

ROUND 1

The Editor in Chief

World Journal of Clinical Cases

Dear Sir or Madam,

We would like to thank the reviewers for the time and the effort taken to review our manuscript (74021). We have read the reviewers' constructive criticisms and have made the necessary corrections.

Please allow us to submit a revised version with changes marked in bold type and also listed in point fashion below:

- Reviewer 1 Commented: "The data examined in the Caribbean are very poor, compared to the data in the literature review of high-volume centers for pancreaticoduodenectomy. From these situations, your conclusion, "despite low-volumes, the postoperative outcomes are acceptable with a modified centralization concept", cannot be obtained.

We note the comments from reviewer 1 and respect that this is their opinion. However, we believe this reviewer has missed the point we are attempting to make. We are not attempting to argue that the results in this setting are the same as those in high volume centres. In fact, we fully agree that the outcomes are better in high-volume centers.

What we are addressing in our paper is the fact that the majority of patients in low and middle-income nations do not have the option to have their pancreaticoduodenectomy performed in high volume hospitals in first world countries. Therefore, the centralization concept is simply not relevant to developing nations. In these nations, patients have no options but to have their pancreaticoduodenectomies done by low volume general surgeons – or in a facility with a modified centralization concept.

We have shown, with supporting data, that the results are better than the historic normal in these low volume countries. Therefore, we have made no changes in response to this comment.

- Reviewer 2 Commented: "In this paper, the authors review the evolution of the concept of the high-volume center and discuss the feasibility of this concept and the incorporation of PD into low-volume and resource-poor countries, such as those in the Caribbean. This paper has two parts. First, the authors performed a literature review evaluating studies published on outcomes after PD in high volume centers. The data in

the Caribbean is then examined and discuss the incorporation of this operation into resource-poor hospitals with modifications of the centralization concept. In conclusion, most patients who require PD in the Caribbean do not have realistic opportunities to have surgery in high-volume centers in developed countries. In these settings, their only options are to have their operations in the resource-poor, low-volume settings in the Caribbean. However, it has been demonstrated that, despite low-volumes, the post-operative outcomes are acceptable with a modified centralization concept. The authors discuss the strategies employed in this setting to ensure good outcomes. It is a topic of interest to the researchers in the related areas but the paper needs large improvements before acceptance for publication. My detailed comments are as follows: 1. In this review, the authors review the evolution of the concept of the high-volume center and discuss the feasibility of this concept and the incorporation of PD into low-volume and resource-poor countries, such as those in the Caribbean.

We thank reviewer 2 for their comments. This paragraph summarizes the contents of our paper, but no specific criticism or suggestion for change is made in this paragraph. Therefore, no change is required in response to this comment.

- Reviewer 2 Commented: 2. The authors perform a literature review evaluating studies published on outcomes after PD in high volume centers. The data in the Caribbean is then examined and discuss the incorporation of this operation into resource-poor hospitals with modifications of the centralization concept, but the part of Surgeon Volumes and CARIBBEAN EXPERIENCE are too verbose and should be shortened to 300 words and the part of **Male Fertility: How to Spot** It is too simple ,it should be discussed completely combined with references(should be add to 150-200words)

We thank reviewer 2 for their comments. However, the comments are confusing. The reviewer states that the “*part of Male Fertility: How to Spot It is too simple, it should be discussed completely combined with references.*” However, this paper does not have any “part on Male Fertility.” Our paper is discussing pancreatico-duodenectomy and centralization. Male Fertility has no part in this discussion and neither does a “how to spot it” section. I suspect that these comments may be in relation to another paper and, therefore, we have made no change in response to this comment.

However, the first comment that the Caribbean Experience is too verbose is accepted. The reviewer suggested that we shorten this to 300 words. In response, we have made significant changes to this section and reduced the word count from 732 words to 300 words.

- Reviewer 2 Commented: 3. The references are not up-to-date, references of the last 10 years should be cited, please cite last 10 years references ,especially references for the last 5 years. Please make large revisions of references, especially in the parts of introduction and the part of Surgeon Volumes and CARIBBEAN EXPERIENCE .After making large revisions,the paper may be considered for publication.

Thank you for this comment. The references have been completely revised, including more references from the last decade and reducing the number of self-citations. However, there are still some earlier references as these are important landmark papers that appear in the systematic review.

- Reviewer #3: Thanks for giving me the opportunity to revise the manuscript that deals with a topic I am keen on. Particularly, I find it novel and interesting, not in terms of the topic (“hospital-volume and outcomes of pancreatic surgery”) faced, that has been, instead, very investigated so far. Rather I appreciate the fact that it has been selectively applied to a geographic area (such as the Caribbean) that may be paradigmatic of poor-resource regions worldwide.

We thank reviewer 3 for the constructive criticisms. The comments are noted and no change is required in response to these comments.

- Reviewer #3: 1) Why do the Authors started the manuscript with a “literature review” of one page and a half of history of pancreatic surgery description? The topic is well known and the Authors do no need to re-examine what has been done in the last century. The manuscript may benefit from having its own structure, even starting from a literature review but of the concept of “hospital-volume and pancreatic surgery”, not of “pancreatic surgery” per sé.

We would like to thank reviewer 3 for this constructive criticism. We do agree that the historic review of pancreatoduodenectomy is over-reaching and well-known. Consequently, in keeping with the suggestion from reviewer 3, we have removed this section on literature review that discusses the history of pancreatoduodenectomy. The manuscript, therefore, moves from the introduction to the hospital volume theme. We do agree that this suggestion from reviewer 3 strengthens the manuscript.

- Reviewer #3: 2) The Authors state: “We conducted a systematic literature search”. However this form is simplistic. The Authors should at least provide the period of the research queries, and the search strategy adopted (this latter may be reported as Supplementary content).

The point made by reviewer 3 is noted and reasonable. Therefore, we have added four sentences to the section on “data from high volume centers” that explain the systematic literature review in detail. These lines now appear in the second paragraph, lines 6-12.

- Reviewer #3: 3) The manuscript by Balzano et al., BJS 2020, on the topic is missing at it should be added.

We thank the reviewer for bringing our attention to this important paper. It has been included in the manuscript data and discussion and added to the references.

- Reviewer #3: 4) “Caribbean Experience” chapter: can the Authors provide insights on the distribution and the HPB volumes of the three Caribbean Centers mentioned? Any info about the number of surgeries performed, apart from the caseload of T&Tobago? Which is the estimated incidence of pancreatic cancer, to mention the most frequent indication to pancreatic surgery, in the Caribbean? Any information about pancreatic surgery in the other Countries, such as Cuba, Dominican Republic, Puerto Rico, Giamaica? How do the health systems work? Are they mostly private, insurance-based? The readership may appreciate it.

We thank reviewer 3 for this comment. Some of this information is available – estimated incidence of pancreatic cancer, most frequent indication for pancreatic surgery is available. However, reviewer 2 definitively stated that the Caribbean Experience section was too long and asked that we significantly reduce the word count. In an attempt to do this, we have shortened this section. Consequently, we could only insert one line in this section to state that the most frequent indication for surgery was pancreatic adenocarcinoma and to state that the estimated incidence of pancreatic cancer was 4.5 per 100,000 population in 2019. This also required updated references from Rawla et al, 2019. We hope that this provides a compromise between the opposing suggestions from reviewer 2 and reviewer 3.

- Reviewer #3: 5) Considering their Caribbean Experience, can the Authors re-evaluate their considerations in light of the manuscript “A Partnership Model Between High- and Low-Volume Hospitals to Improve Results in Hepatobiliary Pancreatic Surgery”, Annals of Surgery, 2014? Is such a partnership model applicable to the Caribbean?

Thank you for this suggestion. We agree that this paper adds value to this manuscript. The concept is similar and we have included this in the manuscript. The reference is discussed in the section on partnerships.

- Reviewer #3: 1) The table 1 should include the year of the study, if not the study period as well.

Thank you for this suggestion. We have added the year of the study as well as the study period to the table.

- Reviewer #4 commented: This manuscript showed Whipple’s operation outcomes in low-volume caribbean centers. This paper is interesting. However, it dose not receive a high enough for publication. 1, There are two Table 1 in this paper. Please make renumbering tables 2,

In keeping with the suggestion from reviewer 4, the tables have been re-numbered from table 1 to table 5.

- Reviewer #4 commented: Table 1 (Hospital volumes) showed that the perioperative mortality in high-volume centers was high. Is it correct?

In follow up with the reviewer's query, we have double checked the information presented in Table 1. The error has been corrected and the data entered under the correct heading in the tables.

- Reviewer #4 commented: 3, The authors said that Table 2 outlines the proportion of PDs performed by low-volume hospitals in developed countries. Where were the data of low-volume hospitals in developed countries?

That you for this comment. The peri-operative mortality for low volume hospitals in developed countries has already been presented in table 1. Column 2 in Table 1 is dedicated to presenting the mortality outcomes from low-volume hospitals in developed countries. Therefore, no change has been made.

- Reviewer #4 commented: 4, Please show the data of Caribbean countries using table. There was weak evidence to support the conclusion in this paper.

We agree with reviewer 4 that the relevant data would be valuable in a table. However, there is very little published on PD from the Caribbean region. Nevertheless, we have added table 6 to visually represent these data.

- Reviewer #5: The concept presented here is very interesting. The analysis of the significance of hospital volume and surgeon volume in particular provides an important basis for the discussion. The data will certainly be of interest to our readers. However, a serious mistake must be corrected. The first PD was not carried out by Whipple, but by Walter Kausch 25 years earlier. Kausch W. Das Carcinom der Papilla duodeni und seine radikale Entfernung. Beiträge zur Klinische Chirurgie. 1912;78:439-486.

Thank you for this encouraging comment. We do apologize for the error in not attributing the first PD to Walter Kauch in 1912. We would have made this correction, but reviewer 3 has asked that we remove the entire section on a review of pancreatic surgery and PD as it is not necessary for an audience experienced with PD. We thought this was a reasonable point and so the history section has been omitted.

- (8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue

sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.

Thank you for this comment. However, there are no figures included in this manuscript. Therefore, no changes are required in response to this comment.

- **Tables:** Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.

We confirm that all abbreviations used in the tables have been defined directly beneath each of the tables.

- The Science Editor commented: The manuscript analyzes the importance of hospital capacity, especially surgeon capacity. I find it an interesting study. 1. Research data in underdeveloped areas such as the Caribbean are very poor.

Thank you for this comment. We agree that there is a paucity of research data from underdeveloped areas such as the Caribbean and we are happy to be given the opportunity to add to the data. No changes were made in response to this comment.

- The Science Editor commented: 2. Self-Citation Count:4 The self-referencing rate should be less than 3%.

We have reduced the self-citations in this paper to only 3 references out of 56. This works out to a self-citation rate of 5%, but we cannot reasonably reduce the citation rate any further and still have meaningful discussion about Caribbean data.

- The Science Editor commented: 3. It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly.

We do not understand this recommendation. After a systematic literature review was done, the relevant citations were referenced. Most of these articles would be published in high quality journals and, therefore, these journals would contain several good articles. We think it would not be reasonable or honest for us to exclude these high-quality papers just because of the name of the journal it was published in. We respectfully ask for this to be reconsidered.

- The Science Editor commented: 4. The format of the table should be a three-line table.

This comment is vague. We are not sure if the editor means three-columns or three rows? Each row has lines – so we are not sure if they are referring to lines within the rows? No change has been made in response to this comment as the comment is unclear.

- Requirements for Article Highlights: If your manuscript is an Original Study (Basic Study or Clinical Study), Meta-Analysis, or Systemic Review, the “Article Highlights” section is required. Detailed writing requirements for the “Article Highlights” can be found in the Guidelines and Requirements for Manuscript Revision.

Thank you for this comment. This was an invited opinion piece. As such, article highlights are not necessary according to these instructions.

- Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as “74021-Figures.pptx” on the system. The figures should be uploaded to the file destination of “Image File”. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper).

Thank you for these comments. However, there are no figures included in this manuscript. Therefore, no changes were made in response to this comment.

- (2) Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as “74021-Tables.docx” on the system. The tables should be uploaded to the file destination of “Table File”.

The tables have all been saved separately as a word file named 74021-Tables.docx and uploaded separately.

- Step 6: Automatically Generate Full-Text Files. Authors cannot replace and upload the “Manuscript File” separately. Since we only accept a manuscript file that is automatically generated, please download the “Full Text File” or click “Preview” to ensure all the contents of the manuscript automatically generated by the system are correct and meet the requirements of the journal. If you find that there is content that needs to be modified in the Full-Text File, please return to the corresponding step(s), modify and update the content, and save. At this point, you then have to click the "Save & Continue" button in Step 5 and the F6Publishing system will automatically regenerate the Full-Text File, and it will be automatically stored.

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However, we have not received any email correspondence regarding the copyright license agreement. We would be grateful if this could be re-sent.

In fact, we have received no email correspondence at all about our manuscript. All instructions were found incidentally by logging onto the F6 system and there is no function to download a copyright agreement there.

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- CONFLICT-OF-INTEREST DISCLOSURE FORM
We have downloaded and completed the ICMJE form for disclosure and conflicts.

We would like to again thank the authors for their constructive criticisms and the journal for the opportunity to submit a revised version of our work.

Regards

Shamir cawich

ROUND 2

The Editor in Chief
World Journal of Clinical Cases

Dear Sir or Madam,

We would like to thank the reviewers for the time and the effort taken to review our manuscript (74021). We have read the reviewers' constructive criticisms and have made the necessary corrections.

Please allow us to submit a revised version with changes marked in bold type and also listed in point fashion below:

- Reviewer 1 Commented: "The paper reviewed the evolution of the concept of the high-volume center. And discussed the feasibility of this concept and the incorporation of PD into low-volume and resource-poor countries, such as those in the Caribbean. Results are good, and the figures are clear

Thank you for this comment. There are no corrections required in response to this comment.

- Reviewer 1 Commented: "The language is fluent"

Thank you for this comment. There are no corrections required in response to this comment.

- The references are not up-to-date, references of the last 10 years should be cited, please cite last 10 years references, especially references for the last 5 years.

The references have been revised, including more references from the last decade. Earlier references still appear and we are not willing to remove as these are important landmark papers that appear in the systematic review.

- The tables should use the format of 3-line table, please revise the format of the tables to 3-line table, especially Table1-6.

This comment is vague. We are not sure if the reviewer means three-columns or three rows? Each row has lines - so we are not sure if they are referring to lines within the rows?

Really, there is no way to condense this information into a table of three rows or lines or even columns. We do not believe this is a reasonable request.

- Please make some revisions, especially in the parts of references. After making some revisions, the paper may be considered for publication.

The references have been revised. There are still earlier references that we are not willing to remove as these are important landmark papers that form a part of the systematic review.

- Reviewer 2 Commented: “In its present form, the manuscript should be published in our journal.”

Thank you for this comment. There are no corrections required in response to this comment.

- Reviewer 3 commented: “This manuscript showed Whipple’s operation outcomes in low-volume caribbean centers. This paper is well revised and acceptable for publication.

Thank you for this comment. There are no corrections required in response to this comment.

We would like to again thank the authors for their constructive criticisms and the journal for the opportunity to submit a revised version of our work.

Regards
Shamir Cawich