MIREC

Maternal-Infant Research on Environmental Chemicals

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PhD (c) Université de Montréal

Funding Agencies

Health Canada
Santé Canada

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Ontario

Investigators

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Study coordinating centre

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant

Pour l'amour des enfants

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Objectives

- To obtain national-level data on maternal and neonatal exposure to priority environmental contaminants
- To obtain Canadian data on smoking behaviour and exposure to tobacco smoke (active and passive) in pregnancy
- To determine if heavy metal exposure is related to elevated maternal blood pressure, hypertension, altered sex ratio and fetal growth restriction

Objectives

- To obtain contemporary levels of priority environmental chemicals, selected nutrients and relevant immunoprotective endpoints in mature human milk
- To obtain contemporary levels of maternal hair-mercury
- To characterize dietary exposure of breastfed infants ages 2-8 weeks to allow for time-trend analyses for those analytes which were included in previous human milk surveys

Epidemiological evidence for causal relationships between reproductive and child health outcomes and environmental chemical contaminants.

Wigle DT, Arbuckle TE, Turner MC, Bérubé A, Yang Q, Liu S, Krewski D.
J Toxicol Environ Health B Crit Rev. 2008 May;11(5-6):373-517. Review.

- Prenatal high-level methylmercury (CH(3)Hg) exposure:
  - delayed developmental milestones and cognitive, motor, auditory, and visual deficits.

- High-level prenatal exposure to polychlorinated biphenyls (PCBs), and related toxicants:
  - neonatal tooth abnormalities, cognitive and motor deficits.

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- Maternal active smoking:
  - delayed conception, preterm birth, fetal growth restriction and sudden infant death syndrome,
- Prenatal environmental tobacco smoke (ETS) exposure:
  - preterm birth

- However, evidence for some proven relationships came from investigation of relatively small numbers of children with high-dose prenatal exposures, e.g., CH(3)Hg poisoning episodes in Japan and Iraq.

Background
Prenatal Exposure to endocrine modulating chemicals

- The endocrine system is essential to development and reproduction
- Plasticizers (phthalates and bisphenol A), surfactants (perfluorinated compounds), brominated flame retardants
- Adverse health effects in an intact organism, its progeny, and also in subsequent generations

Phthalates:
Potential developmental and reproductive effects

- Decreased Anogenital Distance (AGD) in males
  - Disbalance in testosterone production
  - leydig cells differentiation

- Decreased AGD in 106 boys (1, 2)
- Lower post-natal surge of reproductive hormones (3)

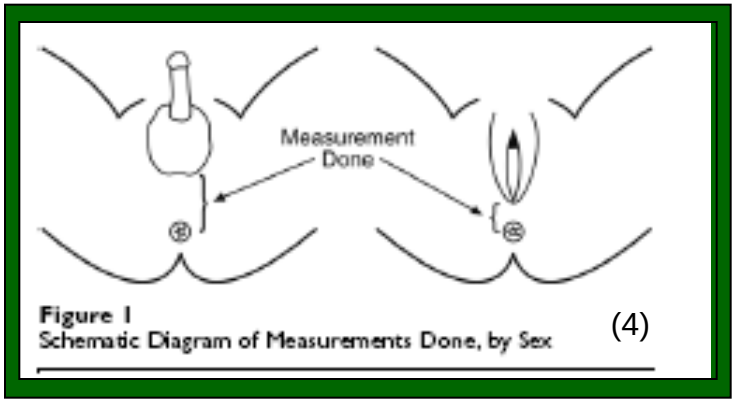

Figure 1
Schematic Diagram of Measurements Done, by Sex (4)

(1) *Swan et al, 2005*
(2) *Swan et al, 2008*
(3) *Main et al, 2006*
(4) *Salazar-Martinez, 2004*

Epidemiological evidence for causal relationships between reproductive and child health outcomes and environmental chemical contaminants.

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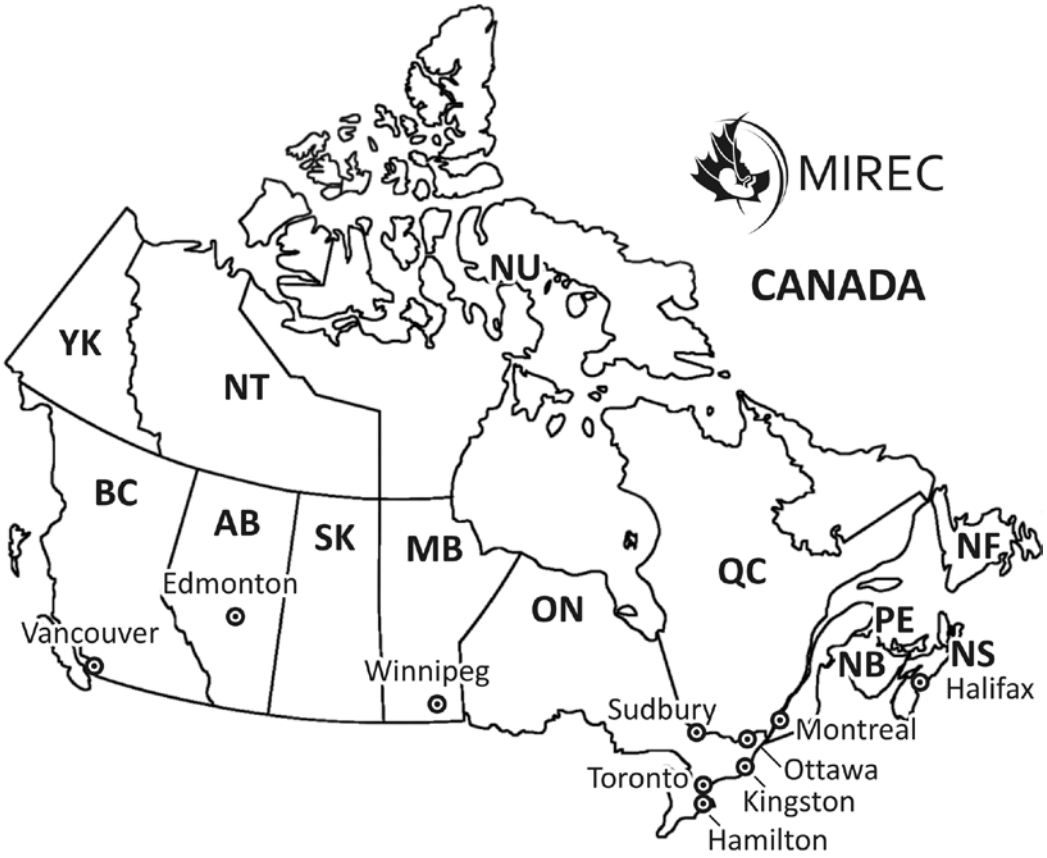
“There is a great need for population-based, multidisciplinary and collaborative research on the many relationships supported by inadequate evidence, as these represent major knowledge gaps”.

Study Design

- A National-level pregnancy cohort study,10 Clinical sites across Canada



Participating Hospitals

01 BC Children and Women's Health Centre, **Vancouver** - Dr. Peter von Dadelszen

02 University of Alberta**, Edmonton** – Dr. Denise Hemmings and Jungwei Wang

03a St-Boniface Hospital, **Winnipeg** - Dr. Michael Helewa

03b The University of Manitoba , **Winnipeg** - Dr Shayne Taback

04 Mount-Sinaï Hospital, **Toronto** - Dr. Mathew Sermer

05 McMaster University Hospital, **Hamilton** - Dr. Warren Foster

06 **Sudbury** - Dr. Greg Ross /Dr. Paul Fredette

07 **Kingston** General Hospital - Dr. Graeme Smith

08 **Ottawa** General Hospital - Dr. Mark Walker

09a CHU Ste-Justine, **Montreal** - Dr. William Fraser

09b Jewish General Hospital, **Montreal** - Dr. Roberta Shear

10 IWK Health Centre, **Halifax** - Dr. Linda Dodds

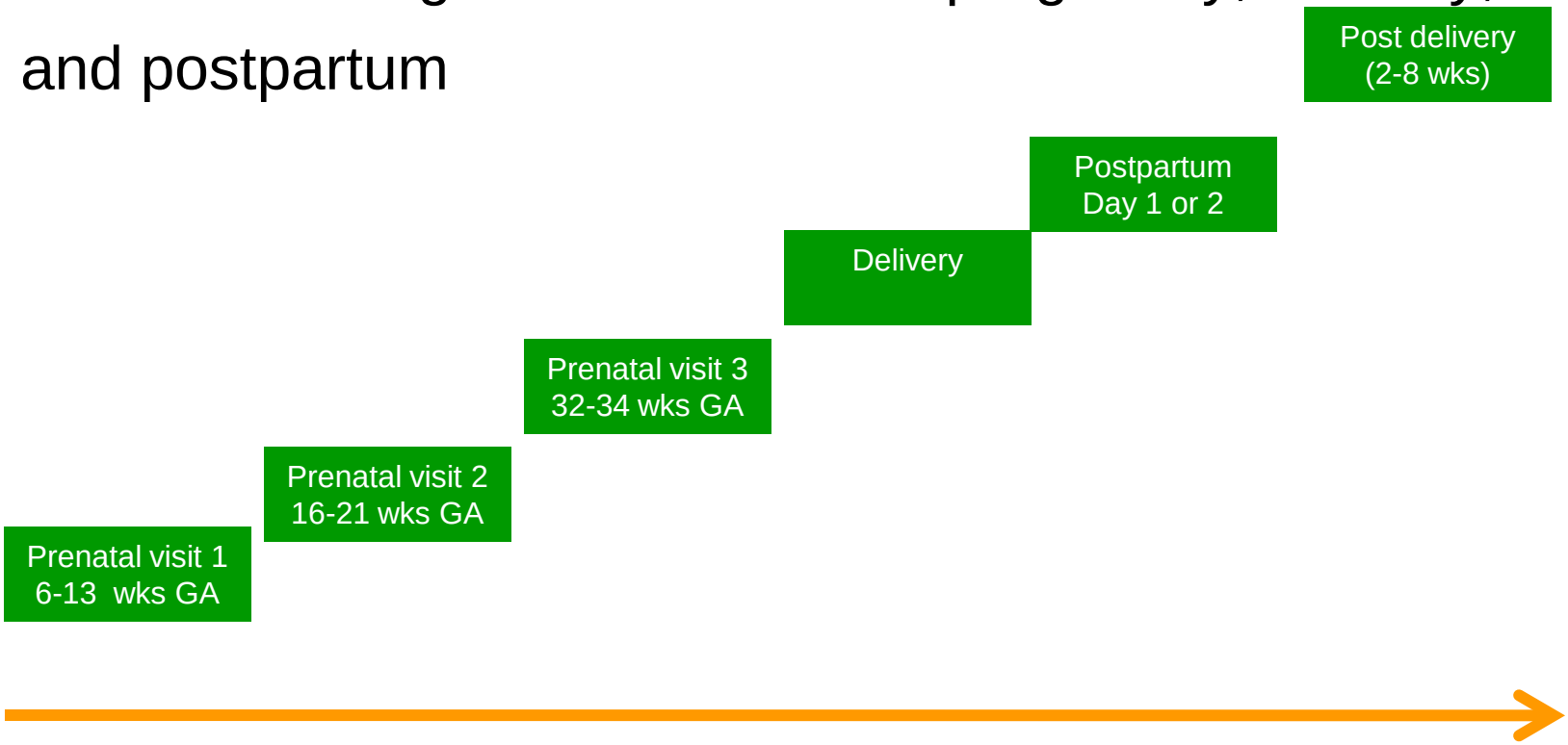
Study population
Eligibility criteria

- Inclusion criteria

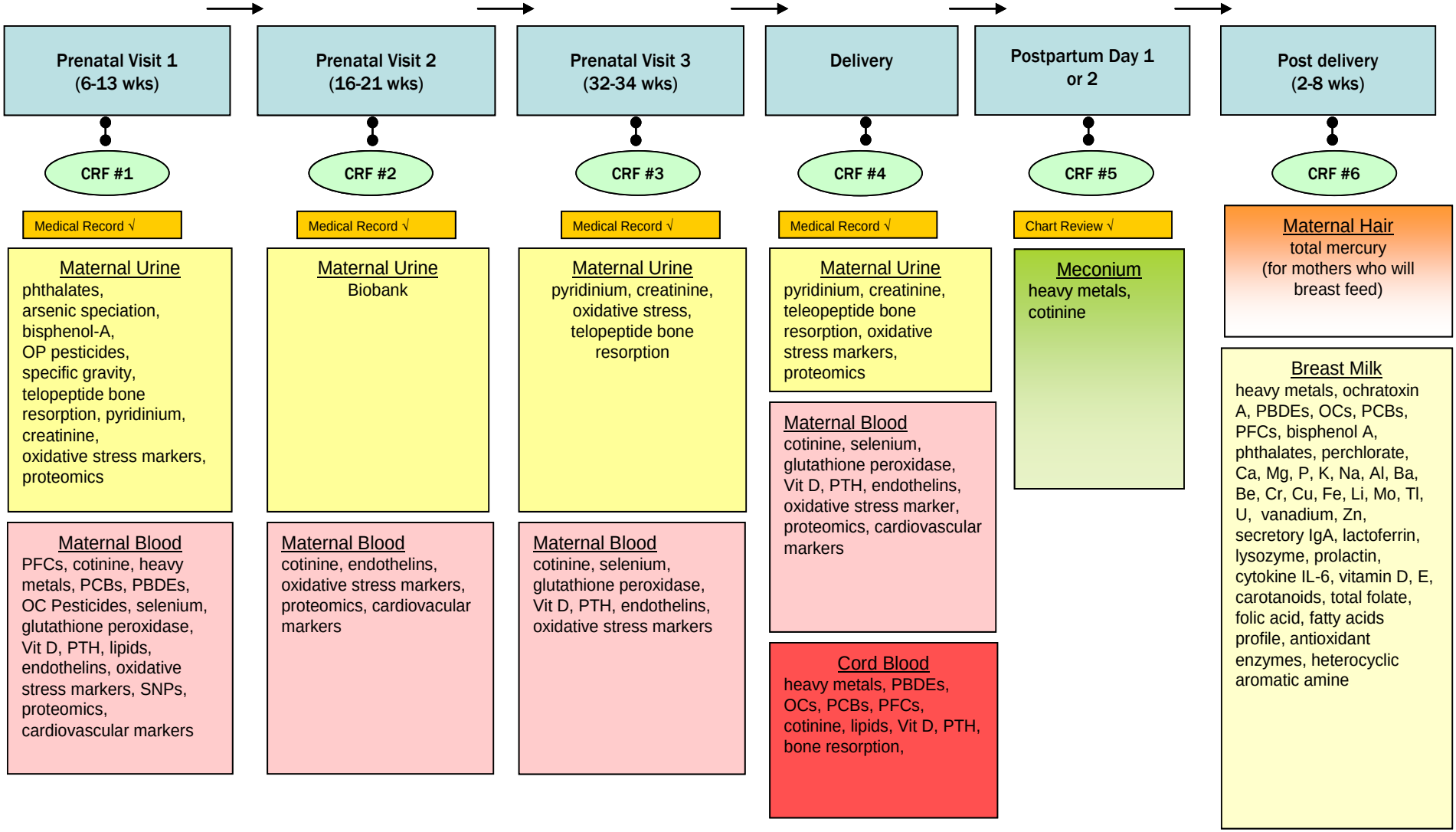
1. The woman is pregnant between $6^{0/7}$ and $13^{6/7}$ completed weeks
2. Age $\geq$ 18 years
3. Speaks a language known by the medical staff (French or English)
4. Plans to deliver in a study participating hospital
5. The woman is able to understand and sign a consent form

Study Design

- 2,000 pregnant women recruited during 1st trimester
- Hospital-based sample
- Contacts during each trimester of pregnancy, delivery, and postpartum



Data Collection



Sources of Exposure

Chemical Group	Biomarkers	Uses and Sources of Exposure
Metals/metalloids	Lead	Gasoline, paint, dust, drinking contaminated water
	Mercury	Batteries, fluorescent light bulbs, fish consumption, dental amalgams
	Cadmium	Pigments, municipal waste incineration, cigarette smoke
	Arsenic	Pressure-treated wood, drinking contaminated water
	Manganese	Burning of fossil fuels
Plasticizers	Bisphenol A (BPA)	Polycarbonate food containers, refillable water bottles, metal food and beverage cans, dental sealants
	Phthalate metabolites	Polyvinyl chloride flooring, toys, detergents, personal care products, food packaging, dust

Sources of Exposure

Chemical Group	Biomarkers	Uses and Sources of Exposure
Surfactants	Perfluorinated compounds (e.g., PFOS, PFOA)	Non-stick cookware, stain repellent furnishings, fast-food packaging
Pesticides	Organophosphate metabolites	Insecticides, food contaminant
Flame Retardants	Polybrominated diphenyl ethers (PBDEs)	Electronic equipment, furniture, construction materials, textiles, foods, house dust
Persistent Organic Pollutants (POPs)	Polychlorinated biphenyls (PCBs)	Industrial equipment, food
	Organochlorine metabolites (e.g., DDE, aldrin, mirex)	Insecticides, food contaminant
Tobacco Smoke	Cotinine	Active and passive exposure to tobacco smoke

Nutritional Data Collected
Nutrient-Heavy Metals Interaction

Nutritional status can play a role in altering absorption or susceptibility to toxicity of heavy metals:

- Calcium
  - Bone demineralization may be caused by insufficient maternal dietary sources of calcium
- Iron
  - Animal studies suggest that iron supplementation partially reduces the impaired fetal growth caused by cadmium
- Selenium
  - may also play an active role in maternal defence systems against the toxicity of metals and constituents of cigarette smoke

Nutritional Data Collected

- **First Trimester**
  - Supplements (product names)
    - Prenatal vitamins
    - Folic acid supplements
    - Other supplements
  - Beverages (milk, water, juice, tea, coffee, alcohol)
  - Species of fish
- **Second Trimester** (take home questionnaire)
  - Within past 24 hours

    Name of product, amount taken, frequency
  - During last 30 days

    Name of product, amount taken, frequency

Nutritional Data Collected

- **Second Trimester (continued)**
  - Food Frequency Questionnaire
    - During the past month
    - Frequency
    - Serving size
    - Primarily focusing on calcium and iron sources
- **Third Trimester**
  - Beverages (milk, water, juice, tea, coffee, alcohol
  - Species of fish
- **Lactational questionnaire**
  - Fish species
  - Beverages
  - Nutrient supplements while breastfeeding

Other Data Collected

- 1st and 3rd Trimesters
  - Smoking (active and passive)
  - Socio-demographics
  - Obstetrical history
  - Employment
  - Environmental exposures (work, home)
  - Physical activity
  - Sunlight exposure
  - Anthropometry
  - Blood pressure
- Pregnancy outcomes

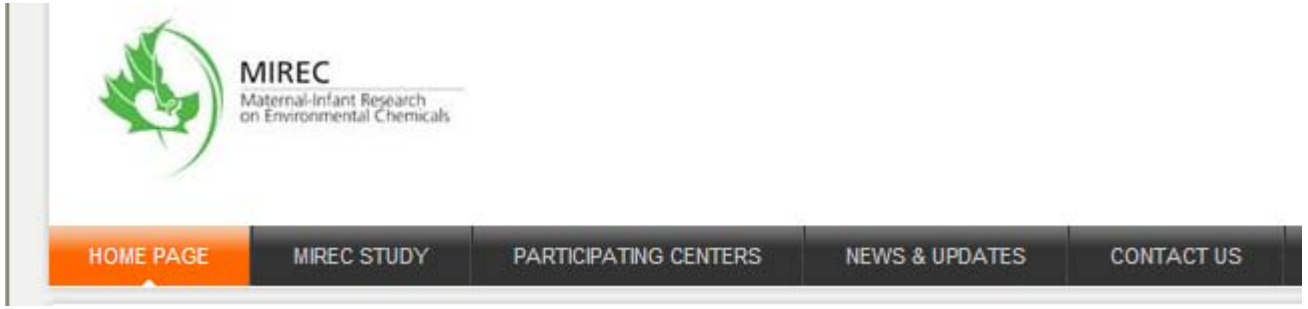
Communication Strategy

- Public Awareness
  - Websites

    www.hc-sc.gc.ca/ewh-semt/contaminants/mirec/index_e.html

    www.chemicalsubstanceschimiques.gc.ca/bio_e.html

    www.mirec-canada.ca



Reporting of Laboratory Results to Participants

- Report Advisory Committee
  - Toxicologists, risk assessors, communications
  - Develop material to accompany individual chemical test results to participants
    - Where available, guidelines
    - Sources of exposure
  - Physicians Guidance Documents for Pb, Hg, Cd

Reporting of Laboratory Results to Participants

- Metals: INFORM patients and physicians with information on potential sources of exposure and current intervention level (e.g. Health Canada Lead Information Package)
  - 3 to 6 months
- Other contaminants: WHAT TO DO WITH RESULTS WHEN EFFECTS OF AN EXPOSURE ARE UNKNOWN?

Ethical issues

- Ste-Justine's REB: Results communicated to participants are those where results exceed health-based guidelines:
  - Are scientifically proven to be significant for the health of the participant and,
  - There are preventive measures or treatments available
- Through physician

Additional and Future Research

- **Biobank** of maternal and infant biospecimens (blood, urine, meconium, cord blood, maternal hair, breast milk)
- About 65% of the aliquots are in the MIREC biobank.
- The MIREC biobank is housed at the Ste-Justine Hospital and is governed by a biobank management committee, which is comprised of some of the MIREC study investigators and co-investigators.
- Long-term storage of these valuable samples in the biobank will be used for future research on environmental chemicals and maternal and infant health.

Paediatric and Perinatal Epidemiology
Affiliated to the Society for Pediatric and Perinatal Epidemiologic Research

doi: 10.1111/ppe.12061

Study design article

Cohort Profile: The Maternal-Infant Research on Environmental Chemicals Research Platform

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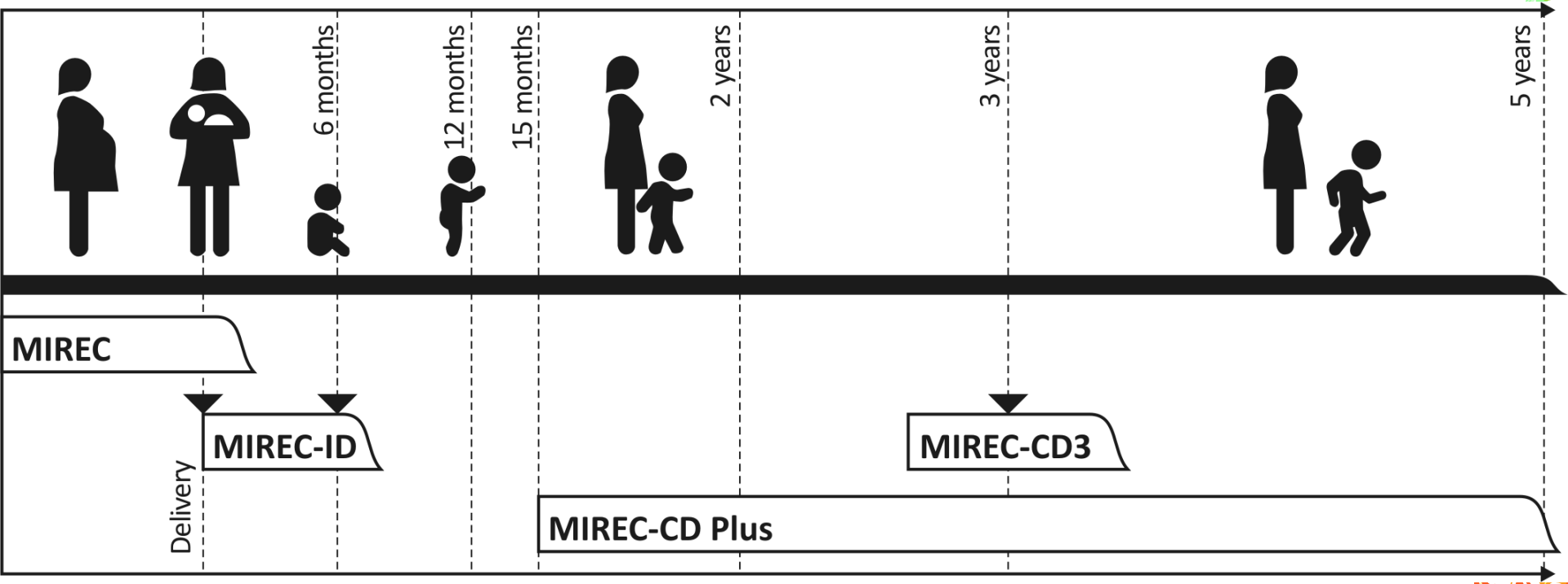
6 months
12 months
15 months
2 years
3 years
5 years
MIREC
Delivery
MIREC-ID
MIREC-CD3
MIREC-CD Plus

Looking for…

- Opportunities to increase longer follow-up, and additional research questions

Acknowledgments

- Participants
- Principal investigators
- Co-investigators
- Site nurses and research assistants
- Study Coordinating Centre

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Instituts de recherche en santé du Canada


MIREC
Maternal-Infant Research
on Environmental Chemicals
Étude mère-enfant
sur les composés chimiques
de l'environnement
Funding agencies
Health Canada
Ontario Ministry of the Environment
Canadian Institutes of Health Research
Project initiated by Health Canada,
in collaboration with Hôpital Ste-Justine
Health Canada
Santé Canada
Ontario
IRSC CIHR
CHU Sainte-Justine
Le centre hospitalier
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Thank you