

RESEARCH

Open Access



The 'Ironclad friendship' of China-Cambodia, lays the first step in the foundation of early diagnosis and treatment of asymptomatic congenital heart Defects- A multi-national screening and intervention project, 2017–2020

Honglin Song^{1,2†}, Xi Li^{3,4†}, Jiang Lu¹, Junjie Song¹, Teng Wang¹, Min Gao⁵, Xingyi Zhang³, Min Ma², Yi Shi¹, Jiayu Fang², Hongchen Fu², Huadan Wang², Lin Duo¹, Mingjing Tang^{1*} and Linhong Pang^{1,2*}

Abstract

Background Congenital heart disease (CHD) is the leading cause of mortality in childhood worldwide. However, a large number of children with CHD are not diagnosed promptly in low- and middle-income regions, due to limited healthcare resources and lack the ability of prenatal and postnatal ultrasound examinations. The research on asymptomatic CHD in the community is still blank, resulting in a large number of children with asymptomatic CHD can not be found and treated in time. Through the China-Cambodia collaborative health care initiative, the project team conducted research, screened children's CHD through a sampling survey in China and Cambodia, collected relevant data, and retrospectively analyzed the data of all eligible patients.

Objectives The project aimed to evaluate the prevalence of asymptomatic CHD in a sample population of 3-18years old and effects on their growth status and treatment outcomes.

Methods We examined the prevalence of 'asymptomatic CHD' among 3-18years old children and adolescents at the township/county levels in the two participating. A total of eight provinces in China and five provinces in Cambodia were analyzed from 2017 to 2020. During 1 year follow-up after treatment, the differences in heights and weights of the treated and control groups were evaluated.

[†]Honglin Song and Xi Li contributed equally to this work.

*Correspondence:
Mingjing Tang
candysabrina@126.com
Linhong Pang
plh2835@163.com

Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Results Among the 3,068,075 participants screened from 2017 to 2020, 3967 patients with asymptomatic CHD requiring treatment were identified [0.130%, 95% confidence interval (CI) 0.126–0.134%]. The prevalence rate of CHD ranged from 0.02 to 0.88%, and was negatively related to local per capita GDP ($p=0.028$). The average height of 3310 treated CHD patients were 2.23% (95% CI: -2.51%~–1.9%) lower than that of the standard group and the average weight was -6.41% (95% CI: -7.17%~–5.65%) lower, the developmental gap widening with advancing age. One year after treatment, the relative height difference remained comparable while that, in weight was reduced by 5.68% (95% CI: 4.27% ~7.09%).

Conclusions Asymptomatic CHD now is often overlooked and is an emerging public health challenge. Early detection and treatment are essential to lower the potential burden of heart diseases in children and adolescents.

Keywords Congenital heart disease, Prevalence, China, Cambodia, Asymptomatic, Children

Background

Congenital heart defects (CHD) are the leading cause of mortality in childhood worldwide [1], affecting 13.3 million people worldwide in 2019 [2]. CHD accounts for more than 40% of deaths related to congenital defects and causes a serious public health burden, especially in low- and middle-income countries, including China and Southeast Asian countries [3–6]. The prevalence of congenital heart disease in China has increased 24-fold from 2015 (0.201‰) to 2019 (4.905‰) [7]. Early detection, followed by surgery or transcatheter intervention, should greatly reduce mortality and morbidity [8]. However, a significant number of asymptomatic patients with CHD are overlooked in antenatal ultrasound and neonatal examinations, resulting in poor prognosis or undernourished and compromised growth status [9].

In many aspects, asymptomatic CHD remains largely understudied. One major issue is the underdiagnosis of the disease, which often leads to serious hypoxia, shock, acidosis, pneumonia, and other complications including death [10–11]. Pulse oximetry is a highly specific and moderately sensitive test for detection of critical CHD with very low false-positive rates [12–13]. The use of pulse oximetry for newborn screening has led to remarkable improvements in detection in recent years but is still not widely available in low and middle-income countries [12–14]. Result from a meta-analysis suggest that a quarter of asymptomatic patients with critical CHDs remain undiagnosed due to its 76% sensitivity of pulse oximetry [14]. Furthermore, there is no data to the knowledge of the authors, or in scientific literature on the potential health effects and treatment outcomes in asymptomatic patients, including—how CHD influences growth status in childhood and strategies to overcome the condition. The above information is crucial in the development of public health policies and resource allocation in the sector of pre-school and early childhood health services.

‘The Children’s CHD Free Screening Project’ in China [15] and the ‘Love Heart Journey Project’ [16] in Cambodia, two screening and intervention programs for asymptomatic children and adolescents with CHD, have been

implemented since January 2017. The primary goal of this study was to determine the prevalence and subtypes of asymptomatic CHD by screening children in kindergarten, primary, middle and high schools via cardiac auscultation and ultrasound. The second objective was to determine the patient growth status and efficacy of treatment in narrowing the gaps in growth and development.

Methods

Design overview and study cohort

In this study, we examined the prevalence of ‘asymptomatic CHD’ among 3–18 years old children and adolescents at the township/county level. The study area incorporated different districts in the two participating nations, China and Cambodia. The author’s affiliated institution (Fuwai Yunnan Cardiovascular Hospital) is located in Yunnan province, which is the largest specialized hospital for cardiovascular disease in southwest China. We selected most counties in Yunnan Province (on our way to cover all areas), as well as relatively remote and poor areas in 7 provinces in western China with local screening needs as screening sites. A total of eight western provinces in China comprising 74 counties and 700 townships were included in the study. On average, approximately 7.3 million children are residents in each of these selected provinces in China, and the population density in the study areas is around 200 individuals per square kilometer. With the cooperation of an intergovernmental program, a ‘Love Heart Journey Project’ was launched in Cambodia in January 2018. Five provinces of Cambodia with an average of 87 children per square kilometer were selected for the study as the whole process required the commitment and support of the local governing boards at different administrative/prefectural levels in Cambodia. A map of the study area incorporating the provinces and counties of both nations is shown (Additional file 1). Far-flung and underdeveloped areas with limited medical resources were included as part of the study plan. Children from kindergarten were thoroughly evaluated at our screening camps. Those diagnosed with CHD and eligible

for higher center treatment received appropriate surgical or interventional therapy at a specialist cardiology center.

The overall response rate from the participating was 98.2%. Patients who underwent treatment at tertiary cardiology centers, such as Fuwai Yunnan Cardiovascular Hospital had 95% of their medical costs covered by health insurance schemes offered by governments and philanthropic foundations. The parents of the patients were followed up for at least one year following their discharge from postsurgical intervention. Geographic information system (GIS) was applied to generate a prevalence map of CHD. We further explored the associations among high-prevalence clustering patterns of CHD, height and weight growth gap patterns.

Procedures

The screening team consisted of a cardiologist or cardiac surgeon, three specially trained nurses, two ultrasound specialists, and local community members. For some planned screening sites with a large number of children, the screening team added additional 3–5 cardiologists and nurses to cope with the task. As part of the screening process, a standardized physical examination was initially performed by qualified practice nurses who were vigilant for specific signs (such as abnormal pulse, clubbing fingers, pedal edema, fluid overload, rapid breathing and poor posture) [17]. During this time, detailed history of the child's mental status, and breathlessness during feeding leading to poor weight gain and easy fatigability were noted [17]. An experienced nurse or a qualified doctor then auscultated the heart in the aortic, pulmonary, tricuspid, and mitral areas with stethoscope B type (Suzhou Yuyue Medical Technology Co., Ltd, China), during which any cardiac souffle or a functional murmur was considered abnormal (Additional file 2). For patients with abnormal heart sounds, further echocardiography was performed using ultrasound Phillip CX 50, Probe S5-1, systematically and comprehensively to assess structural and hemodynamic changes in the heart, from various views, including (a). parasternal long axis, (b). parasternal short axis (at apical, papillary muscle, mitral valve, aortic valve levels), (c). apical (two, three, four, five-chamber), (d). subcostal, and (e). suprasternal views. Various jet flows, pressures, volumes, and chamber areas in both the systole and diastole phases were measured. Based on results obtained by specialists in echocardiography, the cardiologist or cardiac surgeon determined whether the clinical phenotype warranted surgical or interventional treatment, which was ultimately provided at Fuwai Yunnan Cardiovascular Hospital.

Data collection and measurement

The centers recorded all forms of CHD, mainly, patent ductus arteriosus (PDA Q21.051), tetralogy of Fallot

(TOF), atrial septal defect (ASD Q21.102), and ventricular septal defect (VSD Q21.001, Q21.102), along with other types according to International Classification of Diseases (ICD 10) [18]. With the electronic medical record database of children and adolescents, basic characteristics were extracted, including gender, age, height and weight at admission, CHD subtypes (ASD, VSD, PDA, TOF, and others), after treatment adverse reactions (squatting, shortness of breath after activity, dyspnea, cyanosis, or syncope). We also collected information about annual family income, health insurance, and place of residence through face-to-face interviews with parents.

The parents of treated children and adolescents were contacted one year after discharge to obtain information about their health conditions, including death, reoperation, symptoms, ultrasound manifestations, current weight and height, school attendance, as well as feeding, physical development, and psychological status. To define the natural environment and social development characteristics of patients at each study site, we also searched grey literature, such as statistical yearbooks, for information on average altitude and annual per capita gross domestic product (GDP) in 2017 [19–20].

Statistical analysis

For categorical variables, frequencies and percentages were calculated while for continuous variables, median [interquartile range (IQR)] values were determined. To estimate the prevalence of asymptomatic CHD and its subtypes in screening, we divided the number of identified cases by the number of screened individuals. The prevalence in the two countries (China and Cambodia), was compared along with subtype fractions among three age groups (3–6 years, 7–12 years, and 13–18 years). The differences between groups were visualized and tested using box plots and the Kruskal-Wallis test. Scatter plots and fitting lines were applied to illustrate the correlation between the prevalence and environmental (altitude) and socioeconomic characteristics (per capita GDP) across counties. To determine the height and weight gaps of patients, we calculated the absolute and relative differences with the age-specific Chinese standard lines [21]. Additionally, the changes in relative gaps during follow-up were calculated by subtracting the baseline from the 1-year value. Patients with missing data were excluded from the analysis. All studies were conducted with SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Prevalence of asymptomatic CHD

A total of 3,068,075 participants were screened (3,015,470 in China and 52,605 in Cambodia), which resulted in the identification of 3967 [0.130%, 95% confidence interval

(CI) 0.126–0.134%] children and adolescents with asymptomatic CHD that needed treatment (Additional file 3).

A total of 3,015,470 children were screened from 7,756 schools in 700 villages in China, among which 3,842 children were diagnosed with CHD. Table 1 shows that the prevalence of asymptomatic CHD was highest in North-west China (0.201%). The prevalence of asymptomatic CHD was significantly lower in China than Cambodia (0.127%, 95% CI: 0.123–0.132% vs. 0.238%, 95% CI: 0.198–0.283%, $p < 0.001$). Among the 64 screening sites, the county/district-level prevalence of asymptomatic CHD ranged from 0.022 to 0.883%, which was negatively correlated with local per capita GDP ($p = 0.028$), but not significantly related to local average altitude ($p > 0.05$) (Fig. 1).

Patient characteristics

Among 3310 children with CHD who underwent surgical treatment, 1 child died and 835 were lost to follow-up. Therefore, 2474 children with CHD were followed up (Additional file 3). The median age was 7.0 (3.0 to 11.0) years and 56.4% were female, among which ASD (946, 0.030%, 95% CI: 0.028–0.033%), VSD (703, 0.022%, 95% CI: 0.023–0.024%), and PDA (366, 0.012%, 95% CI: 0.011–0.013%) were the most common subtypes (Table 2). Overall, 89.4% of patients residing in rural areas, 31.1% had an annual household income of less than 10 000 Yuan (equivalent to 1587 USD), and 96.7% had social health insurance (Table 2). Compared with patients from Cambodia, those in China were more likely to have an annual household income over 1587 USD, and social health insurance (both $p < 0.001$).

Among the major subtypes of CHD identified the fraction of ASD increased from 31.9% (95% CI: 28.8–35.0%) in patients aged 3–6 years to 45.0% (95% CI: 41.4–48.9%)

in patients aged 13–18 years ($p < 0.001$), while fraction of VSD [from 33.9% (95% CI: 30.7–37.0%) to 24.0% (95% CI: 20.7–27.4%)] and PDA [from 15.8% (95% CI: 13.4–18.3%) to 11.9% (95% CI: 9.4–14.5%)] (both $p < 0.05$) (Fig. 2).

Growth gaps

The average height of the patient group requiring treatment was 2.84 (95% CI: 2.39–3.28) cm lower than the standard also presenting as a relative difference of -2.23% (95% CI: -2.54%–-1.93%). The average patient weight was 1.89 (95% CI: 1.59–2.18) kg lower relative to the standard weight presenting as a relative difference of -6.41% (95% CI: -7.17%–-5.65%). The height (8.88 vs. 2.84 cm, $p = 0.0054$) and weight gaps (8.59 vs. 1.87 kg, $p < 0.001$) were more significant in Cambodian than those in Chinese patients.

The growth gaps remained across the baseline age groups. The relative gaps in height and weight were -2.51% (-3.01%–-2.00%) and -7.24% (-8.41%–-6.08%) for patients aged 3–6 years at diagnosis, -1.91% (-2.38%–-1.44%) and -5.94% (-7.18%–-4.69%) for those aged 7–12 years, and -2.59% (-3.06%–-2.13%) and -5.88% (-7.50%–-4.26%) for 13–18 years old patients ($p > 0.05$ for all) (Fig. 3). Height and weight gaps were similar, for patients with different subtypes of CHD (Additional file 4).

Recovery after treatment

After the treatment period, 3 (0.1%) patients died during the 1-year follow-up, while 2474 (74.7%) reported their growth situations. In this cohort, the relative height gap persisted from -2.23% (95% CI: -2.54%–-1.93%) at baseline to -2.98% (95% CI: -3.46%–-2.50%) 1 year later, with an insignificant change of -0.80% (95% CI:

Table 1 Prevalence of CHD in different screening regions

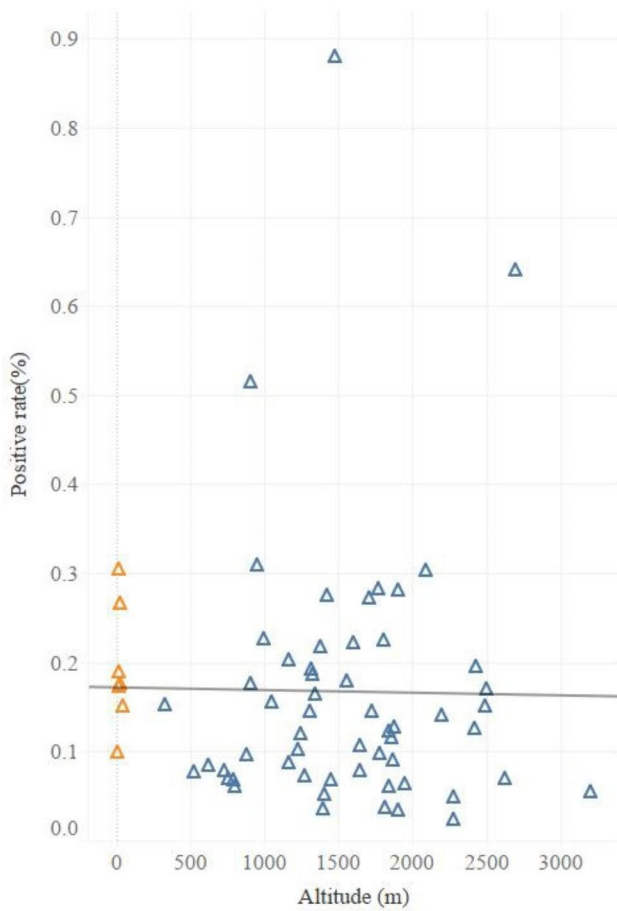
Country	Region	Number of townships	Number of screening schools	Screening children	Confirmed case of CHD	Prevalence rate (%)
China	Western Yunnan	97	1332	390,355	504	0.129
	Southwest Yunnan	189	1674	713,905	1071	0.150
	Northwest Yunnan	65	384	130,257	150	0.115
	Central Yunnan	43	629	253,011	232	0.092
	Northeast Yunnan	193	3086	1,251,676	1410	0.113
	Southern Yunnan	27	184	63,091	122	0.193
	Southwest China [#]	56	230	123,006	172	0.140
	Northwest China [#]	30	237	90,169	181	0.201
	Total		700	7756	3,015,470	3842
Cambodia	5 provinces in total	NA	80	52,605	125	0.238

Abbreviation: CHD congenital heart disease

NA: Indicates that the data was not available

[#] The screening centers in 7 provinces other than Yunnan Province were scattered, so they were categorized as “Southern China provinces” and “Northwestern China provinces”

Altitude-CHD prevalence



Per capital gross domestic product-CHD prevalence

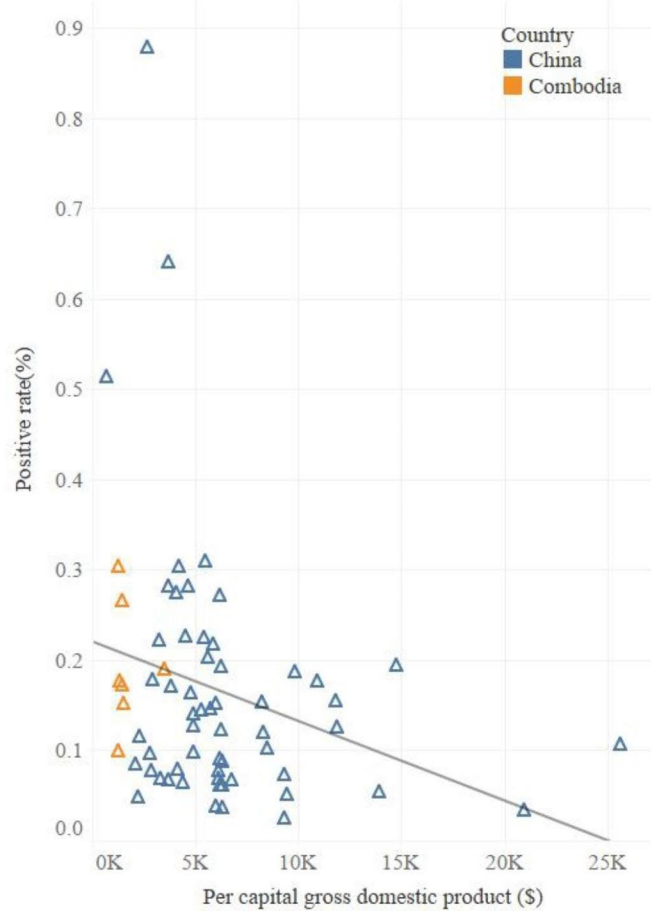


Fig. 1 Correlations of CHD prevalence across counties/districts with local per capital GDP and altitude
Abbreviations: CHD: indicates congenital heart disease

-1.39%~-0.21%); while the relative weight gap was 5.68% lower (95% CI: 4.27%~7.09%) [from -6.41% (95% CI: -7.17%~-5.65%) to -0.76% (95% CI: -1.88%~0.35%)]. These patterns were consistent between the Chinese and Cambodian patient populations.

The “catching-up” steps were larger in patients who were younger during the time of treatment. In patients aged 3–6 years, changes in relative height and weight gaps were 0.09% (95% CI: -0.96%~1.14%) and 8.91% (95% CI: 6.70%~11.10%). In contrast, in patients aged 13–18 years, changes in relative height and weight gaps were -0.81% (95% CI: -1.87%~0.25%) and 0.71% (95% CI: -1.79%~3.21%) (Fig. 4). The changes in growth gaps related to different major subtypes of CHD are presented in Additional file 4.

Discussion

According to data obtained from screening projects involving over 3 million people in China and Cambodia from January 2017 to Jan. 2020, 0.12% of 3-18-year-old children and adolescents had asymptomatic CHD that required treatment, with rates being higher in less well-developed areas. Patients with this condition experienced delayed growth in height and weight, but early detection and treatment could significantly improve development and outcomes.

In addition to being the largest screening project on CHD, this study contributes to the literature in several aspects. We observed a notable prevalence of asymptomatic CHD in children and adolescents requiring treatment. CHD prevalence was markedly lower relative to that reported in earlier screening studies (0.38 -0.49%) [22–23], but it should be noted that the patients identified in our study are a particularly overlooked group, as the majority of current routine prenatal (e.g. ultrasound)

Table 2 Characteristics of patients with congenital heart disease, overall and by country

	Overall	China	Cambodia	P value
Demographic and socio-economic				
Female	56.35 (1394/2474)	56.56 (1384/2447)	44.44 (12/27)	0.207
Age, year (Median and IQR)	7.0 (3.0–11.0)	7.0 (3.0–11.0)	8.0 (6.0–13.0)	0.016
Household income: 10 000 RMB (1587 USD) or above per year	68.88 (1704/2474)	69.47 (1700/2447)	14.81 (4/27)	< 0.001
Social medical insurance	96.68 (2392/2474)	97.75 (2392/2447)	0.00 (0/27)	0.163
Rural residence	89.41 (2212/2474)	89.29 (2185/2447)	100.00 (27/27)	0.106
Clinical profile at admission				
Subtypes of CHD				< 0.001
Patent ductus arteriosus	14.79 (366/2474)	14.91 (365/2447)	3.70 (1/27)	
Tetralogy of Fallot	1.40 (34/2474)	1.14 (28/2447)	22.22 (6/27)	
Ventricular septal defect	28.41 (703/2474)	28.36 (694/2447)	33.33 (9/27)	
Atrial septal defect	38.24 (946/2474)	38.45 (941/2447)	18.52 (5/27)	
Other	17.19 (425/2474)	17.12 (419/2447)	22.22 (6/27)	
Adverse reactions	34.16 (845/2474)	33.75 (826/2447)	70.37 (19/27)	< 0.001

Values in the table indicate percentages (numerator/denominator) unless otherwise noted.

Abbreviations CHD: congenital heart disease; IQR: inter quartile range.

and neonatal (e.g. pulse oximetry) CHD screenings tests focus on critical CHD [24–26]. Moreover, the prevalence of CHD was higher in less developed areas, indicating a higher misdiagnosis rate, which may be attributed to the lack of skilled personnel and advanced facilities for diagnosis and treatment [27–28], as well as parents' willingness to undergo early CHD screening. Considerable evidence indicates that in the majority of developing countries, achieving the goal of early diagnosis and treatment remains a challenge, which significantly hampers overall population development [28–30]. In developing countries, the lack of sufficient healthcare resources for universal screening generally impedes the development of the entire population [31–32]. This vicious cycle between 'poverty caused by illness' and 'poverty caused by CHD' needs to be urgently broken [33].

Furthermore, even in cases with no major symptoms, CHD can cause a lag of growth during childhood and adolescence. In addition, children with CHD are at risk of acute and chronic malnutrition due to difficulties in

feeding and poor digestion and absorption of nutrients [34–35]. Previous studies on the growth and development of children with CHD revealed smaller effects on weight in school-age children than pre-schoolers, but this finding was attributed to survival bias [36, 37]. Our data suggest that both height and weight gaps related to CHD similarly persist with age across countries. Nevertheless, it is reasonable to expect that the relative gaps widen with patient growth. A survival bias could also affect age-dependent trends in gaps, since the fraction of severe CHD cases among the common subtypes (i.e., VSD and PDA) decreased as patients got older, implying that some of these patients may not be able to continue their education or even die.

Third, early treatment can substantially reduce the growth delay of children and adolescents with asymptomatic CHD. Several studies have shown that after CHD surgery, the cardiac functions of children improve, along with nutritional intake growth and development levels gradually approach those of their healthy counterparts [38–39]. In our study, the weight and height of children with suspected CHD improved after treatment, highlighting the importance of timely detection and treatment of asymptomatic coronary heart disease. The potential for improving the growth trajectory of the patient is significantly greater with earlier intervention. Treatment effects are expected to influence future physical functions, psychological status, and quality of life in addition to anthropometric parameters [40–41], which calls attention to the need for longer-term observations in this large cohort.

Our study paves the way for a more comprehensive analysis of asymptomatic CHD, especially in middle- and low-income countries. Our findings have significant implications for the development of health policies in these areas. While recognizing the importance of CHD screening, simple and effective technical protocols are necessary for conducting large-scale projects. Cardiovascular auscultation has been confirmed as the most valuable screening method for CHD [42]. This procedure, combined with echocardiography, has allowed us to scale up CHD screening across countries. The key to improving health outcomes in subsequent prompt CHD treatment. However, surgery for CHD remains an advanced technique that is not universally available. Only three hospitals in Cambodia can perform this procedure. Although interventional treatment for CHD is widely adopted in many areas, expensive angiography equipment is required. In Cambodia, only 10 such systems are available. In recent years, new procedures for structural heart disease such as ASD, PDA, and VSD, which are under echo guidance only, have been established to reduce potential injury related to fluoroscopy and angiography [43–45]. These novel techniques are of particular

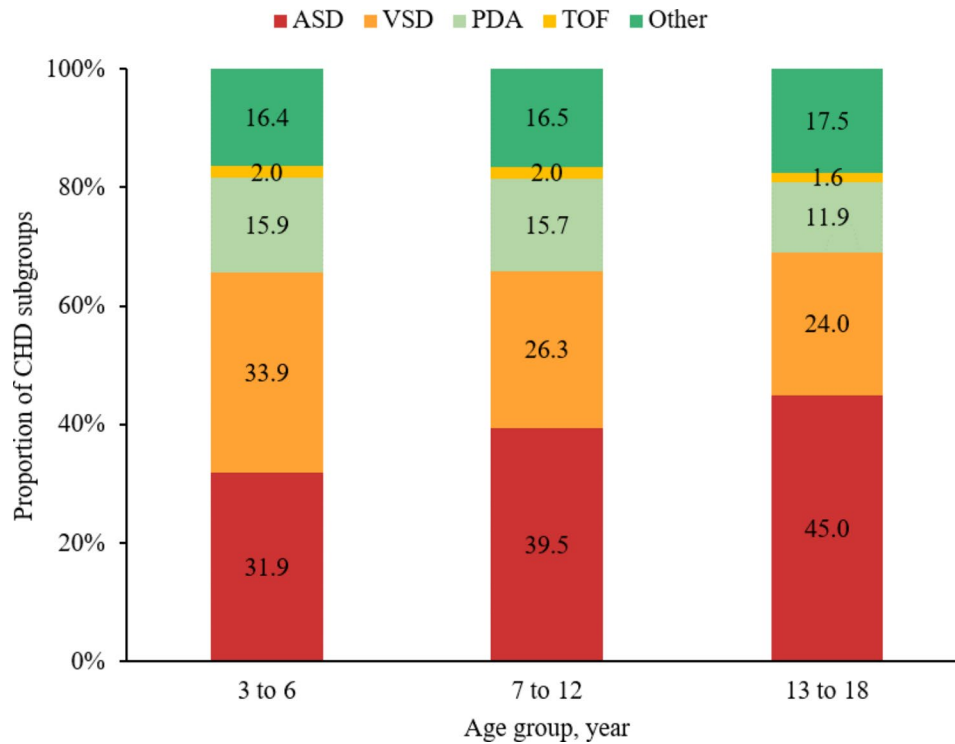


Fig. 2 Proportion of CHD subtypes across age groups
 Abbreviations: CHD: congenital heart disease; PDA: patent ductus arteriosus, TOF: tetralogy of Fallot, ASD: atrial septal defect, VSD: ventricular septal defect

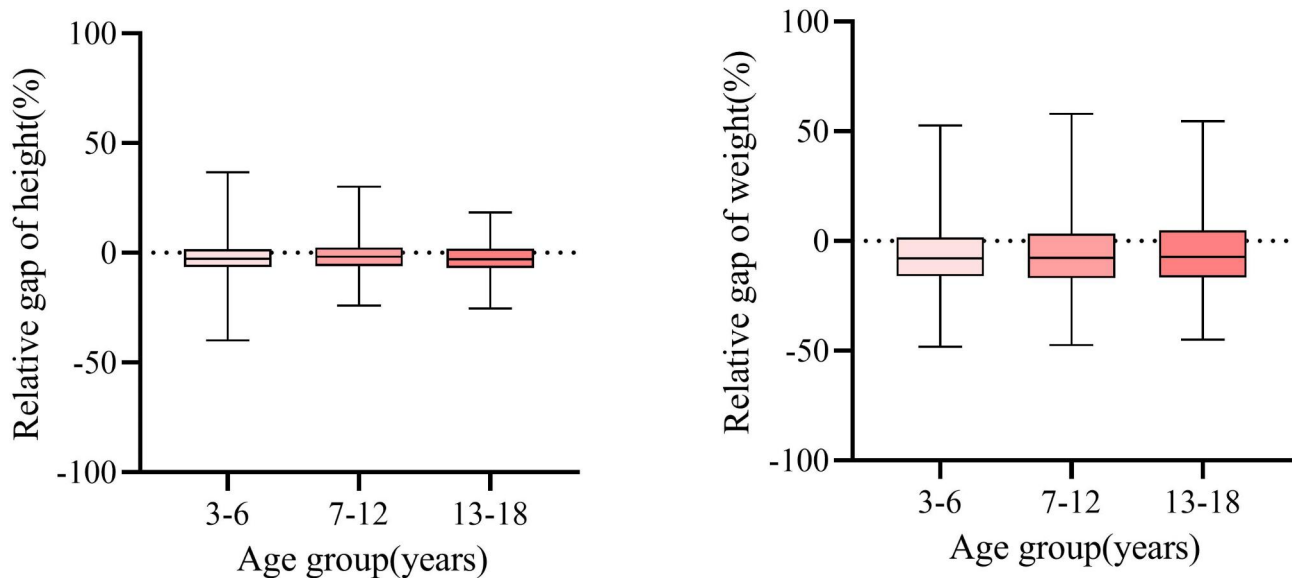


Fig. 3 Relative growth gaps across baseline age groups
 "Relative height or weight gap" = (height or weight of the CHD child divided by the standard height or weight of Chinese child) – 1. Therefore, a value greater than 0 indicated that the child with CHD was developing in accordance with Chinese child growth standards, otherwise the opposite is true

value for access to treatment in less developed regions, due to their independence from cath laboratories.

Several potential limitations need to be considered when interpreting the findings of the current study. Telephone survey methods may have potential bias leading to skewing of results. Follow-up on CHD from the field

is therefore essential. Moreover, the retrospective design of the study raises concerns about the accuracy of recall. However, the concordances between the study and past findings on height and weight growth in children with congenital heart disease give credibility to our findings the effects of CHD on growth and development over

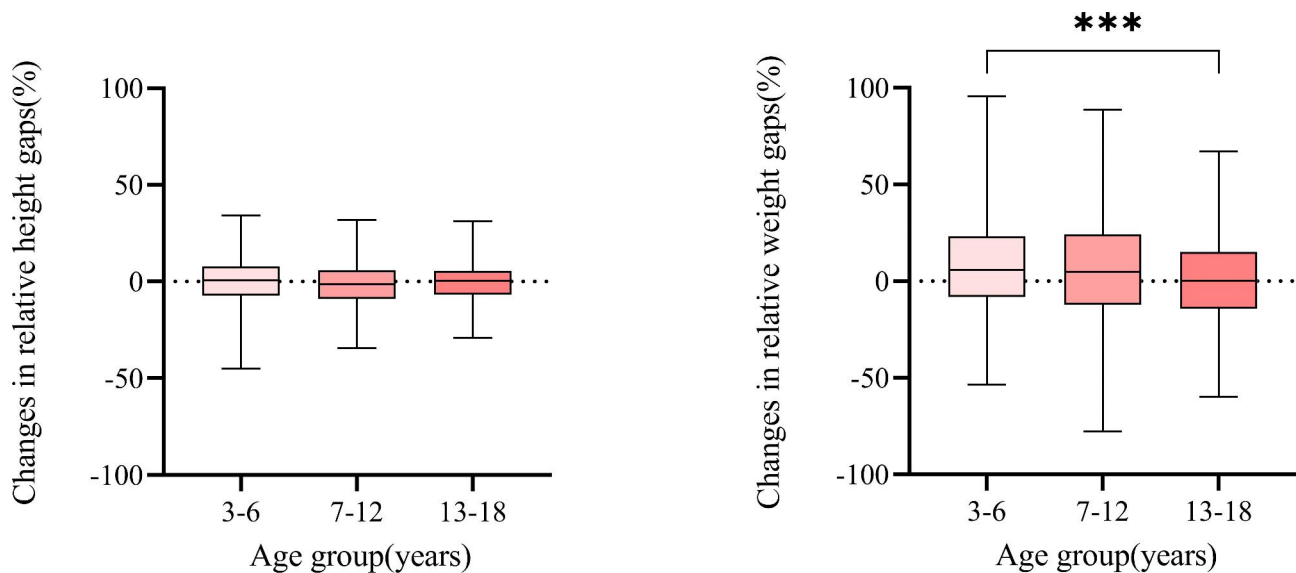


Fig. 4 Catching up in growth across baseline age groups

“Relative height or weight gap” was both calculated at baseline and at follow-up. “Change in relative height or weight gap” = “Relative height or weight gap at baseline” - “Relative height or weight gap at follow-up”

the long term require further study and follow-up. Due to field screening time constraints, we failed to collect the complete socio-demographic information on children without CHD besides total numbers, the confirmed CHD cases data available were not sufficient to support the regression models and further adjust for confounding variables.

Conclusions

To our knowledge, this is the largest community-based congenital heart disease screening project worldwide. This study indicates of many CHD left over in the community, large-scale CHD screening benefits and brought down to low and middle-income countries to reduce the potential high burden of CHD. Further development of surgical and interventional treatment capacities in these countries plays a critical role in improving the growth trajectory of disadvantaged patients.

Abbreviations

PDA	patent ductus arteriosus
TOF	tetralogy of Fallot
ASD	atrial septal defect
VSD	ventricular septal defect
CHD	congenital heart disease
IQR	inter quartile range.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12872-023-03314-8>.

Additional File 1: Project sites

Additional File 2: Auscultation technical protocol and auscultation location

Additional File 3: Flow chart of selected participants

Additional File 4: Height and weight gaps before and after treatment

Acknowledgements

We appreciate the multiple contributions made by study teams at the Cambodia-China Friendship Kossamak Hospital, and the local sites in the collaborative network in the realms of study design and operations, particularly Chea Munyrih and Xia Zhou from Cambodia China Friendship Association, for data collection.

Author contributions

LD and LP conceived of the “Children CHD Free Screening Project” in China and “Love Heart Journey Project” in Cambodia, and take responsibility for all aspects of them. HS and XL designed the study. XL, HS and LP wrote the first draft of the article, with further contributions from LD, JL, XZ, JF, HF, HW and MG collected the data for this study. MT and JS did the statistical analysis, the manuscript was critically revised by TW, MM, and YS. All authors interpreted the data and approved the final version of the article.

Funding

This project was supported by building a joint laboratory for important chronic and epidemic diseases in South and Southeast Asia (Grant No. 202103AF140002), Yunnan Provincial Clinical Research Center for Cardiovascular Diseases-New Technology Research and Development Project for Diagnosis and Treatment of Major Cardiovascular Diseases (Grant No. 202102AA310002); Key Research and Development Program from Yunnan Province Science and Technology Department (Grant No. 202103AF140002); and Provincial Innovation Team Project of Heart Failure Diagnosis and Treatment in Fuwai Yunnan Cardiovascular Hospital (Grant No. 202005AE160020). Study design, data collection, data analysis, data interpretation, and report writing were not influenced by the study funders.

Data Availability

Original data tied to individuals, locations, and times are considered personally identifiable health information. These data cannot be shared. Aggregated data are available to the extent allowed by a data use agreement. The corresponding authors affirm that the manuscript is an honest, accurate, and transparent account of the study, that no important aspect of the study has been omitted, and that any deviations from the study plan have been explained. Final data for this study can be obtained from the corresponding authors upon reasonable request.

Declarations

Ethics approval and consent to participate

The ethics committee at the Fuwai Yunnan Cardiovascular Hospital approved this project (Number 2018-01). Informed consent was obtained from all subjects and/or their legal guardian(s). The study protocol adheres to the ethical guidelines of the 1975 Declaration of Helsinki. Each CHD case was classified and coded according to the International Classification of Diseases version 10 and belonged to the code range from Q20 to Q28. The classification showed that there were more than 15 types of defects in our study area.

Consent for publication

Not applicable.

Competing interests

The authors declared no relevant conflict of interest.

Author details

¹Fuwai Yunnan Cardiovascular Hospital, Affiliated Cardiovascular Hospital of Kunming Medical University, Kunming, China

²School of Public Health, Kunming Medical University, Yu Hua Street Chun Rong Road, Cheng Gong New City, Kunming, China

³National Clinical Research Center for Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China

⁴Central China Subcenter of the National Center for Cardiovascular Diseases, Zhengzhou, China

⁵School of Public Health, Chongqing Medical University, Jinyun Campus, Huxi Town, Shapingba District, Chongqing, China

Received: 9 May 2023 / Accepted: 18 May 2023

Published online: 07 June 2023

References

1. GBD 2017 Congenital Heart Disease Collaborators. 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(3):185–200. [https://doi.org/10.1016/S2352-4642\(19\)30402-X](https://doi.org/10.1016/S2352-4642(19)30402-X).
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM et al. Global Burden of Cardiovascular Diseases and Risk factors, 1990–2019: Update from the GBD 2019 Study. *J Am Coll Cardiol*. 2020;76(25):2982–3021. <https://doi.org/10.1016/j.jacc.2020.11.010>.
3. Lloyd J, Askie L, Smith J, Tarnow-Mordi W. Supplemental oxygen for the treatment of prethreshold retinopathy of prematurity. *Cochrane Database Syst Rev*. 2003;2003(2):Cd003482. <https://doi.org/10.1002/14651858.CD003482>.
4. Zheleva B, Atwood JB. The invisible child: childhood heart disease in global health. *Lancet*. 2017;389(10064):16–8. [https://doi.org/10.1016/S0140-6736\(16\)32185-7](https://doi.org/10.1016/S0140-6736(16)32185-7).
5. Su Z, Zou Z, Hay SI, Liu Y, Li S, Chen H, et al. Global, regional, and national time trends in mortality for congenital heart disease, 1990–2019: an age-period-cohort analysis for the global burden of Disease 2019 study. *EclinicalMedicine*. 2022;43:101249. <https://doi.org/10.1016/j.eclinm.2021.101249>.
6. Richner B, Sok C, Kretschmar O, Pretre R, Babatasi G, Lafont A. Interventional cardiology and cardiac surgery in Cambodia. *Lancet*. 2012;379(9822):1197–8. [https://doi.org/10.1016/S0140-6736\(12\)60510-8](https://doi.org/10.1016/S0140-6736(12)60510-8).
7. Zhao L, Chen L, Yang T, Wang T, Zhang S, Chen L, et al. Birth prevalence of congenital heart disease in China, 1980–2019: a systematic review and meta-analysis of 617 studies. *Eur J Epidemiol*. 2020 Jul;35(7):631–42. <https://doi.org/10.1007/s10654-020-00653-0>.
8. Friedman JK, Newburger JW. Trends in congenital heart disease: the Next Decade. *Circulation*. 2016;133(25):2716–33. <https://doi.org/10.1161/CIRCULATIONAHA.116.023544>.
9. Wren C, Richmond S, Donaldson L. Presentation of congenital heart disease in infancy: implications for routine examination. *Arch Dis Child Fetal Neonatal Ed*. 1999;80(1):F49–53. <https://doi.org/10.1136/fn.80.1.f49>.
10. Singh Y, Lakshminrusimha S. Perinatal Cardiovascular Physiology and Recognition of critical congenital heart defects. *Clin Perinatol*. 2021 Aug;48(3):573–94. <https://doi.org/10.1016/j.clp.2021.05.008>.
11. Huang Y, Zhong S, Zhang X, Kong L, Wu W, Yue S et al. Large scale application of pulse oximeter and auscultation in screening of neonatal congenital heart disease. *BMC Pediatr*. 2022 Aug 12;22(1):483. <https://doi.org/10.1186/s12887-022-03540-7>.
12. Plana MN, Zamora J, Suresh G et al. Pulse oximetry screening for critical congenital heart defects. *Cochrane Database Syst Rev*. 2018 Mar 1;3(3):CD011912. <https://doi.org/10.1002/14651858.CD011912.pub2>.
13. Jain D, Jain M, Lamture Y. Pulse Oximetry Screening for Detecting Critical Congenital Heart Disease in Neonates. *Cureus*. 2022 Dec 23;14(12):e32852. <https://doi.org/10.7759/cureus.32852>.
14. Thangaratnam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. *Lancet*. 2012;379(9835):2459–64. <https://doi.org/10.1016/j.lancet.2012.10.013>.
15. Health Commission of Yunnan Province. Yunnan Province has actively carried out screening and treatment of congenital heart disease in children in ethnic minority areas. 2017. http://ynswsjkw.yn.gov.cn/html/2017/gongzuodongtai_0621/4574.html Accessed 21 March 2023.
16. Cambodia office of the council of ministers. Cambodian and Chinese Premiers Unveil Red Cloth to Officially Launch “Love Heart Journey” Project in Cambodia. 2018. <https://pressocm.gov.kh/en/archives/21902>. Accessed 21 March 2023.
17. Yunnan Science and Technology Press: Screening manual for congenital heart disease children in the community (ISBN: 978-7-5416-8072-4). 2021, Yunnan.
18. World Health Organization. International statistical classification of diseases and related health problems, ICD-10 Volume 2. 2016. https://cdn.who.int/media/docs/default-source/classification/icd/cause-of-death/icd10volume2_en_2016.pdf. Accessed 24 Jun 2022.
19. National Bureau of Statistics of China. China statistical Yearbook. 2022. <http://www.stats.gov.cn/sj/ndsj/2022/indexch.htm>. Accessed 21 March 2023.
20. National Institute of Statistics. Statistical Yearbook of Cambodia 2021. <http://www.nis.gov.kh/index.php/km/>. Accessed 21 March 2023.
21. Zhang YQ, Li H. Reference charts of sitting height, leg length and body proportions for chinese children aged 0–18 years. *Ann Hum Biol*. 2015;42(3):223–30. <https://doi.org/10.3109/03014460.2014.934283>.
22. Zhao L, Chen L, Yang T, Wang T, Zhang S, Chen L, et al. Birth prevalence of congenital heart disease in China, 1980–2019: a systematic review and meta-analysis of 617 studies. *Eur J Epidemiol*. 2020;35(7):631–42. <https://doi.org/10.1007/s10654-020-00653-0>.
23. Liu Y, Chen S, Zühlke L, Babu-Narayan SV, Black GC, Choy MK, et al. Global prevalence of congenital heart disease in school-age children: a meta-analysis and systematic review. *BMC Cardiovasc Disord*. 2020;20(1):488. <https://doi.org/10.1186/s12872-020-01781-x>.
24. Gómez-Rodríguez G, Quezada-Herrera A, Amador-Licona N, Carballo-Magdalena D, Rodríguez-Mejía EJ, Guizar-Mendoza JM. Pulse oximetry as a screening test for critical congenital heart disease in term newborns. *Rev Invest Clin*. 2015;67(2):130–4.
25. Plana MN, Zamora J, Suresh G, Fernandez-Pineda L, Thangaratnam S, Ewer AK. Pulse oximetry screening for critical congenital heart defects. *Cochrane Database Syst Rev*. 2018;3(3). <https://doi.org/10.1002/14651858.CD011912.pub2>.
26. Guillory C, Gong A, Livingston J, Creel L, Ocampo E, McKee-Garrett T. Texas Pulse Oximetry Project: a Multicenter Educational and Quality Improvement Project for implementation of critical congenital heart Disease Screening using pulse oximetry. *Am J Perinatol*. 2017;34(9):856–60. <https://doi.org/10.1055/s-0037-1599214>.
27. Zühlke L, Lawrenson J, Comitis G, De Decker R, Brooks A, Fourie B, et al. Congenital heart disease in low- and Lower-Middle-Income Countries: current status and New Opportunities. *CurrCardiol Rep*. 2019;21(12):163. <https://doi.org/10.1007/s11886-019-1248-z>.
28. Kang G, Xiao J, Wang J, Chen J, Li W, Wang Y, et al. Congenital heart disease in local and migrant Elementary Schoolchildren in Dongguan, China. *Am J Cardiol*. 2016;117(3):461–4. <https://doi.org/10.1016/j.amjcard.2015.10.061>.
29. Zimmerman M, Sable C. Congenital heart disease in low-and-middle-income countries: focus on sub-saharan Africa. *Am J Med Genet C Semin Med Genet*. 2020;184(1):36–46. <https://doi.org/10.1002/ajmg.c.31769>.

30. Trafimow D. Parents do not always have to get their way: why critical congenital heart Disease Screening for Newborns should be mandatory. *Am J Bioeth.* 2016;16(1):35–7. <https://doi.org/10.1080/15265161.2015.1115143>.
31. Van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol.* 2011;58(21):2241–7. <https://doi.org/10.1016/j.jacc.2011.08.025>.
32. Davey B, Sinha R, Lee JH, Gauthier M, Flores G. Social determinants of health and outcomes for children and adults with congenital heart disease: a systematic review. *Pediatr Res.* 2021;89(2):275–94. <https://doi.org/10.1038/s41390-020-01196-6>.
33. Saxena A. Status of Pediatric Cardiac Care in developing countries. *Child (Basel).* 2019;6(2):34. <https://doi.org/10.3390/children6020034>.
34. Argent AC, Balachandran R, Vaidyanathan B, Khan A, Kumar RK. Management of undernutrition and failure to thrive in children with congenital heart disease in low- and middle-income countries. *Cardiol Young.* 2017;27(S6):22–530. <https://doi.org/10.1017/s104795111700258x>.
35. Medoff-Cooper B, Ravishankar C. Nutrition and growth in congenital heart disease: a challenge in children. *Curr Opin Cardiol.* 2013;28(2):122–9. <https://doi.org/10.1097/hco.0b013e32835dd005>.
36. Udholm LF, Gaml-Sørensen A, Arendt LH, Brix N, Lunddorf LLH, Ernst A, et al. Timing of Pubertal Development in Boys and Girls with congenital heart defects: a Nationwide Cohort Study. *J Am Heart Assoc.* 2022;11(7):e023135. <https://doi.org/10.1161/jaha.121.023135>.
37. Li X, Zhu J, An J, Wang Y, Wu Y, Li X. Growth and development of children under 5 years of age with tetralogy of Fallot in a chinese population. *Sci Rep.* 2021;11(1):14255. <https://doi.org/10.1038/s41598-021-93726-3>.
38. Carmona F, Hatanaka LS, Barbieri MA, Bettiol H, Toffano RB, Monteiro JP, et al. Catch-up growth in children after repair of tetralogy of Fallot. *Cardiol Young.* 2012;22(5):507–13. <https://doi.org/10.1017/s1047951111002009>.
39. Correia Martins L, Lourenço R, Cordeiro S, Carvalho N, Mendes I, Loureiro M, et al. Catch-up growth in term and preterm infants after surgical closure of ventricular septal defect in the first year of life. *Eur J Pediatr.* 2016;175(4):573–9. <https://doi.org/10.1007/s00431-015-2676-4>.
40. Sun KP, Xu N, Huang ST, Cao H, Chen Q. Health-Related quality of life in children and adolescents with simple congenital heart defects before and after transcatheter intervention therapy: a single-center study. *Ann Thorac Cardiovasc Surg.* 2021;27(2):105–11. <https://doi.org/10.5761/atcs.0a.20-00078>.
41. Cheung MM, Davis AM, Wilkinson JL, Weintraub RG. Long term somatic growth after repair of tetralogy of Fallot: evidence for restoration of genetic growth potential. *Heart.* 2003;89(11):1340–3. <https://doi.org/10.1136/heart.89.11.1340>.
42. Zhao QM, Niu C, Liu F, Wu L, Ma XJ, Huang GY. Accuracy of cardiac auscultation in detection of neonatal congenital heart disease by general paediatricians. *Cardiol Young.* 2019;29(5):679–83. <https://doi.org/10.1017/s1047951119000799>.
43. Pan XB, Ou-Yang WB, Pang KJ, Zhang FW, Wang SZ, Liu Y, et al. Percutaneous Closure of Atrial Septal Defects under Transthoracic Echocardiography Guidance without Fluoroscopy or Intubation in Children. *J Interv Cardiol.* 2015;28(4):390–5. <https://doi.org/10.1111/joic.12214>.
44. Ou-Yang WB, Li SJ, Wang SZ, Zhang DW, Liu Y, Zhang Z, et al. Echocardiographic guided Closure of Perimembranous Ventricular Septal defects. *Ann Thorac Surg.* 2015;100(4):1398–402. <https://doi.org/10.1016/j.athoracsur.2015.05.036>.
45. Bu H, Yang Y, Wu Q, Jin W, Zhao T. Echocardiography-guided percutaneous closure of perimembranous ventricular septal defects without arterial access and fluoroscopy. *BMC Pediatr.* 2019;19(1):302. <https://doi.org/10.1186/s12887-019-1687-0>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.