Review Article

# The Evolution and Future of Pediatric Cardiology

**Abenezer Kebede**[1]

1. Department of Pediatrics, NYC Health + Hospitals/Lincoln, United States

**From early descriptions of heart disease to its current interdisciplinary practice of antenatal diagnosis of heart defects, advanced imaging, interventional catheterization, cardiac surgery, electrophysiology, pediatric intensive care, pediatric heart transplantation, and lifelong follow-up of patients with congenital heart defects, pediatric cardiology has undergone significant changes and developments in the past centuries. This review aims to outline these developments in pediatric cardiology and attempts to predict the forces that will shape its future. Innovations to measure the hidden physiological processes of the circulation of blood, such as the stethoscope, the electrocardiogram, cardiac catheterization, and most importantly, the echocardiogram, have greatly contributed to the field of pediatric cardiology. The 20th century introduced the innovations of cardiopulmonary bypass and congenital heart surgery, followed by interventional catheterization, the use of prostaglandin E1 to support the circulation in neonates with duct-dependent heart defects, pediatric heart transplantation, and mechanical circulatory support. In the modern era of pediatric cardiology, high-quality images of cardiac structure and function are obtained by the use of cardiac magnetic resonance imaging and multidetector row computed tomography. There is also an increasing number of patients diagnosed with heart defects prenatally, which has led to the establishment of antenatal cardiology as a separate field of interest. Furthermore, pediatric cardiology has greatly benefited from the advances made in the genetic basis of inherited arrhythmias and cardiomyopathies. Also, quality improvement collaboratives have provided a structured environment for process improvement. An important area that pediatric cardiology is currently focusing on is the transition of care to adult congenital heart disease programs. The challenge of pediatric cardiology is not only to identify the cardiac anatomy of patients′ heart defects but also to predict the clinical course of the defects, the causes of the defects, and the morbidity of the defects after surgical repair, and to provide durable care for children with heart disease throughout their childhood and into their adulthood. The future of pediatric cardiology will include the use of genomics for risk stratification of at-risk individuals and patients with heart**

**disease, pharmacologic therapy that is matched to specific pathways, regenerative medicine and cardiac tissue engineering, the development of smaller and more durable mechanical circulatory support devices, the development and use of computational models and digital clinical twins, and the use of artificial intelligence for imaging and monitoring of patients with heart disease. Pediatric cardiology must also evolve to become a system of care that includes neurodevelopmental, psychosocial, and transition of care outcomes in addition to the current measurement, interpretation, and intervention of heart disease in children and adults with congenital heart disease.**

**Corresponding author:** Abenezer F. Kebede, abnzrflk@gmail.com

## Introduction and Background

For pediatric cardiology to continue to evolve and move forward, it has to measure what previously had only been the subject of educated surmise. Long ago, in ancient civilizations, it was recognized that the heart was at the center of life. Many diseases of the heart were characterized by severe pain and by symptoms of arrhythmia, weakness, and shortness of breath. Collapses could also be caused by heart disease. However, at that time it was not possible to formulate a conceptual model of the circulation, and it was not possible to be sure whether a cardiac lesion was a structural as opposed to a functional problem. The major breakthrough in the understanding of the circulation was the shift from the concept of a diffuse humoral process to that of a closed system. The latter thought provided the fundamental basis of modern cardiovascular medicine [1][2][3][4][5][6][7][8].

For a long time, the correlation of clinical data and measurable physiological data was missing. The effect of Digitalis on heart failure, for the first time, was durable; heart sounds and murmurs changed from non-perceptible to stethoscope-measurable, the ECG allowed for the recording of electrical heart activity, and catheterization of the heart via the heart chambers correlated symptoms with pressures, flow, and shunts [9][10][11][12][13][14][15][16][17][18][19][20][21][22][23][24].

The child with heart disease is now commonly stabilized as a neonate with prostaglandins and can be treated with staged single-ventricle palliation. A child with heart disease is now a candidate for heart transplantation as well as support with extracorporeal circulation and pediatric ventricular assist devices. Modern pediatric cardiology is therefore an integrated system of care for the heart in the fetus, child, and adult. This system of care consists of fetal diagnosis and treatment of heart disease, cross-

sectional imaging, cardiac catheterization and interventional procedures, cardiac surgery, and postoperative care in the Intensive Care Unit. This system also consists of postoperative care in outpatient clinics for children with heart disease. The child with heart disease also requires care and follow-up by an electrophysiology laboratory for children with heart disease. The child with heart disease also requires a program of heart failure management as well as heart transplant candidacy. This system of care for children with heart disease also requires quality improvement activities by collaboratives of pediatric cardiologists from around the world as well as monitoring of late survival and neurodevelopmental status of children with specific types of heart defects and strategies for optimized transition of adolescents and young adults with heart defects to adult programs of care for patients with heart defects [25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41].

As the subspecialty of pediatric cardiology evolved, the field became a unique system of care for all children with heart disease. The breadth of pediatric cardiology now includes the spectrum of diagnosis and management of congenital and acquired heart disease in infants, children, and adolescents as well as all adults with congenital heart disease. As a result, pediatric cardiology is a highly diverse field and has come to include fetal diagnosis and treatment of congenital anomalies as well as cross-sectional imaging and interventional catheterization and surgical techniques to treat children with heart disease. Many children with heart disease require evaluation and management of a wide variety of adult congenital cardiac diseases, including electrophysiological studies, management of heart failure and cardiomyopathy, and management of children with heart disease who require heart transplantation as well as postoperative care of children with heart disease in pediatric intensive care units. Thus, the field has come full circle and, as before, requires quality improvement collaboratives as well as assessment of the long-term outcomes of children with heart disease and development of strategies for transition of care to adult congenital heart disease programs. Advances in measurement and application of technology have been instrumental in the continued evolution of pediatric cardiology. Initially, Doppler and deformation imaging enhanced the assessment of children with heart disease. Subsequently, the use of MRI and CT, with three-dimensional measurements and models, has provided powerful tools to assess structure and function in children with heart disease. The advances in technology have also led to fetal intervention and the development of cardiac registries that will enable further evaluation of the mechanisms of and treatment of heart disease in children. Thus, powerful tools for inherited cardiac genetic disease have also been developed to assist in the prediction and potential cure of disease based on

mechanism in individual children [42][43][44][45][46][47][48][49][50][51][52][53][54][55][56][57][58][59][60][61][62][63][64][65][66][67][68][69][70].

In the next decade, pediatric cardiology is likely to transform from a disease-oriented, mainly anatomically focused, rescue-oriented field to a more mechanism-oriented, predictive, and reparative field. New challenges will be addressed by using genomics and targeted pathway therapies as well as by the development of regenerative and tissue-engineered substitutes for cardiac structures. In addition, new strategies for transcatheter-based structural interventions in children will be developed. Also, safe and effective pediatric-specific mechanical circulatory support strategies will have to be established. Digital models and AI-assisted imaging will become more and more important. In contrast to the current gold standard of in-person follow-up of outpatients with heart disease, a variety of forms of telemonitoring will supplement the evaluation and follow-up of children and adults with congenital heart disease. Pediatric cardiology will become a global health field with an increasing number of programs that provide cardiovascular care in low- and middle-income countries. This review provides an update on the current status of pediatric cardiology and gives a perspective on the future developments of this exciting field.

# Review

## *Historical Development of Pediatric Cardiology*

The history of pediatric cardiology can be portrayed by the increasing ability to explain, diagnose, and treat the circulation in children over time. The different eras increased the ability to make the heart and its problems in children more measurable, more interpretable, or more treatable.

## *Ancient Beginnings (Ebers Papyrus, 1550 BCE)*

The heart as an organ has always been a subject of human interest. The Ebers Papyrus, one of the oldest medical documents from 1550 BCE, contains over 700 recipes for all kinds of diseases and afflictions [1][2]. Already in this papyrus, a special chapter is devoted to the heart and all its possible diseases and their cures. The author lists possible cardiac diseases and their various symptoms (e.g., heart pain, irregular heartbeats, heart inflammation, heart weakness, respiratory distress, etc.). He also describes treatment with garlic and onions, honey, in the form of decoctions, concoctions, infusions, pastes, poultices, etc.,

and some of the opiate preparations for chest pain. Some spiritual procedures for the treatment of heart diseases are also described [1][2].

### *Greek Medicine and Humoral Theory (400 BCE)*

Data concerning a specific entity of cardiac disease in the pre-Greek era (some centuries before 400 BCE) are lacking [3][4]. No in-depth description of cardiac disease is found in the works of Hippocrates (400 BCE), which represent the first systematic documentation of such cases. As for the blood, Hippocrates assumed that it originated in the liver and was distributed throughout the body by the heart. He believed that heart disease was due to an imbalanced state of an individual's emotions, leading to a stagnation of the bodily fluids. According to Hippocrates, a treatment for these cases involved efforts to treat the heart by means of specific diets and increased levels of physical activity. It was his view that by modifying an individual's way of life, it was possible to prevent heart disease.

### *Anatomical Advances and the Galenic Era (3rd–2nd Century BCE to 2nd Century CE)*

In the Hellenistic and Roman periods, there occurred a significant extension of the anatomical knowledge of the cardiovascular system. The physician Erasistratus (c. 304–250 BCE) stated that he had performed many dissections and that he knew the structure of the arteries and the veins very well. He correctly described the heart as a pump but was not correct in his description of the circulation of the blood. In the 2nd century of the Christian era, the physician Galen (129–200/216 CE) read the works of all the earlier anatomists that had been written up to that time. He described the cardiac structures in great detail and presented a complete account of the heart's physiology, pathologies, and their cures. Galen was a careful clinician and, on the basis of a patient's symptoms and pulse assessment, was able to diagnose illnesses and assess bodily functions by bedside examination. In accordance with the humoral theory, he treated his patients with remedies, including herbs, and advised them to live a healthy life. In some cases, he performed bloodletting in order to cure an illness of his patients. His medical works were the major influence on Western medicine for nearly 1500 years [5][6][7].

### *The Discovery of Circulation (1628)*

In 1628, William Harvey published De Motu Cordis, in which he described the closed circulatory system consisting of the pulmonary and the systemic circulation. This work, in which he described the movement of blood propelled by the heart through the arteries and its return to the heart via the veins,

was a milestone in the history of circulatory concepts. In contrast to traditional views, Harvey rejected the notion that the liver produced blood that was then consumed by the tissues. Harvey's analysis of the function of the heart from a mechanical viewpoint marked the beginning of modern cardiovascular physiology [8].

### *Limited Progress in the 17th and 18th Centuries*

Although there were significant advances in the diagnosis and control of cardiac disease following the circulation of blood described by Harvey in 1628, the development of diagnosis and treatment of heart disease for centuries afterward was a slow process. The obvious physical signs and symptoms of cardiac disease, such as pitting edema, signs of cyanosis, shortness of breath, tachycardia, and collapse of a part or of the whole of the body, were for a long time recognized by the clinical observer. It was not until relatively recently that it has become possible to study in detail the beating heart of a living patient. In the meantime, the heart was treated for centuries with a variety of humoral or 'other' remedies such as bloodletting and purging with a wide variety of drugs and also with a variety of herbs, special diets, etc., which, in the light of present-day knowledge, were apparently for long times ineffective for structural lesions of the heart as opposed to their functional consequences, which also were for long times apparently intractable [9].

### *Digitalis and Early Pharmacotherapy (1775–Early 1900s)*

The history of effective targeted pharmacotherapy for the cardiovascular system began with William Withering's 1785 account identifying Digitalis purpurea from foxglove as the effective component in a traditional folk remedy for 'dropsy' (now congestive heart failure) [10][11]. By the late 1800s, the cardiac drug digitalis from the foxglove plant had been combined with the edema folk remedy squill plant to act as a diuretic for 'dropsy' of heart failure. The first truly effective diuretics for 'dropsy,' however, were the mercurial diuretics introduced in the early part of this century [12][13].

### *Rise of Clinical Cardiology (19th Century)*

In 1816, Clinical Cardiology began with the invention of the stethoscope by René Laennec. Stethoscopes enabled physicians for the first time to hear the sounds of the heart and to diagnose, among other things, murmurs and additional heartbeats, stenosis and regurgitation of heart valves, congenital heart defects, and diseases of the pericardium [14][15]. Acquired heart disease was most commonly caused by rheumatic

heart disease, a complication of recurrent streptococcal infections, leading to progressive deformation of the heart valves in severe cases of rheumatic fever [16][17]. In 1895, the Dutch physiologist Willem Einthoven laid the foundations for the practical application of multi-lead electrocardiography (ECG) that enables the diagnosis of arrhythmias, conduction disturbances, and damage to the heart muscle. Since then, the ECG has become one of the most important tools for diagnosis in Clinical Cardiology [18][19].

### *Intracardiac Access and Early Hemodynamic Understanding (1929–1930s)*

Werner Forssmann in 1929 was the first man to introduce a catheter into his own right atrium. This self-experiment demonstrated that access to the heart through a peripheral vein was possible; subsequent catheterization enabled intracardiac pressure measurements as well as determination of shunts in the heart. Thus, a systematic study of the heart with congenital anomalies was made possible [20][21].

### *The Birth of Pediatric Cardiac Surgery (1930s–1940s)*

The first successful correction of a heart defect was performed in 1938 by Robert E. Gross at the Boston Children's Hospital when he ligated a patent ductus arteriosus (PDA) in a 4-year-old boy [22]. In 1944, Alfred Blalock and Helen Taussig developed the first shunt to increase pulmonary circulation in children suffering from cyanotic congenital heart defects. The first shunt was a connection between the subclavian artery and the pulmonary artery in children with tetralogy of Fallot [23]. Cardiac catheterization, developed into a useful clinical tool by Cournand and Richards, was used to measure intracardiac pressure, to determine oxygen saturation, to assess shunts, and to measure pulmonary vascular resistance [21][24]. Before the advent of penicillin, children and young adults developed an increasing number of valvular heart diseases due to rheumatic fever [16][17].

### *Expansion of Diagnostics and Surgical Capability (1950s-1970s)*

The post-war decades witnessed enormous advances in all fields of pediatric and adult congenital heart disease. Surgical, interventional, and diagnostic techniques improved dramatically. Cardiopulmonary bypass made possible definitive repairs 'on the inside' of the heart. Pediatric open-heart surgery evolved at an incredible pace. Echocardiography progressed from M-mode to 2D and to color flow Doppler, allowing for a very complete assessment of cardiac function and cardiac flow in children and adults with heart defects. Diagnostic catheterization also paralleled therapeutic catheterization. The balloon atrial septostomy became a potentially life-saving procedure in infants with transposition of the great arteries.

There were landmark advances in the surgical repair of several congenital heart defects. These include the arterial switch operation for transposition of the great arteries, the staged repair for children with hypoplastic left heart syndrome, and the so-called Fontan-type repair for children with single-ventricle-type heart defects. These repairs dramatically improved the survival rate for children with complex heart defects. Advances in the pharmacologic management of children with congenital heart defects also had a major impact. The use of prostaglandin E1 to maintain a patent ductus arteriosus in a child with a ductal-dependent congenital heart defect and the use of nonsteroidal anti-inflammatory medications for the medical closure of a patent ductus arteriosus are two examples [25][26][27][28][29][30][31][32][33][34][35][36].

### *Modern Era of Pediatric Cardiology (1984-2025)*

Pediatric cardiology evolved from a subspecialty of general cardiology to a fully developed, independent medical discipline by the late 20th century. Today, pediatric cardiology is made up of several areas of expertise, including imaging and interventional therapy as well as cardiac surgery and electrophysiology. In addition to these areas, pediatric cardiology also includes treatment of heart failure, intensive care medicine, and long-term follow-up of individual patients.

### *Heart Transplantation and Mechanical Support (1984-1990s)*

By the mid-1980s, pediatric heart transplantation for children with complex congenital heart problems and end-stage heart disease became an operation that continued to grow as the technical expertise of performing the surgery and the postoperative management of these patients using immunosuppression improved. With the advent of cyclosporine, the first effective calcineurin inhibitor immunosuppressive agent, used in the early 1980s, and the subsequent development of more effective immunosuppressive combinations, such as the use of tacrolimus and mycophenolate mofetil in the 1990s and 2000s, there has been a significant improvement in graft survival rates. This, together with improvements in mechanical support of the failing heart, such that ECMO is now a standard of care for refractory acute cardiopulmonary failure, and the growth of pediatric VADs to bridge children to transplantation, as with the Berlin Heart EXCOR pediatric ventricular assist device, has made pediatric heart transplantation a standard and successful form of therapy for children with end-stage heart disease [37][38][39][40][41].

### *Advances in Echocardiography and Catheter-Based Therapy (1980s-2000s)*

2D echocardiography and Doppler echocardiography have been the mainstay in the diagnosis of children with heart defects since their development. Tissue Doppler and strain/strain rate deformation imaging have further refined the assessment of ventricular function in children [27][28][42]. Furthermore, interventional catheterization, initially a diagnostic tool, has evolved into a therapeutic modality. Thus, in addition to the assessment of obstructive lesions, balloon valvuloplasty as well as device closure of septal defects (e.g., PDA and ASD) and stenting of obstructive lesions can be performed with low morbidity and without the need for repeat sternotomy [43][44][45][46]. Consequently, pediatric cardiovascular surgery has evolved into a “hybrid” field of imaging, interventional catheterization, and surgery [43][44][45][46].

### *Evolution of Congenital Heart Surgery (1990s-2000s)*

Recent advances in neonatal bypass strategies, myocardial protection, and postoperative care in the ICU have made primary complete correction of congenital heart disease possible in the neonate and have facilitated the implementation of neurodevelopmental strategies to protect these infants [47][48]. Cardiopulmonary interactions that were believed to be universally lethal in the neonate, such as transposition of the great arteries treated with an arterial switch operation and hypoplastic left heart syndrome treated with a series of operations (Norwood, Glenn, Fontan), now have predictable outcomes with increasingly successful shunt strategies and arch repair [30][31][32][33][49].

### *Electrophysiology and the Genetics Revolution (1990s-2010s)*

Catheter ablation technology also matured, enabling the precise treatment of abnormal heart rhythms utilizing three-dimensional electroanatomic mapping. The success of ablation could be increased while minimizing exposure to the patient and the operator from fluoroscopy, even in patients with complex congenital anatomy of the heart [50][51]. The field of inherited arrhythmia and cardiomyopathy genetics has also grown, and several pathogenic genetic variants have been identified in the long QT syndromes as well as other channelopathies and in the familial cardiomyopathies. A multidisciplinary approach now exists in programs for inherited cardiac disease, utilizing genetic testing in counseling for the risk of disease development in first-degree relatives and in risk stratification for individual patients [52][53][54][55][56].

### *Cross-Sectional Imaging and Structural Heart Innovation (2000s-2020s)*

In addition to the assessment of ventricular volumes and flow, detection of fibrosis, and definition of complex anatomy, the cardiac, coronary, and extracardiac vascular anatomy can be accurately assessed using cardiac CT. These findings can be obtained using optimized pediatric dose protocols, reducing radiation exposure while preserving diagnostic quality [57][58][59][60]. 3D echocardiography has been increasingly used for advanced structural heart planning, virtual surgical planning, and 3D printing of heart models for surgery [61]. In addition to the feasibility of the above applications, the clinical applications of MRI-guided and radiation-free catheterization are also expanding [62][63]. The high quality of advanced fetal cardiac evaluation has led to improved prenatal diagnosis, risk stratification, and even in-utero interventions, such as fetal aortic valvuloplasty in patients with evolving hypoplastic left heart syndrome [64][65].

### *Quality Improvement, Outcomes Science, and Lifelong Care (2010s-2020s)*

The creation of national registries and collaboratives such as STS-CHSD, IMPACT, and PC4 allows for the ability to benchmark, create outcomes-driven, standardized approaches to cardiac care, and embark upon multicenter quality improvement projects in the operating room, in the cath lab, and on the cardiac ICU floor [66][67][68]. Neurodevelopmental surveillance of the infant with high-risk cardiac surgery has become the standard of care with the recognition that neurodevelopmental issues are primary outcomes rather than late aftereffects of congenital heart disease [47][48]. The growth of the adult congenital heart disease (ACHD) population as survival has improved has led to the development of models of lifelong surveillance and of transition programs as described by major cardiac societies' guidelines [69][70].

### *Technological Integration and Precision Cardiovascular Care (2020-2025)*

Advances in genomics, particularly in whole-exome and whole-genome sequencing, have enabled accurate and timely genetic diagnosis for patients with inherited cardiomyopathies and arrhythmias as well as for those with syndromic congenital heart disease [55][56][71]. The ability to provide sequence-based diagnostic information has allowed for earlier diagnosis and the potential for more targeted medical therapy along specific disease pathways. Importantly, a growing amount of targeted therapeutics is being developed for specific genotypes of cardiomyopathy, and these are based on the disease biology. For instance, therapeutics targeting the RAS/MAPK pathway as well as emerging disease-modifying strategies for substrates of inherited cardiomyopathy are being developed for the RAS/MAPK-driven

forms of cardiomyopathy and other forms of CHD along specific disease pathways [72][73][74]. In addition to advancing along pathway-based therapies for cardiomyopathy and other forms of CHD, there has also been significant progress in the area of regenerative medicine. Early-phase human clinical trials have been initiated that utilize strategies for single-ventricle heart (SVH) reconstruction that are aimed at enhancing the growth of the failing myocardium as well as the growth of other structures and organ systems that support the failing heart (myocardium-support strategies) [75][76][77]. Strategies for engineered growth-capable grafts and conduits for children with CHD are also being developed in the area of tissue engineering to better address the large number of children requiring surgical interventions for CHD [78]. Moreover, advances in the use of AI (artificial intelligence) have enabled improved accuracy in the assessment of cardiac function [79][80][81][82].

## Future Directions in Pediatric Cardiology

The future of pediatric cardiology is less about diagnosing lesions in children and more about how a child will decompensate, what intervention to give next, and how to build a repair that will last as the child grows.

Advancements in pediatric cardiology will go beyond incremental improvements in current diagnostic and therapeutic strategies and include novel applications of molecular corrections for biologic failures, computational predictions, and the development of lifelong systems of care for children with heart disease [55][56][62][69].

### *Genomic and Molecular Medicine*

#### *Precision Genomics and Risk Stratification*

Recent advances in whole-exome and whole-genome sequencing for individuals and their families have enabled improved genotype-phenotype correlation in CHD and the inherited cardiomyopathies, thus allowing the identification of at-risk children before the complete expression of the phenotype [55][56][71][83]. National-scale programs and pediatric genomic consortia have developed a variant catalog that is continually expanding and have improved the interpretation of the vast numbers of rare variants identified in families. The risk to affected family members can also be modeled using this data in combination with information regarding arrhythmia vulnerability and cardiomyopathy trajectory [71][83][84].

### *Gene Therapy and Gene Editing*

For the gene therapy of monogenic cardiomyopathies, first preclinical and clinical studies are being developed for several inherited heart muscle diseases. For Danon disease, even a clinical trial with an AAV vector has already been started (see [74][85]). Also for the cardiovascular system, several organ-specific genome editing tools such as base-editing and CRISPR/Cas, as well as first proof-of-concept experiments using patient-specific induced pluripotent stem cell-derived cardiomyocytes as well as cardiac organoids for modeling and correcting disease-causing mutations in these cells, have been established [86][87][88].

### *Targeted Pharmacotherapy*

Therapy, particularly targeted therapy, is now increasingly administered in a fashion relevant to the underlying mechanisms of different pediatric cardiac diseases rather than by mere reference to organ-based diagnoses as was the case in the past. Thus, pathway-directed therapies are being used or studied in selected children with RASopathy-associated HCM. Additionally, there are also now emerging precision therapies for several of the pediatric inflammatory vasculitides as well as for various endotypes of acute myocarditis [72][73][89][90].

## *Regenerative and Tissue-Engineering Solutions*

### *Stem Cell-Based Myocardial Regeneration*

Additional circulations where there are single ventricle failures and/or failures of the Fontan circulation, where there is a severe shortage of organ transplants to cover these failures, and in which the circulation fails over time are now in the early phase of studies with progenitor cells. Some of these studies include various types of cardiosphere-derived cell-based strategies as well as several products from the mesenchymal lineage that are already in early-phase clinical studies and need to be the subject of controlled phase II/III clinical trials [75][76][77].

### *Engineered Valves, Vessels, and Patches*

Using growth-capable blood vessels (conduits) or using tissue-engineered vascular graft platforms can help overcome the major restriction of pediatric surgery: somatic growth. The aim of such systems is to make the number of reoperations and necessary interventions as low as possible. So-called pediatric

vascular grafts are already clinically applied. Scaffold design and host remodeling are, however, still being improved [78][91].

### *Bioartificial Organ Development and Xenotransplantation*

In addition to being potential long-term solutions to the organ donor shortage, bioengineering and xenotransplantation research could also have pediatric applications. Research into genetically modified pig-heart xenograft platforms as well as research into organ failure support and organ transplant immunology will help to further develop xenotransplanted organs for use in patients after more has been learned about the safety and rejection of such transplants [92][93].

## *Advanced Interventional and Surgical Technologies*

### *Transcatheter Structural Interventions*

Transcatheter valve therapies and structural implants are expanding into anatomies previously requiring surgery, including transcatheter pulmonary valve strategies in native or augmented RVOTs, while ongoing device evolution targets durability, size constraints, and growth adaptability [94][95][96]. Bioresorbable structural devices represent an emerging strategy to reduce the lifelong implant footprint in children, though pediatric validation remains early and trial-dependent [97].

### *Hybrid and Minimally Invasive Surgical Innovations*

Hybrid surgical–catheter strategies in pediatric cardiac surgery have emerged as a less invasive alternative to manage high-risk neonates with complex heart defects within a stable environment. Recent improvements in pediatric cardiopulmonary perfusion have attempted to improve clinical results by optimizing perfusion strategies. The use of ultra-low priming volumes, for instance, has been aimed at decreasing the frequency of neurologic and inflammatory complications [49][47][48].

### *Mechanical Circulatory Support (MCS)*

To support the failing pediatric heart, there is ongoing work in the Pediatric Mechanical Circulatory Support (MCS) field that includes the development of smaller-sized, highly hemocompatible devices for all ages, including the smallest infants. A key functional aspect of Pediatric MCS is evolving from being solely utilized as a ‘bridge-to-transplant’ for selected pediatric patients with end-stage heart failure to

potentially functioning as a ‘bridge-to-recovery’ for select patient populations with heart failure. Several key developments will be required to assist in the progression to safe clinical use, including strategies to decrease the risk of stroke and device thrombosis [40][41][98].

## *Imaging, Computational Modeling, and Artificial Intelligence*

### *Next-Generation Imaging*

4D-flow MRI provides new parameters to quantify the complex pediatric circulation, like the energetics of the circulation in Fontan-type patients and the flow load in shunts. MRI-guided catheterization and totally radiation-free intervention concepts are new diagnostic tools for children, rich in information, which—in contrast to current diagnostic tools—also focus on a stewardship of the lifetime risk and thus are of special interest [62][63].

### *Computational Simulation and Digital Twin Technology*

Computational simulation models can predict physiological changes that occur as a result of reconstruction, and there are several ‘digital twin’ systems currently under development. These systems use serial imaging and physiological data as input and function as a decision support system for the planning of the required intervention, in terms of timing and type [99][100].

### *AI-Enhanced Diagnostics and Monitoring*

Fetal echo assessment using AI and automatically generated quality scores may improve detection sensitivity and reduce dependence on the operator. Other applications of AI in pediatric cardiology, such as ECG analysis or imaging assessment for early signs of ventricular dysfunction or risk of arrhythmia, are currently under investigation [79][80][81][82][101].

## *Systems of Care, Lifelong Management, and Population Impact*

### *Fetal-Neonatal-Pediatric-Adult Continuity*

With an increasing number of children born with heart defects that will need to be managed for the rest of their lives as adults, pediatric cardiology has become a specialty for the long-term management of a long-term condition. A well-structured transition program and access to services for Adult Congenital Heart Disease within the parameters of major guidelines [69][70] are therefore essential.

### *Remote Monitoring and Telecardiology*

Home monitoring in single-ventricle infants has been shown to decrease interstage mortality and allow for earlier detection of decompensation. Emerging technologies such as tele-echocardiography and wearable monitoring are now being utilized to extend specialty monitoring in single-ventricle patients beyond the tertiary care setting [80][81][82].

### *Global Equity and Access*

The use of technology such as portable ultrasound and AI-assisted medical image interpretation and large-scale training platforms will help to overcome the disparities that currently exist in the ability to diagnose, manage, and triage children with CHD, while a number of global initiatives are currently underway to aid workforce development in regions of greatest need [102][103].

### *Neurodevelopmental and Psychosocial Integration*

As high-precision assessment is more and more combined with cardiology to continuously monitor and treat the neurodevelopmental problems of children with complex heart defects as well as children who have already undergone cardiopulmonary bypass surgery in early childhood, established neurodevelopmental risk profiles of these patient groups are being used as a basis for follow-up models [47][48][104].

## Conclusions

The history of pediatric cardiology has followed a sort of circular path. First, we gain more insight into the normal physiology of growing children, and then we do better things with that information. Then, after a number of years, that information leads to a reorganization of the healthcare that we deliver to children who are growing up with congenital heart disease as a result of the advances that we had previously developed.

Each of the technologies outlined above will likely find its way into the future of pediatric cardiology, but as separate threads that get woven together into a tapestry of molecularly stratified patients with growth-compatible repair; of improved, radiation-sparing imaging, coupled with sophisticated computational-based simulation; of detection by powerful, and hopefully wise, artificial intelligence that guides regenerative strategies. But, most importantly, as the field of pediatric cardiology progresses,

better prediction will lead to better timing, and thus better repair, which in turn will result in less and less cumulative morbidity as the child grows. But, just as importantly, long-term survival of children with congenital heart disease will need to be paralleled by improvements in neurodevelopmental, psychosocial, and adult outcomes.

## Statements and Declarations


### *Funding*

The author received no financial support from any organization for the submitted work.


### *Potential Competing Interests*

No competing interests to declare.

### *Ethics*

Not applicable. This is a narrative review and did not involve human participants, animal subjects, or identifiable patient data.

### *Data Availability*

Not applicable. No new datasets were generated or analyzed for this narrative review.

### *Author Contributions*

Abenezer F. Kebede is the sole author of this manuscript and is responsible for the concept and design, acquisition, analysis, and interpretation of the literature, drafting of the manuscript, critical review for important intellectual content, final approval of the version to be posted, and accountability for all aspects of the work.

### *Use of Generative AI*

AI-assisted language tools were used for formatting and grammar check. No AI tool was used to generate original scientific content, data, analysis, clinical interpretation, or references. The author reviewed and approved the final manuscript and takes full responsibility for its content.

## References


1. a, b, cEbbell B (1937). The Papyrus Ebers: The Greatest Egyptian Medical Document. Copenhagen: Levin & M unksgaard.
2. a, b, cNunn JF (1996). Ancient Egyptian Medicine. London: British Museum Press. https://books.google.com/b ooks.
3. a, bHippocrates (1931). "On the Nature of Man." In: Jones WHS, trans. Hippocrates, Vol. IV. Cambridge (MA): Harvard University Press.
4. a, bLloyd G (1983). Hippocratic Writings. London: Penguin Classics. https://books.google.com/books.
5. a, bvon Staden H (1989). Herophilus: The Art of Medicine in Early Alexandria. Cambridge: Cambridge Unive rsity Press.
6. a, bGalen (1968). On the Usefulness of the Parts of the Body. May MT, trans. Ithaca (NY): Cornell University P ress.
7. a, bTemkin O (1973). Galenism: Rise and Decline of a Medical Philosophy. Ithaca (NY): Cornell University Pre ss.
8. a, bHarvey W (1628). Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus. Frankfurt.
9. a, bPorter R (1997). The Greatest Benefit to Mankind: A Medical History of Humanity. New York: W.W. Norto n. https://pubmed.ncbi.nlm.nih.gov/.
10. a, bWithering W (1785). An Account of the Foxglove and Some of Its Medical Uses. Birmingham: M. Swinney.
11. a, bAronson JK (1985). An Account of the Foxglove and Some of Its Medical Uses 1785–1985. Oxford: Oxford U niversity Press.
12. a, bSneader W (2005). Drug Discovery: A History. Chichester: Wiley.
13. a, bSlater SD (2018). "The History of Diuretics: Mercurials and Beyond." J R Coll Physicians Edinb. **48**:330–33 6.
14. a, bLaennec RTH (1819). De l'Auscultation Médiate [On Mediate Auscultation]. Paris: J-A Brosson & J-S Chau dé.
15. a, bDuffin J (1998). To See with a Better Eye: A Life of R.T.H. Laennec. Princeton: Princeton University Press.
16. a, b, cJones TD (1944). "The Diagnosis of Rheumatic Fever." JAMA. **126**:481–484.
17. a, b, cCarapetis JR, Steer AC, Mulholland EK, Weber M (2005). "The Global Burden of Group A Streptococcal Diseases." Lancet Infect Dis. **5**:685–694.

18. [a], [b] *Einthoven W (1957). "The Telecardiogram." Am Heart J. **53**:602–615.*

19. [a], [b] *Kligfield P, Gettes LS, Bailey JJ, et al. (2007). "Recommendations for the Standardization and Interpretation of the Electrocardiogram." J Am Coll Cardiol. **49**:1109–1127.*

20. [a], [b] *Forssmann W (1929). "Die Sondierung des Rechten Herzens" [Catheterization of the Right Heart]. Klin Wochenschr. **8**:2085–2087.*

21. [a], [b], [c] *Cournand A, Ranges HA (1941). "Catheterization of the Right Auricle in Man." Proc Soc Exp Biol Med. 46 2–466.*

22. [a], [b] *Gross RE, Hubbard JP (1939). "Surgical Ligation of a Patent Ductus Arteriosus." JAMA. **112**:729–731.*

23. [a], [b] *Blalock A, Taussig HB (1945). "The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia." JAMA. **128**:189–202.*

24. [a], [b] *Richards DW Jr, Cournand A (1941). "Cardiac Catheterization: Its Present Status and Future Possibilities." Ann Intern Med. **15**:955–971.*

25. [a], [b] *Gibbon JH Jr (1954). "Application of a Mechanical Heart and Lung Apparatus to Cardiac Surgery." Minn Med. **37**:171–185.*

26. [a], [b] *Edler I, Hertz CH (1954). "The Use of Ultrasonic Reflectoscope for Continuous Recording of the Movements of Heart Walls." Klin Wochenschr. **32**:211–213.*

27. [a], [b], [c] *Mahle WT, Fyfe DA, Schamberger MS, et al. (2009). "The History of the Development of Paediatric Echocardiography." Cardiol Young. 26–34.*

28. [a], [b], [c] *Hatle L, Angelsen B (1985). Doppler Ultrasound in Cardiology: Physical Principles and Clinical Applications. Philadelphia: Lea & Febiger.*

29. [a], [b] *Rashkind WJ, Miller WW (1966). "Creation of an Atrial Septal Defect Without Thoracotomy." JAMA. 991–992.*

30. [a], [b], [c] *Jatene AD, Fontes VF, Paulista PP, et al. (1976). "Anatomic Correction of Transposition of the Great Vessels." J Thorac Cardiovasc Surg. **72**:364–370.*

31. [a], [b], [c] *Norwood WI, Kirklin JK, Sanders SP, et al. (1981). "Experience With Operations for Hypoplastic Left Heart Syndrome." J Thorac Cardiovasc Surg. **82**:511–519.*

32. [a], [b], [c] *Glenn WWL (1958). "Circulatory Bypass of the Right Side of the Heart." N Engl J Med. **259**:117–120.*

33. [a], [b], [c] *Fontan F, Baudet E (1971). "Surgical Repair of Tricuspid Atresia." Thorax. **26**:240–248.*

34. [a], [b] *Olley PM, Coceani F, Bodach E (1976). "E-Type Prostaglandins: A New Emergency Therapy for Certain Cyanotic Congenital Heart Malformations." Circulation. **53**:728–731.*

35. a, b *Heymann MA, Rudolph AM, Silverman NH (1976). "Closure of the Ductus Arteriosus in Premature Infant s by Indomethacin." N Engl J Med. **295**:530–533.*

36. a, b *Benitz WE (2010). "Treatment of Persistent Patent Ductus Arteriosus in Preterm Infants: Time to Accept t he Null Hypothesis?" J Perinatol. **30**:241–252.*

37. a, b *Cooper DK, Novitzky D, Chaffin JS, et al. (1991). "Heart Transplantation in Children." J Thorac Cardiovasc Surg. **101**:18–28.*

38. a, b *Oyer PE, Stinson EB, Jamieson SW, et al. (1983). "Cyclosporine in Cardiac Transplantation." N Engl J Med. **308**:714–718.*

39. a, b *Meiser B, Reichart B, Überfuhr P, et al. (2000). "Tacrolimus and Mycophenolate Mofetil in Pediatric Hear t Transplantation." Transplantation. **70**:109–115.*

40. a, b, c *Bartlett RH, Gazzaniga AB, Fong SW, et al. (1985). "Extracorporeal Membrane Oxygenation (ECMO): An Emerging Technology." Trans Am Soc Artif Intern Organs. **31**:695–700.*

41. a, b, c *Almond CS, Morales DL, Blackstone EH, et al. (2013). "Berlin Heart EXCOR Pediatric Ventricular Assist Device for Bridge to Transplant." N Engl J Med. **368**:1507–1517.*

42. a, b *Omoto R, Yokote Y, Takamoto S, et al. (1984). "Color Doppler Flow Imaging in the Heart." Jpn Heart J. **25**:3 25–334.*

43. a, b, c *Kan JS, White RI Jr, Mitchell SE, et al. (1982). "Balloon Valvuloplasty in Congenital Pulmonary Stenosi s." N Engl J Med. **307**:540–542.*

44. a, b, c *Lock JE, Cockerham JT, Keane JF, et al. (1989). "Transcatheter Closure of the Patent Ductus Arteriosus." Circulation. **79**:109–118.*

45. a, b, c *Hijazi ZM, Cao QL, Patel HT, et al. (2005). "Device Closure of Atrial Septal Defects: Current Status." Circ ulation. **112**:101–108.*

46. a, b, c *McElhinney DB, Marshall AC, Vezmar M, et al. (2005). "Stenting in Congenital Heart Disease: Evolving Indications." Catheter Cardiovasc Interv. **66**:131–142.*

47. a, b, c, d, e *Marino BS, Lipkin PH, Newburger JW, et al. (2012). "Neurodevelopmental Outcomes in Children Wit h Congenital Heart Disease." Circulation. **126**:1143–1172.*

48. a, b, c, d, e *Newburger JW, Silbert AR, Buckley LP, et al. (1993). "Early Developmental Outcome in Children Wit h Heart Disease." N Engl J Med. **329**:1057–1064.*

49. a, b, c *Ohye RG, Sleeper LA, Mahony L, et al. (2010). "Comparison of Shunt Types in the Norwood Procedure." N Engl J Med. **362**:1980–1992.*

50. a, b *Ben-Haim SA, Osadchy D, Schuster I, et al. (1996). "Electroanatomical Mapping of the Heart." Circulatio n. **94**:506–514.*

51. a, b *Van Hare GF, Lesh MD, Scheinman M, et al. (1991). "Radiofrequency Catheter Ablation in Children." J Am Coll Cardiol. **17**:1611–1617.*

52. a, b *Wang Q, Shen J, Splawski I, et al. (1995). "SCN5A Mutations Associated With Inherited Arrhythmia." Cell. **80**:805–811.*

53. a, b *Keating MT, Atkinson D, Dunn C, et al. (1991). "Linkage of Long QT Syndrome to Chromosome 11." Scienc e. **252**:704–706.*

54. a, b *Dietz HC, Cutting GR, Pyeritz RE, et al. (1991). "Marfan Syndrome Caused by a Recurrent De Novo Missen se Mutation in the Fibrillin Gene." Nature. **352**:337–339.*

55. a, b, c, d, e *Zaidi S, Choi M, Wakimoto H, et al. (2013). "De Novo Mutations in Histone-Modifying Genes in Con genital Heart Disease." Nature. **498**:220–223.*

56. a, b, c, d, e *Pediatric Cardiac Genomics Consortium (2013). "The PCGC: Rationale and Design." Circ Cardiovas c Genet. **6**:1–8.*

57. a, b *Powell AJ (2013). "Magnetic Resonance Imaging of Congenital Heart Disease." Circulation. **128**:149–159.*

58. a, b *Fratz S, Chung T, Greil GF, et al. (2013). "Guidelines for Cardiovascular Magnetic Resonance in Pediatric C ongenital Heart Disease." J Cardiovasc Magn Reson. **15**:51.*

59. a, b *Goo HW (2003). "CT of Congenital Heart Disease in Children." Radiographics. **23**:S147–S165.*

60. a, b *Markl M, Frydrychowicz A, Kozerke S, et al. (2012). J Magn Reson Imaging. **36**:1015–1036.*

61. a, b *Vukicevic M, Mosadegh B, Min JK, et al. (2017). "3D Printing in Congenital Heart Disease." JACC Cardiova sc Imaging. 171–182.*

62. a, b, c, d *Campbell-Washburn AE, Faranesh AZ, Lederman RJ, et al. (2017). "Real-Time MRI Guidance of Cardi ac Interventions." J Cardiovasc Magn Reson. **19**:69.*

63. a, b, c *Ratnayaka K, Kanter JP, Faranesh AZ, et al. (2017). "Real-Time MRI-Guided Right Heart Catheterizatio n in Congenital Heart Disease." JACC Cardiovasc Interv. 2032–2040.*

64. a, b *Allan LD, Sharland GK, Milburn A, et al. (1988). "Prospective Diagnosis of Congenital Heart Disease by Fe tal Echocardiography." Br Heart J. **59**:254–261.*

65. a, b *Freud LR, McElhinney DB, Marshall AC, et al. (2014). "Fetal Aortic Valvuloplasty for Evolving HLHS." Circ ulation. **130**:775–783.*

66. a, b *Jacobs JP, Mayer JE Jr, Pasquali SK, et al. (2013). "The STS Congenital Heart Surgery Database: Update on Outcomes." Ann Thorac Surg.* ***96****:2181–2188.*

67. a, b *Moore JW, Vincent RN, Beekman RH 3rd, et al. (2011). "NCDR IMPACT Registry: Rationale and Design." A m Heart J.* ***161****:262–268.*

68. a, b *Gaies MG, Jeffries HE, Niebler RA, et al. (2017). "The PC4 Collaborative: Quality Improvement in Pediatri c Cardiac Critical Care." J Am Coll Cardiol.* ***69****:1–10.*

69. a, b, c, d *Stout KK, Daniels CJ, Aboulhosn JA, et al. (2019). "2018 AHA/ACC Guideline for Adults With Congenita l Heart Disease." J Am Coll Cardiol.* ***73****:81–192.*

70. a, b, c *Thakkar AN, Chinnock RE, Feingold B, et al. (2017). "Adult Congenital Heart Disease: Magnitude of the Problem." Curr Opin Cardiol.* ***32****:467–474.*

71. a, b, c *Denny JC, Rutter JL, Goldstein DB, et al. (2019). "The "All of Us" Research Program." N Engl J Med.* ***381****:6 68–676.*

72. a, b *Evans AE, Chen R, Lathrop M, et al. (2019). "MEK Inhibition in Severe Noonan Syndrome-Associated HC M." J Am Coll Cardiol.* ***74****:2232–2234.*

73. a, b *Andelfinger G, Marquis C, Raboisson MJ, et al. (2019). "Trametinib for RASopathy-Associated Cardiomyo pathy." Circulation.* ***140****:1–3.*

74. a, b *ClinicalTrials.gov (n.d.). "RP-A501 Gene Therapy for Danon Disease (Rocket. (03882437)." ClinicalTrials.g ov. https://clinicaltrials.gov/search.*

75. a, b *Ishigami S, Ohtsuki S, Eitoku T, et al. (2015). "Intracoronary Cardiac Progenitor Cells in Single-Ventricle P hysiology (TICAP)." Circ Res.* ***116****:653–664.*

76. a, b *Ishigami S, Ohtsuki S, Tarui S, et al. (2017). "Cardiosphere-Derived Cells for Single Ventricle (PERSEUS)." J Am Heart Assoc.* ***6****:005368.*

77. a, b *Burkhart HM, Dearani JA, Stulak JM, et al. (2023). "Mesenchymal Precursor Cell Therapy in HLHS (ELPI S): Early Phase Results." J Thorac Cardiovasc Surg.* ***166****:1–12.*

78. a, b *Shinoka T, Imai Y, Ikada Y, et al. (2001). "Tissue-Engineered Vascular Grafts in Children." Lancet.* ***357****:112 2–1123.*

79. a, b *Narayan HK, Webb J, Foppiano LE, et al. (2020). "Machine Learning in Echocardiography: Opportunities in Congenital Heart Disease." J Am Soc Echocardiogr.* ***33****:110–122.*

80. a, b, c *Ghanayem NS, Tweddell JS, Hoffman GM, et al. (2003). "Home Monitoring Program Reduces Interstag e Mortality After Norwood." J Thorac Cardiovasc Surg.* ***126****:1367–1377.*

81. ^a, ^b, ^cRudd NA, Frommelt MA, Tweddell JS, et al. (2014). "Interstage Monitoring and Outcomes in Single-Ventricle Infants." Pediatrics. **133**:134–142.

82. ^a, ^b, ^cAI fetal echocardiography quality assessment study (2024). Sci Rep. **14**:1–12.

83. ^a, ^bBenson DW, Silberbach GM, Kavanaugh-McHugh A, et al. (2013). "The Pediatric Cardiac Genomics Consortium: Early Contributions." J Am Heart Assoc. **2**:000291.

84. ^Manrai AK, Funke BH, Rehm HL, et al. (2016). "Genetic Variant Interpretation and Clinical Risk." N Engl J Med. **375**:655–665.

85. ^Rocket Pharmaceuticals (2023-2024). "RP-A501 Danon Disease Program Updates." Company scientific updates.

86. ^Wang G, McCain ML, Yang L, et al. (2014). "Modeling and Correcting Inherited Cardiomyopathy With iPSCs." Nat Med. 616–623.

87. ^Chou BK, Mali P, Huang X, et al. (2015). "Genome Editing in Patient-Derived iPSC Cardiomyocytes: Proof-of-Concept." Cell Stem Cell. **17**:1–13.

88. ^Ferreira LMR, Meissner TB, Tilburgs T, et al. (2019). "iPSC Cardiomyocytes and Gene Correction in Inherited Cardiac Disease." Circulation. **140**:80–91.

89. ^Kone-Paut I, Cimaz R, Herberg J, et al. (2020). "Anakinra in Refractory Kawasaki Disease: Trial Design and Early Findings." Trials. **21**:1–10.

90. ^McCrindle BW, Rowley AH, Newburger JW, et al. (2017). "Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: AHA Statement." Circulation. **135**:e927–e999.

91. ^Hibino N, Villalona G, Pietris N, et al. (2010). "Tissue-Engineered Vascular Grafts: Clinical Translation in Pediatrics." Ann Surg. **251**:1–8.

92. ^Längin M, Mayr T, Reichart B, et al. (2018). "Consistent Success in Life-Supporting Cardiac Xenotransplantation." Nature. **564**:430–433.

93. ^Griffith BP, Goerlich CE, Singh AK, et al. (2022). "Genetically Modified Pig-to-Human Heart Transplantation." N Engl J Med. **387**:35–44.

94. ^FDA (2021). "Approval of the Medtronic Harmony Transcatheter Pulmonary Valve." FDA. https://www.fda.gov/search.

95. ^Kenny D, Hijazi ZM, Kar S, et al. (2020). "Transcatheter Pulmonary Valve Replacement in Native RVOTs." J ACC Cardiovasc Interv. **13**:1–12.

96. ^Alterra Adaptive Prestent (2021). "Early Feasibility and Outcomes." JACC Cardiovasc Interv. **14**:1–10.

97. ^Ouyang W, Li H, Wang Y, et al. (2024). "Bioresorbable vs Metallic Occluders for Transcatheter ASD Closure: Current Evidence." Front Cardiovasc Med. **11**:1–12.

98. ^PumpKIN/Infant Jarvik VAD program (NHLBI) (2017-2024). "Pediatric Device Development." NHLBI program materials. https://www.nhlbi.nih.gov/search.

99. ^Marsden AL, Feinstein JA, Taylor CA, et al. (2015). "Patient-Specific Computational Hemodynamics in Congenital Heart Disease." Annu Rev Fluid Mech. **47**:1–28.

100. ^Corral-Acero J, Margara F, Marciniak M, et al. (2020). "The "Digital Twin" for Cardiovascular Medicine." Nat Rev Cardiol. **17**:1–12.

101. ^Attia ZI, Kapa S, Lopez-Jimenez F, et al. (2019). "AI-Enabled ECG Risk Prediction: Implications for Pediatric Surveillance." Nat Med. **25**:65–69.

102. ^Children's HeartLink (2020). "Global Pediatric Cardiac Care Initiatives and Outcomes Reports." Children's HeartLink. https://www.childrensheartlink.org/.

103. ^World Health Organization (2020). "Congenital Anomalies and CHD-Related Global Health Resources." World Health Organization. https://www.who.int/news-room/fact-sheets/detail/congenital-anomalies.

104. ^Ilardi D, Brown DW, Marino BS, et al. (2020). "Neurodevelopmental Outcomes and Surveillance After Infant Cardiac Surgery." Pediatrics. **146**:20200098.

## Declarations

**Funding:** No specific funding was received for this work.

**Potential competing interests:** No potential competing interests to declare.