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Reviewer A

And I bring you the following constructive comments:

1. It is unclear what the difference is between the two logistic regression models used to identify the risk factors associated with congenital heart defect children.

Reply 1: Thank you for your suggestions. The results of the two logistic regression models are detailed in Table 4. Model 1 did not adjust for any covariates, while Model 2 adjusted for all covariates listed in Table 4. We have added an asterisk to the title of Table 4 with an associated footnote to point this out to the reader. We have also added this information to the revised Results section. (See page 12-13, line 300-334, page 28-30, line 561-564)

2. It would also be interesting to know quality measures of the logistic regression model such as the confusion matrix, the area under the receiver operating characteristic curve (AUC), and Hosmer and Lemeshow test. Best regards, João Chang Junior.

Reply 2: We understand your request, but we did not build a multivariate prediction model for this study. Therefore, we could not perform the calculations for the confusion matrix, AUC, or Hosmer-Lemeshow test. Thank you for your suggestions. We will pay attention to this problem in future studies.

Reviewer B

The Authors should be appraised for analyzing impressive number of data. Nevertheless, the study design is questionable. Since data were collected retrospectively outside professional medical centers, details such as mother's gain during pregnancy or complications during pregnancy could not be thoroughly verified. It is not fully justifiable to discuss the results with prospective studies enrolling live births and performed in medical centers. In this study, only survivors are included, which means that patients who died of uncorrected life-threatening congenital heart defects (or of any other reasons) are left out. As result, we cannot consider it high-quality data. Very importantly, the Authors analyze 18 ethnic groups, not providing the ethnical structure of the population. Last but not least the enrollment has many limitations. We do not find out the number of children whose parents were

offered participation it this study. It is crucial to present the percentage of children whose parents responded positively among different ethnic groups.

1. Since data were collected retrospectively outside professional medical centers, details such as mother's gain during pregnancy or complications during pregnancy could not be thoroughly verified. It is not fully justifiable to discuss the results with prospective studies enrolling live births and performed in medical centers.

Reply 1: Thank you for your suggestions. Through the Congenital Malformation Registration database (CMRD) of Yunnan Province, we collected the incidence of congenital heart defects in children aged 0-18 in cooperation with local education bureaux and the Red Cross society, and the corresponding data of maternal prenatal and obstetric examination were also collected. The maternity examination information is shown in the attachment 1-2.

2.In this study, only survivors are included, which means that patients who died of uncorrected life-threatening congenital heart defects (or of any other reasons) are left out. As result, we cannot consider it high-quality data.

Reply 2: Thank you for your suggestions. We have already mentioned this part in line 445-450 of the text "Although we attempted to screen the entire population of the CMRD, a portion of children died before performance of the screen; some of these succumbed to acute severe CHD, which means that the morbidity of CHD could be underestimated."

3.Very importantly, the Authors analyze 18 ethnic groups, not providing the ethnical structure of the population.

Reply 3: Thank you for your suggestions. According to the latest census data of China, the total population of Yunnan province is 47209277, and the Han population is 31573245, accounting for 66.88% of the total population. The population of ethnic minorities is 15636,032, accounting for 33.12% of the total population. Among them, the population of ethnic minorities (Yi: 4.79 million, Bai: 1.81 million, Hani: 1.49 million, Dai: 1.19 million, Zhuang: 1.18 million, Miao: 1.07 million, Hui: 720,000, Lisu: 640,000, Lahu: 460,000 people, Wa 410,000 people, Naxi 330,000 people, Yao 210,000 people, Tibetan 160,000 people, Jingpo 140,000 people, Bulang 100,000 people, Buyi 87,000 people, Achang 53,000 people, Pumi 46,000 people, Mongolian 34,000 people, Nu 30,000 people, Jinuo: 27,000, 21,000 of De 'ang, 19,000 of Shui, 13,000 of Manchu, and 7,400 of Dulong) as shown in the attachment 3 figure 1.

4.We do not find out the number of children whose parents were offered participation it this study. It is crucial to present the percentage of children whose parents

responded positively among different ethnic groups.

Reply 4: Thank you for your suggestions. In cooperation with local education bureaus, the Red Cross and other organizations, we conducted screening activities for children aged 0-18 through family telephone consultation, family visits, on-site screening on campus, on-site screening in maternal and child health centers and other methods. Although we did not conduct specific statistics, the screening rate of parents and their children of all ethnic groups exceeded 95%.

Minor considerations:
The Authors should clarify, why they state that ‘in cases where multiple CHD defects were observed, the case was identified by the most severe anomaly’ (page 6). ‘Compound type’ CHD is a separate number in Table 2 (65) included in the number of patients enrolled (2421). Also, it should be defined, which defects were encountered in the category ‘Other lesions’. Additional column showing percent values would be helpful; please comment what included ‘other lesions’?

1. The Authors should clarify, why they state that ‘in cases where multiple CHD defects were observed, the case was identified by the most severe anomaly’ (page 6). ‘Compound type’ CHD is a separate number in Table 2 (65) included in the number of patients enrolled (2421).

Reply 1: Thank you for your suggestions. For example, we found a case in the screening process and changed the medical record (attachment 3 figure 2): "male, 12 years old. Diagnosis: 1. aortopulmonary septal defect 2. congenital ventricular septal defect 3. congenital atrial septal defect 4. persistent left superior vena cava 5. overriding aorta." Cases of multiple congenital heart diseases in the same child are classified as' Compound types'. But，If a patient has more than one heart malformation, such as perimembrane or inferior trunk ventricle, it is not compound types but inferior trunk ventricle (which is more harmful).

2.Also, it should be defined, which defects were encountered in the category ‘Other lesions’. Additional column showing percent values would be helpful; please comment what included ‘other lesions’?

Reply 2: Thank you for your suggestions. 'Other lesions' are rare types of congenital heart diseases, including tricuspid atresia, Complete transposition of the great arteries, persistent truncus arteriosus , coronary arteriovenous fistula, etc. Because some of patients died before they took into superior hospitals for further cardiac catheterization and dual-source CT examination, we could not confirm the final subtypes of congenital heart defects. Then it is regretful that we could not provide the percent of this group.