

maternal infant
child & youth
research network



réseau de recherche
en santé des
enfants et des mères

Canadian Maternal Clinical Trials Activity 2005-2009

Report completed September 2010

Anne Junker, MD
Director, Mother Infant Child Youth Research Network (MICYRN)
Réseau de Recherche en Santé des Enfants et des Mères (RRSEM)

Table of Contents

Introduction	2
Methods	3
Results	4
Frequency of Clinical Trials	4
Table I Number of registered maternal clinical trials by country	4
Primary Sponsor	5
Figure 1 Academic sponsors of maternal clinical trials in Canada	5
Figure 2 Home Province of Primary Sponsor for Academic Trials	5
Table II Studies sponsored by member institutions of CCCHR	6
Table III Non CCCHR institutions sponsoring maternal trials	7
National nature of Academic Trials	7
Recruitment	7
Figure 3 Recruitment Status of Maternal Clinical Trials	8
Subject of study	8
Figure 4 Health Conditions Studied in maternal clinical trials	8
Comments	9
Appendix I World Health Organization Registration requirements	10

Introduction

The Maternal Infant Child Youth Research Network (MICYRN)/Réseau de Recherche en Santé des Enfants et des Mères (RRSEM) was formed in 2006 to build capacity for high quality clinical research in Canada and beyond. The origin of MICYRN-RRSEM was with the 17 academic health centres joined by the Canadian Council for Child Health Research (CCCHR). About half of these centres also have a commitment to maternal and/or women’s health research. On September 11th, 2010, at a meeting of CCCHR representatives, there was unanimous agreement to include in the membership of MICYRN-RRSEM, organizations with a focus on maternal health research. And that MICYRN-RRSEM should facilitate development of an integrated strategy to support pediatric, perinatal and maternal clinical

trials across Canada. MICYRN-RRSEM is committed to enhancing the productivity of the Canadian maternal-child research community, through sustaining and augmenting existing activities, and reducing impediments to multicentre research activity. A key contribution of MICYRN-RRSEM is information about maternal-child clinical research activity in Canada. This report provides information about Canada's involvement in maternal clinical trials, with the intent to promote discussion on developing a national framework for multicentre clinical trials.

Methods

The World Health Organization (WHO) established an International Clinical Trials Registration Platform (ICTRP) following a Ministerial Summit on Health Research that took place in Mexico City, Mexico, in November 2004. Participants of the Summit called for the WHO to facilitate the establishment of: *“a network of international clinical trials registers to ensure a single point of access and the unambiguous identification of trials”*. As stated by the WHO, *“Registration of all interventional trials is considered to be a scientific, ethical and moral responsibility”*. This sentiment was supported by the International Committee of Medical Journal Editors (ICMJE) which had a parallel effort and in September 2005, implemented a policy that requires registration of clinically directive trials as a condition of consideration for publication in their journals. The WHO Registry Network is composed of 12 Registries which meet the reporting requirements of the ICMJE. Datasets from Registry data providers are updated regularly: weekly from the Australian New Zealand Clinical Trials Registry, ClinicalTrials.gov, and ISRCTN; and every four weeks from registries in China, India, Republic of Korea, Germany, Iran, Japan, Africa, Sri Lanka, and the Netherlands. Complete information about the Platform can be found at <http://www.who.int/ictcp/en/>.

The WHO Trial Registration Data Set currently includes 20 items. (see Appendix I for item list and definitions) The ICTRP Search Portal includes the ability to search on countries of recruitment; date of registration; recruitment status; and on phrases in the title, condition or intervention.

This report covers a review of data retrieved from the WHO ICTRP to study interventional and observational maternal clinical trials over the past 5 years where Canada was listed as a 'country of recruitment'. Selection of trials was made on the “condition” field, using the terms “pregnancy OR postpartum OR perinatal OR fetal OR maternal OR obstetric OR gestation”.

Results

Frequency of Clinical Trials

As at September 18th, 2010, the WHO database showed a total, world-wide of 85,876 registered clinical trials for the study period 2005-2009, with 823 (0.9%) of these matching the search terms. Sixty-eight (8%) of the 823 maternal clinical trials listed Canada as a country of recruitment. Interventional clinical trials accounted for 77%, and observational trials 23%, of Canadian maternal trials activity. Canada was second only to the USA in the total number of maternal clinical trials being conducted world-wide, and third after the Netherlands and Australia for the number of actively recruiting trials per million births in the population. (Table I) Births were chosen as a comparator because this is an easily obtained statistic, and reflects the reality of maternal activity in a population, compared to the age of women in a population.

Table I Number of registered maternal clinical trials by country

Country	Total Trials 2005-2009	No. Actively Recruiting Maternal Trials in 2008 [#]	Births x 1000* in 2008	Trials per million births (2008)
India	19	4	26,913	0.15
China	13	2	18,134	0.11
USA	286	87	4,399	19.8
France	31	16	752	21
United Kingdom	46	7	743	9.4
Germany	14	5	666	7.5
Italy	14	4	546	7.3
Canada	73	20	353	56.6
Australia	57	21	267	78.7
Netherlands	56	22	185	118.9

* From United Nations Data for year 2008 <http://data.un.org/Data.aspx?d=SOWC&f=inID%3A75>

From WHO ICTRP for all actively recruiting trials registered 01/01/2003 – 31/12/2008

Seven studies were not included in the following analysis: one of these studies was being conducted at sites outside Canada by a Canadian sponsor; 5 studies were not yet recruiting; and 1 study had not listed the projected subject enrolment.

Primary Sponsor

Only 1/61 clinical trials was sponsored by industry. All the rest had academic sponsors. Figure 1 shows the distribution of trials by academic sponsors. Overall, Canadian sponsors were responsible for 55/60 (92%) of these trials, with 50/55 (91%) of these being province-based academic institutions.

Figure 1 Academic sponsors of maternal clinical trials in Canada

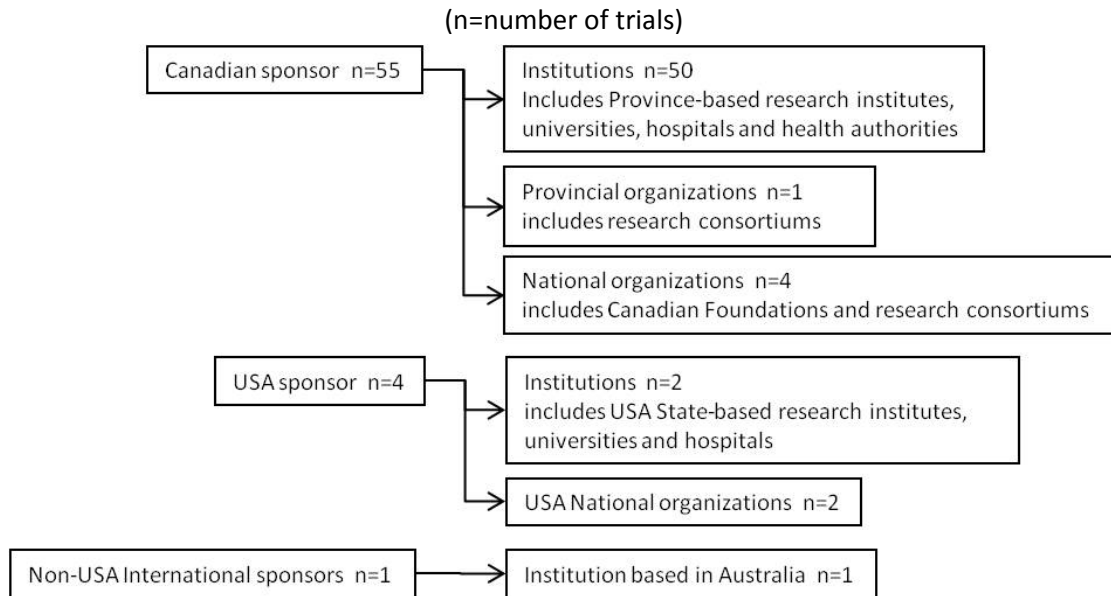
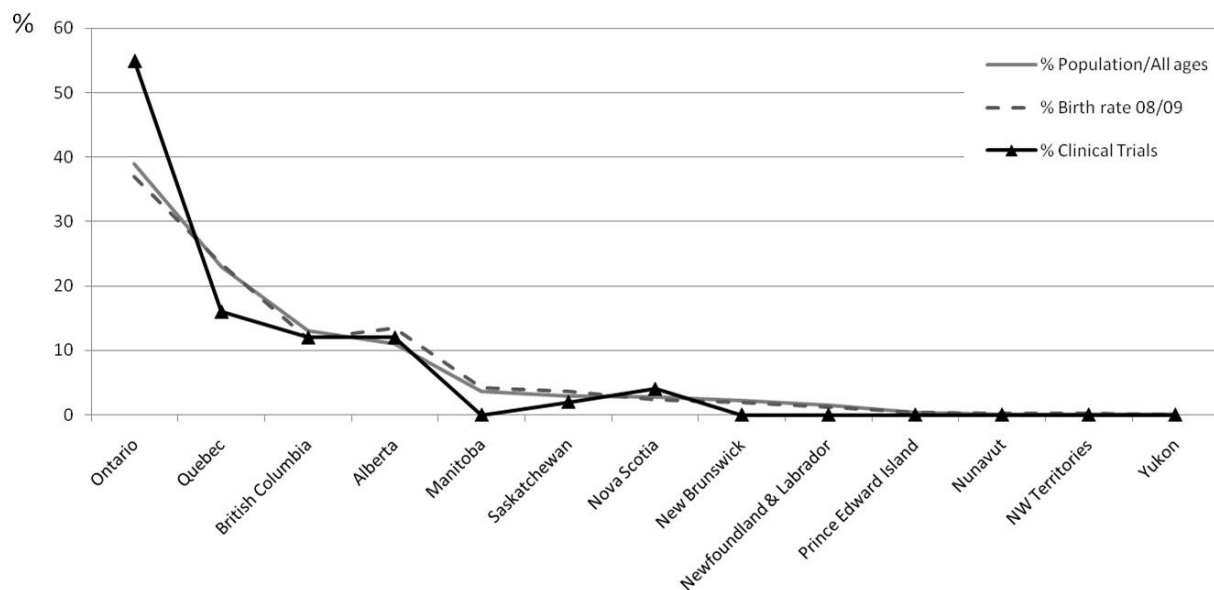


Figure 2 shows the home province of the primary sponsor for academic trials. The proportion of trials was higher than the proportion of population and birth rates for Ontario, and lower than expected for Quebec and Manitoba.

Figure 2 Home Province of Primary Sponsor for Academic Trials



Canadian academic health science centres with a focus on child and youth health which comprise the membership of the Canadian Council of Child Health Research (CCCHR) were responsible for 18/50 (36%) institution-sponsored trials. (Table II) Other institutions listed in Table III were responsible for 32/50 (64%) of institution-sponsored trials.

Table II Studies sponsored by member institutions of CCCHR

Number of trials sponsored	Academic Institution			
3	Child and Family Research Institute	University of British Columbia	Vancouver	British Columbia
2	Women and Children's Health Research Institute	University of Alberta	Edmonton	Alberta
2	Institute of Maternal and Child Health	University of Calgary	Calgary	Alberta
1	Royal University Hospital	University of Saskatchewan	Saskatoon	Saskatchewan
0	Manitoba Institute of Child Health	University of Manitoba	Winnipeg	Manitoba
0	Children's Health Research Institute	University of Western Ontario	London	Ontario
1	McMaster Children's Hospital	McMaster University	Hamilton	Ontario
2	The Hospital for Sick Children	University of Toronto	Toronto	Ontario
0	Kingston General Hospital	Queen's University	Kingston	Ontario
1	Children's Hospital of Eastern Ontario (CHEO)	University of Ottawa	Ottawa	Ontario
0	Sudbury Regional Hospital	Laurentian University	Sudbury	Ontario
0	Montreal Children's Hospital Research Institute	McGill University	Montreal	Quebec
1	Le Centre de recherche du CHU Sainte-Justine	Université de Montréal	Montreal	Quebec
3	Sherbrooke University Hospital	Université de Sherbrooke	Sherbrooke	Quebec
1	Hospitalier Université Laval (CHUL)	Université de Laval	Quebec City	Quebec
1	IWK Health Centre	Dalhousie University	Halifax	Nova Scotia
0	Janeway Children's Health and Rehabilitation Centre	Memorial University	St. John's	Newfoundland

Table III Non CCCHR institutions sponsoring maternal trials

Number of trials sponsored	Academic Institution		
3	Women’s Health Research Institute	Vancouver	British Columbia
1	Calgary Health Region	Calgary	Alberta
7	Samuel Lunefeld Research Institute Mt Sinai	Toronto	Ontario
5	University of Toronto	Toronto	Ontario
3	St. Michael’s Hospital	Toronto	Ontario
1	University of Toronto Health Network	Toronto	Ontario
1	Maternal Infant Reproductive Health Unit	Toronto	Ontario
2	Hamilton Health Services	Hamilton	Ontario
1	University of Hamilton	Hamilton	Ontario
1	St Joseph’s Hospital	Hamilton	Ontario
2	Ottawa Hospital Research Institute	Ottawa	Ontario
1	Ottawa Fertility Centre	Ottawa	Ontario
3	University of McGill	Montreal	Quebec
1	Dalhousie University	Halifax	Nova Scotia

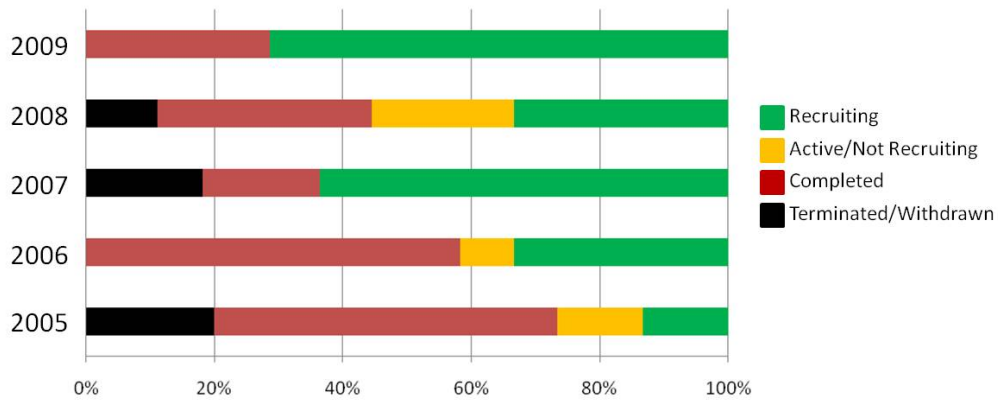
National nature of Academic Trials

Of the 60 trials with an academic sponsor, 54 (90%) listed Canada as the only country of recruitment. Canadian institutions sponsored only 3 studies involving sites outside Canada.

Recruitment

Figure 3 illustrates the recruitment status of trials. Note that the data for this report was linked to the date of trial registration, not commencement of enrolment. The Registry systems in place allow registration of studies at any time prior to initiation through to completion of enrolment, so it is possible to register a trial even when enrolment is completed. However, ICMJE journals have indicated that for trials beginning on or after July 1, 2005 they would only consider trials where registration occurred before the first patient was enrolled (“prospective registration”).

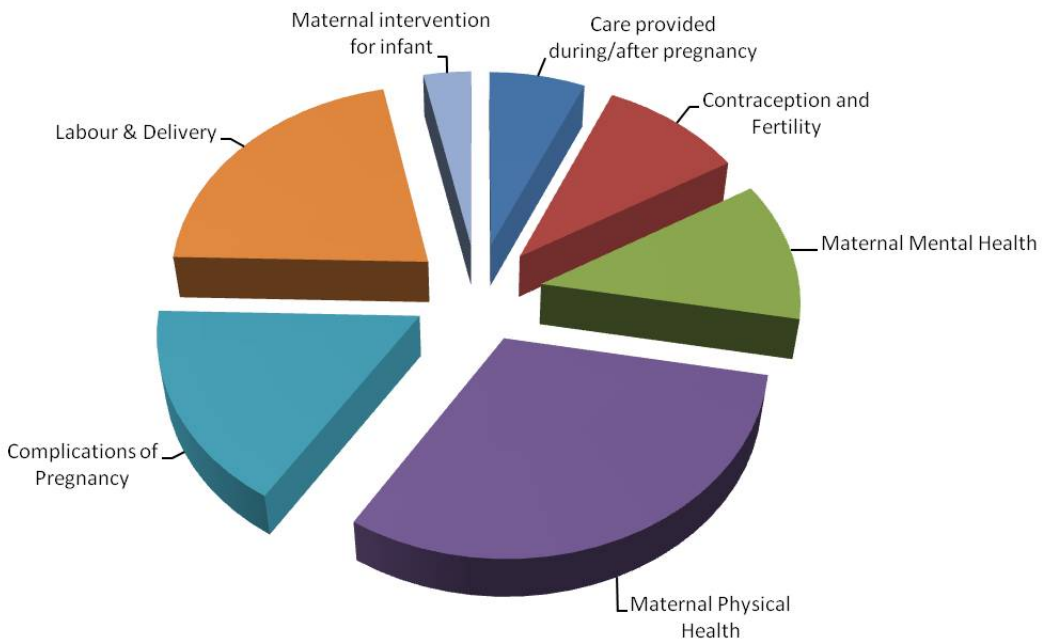
Figure 3 Recruitment Status of Maternal Clinical Trials



Subject of study

The distribution of conditions studied in maternal clinical trials is illustrated in Figure 4. Maternal physical health included studies related to diabetes (n=7), infectious diseases (n=4), and hypertension (n=4). Complications of pregnancy included studies of fetal loss and placental dysfunction (n=4). Two studies specifically involved a maternal intervention directed to child health – vaccination of the mother to promote infant antibody levels; and maternal nutritional supplementation to promote infant brain development.

Figure 4 Health Conditions Studied in maternal clinical trials



Comments

- The WHO ICTRP provides a rich resource of information about clinical trials
- World-wide, there is a striking paucity of industry-sponsored clinical trials related to pregnancy
- Compared to other countries, there is a reasonable amount of maternal-focused clinical trials activity in Canada
- Canadian academic organizations sponsor the overwhelming majority of maternal clinical trials conducted by investigators in Canada
- Canadian academic organizations are infrequent sponsors of multi-national maternal clinical trials. This was the same finding for pediatric clinical trials.

Appendix I World Health Organization Registration requirements ¹

The minimum amount of trial information that must appear in a register in order for a given trial to be considered fully registered, and the description of this information, is detailed following.

1. Primary Registry and Trial Identifying Number

Name of Primary Registry, and the unique ID number assigned by the Primary Registry to this trial.

2. Date of Registration in Primary Registry

Date when trial was officially registered in the Primary Registry. If relevant, also include the date of registration in the Partner Registry.

3. Secondary Identifying Numbers

Other identifiers besides the Trial Identifying Number allocated by the Primary Registry, if any. These should include:

- The Universal Trial Number (UTN)
- Identifiers assigned by the sponsor (record sponsor name and sponsor-issued trial number (e.g., protocol number))
- Other trial registration numbers
- Identifiers issued by funding bodies, collaborative research groups, regulatory authorities, ethics committees / institutional review boards, etc.

All secondary identifiers will have 2 elements: an identifier for the issuing authority (eg NCT, ISRCTN, ACTRN) plus a number.

There is no limit to the number of secondary identifiers that can be provided.

4. Source(s) of Monetary or Material Support

Major source(s) of monetary or material support for the trial (e.g., funding agency, foundation, company).

5. Primary Sponsor

The individual, organization, group or other legal entity which takes responsibility for initiating, managing and/or financing a study. The Primary Sponsor is responsible for ensuring that the trial is properly registered. The Primary Sponsor may or may not be the main funder.

6. Secondary Sponsor(s)

Additional individuals, organizations or other legal persons, if any, that have agreed with the primary sponsor to take on responsibilities of sponsorship. A secondary sponsor may have agreed:

- to take on all the responsibilities of sponsorship jointly with the primary sponsor; or
- to form a group with the primary sponsor in which the responsibilities of sponsorship are allocated among the members of the group; or

¹ <http://www.who.int/ictrp/en/>

- to act as the sponsor’s legal representative in relation to some or all of the trial sites; or
- to take responsibility for the accuracy of trial registration information submitted.

7. Contact for Public Queries

Email address, telephone number, or postal address of the contact who will respond to general queries, including information about current recruitment status.

8. Contact for Scientific Queries

Email address, telephone number, or postal address, and affiliation of the person to contact for scientific queries about the trial (e.g., principal investigator, medical director employed by the sponsor). For a multi-center study, enter the contact information for the lead Principal Investigator or overall scientific director.

9. Public Title

Title intended for the lay public in easily understood language.

10. Scientific Title

Scientific title of the study as it appears in the protocol submitted for funding and ethical review. This title should contain information on population, intervention, comparator and outcome(s). Include trial acronym if available.

11. Countries of Recruitment

The countries from which participants will be, are intended to be, or have been recruited at the time of registration.

12. Health Condition(s) or Problem(s) Studied

Primary health condition(s) or problem(s) studied (e.g., depression, breast cancer, medication error).

If the study is conducted in healthy human volunteers belonging to the target population of the intervention (e.g. preventive or screening interventions), enter the particular health condition(s) or problem(s) being prevented.

13. Intervention(s)

For each arm of the trial record a brief intervention name plus an intervention description.

Intervention Name: For drugs use generic name; for other types of interventions provide a brief descriptive name.

- For investigational new drugs that do not yet have a generic name, a chemical name, company code or serial number may be used on a temporary basis. As soon as the generic name has been established, update the associated registered records accordingly.
- For non-drug intervention types, provide an intervention name with sufficient detail so that it can be distinguished from other similar interventions.

Intervention Description: Must be sufficiently detailed for it to be possible to distinguish between the arms of a study (e.g., comparison of different dosages of drug) and/or among similar interventions (e.g., comparison of multiple implantable cardiac defibrillators). For example, interventions involving drugs may include dosage form, dosage, frequency and

duration.

- If the intervention is one or more drugs then use the International Non-Proprietary Name for each drug if possible (not brand/trade names). For an unregistered drug, the generic name, chemical name, or company serial number is acceptable.
- If the intervention consists of several separate treatments, list them all in one line separated by commas (e.g., "low-fat diet, exercise").
- For controlled trials, the identity of the control arm should be clear. The control intervention(s) is/are the interventions against which the study intervention is evaluated (e.g., placebo, no treatment, active control). If an active control is used, be sure to enter in the name(s) of that intervention, or enter "placebo" or "no treatment" as applicable. For each intervention, describe other intervention details as applicable (dose, duration, mode of administration, etc).

14. **Key Inclusion and Exclusion Criteria**

Inclusion and exclusion criteria for participant selection, including age and sex. Other selection criteria may relate to clinical diagnosis and co-morbid conditions; exclusion criteria are often used to ensure patient safety.

If the study is conducted in healthy human volunteers not belonging to the target population (e.g., a preliminary safety study), enter "healthy human volunteer".

15. **Study Type**

Study type consists of:

- Type of study (interventional or observational)
- Study design including:
 - Method of allocation (randomized/non-randomized)
 - Masking (is masking used and, if so, who is masked)
 - Assignment (single arm, parallel, crossover or factorial)
 - Purpose
- Phase (if applicable)

16. **Date of First Enrollment**

Anticipated or actual date of enrollment of the first participant.

17. **Target Sample Size**

Number of participants that this trial plans to enrol in total.

18. **Recruitment Status**

Recruitment status of this trial:

- Pending: participants are not yet being recruited or enrolled at any site
- Recruiting: participants are currently being recruited and enrolled

- Suspended: there is a temporary halt in recruitment and enrollment
- Complete: participants are no longer being recruited or enrolled
- Other

19. **Primary Outcome(s)**

Outcomes are events, variables, or experiences that are measured because it is believed that they may be influenced by the intervention.

The Primary Outcome should be the outcome used in sample size calculations, or the main outcome(s) used to determine the effects of the intervention(s). Most trials should have only one primary outcome.

For each primary outcome provide:

- The name of the outcome (do not use abbreviations)
- The metric or method of measurement used (be as specific as possible)
- The time point(s) of primary interest

Example: Outcome Name: Depression; Metric/method of measurement: Beck Depression Score; Timepoint: 18 weeks following end of treatment

20. **Key Secondary Outcomes**

Secondary outcomes are outcomes which are of secondary interest or that are measured at timepoints of secondary interest. A secondary outcome may involve the same event, variable, or experience as the primary outcome, but measured at timepoints other than those of primary interest.

As for primary outcomes, for each secondary outcome provide:

- The name of the outcome (do not use abbreviations)
- The metric or method of measurement used (be as specific as possible)
- The time point(s) of interest