CRITICAL PATH INSTITUTE

Amidst Rare Disease Awareness Month, C-Path Shines a Light on Listening As a Form of Precision Medicine

This perspective builds on insights shared during C-Path's Global Impact Conference 2025 panel, "Ensuring a Focus on Patients in Pediatrics and Rare Diseases," where experts and advocates discussed how listening to families early leads to better trial design and the generation of more meaningful evidence.

The most essential components of any clinical trial are the study participants, who generously donate their bodies, time, and data to help develop new treatments. But the research community has been slow to recognize what participation actually demands of these families, and how those demands impact the quality of evidence when they become unbearable.

Through our rare disease initiatives and engagement with patient communities, C-Path has a clearer picture of what trial participation looks like from the family's side. Imagine a parent driving five hours to a study site with a child who has a seizure disorder. Now imagine that child seizes on the highway, and the parent has to pull onto the shoulder to manage it alone. Or imagine a family that encounters a medical emergency en route and arrives at a local hospital only to discover it lacks the pediatric equipment to intubate their child. These scenarios are not uncommon. For families managing complex, life-threatening conditions, the logistics of getting to and from a trial site can become safety risks in themselves. And when the risks become untenable, families leave the trial, taking with them observations that rare disease research cannot afford to lose and depriving patients of potentially beneficial treatment.

The underlying issue is structural. Trials are frequently built around the assumption that participants live near major academic centers, that caregivers have the flexibility to manage repeated long-distance travel, and that patients are stable enough to tolerate full days of assessment after hours in a car. For families living with complex, unpredictable conditions, those assumptions are likely unreasonable and place responsibility on

families rather than on the study sponsor.

C-Path views these logistical realities as design constraints with the same rigor we'd bring to any scientific variable. That means advocating for decentralized trial elements: local blood draws, home-based assessments, visit windows that flex around the unpredictability of living with a rare disease. A protocol that allows a family to stay near their own clinician, their own hospital, and their own support network supports participant retention and generates more complete and representative evidence.

C-Path also works with the lived experience community and with partners across the public, private, and nonprofit sectors to advance new digital health tools that can track how rare diseases change over time and measure the impact of potential new treatments. These efforts include utilizing wearable technologies that can support more human?centered clinical trial designs. For example, C-Path's program for Rare Neurodegenerative Diseases is leading work to create digital mobility measures for amyotrophic lateral sclerosis (ALS) using data gathered from wearable devices. This progress is made possible by people living with ALS, who generously share their time and data to drive research forward.

The same principle applies to what is measured. Legacy assessment tools, many designed for broader populations, routinely appear in rare disease trials with little thought to whether adaptation is needed. Imagine a caregiver sitting through a three-hour interview that asks, question after question, whether their child can cross the street, ride a bike, or climb stairs. Now imagine that child has a condition that will likely prevent them from ever walking. Those questions produce no useful information for the study. They do, however, require a parent to catalog their child's limitations in exhaustive detail, visit after visit.

C-Path's programs develop or modify assessment tools that more accurately measure meaningful changes in function. To do that, it's imperative to understand what outcomes matter to patients and their families. Seizure reduction is a meaningful clinical endpoint. So is a nonverbal child gaining the ability to use an eye-gaze device to communicate pain. In developing outcome measures and informing clinical trial designs, qualitative research is conducted where families are asked to recount their most difficult experiences. Currently, if different sponsors want to learn this information, they must each conduct their own interviews. This means that the same patient and family may have to recount the same crises, the same barriers, and the same near-misses for every new study. C-Path is working to build qualitative repositories, modeled on the way C-Path's Data Collaboration Center already compiles clinical trial and natural history datasets, so that families are spared that repetition and sponsors can build on a collective understanding rather than starting from scratch each time.

Timing matters enormously in all of this. If patients are consulted after a protocol has been finalized, the endpoints, visit schedules, and inclusion criteria have already been decided. Programs that consider the lived experience during study design can more effectively meet the unique needs of the study population and are better able to evaluate what matters most to families. As a result, these more thoughtfully designed trials stand to generate the strongest evidence in therapeutic development for rare diseases.

At C-Path, we are committed to smoothing the regulatory road by ensuring that the evidence generated reflects the full reality of the disease. That means listening early, listening carefully, and building that evidence into every layer of the research process. In rare disease, where the margin for error is thin and the stakes for families are enormous, listening is its own form of precision medicine.