Canadian Rare Disease Network (CRDN)

Francois Bernier on behalf of the CRDN interim steering committee

Alberta Children's Hospital Research Institute (ACHRI), University of Calgary

CORD Meeting

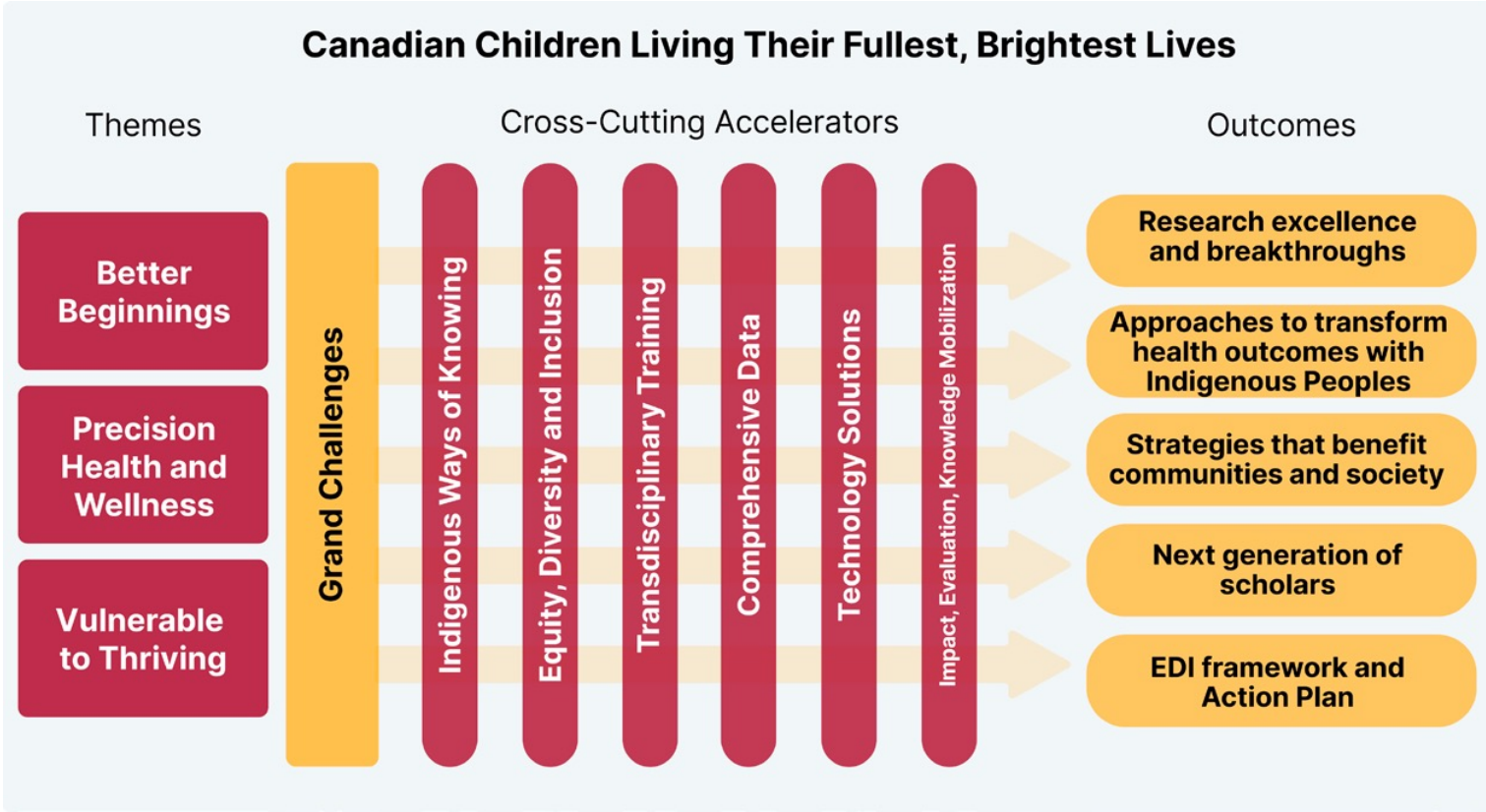
November 29-30, 2023, Calgary, AB

Acknowledgements

one child every child

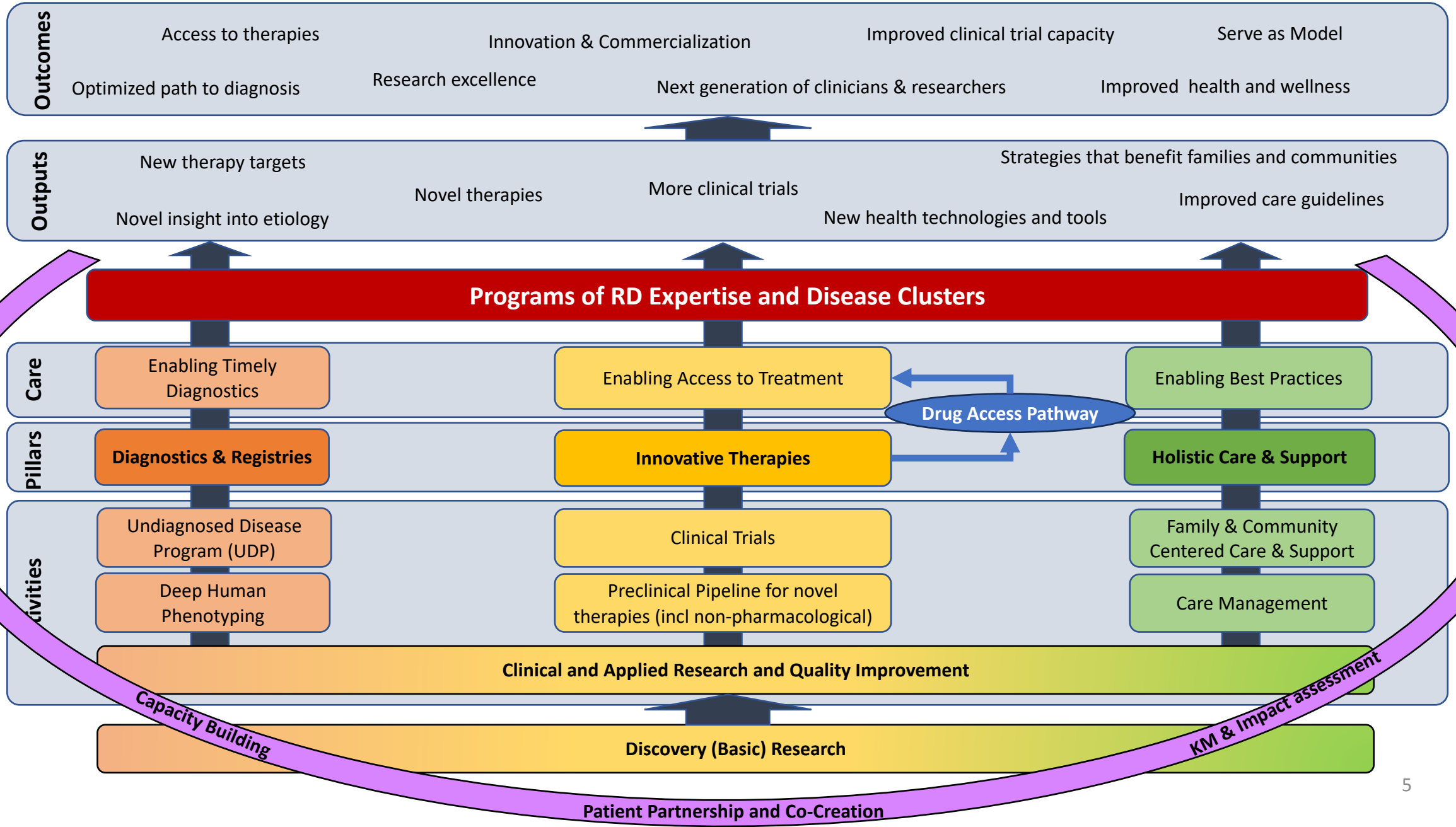
UNIVERSITY OF CALGARY | Alberta Children's HOSPITAL RESEARCH INSTITUTE | CANADA FIRST RESEARCH EXCELLENCE FUND

A Canada-first research initiative, with a vision for all children to be healthy, empowered, and thriving.



Programs of Excellence in Rare Diseases

CRDN - Overview of Goals and Structure



Benefits of the Network of Networks Approach

Coordination & Collaboration: Ensuring efforts are aligned and complementary rather than fragmented and possibly duplicated, thus empowering the rare disease community.

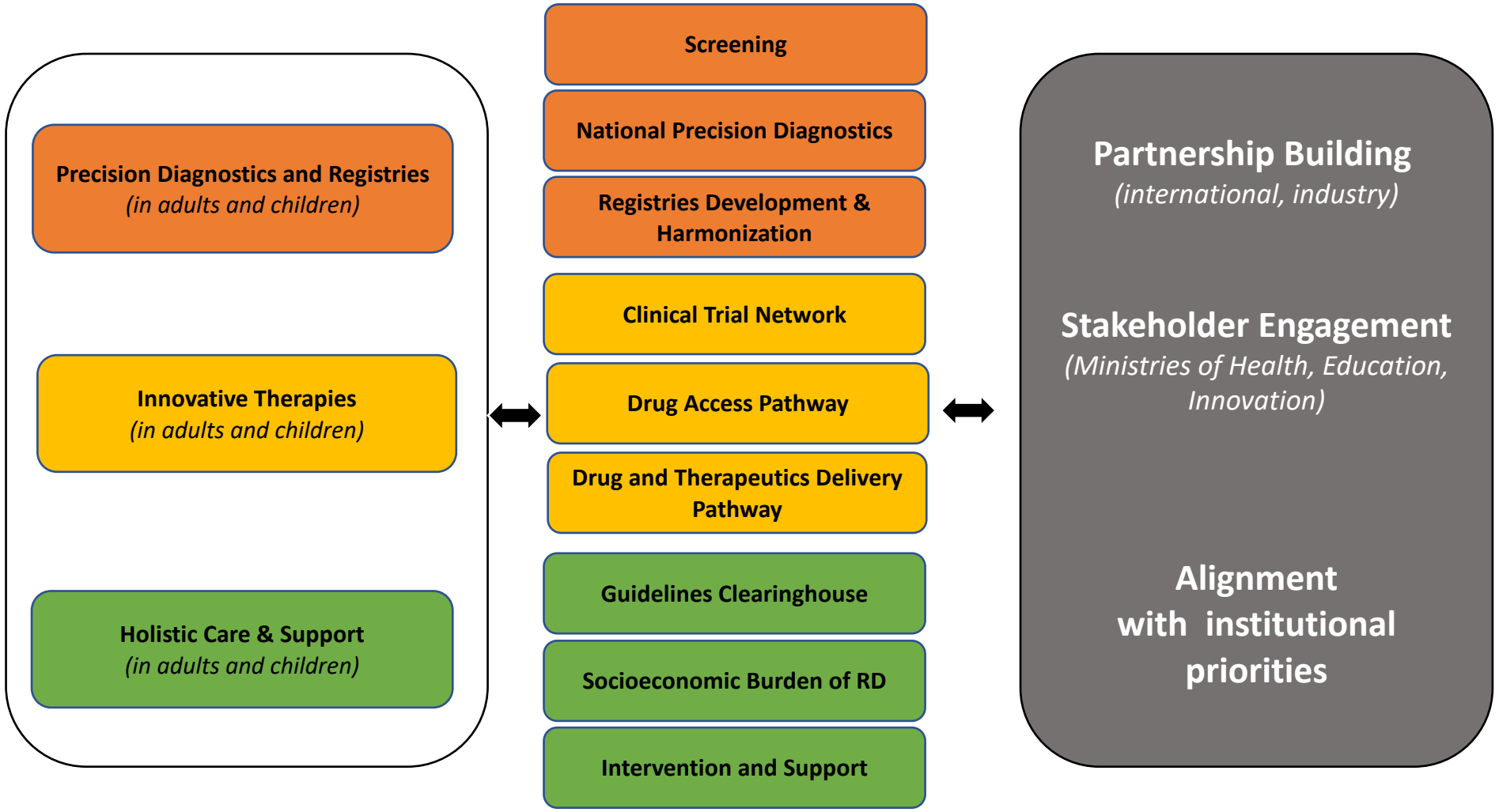
Resource Sharing: Efficient sharing of resources, such as expertise, best practices, and funding that can enhance learning and save costs.

Increased Impact: Greater visibility of individual networks and initiatives as well as coordinating and amplifying collective efforts to achieve larger-scale, cross-sectoral outcomes.

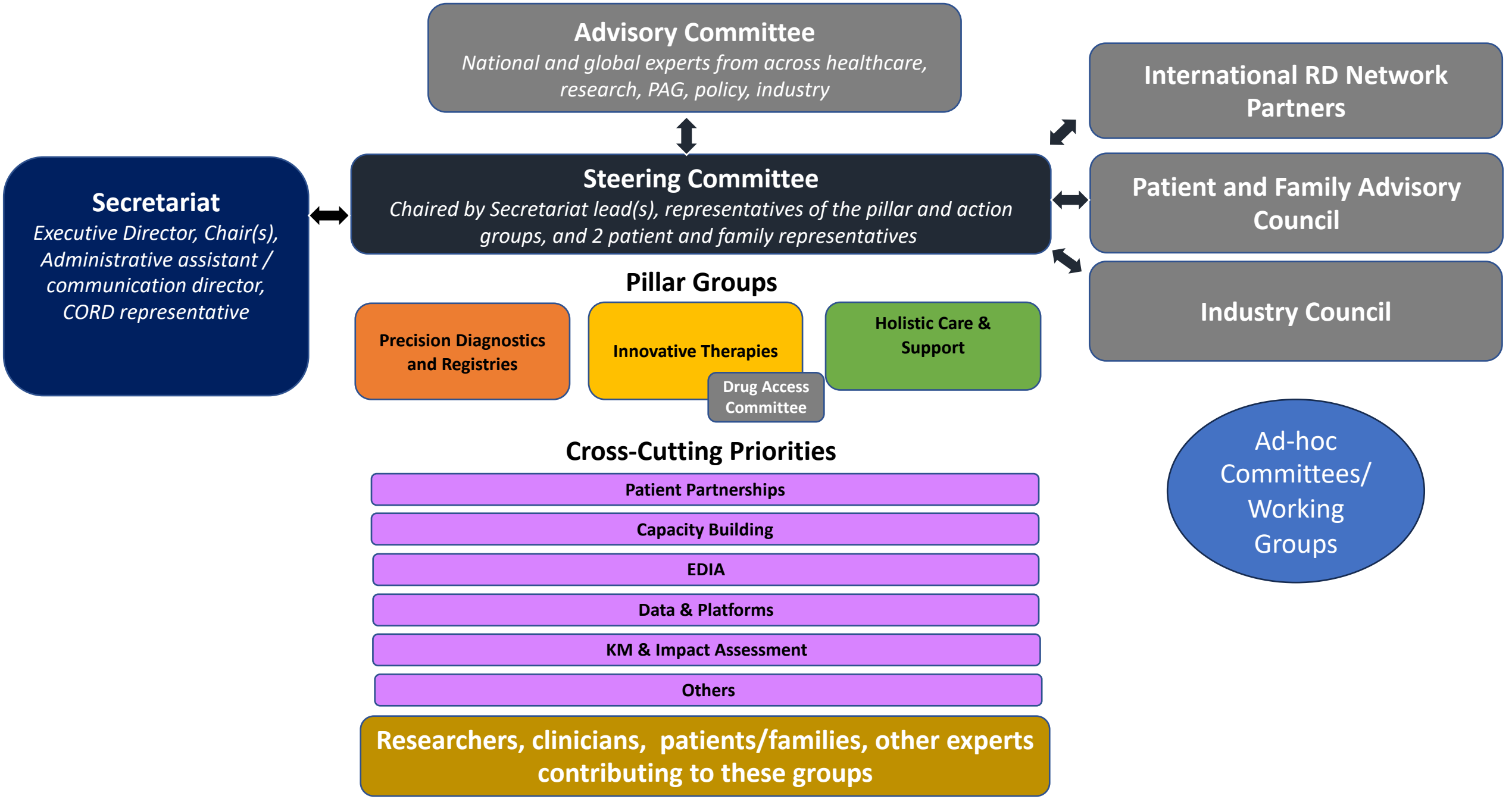
Capacity Building: Opportunities for capacity building and professional development, benefitting all members.

Global Engagement: Support international engagement and partnerships, fostering collaboration and knowledge-sharing for research, innovation, care, and advocacy.

Pillar Priorities – Short-Term



CRDN - Governance



Steering Committee Members

Francois Bernier, MD
Alberta Children's Hospital Research Institute (ACHRI),
University of Calgary

Durhane Wong-Rieger, PhD
Canadian Organization for Rare Disorders (CORD)

Jim Dowling, MD, PhD
Sick Kids Hospital,
University of Toronto

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Génétique simplement,
Former RQMO

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Hotchkiss Brain Institute,
University of Calgary

Angela Genge, MD
Montreal Neurological Institute – Hospital,
McGill University

Jonathan Pratt
Regroupement Québécois des maladies orphelines (RQMO)

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Western University

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University of Ottawa

Ian Stedman, PhD
York University

Thierry Lacaze-Masmonteil, MD, PhD
University of Ottawa,
University of Calgary,
MICYRN

Deborah Marshal, PhD
Alberta Children's Hospital Research Institute (ACHRI),
University of Calgary

Network Membership

Researchers and Healthcare Professionals

- ✓Get involved in a committee and/or task force, according to expertise.
- ✓Access to a national network of stakeholders and experts.
- ✓Chair or present at one of our monthly webinars “Rarely Explored”.
- ✓Promote your opportunities (research studies, webinars/workshops, funding, events, job postings) to our members.
- ✓Access to shared resources to advance research and best practices, and information on the State-of-Play in rare disease.

Patients, Families, and Advocacy Groups

- ✓Get involved in a committee and/or task force, according to expertise.
- ✓Be involved in influencing research priorities and setting guidelines, recommendations, policies, and CRDN activities.
- ✓Learn about clinical trials and research studies, and potential opportunities to participate.
- ✓Access to a support network through patient organizations and advocacy groups, which can provide information, educational resources, and advocacy opportunities.
- ✓Promote your opportunities (events, advocacy and policy initiatives) to our members.

Industry Representatives

- ✓Get involved in the Industry Council, according to needs and expertise.
- ✓Access to a national network of stakeholders and experts active in the field of rare disease.
- ✓Access to information about pediatric and adult rare disease research initiatives and clinical trials work and sites for therapy development.
- ✓Opportunity to collaborate and support rare disease research initiatives and clinical trials.

Getting Going

March 1st 2024!

Phase 1

May 2023 to January 2024: soft launch

> Stand up governance

> Engage stakeholders

> Finalize initial priorities and working groups and initiate partnerships with established networks

> Establish Secretariat resources

> Create web presence and communication/engagement strategy

Phase 2

February to April 2024: public launch

> Public launch on Rare Disease Day (Mar 1st), including media release and event

> Consolidate priorities and working groups and continue partnership development

> Indigenous engagement and impact plans

Phase 3

Beyond year one…

> Strategic, funding, resource, and evaluation planning

> Integrating national and international partners

> Accelerating research, innovation and care

We need your feedback to decide on a logo for the CRDN!

CRDN
CANADIAN RARE
DISEASE NETWORK

Canadian
Rare
Disease
Network

CANADIAN
RARE
DISEASE
NETWORK

CANADIAN
RARE
DISEASE
NETWORK

Use QR code:

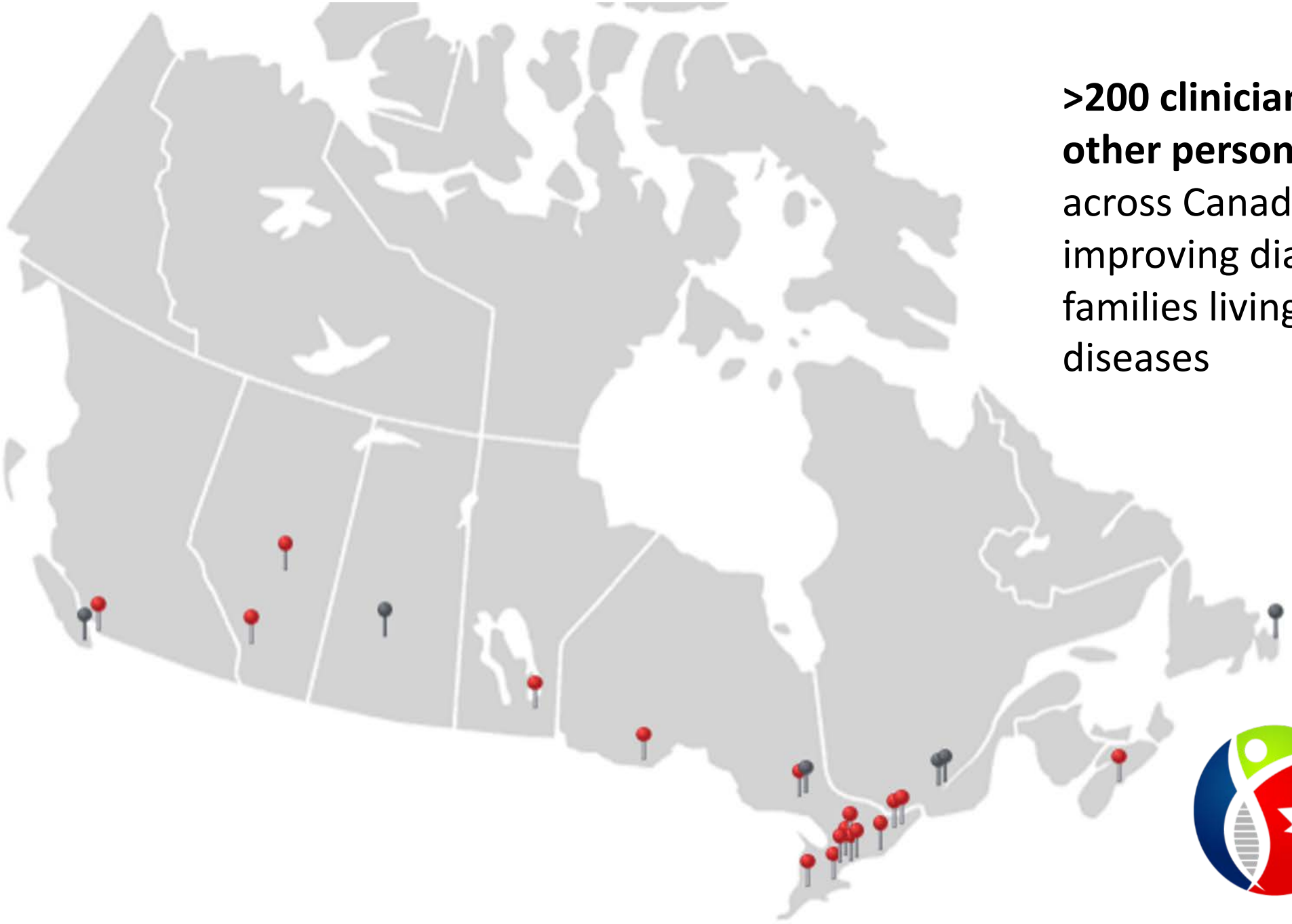
Value of Genomic Sequencing

Canadian Organization for Rare Disorders, Fall Conference 2023

Taila Hartley, PhD, MSc, MSc, CCGC

Genetic Counsellor and Operations Director, Care4Rare Canada

CHEO Research Institute



>200 clinicians, scientists and other personnel from 21 sites across Canada devoted to improving diagnostic care for families living with rare genetic diseases

CARE forRARE

What we do

CARE forRARE

Define utility of new genetic technologies

Collect, harmonize, and share clinical and ‘omic data for research

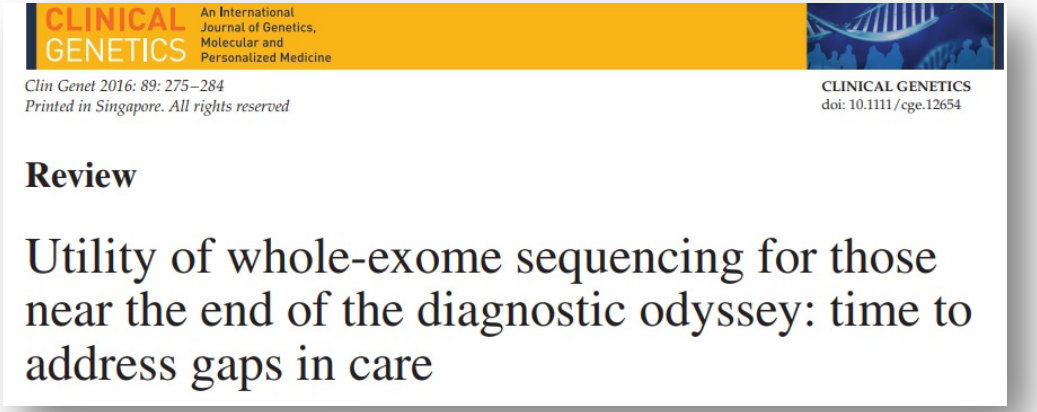
genomics4rd

Describe Rare Diseases to improve clinical care for specific diseases

Engage with different players to advance diagnostic care more generally for Rare Diseases

Genomic sequencing is the best diagnostic test we have ever had for rare genetic disease

https://www.futurelearn.com/info/courses/whole-genome-sequencing/0/steps/16773



CLINICAL GENETICS An International Journal of Genetics, Molecular and Personalized Medicine

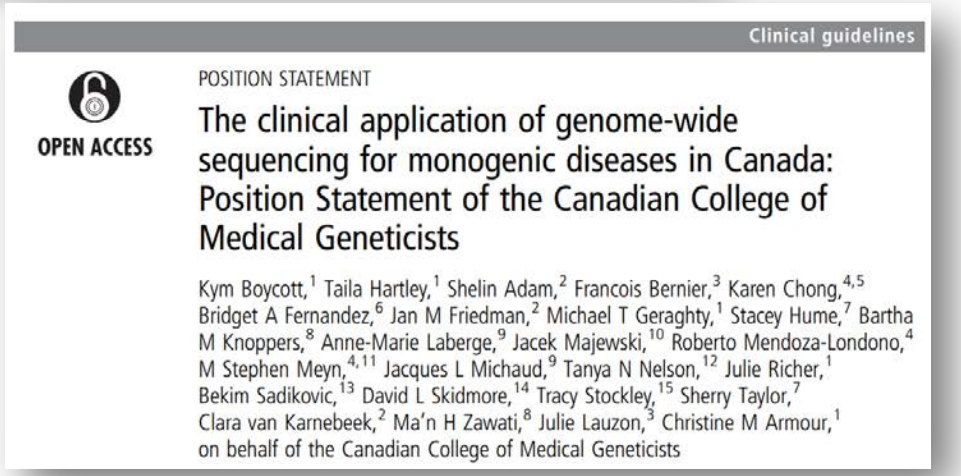
Clin Genet 2016: 89: 275–284
Printed in Singapore. All rights reserved

CLINICAL GENETICS
doi: 10.1111/cge.12654

Review

Utility of whole-exome sequencing for those near the end of the diagnostic odyssey: time to address gaps in care

Generate Canadian evidence
>2,000 families living with Rare Diseases and almost 1000 clinical and scientific collaborators



Clinical guidelines

OPEN ACCESS

POSITION STATEMENT

The clinical application of genome-wide sequencing for monogenic diseases in Canada: Position Statement of the Canadian College of Medical Geneticists

Kym Boycott,[1] Taila Hartley,[1] Shelin Adam,[2] Francois Bernier,[3] Karen Chong,[4,5] Bridget A Fernandez,[6] Jan M Friedman,[2] Michael T Geraghty,[1] Stacey Hume,[7] Bartha M Knoppers,[8] Anne-Marie Laberge,[9] Jacek Majewski,[10] Roberto Mendoza-Londono,[4] M Stephen Meyn,[4,11] Jacques L Michaud,[9] Tanya N Nelson,[12] Julie Richer,[1] Bekim Sadikovic,[13] David L Skidmore,[14] Tracy Stockley,[15] Sherry Taylor,[7] Clara van Karnebeek,[2] Ma'n H Zawati,[8] Julie Lauzon,[3] Christine M Armour,[1] on behalf of the Canadian College of Medical Geneticists

Mobilize evidence to **co-produce Canadian clinical guidance** with professional societies

Implement and evaluate with Ministries of Health

What is the value of genomic sequencing?

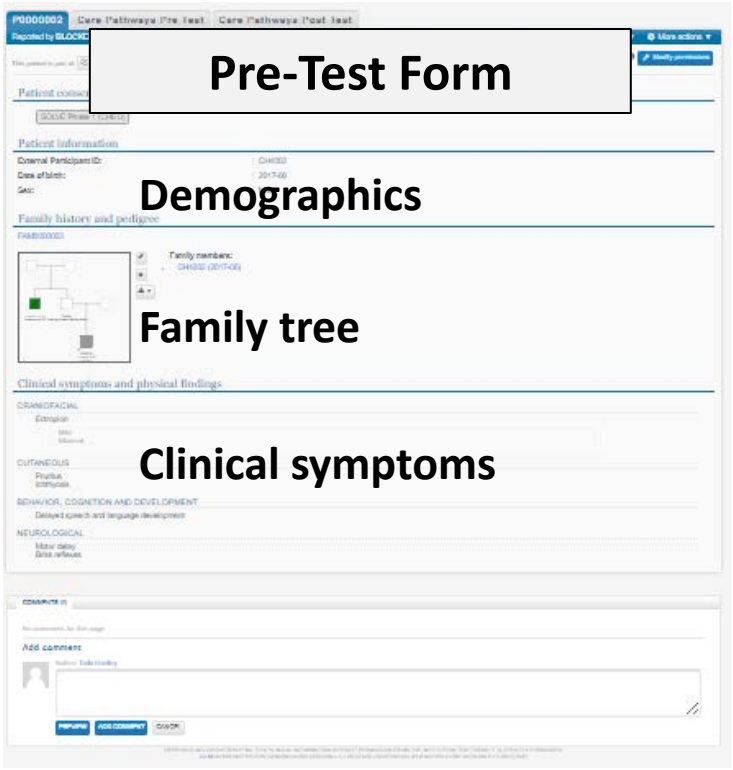
(preliminary Care4Rare-SOLVE results)

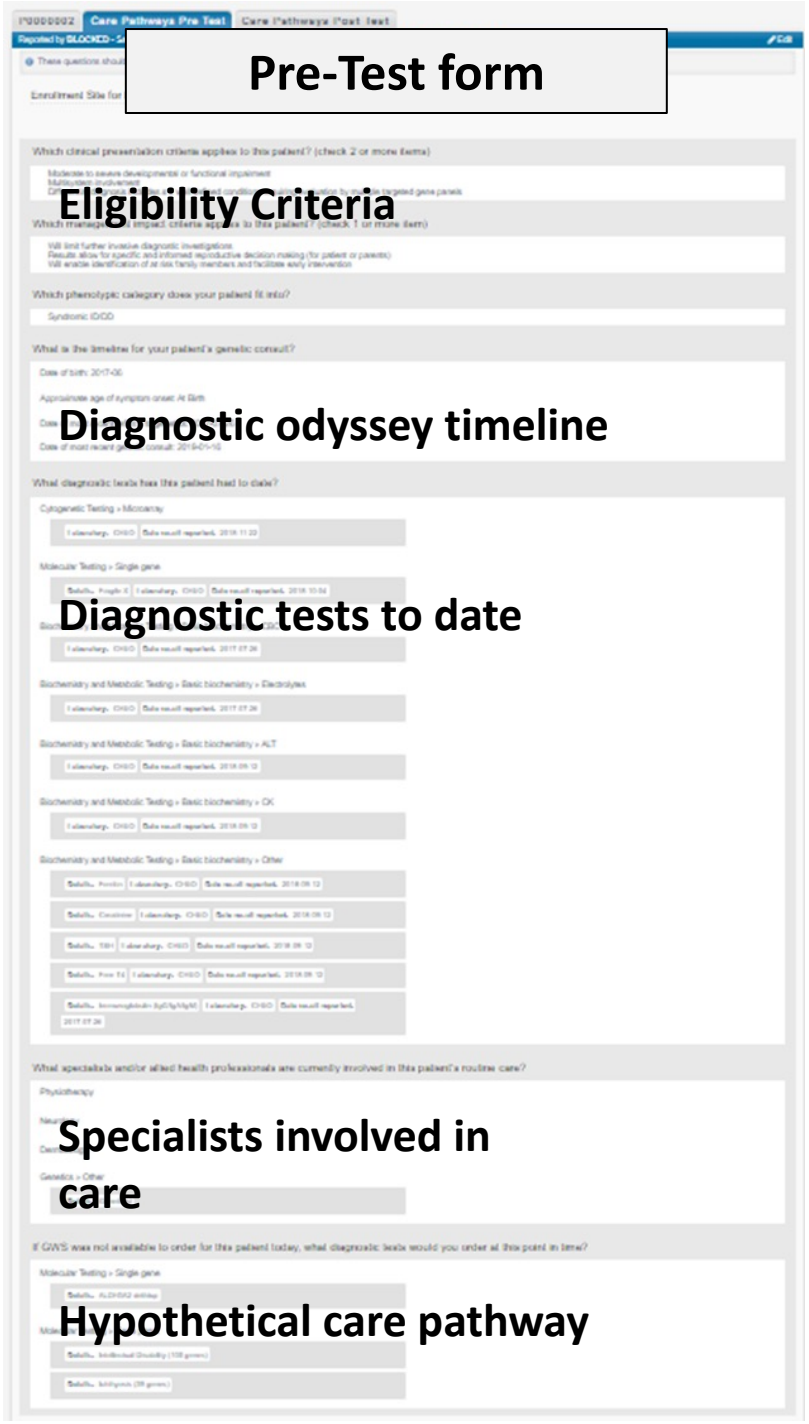
Deborah Marshall
University of Calgary

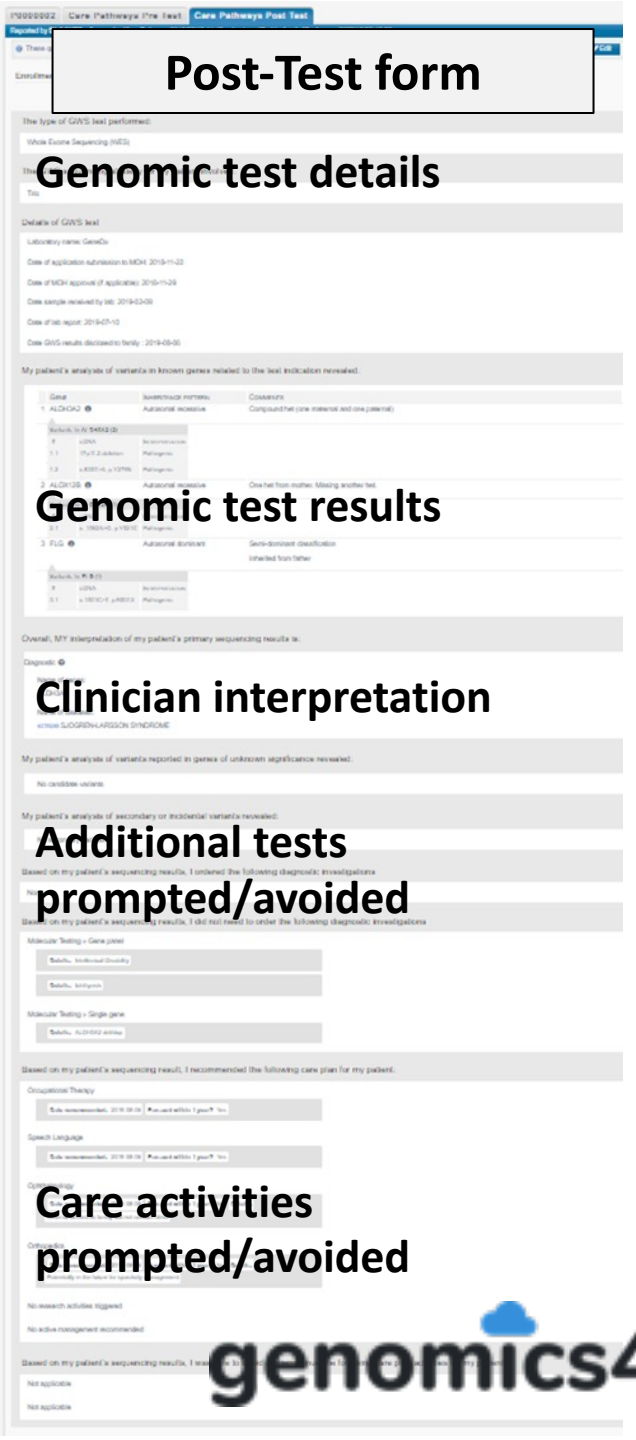
Robin Hayeems
University of Toronto

Francois Bernier
University of Calgary

Kym Boycott
University of Ottawa







Prospectively collected data for **718 individuals** who had clinical genomic sequencing in Ontario or Alberta

genomics4rd

Families with rare diseases experienced long, test intensive, and expensive diagnostic odysseys prior to genomic sequencing

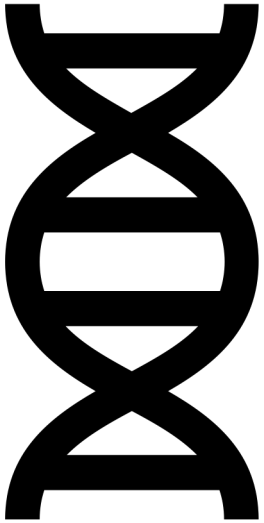
On average, individuals received **24 tests over a 3-year period before genomic sequencing**

The mean total cost of these tests was **$6,789 per person**

CARE forRARE

Data not yet published, manuscript is in preparation

Genomic sequencing had **diagnostic value**; it made diagnoses and impacted clinician thinking



Genomic sequencing identified **diagnoses** in **35% of families**

More than **one third (39%)** of the diagnoses **would be missed** by hypothetical care pathways proposed by ordering clinicians.

CARE forRARE

Hartley et al (2023) PMID: 37924259; *In press at Genetics in Medicine*

Genomic sequencing has **economic value** for healthcare payers

$

A **Health Technology Assessment** by Ontario Health (2020) recommended publicly-funded genomic sequencing as a second-tier test.

Our preliminary findings suggest genomic sequencing as the first test (instead of the second test) would **decrease cost and time to diagnosis** with minimal change in diagnostic yield

UNIVERSITY OF CALGARY

Time to Diagnosis and Cost Effectiveness of Whole Exome Sequencing (WES) Position in the Diagnostic Pathways of Patients with Suspected Rare Genetic Disease

Degeling K[1], Hayeems RZ[2], Tagimacruz T[3], MacDonald KV[3], Seeger TA[3],Hartley T[4], Boycott KM[4], Bernier FP[5], Mendoza-Londono R[6], Marshall DA[3]

[1] Cancer Health Services Research, Center for Health Policy & Centre for Cancer Research, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Australia; [2] Child Health Evaluation Sciences, The Hospital for Sick Children, Toronto, ON, Canada; [3] University of Calgary, Calgary, AB, Canada; [4] Children's Hospital of Eastern Ontario Research Institute, University of Ottawa, Ottawa, ON, Canada; [5] Department of Pediatrics, University of Toronto, Toronto, ON, Canada; [6] Alberta Children's Hospital, Calgary, AB, Canada; [6] Division of Clinical and Metabolic Genetics, The Hospital for Sick Children, Toronto, ON, Canada

CARE forRARE

Data not yet published, manuscript is in preparation

Genomic sequencing had **clinical value** regardless of whether a diagnosis was made

Medical management was changed (diagnostic test and/or therapeutic changes) for **90% of individuals** (650 of 718)

Genomic sequencing results changed management for **family members** of **21%** (151 of 718)

Genomic sequencing resulted in **research opportunities** for **40% of people** (288 of 718)

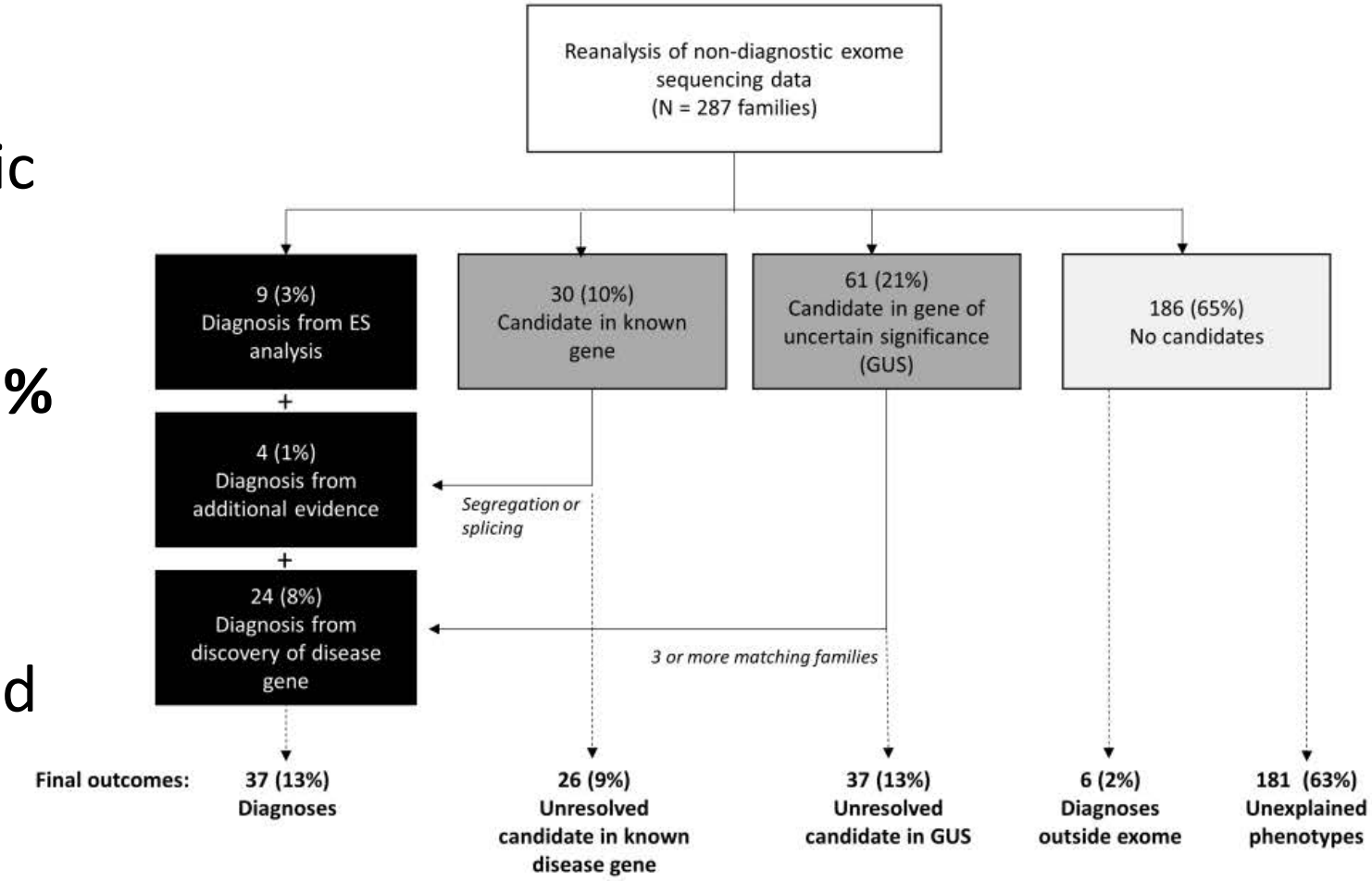
CARE forRARE

Data not yet published, manuscript is in preparation

Genomics sequencing has **research value**

We reanalyzed the genomic sequencing data from clinical labs with clinicians and found **diagnoses in 13%** in **candidates in 21%**

The majority of diagnoses come from newly described diseases



Hartley et al (2022) *Clinical Genetics.* 103(3):288-300 PMID: 36353900

What is the value of genomic sequencing?

For clinicians: A powerful test that can provide clinically-valid diagnoses, avoiding additional testing, enabling informed management

For payers: Decreased costs compared to current diagnostic pathways

For families with RD: Earlier diagnoses (time, avoiding unnecessary tests, earlier informed management), clinical implications for those that are affected and their family members, access to research opportunities

CARE forRARE

Despite its value, access to genomic sequencing remains limited

Publicly funded genomic sequencing, performed-in province, for all patients that meet evidence-informed criteria

Horizon scan, October 2023

5,000+ participants **21** sites **200** clinicians

500 collaborators **100** scientists **32** countries

Questions? Comments? Contact me: thartley@cheo.on.ca

Driving toward Consensus on Optimizing Patient Care Pathway

CORD Calgary Conference 2023

Kim L McBride
Department of Medical Genetics, University of Calgary
Section of Medical Genetics, Alberta Children's Hospital

November 29 and 30, 2023

Personal Perspective (And Biases!)

- Previous Chair of American College of Medical Genetics and Genomics Therapeutics Committee
  - Policy, development of evidence-based treatment guidelines
- Former Director NORD Center of Excellence, Nationwide Children's Hospital/Ohio State University, Columbus, Ohio
- Active clinical trial research in rare disorders

…Now what?

Treatment Guidance Uncertainties

- Most rare diseases do not have detailed natural history studies
- Rare disease therapeutics will continue to be challenging
  - Endpoints difficult and not always practice friendly
  - Evidence will likely always be very incomplete
- Systematic evidence-based reviews often not fruitful
  - Frequently not enough evidence for practice guideline
- Reliable source of clinical practice information still needed
- ***Patient and family experiences need to be incorporated***

Delivering Care for Rare Disorders

- Applying clinical recommendations requires organizational structure
- Develop a process to establish a care pathway approach
  - Some disease specific CoE (CF) have good model for CoE structure
  - Many RD are very rare, not enough expert people, lack of good evidence for CoE
- Network of expertise to optimize/distribute and ensure equity of care
  - Not just specialist care - Chronic care, allied health care, etc.
  - Infrastructure – hospitals, institutes
- ***Use patient and family community to guide***

Care Pathway Definition

1. Intervention is a structured multidisciplinary plan of care
2. Intervention is used to translate guidelines or evidence into local structures
3. Intervention details steps in a course of care (i.e., the intervention has timeframes or criteria-based progression)
4. Intervention aims to standardize care for a specific population

"the right person, in the right place, doing the right thing, at the right time, with the right outcome and all with attention to the patient experience."

Lawal AK, et al. *BMC Med.* 2016

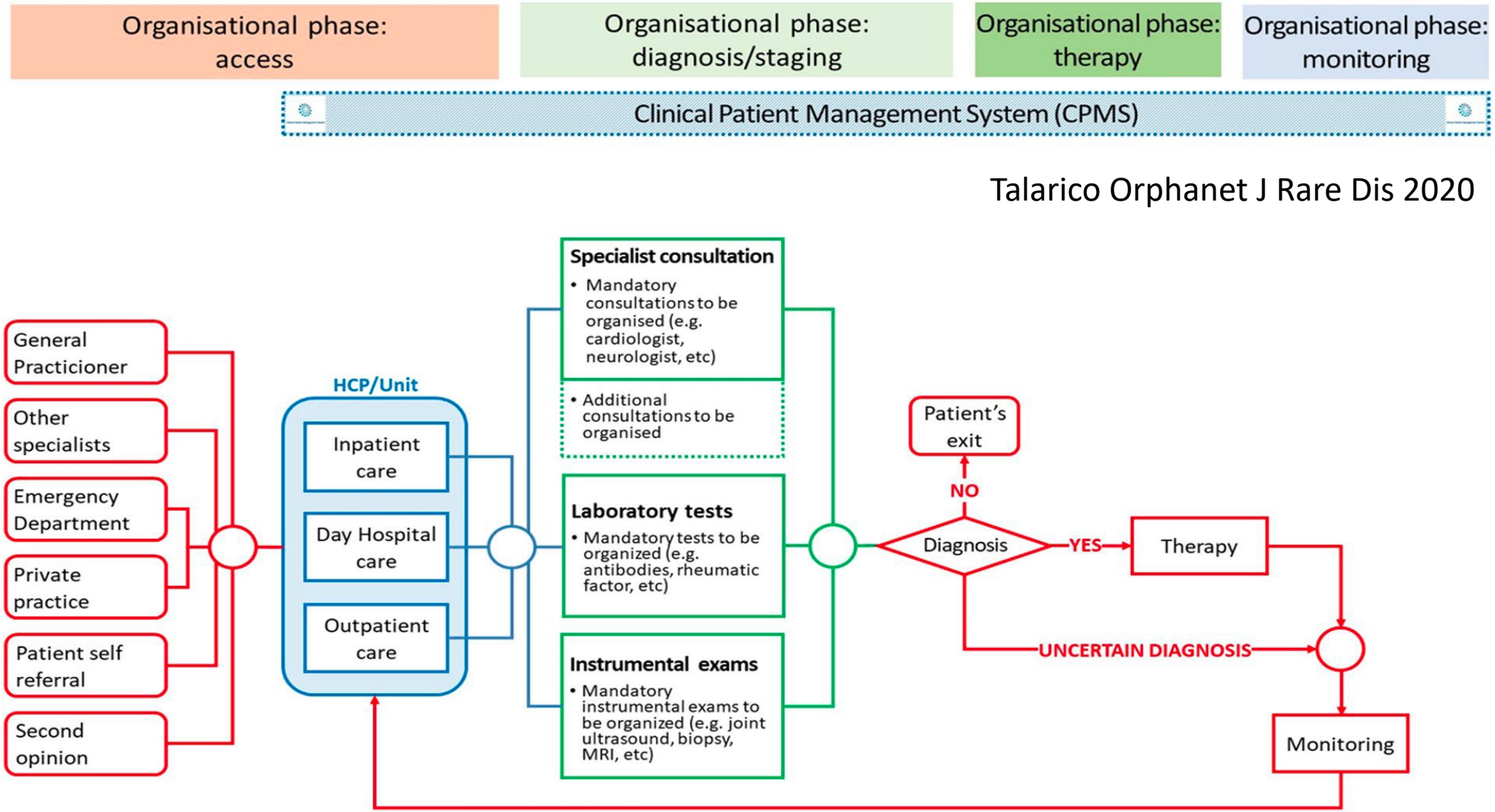
Challenges of RD Care Pathways

- Limited abilities to recognize RD at entry to healthcare
- Lack of care pathway leads to delays (diagnosis, treatment) and inequity and places high burden of care coordination on families
- Large scope and complexity of heterogenous group of RD
- Lack of resources:
  - Financial, psychosocial support, evidence to guide care
- How to benchmark
- Integration into provincial/national systems
- Education and training

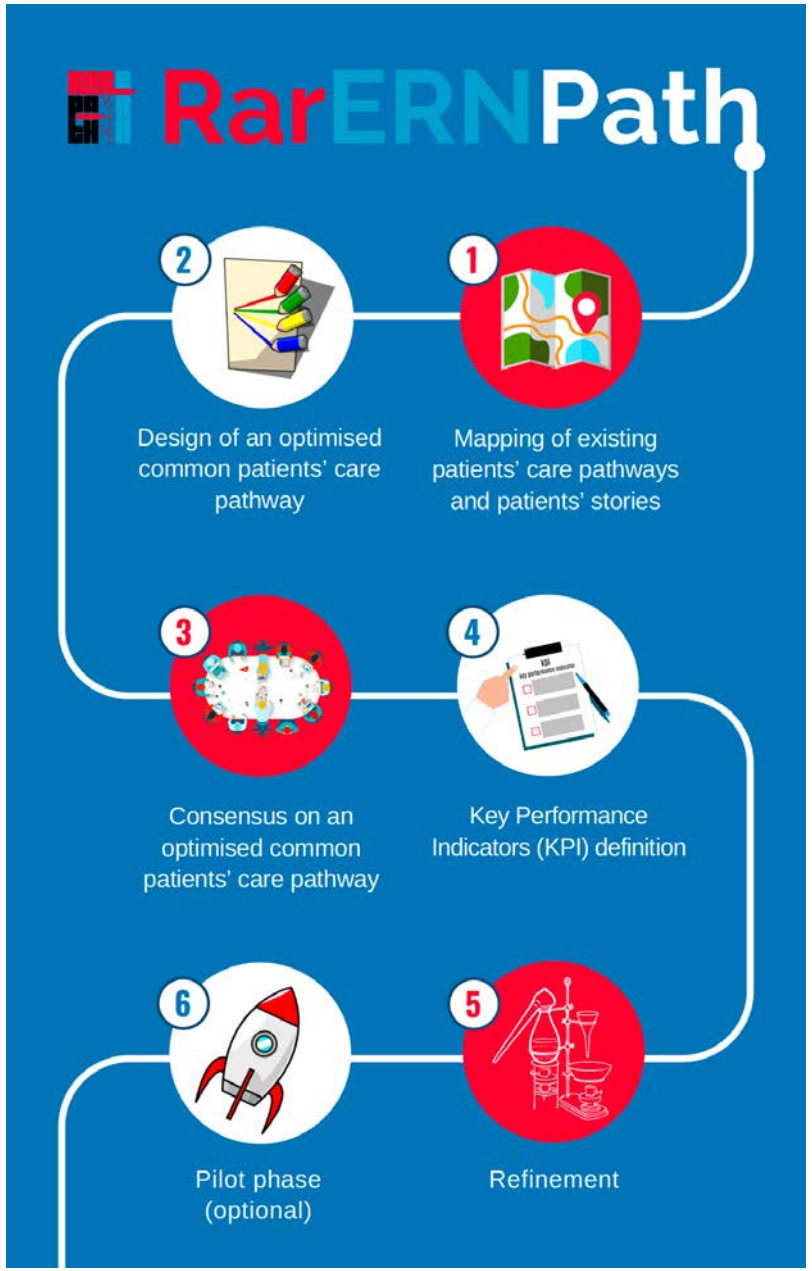
Characteristics of RD Care Pathways

- Large load onto highly specialized services
- Centralization of services
- Balance between specialized expertise, accessibility
- Patients and families empowerment
- Blurring or boundaries between clinical care and research
- Need for complex care:
  - Psychosocial, ancillary services, community care

European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases



Talarico Orphanet J Rare Dis 2020



Patient First RD Care Pathway

- European Reference Network created a method to provide care plan organization across the different EU Member States.
- Based on sharing expertise and patient-centred approach: RarERN Path™

Concluding Thoughts on Canadian RD Care Pathway

- Patient/family centered multidisciplinary and chronic care
- Centre of Excellence model not as optimal
  - Creation of network(s) in response to need for equity of care across country and account for provincial/federal framework of health care
- Incorporation of research and education into care pathway
- Enabling access to innovative therapies

Canadian Organization for Rare Disorders

Amyloidosis Program of Calgary

Unique Challenges of Diagnosis and Care for Adults with Rare Diseases

Canadian Organization for Rare Diseases Fall Conference

Nowell Fine, MD SM

November 29th 2023

LIBIN CARDIOVASCULAR INSTITUTE

Alberta Health Services

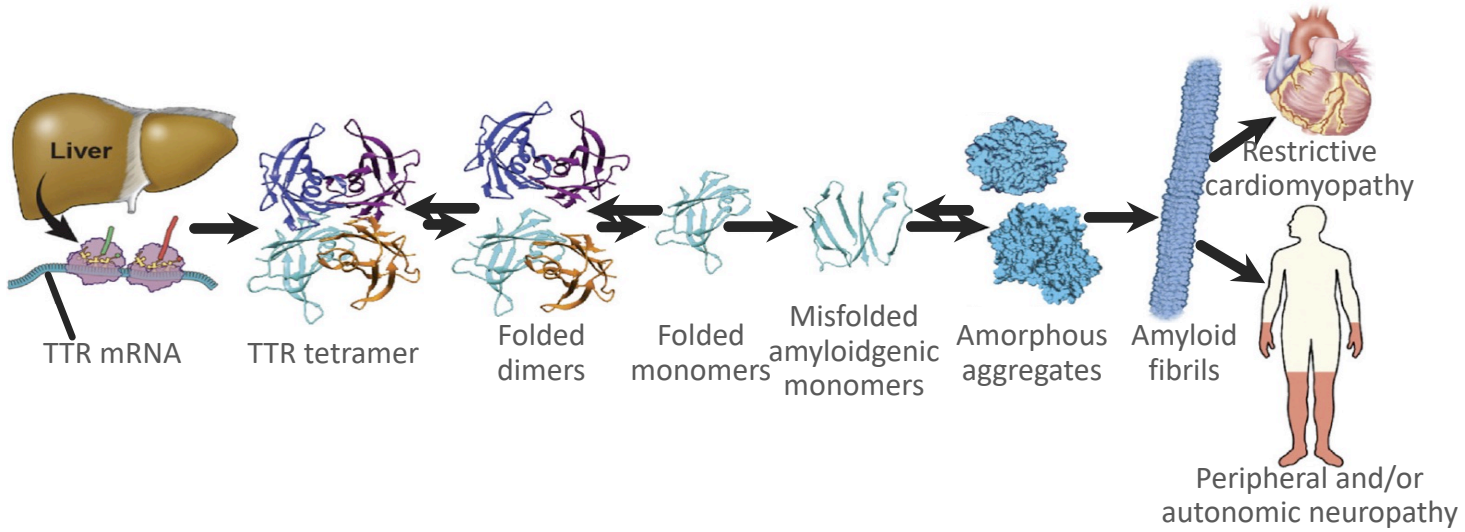
UNIVERSITY OF CALGARY CUMMING SCHOOL OF MEDICINE

Disclosures

- **Grants/Research Support:** Pfizer, Ionis, Servier, Takeda, Novartis, BridgeBio-Eidos

- **Speaking/Consulting Honoraria:** Pfizer, Ionis, Sobi, Alnylam, Sanofi-Genzyme, Astra-Zeneca, Takeda, NovoNordisk

Transthyretin Amyloidosis (ATTR)



Diagnosed in older adults 70's, 80', 90's!

New (and expensive) therapies!

Transthyretin Amyloidosis (ATTR)

- **Hereditary ATTR** — **TTR gene mutation, endemic ethnic/racial groups**
- **Wild-type ATTR** — **Age-related disorder, no gene mutation, male predominance**

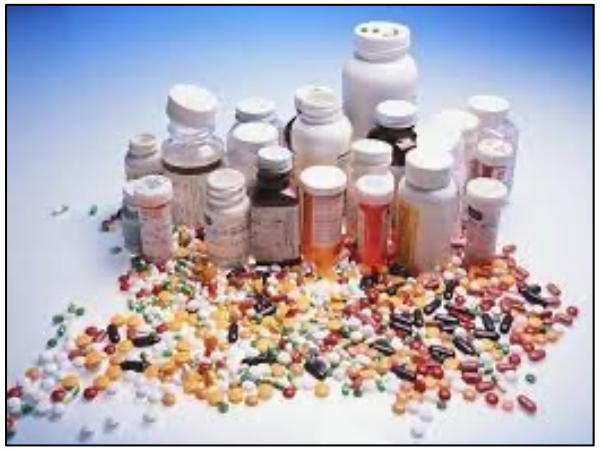
Ruberg. JACC 2019;73:2872

Diagnosis

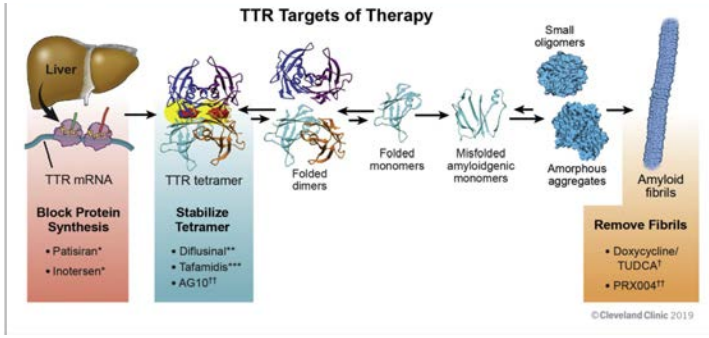
Hiding in plain sight!

Clinical Care Issues

Comorbidities

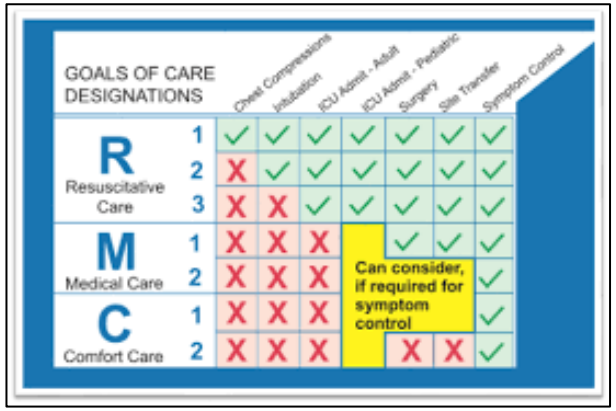


Polypharmacy



Disease Modifying Therapy

- Projected benefit and lifespan



Goals of Care

Ageism

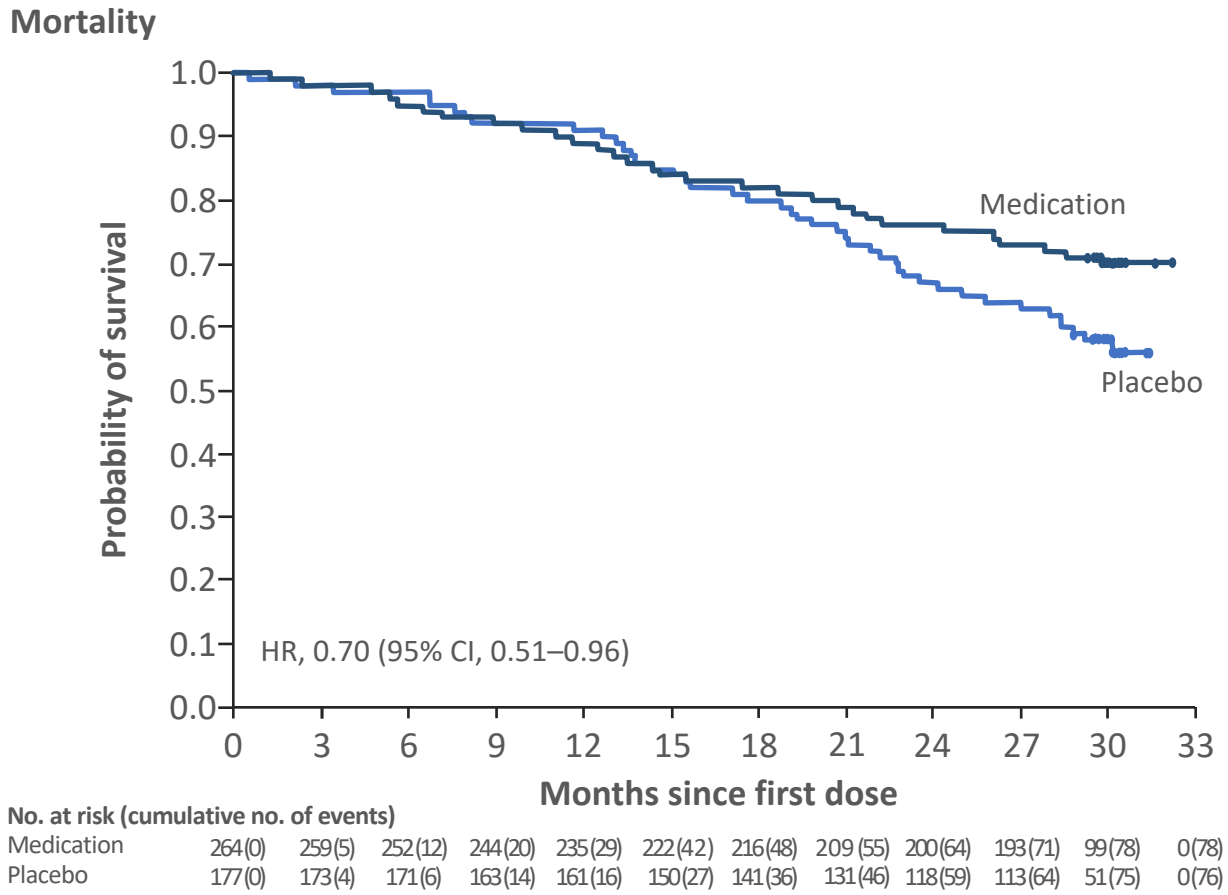
Multidisciplinary Care

It takes a village!

Avengers assemble!

Genetic Testing

Drug Development



Amyloidosis
Program of Calgary

Adult Rare Diseases

- Thank you!

- nmfine@ucalgary.ca

CORD Canadian Organization for Rare Disorders

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Alberta Health Services

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CUMMING SCHOOL OF MEDICINE

IRARE Centre: Supporting the Whole of the RD Community

Gail Ouellette, Regroupement québécois des maladies orphelines

Quebec Coalition of Orphan Diseases

CORD meeting, Calgary
November 29-30, 2023

REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES / QUEBEC COALITION OF ORPHAN DISEASES

RQMO
REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES

MISSION

- Inform & support
- Awareness
- Disseminate information
- Facilitate research

RQMO
REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES

+ the most orphan:

PATIENTS
PARENTS
CAREGIVERS

WITHOUT
A PATIENT ORGANIZATION

- CORAMH (Corporation de recherche et d'action sur les maladies héréditaires)
- Association d'acidose lactique du Saguenay-Lac-Saint-Jean
- Groupe d'aide aux enfants tyrosinémiques du Québec
- Association canadienne des ataxies familiales - Fondation Claude St-Jean
- Association québécoise des personnes de petite taille
- Fondation sur les leucodystrophies
- Association canadienne de Fabry
- National Gaucher Foundation of Canada
- Fondation Jean-Michel Dufour
- Fondation du syndrome de Loeys-Dietz du Canada
- Encéphalite anti-NMDA Canada
- Fondation hypertension artérielle pulmonaire du Québec
- Fondation du syndrome d'Angelman du Québec
- PKU Canada (phénylcétonurie)
- Eeyou Awaash Foundation (leucoencéphalopathie et encéphalite des Cris)
- Dystrophie musculaire Canada
- Association de la neurofibromatose du Québec
- Soutien hétérotopie nodulaire périventriculaire
- Sclérodermie Québec
- Association d'anémie falciforme du Québec
- Association canadienne de l'anémie aplasique et la myélodysplasie
- Association des patients immunodéficients du Québec
- Association du syndrome de Turner du Québec
- Association québécoise de la névralgie du trijumeau
- Vivre avec la fibrose kystique
- Association québécoise du syndrome de Rett
- Association du spina bifida et de l'hydrocéphalie du Québec
- Fondation La Force
- Fondation Simon-le-zèbre
- Communauté Morquio du Québec

centre iRARE

iNFORMATION
RESSOURCES
AIDE
RÉFÉRENCES
EDUCATION

Pour toute **maladie rare** et **maladie non diagnostiquée**

- Free
- Bilingual
- Professional

iRARE centre

iNFORMATION
RESOURCES
AID
REFERENCES
EDUCATION

For any **rare** or **undiagnosed disease**

INFORMATION AND SUPPORT are the keys to a better management of your disease.

INFORMATION

- Articles in lay language, practice guidelines
- Research projects and clinical trials
- Rare disease experts and specialized clinics
- Basic genetic counselling
- Orphan drugs, on the market or in development
- Patient registries and biobanks

SUPPORT

Matching

Matching with individuals/families with the same or similar rare disease

Listening

Referral to

- Patient organizations
- Support groups

Medical, government and community resources

ESTABLISHING AND OPERATING A CANADIAN NETWORK OF

iRARE centre

INFORMATION AND SUPPORT CENTRES FOR RARE DISEASES

RQMO
REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES

CANPKU+ CANPKU+

www.CANPKU.org

CANADIAN PKU AND ALLIED DISORDERS INC.
PCU ET MALADIES APPARENTÉES CANADA INC.

IMPLEMENTATION OF A DIGITAL PLATFORM TO BRING TOGETHER RARE COMMUNITIES

RQMO
REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES
iRARE centre

Funded by the Government of Canada's Community Services Recovery Fund

Canada

Community Services Recovery Fund

Canadian Red Cross

COMMUNITY FOUNDATIONS OF CANADA

United Way Centraide Canada

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REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES

iRARE centre

i NFORMATION
R ESOURCES
A ID
R EFERENCES
E DUCATION

For any **rare** or **undiagnosed disease**

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