Inter-provincial Barriers to Pediatric Clinical Research

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Maternal Infant Child and Youth Research Network (MICYRN)
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Background

Economic, ethical, regulatory and infrastructure considerations associated with the conduct of child health research have limited the number of drug clinical trials conducted with children. Several challenges, more frequently encountered when conducting clinical trials with a pediatric population, have contributed to current gaps in the evidence base on medicines for children. On one hand, many diseases occur less frequently in children and neonates, compared to adults. On the other hand, some diseases only occur in children or have etiology or physiopathology different from the adult population. Other challenges with neonatal or pediatric clinical trials include the frequent lack of age-appropriate and validated clinical endpoints, the paucity of data on normal laboratory values, the need for sensitive assays to minimize blood sampling, and the fact that, while they cannot legally provide consent, children should be informed and have a voice regarding participation. Therefore, in order to engage sufficient participants in a timely fashion and to execute well and appropriately powered studies, pediatric clinical trials often require recruitment and enrollment at multiple sites across multiple jurisdictions. The result of expansion across multiple jurisdictions requires considerable effort and there is complexity due to the need to obtain clearance from the competent authority, negotiating budgets, execution of contracts and data sharing agreements, and undergoing institutional ethics committees review.

As a result, and despite Canada's relative wealth as a nation with universal healthcare and world class investigators, our country was not optimally positioned to be among the world leaders in COVID19 pediatric clinical research during the pandemic. What we have clearly learned from this experience is that improving our pediatric clinical health research efficiency and effectiveness now will not only help us prepare for events in the future, but will support a productive child health research agenda that benefits Canadian children and their families.

The establishment of a pediatric clinical research infrastructure is particularly important in addressing the knowledge gap in the rare diseases space. It is estimated that 1 in 15 children are born with a rare disease, and many of these children die before their first birthday; rare diseases account for 30-40% of neonatal deaths in Canada. Over 70% of all rare diseases manifest in childhood. Given their young age and productive potential, children diagnosed with a rare disease represent many lost year years of potential to make positive contributions to society. One in four paediatric hospital beds are currently being occupied by a child with a rare disease. Treatments for rare diseases are limited and when available, can be extremely expensive with overall costs ranging from $100,000 to over $2 million per patient annually. Further, the percentage of drugs costing over $200,000 per year has continued to increase over recent years, from 36% in 2015 to 73% in 2019. Genome sequencing, other diagnostic technologies and innovative therapeutic approaches are driving the shift toward precision medicine and health.

Unfortunately, Canada is lagging when it pertains to ensuring the right drug for the right patient is adequately evaluated and available to every child in Canada. Among the root causes of the problem is inefficient research infrastructure; another reason includes a disjoint between clinical research efforts at the point of care within the healthcare ecosystem due to the cultural perception that research is unconnected to clinical practice. Finally, the lack of a federated mechanism to easily and safely share data or ethics oversight given the provincial coordination of healthcare results in replication of effort and inefficiencies. Building on previous efforts, MICYRN and its 21 affiliated maternal/child academic health care centres are well positioned to create a sustained national coordinated, expertise, and infrastructure that ensures that effective and novel therapeutics and interventions are available for Canadian children and their families.

Recommendations

Recommendation #1: Commit $25 million to support the development of a national child health clinical trial infrastructure with a focus on rare disease.

The establishment and long-term sustainability of a national child health clinical trial infrastructure is crucial for Canadian children and their families. An initial injection of funding will establish the foundation for a national coordinated approach to child health research. A shared, efficient pediatric clinical trial infrastructure will eliminate replication of work and generate real cost savings for federal and provincial research granting agencies, allowing new and innovative projects to be conducted at a lower cost.

A national pediatric clinical trial infrastructure will:

- **facilitate early access** to new and potentially life-saving therapies for Canadian children through a single point of contact for all sponsors - both industry and academia
- **foster collaborations** with experts based across Canadian academic institutions and subspeciality networks
- **ensure rapid and efficient trials implementation** through coordination of sites, high quality national and international standards, and rapid study feasibility assessments
- **promote innovation** in the design of paediatric clinical trials using platform trial design and Bayesian methods in order to foster the development of novel therapies
- **enable Canada's participation in global studies**, and thus support rapid delivery and participation in studies which Canada cannot deliver alone.

The Rare Diseases High Cost Drug National Strategy offers a unique opportunity to establish this infrastructure. We propose a fraction (25 million) of the funds already allocated to The Strategy to be invested in the establishment of a pediatric clinical trial infrastructure. Such an investment would bring Canada's internationally-recognized expertise in rare disease research together and position the country as a global hub for

drug development, evaluation, and market authorization. Canadian children and their families would benefit from early access to trials and therapies and the Canadian health care system would be strengthened economically from the efficiencies born from a standardized, streamlined clinical trials process informed by the best evidence and highest safety standards.

Recommendation #2: Facilitate a partnership among the provincial health systems and research institutes and organizations to foster the initial development of a national Learning Healthcare System that embeds research into clinical practice.

A Learning Healthcare System seeks to apply evidence, innovation, quality and value in the health system, thereby increasing the value of health care via rapid learning from data and immediate translation to practice and policy. Bridging the gap between clinical research and health care is crucial to optimize our publicly funded health systems that measure their effectiveness by continuous, thoughtful evaluation of the clinical cost effectiveness of health interventions.

The federal government has an early opportunity to initiate the necessary conversation of research integration at the point of care across provincial health jurisdictions. Discussion regarding the possibility of implementing early-step structural changes to health research in Canada should involve both federal and provincial governments at the annual federal–provincial negotiations of funding transfers.

Recommendation #3: The federal government to develop a national approach toward realizing open and accessible data across the pediatric research community that enables data sharing across jurisdictions.

Health data access and sharing are increasingly critical for evidence-based scientific discovery and for solving societal challenges; COVID19 underscored the need for cross-jurisdictional data access to mobilize information to support urgent research questions related to the pandemic and child health.

The federal government is well-positioned to take a leadership role in facilitating discussions among jurisdictions toward the development of a data strategy that includes nationwide interoperability, accessibility and use of child health relevant data for evidence-based pediatric healthcare research and data driven precision medicine.

Facilitating national access to quality data engenders the collaboration and innovation needed to answer urgent questions about our children's health.

About Us

The Maternal Child Youth Research Network (MICYRN) is incorporated as a charitable non-profit organization as a national network representing 21 maternal-child health research member organizations and brings together more than 25 affiliated practice-based research networks of investigators from across teaching hospitals affiliated with the 17 medical schools in Canada. Funded by its members, MICYRN's

mandate is to improve the quality and impact of research through the provision of a coordinated infrastructure to support research teams working across Canada and beyond.

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