Author’s response to reviews

Title: Factors Associated with Prolonged Length of Stay for Elective Hepatobiliary and Neurosurgery Patients: A Retrospective Medical Record Review

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Author’s response to reviews:

Responses to Editor and Reviewers

BHSR-D-17-00090

Comments by and Responses to Editor:

1. “Your manuscript "A Retrospective Medical Record Review of Risk Factors Associated with Prolonged Length of Stay for Elective Hepatobiliary and Neurosurgery" (BHSR-D-17-00090) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Health Services Research.”
2. “Thank you for submitting your valuable manuscript into the BMC Health Services Research. Our three reviewers reviewed your manuscript. They said that your manuscript has several critical issues to be resolved. However, they also said that your manuscript has meaningful study results as well. So, I would like to give you further opportunity submitting revised manuscript again. Please carefully read the three-reviewer's comments and submit the revised manuscript again with your note on how you handled the reviewer's comments. Publishable article format with thorough research methods will be deeply appreciated and considered as an opportunity of publication. Current version of the manuscript does not reach to the publication level. I hope to see your revised manuscript pretty soon! Cheers!”

Thank you very much for the opportunity to revise this paper for BMC Health Services Research to communicate the results of our study with sharper focus. We appreciate the comments made by the 3 Reviewers and have attempted address each of them to improve the paper. We are gratified that the reviewers were consistent in their comments and so believe that we have adequately addressed them all. As the result, this paper has greatly expanded, although we believe in an efficient way. Please note that when we refer to a page number, page 1 starts with the abstract. We hope our revisions meet with your and their expectations. Thank you again for an opportunity to improve this paper for BMC Health Services Research.

Comments by and Responses to Reviewer 1:

1. “Although this study investigate an important issue for healthcare providers to care patients with prolonged stay in the hospital, I hesitate to recommend publish as there are some substantial drawbacks in the work.

First, the writings are not clear throughout the manuscript, and a professional editor may be of help.”

Thank you very much for the opportunity to revise and present the results of this study, which seeks to explore areas in the operative pathways that influence prolonged length of stay (LOS). Thank you for your suggestion to engage a professional editor to make the writing clearer. We hope the paper is now easier to read and meets with your expectations.
2. “Second, I cannot see any rationale of studying such important issue in HPB and NS patients. Why did the authors want to investigate the two types of patients?”

Thank you for your question. We have included information in the Background on pages 5 and 6, related to the rationale for investigating these two types of patients as follows, “HPB malignancies, liver tumors, and other liver diseases have the highest incidences in Asia and Southeast Asia compared to the rest of the world due to widespread hepatitis B virus infections [17]. Surgery remains the only option for treatment. However, in Asia HPB procedures are variable and their care management practices are not standardized [18]. Consequently, the LOS for HPB surgical patients varies widely. For NS, the demand for such surgeries is expected to increase because of improved surgical procedures in craniotomy and cranioplasty for intracranial aneurysms, brain tumors, and other cerebrovascular diseases as well as aging populations and changes in lifestyle in developed countries, including Asia [19]. By explicating factors associated with prolonged LOS for HPB and NS elective surgeries, hospitals can design better patient management services [20].” We hope the rationale we gave met with your expectations. Thank you.

3. “Third, I would like to know the details of how the current literature focuses only on the partial perioperative pathways. Do the authors mean that no literature looking at one of the pre-, intra-, or post-operative periods?

Based on the above statements, it looks like current literature has investigated in the intra- and post-operative periods.

Or, do the authors mean that the current literature only look into a certain period of the perioperative period? If this is the case, what makes the differences between three studies separately investigate pre-, intra-, and post-operative periods and one study investigates the entire perioperative period?”

Thank you for your comments. The entire perioperative pathway includes pre-, intra- and post-operative pathways. We have provided more information in the Background on page 8, related to the combination of the perioperative pathways that past studies focused on, “Freitas et al. [7], Reponen et al. [44], and Lukasiewicz et al. [21] focused on the patients’ preoperative clinical conditions, Morimoto et al. [13] investigated preoperative and intraoperative clinical factors, while Collins et al. [2] considered intraoperative and postoperative factors. These studies could not rule out confounding factors from the partial pathway that would otherwise be non-
significant on prolonged LOS if the entire perioperative pathway was considered. In this study, we examined perioperative factors in the entire surgical pathway. By assessing the simultaneous impact of these factors on prolonged LOS, hospitals can set reasonable preoperative expectations for patients and the healthcare team, establish efficient operative protocols, or plan postoperative treatment care and improve discharge planning for patients. Our approach is more likely to yield a more comprehensive surgical services protocol for the entire perioperative care continuum for elective HPB and NS patients.”

While we agree that one could derive generalized insights from looking at all the partial pathway studies in aggregate, we think that there is still value in a simultaneous investigation of the entire perioperative pathway. This approach may yield insights that aggregated partial studies are not able. For example, a significant factor found in a partial study may become insignificant when the entire pathway is considered. Additionally, factors in the pathway may be related to one another, so that a significant factor in the post-operative period may be driven by a factor in the pre-operative period. Hence, the right approach may be to deal with the problem at the pre-operative period. We hope we have communicated how our focus on the entire perioperative pathway contributes to the literature.

4. “Fourth, the statistical analyses are quite confusing. It looks like that the authors group the participants into four groups based on the LOS duration: very long, long, short, and very short. Then, the authors compare long vs. short; very long vs. very short.

However, they did not mention this in the statistical analysis section, and I wonder why they did not compare the four groups but compared every two groups. The redundant comparisons may cause the inflation of Type 1 error.

Also, the Tables are not in good shapes, and I feel very difficult to read them.”

Thank you for pointing out that the results were communicating 4 types of LOS duration. Since this is not our purpose, we have now reanalyzed the results using the common definition of prolonged LOS as above the median LOS. We did this following, Collins et al (1999) and Morimoto et al (2015), as stated in the Measures section on page 10. By removing the outlier definition of prolonged LOS at the 75th percentile, we would also reduce any inflation of Type 1 error that you highlighted. Thank you for your very helpful suggestion. We have revised the paper to focus only on comparisons between above the median LOS (prolonged LOS) and below the median LOS (shortened LOS) that is normal of each type of surgery, accounting for surgical
complexity. We hope that you agree with our decision. We have re-structured the tables and hope they are now easier to follow. Thank you very much again for your insightful comment.

5. “Fifth, although this study is not theory-driven, I wonder how the authors define these risk factors, and why these risk factors are belonged to the pre-, intra-, or post-operative period. For example, why only used lab data and assessments for fall risks in the preoperative period, but not for the postoperative period?”

Thank you for your comments. We have eliminated the term ‘risk factors’ and only use the word ‘factors’ since the purpose of the study is to identify factors that are related to prolonged LOS. The use of the word ‘risk’ was presumptive and therefore we apologize for that. The factors were identified after a thorough literature review of perioperative predictors of LOS. The factors that were chosen in this study were typical of preoperative, intraoperative and post-operative surgical pathways.

We discussed this in the Background section from pages 6 to 8, “…common preoperative patient factors associated with prolonged LOS are the patient’s demographics and presenting conditions at the time of admission [21]. Studies have shown that age, gender, functional status, diagnostic or illness factors, and the major procedure group for surgical patients influenced LOS [2, 3, 12, 13, 14, 22]. Specifically, age was related to prolonged LOS for patients undergoing aortic surgery [23]. In general, elderly patients undergoing a major surgery faced higher risks of bleeding and other physiological dysfunctions that may slow recovery and contribute to prolonged LOS [24]. Seicean et al. [15] found that elective spine surgery patients with higher body-mass index (BMI) reported poorer outcomes. The Braden score on admission, which identifies patients at higher risk for pressure ulcers, was found to predict prolonged LOS for patients undergoing liver transplantation [25], while malnutrition on admission slows recovery [26]. Patients who are frail and cannot ambulate independently have a low functional status score and were reported to have prolonged LOS following elective lumbar spine and arterial vascular surgeries [27, 28]. Comorbidity also predicted prolonged LOS [29]. Gruskay et al. [16] found that the total number of comorbidities predicted prolonged LOS after elective lumbar surgery. Likewise, the number of abnormal laboratory results (labs) indicate the severity of patients’ health status, which influences how fast they will recover after surgery. Fall risk is measured by assessing the patient’s level of confusion, dizziness, altered elimination, and difficulty with mobility at admission [30, 31]. Preoperative fall risks have been found to predict postoperative falls, functional decline, and surgical complications, all of which prolonged LOS [32].
Occupational therapy (OT) improves walking capacity, muscle strength, flexibility, balance, and endurance so patients can quickly return to active lifestyles [33, 34]. However, patients need a minimum capacity to do OT, and preoperative physiotherapy (PT) has been shown to improve exercise tolerance for patients undergoing lung transplantation [35].

Preoperative hospital administrative system factors that contribute to LOS include delays in investigation and procedures [36] as well as the day and time of admission [37]. For example, patients admitted during weekends, on the eve of public holidays, or after 5pm often face delays in the initial physical examination and diagnostic tests due to diminished availability of staff and expertise. In general, perioperative patient care after office hours is limited by a reduced clinical crew. Consequently, the day and time of admission have been associated with increased LOS, preventable adverse events, and mortality of patients with pulmonary embolism and myocardial infarction [37, 38].

Intraoperative variables that affect LOS include the duration of preoperative preparation [39] and operation time [2]. For example, for patients undergoing surgery for endocrine tumor, the duration of preoperative preparation for anesthesiologic management, fluid management, medications involving anti-hypertensive medications, alpha, beta, or calcium channel blockers, and antibiotic prophylaxes, were associated with prolonged LOS [39]. Delays or conflicts in preoperative preparation may lead to a cancellation of the surgery, which further increases LOS. Chang et al. [23] found that operations lasting more than 5 hours, which may be related to intraoperative blood loss, were associated with prolonged LOS for patients undergoing aortic surgery.

Postoperative variables that affected LOS include the number of complications after surgery and hospital-acquired infections (HAI) [2, 23, 40, 41]. For example, complications such as urinary tract infection and pneumonia led to prolonged LOS following cervical discectomy and fusion [41]. Postoperative treatment for wound or surgical site infections [23], polypharmacy [40, 42] where multiple drug consumption increased the risk of drug interactions and adverse reactions, as well as use of dialysis, ventilator support, and other tube insertions [3] also contributed to LOS. Other hospital acquired nosocomial infections include bacterium infections from clostridium difficile colitis [43] or methicillin-resistant Staphylococcus Aureus [6]. Research has also shown that discharge planning affects LOS, where discharge to a nursing home was associated with prolonged LOS by 89% for surgical patients compared to being discharged to home [3, 36].”
We hope that the literature we provided to support our choice of predictor variables meet with your expectations. Thank you.

6. “Lastly, because I feel that the statistical analyses and the rationale of classifying pre-, intra-, and post-operative factors are not clearly presented, please note that I did not review the Discussion. I would like to review the manuscript again if the authors revise it in a good shape, and I hope that my comments are of help.”

We hope that our explanations for why factors were listed as pre-, intra-, and post-operative factors have been clearly explained in the paper. Again, these were derived from the literature, as described in our response to your point 5, above. Because there were many factors, we utilized Student’s t-tests and logistic regression to focus only on those factors that predict prolonged LOS in our sample, as discussed in the Statistical Analysis section on page 11. We hope you would be willing to review the paper again. Thank you.

7. “Some specific comments are as follows:

1. In abstract, (1) I cannot understand what the authors said in "prolonged LOS was defined as above median LOS and above the 75th percentile LOS". Do the authors define two prolonged LOSs? If this is the case, do both prolonged LOSs have the same predictors in HPA and NS patients, respectively?

After I read the Methods in the main text, I understand that the authors defined very long, long, short, and very short LOS. However, this is not clear for those who only read the Abstract.”

Thank you for highlighting the confusion we created with 2 definitions of prolonged LOS. We have now focused only on above median LOS as prolonged LOS and below median LOS as shortened LOS in accordance to the definitions used by Collins et al. [2] and Morimoto et al. [13], as described in the Measures section on page 10. The purpose of this study is to explore which factors affect HPB and NS patients respectively since the patients’ conditions leading to each type of surgery is different (preoperative factors), intraoperative factors are different, and even post-operative care are different. We do not presume that the same factors affect HPB and NS patients similarly.
(2) “I feel somewhat weird in the description of "Practices that enhanced prolonged LOS for both HPB and NS samples were longer intervals between admissions and surgery, longer intraoperative preparations, and longer operation durations after adjusting for surgical complexity."

If the patients have prolonged LOS, of course they may have all the above duration being longer. If not, why do the patients have longer stay?

The point is what makes these procedures longer (i.e., why these patients had longer interval between admissions and surgery, and so on.)”

Thank you for the comment, which indicates that we were unclear in our construct operationalization. We tried to simplify the definition of process duration by breaking up a continuous variable into long, short, etc. Obviously, this did not work. As a result, we have removed the variable ‘interval between admissions and surgery’ from the analysis and used preoperative duration and operation duration as the original continuous variables, without recoding them into short, long, or longer durations. Consequently, the results in this revision is slightly from the first version of the paper since this variable had a very strong influence on prolonged LOS, as one might imagine.

(3) “I cannot understand "fall risks" in the sentence. Do the authors mean that risk for fall (e.g., inappropriate bed; slippery floor), or do the authors mean how many times a patient fell down?

I also cannot understand the number of fall risks should belong to pre-, intra-, or post-operative factors.”

Thank you for your comment. Fall risk is defined in the literature. It is the likelihood that a patient will experience a fall because of some physiological and cognitive factors. We referred to the literature to define fall risk, in the Background section on page 10, as “assessing the patient’s level of confusion, dizziness, altered elimination, and difficulty with mobility at admission [30, 31]. Preoperative fall risks have been found to predict postoperative falls, functional decline, and surgical complications, all of which prolonged LOS [32]”. We hope we have adequately answered your question about the meaning of fall risk and why it should be seen as a preoperative factor rather than an intra- or post-operative factor. Thank you.
(4) “Please keep using the defined abbreviations; that is, LOS, HPB and NS.
Please avoid using inconsistent word; e.g., intra-operative or intraoperative.”

Thank you for your comment. We have kept to the defined abbreviations and avoided using inconsistent words as you suggested. Thus, we have used LOS, HPB, NS, preoperative, intraoperative, and postoperative throughout the paper to be consistent. Thank you.

2. “The first sentence in the Introduction, I do not think that scarce is a good word here because this may let the readers think that patients with LOS do not use any hospital resources at all.”

Thank you for your comment. We have changed the word to ‘more’ to indicate that patients with prolonged LOS utilize more hospital resources.

3. “It is weird to see the statement of "Our contribution is to the literature on surgical safety and quality of care that influence LOS" and with citations.
If this is the contribution of the study, the statement should be put in the Discussion section, and clearly indicate what contributions are. If the contribution belongs to other studies, why did the authors cite other references?”

Thank you for your insightful observation. We have removed the citations at the end of the statement that specified our contributions. Instead, we have motivated our study with a lot more literature and accompanying citations, in the Background section from pages 5 to 9, to justify our choosing HPB and NS, and choice of factors that represent the preoperative, intraoperative, and postoperative pathways. We hope that our explanations for our contribution is clearer and we have adequately stated our contributions to the existing literature.
4. “The second paragraph in the Introduction, the authors have mentioned something in patient-level factors, but they did not clearly indicate what the system-level factors are.”

Thank you for your comment. We now specify that systems factors in the Background section on page 7, as “…hospital administrative system factors that … include delays in investigation and procedures [36] as well as the day and time of admission [37]”. We hope we clarified that system-level factors refer to the hospital administrative policies and functions.

5. “As the authors mentioned that they want to investigate their study in a major international academic center, I wonder how they justify that the tertiary academic hospital in Singapore is a major international academic center.”

Thank you for pointing out our poor choice of words to suggest that our study site is a major international academic center. Instead, we have modified the term in the Design and Setting section on page 9 as, “…tertiary academic center in Singapore, which was the first to receive the Joint Commission International accreditation in the country [47]. Our study site mirrors bed shortages in public hospitals in urban environments as well as incidences of HPB malignancies and demand for NS due to an aging population [48]”. We hope that this meets your expectations that this hospital is an academic center that meets international standards for clinical practices.

6. “The authors should clearly define that very long LOS is above the 75th percentile; long LOS is above the median, short is below the median, and very short is below the 25th percentile.”

Thank you for your insightful observation that we have created a perception of 4 types of LOS duration. Since that is not the purpose of our study, we have now defined prolonged LOS to be above median LOS and thus, shortened LOS is defined as below median LOS in accordance to the extant literature by Collins et al. (1999) and Morimonto et al. (2015), in the Measures section on page 10. We hope that focusing on only 1 definition of prolonged LOS removes some confusion and meets with your expectation. Thank you.
7. “Page 7, "smoking use" is somewhat weird. I think that "tobacco use" is better.”

Thank you for your comment. We have changed the word in the Measures section on page 10 to ‘smoking history’ because ‘tobacco use’ may involve chewing tobacco and not just smoking. We hope you agree with our more precise use of the term. Thank you.

8. “Page 7, what are the lab data? Virus testing, blood pressure, HbA1c, or anything?”

Thank you for your comment. We have changed the term to laboratory results (labs) in the Background section on page 6, which is consistent with the use of this term in the manuscript and tables. The list of lab results that are considered in this study is found in Supplemental Table 1, which includes data for urea, creatinine, potassium, hemoglobin, hematocrit, serum albumin, leucocytes/TWC, prothrombin time, and International Normalized Ratio (INR).

9. “Page 7, what are the fall risks? How did the authors measure this? Did the authors use any standardized instrument?”

We defined fall risk in the Background section on pages 6 and 7 as, “…assessing the patient’s level of confusion, dizziness, altered elimination, and difficulty with mobility at admission [30, 31]. Preoperative fall risks have been found to predict postoperative falls, functional decline, and surgical complications, all of which prolonged LOS [32]”. Supplemental Table 1 also defines fall risks as the risk of falls due to altered mental states, dizziness, altered elimination, and lower limb weakness. These states are clinically assessed using a Falls Assessment Tool as described by Yip et al. (2016). We hope we have adequately answered your question to the satisfaction.

Thank you very much for your insightful and detailed comments. We appreciate very much for the opportunity to revise this paper. From your comments and suggestions, we have attempted to sharpen and focused the paper. Specifically, we have provided more literature to support the
importance of the study and choice of variables in the Background section between pages 5 to 9. We have also clarified our definition and measurement of prolonged LOS, which is in accordance with the literature from Collins et al. (1999) and Morimoto et al. (2015) in the Measures section on page 10. We hope our revisions have met with your expectations. Thank you very much for your guidance to improve this paper.

Comments by and Responses to Reviewer 2:

1. “This is a retrospective cross-sectional study to identify the associated factors of prolonged length of stay (LOS) regarding the hepatobiliary (HPB) and neurosurgeries (NS). The variables should be over-comprehensive and some are not well-justified. The background and discussion is too brief and superficial. However, the findings is important to inform the health care policy and operation plan. I hope to read a revised manuscript.”

Thank you an opportunity to revise this paper. We appreciate your comments and your endorsement that the findings are important to inform health care policy and operations. We have provided more information on the background of the study, justification for the choice of variables and samples, and discussion of the results. We hope that our revision meets with your expectations. Thank you.

2. “Background:

P3. line 20-23, The reason of choosing the elective procedure for this study is not sound enough. Some reasons may be related to the representativeness or sample variance (like limited some confounding factors).”

Thank you for your insight. We have provided more reasons to choose elective procedures in this study. Generally, the rationale is policy driven, because these procedures are managerially meaningful. Specifically, we write in the Background section on page 5 that, “Surgical services represent approximately 30% of all hospital expenses [8] and elective surgeries are far more common than emergency operations [9]. Unlike emergency admissions where it is difficult for
hospital administrators to influence pre-admission factors, knowing the factors that increase LOS in elective surgeries can allow hospital staff to proactively influence the delivery of care and demand for beds [10]. Since hospitals can more readily manage hospital bed capacity in elective than emergency surgeries, identifying factors related to prolonged LOS in elective surgeries can reduce the utilization of scarce hospital beds.”

We further explain in the Background section on pages 5 and 6 that, “While past studies have explored the factors associated with prolonged LOS after cardiac [11], laparoscopic cholecystectomy [12, 13, 14], and spine [15, 16] surgeries, no studies have explored the factors that lead to prolonged LOS in hepatobiliary (HPB) and neurosurgeries (NS). HPB malignancies, liver tumors, and other liver diseases have the highest incidences in Asia and Southeast Asia compared to the rest of the world due to widespread hepatitis B virus infections [17]. Surgery remains the only option for treatment. However, HPB procedures are variable and their care management practices are not standardized [18]. Consequently, the LOS for HPB surgical patients varies widely. For NS, the demand for such surgeries is expected to increase because of improved surgical procedures in craniotomy and cranioplasty for intracranial aneurysms, brain tumors, and other cerebrovascular diseases as well as aging populations and changes in lifestyle in developed countries, including Asia [19]. By explicating factors associated with prolonged LOS for HPB and NS elective surgeries, hospitals can design better patient management services [20].”

We hope our justifications for choosing elective HPB and NS surgeries in this study meet with your expectations. Thank you.

3. “P4, line 9-11. It is strange to state the ethical consideration in the section of "background".”

Thank you for your comment. We have moved the statement on IRB to the Methods section on page 10. We hope that doing so meets with your expectations. Thank you.

4. “The entire background is too brief.”
Thank you for your comment. We have provide more information in the background section in pages 5 to 9 on the aims of this study, more literature review to indicate why this study is necessary and how it aims to contribute to the field as follows, “Length of stay (LOS) is an important measure of resource utilization as patients with prolonged LOS disproportionately account for the consumption of more hospital resources [1]. Prolonged LOS, which is defined as inpatient stay that exceeds the expected LOS for a certain procedure [2], utilizes hospital bed capacity, contributing to shortage. Inpatient bed shortage delays elective admissions and increases emergency department boarding, which denies critically ill patients timely access to treatment as inpatient care conventionally begins only after the patient arrives at the assigned inpatient ward [3, 4]. Patients with prolonged LOS are also at higher risks of nosocomial infections and unplanned readmissions [5, 6]. In short, prolonged LOS disadvantages both hospitals and patients [7].

Surgical services represent approximately 30% of all hospital expenses [8] and elective surgeries are far more common than emergency operations [9]. Unlike emergency admissions where it is difficult for hospital administrators to influence pre-admission factors, knowing the factors that increase LOS in elective surgeries can allow hospital staff to proactively influence the delivery of care and demand for beds [10]. Since hospitals can more readily manage hospital bed capacity in elective than emergency surgeries, identifying factors related to prolonged LOS in elective surgeries can reduce the utilization of scarce hospital beds.

While past studies have explored the factors associated with prolonged LOS after cardiac [11], laparoscopic cholecystectomy [12, 13, 14], and spine [15, 16] surgeries, no studies have explored the factors that lead to prolonged LOS in hepatobiliary (HPB) and neurosurgeries (NS). HPB malignancies, liver tumors, and other liver diseases have the highest incidences in Asia and Southeast Asia compared to the rest of the world due to widespread hepatitis B virus infections [17]. Surgery remains the only option for treatment. However, HPB procedures are variable and their care management practices are not standardized [18]. Consequently, the LOS for HPB surgical patients varies widely. For NS, the demand for such surgeries is expected to increase because of improved surgical procedures in craniotomy and cranioplasty for intracranial aneurysms, brain tumors, and other cerebrovascular diseases as well as aging populations and changes in lifestyle in developed countries, including Asia [19]. By explicating factors associated with prolonged LOS for HPB and NS elective surgeries, hospitals can design better patient management services [20].

Multiple factors at the patient and systems level have been associated with LOS in a variety of disease settings. For example, common preoperative patient factors associated with prolonged
LOS are the patient’s demographics and presenting conditions at the time of admission [21]. Studies have shown that age, gender, functional status, diagnostic or illness factors, and the major procedure group for surgical patients influenced LOS [2, 3, 12, 13, 14, 22]. Specifically, age was related to prolonged LOS for patients undergoing aortic surgery [23]. In general, elderly patients undergoing a major surgery faced higher risks of bleeding and other physiological dysfunctions that may slow recovery and contribute to prolonged LOS [24]. Seicean et al. [15] found that elective spine surgery patients with higher body-mass index (BMI) reported poorer outcomes. The Braden score on admission, which identifies patients at higher risk for pressure ulcers, was found to predict prolonged LOS for patients undergoing liver transplantation [25], while malnutrition on admission slows recovery [26]. Patients who are frail and cannot ambulate independently have a low functional status score and were reported to have prolonged LOS following elective lumbar spine and arterial vascular surgeries [27, 28]. Comorbidity also predicted prolonged LOS [29]. Gruskay et al. [16] found that the total number of comorbidities predicted prolonged LOS after elective lumbar surgery. Likewise, the number of abnormal laboratory results (labs) indicate the severity of patients’ health status, which influences how fast they will recover after surgery. Fall risk is measured by assessing the patient’s level of confusion, dizziness, altered elimination, and difficulty with mobility at admission [30, 31]. Preoperative fall risks have been found to predict postoperative falls, functional decline, and surgical complications, all of which prolonged LOS [32]. Occupational therapy (OT) improves walking capacity, muscle strength, flexibility, balance, and endurance so patients can quickly return to active lifestyles [33, 34]. However, patients need a minimum capacity to do OT, and preoperative physiotherapy (PT) has been shown to improve exercise tolerance for patients undergoing lung transplantation [35].

Preoperative hospital administrative system factors that contribute to LOS include delays in investigation and procedures [36] as well as the day and time of admission [37]. For example, patients admitted during weekends, on the eve of public holidays, or after 5pm often face delays in the initial physical examination and diagnostic tests due to diminished availability of staff and expertise. In general, perioperative patient care after office hours is limited by a reduced clinical crew. Consequently, the day and time of admission have been associated with increased LOS, preventable adverse events, and mortality of patients with pulmonary embolism and myocardial infarction [37, 38].

Intraoperative variables that affect LOS include the duration of preoperative preparation [39] and operation time [2]. For example, for patients undergoing surgery for endocrine tumor, the duration of preoperative preparation for anesthesiologic management, fluid management, medications involving anti-hypertensive medications, alpha, beta, or calcium channel blockers, and antibiotic prophylaxes, were associated with prolonged LOS [39]. Delays or conflicts in
preoperative preparation may lead to a cancellation of the surgery, which further increases LOS. Chang et al. [23] found that operations lasting more than 5 hours, which may be related to intraoperative blood loss, were associated with prolonged LOS for patients undergoing aortic surgery.

Postoperative variables that affected LOS include the number of complications after surgery and hospital-acquired infections (HAI) [2, 23, 40, 41]. For example, complications such as urinary tract infection and pneumonia led to prolonged LOS following cervical discectomy and fusion [41]. Postoperative treatment for wound or surgical site infections [23], polypharmacy [40, 42] where multiple drug consumption increased the risk of drug interactions and adverse reactions, as well as use of dialysis, ventilator support, and other tube insertions [3] also contributed to LOS. Other hospital acquired nosocomial infections include bacterium infections from clostridium difficile colitis [43] or methicillin-resistant Staphylococcus Aureus [6]. Research has also shown that discharge planning affects LOS, where discharge to a nursing home was associated with prolonged LOS by 89% for surgical patients compared to being discharged to home [3, 36].

In sum, there is broad literature to suggest that multifactor perioperative pathways, excluding the operation procedure, have significant impact on prolonged LOS. However, current studies exploring such factors have only focused on partial perioperative pathways. For example, Freitas et al. [7], Reponen et al. [44], and Lukasiewicz et al. [21] focused on the patients’ preoperative clinical conditions, Morimoto et al. [13] investigated preoperative and intraoperative clinical factors, while Collins et al. [2] considered intraoperative and postoperative factors. These studies could not rule out confounding factors from the partial pathway that would otherwise be non-significant on prolonged LOS if the entire perioperative pathway was considered. In this study, we examined perioperative factors in the entire surgical pathway. By assessing the simultaneous impact of these factors on prolonged LOS, hospitals can set reasonable preoperative expectations for patients and the healthcare team, establish efficient operative protocols, or plan postoperative treatment care and improve discharge planning for patients. Our approach is more likely to yield a more comprehensive surgical services protocol for the entire perioperative care continuum for elective HPB and NS patients.

Thus, the objective of this study is to assess the association between preoperative, intraoperative, and postoperative factors on prolonged LOS after adjusting for surgical complexity for a sample of elective HPB and NS patients. Since surgeries are more susceptible to the risk of adverse events than non-surgical procedures [45, 46] and elective surgeries outnumber emergency
procedures, we contribute to the literature on surgical safety and quality of care with greater impact for potential policy interventions that influence LOS.”

We hope our revision to provide more justification for this study meets with your expectations. Thank you.

5. “Measures:
P6, line 55. Operational definitions for all explanatory variables are important, which provides a communication with the literature (e.g., BMI cutoff). Sometimes, it may affect the findings as well. The authors attached the supplemental 1 and 2. which gives better understanding on the selected variables. Nevertheless, there are still some unclear, e.g., nutrition score, number of delays, and so on. Some variables are difficult to understand how it is related to LOS, e.g., operation end after 5pm, discharge after 5pm, when is the admissions. I believe that all variables should be well-justified and the researchers shall not fish the significant results by putting all variables for trials.”

Thank you for your comments. We have included citations to support why these variables are included in the study as described in point 4 above. We hope these justifications meet with your expectations.

6. “P.8, line 4-19. The justification of discriminant analysis needs reference for support.”

Thank you for your comment. Since Reviewer 3 highlighted that the purpose of our study is to identify factors that predict prolonged LOS, and Reviewer 1 had concerns about the way we defined prolonged LOS, we made significant changes to this section. First, we simplified the definition of LOS to above the median LOS for a procedure after accounting for surgical complexity (prolonged LOS), and below the median (shortened LOS), following Collins et al (1999) and Morimoto et al (2015), as stated in the Measures section on page 10. Due to this change, we also changed our model estimation strategy to use stepwise logistic regression. This
is a more common method for these types of data, with the results that the findings are cleaner and easier to interpret. We hope you agree with this analytical strategy. Thank you.

7. “Discussion and conclusion:

The authors comprehensively analyze all associated factors predicting the prolonged LOS. The results deserve a lot of discussion to justify and communicate with the literature. However, the discussion is too short and superficial.”

Thank you for your insightful comments. We have provided more information in the Discussion and Conclusion section on page 12 and 13 to justify and communicate the results vis-à-vis the literature as follows: “…the logistic regression model reports that preoperative factors in the surgical pathway were the most predictive of prolonged LOS. In the HPB sample, these were age and admission after 5pm. Age is a multifactorial demographic characteristic that is related to functional status [27], comorbidities [24, 42], polypharmacy [42], and postoperative complications [23]. Knowing that age is a risk factor allows hospitals to implement evidence-based policies to increase patient safety and reduce LOS for elderly surgical patients. Admission for surgery after 5pm is an indicator of operational inefficiency since no elective surgeries occurred at this time at this academic center. Admission for surgery after 5pm not only added another day of stay but may also expose patients to handoff risks that could prolong LOS from incomplete transfers of patient information between the night and day clinical staff.

In the NS sample, functional status, referrals to OT, and the number of HAI predicted prolonged LOS. Partridge et al. [28] found that low functional status and frailty indicated physiologically vulnerable patients that needed additional plans for dependent care in order to be discharged. The impact of HAI on prolonged LOS in this sample suggests that post-surgical care should focus on wound support and better monitoring by the team on pneumonia and other nosocomial infections.

Our results offer insights for hospital administrators and clinicians to attend to patient and system level factors that could lead to prolonged LOS in elective HPB and NS surgeries. For example, adopting preoperative protocols such as home visits and enhanced recovery after surgery (ERAS) protocols [54] prior to the surgery may better prepare elderly or frail patients for the upcoming elective surgeries [55]. Among system factors, reducing admission after 5pm will minimize
periods when a skeletal night crew must care for patients at a time they are most vulnerable and need optimal care. Postoperative procedures such as TeamSTEPPS may improve teamwork and handoffs among the inpatient care team to reduce HAI and improve patient safety [56].

We hope our discussion which is linked to the extant literature met with your expectations.

Thank you very much for your comments and suggestions. We appreciate very much for the opportunity to revise this paper. As a result of your comments, we believe the paper has significantly improved. Specifically, we have provided more literature to support the importance of the study and choice of variables, and discussed the findings in greater depth. We hope our revisions have met with your expectations. Thank you very much.

Comments by and Responses to Reviewer 3:

1. “This study is to investigate the risk factors associated with prolonged LOS for patients with elective hepatobiliary (HPB) and neurosurgery (NS). The study adopted a retrospective cross-sectional study design and selected group of patients with HPB and NS and looked into those risk factors. The manuscript has several meaningful study results. For an example, intraoperative factors critically impacted on prolonged LOS. However, this study has several drawbacks as a publishable manuscript as follows;”

Thank you very much for an opportunity to revise this paper. We appreciate very much that you noted several meaningful results from our study. We hope that our revision will meet with your expectations.

2. “Major Compulsory Revisions
1. I think that the background section should be rewritten for several reasons; (1) The study purpose is being described at the beginning of the background section, (2) Some methodological explanations seem to be appeared in the background section as well (e.g., elective procedures), (3) You said that "our contribution is to the literature on surgical safety and quality of care that influence LOS [8-13]" By judging from several referenced articles you cited, I think that there are many studies on investigating factors affecting LOS, etc., which degrades the value of your study, etc. Overall, the structure of the background section does not fit well into the research article format. Please rewrite the whole part. This part should include the contents below in the following sequence;

-What is prolonged LOS?
-What are those negative effects of prolonged LOS? (Citing 2 or 3 references is not enough)
-What studies have been so far? Specifically describe other study results. Simply listing risk factors would not be enough.
-Why your study is important? If you say that your study differs from the others, then why does it differ? In this case, you should explain how other study did. Simply saying your study is focusing on the entire surgical pathways is not enough.
-Put the purpose of your study at the end of the background section.
-What could your study give the research or policy implications? Put this part at the end of the background section.”

Thank you very much for your insightful and detailed suggestions and comments. We have addressed all the above points in the revised manuscript to define prolonged LOS, their negative effects, providing a more detailed literature review to justify the importance of this study and how it differs from others and the research and policy implications that could be derived from the results of this study.

We write in the Background section from pages 5 to 9, “Length of stay (LOS) is an important measure of resource utilization as patients with prolonged LOS disproportionately account for the consumption of more hospital resources [1]. Prolonged LOS, which is defined as inpatient stay that exceeds the expected LOS for a certain procedure [2], utilizes hospital bed capacity, contributing to shortage. Inpatient bed shortage delays elective admissions and increases emergency department boarding, which denies critically ill patients timely access to treatment as inpatient care conventionally begins only after the patient arrives at the assigned inpatient ward [3, 4]. Patients with prolonged LOS are also at higher risks of nosocomial infections and
unplanned readmissions [5, 6]. In short, prolonged LOS disadvantages both hospitals and patients [7].

Surgical services represent approximately 30% of all hospital expenses [8] and elective surgeries are far more common than emergency operations [9]. Unlike emergency admissions where it is difficult for hospital administrators to influence pre-admission factors, knowing the factors that increase LOS in elective surgeries can allow hospital staff to proactively influence the delivery of care and demand for beds [10]. Since hospitals can more readily manage hospital bed capacity in elective than emergency surgeries, identifying factors related to prolonged LOS in elective surgeries can reduce the utilization of scarce hospital beds.

While past studies have explored the factors associated with prolonged LOS after cardiac [11], laparoscopic cholecystectomy [12, 13, 14], and spine [15, 16] surgeries, no studies have explored the factors that lead to prolonged LOS in hepatobiliary (HPB) and neurosurgeries (NS). HPB malignancies, liver tumors, and other liver diseases have the highest incidences in Asia and Southeast Asia compared to the rest of the world due to widespread hepatitis B virus infections [17]. Surgery remains the only option for treatment. However, HPB procedures are variable and their care management practices are not standardized [18]. Consequently, the LOS for HPB surgical patients varies widely. For NS, the demand for such surgeries is expected to increase because of improved surgical procedures in craniotomy and cranioplasty for intracranial aneurysms, brain tumors, and other cerebrovascular diseases as well as aging populations and changes in lifestyle in developed countries, including Asia [19]. By explicating factors associated with prolonged LOS for HPB and NS elective surgeries, hospitals can design better patient management services [20].

Multiple factors at the patient and systems level have been associated with LOS in a variety of disease settings. For example, common preoperative patient factors associated with prolonged LOS are the patient’s demographics and presenting conditions at the time of admission [21]. Studies have shown that age, gender, functional status, diagnostic or illness factors, and the major procedure group for surgical patients influenced LOS [2, 3, 12, 13, 14, 22]. Specifically, age was related to prolonged LOS for patients undergoing aortic surgery [23]. In general, elderly patients undergoing a major surgery faced higher risks of bleeding and other physiological dysfunctions that may slow recovery and contribute to prolonged LOS [24]. Seicean et al. [15] found that elective spine surgery patients with higher body-mass index (BMI) reported poorer outcomes. The Braden score on admission, which identifies patients at higher risk for pressure ulcers, was found to predict prolonged LOS for patients undergoing liver transplantation [25], while malnutrition on admission slows recovery [26]. Patients who are frail and cannot ambulate
independently have a low functional status score and were reported to have prolonged LOS following elective lumbar spine and arterial vascular surgeries [27, 28]. Comorbidity also predicted prolonged LOS [29]. Gruskay et al. [16] found that the total number of comorbidities predicted prolonged LOS after elective lumbar surgery. Likewise, the number of abnormal laboratory results (labs) indicate the severity of patients’ health status, which influences how fast they will recover after surgery. Fall risk is measured by assessing the patient’s level of confusion, dizziness, altered elimination, and difficulty with mobility at admission [30, 31]. Preoperative fall risks have been found to predict postoperative falls, functional decline, and surgical complications, all of which prolonged LOS [32]. Occupational therapy (OT) improves walking capacity, muscle strength, flexibility, balance, and endurance so patients can quickly return to active lifestyles [33, 34]. However, patients need a minimum capacity to do OT, and preoperative physiotherapy (PT) has been shown to improve exercise tolerance for patients undergoing lung transplantation [35].

Preoperative hospital administrative system factors that contribute to LOS include delays in investigation and procedures [36] as well as the day and time of admission [37]. For example, patients admitted during weekends, on the eve of public holidays, or after 5pm often face delays in the initial physical examination and diagnostic tests due to diminished availability of staff and expertise. In general, perioperative patient care after office hours is limited by a reduced clinical crew. Consequently, the day and time of admission have been associated with increased LOS, preventable adverse events, and mortality of patients with pulmonary embolism and myocardial infarction [37, 38].

Intraoperative variables that affect LOS include the duration of preoperative preparation [39] and operation time [2]. For example, for patients undergoing surgery for endocrine tumor, the duration of preoperative preparation for anesthesiologic management, fluid management, medications involving anti-hypertensive medications, alpha, beta, or calcium channel blockers, and antibiotic prophylaxes, were associated with prolonged LOS [39]. Delays or conflicts in preoperative preparation may lead to a cancellation of the surgery, which further increases LOS. Chang et al. [23] found that operations lasting more than 5 hours, which may be related to intraoperative blood loss, were associated with prolonged LOS for patients undergoing aortic surgery.

Postoperative variables that affected LOS include the number of complications after surgery and hospital-acquired infections (HAI) [2, 23, 40, 41]. For example, complications such as urinary tract infection and pneumonia led to prolonged LOS following cervical discectomy and fusion [41]. Postoperative treatment for wound or surgical site infections [23], polypharmacy [40, 42]
where multiple drug consumption increased the risk of drug interactions and adverse reactions, as well as use of dialysis, ventilator support, and other tube insertions [3] also contributed to LOS. Other hospital acquired nosocomial infections include bacterium infections from clostridium difficile colitis [43] or methicillin-resistant Staphylococcus Aureus [6]. Research has also shown that discharge planning affects LOS, where discharge to a nursing home was associated with prolonged LOS by 89% for surgical patients compared to being discharged to home [3, 36].

In sum, there is broad literature to suggest that multifactor perioperative pathways, excluding the operation procedure, have significant impact on prolonged LOS. However, current studies exploring such factors have only focused on partial perioperative pathways. For example, Freitas et al. [7], Reponen et al. [44], and Lukasiewicz et al. [21] focused on the patients’ preoperative clinical conditions, Morimoto et al. [13] investigated preoperative and intraoperative clinical factors, while Collins et al. [2] considered intraoperative and postoperative factors. These studies could not rule out confounding factors from the partial pathway that would otherwise be non-significant on prolonged LOS if the entire perioperative pathway was considered. In this study, we examined perioperative factors in the entire surgical pathway. By assessing the simultaneous impact of these factors on prolonged LOS, hospitals can set reasonable preoperative expectations for patients and the healthcare team, establish efficient operative protocols, or plan postoperative treatment care and improve discharge planning for patients. Our approach is more likely to yield a more comprehensive surgical services protocol for the entire perioperative care continuum for elective HPB and NS patients.

Thus, the objective of this study is to assess the association between preoperative, intraoperative, and postoperative factors on prolonged LOS after adjusting for surgical complexity for a sample of elective HPB and NS patients. Since surgeries are more susceptible to the risk of adverse events than non-surgical procedures [45, 46] and elective surgeries outnumber emergency procedures, we contribute to the literature on surgical safety and quality of care with greater impact for potential policy interventions that influence LOS”.

We hope that our revision meets with your expectations. Your comments were very helpful because they pushed us to be more complete in our justification, setup, and discussions.
2. “You said that; your study differs from others because the other studies were about only partial perioperative pathways (PPP), but your study is about the entire surgical pathways (ESP). Are you sure that most of studies are regarding the partial perioperative pathways? If so, please describe examples of other studies which have adopting PPP. Please explain the difference between PPP and ESP?”

Thank you for your comments. We have provide more literature review to shed light on the past studies that focused on PPP and how that is different from ESP as listed in the second last paragraph in Point 1 above. We are not saying that PPP studies are not valuable. However, we think that there is value in a simultaneous investigation of the factors in the ESP. This approach may yield insights that PPP studies may not. For example, a significant factor found in a PPP study may become insignificant when the ESP is considered. Additionally, factors in the pathway may be related to one another, so that a significant factor in the post-operative period may be driven by a factor in the pre-operative period. Hence, the right approach may be to deal with the problem at the pre-operative period. We hope our more in-depth review of past studies on PPP met with your expectations.

3. “There is no demographic information of the study subjects: HPB, NS. Please add table on it. It would be great if you could put type of healthcare services the patients received.

Thank you for your comments. The demographic and health services assessment information of the HPB and NS study subjects are listed in Tables 1 and 2 respectively. We hope that this information is what you were asking for.

4. “This study had several critical draw backs such as small sample size, subjective selection of the study subjects, etc. Authors simply described them in the discussion and conclusion sections. However, I think that they would not be enough.”

Thank you for your comment. Our sample is a complete sample of all patients undergoing elective HPB and NS procedures in a one year period. However, because this is a medical record review study that is labor-intensive in the data collection process, we were only able to collect data for 1 year. The only exclusions, which we stated in the Participants section on page 9, are the day surgeries that did not have LOS, and emergency surgeries (since management cannot
control these). We did not detect anything unusual, in terms of patient flow for that year but acknowledge that our conclusions are limited to the 1 year of data. In summary, there were no subjective decisions on which patients to include; in that sense the data is unbiased. Unfortunately, the small sample size is due to limited resources (this study was unfunded and the researchers used their time, after hours, to collect the data). However, we tried to list all the possible limitations as transparently as we could. We hope our discussion puts you at greater ease. Thank you.

5. “Regarding the research method section, I think that they are too much concise. Can you add more detail description to the manuscript for readers?”

Thank you for your comment. We have included justifications for the variables we included in this paper in Point 1 above. Further descriptions of the variables are listed in Appendix Supplemental Table 2. We have also gone to some lengths to describe the estimation model and to justify it. We hope this meets with your expectations, otherwise, we appreciate some guidance on any additional information you would like to see. Thank you.

6. “This study is about the prolonged LOS. Please see the title. But the potential part of the manuscript is also about shorter LOS. These two subjects seem to make the result table be seen as complicated. Is there any way to present the study result simple? Please think about this issue and suggest your idea.”

Thank you for your insightful comment. We have now focused on the definition of prolonged LOS as above the median LOS. As a result, we now use logistic regression analysis to predict prolonged LOS, following Collins et al (1999), and Morimoto et al (2015) on page 10 in the Methods section. We have removed our discussion on shorter LOS to avoid complication. We hope that makes the results easier to follow and have met with your expectations. Thank you for your suggestion.
7. “There are some possibilities of research result fabrication. You said that two persons extracted data. But there is not any explanation on how they selected study subjects. If you selected the study subject electively or subjectively, I don't think that the study results could be produced objectively. Please add manuscript on how they selected study subjects and what kind of guidelines they did use.”

Thank you for your comments. We highlighted in the participation section on page 9 that all elective HPB and NS surgical patients over 18 years old admitted between Jan 2014 and Jan 2015 were included in the study. There were no subjective decisions on which patients to include. For obvious reasons, we excluded emergency surgeries which were unplanned or day surgeries where LOS = 0 for the repair of inguinal hernia, anal fissure, appendectomy, and cholecystectomy for gallstones. We hope the inclusion and exclusion criteria that we specified in this paper is what you were looking for. Moreover, we indicated in the Data Collection section on pages 9 and 10 that, “One nurse administrator and one operations administrator, who were not involved in surgeries, extracted preoperative, intraoperative, and postoperative information from the medical records with the assistance of five registered nurses.” As a result of an arms-length relationship to the surgery, we sought to ensure that the data collection agents could not guess at what we were looking for to fabricate the result since they were not statisticians. Moreover, 5 registered nurses helped with the data collection to ensure that the data was not fabricated. We hope that the working of 7 persons give you assurance that the group could not have fabricated the data and results since none of them were statisticians. Thank you.

“Minor Essential Revisions

8. There are too many independent variables without having its ways of measurement. Please explain all those variables with its measurement status.”

Thank you for your comment. We provided the explanations and measurement of the independent variables in Appendix Supplemental Table 2 of the paper. We hope this information is what you were looking for. Thank you.

9. “You selected two groups of patients: HPB, NS. Is there any reason? Describe this reason in the manuscript.”
Thank you for your comment. We have provided reasons for the selection of elective HPB and NS patients in the background section as described in our response to you in Point 1 above. We hope these reasons meet with you expectations. Thank you.

“Discretionary Revisions

10. In abstraction section, delete the first sentence: "this study is the first ever on …..center". This is bombastic expression. Who cares about the first trial? Please rewrite this part again with other good reasons for the importance of your study.”

Thank you for your comments. We have revised the statement to provide other reasons for the importance of this study as described in our response to you in Point 1 above. We hope these reasons meet with your expectations. Thank you.

11. “Please think about the way of expressing your study results. It is very hard to understand the tables. Current study results seem to be seen messy. For an example, do they need 95% CI? Why? There is p-value. Please select the core statistics.”

Thank you for your comments. We have removed the 95%CI and provided the standard deviations in Tables 1 and 2 instead. We hope this statistic makes it easier for you to read the tables. Thank you for your suggestion.

12. “Please think about the other way of statistical analysis. If you want to stick to the current method, please add manuscript on the advantages of the current method compared to the others.”

Thank you for your suggestion. We have change the statistical analysis to logistic regression, as stated in the Statistical Analysis section on page 11, since you rightly point out that because our outcome variable is prolonged LOS, then logistic regression is a better technique. We hope you
are in agreement that this is a better statistical analysis. Thank you very much for your suggestion.

13. “Move IRB explanation section from "design and setting" to "data collection" section. Add IRB number in the manuscript.”

Thank you for your comment. We have moved the IRB information to the Data Collection section on page 10, and added the IRB number (DSRB 2015/00229). Thank you.

“These are all my comments. I know well that you guys are all experts on this area and I am just a reviewer. All my comments are for the improvement of your manuscript and I hope for your understanding. I hope to see your revised manuscript in the next round of review process. Good luck!”

Thank you for the opportunity to revise this paper so readers could better understand its importance and the results. Your comments were very helpful and we hope you see that we took your comments very seriously. As a result of your comments, we believe that this is now a more well developed paper.