

## Developing an Integrated Strategy to Support Pediatric and Perinatal Clinical Trials across Canada

May 27<sup>th</sup>-29<sup>th</sup>, 2011

Eastern Townships, Quebec, Canada

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This Workshop was instigated 8 months prior, September 2010, in Vancouver BC, at a MICYRN members meeting held in conjunction with the international StaR Child Health Summit. Given the world-wide attention given to the need for 'better medicines for children' the question was posed as to whether Canada's maternal-child research community should advance an approach to clinical trials. Canada is second only to the USA in the number of pediatric or maternal clinical trials, world-wide; and third after the Netherlands and Australia in the number of trials per million children (pediatric studies) or births (maternal studies) in the population.

The Agenda for this Workshop was designed to touch on issues related to Clinical Trials, and began with a review of international initiatives which are focused on children. It is clear that Canada is well-positioned to expand a Trials focus to include maternal and perinatal studies; and to consider the conduct of studies beyond drugs & devices sponsored by Industry, which again, is the emphasis elsewhere. There is a need to include aspects of complex interventional trials and community cluster randomized trials, in design, statistical analysis, and outcome measures assessed.

Presentations by several national networks drew attention to the important work of Networks to inform on the natural history of disease, and to raise new questions for basic science and the study of the mechanism of disease, thus emphasizing a need for support beyond that which should be provided solely for the conduct of clinical trials.

The inclusion of Drs. Alain Beaudet and Philip Sherman, representing the CIHR, and presentation on the Support for Patient Oriented Research strategy (SPOR), led to discussion about how the maternal-child research community can be positioned to take advantage of new opportunities, and stressed the importance of engaging local/regional charities and governments; as well as CIHR Institutes. However, the workshop participants were in agreement that while we needed to align with the SPOR agenda, "SPOR" is not the 'end game' – improving maternal and child health outcomes through high quality, collaborative research is the goal. There is need to capitalize on, and leverage, existing resources in institutions and networks; and local/site relationships with hospitals, Foundations and governments.

During this workshop meeting, the need to position MICYRN and its role to improve maternal-child health outcomes was emphasized. MICYRN is well-positioned to address key areas, including:

- The need to be cohesive and address key issues at a national level (ie. ethics; safety; data management; knowledge translation; commercialization; governance; liaison with governments)
- The need to engage the periphery (ie. rural, community and aboriginal)
- The need to engage patients and families (ie. adopt the highly successful UK model)
- The importance of training and need to build on success of the CCHCSP (ie. Trials methodology)
- The ability to develop a "Rapid Response" approach to difficult situations like breach of ethics, conflict of interest, and misconduct. (requires foresight, a pool of people to respond, logistics)

See the full report including slide presentations @[www.micyrn.ca](http://www.micyrn.ca) under Reports

## **SATELLITE WORKSHOP at the 2nd National Obesity Summit**

### **Breaking the obesity cycle: Understanding the origins in the maternal/infant dyad**

**April 27th, 2011  
Montreal, Quebec, Canada**

A day long Workshop on, "Breaking the Obesity Cycle: Understanding the origins in the maternal/infant dyad", organized by the Birth Cohort Group of MICYRN attracted an overflow audience of researchers, clinicians and trainees. This Satellite meeting as part of the 2nd National Obesity Summit held by the Canadian Obesity Network was organized by Drs. Stephanie Atkinson, Anne Junker and Rhonda Bell. Financial support for the Workshop was kindly provided by a conference grant from the CIHR Institute of Human Development, Child and Youth Health, Sugar Mommies research program at the University of Alberta, the Early Nutrition Committee of the International Life Sciences Institute of North America in Washington and the Canadian Obesity Network. MICYRN provided 5 travel awards to trainees attending the workshop who had abstracts related to research in early determinants of obesity accepted for presentation at the Obesity Summit.

Two Scientific Sessions provided updates on current evidence of the early origins of obesity from epidemiology, mechanistic (basic) and clinical research perspectives of fetal/neonatal exposures as determinants of obesity risk. Each was followed by a panel of experts in the field to initiate discussion on translation of knowledge and future research directions.

The first session on Maternal Obesity & Pregnancy Outcomes included presentations on mechanisms of how maternal obesity contributes to poor neonatal health based on animal models, the impact of maternal obesity and gestation diabetes on pregnancy and infant outcomes, the determinants of gestational weight gain and post-partum weight retention and possible maternal interventions to modify gestational weight gain. A panel discussion on these topics followed which provided perspectives on the current Canadian practice/guidelines that address obesity in pregnancy from the Society for Obstetrics & Gynecology of Canada and exercise in pregnancy from the Canadian Society for Exercise Physiology. The discussion highlighted the lack of evidence with respect limiting weight gain in obese pregnant women and thus the need for randomized trials upon which evidenced-based reviews can provide the basis for future practice guidelines. Other gaps in research include practices for attaining health pregnancy outcomes in special populations such as Aboriginal communities and those with food insecurity.

The second session focused on Lifestyle Influences & Risk of Obesity in the Infant and Child. Topics included a systematic review of the markers of adult obesity, early determinants of childhood obesity, weight gain in infancy as a predictor of later obesity and breaking the cycle of obesity and type 2 diabetes in Indigenous peoples. The panelists for this session provided updates on ongoing projects of interventions in early childhood for obesity prevention including those linked to primary care practice, school-based and community-based. The importance of employing e-technology and validating direct measures of body composition for use in the community were emphasized.

The closing panel addressed the niche directions for Canadian research in the areas of early determinants of health and disease. Dr. William Fraser provided his perspective on the strengths of research in Canada in this field and how we might work collaboratively. Such strategies included: harmonization of measures of exposure and outcome on existing cohorts; international collaborations both in cohort studies and clinical trials; lobbying governments and NGOs to support cohort studies and clinical trials in this area; collaboration with First Nations communities for a national birth cohort study; work with Health Care system towards standardization of measures and assessment tools.

The MICYRN initiative in Birth Cohorts will continue to support initiatives to advocate for and to foster research collaborations among researchers and practitioners to facilitate transfer of knowledge to practice and health policy with the global aim to improve maternal and child health in early life.

See the full report including slide presentations @[www.micyrn.ca](http://www.micyrn.ca) under Reports



**MIREC**  
Maternal-Infant Research  
on Environmental Chemicals

**Maternal-Infant Research on Environmental Chemicals (MIREC): A National Profile of In Utero and Lactational Exposure to Environmental Contaminants** This \$6-million multicenter study is designed to track whether low level exposure to common household chemicals that expectant mothers encounter can trigger health problems in their children, or even alter the babies (epi-)genetic makeup. Involving 2,000 mother and their offspring, MIREC is funded by Health Canada, CIHR, and the Ontario Ministry of the Environment; and led by co-principal investigators Tye Arbuckle, PhD from the Healthy Environments and Consumer Safety Branch of Health Canada; and William Fraser, MD, Professor and Chair Department of Obstetrics & Gynecology, Université de Montréal. MIREC is a part of the Federal Government's Chemicals Management Plan, and underlines the Government's commitment to protecting Canadians against risks to their personal health and the environment. It also supports the 2004 Stockholm Convention, an international agreement that aims to eliminate the use of many persistent organic pollutants and paves the way for other harmful chemicals to be regulated or banned. These actions will help reduce the levels of environmental chemicals in both the environment and humans.

Women are recruited in the first trimester of pregnancy, when developing foetuses are most vulnerable to outside influence. Blood, hair, breast milk and urine samples from the mothers will be tested for a host of chemicals, like heavy metals such as lead, cadmium and mercury; bisphenol-A, fire retardants and certain pesticides. The women will also be questioned about their lifestyles, diet and occupations. Various measurements and other data on the newborns will be collected at birth, and repeated at six months along with tests of eyesight, hearing and other aspects of the children's development. MIREC aims to measure the extent to which pregnant women and their babies are exposed to common environmental chemicals; to measure some of the beneficial elements in human breast milk; to assess what health risks, if any, are associated with the chemical levels measured, with a focus on heavy metals such as lead and mercury; and, to create a data and biological specimen bank for further research on fetal growth, pregnancy and health of mother and baby.

Recruitment centers are in Halifax, Montreal, Kingston, Ottawa, Hamilton, Sudbury, Winnipeg, Edmonton and Vancouver. For more information, contact the MIREC Study Coordinating Centre at CHU Ste-Justine 514 345-4931 (#4267) or visit the website at <http://www.mirec-canada.ca>

## The Canadian Pediatric Surgery Network Le Réseau Canadien de Chirurgie Pédiatrique

**CAPSNet** was established in 2005 with CIHR funding to study two surgical birth defects: congenital diaphragmatic hernia (CDH) and gastroschisis (GS).

Involving 16 tertiary Canadian centres, CAPSNet captures detailed information about these conditions from fetal diagnosis until neonatal death or birth hospitalization discharge, with a view to determining how differences in management affects outcomes. CAPSNet is closely associated with a spectrum of CIHR-funded trans-Canadian networks including the Perinatal Network (CPN), Neonatal Network (CNN) and Neonatal Followup Network (CNFUN) which target improvement in health services for high risk pregnancy and at risk newborns. The CIHR Team in Maternal Infant Care (MiCARE) provides network linkage and infrastructure for IT, data management, research coordinators, study design and analysis. There is collaboration with Statistics Canada and the Public Health Agency of Canada. Since 2005, CAPSNet has maintained continuous CIHR funding; and in 2009, procured Professional Society investment from the Canadian Association of Paediatric Surgeons (CAPS). Two CIHR funding proposals are under consideration: Secondary Analyses of Databases; and Emerging Teams in Rare Diseases.

As of August 2010, there were 561 GS cases and 347 CDH cases entered in CAPSNet's unique, condition-specific databases—indicating the striking rarity of these conditions. Annual reports to CAPSNet centres and stakeholders provide aggregate network (site anonymized) descriptive data and selected outcomes, and a research output summary. Each CAPSNet site investigator also receives a confidential data summary for their centre. These reports allow institutional benchmarking for birth defect treatment and outcomes. A CAPSNet Steering Committee (SC) meets annually at CAPS meetings. These meetings facilitate smooth network function, database updates, and discussion of provincial privacy legislation, which has enabled continuous compliance with ethical requirements at each CAPSNet centre.

CAPSNet supports research conducted by trainees from a diverse spectrum of undergraduate and postgraduate programs at 8 Canadian universities or Schools including paediatric surgery, general surgery, paediatrics, neonatology, obstetrics and gynecology, plastic surgery, nutrition, Population and Public Health, and Geographic Information Systems. This has led to 14 CAPSNet manuscripts, 12 first-authored by trainees; 17 podium or poster presentations at international surgical meetings; and two Master's of Health Sciences major project theses using CAPSNet data. Research Themes include: i) Derivation and Validation of Risk adjustment tools specific to CDH (SNAP-II) and GS (Bowel injury score); ii) Impact of Perinatal Risk and Treatment Variables on Outcome (eg time of birth, timing and route of delivery, institutional case volume/team complexity, defect size -CDH), maternal exposure risks (GS); iii) Variation in Treatment and Short and Long term Outcome between Canadian centres; and iv) Geographic and ethnic variation in Malformation Incidence and Outcome.

For more information about CAPSNet visit the website at <http://www.capsnetwork.org>



**The Canadian Pharmacogenomics Network for Drug Safety (CPNDS)** is an innovative national program that aims to help solve the drug safety problem by developing genetic tests that predict which patients are at risk of a serious adverse drug reaction. Adverse drug reactions (ADRs) are unintended responses or harmful side effects caused by the normal dose of a drug, and are among the top ten causes of all deaths in North America. In Canada, there are an estimated 200,000 ADRs each year and the annual cost of ADRs has been estimated to be over \$13 billion. Many of these ADRs are caused by inherited genetic differences, as genes determine how drugs are metabolized and whether a drug accumulates in the body in toxic amounts. CPNDS is led by co-principal investigators Bruce Carleton, PharmD, Professor of Paediatrics, University of BC (UBC), and director of the Pharmaceutical Outcomes Programme at BC Children's & Women's Hospital; and Michael Hayden, MD, PhD, Director of the University of British Columbia's Centre for Molecular Medicine and Therapeutics (CMMT) and University Killam professor in the Department of Medical Genetics, UBC.

CPNDS began in 2005 as Genotype-specific Approaches to Therapy in Childhood (GATC). GATC functioned until 2009 when it evolved to become CPNDS to reflect new funding partners, and a larger role with expanded emphasis on adult ADRs. The GATC consortium established an active ADR surveillance network that is unique in the world. It began with one surveillance site at BC Children's Hospital, and grew to include 13 major paediatric teaching hospitals across Canada where surveillance clinicians (pharmacists, registered nurses and physicians) are deployed. The CPNDS clinicians work with local health care professionals who help identify ADRs, then enrol patients and collect clinical data and biospecimens. GATC developed its first pharmacogenomic panel of single nucleotide polymorphisms (SNPs) to study the genetics of ADRs in 2005. This panel allowed for the detection of genetic variation in over 220 key candidate genes that influence the way patients respond to a given medication. Over time, new SNP panels have been developed for specific drug pathways and the initial panel has been further refined. In January 2009 when GATC evolved to become CPNDS, there were over 18,000 ADR cases and matched controls enrolled in the project. Currently, there are more than 40,000 cases and matched controls.

Work done by CPNDS is allowing doctors to prescribe drugs based on a patient's genetic profile: the right drug at the right dose for each child. CPNDS has determined the genetic cause for three ADRs that were initially targeted for surveillance because of the seriousness and long-term consequences of the ADR: cisplatin-induced hearing loss; anthracycline-induced heart damage/failure; and, opiate intoxication of infants. With the discovery that in some mothers, codeine can be metabolized into toxic amounts of morphine that are life-threatening for breastfed infants, Health Canada, the U.S. Food and Drug Administration and industry changed labelling to alert consumers of the potential dangers of codeine.

CPNDS is funded by the Canada Foundation for Innovation, CIHR, Genome BC, UBC, and the BC Child & Family Research Institute. For more information visit the website at <http://www.cpnuds.ubc.ca/>



**Paediatric Emergency Research Canada / Groupe de Recherche en Urgence Pédiatrique du Canada (PERC)** is a network involving health care professionals at 15 sites in 14 cities across Canada with the vision to be international leaders in paediatric emergency research. Now engaging over 100

members, any health care provider involved in the delivery of care for children and youth in paediatric emergency medicine and researchers involved in PEM research can join PERC. Formed in 1995, PERC goals are to create new knowledge through research involving clinical and epidemiological studies in paediatric emergency medicine; to mentor new investigators and fellows in developing research projects; to enhance the image of paediatric emergency medicine as a credible academic discipline with its own research agenda; and to develop cohesiveness between centers involved in the practice of paediatric emergency medicine. PERC began as a "coalition of the willing" with investigator-initiated project-to-project based funding for prospective cohort studies and clinical trials that led to significant findings which now set several PEM clinical practice guidelines. A CIHR Team grant in 2006 provided funding for 7 projects which engaged the entire PEM community and provided matching funding for site coordinators. The collaborative involvement of multiple centres serving a total of over 550,000 children for emergency care each year, provides sufficient patient numbers to allow the completion of large, adequately powered RCTs for common problems usually within 1 to 3 years.

PERC is governed by an Executive Committee which consists of seven positions elected by the PERC membership. The executive committee is responsible for review of new protocols, monitoring on-going studies, development of guidelines and policies that determine how PERC will conduct its business, and planning and setting the agenda for each annual meeting of PERC. The annual meeting allows members to be updated on newly approved and on-going studies, and to hear about and discuss potential new studies. PERC collaborates with the USA Paediatric Emergency Care Applied Research Network (PECARN), and in 2009, was instrumental in creation of a global umbrella network of paediatric emergency research networks (PERN) which conducted its first study to identify historical and clinical features at ED presentation associated with severe H1N1 outcome in children presenting with influenza-like illness.

For more information, including a complete listing of PERC sites and site representatives, see <http://perc.srv.ualberta.ca/>

# Best Practices, Tools & Technology

## Canadian Data Harmonization Roundtable

Canadian research funders convened this invitational meeting on March 28th and 29th in Ottawa, Ontario to explore the elements of a national data harmonization infrastructure initiative that could support research and service functions to enable secondary analysis of publicly-funded data sets. Participants included national and international experts in population research, data standardization, data archiving and data integration across a variety of disciplines. **MICYRN was asked to present** on it's data harmonization efforts which include discussions with principal investigators of Canadian birth cohorts to 'pool' data common to the 50 current studies involving some 96,000 pregnancies; work on ethics to ensure investigators obtain consent for the secondary use of data; and work to promote use of a common research data management platform that would improve the ability to compare data sets from different studies. It was clear that there needs to be a strong national vision and commitment by many stakeholders to realize the goal of cross-jurisdictional integration of data sets, which would allow Canada to capitalize on its considerable investment in population data. The meeting closed with an expression of desire by the organizers to call on a small working group to develop a more concrete vision and accompanying strategy for a pan-Canadian initiative.



**The Public Population Project in Genomics (P<sup>3</sup>G)** is a not-for-profit international consortium dedicated to fostering collaboration between population genomics researchers. This is done through the development of free and accessible research tools, resources and methods that help optimize and harmonize the design of biobank infrastructures and research projects. The goal of population-based biomedical research is to improve health for individuals and populations. By pooling together the results of well-designed studies, statistical power increases and provides rapid replications that can validate key findings. This is why harmonization is vital and why P<sup>3</sup>G was created. The timely funding of this International Consortium Initiative by Genome Quebec and Genome Canada enabled P<sup>3</sup>G to offer a focal point for discussion and coordination at a critical time in the development of this field. Through the use of P<sup>3</sup>G tools, data can be synthesized from over 6 million study participants in 53 large cohorts in Europe, North America and Asia.

Canada's participation in the International Rare Diseases Consortium (led by NIH and the European Commission) provides the opportunity to take a leadership role in the building of infrastructure science. Through a concerted effort by FORGE (CIHR-GC) and **MICYRN**, P<sup>3</sup>G proposes the construction of a Rare Diseases Platform which will build both epidemiological, IT and policy tools to enable international interoperability. It will catalogue current rare disease research efforts, customize already existing P<sup>3</sup>G tools like DataSHAPER and create DataSchema and software particular to rare diseases. Unique ELSI issues are raised by research into rare diseases, the obvious ones being: individual, familial and community (ethnicity) identifiability and the very real need for international sharing of data and samples in order to acquire statistical significance. Moreover, due to the large number of paediatric rare diseases, the recruitment and use of samples and data from children and minors requires specific policy tools as mandated by their ethical and legal status.

P<sup>3</sup>G's Secretariat is based at McGill University, Montreal. For more information see <http://www.p3g.org/>

## Upcoming Events

**Transforming Health & Economics: 8th World Congress on Health Economics** will be held at the Sheraton Centre Toronto Hotel, Toronto, **July 10-13 2011**, <http://www.healtheconomics.org/congress/2011/pre-congress/> Registration is now open for the special symposium "Investing in Child Health to Transform Global Health"

**2011 CAPHC Annual Conference** will be held at the Westin Ottawa and Ottawa Convention Centre, **October 16-19, 2011** <http://www.caphc.org> "The Future of Children's Healthcare: What Can We Expect? How Do We Prepare?" Joint meetings include the annual general meetings of MICYRN; the Canadian Council for Child Health Research (CCCHR); and the Canadian Child Health Clinical Scientist Program (CCHCSP).

**Pregnancy and Birth: Current Clinical Issues Annual Conference, December 15-16, 2011** - Marriott Toronto Eaton Centre, 525 Bay Street, Toronto, Ontario. For further details contact email Judy Cardwell at [cmicr@sunnybrook.ca](mailto:cmicr@sunnybrook.ca); to view the full program, please visit [www.cmicr.ca](http://www.cmicr.ca) or [www.cmicrconference.ca](http://www.cmicrconference.ca).

# Announcements

**Mind the Gap** Health Canada's proposal to the Council of Canadian Academies entitled "Mind the Gap: Therapeutic Products for Infants, Children and Youth" was recommended for approval on May 26, 2011, by the federal Committee on Science and Technology under Industry Canada. As a last step, Health Canada is seeking the Health Minister's concurrence with this proposed study. Should all go well the Minister of Health will forward it to the Minister of Industry Canada to request that he refer the proposal to the Council of Canadian Academies' Board of Governors to conduct. Refer to an editorial from the Canadian Medical Association Journal June 2011 edition on this issue. Industry's neglect of prescribing information for children Bob Peterson MD PhD MPH, Paul C. Hébert MD MHSc, Noni MacDonald MD MSc, Daniel Rosenfield BArtsSc, Matthew B. Stanbrook MD PhD, Ken Flegel MDCM MSc CMAJ 2011. DOI:10.1503 /cmaj.110563

## The MICYRN website content is now bilingual

Enter the French version on the homepage



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français

## News about MICYRN Partners



**INSTITUTE  
OF FAMILIES**  
for Child and Youth Mental Health

**The National Institute of Families for Child & youth Mental Health (IF)** was founded in 2009.

The IF is a central coordinating organization **that acts as the catalyst to connect families** with mental health care providers, policy makers, educators, researchers, service providers and businesses across Canada. IF works to ensure that families have a voice in improving child and youth mental health and leads the Nation in mobilizing and engaging families in support of child and youth mental health. The National Institute of Families for Child & Youth Mental Health (IF) officially launched it's website, April 27, 2011 at <http://www.instituteoffamilies.com>

Family Smart™ is a trademark that will identify and endorse practices, research, policies, programs and services, which relate to child and youth mental health and are meaningful and make a difference to families. The IF is gathering input from families and those working and interested in child and youth mental health to help define criteria for Family Smart™. As a first step, on National Child and Youth Mental Health Day (May 7, 2011) the IF invited youth, parents, caregivers, professionals and others working or interested in child and youth mental health to come together to discuss the vision for Family Smart™ and help define what it will look like to have that vision realized for children, youth and families in Canada. Further consultation will take place across Canada in the months after May 7th.

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*Building capacity for high quality clinical  
research in Canada and beyond*

**The Maternal Infant Child Youth Research Network (MICYRN) was formed in 2006 to build capacity for high quality clinical research in Canada and beyond. MICYRN links 17 participating academic health centers, and hundreds of investigation teams across the country.**

**MICYRN is committed to enhancing the productivity of the Canadian child-maternal research community, through sustaining and augmenting existing activities, and reducing impediments to multicentre research activity.**

maternal infant  
child & youth  
research network



réseau de recherche  
en santé des  
enfants et des mères