Peer Review File
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Reviewer Comments

Reviewer A

Comment 1: excellent paper which deals with laboratory stewardship and the adoption of management science to correctly implement laboratory stewardship in the specific clinical context.
Reply 1: We thank the reviewer for this positive feedback on the manuscript.

Reviewer B

Comment: This is an interesting Review of approaches to solving a crucial problem in Western medicine, inappropriate use of healthcare resources. The Review is scholarly and well-written. The purpose of any Review is to critically assess what is available in the literature and to allow readers to quickly understand the key elements of theory and practice. The authors have achieved this is an area that is not familiar to most readers.
Reply: We thank the reviewer for this positive feedback on the manuscript.

Comment 1: Suggest that the authors change 'lab stewardship' to 'laboratory stewardship.'
Reply 1: This change has now been made throughout the manuscript.

Comment 2: Abstract - line 23. 'spending on tests.' Isn't it costs or value of testing?
Reply 2: 'Spending on tests' has now been changed to 'costs'.

Comment 3: Abstract, line 31 - 'test use' is 'test utilisation' a better term?
Reply 3: We prefer to keep the term 'test use' since in this sentence we are referring to clinicians using tests as part of their practice (i.e. focusing specifically on test use as a behaviour) rather than the area of test utilisation more broadly.

Comment 4: Background. line 45. The problem with over utilisation is mainly in developed countries. In developing countries, the problem is underutilisation of testing.
Reply 4: Evidence syntheses indicate that under- utilisation occurs in high-income countries (Zhi et al. reference 1 in manuscript) and that over-utilisation occurs in low- and middle-income countries (Albarqouni et al. Overdiagnosis and overuse of diagnostic and screening tests in low-income and middle-income countries: a scoping review. BMJ Glob Health. 2022; 7(10): e008696), hence these problems are international in nature.

Comment 5: Background. A significant problem with inappropriate utilisation of testing is the environmental waste it generates (plastics, toxic chemicals).
Reply 5: We thank the review for raising this important implication of over-use. We have now incorporated this into the background, as follows:

> "Over-use also represents wasted healthcare resources which could have been better used, and increasingly, the negative impacts of over-use on the environment are being recognised (6–8)." (lines 50-51)

Comment 6: Line 64. There were significant reductions in test volumes - what impact did this have on patient care? It seems like most tests were inappropriately requested and performed?
Reply 6: One of the reviews summarised in the background section (Rubinstein et al. Reference 14) discusses impacts on patient outcomes. We have added the following summary of their findings to the manuscript:

> "This review also noted that initiatives were not associated with adverse impacts on patient-related outcomes (such as length of stay, morbidity, and mortality)." (lines 81-82)

Comment 7: Line 132. Who was on the multi-hospital lab stewardship committee? Why were they there and how were they selected?
Reply 7: Individuals in various roles relevant to stewardship issues were invited to join the committee. Further details about the committee have now been added to the manuscript, as follows:

> "We formed a multi-hospital laboratory stewardship committee to help guide our stewardship work. Individuals in various roles relevant to stewardship issues were invited to join the committee. As such, the committee includes those in the following roles: Laboratory Director, Laboratory Manager, Division Head, Physician, Patient Advisor, Quality Improvement Specialist, Implementation Scientist, Hospital Senior Management Representative." (lines 128-132)

Comment 8: Line 143 - what were the key metrics?
Reply 8: The key metrics vary depending on the specific stewardship project but may include a measure of test volumes, test costs, blood volumes, blood transfusions, and patient safety outcomes such as hospital length of stay and readmission. This has now been added to the manuscript, as follows:

> "For this step, we identify the key metrics to be measured at baseline and follow-up to evaluate initiative effectiveness and develop a plan for analyzing these metrics. Key metrics can include test volumes, test costs, blood volumes, blood transfusions, and patient safety outcomes such as hospital length of stay, readmission, morbidity, and mortality." (lines 143-146)

Comment 9: How was the project communicated to key stakeholders? There are informal discussions listed.
Reply 9: It is unclear which part of the manuscript the reviewer is referring to. Specific stewardship projects are regularly discussed with key stakeholders at relevant internal committees.

Reviewer C

Comment 1: Thank you for the opportunity to review your research. You have dedicated a lot of time and effort to outline the very important steps in the iterative process of quality improvement. It is of great need in the field of lab stewardship to have practical articles like the one you have written for administrators/scientists in various centers to apply the appropriate QI principles in their respective contexts.
Reply 1: We thank the reviewer for this positive feedback on the manuscript.

Comment 2: Because your article has a practical flavor, I believe it would be greatly enhanced if you could apply principles discussed in each section to a mock "case". This could even appear in a box which the reader could follow along. (e.g. Joe is scientist who works in the lab at University "x". He has noticed a lot of CBC's drawn....etc". And then Joe decides he wants to use a survey to explore reasons that clinicians order CBC etc. This would make it even easier to translate some of the lessons you are teaching to the real world. This could either be added as an appendix or sprinkled in throughout.
Reply 2: We thank the reviewer for this suggestion and have now included a mock case in the Supplementary Appendix. We have added the following sentence to highlight this in the manuscript:

> "A mock case in which a stewardship project team follows these steps is provided in the Supplementary Appendix." (lines 156-157)

Comment 3: As you have acknowledged, your evaluations section is thin. Unfortunately, this is the step which often leads to projects being noticed further success. As a result, your reader will want some more direction on how to achieve this. Not only will the above practical example be helpful to demonstrate a practical approach to evaluation, but I wonder if this section would benefit from mention of a few statistical tricks that can be used to reach statistical significance with smaller overall "N". For example, You will lead to this in your discussion saying RCTs are not usually feasible, but you do not provide practical tips on how this can be achieved. Here is an example for you to consider:
https://jlpm.amegroups.org/reviewer/submission/16377?key=RKJ8ZjHB
Reply 3: The link provided by the reviewer does not seem to work, and we are unsure what is meant by advice for reaching statistical significance with a smaller N. We had previously noted in the discussion that readers can consult detailed guidance on conducting RCTs of implementation interventions and we provided the reference for that guidance. We have now added an example evaluation within the mock case in the Supplementary Appendix and have provided some key metrics that can be used for evaluation purposes along with a statement emphasising the importance of clinical significance, as follows:

> "Key metrics can include test volumes, test costs, blood volumes, blood transfusions, and patient safety outcomes such as hospital length of stay, readmission, morbidity, and mortality. Targets for improvement should be clinically meaningful and realistic." (lines 143-146)

Comment 4: Again, I appreciate the opportunity to review your work and best of luck with the revisions.
Reply 4: We thank the reviewer for taking the time to review the manuscript and providing helpful suggestions for improvement.

Reviewer D

Comment 1: The importance of lab stewardship is established, and the authors build a case for using an implementation science approach to generate data that is useful in understanding stewardship problems and identifying relevant solutions. There are other steps in an overall project approach, but they are only addressed to a limited extent. However, the authors clearly clarify their focus on specific steps. Useful tools are suggested along with illustrations of how they are useful in the lab stewardship context. Table 3 is particularly notable here for demonstrating the myriad of barriers to reducing testing from the test-ordering clinician behaviour perspective.

Reply 1: We thank the reviewer for this positive feedback on the manuscript.

Comment 2: A limitation of this work is the discussion section. As written, it is largely a summation of what has already been presented, rather than being a robust dive into the broader meaning of the work and how it is situated in context of typical approaches to addressing lab stewardship initiatives. For example, what is the relationship of this approach to quality improvement approaches, which are quickly becoming the de facto approach in many lab stewardship studies and initiatives?

Reply 2: We have now added the following paragraph to the discussion which highlights the added value of implementation science approaches in this context:

> "While implementation science has to date not been widely used in laboratory stewardship initiatives, there is widespread use and advocacy for quality improvement methodology (55,56). Quality improvement methods, which tend to focus on processes and systems, can be highly useful for helping to close a specific local gap in quality, such as under- or over-use of tests. Quality improvement projects may be augmented with integration of implementation science approaches for specific purposes, including to i) determine barriers to change using existing literature and locally-gathered data; ii) design an intervention and develop the associated theory of change using evidence-supported theories and associated change techniques; and iii) support the spread of successful projects elsewhere by facilitating fulsome description of all of these elements of the initiative (57). From an evaluation and statistical perspective, integration of interrupted time series analyses offers an opportunity to strengthen the analyses approaches typically used in quality improvement projects (58)." (lines 420-430)

> Supporting references added:
55. Beriault DR, Gilmour JA, Hicks LK. Overutilization in laboratory medicine: tackling the problem with quality improvement science. Critical Reviews in Clinical Laboratory Sciences. 2021 Aug 18;58(6):430–46.
56. Eaton KP, Levy K, Soong C, Pahwa AK, Petrilli C, Ziemba JB, et al. Evidence-Based Guidelines to Eliminate Repetitive Laboratory Testing. JAMA Intern Med. 2017 Dec 1;177(12):1833–9.
57. Øvretveit J, Mittman BS, Rubenstein LV, Ganz DA. Combining Improvement and Implementation Sciences and Practices for the Post COVID-19 Era. J Gen Intern Med. 2021 Nov;36(11):3503–10.

58. Fretheim A, Tomic O. Statistical process control and interrupted time series: a golden opportunity for impact evaluation in quality improvement. BMJ Qual Saf. 2015 Dec 1;24(12):748–52.

Comment 3: The authors could also consider discussing more practical implications of the work, particularly in light of the hierarchical structure of the healthcare system. As it is, the few examples given are about the ordering professional, but there are many other actors, like administrators, pathologists, laboratory scientists, clinical chemists/hematologists/ microbiologists/etc, laboratory managers, laboratory technologists, and then of course the importance of the patient voice.

Reply 3: We wholeheartedly agree that it is essential to consider the multiple actors involved in the system when planning such initiatives and had made reference to this issue (lines 107-110; lines 168-179). We have now reiterated and expanded on this point in the discussion, as follows:

> "Whilst the examples provided in this article focus primarily on supporting change in the behaviours of clinicians involved in the test ordering process, it is important to reiterate that the multiple actors that are involved in the testing process more broadly should be identified and their potential role in the initiative considered at the outset of initiative planning. This may include hospital administrators, clinical biochemists, hematologists, microbiologists, laboratory managers, laboratory technologists, and patients. In some instances, these actors may themselves be targets for intervention. In others, they could play a key role in intervention delivery, or could serve on the project team responsible for developing and evaluating the initiative." (lines 412-419)

Comment 4: There are some instances of unclear writing or sentence structure errors and editing to improve conciseness is recommended. Example: line 298 with a potential typo or incorrect word use.

Reply 4: The identified typo has now been corrected and the manuscript has been reviewed for additional errors and opportunities to improve conciseness.