FAQs for the CCHS Network One World Registry: a Natural History Study of CCHS

Here is a list of questions you may have about the CCHS Network One World Registry. If you have additional questions that are not addressed here, please feel free to contact us at cchsnowregistry@cchsnetwork.org

1. What is a Patient Registry?

A patient registry is a collection of standardized information about a group of patients who share a condition and is used for a variety of purposes such as conducting natural history studies and supporting disease specific clinical trial recruitment. *The CCHS Network One World Registry (CCHS NOW Registry) will collect patient information, securely and confidentially (see more below), to study CCHS.*

2. What is a Natural History Study?

A natural history study is a study designed to track the course of a medical condition or disease over time. A medical natural history study includes people who have a specific medical condition or disease and those who are at risk of developing the medical condition or disease. This method of research explores the disease in a comprehensive way and identifies demographic, genetic, environmental, and other variables that correlate with the disease and its outcomes. Natural history studies have many potential uses such as patient care, best practice developments and clinical trial recruitment.

3. What is a longitudinal study?

A longitudinal study is a research method in which data is gathered for the same subjects repeatedly over a period of time. Longitudinal research projects can extend over years or even decades.

4. This study is sponsored by the CCHS Network. What exactly is a Research Study Sponsor?

The National Health Service defines a study sponsor as, "… the individual, company, institution or organization, which takes on ultimate responsibility for the initiation, management […] of and/or financing […] for that research."[1]

[1] NHS http://www.hra.nhs.uk/resources/before-you-apply/roles-and-responsibilities/sponsor/

The Study Sponsor ensures that the study is conducted in a reputable manner and upholds regulations as they apply to the study.

5. What is a Principal Investigator?

The Principal Investigator is the research group leader or, the person with the primary responsibility for the design and conduct of the research project or study. Sarah Yang, PhD, Melinda Riccitelli, PhD, and Vandana Dole. PhD are sharing responsibility duties for the CCHS NOW Registry. If you have questions *at any time* about this Registry please contact them at cchsnowregistry@cchsnetwork.org

6. What is an Institutional Review Board (IRB)?

According to the Mayo Clinic an IRB is, "[a] specifically constituted review body established to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research."[2] In lay terms, an institutional review board is a group of people who are responsible for protecting the rights and welfare of people who participate in research. *The CCHS NOW Registry has been extensively reviewed for patient protection and confidentiality and study feasibility by the Hummingbird IRB group, a respected member of the IRB community with specialized expertise in medical, ethical and regulatory matters.*

7. Who is a study participant?

A study participant is the individual with the condition who takes part in a research study and whose information is collected for that research. Study participants may consent to enter and share their own personal data. *In the CCHS Now Registry the CCHS patient is the study participant.*

8. Who is a reporter/respondent?

A reporter/respondent is an individual who completes the surveys on behalf of the patient/study participant, when they are unable to do so on their own behalf. *In the CCHS NOW Registry a CCHS parent or Legal Representative (see more below) of a minor CCHS patient or a CCHS patient who cannot answer for him/herself is the reporter/respondent.*

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[2] Mayo Clinic http://www.mayo.edu/research/institutional-review-board/definition-terms

9. What is a legally authorized representative (LAR)?

A legally authorized representative is an individual who, under law, has the ability to act on behalf of another person (such as a minor study participant). The LAR may be a parent, grandparent, caregiver who has the legal authority to grant consent on behalf of another who has been invited to participate in research.

10. What is an Informed Consent?

An informed consent is a document that provides potential participants in a research study information about the study so that participants can make a voluntary, knowledgeable decision to join the study or not. Some (not all) of the information that an informed consent includes are the risks and benefits of the research project, how data will be handled, ethical considerations, the duration of the study, economic considerations, how the study will be conducted, and how data will be used.

11. Do I have to sign the CCHS NOW Registry Informed Consent to participate in the study?

Yes, in order to participate in the CCHS NOW Registry you must sign the informed consent. Two consents are available: one for adult CCHS patients and one for minor/dependent CCHS patients. If you are a CCHS adult you will sign the informed consent for adults. If the CCHS patient is a minor or a dependent, the legal representative of the patient (most of the time a parent) will sign the Legally Authorized Representative (LAR) consent form.

If after reading the informed consent you are confused or have questions about the CCHS NOW Registry informed consent process or research project please direct these inquiries to study investigators @ cchsnowregistry@cchsnetwork.org.

Participation in this research project is completely voluntary.

12. What is the purpose of the CCHS NOW Patient Registry?

One of the most important purposes of the CCHS NOW Registry is to bring the CCHS community together and collect data which could be used to create therapeutics and improve the quality of life for patients. Some other goals of the CCHS NOW Registry are to:

- Conduct a prospectively-planned natural history study that will result in the most comprehensive understanding of CCHS and its progression over time.

- Characterize and describe the CCHS population as a whole.
- Assist the CCHS community with the development of recommendations for standards of care.
- Assist researchers studying the pathophysiology of CCHS
- Assist researchers studying interventional outcomes.
- Support the design of clinical trials for new treatments.

13. What types of data will be collected in the CCHS NOW Patient Registry?

The data collected is uniform and includes but is not limited to:

- Socio-demographics
- Medical and diagnostics
- Treatment and disease progression
- Management of care
- Quality of life

Data will be collected in three study phases: Phases 1 and 2 are patient-reported information about CCHS; Phase 3 is physician-reported information about CCHS. We are only launching Phase 1 of the study at this time: Patient-reported Core Data collection. These questions focus on common core questions from NORD, with input from CCHS NOW study investigators, which are designed to find commonalities between various rare diseases. Phase 2 will focus on CCHS-specific questions. More information will be available about phases 2 and 3 when we launch these initiatives.

14. How is the data collected?

Data is collected through a secure web-based system developed by the National Organization for Rare Disorders (NORD), an independent non-profit committed to the identification, treatment, and cure of all 7,000 rare diseases. Study participants respond to questions grouped within a series of surveys developed per study standards and in collaboration with disease specific experts.

15. How long will it take to complete questionnaires?

You should anticipate each survey section taking between 15 and 30 minutes to complete.

16. Do I have to answer all survey questions asked?

Participation in this registry is completely voluntary. As a study participant you have the right to not answer survey questions that makes you uncomfortable and/or you choose not to answer.

17. Can data be collected worldwide?

The patient registry uses an online platform which allows to contribute data from anywhere in the world.

18. Where is the data from the CCHS Now Registry stored?

The data is stored on NORD's registry platform system which adheres to industry standards regarding security protections.

19. Is the data collected by the CCHS NOW Registry safe?

Yes, the data is safe. The registry follows strict government guidelines to assure patient information is protected. The platform is served over HTTPS, which provides traffic encryptions so as to prevent eavesdropping and man-in-the-middle attacks. Communications between the registry platform application server and the database are also encrypted.

20. Is the data collected by the CCHS NOW Registry kept confidential?

Yes, your data is kept confidential from the public. Confidentiality is protected by limiting access to data and keeping Personal Health Information (PHI) data password protected on a secure server. Access to PHI in the database will be limited to the sponsor's registry research team (see above – "What is a Principle Investigator") via password protected security measures. Data will be maintained on the NORD Natural History Studies platform, which meets or exceeds current guidelines for maintaining security of PHI. **Only** aggregated, de-identified data will be shared with the public as general descriptive statistics regarding database contents. De-identified data will be shared with NORD. PHI will be associated with a unique identifier that is assigned by registry staff to further obscure patient identity. The file linking the unique identifier and the PHI will be kept in a separate password protected database.

While data is kept confidential, a unique feature of the CCHS NOW Registry is that participants, can see the data collected as it is being collected (in an anonymous format, once 10 patients have enrolled), empowering patients

with information in real time. This feature is not typical of most registries where data collected is concealed from participants until the time the researcher published the results.

21. Who can join the study?

This study is open to anyone who has a CCHS diagnosis.

CCHS, for the purpose of this study, is defined as:

- Disease status by genetic testing or lab value: Phox2b Analysis documentation; or
- Disease defining characteristics based on clinical diagnosis (need to provide evidence of 3 of the following 4):
    1. Chronic Respiratory Failure
        i. CO_2 Retention
        ii. Hypoxia
    2. Abnormality in central control of breathing
    3. Lack of confirming differential diagnosis (diagnosis of exclusion method): i.e. metabolic, neuro-muscular, chronic lung disease, and obstructive airway disease is clearly ruled out as a cause of respiratory failure
    4. Clinically confirmed dysautonomia

To participate, you must also be:

- Willing to provide informed consent
- Able to comply with web-based study procedures and data collections

22. Is there a cost to participate?

There is no cost to the patient to join this study. The CCHS Network bears the burden of the cost of the registry for its members, but shares the overall cost of the registry with NORD and the other rare disease groups using the platform.

23. How long will this study last?

This registry will be open for five years with the option to renew registration. There is no date of termination or closure at this time.

24. What might be some benefits of this study to me?

Because CCHS is a rare disorder, effective research into the phenotype, pathophysiology, effectiveness of treatments, etc., requires the accumulation of data from a broad cohort of participants. There are no direct benefits associated with participation in the CCHS Network One World Registry and individual participants should not expect a direct benefit. The CCHS NOW Registry will facilitate collaboration between clinicians at multiple sites as well as assist in recruitment of participants for clinical trials. Conceivable benefits include the potential for future studies that will significantly increase understanding of therapeutic options for CCHS patients. The use of information contained within the CCHS NOW Registry for retrospective research analyses may be of future benefit to patients with CCHS. In addition, participants in the CCHS NOW Registry will be informed of future research studies involving CCHS for which they may be eligible. Certain participants may directly benefit from inclusion in future treatment studies that result from the registry and for which separate informed consent will be obtained.

25. What are some risks of the study?

There are no risks of physical harm associated with participation in the study. Participation in the CCHS NOW Registry does involve the potential risks of a breach of confidentiality of medical information and associated privacy of participants. Such risks will be minimized by ensuring adherence to applicable regulations and data security measures and by performing the following: (1) removing direct participant identifiers from information and data shared or released from the registry; (2) limiting access to linking codes assigned to the CCHS NOW Registry information; 3) and limiting access to information contained within the CCHS NOW Registry to registry investigators and researchers approved by the Advisory Board, and (4) Maintaining the Privacy and Confidentiality of Registry information as described below.

26. Who owns the data of the CCHS Now Registry?

The identifiable and de-identifiable data are owned by the study sponsor, the **CCHS Network**. The **CCHS Network**, in collaboration with a team of CCHS clinical/research experts, CCHS patients, and CCHS family advocates, decides how and with whom to share the data. A subset of the deidentified data collected across the NORD Registry Platform is available to NORD to support cross disease analysis and advocacy activities to members of the rare disease community as a whole.

27. Who will be able to use this data?

One of the goals of this registry is to gather and disperse CCHS information as quickly and securely as possible. In agreement with the standards set by NORD and the IRB, we intend a free sharing of *de-identified* data with *any* researcher who asks for it for a legitimate reason. The CCHS Network in collaboration with the CCHS NOW Registry Advisory Board (comprised of CCHS clinical and research experts, CCHS patients, and CCHS family advocates) will review request for access to de-identified data from researchers. Investigators wanting to use the registry or contact participants will need to apply to the CCHS NOW Advisory Board for access. The application will require information concerning: Principal Investigator, aims and hypotheses of the proposed research, and where the research will be performed, and how the research will be funded. The CCHS NOW Advisory Board will review and approve applications based on study quality, potential, and value to CCHS.

28. How is the Patient Registry maintained?

The registry is maintained by NORD who hosts the registry on its cloud-based Platform and provides oversight and ongoing support of the system. **The CCHS Network** provides the day-to-day management of their patient registry, including the development and adherence to the study procedures.

29. Who is the CCHS NETWORK?

The CCHS Network, founded in 1989**,** is a non-profit, tax-exempt patient advocacy organization registered in the United States. The CCHS Network promotes communication across physician - patient communities in the US and around the world, while our **CCHS Foundation** and **Research Advisory Board** focus upon funding and facilitating critical CCHS research in the US and abroad. We have learned that sharing our CCHS children's or young adults' challenges and successes through the CCHS Website and online

discussion pages is an important source of inspiration and improved medical support for CCHS patients. Family discussions of high-tech homecare, medical issues and coping challenges have also yielded ideas for new areas of research on this rare disorder. By sharing patient experiences, new research and healthcare strategies and information with families, physicians, and researchers around the US and the world, the CCHS Network provides the CCHS community with a meaningful and powerful voice.

30. Who is NORD – the National Organization for Rare Disorders?

NORD, a 501(c)(3) organization, is a patient advocacy organization dedicated to individuals with rare diseases and the organizations that serve them. NORD was founded by patients and families who marshaled grass-roots efforts to secure the passage of the Orphan Drug Act in 1983. Today, NORD represents the united voice of more than 250 rare disease-specific groups and thousands of patient advocates. Together, we are committed to the identification, treatment and cure of rare disorders through programs of advocacy, education, research and patient support services. Learn more about NORD at https://rarediseases.org/.

For more information about registries you may want to listen to the video available on the CCHS NOW Registry website at https://cchsnowregistry.iamrare.org/ (under About, For Researchers) – Marshall Summer, Chief of Genetics and Metabolism at Children's National Medical Center in Washington DC explains the goals and value of Patient-centered Registries.