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Dear Editor and Reviewer:

Thank you for your decision and professional comments on our manuscript. We have carefully considered the valuable suggestions and made some revisions. We also followed SQUIRE 2.0 checklist. The revised manuscript (keep the track changes), its clean version and reporting checklist are attached. **The line numbers for the replies and reporting checklist can be found in the clean version** for your convenience.

Below we provide the point-by-point responses.

Reviewer A

The paper titled "An Intelligent Platform for Neonatal Congenital Heart Disease Whole-Course Management Based on Big data and Parental Self-report" is interesting. This article reviewed the challenges to implementation and surveillance of neonatal CHD and the applications of Mobile health (M-Health) based on big data technology. Also, the detailed architecture and workflow of the platform are provided. However, there are several minor issues that if addressed would significantly improve the manuscript.

Comment 1: Suggest adding relevant content on the advantages of big data assistance management and the working mechanism of online and offline collaboration. **Reply 1:** Thank you very much for your suggestions. Relevant sentences have been added. (see Page 14, line 391-401)

Changes in the text: Big data management can help healthcare institutions in creating extensive databases of congenital heart disease patients. By monitoring clinical data of newborns, it can provide congenital heart disease-related knowledge to parents, enhancing their cognitive level of this condition. This, in turn, facilitates early detection of congenital heart disease and increases the likelihood of positive cardiac ultrasound screening for newborns. Furthermore, by analyzing a vast array of newborn data, healthcare institutions can gain deeper insights into the progression of newborns' conditions. Parents can also seek advice about their newborn 's health issues online on the platform and share pictures. Medical experts will provide prompt responses through the platform. In cases where the newborn's condition is too complex to handle online or if online consultations prove ineffective, parents will be advised to seek offline medical attention.

Comment 2: What is the biggest problem encountered during the process of system building and platform building? How to overcome it? Suggest adding relevant content.

Reply 2: Thanks for your constructive comments. The biggest problem is the limited stickiness of parents using the platform. Other potential issues and the solutions are also added. (see Page 22, line 547-560)

Changes in the text: It is crucial to maintain close communication with the technical team and users (the parents) throughout the development and use of the platform. To guarantee the usability of the platform, it is imperative to swiftly communicate user requirements to the technical team and implement necessary modifications to features or interfaces. Our goal is to offer prompt responses to parents' queries, consistently improve the user experience, and fulfill

user requirements. It is crucial for medical staff to effectively track the condition of newborns by encouraging parents to consistently use the platform and report their condition regularly. The challenge of limited parental stickiness on the platform will be significant. To motivate data self-reporting, we will prioritize platform promotion in the initial stages, alongside offering medical consultation services, updating scientific knowledge on the platform, and emphasizing the need for monitoring potential conditions. Another issue arises due to parents having to report information individually, which is the accuracy of the data. In light of this fact, we strongly encourage parents to capture a photo of their exam results and upload it onto the platform.

Comment 3: How to routinely collect real-time clinical data to observe the development of the disease? Suggest adding relevant content.

Reply 3: Thank you for your reminder. We gave more details of the data collecting process. (see Page 14, line 379-383)

Changes in the text: Parents input information on the platform, which is uploaded to the system, and the medical staff monitor the condition of newborns in the back-end data management system. In cases where information input is incomplete, the system sends reminder message or conducts follow-up actively via phone to inform parents about the need for their newborn to undergo diagnosis or treatment.

Comment 4: It is recommended to comprehensively draw a national map of congenital heart disease incidence based on the results of this research platform, to play a guiding role in scientifically formulating prevention and treatment strategies for congenital heart disease. **Reply 4:** Thank you very much for your constructive suggestions. We collected and analyzed the existing data from the platform, preliminarily showing the result (see Page 20, line 500-513) Figure 9 was added as the Spectrum of CHD diagnosed by echocardiography. We also described the process of data collection in the Methods (see Page 13, line 365-372).

Changes in the text: We successfully enrolled a total of 891 infants in the two settings from June 1, 2023, to August 31, 2023. Out of these infants, 95.06% tested negative, whereas 4.93% tested positive. Echocardiography was performed within 7 days after birth for all babies who were classified as test positive. Table 1 shows that a total of 42 cases of CHD were detected. Two infants were diagnosed with mild pulmonary hypertension and no obvious abnormalities, respectively. We will persist in monitoring the diagnosed cases via the platform, send reminder messages to parents to guarantee their children attend check-ups or receive treatment on a regular basis, and disseminate pertinent disease-related scientific knowledge to alleviate parents' stress. (see Page 20, line 500-513)

During the design and construction of this information platform, interviews were conducted with some medical staff to collect constructive suggestions. We also initiated the initial trial run of our platform at two hospitals in China. All parents were given informed consent forms and used this platform voluntarily. There was no limitation for registration. We analyzed the information provided by parents and the verification process results obtained from the hospital management system. The screening and diagnosis data of neonatal congenital heart disease form June 1, 2023, to August 31, 2023 were collected. (see Page 13, line 365-372)

Comment 5: How to explore the correlation and interaction effects between atmospheric pollutants, extreme temperatures, green space index, and the incidence and prognosis of neonatal congenital heart disease based on the results of this research platform? Suggest adding relevant content.

Reply 5: Thank you very much for your constructive suggestions. As suggested by the reviewer, we reviewed the relevant papers, and exploring more usage of our platform and its data. (see Page 21, line 540-546)

Changes in the text: After obtaining all the CHD records from the platform, we can delve into the risk factors associated with the disease. Research indicates that several risk factors, such as maternal exposure to air pollutants (SO2, NO2, PM10, and PM2.5) (52), daily temperatures exceeding 30°C (53), and limited access to green spaces (54) that are often associated with lower household income, can heighten the risk of CHDs. Further studies are warranted to validate these findings by analyzing the valuable data from our platform and other pertinent information from external databases.

Comment 6: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Predicting the postoperative blood coagulation state of children with congenital heart disease by machine learning based on real-world data, Transl Pediatr, PMID: 33633935". It is recommended to quote the article.

Reply 6: As suggested by the reviewer, we have added more information to support this part of review. (see Page 7, line 194-199)

Changes in the text: Guo et al. (30) utilized machine learning (ML) technology and data mining algorithms to predict postoperative coagulation function in children with congenital heart disease. Demographic characteristics and laboratory test results were collected from electronic medical records. This research has identified key features that can assist doctors in predicting the risk of postoperative coagulation abnormalities in children with CHD and facilitating early clinical intervention.

Comment 7: What is the biggest advantage of this model? Does it affect the quality of life of children with congenital heart disease? Suggest adding relevant content.

Reply 7: Thank you very much for your comments. We have considered carefully of the advantages of our platform, making it more clear and comprehensive. (see Page 21, line 528-539)

Changes in the text: Involving parents in managing congenital heart disease on this platform has several advantages. Not only does it help change their health behaviors and increase their understanding of the condition, but also provides a follow-up mechanism for newborns with negative screenings. This enables parents to be more vigilant about their children's well-being in their daily lives. If any newborns show symptoms of congenital heart disease, parents can seek medical attention promptly for a timely diagnosis, thereby reducing the mortality rate of congenital heart disease in newborns and infants. Additionally, this not only improves the quality of life for affected children but also has a positive impact on the overall health of the family. Conversely, for newborns with positive screenings, the platform can track and monitor their cardiac ultrasound. The results should serve as a reminder to parents to schedule timely rechecks, which will in turn enhance the chances of positive cardiac ultrasound screenings.

Reviewer B

Comment 1: First, the title is not accurate, which needs to indicate a review on challenges to implementation and surveillance of neonatal CHD and the implication of AI in this area, as well as the authors' experiences or their AI platform.

Reply 1: We sincerely appreciate the valuable comments. We have modified the title. (see Page 1, line 1-2)

Changes in the text: Intelligent Platform for Surveillance of Neonatal Congenital Heart Disease: Big Data and Parental Self- Report Based Innovative Strategies

Comment 2: Second, the abstract is not informative and needs further revisions. The authors need to briefly describe the clinical needs for this review, the challenges in the traditional management of CHD in China, the strengths of mHealth based on big data and AI technology, and how the authors' AI model was developed. Finally, please have comments on the prospect of the proposed platform and challenges to be addressed to facilitate its implications.

Reply 2: Thank you very much for your constructive and detailed suggestions. We added more information to the abstract. (see Page 2, line 39-76)

Changes in the text:

Background: The neonatal congenital heart disease screening program has advanced in China. However, there are still some missed cases after discharge from maternity hospitals. Moreover, parents' cognitive level and compliance with CHD management are limited. The current disease reporting system, which relies on medical personnel, encounters issues with data omission and misreporting, exacerbated by the manual follow-up process's inefficiency. Involving parents in congenital heart disease management mitigates challenges arising from population mobility, deepens parents' comprehension of the disease, and promotes active data input, ultimately enhancing health management efficiency.

Methods: We performed the key technologies, design, and architecture of the developed platform. It explores the applications of Mobile Health (M-Health) based on big data technology, representing an innovative approach to monitoring neonatal congenital heart disease that emphasizes the integration of advanced technologies such as data integration, online consultation, message reminders, and parental involvement. A feasibility assessment was conducted, involving interviews with medical staff, to evaluate the practicality and effectiveness of the system. Additionally, a preliminary analysis of platform usage was undertaken. **Results:** The platform demonstrated successful integration across the entire CHD management spectrum, including Parent Registration, Screening Phase, Diagnosis Phase, and Treatment Phase. It consists of a mobile APP and a back-end data management system. Parents input information on the platform, which is uploaded to the system. Then, the back-end data management system monitors the case course and provides regular reminders for the treatment and valuable related knowledge for CHD. Based on feedback from medical staff, valuable suggestions for platform enhancement were identified. A total of 891 infants from June 1, 2023, to August 31, 2023, were enrolled at two hospitals in China.

Conclusions: This article reviewed the challenges to the implementation and surveillance of neonatal CHD as well as the applications of Mobile health (M-Health) based on big data technology. This is the first big data management platform for neonatal congenital heart disease (CHD), involving the whole-course management of CHD screening, diagnosis, treatment, and follow-up. It is incorporated into the parental self-report and management with big data mining,

the characteristics of humanization, intelligence, and integration to meet the actual needs of the patients, families, and clinical practice and achieve the expected design effect. Also, the detailed architecture and workflow of the platform are provided. It is crucial to remain vigilant about technical and security concerns while using the platform. Timely feedback and adjustments should be provided to address any identified issues.

Comment 3: Third, in the review part of the challenges, the authors need to analyze the solution strategies for these difficulties. I also suggest the authors to do a small SWOT analysis to indicate the needs for the AI-based platform.

Reply 3: Thanks very much for giving the suggestion of doing a SWOT analysis, which really helps us to revise the part of the challenges more logically. We have modified our text as advised (see Page 8, line256-293). The SWOT analysis is displayed in Figure 1.

Changes in the text: The SWOT analysis is a strategic planning technique that is employed to evaluate the project's strengths, weaknesses, opportunities, and threats (46). The information platform stands out due to its several key advantages. In order to achieve widespread promotion and application in clinical practice, a system must be easy to learn and highly efficient. This is referred to as "usability," which is determined by how effectively a product can be used by specific users to achieve specific goals in a specific context of use. A user-friendly graphical user interface (GUI) has the potential to entice a substantial number of users, and the access to menus must be effortless and straightforward (20,47). With its user-friendly interface, the ease of use ensures that healthcare professionals and parents can easily access it, promoting widespread adoption. The platform is renowned for its proficiency in data integration, offering a holistic perspective on a neonate's health history, thereby aiding in well-informed healthcare decisions. It also provides healthcare providers with advanced tools by offering innovative functions driven by big data. Parents can access health information in the platform to enhance their understanding of congenital heart disease. By means of self-reporting, parental involvement promotes a collaborative approach, thereby improving data sharing and integration, as well as parent engagement. The platform's intelligent algorithms can further facilitate the early detection of CHD, ultimately enhancing patient outcomes.

Despite the offered benefits, the usability challenges in M-Health APPS were technological issues, necessitating regular evaluation and monitoring for adjustment and improvement of the tool (20). The use of big data in managing health information has the potential to improve public health surveillance; however, it also presents substantial challenges. The amalgamation and evaluation of extensive health datasets can result in the involuntary identification of individuals, posing a risk to user privacy." Even within healthcare organizations, employees who have access to large data repositories can potentially compromise data security. To reduce security threats, it is necessary to implement certain measures, including: (1) Implementing strong data encryption techniques for both transit and at-rest data to guarantee that only authorized users have access to confidential information (48). (2) Ensure that both the systems and data management processes adhere to the regulations and legal constraints and requirements (49). ③ Security testing is critical for APP developers to identify security and privacy vulnerabilities. Potential security threats, such as unauthorized access, tampering with health data, or reporting invalid data, are expected to be resolved (50). Additionally, the collection and utilization of personal health data for medical care-related purposes may give rise to ethical concerns (51). Therefore, users must be provided with comprehensive details regarding the intended applications of their data, and

they must provide active consent for these applications prior to data collection and processing. The SWOT analysis is displayed in Figure 1.

Comment 4: In the discussion, please also discuss the possible challenges for the implications of the AI-based platform and the strategies to facilitate its implications. Given the complex environment in China's medical service system, there is no one-size-fits-all strategy. The authors need to discuss more on this.

Reply 4: Thank you very much for your suggestions. We added more information to the discussion. (see Page 22, line 561-572).

Changes in the text: In the complex context of China's healthcare system, the implementation of an intelligent platform for neonatal CHD management holds significant benefits, including improved efficiency, data-driven insights, and remote healthcare delivery. However, several challenges must be addressed, such as data security and privacy, integration with existing healthcare systems, regulatory compliance, and varying levels of technological infrastructure across regions. To maximize its benefits, a tailored approach is required, acknowledging that one-size-fits-all strategies may not be effective. Strategies should include robust data encryption, collaboration with regulatory authorities, and pilot programs. public awareness initiatives, infrastructure investment, and continuous improvement efforts. To effectively navigate the intricate healthcare system in China and unlock the full potential of intelligent platforms for improved management of neonatal heart disease, it is imperative to implement these measures.

Comment 5: Finally, please review and cite several related papers:

5.1 Verrall CE, Patel S, Travitz L, Tchieu J, Dale RC, Kasparian NA, Winlaw DS, Blue GM. Biological and structural phenotypes associated with neurodevelopmental outcomes in congenital heart disease. Transl Pediatr 2023;12(4):768-786. doi: 10.21037/tp-22-687.
Reply 5.1: Thank you very much for your constructive suggestions. We have cited these articles, which have greatly enriched the content of our manuscript. (see Page 4, line 120-124).
Changes in the text: Research has discovered that the mental health of parents is correlated with the psychosocial functioning and quality of life for their children with CHD (8). Therefore, incorporating psychoeducation focused on parents, more knowledge about CHD, and parental involvement in CHD management can yield favorable effects on children's initial diagnosis, prognosis, and overall quality of life.

5.2 Van De Bruaene A, Budts W. Collaterals in congenital heart disease: when and how to treat? Cardiovasc Diagn Ther 2023;13(2):418-426. doi: 10.21037/cdt-23-10.

Reply 5.2: Relevant sentences have been added. (see Page 7, line 224-228)

Changes in the text: Complications might occur in those who have undergone percutaneous closure, a low-risk intervention (41). If online consultation is feasible, parents can pose their queries online and report any complications that may arise post-surgery. Additionally, doctors can keep track of special cases.

5.3Wray J, Layton S, Biglino G. My Core: conveying the everyday normality of living with congenital heart disease. Cardiovasc Diagn Ther 2021;11(6):1436-1438. doi: 10.21037/cdt-21-387.

Reply 5.3: Relevant sentences have been added. (see Page 7, line 222-223)

Changes in the text: For families who have children born with CHD, regular hospital appointments are a common practice (40).