet Hiscock Murdoch Children's Research Institute Melbourne, Australia
REVIEW RETURNED	16-Sep-2019

GENERAL COMMENTS	<p>This is a well written manuscript addressing an important area - low value care practices in pathology testing pre-surgery in children. I have some minor comments which need to be addressed:</p> <ol style="list-style-type: none"> 1. Abstract - state up front that these tests might be unnecessary - otherwise it's unclear as to why you have examined them. 2. Abstract - state that you are only including non-cardiac surgery. 3. Data sources- you include claims from > 100 health insurance associations. What proportion is this (i.e. what is your denominator)? 4. Data sources- in this section, for international reviewers, explain whether this database covers inpatient, outpatient and ED claims and describe the public vs private service landscape in Japan. Were any private hospitals included in the dataset? 5. Study population- how valid are the codes that you used to exclude patients with high-risk comorbidities for bleeding? Has any work been done to examine the validity of these codes? If not, this should be mentioned as a limitation. 6. Individual clinician variation is common in low value care - did you have any access to data on clinician variation? If not, this might also be worth including as a limitation and potential for future exploration at a hospital/service level. 7. Discussion - on page 19, I don't think you can say "problems of low value care have not been well described, especially in paediatrics" given our 2018 SR found > 60 studies and there have been more published since. See: Hiscock H, Neely RJ, Warren H, Soon J, Georgiou A. Reducing unnecessary imaging and pathology tests: a systematic review. Pediatrics. 2018 Feb 1;141(2):e20172862. 8. Discussion- on page 21 you say the efficacy of pre-op coagulation tests remains controversial but your results suggest they are largely unnecessary - consider re-wording this to emphasize how much low value care is being done and the need to reduce these tests unless there is a clear clinical indication. 9. Similarly, in your Conclusion, I think you can be bolder and say more than "it is necessary to reconsider routine preoperative testing in this cohort". Given your MOR for inter-institutional variation was 2.89, could the next step be to compare high vs low ordering services to determine why some services are ordering more of these tests and for those that do, to learn how not to from their low ordering service counterparts.
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REVIEWER	GHALEB ELYAMANY PRINCE SULTAN MILITARY MEDICAL CITY, SAUDI ARABIA
REVIEW RETURNED	22-Sep-2019

GENERAL COMMENTS	the study limitations should be discussed adequately and in details
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VERSION 1 – AUTHOR RESPONSE

Response to Reviewer #1 (Dr. Aryeh Shander)

We wish to express our appreciation to the Reviewer for the insightful comments, which have helped us improve our manuscript significantly. We agree with all comments and have incorporated them into the R1 version of our manuscript.

Comment 1: "Medical Claim" should be changed to "medical billing". It might confused some readers.

Response: We appreciate the Reviewer's valuable suggestions. In accordance with the Reviewer's comment, we have modified the following text in the Methods section (page 8, lines 39):

Medical billing within 60 days before the index procedure

Comment 2: If possible, adding the burden (I am certain there are publications) of phlebotomy in children can be better described than "discomfort".

Response: Thank you for your valuable comment. As you have pointed out that children consider phlebotomy as one of the most frightening and painful health-related events. Pain experienced in childhood may have an impact on a child's life subsequently. Poorly managing their experiences can lead to increased distress in the future procedures, the development of needle fears, and potentially leading to health care avoidance behaviours:

In accordance with the Reviewer's comment, we have modified the following text in the Discussion section (page 20, lines 21–29):

The increasing number of blood tests can burden children and parents. As children consider phlebotomy as one of the most frightening and painful health-related events, frequent experiences can lead to increased distress in future procedures and development of needle fears, potentially leading to health care avoidance behaviours. [28]

Additionally, in accordance with the Reviewer's comment, we have added the following literature to the References to provide information about burden of phlebotomy (painful procedures) in children (page 29):

[28] Aydin D, Sahiner NC. Effects of music therapy and distraction cards on pain relief during phlebotomy in children. *Appl Nurs Res* 2017;33:164–8.

We wish to thank the Reviewer again for the valuable comments.

Response to Reviewer #2 (Dr. Ehrenfried Schindler)

We wish to express our appreciation to the Reviewer for the insightful comments, which have helped us improve our manuscript significantly. We agree with all comments and have incorporated them into the R1 version of our manuscript.

Comment 1: In the discussion the authors pointed out that outpatient surgery is not common in Japan. Nevertheless of the significance of this information for the reader this has nothing to do with prevalence of bleeding disorders and lab testing.

Response: We appreciate the Reviewer's valuable suggestions. In accordance with the Reviewer's comment, we have deleted the following text in the Discussion section:

Compared to other developed countries, ambulatory surgery is not popular in Japan (only 0.8% of general anaesthesia cases underwent surgery in the outpatient setting).[26,27]

Comment 2: On page 19 ff the authors are discussing the importance of "standard" coagulation system parameters like PT and PTT and its significance to identify preoperatively bleeding disorders. It might be worth to discuss a little bit more detailed that the most common congenital bleeding disorders like vWillebrands disease or F VIII deficiency are not detected by this parameters. IN older children a standardized questionnaire is superior or equal to lab parameters like some investigations have found.

Response: Thank you for your valuable comment. In accordance with the Reviewer's comment, we have added the following text to clarify the misuse of "standard" coagulation tests in the Discussion (page 19–20, lines 53–15) accordingly:

Standard haemostatic assessments (PT, aPTT, and platelet count) cannot help in detecting the most common congenital bleeding disorders, such as von Willebrand disease or haemophilia A, and cannot help in predicting perioperative bleeding risk. The predictive value of haemostatic tests (PT, aPTT, and platelet count) for determining perioperative bleeding risk of children undergoing tonsillectomy is generally poor, with a low sensitivity of <44% and a positive predictive value of <29%.^[7] In walking-age children, a standardized questionnaire (personal or family history of haemorrhagic diathesis) and physical examination are more sensitive than laboratory tests in the detection of bleeding risk.^[7,27] Additionally, in accordance with the Reviewer's comment, we have added the following literature to the References to present more details about the prognostic accuracy of standard haemostatic tests in children (page 28):

[27] Licameli GR, Jones DT, Santosuosso J, et al. Use of a preoperative bleeding questionnaire in pediatric patients who undergo adenotonsillectomy. *Otolaryngol Head Neck Surg* 2008;139:546–50.

We wish to thank the Reviewer again for the valuable comments.

Response to Reviewer #3 (Dr. Harriet Hiscock)

We wish to express our appreciation to the Reviewer for the insightful comments, which have helped us improve our manuscript significantly. We agree with all comments and have incorporated them into the R1 version of our manuscript.

Comment 1: Abstract - state up front that these tests might be unnecessary - otherwise it's unclear as to why you have examined them.

Response: We appreciate the Reviewer's valuable comments. In accordance with the Reviewer's comment, we have modified the following text in the Abstract section to clarify our objectives (page 2, lines 9):

Objectives: To describe the prevalence and factors associated with preoperative haemostasis and ABO blood typing tests for children because these tests might represent low-value care.

Comment 2: Abstract - state that you are only including non-cardiac surgery.

Response: We appreciate the Reviewer's valuable comments. In accordance with the Reviewer's comment, we have modified the following text in the all section to clarify our participants (page 2, lines 19):

Participants: Patients aged 1–17 years who underwent common non-cardiac surgeries

Comment 3: Data sources- you include claims from > 100 health insurance associations. What proportion is this (i.e. what is your denominator)?

Response: We appreciate the Reviewer's valuable comments. As estimated by the Japanese Ministry of Health, Labour, and Welfare, there are 1,405 society-managed health insurance associations in 2015 (<https://www.mhlw.go.jp/english/database/db-hh/5-1.html>). In accordance with the Reviewer's comment, we have modified the following text in the Methods section to clarify our data sources (page 7, lines 27–31):

with claims from approximately 18% of all society-managed health insurance associations in Japan.^[14]

Additionally, in accordance with the Reviewer's comment, we have added the following literature to the References (page 27):

[14] Japan Medical Data Center. Features of JMDC claims database, <https://www.jmdc.co.jp/en/pharma/>; 2016 (accessed 10 October 2019).

Comment 4: Data sources- in this section, for international reviewers, explain whether this database

covers inpatient, outpatient and ED claims and describe the public vs private service landscape in Japan. Were any private hospitals included in the dataset?

Response: We appreciate your valuable comments. Since the Japanese health care system is characterized by universal health care coverage and free access to hospitals, our database includes population-based longitudinal medical claims data (inpatient, outpatient, and ED claims) in all medical facilities, including public and private hospitals. In accordance with the Reviewer's comment, we have modified the following text in the Methods section to clarify our data sources in more details (page 7, lines 37, 41):

medical and pharmacy claims data (inpatient, outpatient, and emergency department)
and

In particular, the JMDC database contains claims data of employees as well as their families, who can access freely to any health care facility (public and private) under universal health coverage in Japan.

Comment 5: Study population- how valid are the codes that you used to exclude patients with high-risk comorbidities for bleeding? Has any work been done to examine the validity of these codes? If not, this should be mentioned as a limitation.

Response: We thank you for your valuable suggestion. The high-risk comorbidities for bleeding were assessed using the Quan modification of the Elixhauser comorbidity measure system. The Elixhauser comorbidity index is a validated measure of comorbidities (C statistics over 0.80) in the same databases in Japan [Japanese J Pharmacoepidemiol ekigaku 2019;24:53–64.]. However, each component of the Elixhauser comorbidity index has not been investigated in previous studies. In accordance with your valuable comments, we have added the following text in the Discussion section (page 22, lines 13–25):

The exclusion of patients with high-risk comorbidities for bleeding was based on ICD-10 codes using components of the Elixhauser comorbidities index.[18] Although the Elixhauser comorbidities index is a validated measure of comorbidities in insurance claims databases, similarly to that used in this study,[32] the diagnostic accuracy of each component was not validated in Japan. Thus, misclassification of comorbidities can lead to underestimation.

Additionally, in accordance with the Reviewer's comment, we have added the following literature to the References to discuss more details about the coding algorithms and validity of comorbidities (page 27, 29):

[18] Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9.

[32] Kimura T, Sugitani T, Nishimura T, et al. Validation and recalibration of Charlson and Elixhauser Comorbidity Indices based on data from a Japanese insurance claims database. *Japanese J Pharmacoepidemiol/ Yakuzai ekigaku* 2019;24:53–64.

Comment 6: Individual clinician variation is common in low value care - did you have any access to data on clinician variation? If not, this might also be worth including as a limitation and potential for future exploration at a hospital/service level.

Response: We thank you for your valuable suggestion. As you have pointed out, a recent study [N Engl J Med 2015;372:1530–8] demonstrated that preoperative testing before cataract surgery was more likely to be associated with the practice patterns of the physicians rather than with patients' comorbidities. Individual clinician variation plays important roles in low-value care. However, our database lacks data documented by the physician who ordered the preoperative tests. Thus, we could not investigate the effects of provider-related practice pattern. In accordance with your valuable comments, we have added the following text in the Discussion section (page 22, lines 41–59):

Fourth, we could not access the data from the physician who ordered the preoperative tests and could not investigate the effects of clinician-related practice pattern. A previous study of low-risk surgery revealed that the practice patterns of the physicians were more likely associated with the preoperative testing rather than patients' comorbidities.[22] In future exploration, it is necessary to determine whether the degree of variation is rooted at the institutional or individual provider levels.[33] Given that

our MOR for inter-institutional variation was 2.89, it would be important to compare institutions with high and low orders for these tests to investigate the reasons for their practice variation.

Comment 7: Discussion - on page 19, I don't think you can say "problems of low value care have not been well described, especially in paediatrics" given our 2018 SR found > 60 studies and there have been more published since. See: Hiscock H, Neely RJ, Warren H, Soon J, Georgiou A. Reducing unnecessary imaging and pathology tests: a systematic review. *Pediatrics*. 2018 Feb 1;141(2):e20172862.

Response: We thank you for your valuable comments and reference. In accordance with your valuable comments, we have modified the following text in the Discussion section (page 19, lines 19–21):

problems of low-value care have gained more attention recently

Comment 8: Discussion- on page 21 you say the efficacy of pre-op coagulation tests remains controversial but your results suggest they are largely unnecessary - consider re-wording this to emphasize how much low value care is being done and the need to reduce these tests unless there is a clear clinical indication.

Response: We thank you for your valuable suggestion. In accordance with your valuable comments, we have deleted the following text in the Discussion section (page 21, lines 31–39):

The preoperative coagulation tests before paediatric non-cardiac surgery are largely unnecessary. It is important to reduce these tests, unless there is a clear indication not only because of the low-value care, which provides little or no benefit at all, but also increasing cost of related health care. In 2016,

Comment 9: In your Conclusion, I think you can be bolder and say more than "it is necessary to reconsider routine preoperative testing in this cohort". Given your MOR for inter-institutional variation was 2.89, could the next step be to compare high vs low ordering services to determine why some services are ordering more of these tests and for those that do, to learn how not to from their low ordering service counterparts.

Response: We thank you for your valuable suggestion. In accordance with your valuable comments, we have modified the following text in the Discussion section (page 22, lines 49–59):

In future exploration, it is necessary to determine whether the degree of variation is rooted at the institutional or individual provider levels.[33] Given that our MOR for inter-institutional variation was 2.89, it would be important to compare institutions with high and low orders for these tests to investigate the reasons for their practice variation.

We wish to thank the Reviewer again for the valuable comments.

Response to Reviewer #4 (Dr. GHALEB ELYAMANY)

We wish to express our appreciation to the Reviewer for the insightful comments, which have helped us improve our manuscript significantly. We agree with all comments and have incorporated them into the R1 version of our manuscript.

Comment 1: the study limitations should be discussed adequately and in details

Response: We appreciate the Reviewer's valuable suggestions. In accordance with the Reviewer's comment, we have added the following text in the Discussion section to reflect the limitations (Page 22, lines 13–25):

The exclusion of patients with high-risk comorbidities for bleeding was based on ICD-10 codes using components of the Elixhauser comorbidities index.[18] Although the Elixhauser comorbidities index is a validated measure of comorbidities in insurance claims databases, similarly to that used in this study,[32] the diagnostic accuracy of each component was not validated in Japan. Thus,

misclassification of comorbidities can lead to underestimation.

And (Page 22, lines 41–59)

Fourth, we could not access the data from the physician who ordered the preoperative tests and could not investigate the effects of clinician-related practice pattern. A previous study of low-risk surgery revealed that the practice patterns of the physicians were more likely associated with the preoperative testing rather than patients' comorbidities.[22] In future exploration, it is necessary to determine whether the degree of variation is rooted at the institutional or individual provider levels.[33] Given that our MOR for inter-institutional variation was 2.89, it would be important to compare institutions with high and low orders for these tests to investigate the reasons for their practice variation.

VERSION 2 – REVIEW

REVIEWER	Harriet Hiscock Murdoch Children's Research Institute Australia
REVIEW RETURNED	28-Oct-2019
GENERAL COMMENTS	I am happy with this revised manuscript.