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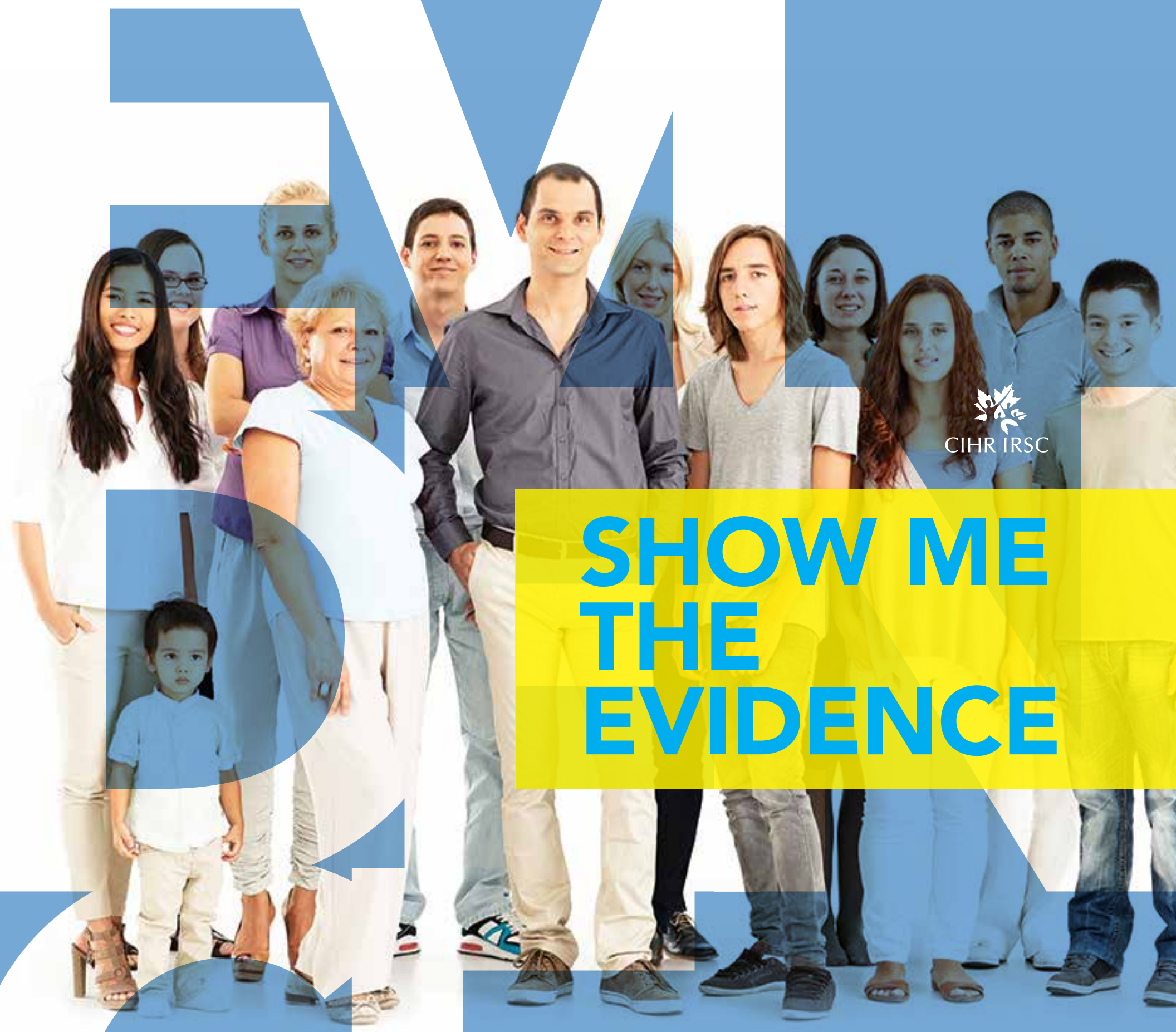

CIHR IRSC

SHOW ME THE EVIDENCE

CIHR SUPPORTED RESEARCH PUTTING PATIENTS FIRST

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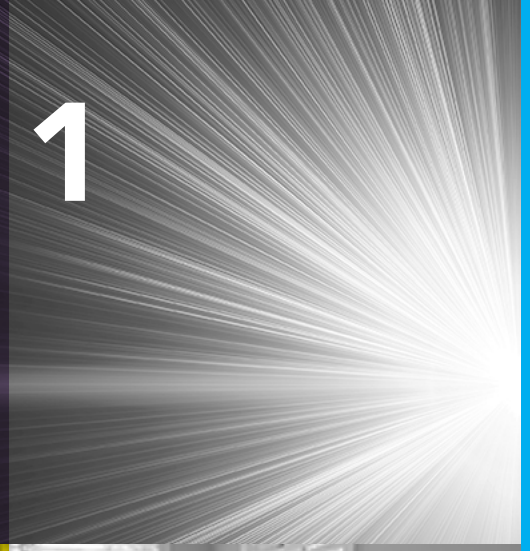
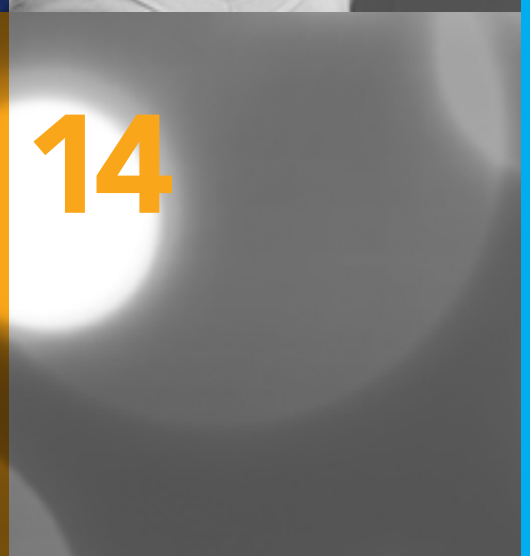
For more than a decade, the Canadian Institutes of Health Research (CIHR) has supported some of the best and brightest health researchers in the world in their quest to improve the health and well-being of Canadians through research. CIHR-funded research and researchers have delivered better care, earlier diagnosis, improved quality of life and cost savings.





As the Government of Canada's health research investment agency, the Canadian Institutes of Health Research (CIHR) enables the creation of evidence-based knowledge and its transformation into improved treatments, prevention and diagnoses, new products and services, and a stronger, patient-oriented health care system. Composed of 13 internationally recognized Institutes, CIHR supports health researchers and trainees across Canada. **www.cihr-irsc.gc.ca**

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Canadian Institutes of Health Research
160 Elgin Street, 9th Floor
Address Locator 4809A
Ottawa, Ontario K1A 0W9

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All people profiled in this magazine have agreed to their appearance in it and approved their individual stories.

WELCOME TO SHOW ME THE EVIDENCE

Achieving the goal of patient-oriented care, where the right patient receives the right treatment at the right time, takes time and effort. What kinds of changes are necessary to ensure that promising research advances are brought quickly to the point of care? How do we alter the research process and the health care system to fully integrate the patient point of view? CIHR-supported researchers are already conducting work that illustrates the benefits of patient-oriented care.

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's health research investment agency. CIHR provides support for investigator-driven health research, but also sets strategic investment priorities to respond to key health and health system challenges. CIHR has established five research priorities for the organization and health research across the country:

- Enhance patient-oriented care and improve clinical results through scientific and technological innovations.
- Support a high-quality, accessible and sustainable health care system.
- Reduce health inequities of Aboriginal people and other vulnerable populations.
- Prepare for and respond to existing and emerging global threats to health.
- Promote health and reduce the burden of chronic disease and mental illness.

Show me the Evidence showcases some of the evidence being produced by Canadian health researchers in response to the challenges listed above. In this issue, we report the progress of several researchers who are working to make patient-oriented care a reality. This research is directly supporting efforts by policy makers to deliver more patient-responsive health care, and is providing new tools to help clinicians and patients work together to address the uncertainty that often arises with disease. These stories highlight:

- An innovative research initiative that is using advances in genomic technology to provide answers to parents of children with rare diseases;
- Efforts to synthesize relevant research to inform Saskatchewan's health care reform plans; and,
- A new evidence-based tool to improve classification of the impacts caused by cerebral palsy.

These CIHR-funded research projects have delivered:

- **COST SAVINGS RESULTING FROM THE PROPER DIAGNOSIS OF RARE DISEASES;**
- **RESEARCH THAT HAS HELPED ENABLE PROVINCIAL HEALTH CARE REFORMS; AND,**
- **IMPROVED COMMUNICATION BETWEEN PATIENTS AND CLINICIANS ABOUT CEREBRAL PALSY DIAGNOSES.**

WHAT DOES THE FUTURE HOLD? SOLVING THE MYSTERIES OF RARE DISEASES

Next-generation gene sequencing can help spare parents years – sometime decades – of not knowing what's wrong and how to best care for their children.

AT A GLANCE

WHO: DR. KYM BOYCOTT, CHILDREN'S HOSPITAL OF EASTERN ONTARIO RESEARCH INSTITUTE

ISSUE: THERE ARE AN ESTIMATED 7,000 RARE DISEASES, MOST OF WHICH AFFECT CHILDREN AND ONLY HALF OF WHICH HAVE AN IDENTIFIED GENETIC ORIGIN – LEAVING ABOUT 3,500 IDENTIFIABLE ONLY BY THE SYMPTOMS THEY CAUSE. FAMILIES OF CHILDREN WITH A SUSPECTED RARE DISEASE ARE LEFT IN THE DARK, OFTEN WAITING YEARS TO GET A DEFINITIVE DIAGNOSIS AND, WITH IT, APPROPRIATE CARE.

PROJECTS: OVER THE PAST TWO YEARS, DR. BOYCOTT, A CLINICIAN-RESEARCHER WHO SPECIALIZES IN THE GENETIC ORIGINS OF NEUROLOGICAL DISORDERS, HAS LED A CONSORTIUM CALLED FORGE CANADA (FINDING OF RARE DISEASE GENES IN CANADA) TO STUDY THE GENETIC CAUSES OF 200 RARE DISEASES. FORGE SOLICITED PROPOSALS FROM CLINICIANS ACROSS THE COUNTRY TO IDENTIFY THE SPECIFIC RARE DISEASES THAT THEY WOULD STUDY. THE CONSORTIUM BRINGS TOGETHER 150 CLINICIANS AND SCIENTISTS WORKING AT 21 CENTRES ACROSS CANADA AND HAS ENLISTED THE HELP OF GENETICISTS IN 17 COUNTRIES.

RESEARCH EVIDENCE: USING HIGH-THROUGHPUT, NEXT-GENERATION SEQUENCING, FORGE HAS ALREADY FOUND THE DISEASE-CAUSING GENE MUTATIONS FOR MORE THAN 100 RARE DISEASES. THE SCIENTISTS EXPECT THEY WILL HAVE IDENTIFIED THE GENETIC ORIGINS OF 130 – OR ABOUT TWO-THIRDS OF THESE DISEASES – BY THE END OF THE YEAR.

EVIDENCE IN ACTION: MORE THAN 500 FAMILIES HAVE RECEIVED DIAGNOSES FOR THEIR CHILDREN'S CONDITIONS SINCE FORGE SET TO WORK IN APRIL OF 2011. THIS HAS SAVED FAMILIES FROM YEARS OF NOT KNOWING WHAT WAS WRONG WITH THEIR CHILD AND SPARED THE CHILDREN FROM UNDERGOING (AND THE HEALTH CARE SYSTEM FROM PROVIDING) NEEDLESS TESTS AND PROCEDURES. CHILDREN GET CARE TAILORED TO REDUCE OR PREVENT COMPLICATIONS, EVEN IF THERE IS NO CURE FOR THEIR DISEASE.

SOURCES: MCMILLAN, HUGH, ET AL., "SPECIFIC COMBINATION OF COMPOUND HETEROZYGOUS MUTATIONS IN 17β-HYDROXYSTEROID DEHYDROGENASE TYPE 4 (HSD17B4) DEFINES A NEW SUBTYPE OF D-BIFUNCTIONAL PROTEIN DEFICIENCY," *JOURNAL OF RARE DISEASES* 7, 90 (2012): DOI:10.1186/1750-1172-7-90. INTERVIEWS WITH DR. KYM BOYCOTT. FORGE CANADA WEBSITE: WWW.CPGDSCONSORTIUM.COM/ABOUTUS.ASPX.

EVIDENCE IN ACTION: COST SAVINGS RESULTING FROM A FIRM DIAGNOSIS OF RARE DISEASES

FORGE'S WORK HAS GIVEN CONCLUSIVE DIAGNOSES TO MORE THAN 500 FAMILIES WITH CHILDREN WHO HAVE RARE DISEASES. A PROPER DIAGNOSIS HELPS DOCTORS PLAN APPROPRIATE CARE AND ELIMINATES THE NEED FOR FURTHER TIME AND EXPENSE SPENT ON DIAGNOSTICS. IN THE CASE OF T.J. AND CASEY O'CONNOR, HEALTH CARE SYSTEM COSTS FOR INCONCLUSIVE TESTS AMOUNTED TO $20,000. THE DNA SCAN THAT PROVIDED A FIRM DIAGNOSIS COST JUST $1,100.

Photos:

Opposite page: The O'Connor family (T.J., Kevin, Kathy and Casey) at clinic for a leg brace fitting appointment. For Casey (seated on the bench) this is his first set of leg braces; up until now he had been wearing orthotics. As the boys grow, they must return to the clinic roughly every six months to be fitted for new braces.

This page: T.J. O'Connor (left) and his younger brother Casey.

WHAT IS A RARE DISEASE?

IT IS ESTIMATED THAT THERE ARE AS MANY AS 7,000 RARE DISEASES[1] (SOMETIMES CALLED ORPHAN DISEASES). MANY ARE GENETIC IN NATURE WITH THE SYMPTOMS FIRST APPEARING IN CHILDHOOD. IN FACT, ABOUT 75% OF RARE DISEASES AFFECT CHILDREN AND ALMOST ONE-THIRD OF CHILDREN WITH RARE DISEASES DIE BEFORE THEIR FIFTH BIRTHDAY.[2] DEFINITIONS OF WHAT CONSTITUTES A RARE DISEASE VARY AROUND THE WORLD. IN THE UNITED STATES, THE NATIONAL INSTITUTES OF HEALTH DEFINE A RARE DISEASE AS ONE AFFECTING FEWER THAN 200,000 AMERICANS – ROUGHLY THE EQUIVALENT TO ONE IN 1,500.[3] THE EUROPEAN COMMISSION SUGGESTS THAT RARE DISEASES ARE THOSE THAT AFFECT FEWER THAN ONE IN 2,000 PEOPLE.[4]

NEXT-GENERATION SEQUENCING: MUCH FASTER, FAR LESS EXPENSIVE

Gene sequencing used to be a slow, laborious and costly enterprise. The most popular method, Sanger Sequencing, has been in use since 1977 and, in essence, involves studying the DNA sequence of one section of a single gene at a time. If you were looking for a needle in the haystack, this would be like searching the pile one strand of hay at a time. With next-generation sequencing, all 22,000 genes in the human genome can be sequenced in parallel. The process takes two to three weeks and costs about the same as sequencing a single gene the old way – about $1,100. While the use of next-generation sequencing to track the genetic roots of rare diseases is becoming more common, Dr. Boycott was a very early adopter of the technology – thanks to funding from the Canadian Institutes of Health Research (CIHR): "The first description of this being applied to rare diseases was in 2009. CIHR jumped on this early on – because we started with this in 2010 when we had our first workshop. That's how early we got in the game."

Kathy O'Connor could tell something was seriously wrong with her two sons. Instead of growing stronger, they were regressing.

At 11 years old, the once robust T.J., who played hockey and soccer, was having difficulty walking in a straight line and started bumping into walls. His speech slowed and his fine motor skills deteriorated. Casey, about two-and-a-half years younger, experienced similar difficulties – although not as pronounced.

"I guess 'a nightmare' is the best description," says Ms. O'Connor, a nurse practitioner who lives in Pembroke, Ontario.

What followed was four years of tests and doctors' visits as the family attempted to find the cause behind T.J.'s and Casey's declining health and wellbeing. The boys underwent multiple biopsies and MRIs, CT scans and blood tests. Neurologists and cardiologists, urologists and endocrinologists studied the boys but no one could find an answer.

"The not knowing – you can only imagine," says Dr. Kym Boycott, a clinician-researcher at the Children's Hospital of Eastern Ontario in Ottawa, who assessed the O'Connor boys. "It is one of the most difficult things in my job: to watch a beautiful child go backwards, to regress, and not know why."

Until recently, there was not much Dr. Boycott could do. Her specialty is neurogenetics, which involves studying the genetic factors that contribute to the development of neurological disorders. "When a child who had some undiagnosed degenerative condition came to my clinic and they had all kinds of tests and we still didn't know what was going on, we'd be stuck. We would have to tell the parents, 'We don't have an explanation and we don't know what's going to happen.'"

However, the use of next-generation gene sequencing in tracing the genetic origins of rare diseases has "revolutionized the way we look after these kids," says Dr. Boycott.

She leads FORGE Canada, a consortium comprised of 150 clinicians and scientists – most of them clinical geneticists – studying the gene mutations behind 200 rare diseases. The FORGE team chose the list of diseases following a national request for proposals to suggest targets for study. Up and running since 2011, FORGE has used next-generation sequencing to crack the mysteries behind more than 100 rare conditions and its investigators are confident they will unravel many more.

One of the major mysteries solved by Dr. Boycott and FORGE involved T.J. and Casey O'Connor. The boys have a rare version of a disease called D-bifunctional protein (DBP) deficiency, which is triggered by a genetic mutation that inhibits the function of an enzyme. The mutation causes damage to the nervous system, hearing, vision and balance. Dr. Boycott co-authored a paper on the discovery in 2012.[5]

The DBP revelation is the kind of discovery that can vastly improve a child's life – even if there is no treatment or cure available. "If you're a child with developmental delay in the public school system, you don't have the same access to services that you would if you have an actual diagnosis," says Dr. Boycott. "As well, they may be at risk for some long-term health complications that we can screen for and possibly impact. We can improve outcomes this way."

Beyond providing peace of mind, there are considerable cost savings to be realized in quickly and efficiently diagnosing rare diseases. In a 2011 *Ottawa Citizen* article, Dr. Boycott estimated she had spent about $20,000 in health care costs on various tests for the O'Connor brothers before next-generation sequencing technology came into use as a way to track rare diseases. The DNA scan that identified the deviant gene cost about $1,100. Multiply those savings by the thousands of patients Canada's geneticists see every year – FORGE investigators estimate genetic disorders affect the lives of about 500,000 children in Canada[6] – and the health care costs saved could amount to billions of dollars.

While knowing the genetic root of a disease does not mean treating it or curing it – genes can't simply be repaired or even tweaked – it may point to a possible therapy.

"We've had a couple of the 100 disorders solved so far where there's an obvious treatment that might be considered," says Dr. Boycott. "One was a vitamin deficiency that caused a neuropathy. Another was a manganese deficiency – the children can't absorb manganese in their diet, which might indicate that supplemental manganese could have a positive effect. These, of course, would require clinical trials, which is beyond the current scope of FORGE, but these opportunities for possible straightforward treatments need to be pursued for these patients."

The next best scenario, she says, is the possibility of repurposing existing pharmaceutical treatments for rare diseases. "For example, if they have over-activation of a pathway and there are inhibitors that have been developed by drug companies, often for cancer treatments, these could be possible routes to treat some of these diseases," says Dr. Boycott. That option is far more realistic than designing new drugs to treat rare diseases, which can take decades and cost tens of millions of dollars.

In most cases, parents are just happy to know what is wrong. The discovery came as a relief to the O'Connor family – even though there is no treatment or cure for DBP. "We definitely wanted a diagnosis. Otherwise, it's hard to look ahead," says Ms. O'Connor.

The O'Connors' reaction is typical, says Dr. Boycott. "Even if their child has something terrible, the parents want to know. They want a name for it. They want to know, 'Are there any other kids like this in the world that we can learn from? What sorts of things have helped in the past with the kids' day-to-day lives to make things as good as possible? And what does the future hold?'"

FORGE-ING FORWARD

WHILE THE FORGE CONSORTIUM HAS THREE LEAD INSTITUTIONS – THE UNIVERSITY OF OTTAWA, THE UNIVERSITY OF BRITISH COLUMBIA, AND THE CHU SAINTE-JUSTINE RESEARCH CENTRE – IT BRINGS TOGETHER DOCTORS FROM GENETICS CENTRES ACROSS CANADA, INTERNATIONALLY-RECOGNIZED CANADIAN SCIENTISTS WITH EXPERTISE IN FINDING GENES, AND TEAMS FROM THE THREE GENOME CANADA SCIENCE AND TECHNOLOGY INNOVATION CENTRES IN TORONTO, MONTREAL AND VANCOUVER.[7]

FOR MORE INFORMATION

FORGE consortium website: www.cpgdsconsortium.com/AboutUs.aspx.

Orphanet Canada website: www.orpha.net/national/CA-EN/index/homepage/.

Canadian Organization for Rare Disorders website: www.raredisorders.ca/.

National Institutes of Health Office of Rare Diseases Research: rarediseases.info.nih.gov/Resources/Patient_Advocacy_Groups.aspx.

Video with Dr. Boycott: www.youtube.com/healthresearchcanada.

1 Orphanet Canada. *About Rare Diseases*. Available at www.orpha.net/national/CA-EN/index/about-rare-diseases/.

2 European Society of Paediatric Oncology (SIOPE). *Rare Diseases: Did you know?* Available at www.siope.eu/page.aspx/3.

3 National Institutes of Health, Office of Rare Diseases Research. *Frequently Asked Questions*. Available at rarediseases.info.nih.gov/about-ordr/pages/31/frequently-asked-questions.

4 European Commission. *Useful Information on Rare Diseases from an EU Perspective*. 2004. Available at ec.europa.eu/health/ph_information/documents/ev20040705_rd05_en.pdf.

5 McMillan, Hugh, et al., "Specific combination of compound heterozygous mutations in 17β-hydroxysteroid dehydrogenase type 4 (*HSD17B4*) defines a new subtype of D-bifunctional protein deficiency," *Journal of Rare Diseases* 7, 90 (2012): doi:10.1186/1750-1172-7-90. www.ojrd.com/content/7/1/90.

6 Genome British Columbia. *Finding of Rare Disease Genes in Canada (FORGE)*. Available at www.genomebc.ca/portfolio/projects/health-projects/finding-of-rare-disease-genes-in-canada-forge-canada/.

7 Ibid.

GET REAL FAST: RESEARCH TEAM HELPS SASKATCHEWAN TRANSFORM ITS HEALTH CARE SYSTEM

"Rapid realist review" helps decision makers achieve patient – and family – centred health care

AT A GLANCE

WHO: DR. ALLAN BEST, UNIVERSITY OF BRITISH COLUMBIA

ISSUE: RECOGNIZING THAT THEIR HIGH-COST SYSTEM WAS NOT DELIVERING HIGH-VALUE SERVICES, THE GOVERNMENT OF SASKATCHEWAN BEGAN TRANSFORMING HEALTH CARE IN 2010. TO GUIDE THEM, DECISION MAKERS SOUGHT INFORMATION ON HOW OTHER JURISDICTIONS HAD WORKED TO TRANSFORM THEIR HEALTH CARE SYSTEMS.

PROJECTS: THROUGH CIHR'S EXPEDITED KNOWLEDGE SYNTHESIS PROGRAM, DR. BEST AND A TEAM OF COLLEAGUES CONDUCTED A "RAPID REALIST REVIEW" SYNTHESIZING THE MOST RELEVANT PUBLICATIONS THAT EXAMINED THE HEALTH REFORM EXPERIENCES OF CENTRES AND SYSTEMS INCLUDING CANADA, THE UNITED STATES, THE UNITED KINGDOM, SWEDEN, DENMARK AND THE NETHERLANDS.

RESEARCH EVIDENCE: SIX MONTHS AFTER THE PROJECT LAUNCH, RESEARCHERS DELIVERED A REPORT THAT PRESENTED FIVE KEY "EVIDENCE STATEMENTS" FOR IMPLEMENTING A "LARGE SYSTEM TRANSFORMATION" AND A SET OF SPECIFIC RECOMMENDATIONS FOR GOVERNMENT ACTION.

EVIDENCE IN ACTION: WHILE A SASKATCHEWAN MINISTRY OF HEALTH OFFICIAL CAUTIONS THAT THE PROVINCE IS STILL IN THE EARLY STAGES OF RECONFIGURING THE SYSTEM, "WE'RE SEEING POCKETS OF IMPROVEMENT THAT ARE EXCITING" AND SOME SIGNIFICANT PROGRESS HAS BEEN MADE, WITH WAIT TIMES FOR ELECTIVE SURGERY CONTINUING TO DECREASE.

SOURCES: SAUL, JESSIE, ET AL. "A TIME-RESPONSIVE TOOL FOR INFORMING POLICY MAKING: THE RISE OF RAPID REALIST REVIEW," *IMPLEMENTATION SCIENCE* (IN PRESS). BEST, ALLAN, ET AL. "LARGE-SYSTEM TRANSFORMATION IN HEALTH CARE: A REALIST REVIEW," *THE MILBANK QUARTERLY* 90, 3, (2012): 421–456.

EVIDENCE IN ACTION: RESEARCH THAT HAS HELPED ENABLE PROVINCIAL HEALTH CARE REFORMS

THE RESEARCH PLAYED AN IMPORTANT ROLE IN HELPING THE PROVINCE ACHIEVE ITS GOALS. AS AN EXAMPLE, WAIT TIMES FOR SURGERY CONTINUE TO DECREASE. AT THE END OF JANUARY 2013, ALMOST 80% OF PEOPLE NEEDING ELECTIVE SURGERY WERE GETTING IT WITHIN THREE MONTHS. THE GOAL IS TO ACHIEVE 100% BY APRIL 2014. (SURGICAL WAIT TIMES CONTINUE TO DROP, 2013)

In 2009, Saskatchewan residents and the provincial government faced bad news about the province's health care system. A provincial-government commissioned report released at the time concluded that "Saskatchewan residents continue to pay high costs for health care services that do not appear to offer high value... Rather, the system struggles to meet demand and maintain basic safety and accessibility standards while often failing to adopt practices that ensure high quality." [1]

According to the report, the problems stemmed from the basic design of the health care system, which had been built around the people who were providing the care, not those who were receiving it.

Within months of the report's release, the Government of Saskatchewan launched its patient- and family-centred care initiative to transform health care – the mission for which involved "putting patients first". The initiative had several goals, including improving primary care, reducing surgical wait times, and implementing a "lean" management approach to streamline processes and improve outcomes.

However, before policy makers and health care leaders began reconfiguring a service that costs provincial residents almost $5 billion per year, they sought out information and analysis on how other jurisdictions had managed to transform their health care systems.

"They wanted to know what had and hadn't worked and why," says University of British Columbia's Dr. Allan Best, whose health research is focused on planning, implementation and evaluation of large-scale organizational change.

Through the CIHR's Expedited Knowledge Synthesis Program**,** Dr. Best, working with his InSource Research Group and other colleagues, led a six-month "rapid realist review" that synthesized and simplified academic studies of large system transformations in health care across the globe, including health centres and systems in Canada and the United States, the United Kingdom, Sweden, Denmark and the Netherlands.

For the project, Dr. Best and his colleagues adapted the "realist review" model developed by researchers in the United Kingdom to meet the needs of the National Health Service. Systematic reviews, which are a well-known tool in health research, summarize studies that measure strictly quantifiable changes around a health issue, for example the use of *Echinacea* to prevent colds. A realist review provides additional qualitative analysis addressing issues on how to use the review, in other words, another "realist" perspective on how to achieve desired change. For example, a realist review that endorses rigorously assessing treatment outcomes will also provide guidance about situations where the approach requires modification.

"It's a much more powerful tool that answers the question: what works, when and why?," says Dr. Best. "It allows you to look at more complex problems than a typical method would and, by incorporating both theoretical and front-line knowledge, reach broader conclusions rather than just 'more research is needed'."

Realist reviews, however, are exhaustive and can take a year or longer to conduct – something policy makers in Saskatchewan didn't have. "So, we developed an adaptation of the method that is much more rapid and fits the timeline decision makers have to work with," added Dr. Best.

Instead of doing a comprehensive review of all the literature available, with a rapid realist approach, a research synthesis team – with input from a seven-member international panel of experts – short-listed 84 of the most relevant research papers from nearly 1,000 originally considered. "We chose those that were most important to grasp the critical things we need to include," says Dr. Best.

Titled Knowledge and Action for System Transformation (KAST), the rapid realist review delivered to the Saskatchewan Ministry of Health in late 2010 not only laid out the five key steps to transform the Saskatchewan system, it included "contextual factors" and "mechanisms" for each step, and a set of recommendations for government action. For example, in terms of what kind of leadership works best, the report suggests that those in positions of authority should "specify outcomes and provide resources but not dictate how the work is to be done."

For Kathleen Peterson, Director of Health System Planning at the Saskatchewan Ministry of Health, the KAST review – coming in at just 55 pages plus appendices – provided precisely what policy makers and health care managers needed to move forward with their reforms.

"It's not a big research paper; it's easier to digest," says Ms. Peterson. "Academics love the details, but when you're in real situation and trying to deal with the practicalities – give us the highpoints so that we have something to guide us."

Four years into the process of transforming its health care system, one key question looms: how is Saskatchewan doing?

"It's looking very good in terms of getting us to where we need to be," says Ms. Peterson.

Wait times for surgery continue to decrease. At the end of January 2013, almost 80% of people needing elective surgery were getting it within three months. The goal is to achieve 100% by April, 2014.[2]

"We're seeing some pockets of improvement that are exciting, but it's early days," says Ms. Peterson. "A cultural transformation is not going to happen overnight. We're working our way through and it's tough slogging. But when people get through the messiness and the difficult parts of it they say, 'This is really great.'"

1 Saskatchewan's Patient First Review Commissioner. *For Patients' Sake*, Patient First Review Commissioner's Report to the Saskatchewan Minister of Health (2009). Available at www.health.gov.sk.ca/patient-first-commissioners-report.

2 Government of Saskatchewan. *Surgical Wait Times Continue to Drop* (March 18, 2013). Available at www.gov.sk.ca/news?newsId=04125d8c-c4a0-4b12-89de-34818131b783.

3 Best, Allan, et al. "Large-System Transformation in Health Care: A Realist Review," *The Milbank Quarterly* 90, 3 (2012): 421–456.

FOR MORE INFORMATION

Putting Patients First video: www.youtube.com/watch?v=pDyAAqlJXtw.

For Patients' Sake, Patient First Review Commissioner's Report to the Saskatchewan Minister of Health: www.health.gov.sk.ca/patient-first-review-documents.

Going Lean in Health Care. IHI Innovation Series white paper. Cambridge, MA: Institute for Healthcare Improvement; 2005. Available at www.ihi.org/knowledge/Pages/IHIWhitePapers/GoingLeaninHealthCare.aspx.

Saskatchewan Ministry of Health: Applying Lean Principles to Health Services: www.health.gov.sk.ca/lean.

InSource website: www.in-source.ca.

Video with Dr. Best: www.youtube.com/watch?v=-G_7jWr51tM.

RELEVANT RESEARCH IN REAL TIME FOR HEALTH REFORM

CIHR'S EXPEDITED KNOWLEDGE TRANSLATION GRANTS SUPPORT TEAMS OF RESEARCHERS WHO CAN DELIVER THE KIND OF SYNTHESIZED KNOWLEDGE THAT PROVINCIAL MINISTRIES OF HEALTH NEED TO MAKE PRUDENT DECISIONS IN THESE TIMES OF EVER-RISING HEALTH CARE COSTS AND LIMITED RESOURCES. FUNDED TEAMS, SUCH AS DR. BEST'S INSOURCE RESEARCH GROUP AND THEIR ASSOCIATED COLLEAGUES, PROVIDE TIMELY, ACCESSIBLE AND RELEVANT EVIDENCE TO DECISION MAKERS. THE TEAMS ALSO WORK DIRECTLY WITH THE KNOWLEDGE USERS SO THAT THE RESEARCH THEY PRODUCE IS DIRECTLY APPLICABLE IN HELPING HEALTH SYSTEMS DEVELOP NEW MODELS OF FINANCING AND DELIVERING CARE.

COUNT TO FIVE: ACHIEVING 'LARGE-SYSTEM TRANSFORMATION'[3]

Dr. Best's InSource Research Group synthesized their findings into five simple rules to guide Saskatchewan as it reforms its health care system:

1. **Blend in designated leadership** (those formally in charge of a program) with distributed leadership (health care professionals/administrators/partners) to mobilize efforts and deliver program components.
2. **Establish feedback loops** so that stakeholders understand how the transformation is proceeding. Provide them with an ongoing blend of quantitative metrics (e.g., number of patients processed) and qualitative measures (e.g., observations on patients' quality of life). Establish indicators that will help identify which transformation strategies are working and how to fine tune them.
3. **Attend to history** to avoid repeating it. Past failures in attempts to change a system shouldn't be seen as predictors for the future but opportunities to discuss how to sidestep setbacks.
4. **Engage physicians** because they are often the principal players in either opposing change efforts or supporting successful transformative ones.
5. **Include patients and families** by sharing information with them on a regular basis, treating them with respect and dignity, and encouraging their participation and collaboration (e.g., asking patients to envision their ideal experience for cancer care).

PAINTING WORD PICTURES: ACCURATELY DESCRIBING THE FUNCTIONAL IMPACT OF CEREBRAL PALSY

Using research evidence to create a common working language for doctors, patients, families and researchers

AT A GLANCE

WHO: DR. PETER ROSENBAUM, MCMASTER UNIVERSITY

ISSUE: ASSESSING THE FUNCTIONAL SEVERITY OF A CHILD'S CEREBRAL PALSY USED TO BE A BEST GUESS. SPECIALISTS RELIED ON THEIR OWN EXPERIENCES TO RATE PATIENTS' DEGREE OF MOTOR FUNCTION IMPAIRMENT AS "MILD," "MODERATE" OR "SEVERE". BUT THE LACK OF A UNIVERSAL, OBJECTIVE RATING TOOL MADE IT DIFFICULT TO REACH CONCLUSIONS ABOUT HOW THE DISORDER WOULD AFFECT THE CHILD OVER TIME AND HOW TO CHOOSE THE BEST THERAPY.

PROJECTS: DR. ROSENBAUM LED A CIHR-SUPPORTED PROJECT THAT ASSESSED MORE THAN 650 CHILDREN WITH CEREBRAL PALSY DURING THE PERIOD OF 1996 TO 2001 USING THE RELIABLE AND VALID FIVE-LEVEL GROSS MOTOR FUNCTION CLASSIFICATION SYSTEM (GMFCS) THAT HIS GROUP HAD DEVELOPED.

RESEARCH EVIDENCE: DR. ROSENBAUM'S 2002 PAPER, "PROGNOSIS FOR GROSS MOTOR FUNCTION IN CEREBRAL PALSY", DEMONSTRATED THAT IT WAS POSSIBLE TO CLASSIFY AND PREDICT FUTURE MOTOR FUNCTION AND ASSESS CHANGES OVER TIME. GMFCS GIVES RESEARCHERS A COMMON LANGUAGE TO SHARE KNOWLEDGE AND HELPS PARENTS AND CLINICIANS CHOOSE THERAPIES AND INTERVENTIONS THAT BEST SUIT A CHILD'S FUNCTION LEVEL.

EVIDENCE IN ACTION: TRANSLATED INTO MORE THAN 25 LANGUAGES, GMFCS HAS BECOME THE WORLD-STANDARD TOOL FOR DESCRIBING THE SEVERITY OF CEREBRAL PALSY AND PROGNOSTICATING OUTCOMES. IT LED TO THE CREATION OF THE 2006 MANUAL ABILITY CLASSIFICATION SYSTEM (MACS) AND THE 2011 COMMUNICATION FUNCTION CLASSIFICATION SYSTEM (CFCS) FOR INDIVIDUALS WITH CEREBRAL PALSY, BOTH OF WHICH DR. ROSENBAUM HELPED DEVELOP WITH INTERNATIONAL PARTNERS.

SOURCES: ROSENBAUM, PETER, ET AL. "PROGNOSIS FOR GROSS MOTOR FUNCTION IN CEREBRAL PALSY: CREATION OF MOTOR DEVELOPMENT CURVES," *JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION* 288, 11 (2002): 1357–63. ROSENBAUM, PETER, ET AL. "DEVELOPING THE GROSS MOTOR FUNCTION CLASSIFICATION SYSTEM FOR CEREBRAL PALSY: LESSONS AND IMPLICATIONS FOR CLASSIFYING FUNCTION IN CHILDHOOD DISABILITY," *DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY* 50, 4 (2008): 249–53.

Parents usually suspect something is not right. Their infant is slow to learn basic movements and motor skills, such as how to roll over, how to sit unsupported, and how to crawl around a room. When their child's diagnosis is cerebral palsy, a disorder of movement and motor control that affects two or three of every 1,000 children, they are anxious to understand how the disorder will affect their child over time.

Until fairly recently, providing an answer to that question was a best-guess proposition: physicians drew upon their experiences with the disorder, broadly labeling the child's disability as either "mild," "moderate" or "severe." But, because these terms have never been defined operationally, one expert's "mild" diagnosis might equal another's "moderate" verdict.

According to McMaster University's Dr. Peter Rosenbaum, the labels were almost meaningless in any practical sense and, in essence, created a barrier to truly high-quality care and research. Such diagnoses did not help predict outcomes for a child with cerebral palsy, or indicate what level of physical activity might be possible – two crucial questions parents always asked. Nor did they help in determining which therapies and interventions would be most beneficial – and which might be a frustrating waste of time.

"I wanted to get away from the 'in-my-experience' diagnosing," says Dr. Rosenbaum in explaining the impetus for a study that would eventually change practice. "Because I don't know what someone else's experience is. I don't even know what my own experience is – in the sense that I don't know if I've seen the most complicated cases of cerebral palsy or the simplest kinds."

Funded by CIHR, Dr. Rosenbaum's group created the Gross Motor Function Classification System (GMFCS)[1] in 1997. The GMFCS replaced the mild-to-severe scale with a much more rigorous five-level ranking of the severity of cerebral palsy – from Level I (*most able*) to Level V (*most limited*). The scale provides a detailed series of 'word pictures' of functions that a child likely will perform at different stages of development from birth to age 12. For example, between their second and fourth birthday, a Level II child can "floor sit but may have difficulty with balance when both hands are free to manipulate objects."

EVIDENCE IN ACTION: A TOOL TO ACCURATELY QUANTIFY THE IMPACT OF CEREBRAL PALSY

AVAILABLE IN 25 LANGUAGES, DOWNLOADED MORE THAN 245,000 TIMES, CITED IN RESEARCH LITERATURE OVER 1,200 TIMES, THE GMFCS HAS BECOME A WORLD STANDARD FOR CLASSIFYING CEREBRAL PALSY AND PREDICTING OUTCOMES.

GROSS MOTOR FUNCTION CLASSIFICATION SYSTEM LEVELS FOR CHILDREN WITH CEREBRAL PALSY BETWEEN AGES 6-12

Level I: Walks without restrictions; limitations in more advanced gross motor skills.

Level II: Walks without assistive devices; limitations in walking outdoors and in the community.

Level III: Walks with assistive mobility devices; limitations in walking outdoors and in the community.

Level IV: Self-mobility with limitations; children are transported or use power mobility outdoors and in the community.

Level V: Self-mobility is severely limited even with the use of assistive devices.

SPREADING THE WORD ABOUT THE NEW CLASSIFICATION SYSTEM

"When we first published it in 1997, it was the early days of the world wide web," says Dr. Rosenbaum. "So we basically just put this under people's noses. We printed up 20,000 copies and every time we went to a meeting, every time we went to a presentation, we left copies for people." After disseminating the original 20,000 copies – quickly followed by another 10,000 in response to requests from around the world – Dr. Rosenbaum "put the whole thing on our web page" so that anyone could download it. "We never had an interest in selling it."

With the 2002 publication by his group of Prognosis for Gross Motor Function in Cerebral Palsy in the *Journal of the American Medical Association (JAMA)*, Dr. Rosenbaum's GMFCS became the international standard to assess cerebral palsy and predict outcomes. The original GMFCS article has been cited more than 1,200 times – a remarkable figure for a rare condition. Available in 25 languages from Arabic to Turkish, the classification system has been downloaded 245,428 times from McMaster's *CanChild* Centre for Childhood Disability Research website (www.canchild.ca).

Researchers, clinicians, parents and patients now routinely use the GMFCS to exchange information about cerebral palsy, assess its severity and devise appropriate interventions to maximize quality of life for people with the incurable condition.

"It has allowed clinicians and researchers to develop a common picture of the severity of a child's motor disability," says Dr. Darcy Fehlings, Physician Director of the Child Development Program at the Bloorview Research Institute in Toronto. "It is used in all corners of the world."

From the perspective of patients and families, by creating a common language, the GMFCS and its analogues have helped level the playing field between experts and health consumers, allowing for more active participation by patients and their families in decisions about how to manage this disorder.

Increased patient engagement and participation has also opened new possibilities for expanding care options. As an example, while the GMFCS was created primarily to get beyond describing cerebral palsy in non-specific terms – mild, moderate, severe – , it has also proven useful in helping select treatments, and when and for whom to provide them.

"These are things we hadn't thought about originally," says Dr. Rosenbaum. "But, for example, a parent asked me a couple of weeks ago, 'What about Botox for my child?' Botox is a useful intervention for the treatment of spasticity in certain circumstances. But now that we have evidence-based ideas about different levels and patterns of function, we have a much better idea about who is likely to respond to what intervention at what age. So instead of saying Botox is a good treatment for cerebral palsy, we can specify under what circumstances, at what age and at what GMFCS level."

In addition to facilitating treatment discussions, the GMFCS is changing the way we talk about life with cerebral palsy.

"The GMFCS is worded in a much more positive way than the traditional descriptive terminology of 'mild, moderate or severe'," says Clarence Meyers, Executive Director at the Ontario Federation for Cerebral Palsy. "It states what an individual 'can' do rather than 'cannot' do – abilities are emphasized rather than limitations. It provides a clear, more human language that everyone worldwide can understand."

Finally, the classification system has also helped provide a bridge to other allied health professionals. With Dr. Rosenbaum's assistance, the GMFCS approach has been adapted by speech therapists to develop the Communication Function Classification System (CFCS).[2]

"Cerebral palsy often affects the speech motor system, which controls the tongue and jaw movement, breath support and the larynx," says Dr. Mary Jo Cooley Hidecker of the University of Central Arkansas. "By creating a communication version of the GMFCS, we can now describe how these kids are able to communicate in daily life. Any clinician or researcher can use it. And because these systems are all set up similar to the GMFCS, it becomes a way to talk interdisciplinarily."

SUCCESSFUL CLASSIFICATION SYSTEM LEADS TO NEW PROJECTS

THE WORLDWIDE ADOPTION OF THE GMFCS LED TO CALLS TO CREATE SIMILAR CLASSIFICATION SYSTEMS FOR OTHER CEREBRAL PALSY DEFICITS. SWEDISH RESEARCHERS REACHED OUT TO DR. ROSENBAUM TO HELP THEM CREATE A MANUAL ABILITY EQUIVALENT, SAYS DR. ANN-CHRISTIN ELIASSON OF STOCKHOLM'S KAROLINSKA INSTITUTE. THE SWEDISH-CANADIAN COLLABORATION, BEGUN IN 2002, LED TO THE PUBLICATION OF THE MANUAL ABILITY CLASSIFICATION SYSTEM IN 2006, WHICH DR. ROSENBAUM CO-AUTHORED.[3] IT HAS SINCE BEEN TRANSLATED INTO 24 LANGUAGES AND IS USED AROUND THE WORLD BY RESEARCHERS AND CLINICIANS WHO WORK WITH CHILDREN WITH CEREBRAL PALSY, SAYS DR. ELIASSON.

1 Palisano, Robert, et al. "Development and reliability of a system to classify gross motor function in children with cerebral palsy," *Developmental Medicine & Child Neurology* 39, 4 (1997): 214–23.

2 Hidecker, Mary Jo, et al. "Developing and validating the Communication Function Classification System for individuals with cerebral palsy," *Developmental Medicine & Child Neurology* 53, 8 (2011): 704-10.

3 Eliasson, Ann-Christin, et al. "The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability," *Developmental Medicine & Child Neurology* 48, 7 (2006): 549–54.

FOR MORE INFORMATION

CanChild Centre for Childhood Disability Research, McMaster University: www.canchild.ca/en/.

Video with Dr. Rosenbaum: www.youtube.com/watch?v=rSof3xeeDOc.

GATHERING MORE EVIDENCE

FOR MORE INFORMATION

Strategy for Patient-Oriented Research: www.cihr-irsc.gc.ca/spor.html.

Roadmap Signature Initiatives: www.cihr-irsc.gc.ca/e/43567.html.

CIHR Strategic Initiatives: www.cihr-irsc.gc.ca/e/12679.html.

Transformational Research in Adolescent Mental Health: tramcan.ca/.

CANADA'S STRATEGY FOR PATIENT-ORIENTED RESEARCH

Promoting and supporting patient-oriented research is a key priority for the Canadian Institutes of Health Research

Canada's Strategy for Patient-Oriented Research (SPOR) is a national coalition of federal, provincial and territorial partners (patient advocates, provincial health authorities, academic health centres, charities, philanthropic organizations, pharmaceutical sector, etc.) dedicated to the integration of research into care – the right patient receives the right treatment at the right time. Patient-oriented research focuses on patient-identified priorities. It produces information for decision makers and health care providers that will improve health care practices, therapies and policies. It ensures that new and innovative diagnostic and therapeutic approaches are applied when and where needed.

Putting SPOR into practice
Achieving the goals of SPOR involves mobilizing the expertise and resources of stakeholders that have come together in support of the strategy.

Patient Engagement: An active collaboration with patients and stakeholders to guide and facilitate patient involvement in the development and implementation of SPOR.

Support Units: Locally accessible, multidisciplinary clusters of specialized research resources, policy knowledge and patient perspective. Provide the necessary expertise to pursue patient-oriented research and help lead reforms in response to locally-driven health care needs.

SPOR Networks: National, collaborative research networks involving the full range of SPOR stakeholders (patients, researchers, policy makers, academic health care centres, health charities, etc.). Focus on specific health challenges identified as priorities in multiple provinces and territories. Networks pursue research and help bridge the gap between research evidence and health care practice.

Clinical Trials: A national public-private-patient collaboration to establish a modernized Canadian clinical research infrastructure able to engage patients and attract financial support for patient-oriented clinical studies.

Training and Mentoring: A strategy to support researchers to receive training and build skills in patient-oriented research.

NEED MORE EVIDENCE?

Thank you for reading *Show me the Evidence.* We hope that you enjoyed learning more about the impact of Canadian health researchers and encourage you to visit CIHR's website **www.cihr-irsc.gc.ca** and social media sites **www.cihr-irsc.gc.ca/e/42402.html** to learn about other CIHR-funded success stories.

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