HeartWorks
WE BUILD HEARTS

Protocol Administrative Information

Protocol Title	The Co-Op @ HeartWorks
Protocol Number	Co-Op 001
Version Number/ **Version Date**	01 29-JAN-2024
Sponsor/Funding Source	HeartWorks, Inc.

By signing this form, I confirm:

I have read and understand the contents of this clinical protocol and will adhere to study requirements as presented.

I will conduct this study in accordance with this protocol, the applicable principles as described in the United States Code of Federal Regulations (CFR) 21 Parts 11, 50, 54, 56 and 312, and the International Conference on Harmonisation (ICH) Harmonised Guideline for Good Clinical Practice E6 (R2).

I will submit a copy of this protocol to the Ethics Review Board (ERB) of record for this study, and I will not conduct research under this protocol until written approval by the ERB has been received.

Neither my sub investigator(s) nor I, are members of the ERB of record for this study at this institution, *OR* my sub investigator(s) or I are members of the ERB of record for this institution but will not participate in the initial or continuing review of this protocol.

Principal Investigator Name	Clinton Hagen MS 3033 41st St NW Suite 200 Rochester, MN 55901
Principal Investigator Signature	
Date	

Summary

This protocol is a research study involving human subjects diagnosed with Congenital Heart Defects/Disease (CHD). *The Co-Op @ HeartWorks* is a cooperative between the research platform at HeartWorks and members of the CHD community. Individuals choosing to participate will be referred to as 'members' of the co-op. This study aims to create a database of members medical journey data to inform future clinical innovation and design of clinical trials which address the needs of the members. The knowledge generated from this study will help advance the care of CHD patients through the deliberate action of *The Co-Op @ HeartWorks* members. Unlike a traditional disease registry, the members of *The Co-Op @ HeartWorks* will actively inform and contribute to the future studies affecting their health.

Background

Congenital heart defects are the most common birth defect[1] effecting about 1%[2,3] births annually, roughly one birth every 15 minutes. Of those, approximately 25% are critical CHDs[4].

While mortality remains high[4], survival for CHD and critical CHD is improving and CHD in adults is becoming more common. Overall, there were more 48 million people living worldwide in 2015 with a CHD[5]. It's estimated that two to three million CHD individuals live in the US. There is no system to track CHDs beyond childhood making more precise estimates unavailable. Despite the large numbers of CHD patients, new therapies and devices to treat CHD are limited. Surgery is often not a cure for CHD, many individuals with CHDs require multiple surgeries and medications well into adulthood.

As more individuals with CHDs are living into adulthood, the long-term care needs and challenges are an evolving topic. Few comprehensive datasets exist describing the natural history of CHD patients. To date, existing CHD registries require institutions to release patient data, the CHD patients and their families have no part in this process. None are patient centric or comprised of patient donated data. Furthermore, individuals with CHD and their caregivers are left to wonder if their outcomes are comparable to other CHD patients due to the lack of CHD normative values for most health measures (i.e. a CHD growth chart doesn't exist).

The CHD effected and aware community is very active in creating awareness and raising money for CHD care and research. Their role in a research study is most typically as a subject and not as a study team contributor. *The Co-Op @ HeartWorks* will change that through an adapted Participatory Action Research Study design where CHD patients have a voice in the research intended to affect their lives.

Participatory Action Research is a framework for creating knowledge that is rooted in the belief that those who are most impacted by research should take the lead in framing the questions, design, methods, analysis and determining what products and actions might be most useful in effecting change[6]. This type of research design is practiced commonly in social justice work and is perfectly adaptable to medical research. The CHD effected community deserves a voice in the research affecting their lives.

Study Design

In a traditional sense, one might call this a disease registry. However, this is a Data Cooperative (modeled after a Participant Action Research study design) which will collect a mix of retrospective clinical and demographic data and prospective current health data to create a natural history for individuals with a CHD. *The Co-Op @ HeartWorks* will allow members to donate their medical journey data to create database intended to inform future clinical innovation and design of clinical trials which address the needs of the members. Medical journey data consist of electronically linked electronic health record, clinical reports and surveys collected on current medical state data. Members will be recruited by the Sponsor through community outreach, and referred by CHD advocacy groups. Individuals wishing to become members of *The Co-Op @ HeartWorks* will consent and donate their medical journey data using the Matrix Platform from Across Healthcare. Additionally, members will be presented with opportunities to inform the research future for CHD patients through feedback surveys.

The primary objective of this study is to collect member donated, medical journey data used to inform future clinical innovation and design clinical trials that address the needs of the CHD population. Members of *The Co-Op @ HeartWorks* may be contacted for clinical studies for which they may be eligible.

The Secondary Outcome for *The Co-Op @ HeartWorks* is to build a natural history database creating a worlds-first CHD benchmarking for a multitude of clinical metrics. This will include prevalence of the medical conditions captured in the member donated data.

Members will provide their data on a schedule of their choosing. There are no scheduled visit windows. Members will be presented with the following data donation options (collection frequency):

- Demographics and contact information survey (collected once, updated as needed)
- CHD diagnoses and surgical history survey (once to start, updated as needed)
- Previous clinical trial and experimental therapy participation survey (once to start, updated as needed)
- Level 1 ClinGen Health and Development Survey (annually)
    - Level 2 ClinGen surveys based on Level 1 responses (annually as triggered above)
    - Level 3 ClinGen surveys based on Level 2 responses (annually as triggered above)
- Member's Voice Survey (always available, no limit to the number or frequency of submissions)
- EHR data synchronization (weekly, once activated)
- Clinical and genetic report file uploads (once to start, updated as needed)

All data collected in this study will be from members directly providing the data into the Matrix Platform via a website. These data will be stored in the Matrix Platform database, maintained by Across Healthcare stored on servers physically present in the United States.

Data integrity is the responsibility of HeartWorks, Inc and members may be queried by staff assigned to The Co-Op @ HeartWorks.

Privacy and Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Additionally, members who provide their genetic related health information are protected under the Genetic Information Non-discrimination Act (GINA).

Collected participant data is stored in *The Co-Op @ HeartWorks* specific Matrix database, provided to HeartWorks Inc. under contract from Across Healthcare Inc. Matrix is a hosted environment which is rigorously controlled for both physical and electronic threats. The Matrix system and Across Healthcare Inc. maintain HIPAA compliant internal systems and procedures as well as complying with current applicable data security standards such as ISO-27001, ISO-22307, NIST SP 800-53 and 21CFR Part 11. Data is encrypted, and the system has a regular schedule of third-party security and threat vulnerability testing. Access to the Co-Op database is limited only to authorized personnel with documented training.

The technology host is a leader in developing data cooperative systems that connect patient communities with researchers studying those conditions. The technology host's Matrix Platform complies with the important research and privacy regulations above to protect member data. Also, you will select a username (email) and password at setup as an extra step to protect your information.

Generally, only HeartWorks Inc. personnel will have access to member donated identifiable health information. However, there are a few exceptions that are listed here.

The following parties are authorized to have access to your identifiable health information in connection with this research study:

- Clinicians connected to their account by the member
- Technology Host
- The Ethics Review Board (ERB) overseeing this study

Withdrawal from the Data Cooperative

Members providing information to the data cooperative is voluntary. If a member chooses to participate, they can withdraw from the data cooperative at any time and for any reason. Should they change your mind about continued participation, they will be free to do so without having to provide any explanation.

Should a member want to withdraw from The Co-Op @ HeartWorks, they can send a request to matrixsupport@acrossmatrix.com (can also click "Contact Us" in the application) and indicate they would like to withdraw. Matrix staff will ask about whether they just want to stop participating or if they would also like their data removed from the data cooperative.

Data Sharing and Dissemination

Researchers or clinicians associated with national/international hospitals as well as for-profit commercial research or biopharmaceutical companies who want to use data cooperative data will only be allowed to see

de-identified information after an approval process that assesses the ethics and appropriateness of the request. HeartWorks Inc. Administration including the Principal Investigator, all of whom are required to receive human subjects protection training, will review all requests for data sharing to approve or deny. Approved researchers, clinicians and for-profit commercial research biopharmaceutical companies may only use the de-identified information to conduct research on CHD. If researchers or clinicians want to recruit patients for their studies, only HeartWorks Inc. Administration personnel will identify members and serve as the intermediary for such researchers and clinicians, on behalf of the members. If a member may be eligible for a researcher's study, HeartWorks Inc. Administration personnel will contact the member to provide information about the study and a way to contact the researcher. The researcher will not be able to contact the members directly. Members will not share in any profit resulting from the use of their data and research results. HeartWorks Inc. will share with members all published results of research conducted with these data via the Technology Host's messaging capability. If the information in this data cooperative is published or presented at meetings, the member will not be identified.

Additionally, members data will be shared with other members directly in the Matrix platform in aggregate only. This may include benchmarking a member's clinical measures with other members with similar conditions (i.e. growth chart for individuals with single ventricle cardiac anatomy). No member identifying information will be used in this benchmarking, aggregated data will not be presented until at least 10 members data are present for any given measure.

Participant Characteristics and Recruitment Strategy

Potential members will self-declare their eligibility as a CHD patient (or caregiver of a CHD minor) and provide diagnoses upon enrollment. Staff members of *The Co-op @ HeartWorks* will review diagnosis data for each enrolled member to ensure inclusion criteria are being met. Member data that do not support a CHD diagnosis will be contacted by staff members of *The Co-op @ HeartWorks* to clarify eligibility. Those not meeting eligibility will be withdrawn.

This data cooperative will not cap the number of members enrolled; it is anticipated 500 members will enroll annually.

Potential members will learn about the opportunity to participate in the data cooperative in many ways.

- Through partnership with CHD advocacy groups and hospitals to distribute recruiting materials
- Social media campaigns by HeartWorks, Inc.
- Promotion on the www.WeBuildHearts.org website
- Member referral in the Matric Platform

Individuals who are interested and qualified to be part the data cooperative will be provided a web address to the Matrix Platform where they can register an account and begin the informed consent process.

Family members of deceased CHD individuals will be allowed to create accounts within The Co-Op @ HeartWorks and enter data of the deceased individual. These members will have the opportunity to donate all

the same data as other members. However, will not be asked to update their information after the initial data donation.

Process to Attest Consent to Participate

Before the conduct of any study data collection, Informed Consent will be obtained from the subject or their authorized caregiver. A parent or authorized caregiver will provide consent for subjects under age 7. Subjects aged 7-age of majority will provide assent in addition to the parental consent, once reaching age of majority they will need to consent for themselves. Members are considered enrolled at the point consent is signed.

Family members of deceased CHD individuals will be allowed to create accounts within The Co-Op @ HeartWorks and enter data of the deceased individual. These members will sign the consent form giving The Co-Op @ HeartWorks permission to use these data.

The informed consent process is entirely electronic where the member checks a box after reading the consent form online to indicate their consent to participate in the data cooperative.

Justice

The Co-Op @ HeartWorks aims to be very inclusive and is committed to Justice in research. We acknowledge this data cooperative does have barriers to entry in the fact members need a device capable to establish a connection to the internet to contribute. Currently, individuals from underrepresented in research communities face a larger burden to coordinate their care and are not always made aware of clinical trial opportunities. We hope this data cooperative can remove some of those burdens by providing a comprehensive instance of their donated health journey data to reduce or eliminate records transfer requests, provide awareness of clinical trials which may benefit the member, and allow the underrepresented in the CHD community a voice in future research. The only way this can happen is if *The Co-Op @ HeartWorks* can enroll them as members, and we plan to recruit directly at community events, provide study flyers to all new CHD births in hospitals agreeing to share the study, member referrals, and share far and wide via social media and advocacy groups to attempt to reach as many as possible to best represent the underlying community.

Risks and Benefits for Participants

Members of *The Co-Op @ HeartWorks* will have access to all their donated data, including aggregated Electronic Health Record (EHR) data, which they can securely share with their providers. Additionally, members will have the option to track their symptoms, medications and medical journey real-time through the Matrix platform and have access to graphical summaries of these data. These data may provide insights to member's care and condition. Additionally, members will have access to clinical trial results and may be contacted for future clinical trial participation if they are possible candidates.

There may be data privacy risks on collecting patient data for any study, including this study

Costs and Payment for participation

Members of *The Co-Op @ HeartWorks* will not be charged to participate, all costs are fully funded by HeartWorks Inc.

Members of *The Co-Op @ HeartWorks* will be offered a $75 merchandise credit in the HeartWorks Inc. online store at www.WeBuildHearts.org.

References

1. Mendis, Shanthi, Puska, Pekka, Norrving, B, World Health Organization, World Heart Federation. et al. (2011). Global atlas on cardiovascular disease prevention and control / edited by: Shanthi Mendis ... [et al.]. World Health Organization. https://iris.who.int/handle/10665/44701
2. Hoffman JL, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol.* 2002;39(12):1890-1900.
3. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in Atlanta, 1998-2005. *J Pediatr.* 2008;153:807-13
4. Oster ME, Lee KA, Honein MA, Riehle-Colarusso T, Shin M, Correa A. Temporal trends in survival among infants with critical congenital heart defects. Pediatrics. 2013 May;131(5):e1502-8. doi: 10.1542/peds.2012-3435. Epub 2013 Apr 22. PMID: 23610203; PMCID: PMC4471949.
5. Vos, Theo et al. , Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, The Lancet, Volume 388, Issue 10053, 1545 – 1602
6. Cornish, F., Breton, N., Moreno-Tabarez, U. *et al.* Participatory action research. *Nat Rev Methods Primers* **3**, 34 (2023). https://doi.org/10.1038/s43586-023-00214-1

Additional Information

The following additional documents should be submitted to the IRB along with the protocol:

- the Principal Investigator's CV;
- evidence (*e.g.,* a certificate) of training in human subject protections for the Principal Investigator and other members of the research team;
- all material that will be used to recruit participants (*e.g.,* social media posts, website language, email blasts);
- informed consent documents, including web forms and attestation form if those are used. Some registries also include separate forms for those who are providing consent for another (*e.g.,* parents who are enrolling their affected child).

REVISION HISTORY

Version 01 Effective on 29-Jan-2024
New

DOCUMENT ELECTRONIC SIGNATURES

DOCUMENT APPROVAL WORKFLOW

Author Approval

Clint Hagen
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I am the author of this document.
Signed 7:03:15 PM UTC 29-Jan-2024

Required Workflow Steps for this Category

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QA
I have reviewed and approve this document.
Signed 7:08:02 PM UTC 29-Jan-2024