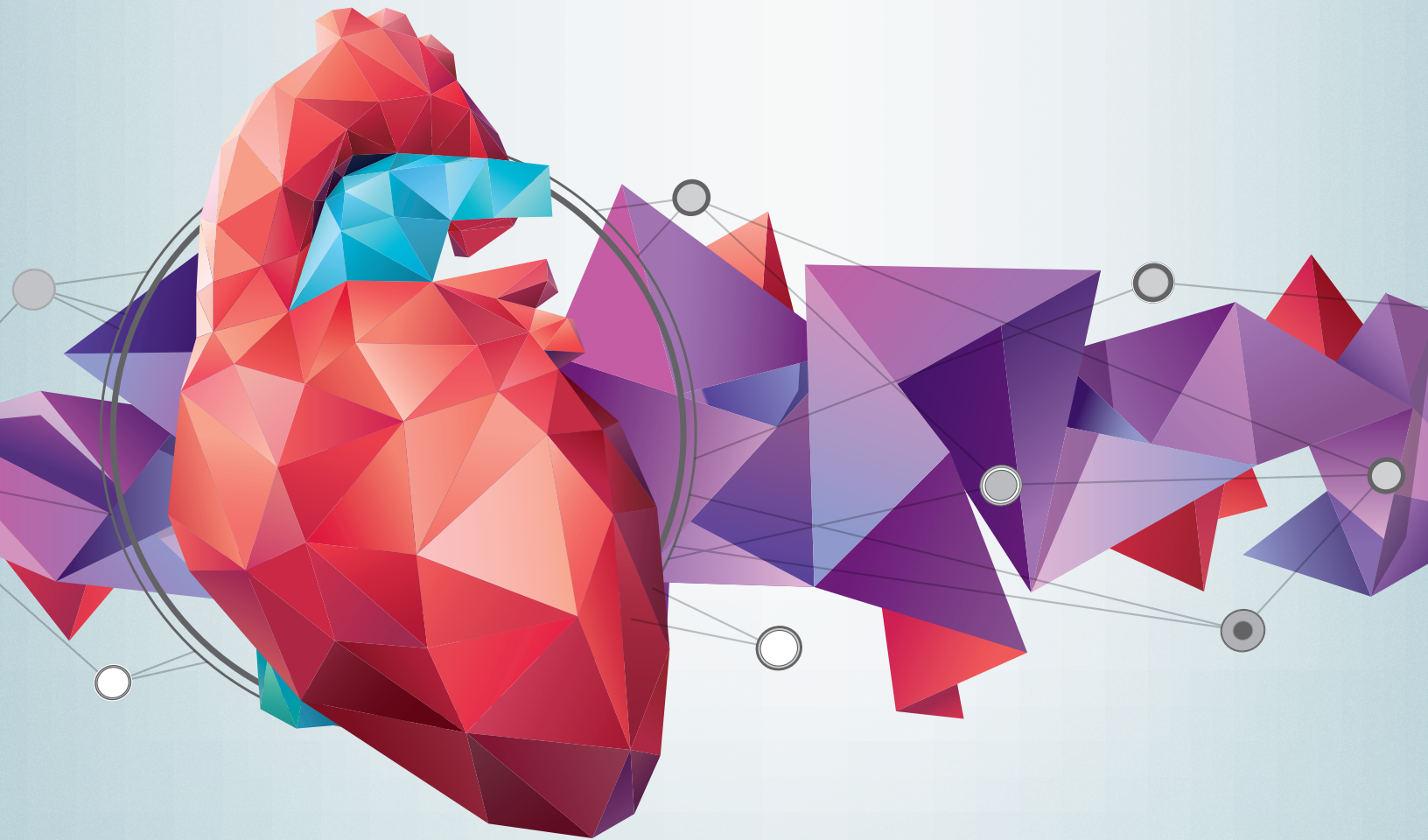




American  
Heart  
Association.

END OF NETWORK REPORT

# CHILDREN'S



STRATEGICALLY FOCUSED RESEARCH NETWORK



**Dr. Timothy Gardner**  
Oversight Advisory  
Committee Chairperson

**F**or nearly 100 years, the American Heart Association has funded lifesaving research to battle cardiovascular disease, the No. 1 killer worldwide.

With research as the foundation of all of its work, the organization has invested over \$5 billion to spur scientific advances so that all people can live longer and healthier lives. As science evolves, the AHA has adapted its research to keep pace.

In 2014, the AHA established the Strategically Focused Research Network (SFRN), a unique venture that brings together scientists from multiple disciplines to create innovative ideas, approaches and expertise on a common topic.

The AHA Board of Directors chooses the topic of each SFRN. Since cardiovascular health during childhood is an essential first step to improve heart health for all, the AHA committed \$15 million to establish the Children's SFRN. It gave researchers a unique opportunity to collaborate in exploring complex questions about cardiovascular health related to children and adolescents.

In 2017, the AHA awarded four centers \$3.7 million each for research on cardiovascular health in children:

**Children's National Research Institute** — to investigate evidence-based strategies to prevent rheumatic heart disease.

**University of Utah** — to develop best methods to leverage data science to improve the health of children with congenital heart disease.

**Northwestern University** — to examine early life origins of cardiovascular health and deliver new ways to measure, monitor and improve heart health during childhood.

**Duke University** — to study the basic biology and effective treatment of pediatric and adolescent obesity.

Each center was required to include a basic, clinical and population science research component. Each also had a two-year research postdoctoral training program for three fellows, who built relationships with faculty across multiple disciplines in their institution and throughout the research network.

"It's exciting to see the American Heart Association support important, leading-edge research on such a timely issue," said **Timothy Gardner, M.D., FAHA**, Oversight Advisory Committee Chairperson. "We clearly need to start early in terms of understanding the best ways to prevent and treat heart disease. This multicenter network really moved things in the right direction."

"The four centers covered the spectrum from global issues to very specific issues, but the question was always the same: 'How can we really make an impact?' Not only did the network provide some very relevant and impressive outcomes, it also trained fellows to conduct even more important research in the future."

**Children's SFRN Awardees and Oversight Advisory Committee**



## SFRN CENTERS

### Children's National Research Institute

Center Director: **Craig Sable, M.D.**

Rheumatic heart disease is rare in children in the U.S., thanks to proper diagnosis and treatment of strep throat. However, it remains a devastating health problem around the world, mostly in low- and middle-income countries, causing 345,000 deaths each year.

Scientists at Children's National Research Institute set out to develop prevention strategies that will strengthen the health system's response to rheumatic heart disease around the globe.

For the basic research project, the team followed 300 patients in Cape Town, South Africa, for three years to learn how the immune system responds to strep throat. They're using the data to help develop a strep vaccine — an ongoing process.

The clinical project sought a better understanding of acute rheumatic fever, a condition in which strep throat can cause permanent damage to the heart's valves (rheumatic heart disease).

Scientists working in Uganda confirmed that rheumatic fever still exists and that advanced testing isn't available in most places where the fever occurs.

Next, they began to develop a simple blood test to detect rheumatic fever in countries where it's most needed. Their research generated an ongoing \$8 million grant from the Leducq Foundation.

The population project focused on the economic impact of rheumatic heart disease and the best methods to convince governments to invest in prevention and control. The project helped spur

two grants to study the disease: an NIH RO1 grant and an AHA grant for a rheumatic heart disease center in its research network on Health Technologies and Innovation.

"Rheumatic heart disease is one of the most historically underfunded diseases because it's primarily a disease of the impoverished," said Center Director **Craig Sable, M.D.** "A lot of cardiologists had basically forgotten about it.

"In addition to the science, our research is significant because it's brought in investments from the public and private sides. Hopefully, this will cause a huge uptick in the world caring about the disease and bring in additional investments for research and prevention."

Sable thanked the AHA for helping convince the World Health Organization in 2018 to launch a coordinated global response to rheumatic heart disease.

"Now that we've raised the profile of the disease, we're hopeful it will improve prevention and help to advance a vaccine," he said.

**Dr. Craig Sable**



**Dr. Asheley Skinner**

### Duke University

Center Director: **Asheley Skinner, Ph.D.**

Childhood obesity is a growing threat to public health, affecting one-third of U.S. children likely to become part of the 70% of adults who are overweight or obese. It also disproportionately affects Black, Hispanic, Asian and Pacific Islander people and worsens health disparities.

To tackle this epidemic that often leads to cardiovascular disease, Duke University scientists sought a better understanding of the biology behind obesity and the best ways to treat it.

In the basic project, scientists discovered significant differences in the gut bacteria of obese children compared to healthy children — paving the way for future research on microbiota.

For the clinical project, scientists conducted a randomized trial to see how obese children ages 6 to 17 responded to fitness and education programs at parks and recreation centers. They found that while children didn't lose weight in the programs, their heart rates and cardiovascular health improved.

The population project set out to determine who's being treated for childhood obesity in the U.S., how they're treated and which treatments seem most effective.

Studying data from obesity treatment clinics across the U.S., researchers detected significant rates of high blood pressure. But they also found those rates often decreased during the program. The project also found socioeconomic factors play a major role in which children start and finish the programs.

"As a society, we're getting better at delivering lifestyle options to fight obesity, but we have a long way to go," said Center Director **Asheley Skinner, Ph.D.** "I hope to see more insurance companies paying for these kinds of programs for kids and more health care systems partnering with community programs to deliver high-quality care. All of this will help lower the stigma around obesity for kids and give us new directions for treatment."

Skinner commended the American Heart Association for "creating a network that pulls together these three disciplines — the basic, clinical and population. It's a unique model that really allows us to look at the big picture and get a better understanding."

## Northwestern University

### Center Directors:

**Bradley Marino, M.D., MPP, MSCE, FAHA;**

**Donald Lloyd-Jones, M.D., SCM, FAHA**

Recognizing a serious knowledge gap in children's heart health, Northwestern University set out to define new standards for defining, tracking and modifying it from birth to age 12.

For the basic science portion, researchers used blood samples to discover markers of how heart-healthy behaviors and environments can affect the way genes work.

While the project is still ongoing due to COVID-19-related delays, Center Director **Donald Lloyd-Jones, M.D., SCM, FAHA**, said "we expect to get a reliable molecular tracking device to show us when cardiovascular health is doing well or when it's falling down a slippery slope."

In the clinical project, nicknamed "Kidfit," scientists created metrics to see how a healthy diet for pregnant mothers and children ages 3-5 impacted a child's body mass index and heart health.

"The preliminary evidence was compelling in that it really will help launch these kids into better health trajectories," Dr. Lloyd-Jones said.

The population project created a way for pediatricians to track a child's cardiovascular health as a new vital sign for children.

"It's essentially an app or a plug-in for an electronic health record system to help clinicians, and it's an important step forward to know when we need to intervene," Dr. Lloyd-Jones said.

The National Heart, Lung, and Blood Institute, one of the largest of the institutes at the NIH, recently provided additional funding for the project.



**Dr. Bradley Marino**



**Dr. Donald Lloyd-Jones**

Lloyd-Jones said Northwestern's research was a stark reminder of the many challenges facing children's heart health, including an unhealthy food supply and lack of physical activity or emphasis on breastfeeding.

"If we continue to let our children grow and develop in unhealthy ways, it's going to be a tsunami of cardiovascular disease," he said. "It's urgent that we focus on monitoring, maintaining and improving it as quickly as we possibly can."

"I'm hopeful the insights our center has made will help the process. But we really need to think about policies at the community, state and federal levels. We need to get everybody's buy-in to refocus on the health of our children, so we have longer, healthier lives for everybody."



**Dr. Martin Tristani-Firouzi**

## University of Utah

### Center Director: Martin Tristani-Firouzi, M.D.

Congenital heart disease (CHD) is life threatening and not well understood. Evidence suggests it has a genetic cause, but in 60-80% of cases, scientists are unable to find one.

And like many children's diseases, it also affects the whole family's health and quality of life.

That's why the University of Utah took a two-pronged approach: Using big data science to delve into the causes of congenital heart disease while exploring ways to improve the shared decision process between parents and physicians.

For the basic project, researchers created an analytical pipeline, using more than 1.6 million medical records to predict which patients are most likely to have a genetic cause. They learned that mothers with high blood pressure during pregnancy were more likely to have a child with CHD. And in those cases, the risk that the child would have a neurological defect increased 11-fold.

Scientists in the clinical research project found the vast majority of CHD cases aren't driven by a genetic defect in the mother or child. Researchers also discovered important differences between placentas of healthy children compared to placentas of children with CHD.

While the study was small due to COVID-19 restrictions, "it would be a monumental discovery if it holds up in bigger studies because it would suggest congenital heart disease could be caused by inflammation or abnormal vasculature in the placenta," said Center Director **Martin Tristani-Firouzi, M.D.**

The population project sought the best new methods to improve health care with a family-centered outcomes approach and shared decision-making.

"These are really hard conversations to have at the moment that you've just told a family that their child has a severe heart defect," Dr. Tristani-Firouzi said. "We need to engage physicians and make sure the family's needs are met."

To do that, researchers used data from the basic project and focus groups to create a unique "decision aid" tool that could be used in a wide variety of medical and counseling settings.

Dr. Tristani-Firouzi praised the AHA's Strategically Focused Research Network "as a phenomenal approach to solving a problem. By having four centers working independently to answer the question and collaborating where they can, the progress is faster, more efficient and impactful than anything else I've been involved in."

## THE FELLOWS: A CLOSER LOOK

### The Fellowship Program

An integral part of the Children's Strategically Focused Research Network is its fellowship program. Thirteen postdoctoral fellows were trained and mentored to become part of an innovative new generation of children's heart health investigators.

Fellows were assigned to teams at each SFRN center, where they forged relationships with scientists inside and outside of their centers and conducted research on new ways to prevent and treat heart disease in children. The fellows also advanced their careers by networking and presenting research at AHA conferences and meetings.

"The fellows were an extremely important part of the success of the network," said **Timothy Gardner, M.D., FAHA**. "Other programs focus their research on what the primary investigator is doing, but I think it's smart the way the AHA encourages fellows to really get involved."

**Asheley Skinner, Ph.D.**, Duke University Center Director, called the trainee program "a critical piece of the work we're doing. They were integral to analyzing and presenting the data in a way anyone can understand. This project would not have happened without our fellows."

Northwestern University Center Co-Director **Donald Lloyd-Jones, M.D., SCM, FAHA**, called the fellowship program "one of the best things about the SFRN."

"Fellows often have some of the best new ideas," he said. "They're coming out of intensive education with the latest expertise, and then you put them in an environment with access to data and senior people who can help them make their ideas a reality. It's a wonderful structure."



Children's National Research Institute



Dr. Babu Muhamed

Here are the stories of four of the fellows:

### **Babu Muhamed, Ph.D., MPH** Children's National Research Institute

For **Babu Muhamed** the AHA's SFRN fellowship marked the midway point of a full-circle journey.

Muhamed grew up in Burundi and South Africa, countries where rheumatic heart disease is still a major cause of death and disability. After researching the disease in the U.S., he hopes to return to Africa to apply what he learned during his AHA fellowship.

"This was a life-changing experience for me," he said. "It really opened up my eyes."

Muhamed worked with scientists at Children's National Research Institute to uncover the ways in which the immune system responds to a strep throat, which, if left untreated, can cause rheumatic fever and rheumatic heart disease.

His team followed South African children with suspected strep throat, checking in with them for three years. After studying blood samples, they confirmed that antibiotics are not used often enough.

"We showed that even children that are flying under the radar without many symptoms often have an aggravated reaction to strep throat," he said. "Since there's no vaccine for strep throat yet, doctors need to be more aggressive about using antibiotics, in this case, penicillin."

As part of his AHA fellowship, Muhamed received training from the National Institutes of Health and earned a masters of public health degree from George Washington University in global health epidemiology and disease control. He has since been hired as a laboratory specialist at the Maryland Department of Health.

He said he'd like to work at the World Health Organization "or another global organization where I can help answer the big questions about heart disease."

He thanked the AHA for "training me, exposing me to so many great mentors, and connecting me with a wider network of people for possible future collaboration. This was really a one-of-a-kind fellowship."

Duke University



**Cody Neshteruk, Ph.D.**

**Duke University**

The rules of scientific research training are often rigid. But the beauty of the AHA's Children's SFRN was how pliable it was at times, **Cody Neshteruk** said.

"There was a lot of flexibility to ask and answer a whole range of questions and expand beyond your focus area," he said. "I was really able to pursue my own interests."

Working with the Duke University center on pediatric obesity, Neshteruk took part in the clinical and population projects to seek out the best methods to treat obesity. The latter project "evolved and pivoted," he said, as the team created a new data set to find out why some children stay enrolled in weight management programs while others drop out.

"We found some pretty clear disparities and a great need to explore the social and cultural factors of why some people respond to treatment and others don't," he said.

"A lot of families have more important issues than nutrition and physical activity. They're struggling to pay the bills and buy food. So we need to understand how to integrate social care into these obesity treatment programs so we can start to address some of the downstream drivers."

Neshteruk's work earned him an AHA Career Development Award and grants from the National Institutes of Health and The Obesity Society to further study childhood obesity. He was recently hired by Duke University as a medical instructor in the Department of Population Health Sciences.

He's now examining the benefits of "patient navigation" in helping with childhood obesity treatment.

"I'm very interested in individuals who can help families navigate both the health care system and community resources, whether that's a food pantry or financial education. We need to be talking more about bridging the clinical sector with the community sector."

**Dr. Cody Neshteruk**



**Liliana Aguayo, Ph.D., MPH**

**Northwestern University**

For **Liliana Aguayo**, the AHA fellowship didn't end when the program wrapped up.

"I feel like everyone still has my back," she said. "The people I worked with still support me if I reach out to them. They're legitimately interested in seeing me grow. Everyone's been incredibly generous."

Aguayo applied for the SFRN fellowship because of her fascination — and frustration — with early-life cardiovascular health.

"The information can be very limited, which leaves us ill-prepared and being more responsive than proactive," she said.

She worked on Northwestern University's basic science project to find that children with a genetic variation were more likely to be born with excessive birth weight. She also worked on the population project, studying how adverse and positive childhood experiences impact cardiovascular disease in men, women and children of different races.

**Dr. Liliana Aguayo**



Northwestern University



Aguayo was lead author in a JAHA study on the topic, one of several publications that came out of her fellowship. Her work also earned her the AHA's Epi-Minority Travel Award and a Career Development Award, and it paved the way for her current job as research assistant professor at Rollins School of Public Health at Emory University.

In the future, she wants to dig deeper into the behavioral and environmental causes and impact of cardiovascular health inequalities during childhood.

"It's amazing how much I learned during my fellowship," she said. "Everyone opened doors for me and helped me navigate and gain confidence in my research and who I am as a scholar. It's changed my way of thinking, and it's been critical for my career. I loved it."



**Dr. Alistair Thorpe**

**Alistair Thorpe, Ph.D.**  
**University of Utah**

One of the more unique chapters in the Children's SFRN focused less on children's heart health and more on the parents' wellbeing. **Alistair Thorpe** was an ideal fellow to help write it.

Thorpe earned his doctorate in psychology at the University of Essex, where he studied the intersection of health communications and treatment decisions. So when he saw a posting on Twitter for the University of Utah's population project on family-centered outcomes and shared decision making, he jumped to apply.

The project focused on parents trying to deal with a diagnosis of life-threatening congenital heart disease in their child. To help them cope with the diagnosis and improve the shared decision process between parents and physicians, Thorpe contributed to studies seeking to better understand their experiences during this time and to assess the impact of a decision-aid tool involving values-clarification exercises.

"We found there's a real need for support during this stressful time that is tailored to parents' unique experiences," he said. "We need more research to understand the best kind of decision-making support we can give to them."

Thorpe helped write two papers from the research, presented research from the project at the Society of Behavioral Medicine conference. He said his work in the AHA's SFRN helped him land his current fellowship at University College London. It also reinforced his goal to one day lead his own medical decision-making research lab.

"We need ongoing research that can provide a steady arsenal of decision support tools and communication guidance to help people come together and reach more informed and value-driven decisions about their health or the health of their children," he said.

Thorpe thanked the AHA for "an invaluable experience that gave me a lot of insight into the best ways to analyze data, collaborate with others and share ideas. I met so many supportive senior investigators whose excitement about research inspired me to keep doing this type of work that can help make people's lives better."

University of Utah



## COLLABORATIONS

**B**y design, the Children's SFRN operated as a strong partnership, with scientists of different disciplines working together inside and outside the four centers. The goal was to share the best methods, models and approaches for studying children's health.

"There was a lot of collaboration, both scientific collaborations as well as educational collaborations, where one center was doing leading-edge research that inspired the others," said Dr. Timothy Gardner, Oversight Advisory Committee Chairperson.

For example, investigators studying gut bacteria at Northwestern's center on early-life origins of heart health partnered with Duke's group, which was doing similar work on the origins of obesity, said Donald Lloyd-Jones, M.D., SCM, FAHA, Northwestern Center Director.

Scientists from Duke and Northwestern's centers also teamed up with non-SFRN research institutions to publish a paper in the Journal of the American Heart Association, "Rheumatic Heart Disease in the United States: Forgotten But Not Gone."

Additionally, the University of Utah teamed up with Duke, Northwestern and Children's National Research Institute for their population project on shared decision making between doctors and families that have a child with congenital heart disease.

"The collaborative spirit was great," said Martin Tristani-Firouzi, M.D., Utah Center Director. "We accomplished a lot. Centers working so well together is exactly what you expect from a SFRN like this one."

## CONCLUSION

Since 2014, the AHA has launched an ever-growing array of Strategically Focused Research Networks, including ones on Prevention, Hypertension, Disparities in CVD & Stroke, Go Red For Women, Heart Failure, and Obesity.

In addition to Children's, other networks are focusing on Vascular Disease, Atrial Fibrillation, Arrhythmias and Sudden Cardiac Death, Cardiometabolic Health and Type 2 Diabetes, Health Technologies and Innovation, Disparities in Cardio-Oncology, Science of Diversity in Clinical Trials, and Biologic Pathways of Chronic Psychosocial Stressors on Cardiovascular Health.

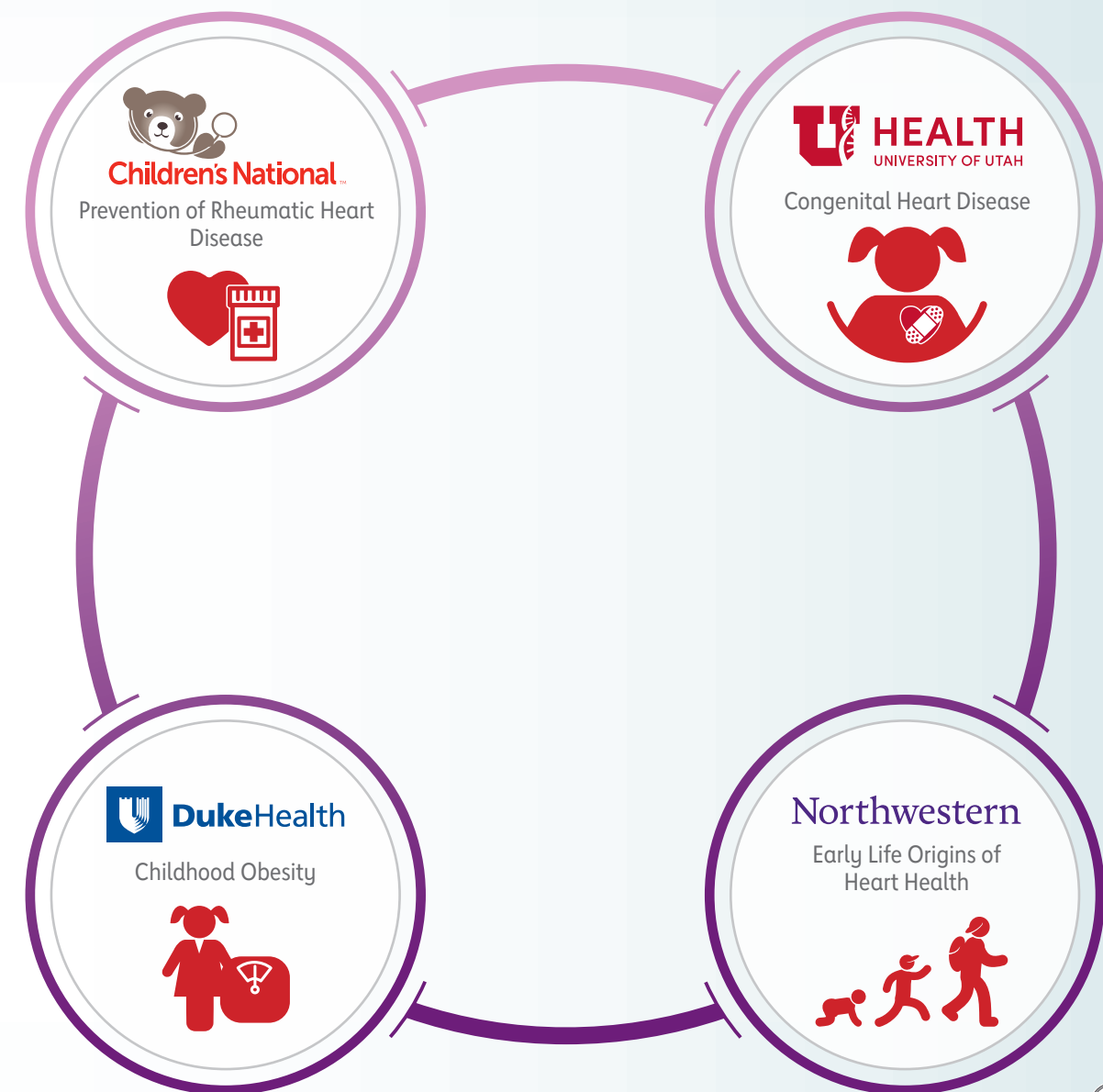
But one thing that set Children's apart from most of the others was the challenge of COVID-19. The pandemic hit as the program was well underway.

"The network was still an unmitigated success, even though COVID limited some of the clinical research" said Dr. Timothy Gardner, Oversight Advisory Committee Chairperson. "The community kept collaborating through virtual meetings, and as a result, the network was largely unaffected."

Since its founding, the AHA's primary focus has been on adult cardiovascular health and disease prevention. But the Children's SFRN is an important reminder that early heart health plays a direct role in heart health later in life.

Discoveries and innovations from the Children's network will further the AHA's mission so people of all ages can strive to maintain ideal health, Gardner said.

"It's exciting to see so much important research being done to improve cardiovascular health for everyone," he said.





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