Replies to reviewer A

The authors present an analysis of healthcare utilization by surgical patients with congenital heart disease (CHD) in the western highlands area of China between 2010-2019 using single-center data contributed to the International Quality Improvement Collaborative for Congenital Heart Surgery (IQIC). They find that costs are high and increasing, with longer length of stay, young age, progressive disease, surgical complexity, and drug and traditional Chinese medicine use were associated with increased hospitalization costs. I thank the authors for their work and have some comments to improve their manuscript:

Major Comments:
Comment 1: Introduction: the authors state (on Lines 72-73) that the disease burden due to CHD increased in low- and middle-income countries. Can the authors support this statement with data? Epidemiological data suggest that this may be more reflective of greater diagnosis of CHD as well as CHD becoming more "visible" due to other conditions (e.g., neonatal disorders and infectious diseases) being addressed, making CHD more likely to be the (diagnosed) cause of death. As CHD is congenital and CHD burdens are largely similar and stable across the globe, this statement deserves clarification or rephrasing.
Reply 1: Thank you very much for your comments. The Global Burden of Diseases (GBD) study reported that approximately three million neonates were born with CHD in 2019. From 1990 to 2019, the overall mortality of CHD declined from 7.1 to 2.8 per 100,000, but remained relatively high in low and middle-income countries. Significant improvements in diagnostic and treatment capabilities for CHD have led to significant improvements in survival rates in developed regions of the world, but success rates in undeveloped regions have not yet reached the same level. Despite improvements over the past decades, newborns in low- and middle-income countries with severe congenital heart disease and no access to surgical care are more likely to die before the age of five than newborns in high-income countries. According to a systematic analysis of the global burden of prevalent heart disease published in the Lancet Adolescent Health journal, the areas with the highest infant mortality rates resulting from CHD, in descending order, are Oceania, North Africa and the Middle East, the Caribbean, Central Sub–Saharan Africa, and Southeast Asia[1].
Reference
[1] Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Child Adolesc Health 2020;4:185-200.
Changes in the text: None.

Comment 2: Introduction/Discussion: the authors evaluate the costs for individuals who do get surgery but note in their introduction that resources are not evenly distributed across China and surgery is often performed late (if at all). Moreover, over 90% of children with CHD in low- and middle-income countries do not get the care they need. Can the authors comment/provide data on patients needing but not getting surgery for CHD in the first place?

Reply 2: Thank you very much for your comments. Distance from medical facilities was an important factor in timely diagnosis of these children. Uneven access to quality healthcare resources can lead to children with CHD missing out on the optimal age for treatment. The results of a cross-sectional survey conducted in eight western provinces showed a high rate of delayed diagnosis of CHD of 66.3%[1]. And the study pointed out that in the less developed areas of western China, medical resources are relatively backward, resulting in many children with CHD not being diagnosed in time. As the age of the children increases, the condition becomes more serious, and only after complications arise can they attract the attention of their parents or medical personnel, so that they can be screened and diagnosed. A report published in 2008 said that about 90% of children with CHD do not receive an appropriate basic diagnosis or intervention each year [2]. Unfortunately, the article is not accompanied by relevant data. We have not yet found any recent literature on the subject.

Reference

[1] PANG Linhong, LU Jiang, SONG Honglin, et al. Comparative analysis of different delayed diagnosis duration and postoperative rehabilitation outcomes of congenital heart disease in children ≤18 years of age in eight provinces in western China[J]. China Public Health,2022,38(06):671-675.(in Chinese)

[2] Tchervenkov CI, Jacobs JP, Bernier PL, Stellin G, Kurosawa H, Mavroudis C, et al. The improvement of care for paediatric and congenital cardiac disease across the world: a challenge for the World Society for Pediatric and Congenital Heart Surgery. Cardiol Young. 2008;18(Suppl 2):63–69.

Changes in the text: None.

Comment 3: Methods: did the authors assess and, if appropriate, adjust for multicollinearity, endogeneity, and heteroskedasticity in their data? For example, age and CHD complexity are likely collinear due to high CHD complexity resulting in either early presentation or early death, whereby surgery is generally needed in the first year(s) of life to avoid death.

Reply 3: Thank you very much for the suggestion. Prior to the linear regression analysis, we performed multicollinearity tests using the tolerance and variance inflation factor (VIF) in SPSS. In general, a higher VIF indicates a higher likelihood of multicollinearity. VIF<10 indicates the absence of multicollinearity. The results of the multicollinearity run are shown in Table 1. The covariance statistics result column contains tolerance and VIF, the tolerance value is less than 1, and the value is greater than 0.1; VIF value is less than 10, so it can be seen that the complementary in the covariance problem between these independent variables, and the model composed by

these variant faces as independent variables is more stable.

Table 1 Covariance statistics table

Model		covariance statistics	
		tolerances	VIF
1	Constant		
	Sex	0.988	1.012
	Type of CHD	0.935	1.069
	Age at hospitalization	0.724	1.380
	Length of stay	0.876	1.141
	Use of traditional Chinese medicine	0.905	1.105
	Proportion of drug costs	0.880	1.137
	Proportion of surgery costs	0.773	1.294

We used the more traditional method, the heteroskedasticity scatterplot, to test for the presence of heteroskedasticity in the regression model, which is indicated if the squares of the residuals vary against changes in either the independent or dependent variables. The scatterplot of the squared residuals in this study is irregularly distributed and there is no heteroskedasticity in this regression model.
Changes in the text: None.

Comment 4: Methods: costs are presented as average costs, even though costs generally do not follow normal distributions as also noted by the authors' normality testing. As such, costs are better presented as medians with interquartile ranges instead of being log-transformed, thereby also enabling easier comparison with other studies (which most commonly present data in their non-normal distributions). Can the authors modify their results accordingly and present figures with box-and-whisker plots?
Reply 4: Thank you very much for your valuable advice. We apologize for any inconvenience we may have caused. We didn't make it clear in our methodology and you misunderstood. In our study, the costs are represented as medians with interquartile ranges (IQR) (see Table 3 for details). We have elaborated on the presentation of average hospitalization costs in the methodology section. After consulting some literature, we only log-transformed the costs when constructing the linear regression model.
Changes in the text: we have modified our text as advised (see page 7, lines 209-210; page 19, line 575).

Comment 5: Methods: readers without an econometrics background, which include the majority of the journal's readership, will have difficulty understanding the grey relational analysis model as currently written. The authors are encouraged to rephrase or elaborate their methodological description to facilitate other readers' understanding.
Reply 5: Thank you very much for your suggestions, your valuable suggestions are very helpful for our article. We apologize for any inconvenience caused to our readers

due to our negligence. To make it more understandable to the readers, we have added a brief description of the gray correlation model in the methods section.

Changes in the text: we have modified our text as advised (see page 6, lines 170-176).

Comment 6: Methods/Discussion: how representative is the patient sample operated at the authors' center? Are there patients who may be treated elsewhere (either a different local hospital or another region of China) because of complexity or cost reasons? Depending on the answer, this may be reflective of information and/or selection bias that deserves discussion.

Reply 6: Thank you very much for your comments. All study subjects were hospitalized patients with CHD who underwent surgery in the hospital in the study. Although the study was conducted in a single center, the Department of Cardiovascular Surgery of the First Affiliated Hospital of Lanzhou University, as the largest cardiovascular surgical center in the western plateau region, accommodates patients with CHD from several provinces, including Gansu, Qinghai, and Ningxia, and therefore the patient sample is well represented.

Changes in the text: None.

Comment 7: Results/Discussion: a considerable part of the journal's readership resides/practices outside China and may note that the use of traditional Chinese medicine resulted in a $2,000 increase ($7,163.08 vs. $5,148.12, P<0.01) in costs. Can the authors comment on the use of traditional Chinese medicine in these cases and whether this is (or is not) a potential area for cost reduction in the eyes of the authors? The authors discuss other factors in their discussion but do not do so for traditional Chinese medicine, which would benefit from elaboration.

Reply 7: Thank you very much for your comments. In our study, the average hospitalization costs of patients with CHD who were treated with traditional Chinese medicine were significantly higher ($7,163.08 vs. $5,148.12, P<0.01). Also, the results of multiple linear regression suggest that whether or not to use traditional Chinese medicine is an influential factor in the hospitalization cost of patients with CHD. In my opinion, appropriate control of the use of traditional Chinese medicines or price adjustments of traditional Chinese medicines may be able to reduce the hospitalization costs of patients with CHD. We have added to the revised manuscript a discussion of the use of traditional Chinese medicine on the cost of hospitalization for patients with congenital heart disease.

Changes in the text: we have modified our text as advised (see page 12, lines 366-371).

Comment 8: Discussion: can the authors comment on early extubation and enhanced recovery after surgery practices for congenital heart surgery in China and/or the potential thereof in reducing hospital length of stay?

Reply 8: Thank you very much for your suggestion. Early postoperative extubation after preoperative surgery has been defined as in-operating theatre extubation or

extubation within 1-6 hours postoperatively in China. Fast-track anaesthesia can be established in many cases of thoracoscopic atrial and ventricular defect repair, mitral valvuloplasty and other cardiothoracic surgery. Early extubation in the postoperative period can improve patients' cardiopulmonary function, increase patient comfort, reduce respiratory complications, safely reduce ICU time and hospital stay, improve resource utilisation, save costs, and at the same time reduce the perioperative morbidity and mortality rate. Statistically, patients who are extubated early can have their stay in the ICU shortened by one day, thus reducing their postoperative hospital stay by one-third[1].

Lung infection is one of the main complications after CHD surgery, and lung infection and respiratory infection advantage affect the children's postoperative recovery and aggravate the disease burden of the main factors, so the early rehabilitation after CHD surgery is particularly important. By using comprehensive intervention rehabilitation methods such as back percussion, postural drainage, correct suctioning, and strengthening postoperative nutritional support, medical staff can reduce the incidence of pulmonary complications in CHD operated patients, improve the postoperative cure rate, and shorten the length of hospital stay, thus further reducing the hospitalisation cost[2].

Reference

[1] Gao YC, Wang YY, Wang CR, et al. Research progress on the effect of fast-track anaesthesia on postoperative complications in adult cardiac surgery[J]. International Journal of Anaesthesiology and Resuscitation,2019,40(6):585-589.

[2] Liu Z, Chen XY, Chen DY, et al. Evaluation of the effect of postoperative early comprehensive intervention rehabilitation model in children with congenital heart disease. Lingnan Journal of Cardiovascular Disease, 2017, 23(04): 448-450-478

Changes in the text: None.

Comment 9: Limitations: the limitations are far too brief (less than three lines) and require elaboration. For example, the authors should acknowledge the potential multicollinearity in their data, as well as the risk for selection and information bias and unknown confounders. In addition, can the authors speculate how these limitations may affect their findings and interpretation of findings?

Reply 9: Thank you very much for your comments. We have added to the limitations in the revised manuscript. There are inherent limitations due to the use of administrative data and to the retrospective nature of our study. In addition, hospitalized patients with CHD were identified by diagnostic codes, and the results of the study need to be interpreted with caution because of concerns about the accuracy of coding. Despite the high coding accuracy, a formal validation study is needed. Although inpatient hospitalization costs account for a large majority of costs, the lack of outpatient costs data constitutes a limitation of the study.

Changes in the text: we have modified our text as advised (see page 14, lines 432-435).

Minor Comments:

Comment 1: Throughout manuscript: please replace "Patients with CHD" with "patients with CHD" as to not reduce individuals to their condition (i.e., use person-first language).

Reply 1: Thank you very much for your comments. We've made changes in the appropriate section of the article.

Changes in the text: All of the manuscript.

Comment 2. Line 104: can the authors provide the categories for "ethnic group" and how these are defined (i.e., research guidelines, census, other)?

Reply 2: Thank you very much for your comments. We have elaborated on ethnicity in the notes section in Table 2.

Changes in the text: we have modified our text as advised (see page 18, lines 569-572).

Comment 3. Line 128: the authors state that "The exclusion criteria included incomplete case records." Can the authors clarify whether this means that the final dataset did not have any missing data? If there were missing data, how were these handled?

Reply 3: Thank you very much for your comments. We have removed the data with missing values prior to the statistical analysis, so the final data for statistical analysis does not have any missing values.

Changes in the text: None.

Comment 4. Methods/Results: please provide a flowchart showing the number of patients overall, excluded (for each reason), and included for analysis.

Reply 4: Thank you very much for your comments. We have added a flowchart in the revised manuscript.

Changes in the text: we have modified our text as advised (see page 21, lines 583-585).

Comment 5. Methods, Lines 191-194: how were variables chosen and sequentially included in their models?

Reply 5: Thank you very much for your comments. We included variables that were statistically significant in the one-way analysis of variance in the models.

Changes in the text: None.

Comment 6. Lines 318-320: can the authors elaborate on the policies by the government in 2013? What actions were taken to improve overall healthcare and/or specifically CHD care? In addition, how were prices adjusted in 2017?

Reply 6: Thank you very much for your comments. We apologize very much for the inconvenience caused by our error, and we have corrected the manuscript section. The

point we are trying to make here is that the decline during two of the studied years (2014 and 2018) in hospitalization costs may be due to the policies by the government in 2013 and 2017. The provincial government issued an implementation plan for improving the reform of the medical and health system in 2013. Gansu Provincial Government adjusted the prices of medical services in public hospitals in 2017.

In 2013, Gansu Province reformed its medical institutions by invoking social forces to participate in public services, standardizing diagnostic and treatment behaviors, strictly controlling unreasonable check-ups and laboratory tests, freeing up space for price adjustments of medical services, and eliminating the situation of "medicines to support doctors", thereby reducing the financial burden on patients.

In 2017, the Gansu provincial government comprehensively launched the comprehensive reform of public hospitals by adjusting the prices of medical services in public hospitals, and further reduced patients' hospitalization costs by promoting the construction of a system of hierarchical diagnosis and treatment, universal healthcare insurance, security of drug supply, and comprehensive supervision, and by abolishing the drug mark-up and making adjustments to the prices of medical services.

Changes in the text: we have modified our text as advised (see page 11, lines 338-348).

Comment 7. Tables/Figures: all table/figure legends must introduce the abbreviations used in the table/figure to enable tables/figures to stand alone and be fully understood by the reader.

Reply 7: Thank you very much for your comments. We have ensured that all table/figure legends introduce the abbreviations used in the table/figure.

Changes in the text: None.

Comment 8. Figures: please make sure that all figures are color-blind-friendly.

Reply 8: Thank you very much for your comments. We have made sure that all figures are color-blind-friendly.

Changes in the text: None.

Comment 9. The supplemental STROBE Statement appears to be empty (no cells are filled in).

Reply 9: Thank you very much for your comments. We are very sorry for the inconvenience caused by our negligence, we have already made up the content of the STORE, and finally, once again, we apologize for our negligence.

Changes in the text: None.

Thank you for the opportunity to review the manuscript titled "Analysis of the hospitalization costs of surgical patients with congenital heart disease in the plateau region of western China, 2010–2019." I want to congratulate the authors for their

initiative. More related studies should be carried out to think about a sustainable program of congenital heart surgery, mainly in developing countries. Although the authors used GDP, which refers to the value calculated using the price level of a specific period as the constant price, calculating the cost may depend on many other factors that also vary from region to region.

Before the article is accepted for publication, I believe that the authors must make the following details clear in the methods: the type of matrix used to carry out the main time of each of the types of CHD proposed to be studied. There are different costs to using bovine pericardium to close a VSD versus using a Teflon patch or polytetrafluoroethylene patch. What type of oxygenator is used? All of this includes the cost of the surgery. Ideally, it should be included in the methods, but at least in the discussion, it should also be included.

Reply: Thank you very much for your comments. Surgical procedures for different types of CHD vary, for example, atrial septal repair for ASD, atrial septal repair for VSD, arterial ductal occlusion for PDA, tetralogy of Fallot for TOF, endocardial cushion correction for ECD, and right ventricular bi-outlet valve orthopedic surgery for DORV. The occlusive materials used for different surgical procedures for CHD vary. The cost of repair materials such as autologous pericardium, bovine pericardium, and polyester patches used in precordial surgery is included in the cost of materials.

The main objective of this study was to investigate the trends in the cost of hospitalization for congenital heart disease over a ten-year period in the Western Highlands region and the main factors affecting the cost of hospitalization. In the grey correlation analysis model, material costs were highly correlated with hospitalization costs, which suggests that material costs have a greater impact on hospitalization costs for patients with preexisting heart disease. To enhance comparability, material costs in hospitalization costs were converted to material costs as a proportion of hospitalization costs.

Changes in the text: None.

Please pay attention to the references; there are tables and figures in the middle of this section.

Reply: Thank you very much for your comments. We are sorry for the misunderstanding. Supplementary material is appended to the references in the body of the text, and the supplementary material contains additional tables and images as well as references. For greater reader-friendliness, we have renumbered the references in the supplementary material.

Changes in the text: we have modified our text as advised (see pages 26-27, lines 624-640).