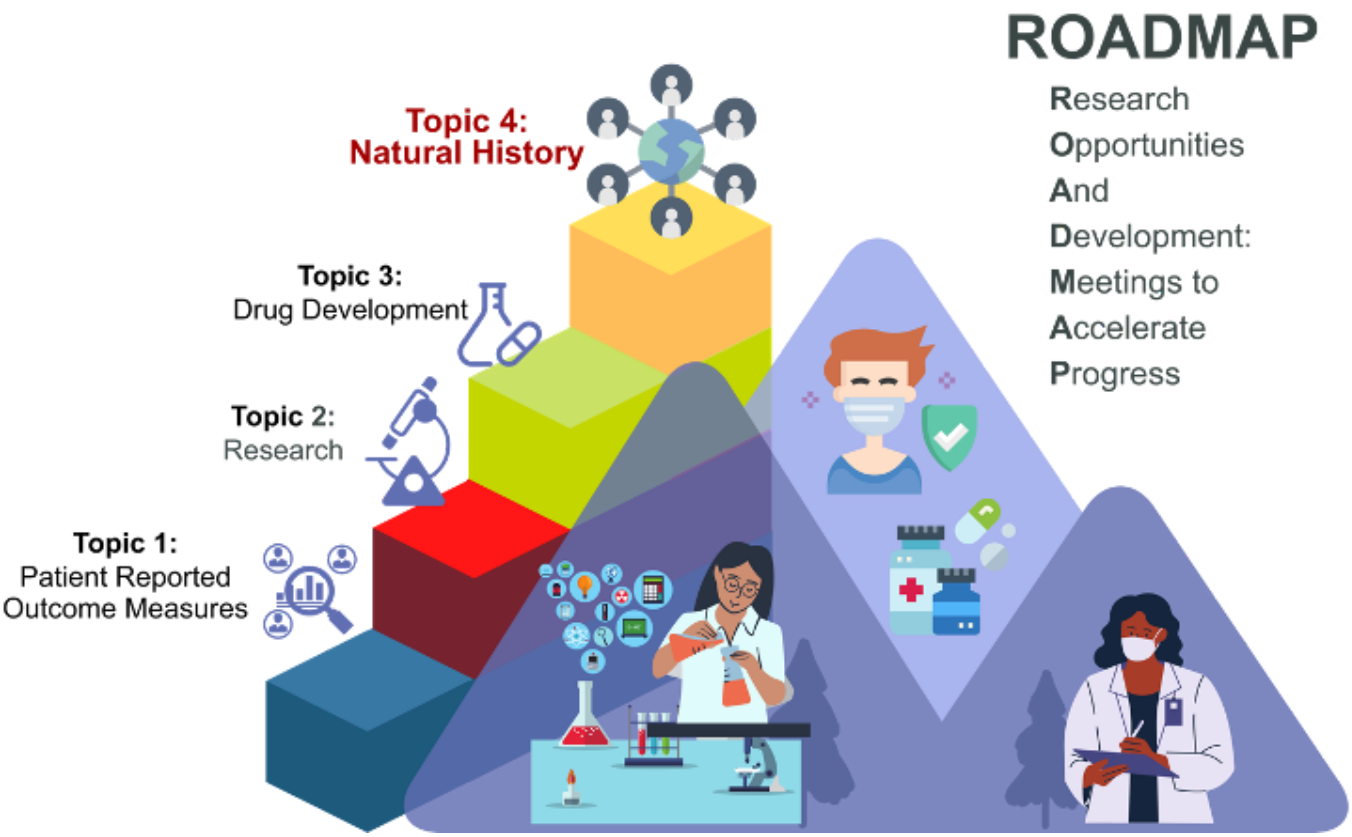
ROADMAP 101 Warm-up:
An Introduction to Natural History Registries and Studies

This year, PSC Partners is developing a natural history project. During the ROADMAP Initiative Natural History 101 session on February 24th, Gideon Hirschfield, BChir, PhD, University of Toronto, Cara Mack, MD, Children's Hospital Wisconsin, and Bettina Hansen, PhD, Toronto General Hospital, will provide us with basic terminology and concepts related to **natural history registries and studies**. Afterwards, we'll have time in breakout rooms to ask questions of the experts.

We hope you will leave the Natural History 101 session with a clear understanding of how patient participation in natural history studies harnesses the power of the PSC patient experience to drive research and drug development. Then, during the ROADMAP Initiative Natural History 201 session on March 23rd, we will discuss the NEW PSC Partners Natural History Project and how we are charting a path forward on our pursuit of a cure for PSC.



What is *natural history* and what does it mean to *study natural history*?

Natural history refers to the usual course of a disease over time. When we capture natural history, we follow a patient over time as their PSC progresses. For example, we may document the treatments that are given, how liver function tests change, and any complications experienced. All of these components are **natural history data** and, with the patient's consent, can be stored securely in a **natural history registry**.

When we ask specific questions about the natural history of PSC, and develop a strategy to answer those questions using specific data, this is called a **natural history study**. These studies are a crucial type of PSC research and will, one day, enable us to get the right treatment to the right PSC patients at the right time.

How is a *natural history registry* different from a *patient registry*?

The PSC Partners Registry is a **patient-reported registry**. Patient registries are a powerful tool to capture patient-reported outcome measures, study quality of life, recruit for clinical trials, and more. Through the PSC Partners Registry, we are able to advocate for the unmet needs of PSC patients and connect the patient voice in ongoing **natural history studies**.

The key piece that differentiates a **natural history registry** from a **patient registry** is the systematic and regular collection of past or current data elements from medical records, like imaging data, hospitalization records, and laboratory test results. The systematic capture of these health data over time are a key component necessary to enable the completion of **natural history studies**.

While researchers have traditionally used only **natural history registries** to complete these studies, it is becoming increasingly common to also leverage patient-reported data from **patient registries,** as well.

Who can participate in a natural history registry?

PSC patients are able to enroll in natural history registries offered by their PSC medical provider. Similar to clinical trials, patients need to meet certain inclusion and exclusion criteria in order to join a **natural history study.** The reason for these criteria is to make sure the study is appropriately structured to answer the questions at hand. Patients who meet the inclusion criteria will fill out a consent form through which they agree to share specific health information with researchers.

However, a natural history is different from a clinical trial, because patients are not given a specific intervention, like a drug or other treatment. Because of this, natural history studies are sometimes referred to as **observational studies**. Also, natural history studies tend to be much more inclusive, enrolling PSC patients who are often excluded from clinical trials, like those with cirrhosis and pregnant women.

Who are the key players involved in natural history registries and studies?

Patients: Patients are at the center of natural history studies. They consent to sharing their health data and may also be asked to share biosamples to enable research as part of a natural history study.

Researchers: Biostatisticians, data scientists, and other experts contribute to the analysis of natural history data. They may also contribute to the design of natural history studies, guiding us all towards an increased understanding of PSC.

Pharmaceutical Companies: Pharmaceutical companies benefit from an increased understanding of the natural history of PSC. Patients and patient advocacy groups may also communicate unmet needs, and this results in targeted drug development that is informed by the natural history and PSC patient experience.

Regulatory Agencies: Regulatory agencies, like the FDA (Food & Drug Administration) in the USA, provide guidance on the development of natural history registries. Natural history data may be submitted to regulatory agencies to support drug development.

Clinicians: Clinicians, or medical providers, are trained to care for patients and are often involved in recruiting patients to join natural history studies. Many clinicians also participate in clinical research, designing studies, analyzing data, and writing scientific articles with their colleagues.

Patient Advocacy Groups: PSC Partners' role in this process started in 2014 with the launch of the PSC Partners Patient Registry: https://www.pscpartnersregistry.org/

In 2022, PSC Partners has expanded its efforts to develop a separate natural history database through the establishment of the PSC Partners Natural History Project, which we will introduce during the ROADMAP Initiative Natural History 201 session on March 24th. We hope to see you there!