Challenges in implementing Perinatal Clinical Studies in Canada: lessons learned

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CIHR sponsored Trials I have led

- The Amniotomy Trial (Fraser et al)
- VBAC Education Trial (Fraser et al)
- The Delayed Pushing Trial (Fraser et al)
- The Amniofusion Trial (Fraser et al)
- International Trial of Antioxidants in the Prevention of Preeclampsia (Fraser et al)

Trials where I've been co-Investigator :

- Structured Early Labour Assessment and

Care by Nurses (SELAN) (Hodnett et al)

- TRIGR (Akerbloom, Knip, Dupré et al)
- Trial of Home versus Hospitalized Care for High Risk Pregnancy (Goulet)
- Quarité trial (ongoing) (Dumont et al)
- Quarisma (ongoing) (Chaillet et al)

‘Impossible to do a RCT of Amniotomy’: Emmanuel Friedman

EFFECT OF EARLY AMNIOTOMY ON THE RISK OF DYSTOCIA IN NULLIPAROUS WOMEN

WILLIAM D. FRASER, M.D., M.SC., SYLVIE MARCOUX, M.D., PH.D., JEAN-MARIE MOUTQUIN, M.D., ANDRÉE CHRISTEN, M.SC., AND THE CANADIAN EARLY AMNIOTOMY STUDY GROUP*

Abstract *Background.* Early amniotomy has been advocated as a means of preventing dystocia, but its efficacy has not been studied prospectively. The purpose of this multicenter study was to determine whether routine early amniotomy reduces the risk of dystocia for nulliparous women in spontaneous labor.

Methods. We studied 925 nulliparous women in labor, who were stratified according to the degree of cervical dilatation (<3 cm vs. ≥3 cm) and randomly assigned to either early rupture of the membranes (amniotomy group) or conservative management of labor (conservative-management group). Dystocia was defined as a period of at least four hours after dilatation of the cervix to 3 cm had been reached during which the mean rate of cervical dilatation was less than 0.5 cm per hour.

utes shorter in the amniotomy group, and there was a trend toward less frequent use of oxytocin among the women assigned to amniotomy (36 percent vs. 41 percent; relative risk, 0.9; 95 percent confidence interval, 0.8 to 1.0). In a stratified analysis, the frequency of dystocia associated with amniotomy was reduced only among women with ≥3 cm initial dilatation. The cesarean-section rate was similar in the two groups (amniotomy, 12 percent; conservative manag

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were no statistically significa

between the infants delivered by the women in the two groups; the measures of an adverse outcome included admission to a neonatal intensive care unit, five-minute Apgar score below 7, and arterial cord-blood pH below 7.2.

Results – Amniotomy Trial

Variable	Amniotomy (N = 462)	Conservative Management (N = 463)	Relative Risk (95% CI)*
	no. (%)		
Dystocia	155 (34)	207 (45)	0.8 (0.6–0.9)
Use of oxytocin	168 (36)	190 (41)	0.9 (0.8–1.0)
Type of delivery			
Spontaneous	266 (58)	280 (60)	—
Vacuum or forceps	140 (30)	133 (29)	—
Cesarean section	56 (12)	50 (11)	1.1 (0.8–1.6)
First stage of labor	38 (8)	31 (7)	1.2 (0.8–1.9)
Second stage of labor	18 (4)	19 (4)	1.0 (0.5–1.8)

*The conservative-management group was used as the reference group. CI denotes confidence interval.

Meta-analysis, amniotomy, nulliparous women

Analysis 1.2. Comparison 1 Amniotomy versus no amniotomy, Outcome 2 Caesarean section.

Review: Amniotomy for shortening spontaneous labour

Comparison: 1 Amniotomy versus no amniotomy

Outcome: 2 Caesarean section

Study or subgroup	Amniotomy n/N	No amniotomy n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Primiparous women					
Fraser 1991	8/47	4/50		3.9 %	2.13 [0.69, 6.60]
Fraser 1993	56/462	50/463		49.9 %	1.12 [0.78, 1.61]
Johnson 1997	19/346	10/254		11.5 %	1.39 [0.66, 2.95]
UK Amniotomy 1994	20/436	23/427		23.2 %	0.85 [0.47, 1.53]
Wetrich 1970	0/16	0/16		0.0 %	Not estimable
Subtotal (95% CI)	**1307**	**1210**		**88.6 %**	**1.13 [0.86, 1.49]**

Total events: 103 (Amniotomy), 87 (No amniotomy)

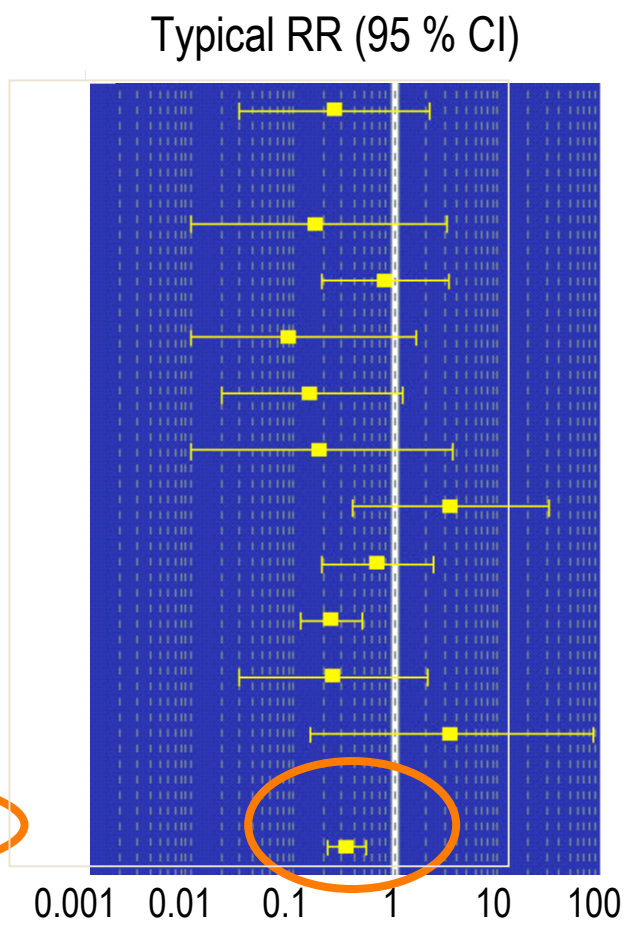
Heterogeneity: $Chi^2 = 2.41$, $df = 3$ ($P = 0.49$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.88$ ($P = 0.38$)

Meta analysis of Amnioinfusion for Meconium Stained Liquor -12 RCTS

Meta-analysis of the effect of amnioinfusion for MSAF on MAS

Trials		AI	Controls
Adams	1989	1 / 17	4 /18
Sadovsky	1989	0 / 19	0 / 21
Wenstrom	1989	0 / 36	3 / 44
Llagan	1992	3 / 38	4 / 40
Macri	1992	0 / 85	5 / 85
Cialone	1994	1 / 47	8 / 58
Eriksen	1994	0 / 65	2 / 59
Spong	1994	3 / 43	1 / 50
Hofmeyr	1998	4 / 162	6 / 163
Mahomed	1998	10 / 323	42 / 329
Moodley	1998	1 / 30	4 / 30
Alvarez	1999	1 / 53	0 / 62
TOTAL		**24 / 918**	**79 / 959**



Unethical to do a RCT of Amnioinfusion?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Amnioinfusion for the Prevention of the Meconium Aspiration Syndrome

William D. Fraser, M.D., Justus Hofmeyr, M.D., Roberto Lede, M.D., Gilles Faron, M.D., Sophie Alexander, M.D., François Goffinet, M.D., Arne Ohlsson, M.D., Céline Goulet, Ph.D., Lucile Turcot-Lemay, M.D., Ph.D., Walter Prendiville, M.D., Sylvie Marcoux, M.D., Ph.D., Louise Laperrière, M.Sc., Chantal Roy, M.Sc., Stavros Petrou, Ph.D., Hai-Rong Xu, M.Sc., and Bin Wei, M.Sc., for the Amnioinfusion Trial Group*

Table 3. Distribution of Primary Outcomes and Other Indicators of Perinatal Status, According to Study Group.*

Outcome or Indicator	Amnioinfusion (N=986)	Control (N=989)	Relative Risk (95% CI)
	no. (%)		
Primary outcomes			
Perinatal death or meconium aspiration syndrome	44 (4.5)	35 (3.5)	1.26 (0.82–1.95)
Perinatal death	5 (0.5)	5 (0.5)	1.00 (0.29–3.45)
Moderate or severe meconium aspiration syndrome			
According to clinical criteria†	43 (4.4)	31 (3.1)	1.39 (0.88–2.19)
On chest radiography‡	19 (1.9)	13 (1.3)	1.47 (0.73–2.95)
Neonatal resuscitation			
Oropharyngeal suctioning§	921 (93.6)	941 (95.3)	0.98 (0.96–1.00)
Laryngoscopy§	236 (24.0)	254 (25.8)	0.93 (0.80–1.08)
Suctioning of meconium below the cords	54 (5.5)	70 (7.1)	0.77 (0.55–1.09)
Any resuscitation	303 (30.7)	322 (32.6)	0.94 (0.83–1.07)
Oxygen only	205 (20.8)	213 (21.5)	—
Ventilation with bag and mask	79 (8.0)	90 (9.1)	—
Intubation with ventilation	19 (1.9)	19 (1.9)	—
Intubation of infant on departure from delivery room	7 (0.7)	7 (0.7)	1.00 (0.35–2.84)

Table 3. The effect of AI on the risk of MAS

Study	Treatment	Control	RR (95% CI)
	n/N	*n/N*	
Standard peripartum surveillance			
Sadovsky *et al.*[35]	0/19	0/21	—
Wenstrom and Parsons[37]	0/36	3/44	0.17 (0.01–3.26)
Macri *et al.*[32]	0/85	5/85	0.09 (0.01–1.62)
Cialone *et al.*[28]	1/47	8/58	0.15 (0.02–1.19)
Eriksen *et al.*[29]	0/65	2/59	0.18 (0.01–3.71)
Spong *et al.*[36]	3/43	1/50	3.49 (0.38–32.32)
Hofmeyr *et al.*[30]	4/162	6/163	0.67 (0.19–2.33)
Moodley *et al.*[34]	1/30	4/30	0.25 (0.03–2.11)
Puertas *et al.*[17]	3/103	4/103	0.75 (0.17–3.27)
Fraser *et al.*[16]	43/986	31/989	1.39 (0.88–2.19)
Subtotal*	55/1576	64/1602	0.59 (0.28–1.25)
Limited peripartum surveillance			
Mahomed *et al.*[33]	10/323	42/329	0.24 (0.12–0.48)
Rathore *et al.*[18]	0/100	1/100	0.33 (0.01–8.09)
Subtotal**	10/423	43/429	0.25 (0.13–0.47)
Total* **	65/1999	107/2031	0.47 (0.22–0.99)

*$\chi^2 = 14.32$, test for heterogeneity $P = 0.07$, $I^2 = 44.1\%$.
**$\chi^2 = 0.04$, test for heterogeneity $P = 0.85$, $I^2 = 0\%$.
***$\chi^2 = 27.66$, test for heterogeneity $P = 0.002$, $I^2 = 63.8\%$.

A trial of KT for an an approach to care that was not based on strong evidence:

Randomized controlled trial of a prenatal vaginal birth after cesarean section education and support program

William Fraser, MD, MSc,[a] Elizabeth Maunsell, PhD,[b] Ellen Hodnett, RN, PhD,[c] Jean-Marie Moutquin, MD, MSc,[a] and the Childbirth Alternatives Post-Cesarean Study Group

Quebec, Quebec, and Toronto, Ontario, Canada

OBJECTIVE: Our objective was to assess whether, for women with previous cesarean section, a prenatal education and support program promoting vaginal birth after cesarean delivery increases the probability of vaginal delivery.

Vitamins C and E for prevention of Preeclampsia

RESEARCH www.AJ

OBSTETRICS

An international trial of antioxidants in the prevention of preeclampsia (INTAPP)

Hairong Xu, MD, MSc; Ricardo Perez-Cuevas, MD, PhD; Xu Xiong, MD, PhD; Hortensia Reyes, MD, PhD; Chantal Roy, MSc; Pierre Julien, PhD; Graeme Smith, MD, PhD; Peter von Dadelszen, MBChB, DPhil; Line Leduc, MD; François Audibert, MD, PhD; Jean-Marie Moutquin, MD, MSc; Bruno Piedboeuf, MD; Bryna Shatenstein, PhD; Socorro Parra-Cabrera, PhD; Pierre Choquette, MD; Stephanie Winsor, MD; Stephen Wood, MD; Alice Benjamin, MD; Mark Walker, MD, MSc; Michael Helewa, MD; Johanne Dubé, MD; Georges Tawagi, MD; Gareth Seaward, MD; Arne Ohlsson, MD, MSc; Laura A. Magee, MD, MSc; Femi Olatunbosun, MD; Robert Gratton, MD, MSc; Roberta Shear, MD; Nestor Demianczuk, MD; Jean-Paul Collet, MD, PhD; Shuqin Wei, MD, PhD; William D. Fraser, MD, MSc; and the INTAPP study group

RESULTS - INTAPP

TABLE 2. Primary outcomes

Characteristic	Vitamins C and E n = 1167	Placebo n = 1196	RR (95% CI)	*P*
GH and its adverse conditions [a]	118 (10.11)	122 (10.20)	0.99 (0.78–1.26)	.94
GH	253 (21.68)	249 (20.82)	1.04 (0.89–1.22)	.61
Preeclampsia	69 (5.95)	68 (5.71)	1.04 (0.75–1.44)	.81
Eclampsia	1 (0.10)	0	–	.50
Diastolic pressure ≥110 mm Hg	32 (2.74)	27 (2.26)	1.21 (0.73–2.01)	.45
Systolic pressure ≥160 mm Hg	53 (4.54)	68 (5.69)	0.80 (0.56–1.13)	.21
Hematocrit <24%	3 (0.26)	5 (0.42)	0.61 (0.15–2.57)	.50
Blood transfusion	3 (0.26)	6 (0.50)	0.51 (0.13–2.04)	.33
Thrombocytopenia	7 (0.60)	7 (0.59)	1.02 (0.36–2.91)	.96
Elevated liver enzyme levels (AST or ALT >70 U/L)	9 (0.77)	7 (0.59)	1.32 (0.49–3.53)	.58
IUGR (<3rd percentile) [b]	18 (1.54)	15 (1.25)	1.23 (0.62–2.43)	.55
Perinatal death [c]	5 (0.43)	1 (0.08)	5.12 (0.60–43.79)	.10

Lessons Learned from INTAPP

- Phase 3 Trials of medications where the biological mechanisms are not elucidated and where there are no strong phase 2 studies are at high risk of being negative trials.
- Biobanking is a complex endeavour
- Don’t take data quality for granted
- Don’t take competent financial management in centres for granted.

A trial of KT – a complex, evidence based intervention in a complex setting

Trials

BioMed Central

Study protocol

Open Access

QUARITE (quality of care, risk management and technology in obstetrics): a cluster-randomized trial of a multifaceted intervention to improve emergency obstetric care in Senegal and Mali

Alexandre Dumont*[1,2,3,13], Pierre Fournier[2,4], William Fraser[1,3], Slim Haddad[2,4], Mamadou Traore[5], Idrissa Diop[6], Mouhamadou Gueye[7], Alioune Gaye[8], François Couturier[9], Jean-Charles Pasquier[10], François Beaudoin[1,3], André Lalonde[11], Marie Hatem[2] and Michal Abrahamowicz[12]

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Lessons learned from Quarité

- Provides an opportunity to test the SOGC's ALARM in an International setting
- Demonstrates the importance of professional organisations as partners in studying quality of care
- Cluster randomized trials are feasible in underresoursed country settings

NEJM, Bergeron et al.

RAPID DETECTION OF GROUP B STREPTOCOCCI IN PREGNANT WOMEN AT DELIVERY

MICHEL G. BERGERON, M.D., DANBING KE, M.SC., CHRISTIAN MÉNARD, PH.D., FRANÇOIS J. PICARD, PH.D., MARTIN GAGNON, B.SC., MARTHE BERNIER, B.SC., MARC OUELLETTE, PH.D., PAUL H. ROY, PH.D., SYLVIE MARCOUX, M.D., AND WILLIAM D. FRASER, M.D.

ABSTRACT

Background Group B streptococcal infections are an important cause of neonatal morbidity and mortality. A rapid method for the detection of this organism in pregnant women at the time of delivery is needed to allow early treatment of neonates.

were fatal.[2] Infants who have such infections may require prolonged hospitalization, and those who survive may have mental retardation or visual loss. Among pregnant women, the prevalence of colonization with group B streptococci ranges from 15 to 40 percent.[1] Women who are carriers are also at risk for severe in-

DSMB contribution

- Caffeine for Apnea of Prematurity (CAP) (Schmidt) (DSMB member)
- TIPP (Indomethecin) trial (Schmidt) (DSMB member)
- Canadian Oxygen Trial (Schmidt, DSMB Chair)

Summary: Lessons learned from Clinical Trials

- In TRIALS - Less is More (get primary objective) (INTAPP)
- Data management team is critical (INTAPP)
- TRIAL Coordinator is just as critical
- Be on top of ethical issues and anticipate results of parallel trials (INTAPP, COT)

Summary: Lessons learned

- Monitoring is critically important (Amnioinfusion, INTAPP) :
  - don’t take data quality for granted,
  - don’t take competence in financial managment for granted.
- Large trials on medical treatments for which there are no clear biological mechanisms are high risk of being negative trials (INTAPP)

Lessons learned

- Maintain close relationship with funding agency – keep them **informed**
- International Collaboration between Formal networks is a political challenge; international collaborations with scientists you can trust is the way to go, but infrastructure is fragile and can change rapidly.

Lessons learned trials

- Centres where prenatal obstetrical care is widely distributed in private clinics and where there is no common **'Point of Contact'** in early pregnancy present a special problem.

- The infrastructure to support academic trials in the perinatal network in Canada is limited and depends on the good will of 1 or 2 individuals in most centres.

Cohort Studies

- Why cohort studies?
  - Many important research questions cannot be addressed through clinical trials
  - Ex. Ethical issues – cannot randomize women and children to certain exposures of interest
  - Need life course approach with long term follow-up
  - Unique challenges of cohort studies: confounding, measuring exposures and measuring confounders,

MIREC

Maternal-Infant Research
on Environmental Chemicals

Project description

Funding Agencies

Health Canada
Santé Canada

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

Ontario

Investigators

Principal Investigators:

Tye Arbuckle, PhD	Senior Epidemiologist & Research Scientist, Health Canada
William D. Fraser, M.D	Professor and Chair Obstetrics and Gynecology Université de Montréal & CHU Ste-Justine

Co-investigators:

Jean-Philippe Weber, Melissa Legrand, Premkumari Kumarathasan, Renaud Vincent, Zhong-Cheng Luo, Adrienne Ettinger, Robert Platt, Grant Mitchell, Kevin Cockell, Maya Villeneuve, Sheryl Tittlemier, Pierre Julien, Denise Avard, Nick Hidiroglou, Hope Weiler, Alain LeBlanc, **Site Investigators:** Peter von Dadelszen (Vancouver), Michael Helewa (Winnipeg), Mathiew Sermer (Toronto), Warren G. Foster (Hamilton), Gregory Ross and Paul Fredette (Sudbury), Graeme Smith (Kingston), Mark Walker (Ottawa), Roberta Shear (Montreal), and Linda Dodds (Halifax).

Study coordinating centre

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant

Pour l'amour des enfants

Université de Montréal

CHU Ste-Justine
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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

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. Suzanne Tough

03 St-Boniface Hospital, **Winnipeg** - Dr. Michael Helewa & The University of Manitoba

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

09aCHU Ste-Justine, **Montreal** - Dr. William Fraser

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

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

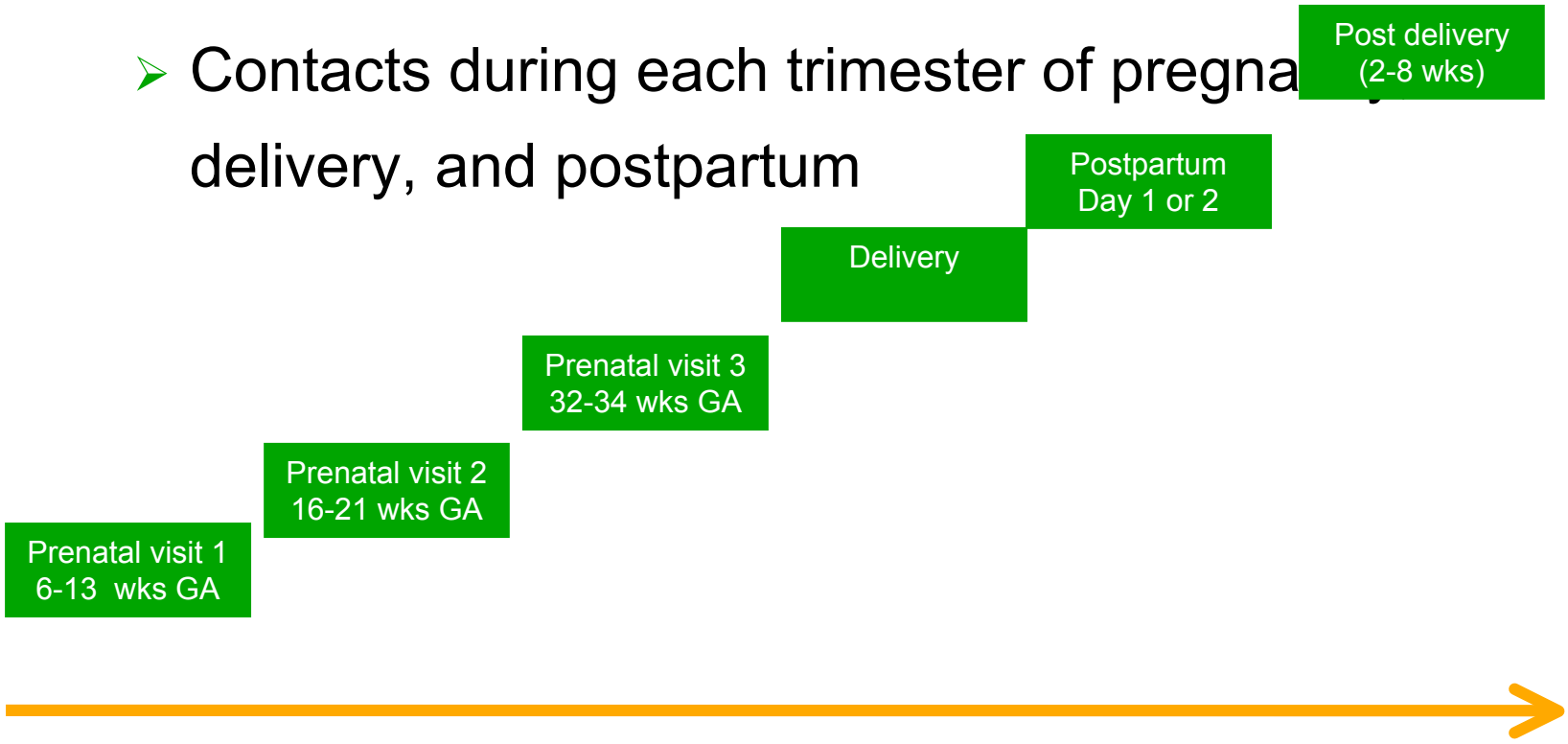
Study population
Eligibility criteria

- Inclusion criteria

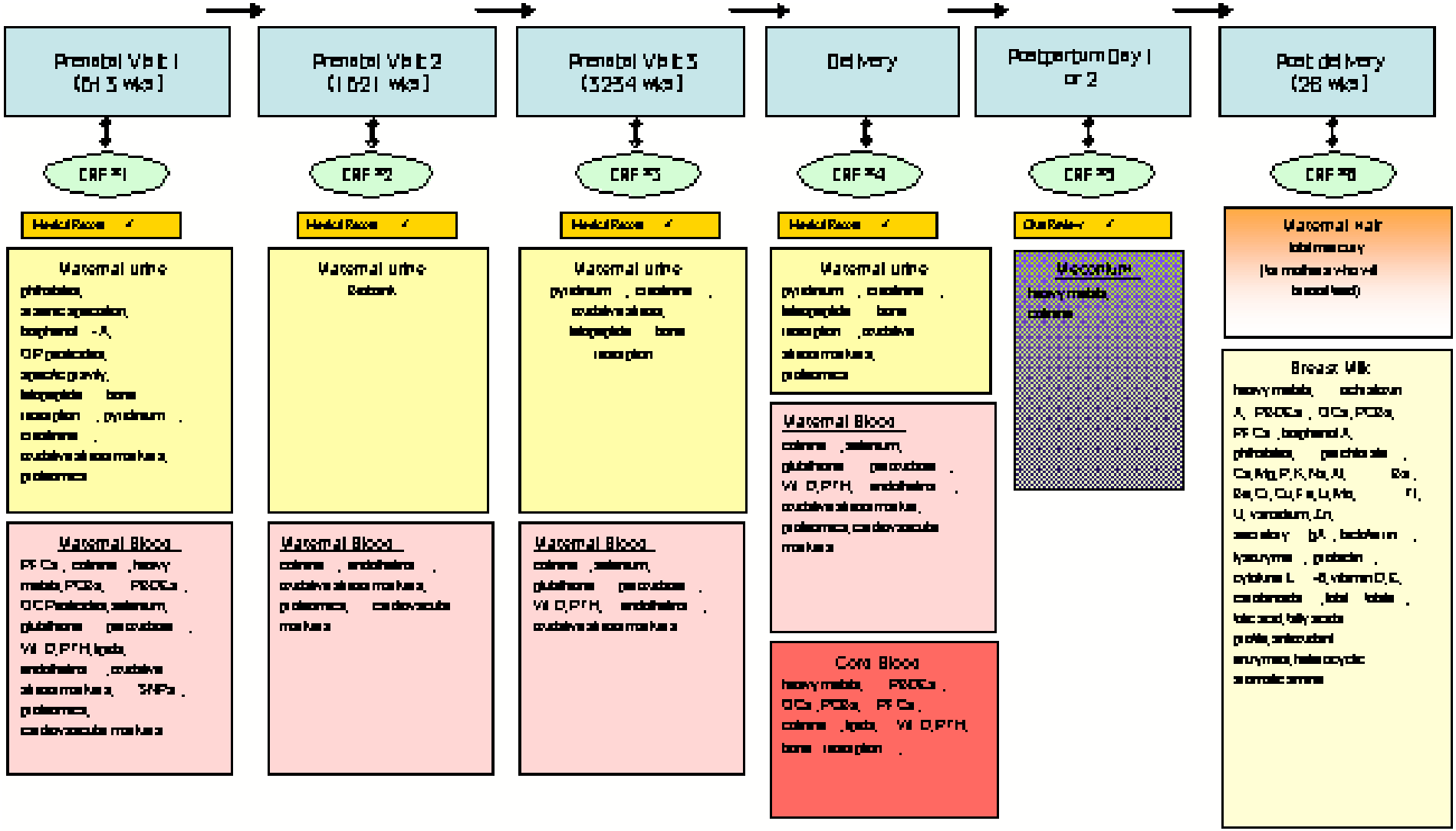
1. The woman is pregnant between $6^{0/7}$ and $13^{6/7}$ completed weeks
2. Age ≥ 18 years
3. Speaks a language known by the medical staff (French or English)
4. Plans to deliver in a study participating hospital
5. The woman is able to understand and sign a consent form

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

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

Why cohort studies?

Challenges for MIREC

- Which are the priority chemicals to be measured?
- Which chemicals are likely to be stable over time and which chemicals need repeat measurement?
- Exploring disease mechanisms: if we find an association between an exposure and a trait, how do we select the pathways to be explored?

Réseau intégré de recherche en périnatalité du Québec et de l'est Ontario/

Integrated Research Network in Perinatology of Quebec and Eastern Ontario. (IRNPQEO)

Financé par les IRSC et la FCI dans le cadre du programme des Initiatives de recherche clinique en avril 2008

Researchers IRNPQEO

Chercheur Principal :

- Dr. William Fraser - Université de Montréal

Co- Chercheurs principaux :

- Lise Dubois - Université d'Ottawa
- Zhong-Cheng Luo - Université de Montréal
- Jacques Michaud - Université de Montréal
- Jean-Marie Moutquin - Université de Sherbrooke
- Gina Muckle - Université Laval
- Jean Seguin - Université de Montréal
- Margaret Somerville - Université McGill
- Jacquetta Trasler - Université McGill
- Richard E. Tremblay - Université de Montréal

Mission du réseau IRNPQEO et de son programme de recherche

Servir de catalyseur pour:

- Increase the quality of perinatal research in Québec and in Canada
- Train a new generation of researchers in a ‘4 pillar’ environment
- Create a provincial – regional model of perinatal research that will lead to innovations and that will ensure that care is evidence based.

Collaborations:

RUIS Université de Montréal
18 delivery units
> 27 000 deliveries / Year

CHU Ste-Justine
> 3 200 deliveries / Year
Expertise
- Genetics / epigenetics
- Neurodevelopment
- Cardiovascular disorders
- Metabolism / growth
- Psycho-socio economic
- Environmental exposures
- Artificial reproductive tech.

Network pillars

Clinical research
Methodological development
Technical support
- Clinical study reports
- Human resources
- Data-mining

Data-bank
Data-management

Bio banks
Laboratories

Training
Student
Clinical researchers
- Clinical research
- Biostatistics
- Bioethics
- Knowledge translation
- Evaluation of health program
- Training of qualified personnel

Social policies

Bioethics research group

Knowledge transfer & translation research group

RUIS Université Laval
25 delivery units
> 16 000 deliveries / Year

CHU de Québec (CHUQ)
> 6 200 deliveries / Year
Expertise
- Genetics
- Cardiovascular disorders
- Placental disorders
- Metabolism / growth
- Health service
- Environmental exposures
- ERB base learning

RUIS Université de Sherbrooke
10 delivery units
> 12 000 deliveries / Year

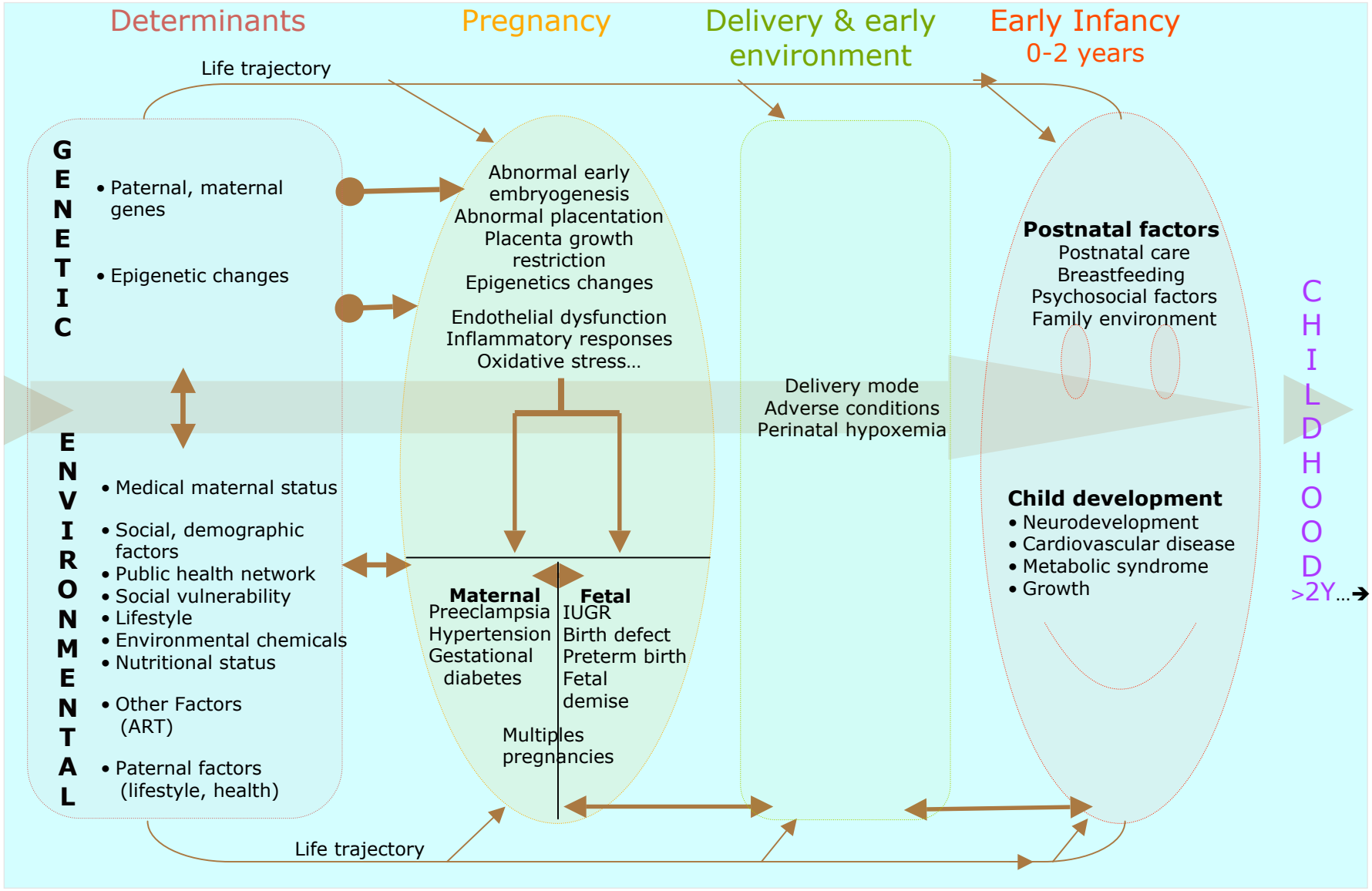
CHU de Sherbrooke
> 2 500 deliveries / Year
Expertise
- Genetics / epigenetics
- Neurodevelopment
- Cardiovascular disorders
- Placental disorders
- Psycho-socio economic
- Clinical epidemiology
- WEB-based learning

University of Ottawa
Perinatal Programme of Eastern Ontario
> 3 500 deliveries / Year

Ottawa General Hospital
> 3 500 deliveries /Year
Expertise
- Epidemiology
- Neurodevelopment
- Health service
- Artificial Reproductive Tech.
- Nutrition

CUSM
> 3 500 deliveries / Year
Expertise
- Epigenetics
- Neurodevelopment
- Stress & psycho-sociology
- Metabolism / growth
- Assisted reproductive tech.
- Biostatistics
- Health service

SCIENTIFIC PARADIGM of IRNPQEO



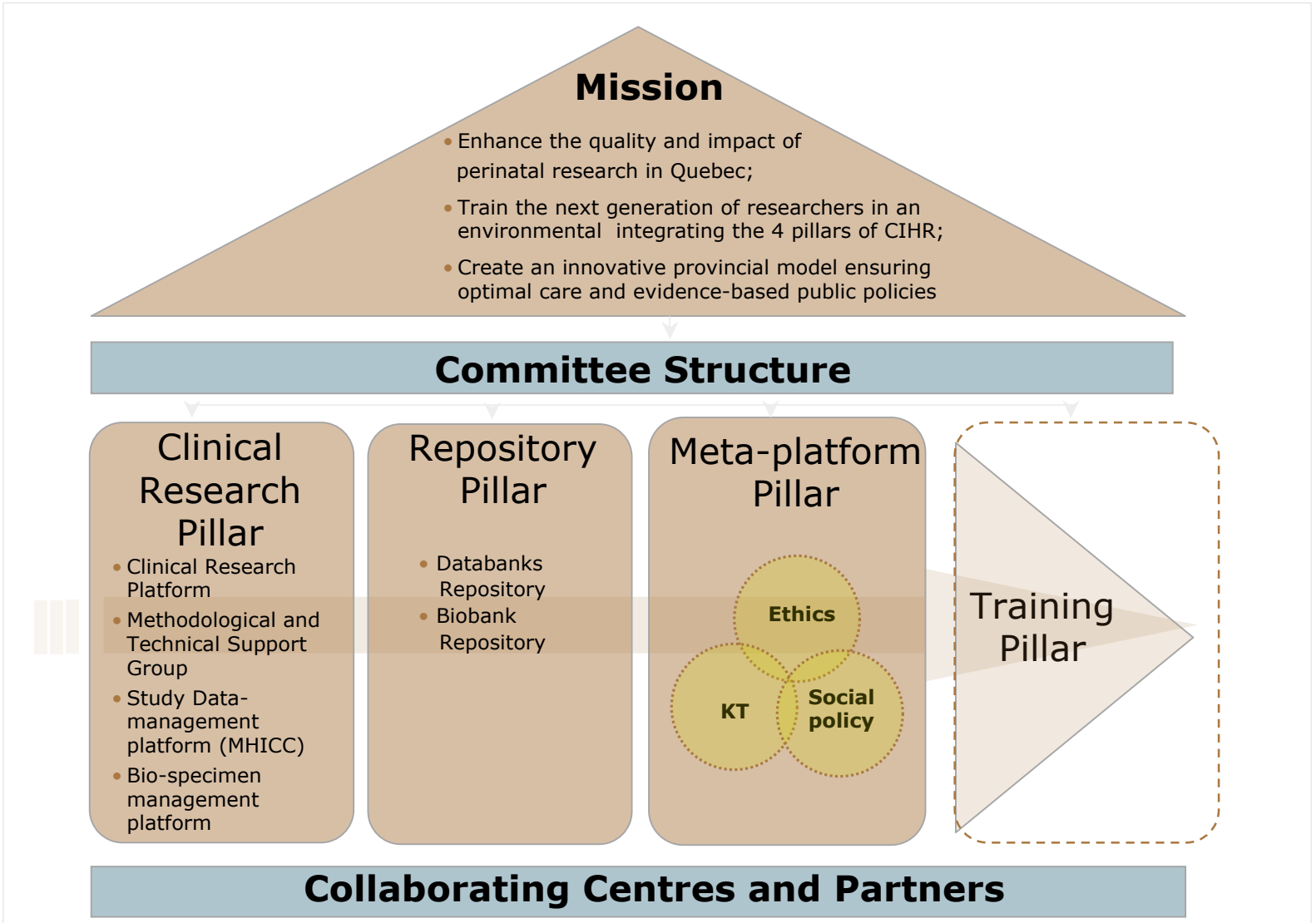
Research Programme - Projets

- Projet 1. ART Cohort
- Projet 2. IUGR sub cohort
- Projet 3. Preterm Birth Subcohort
- Projet 4. Birth Defects Subcohort

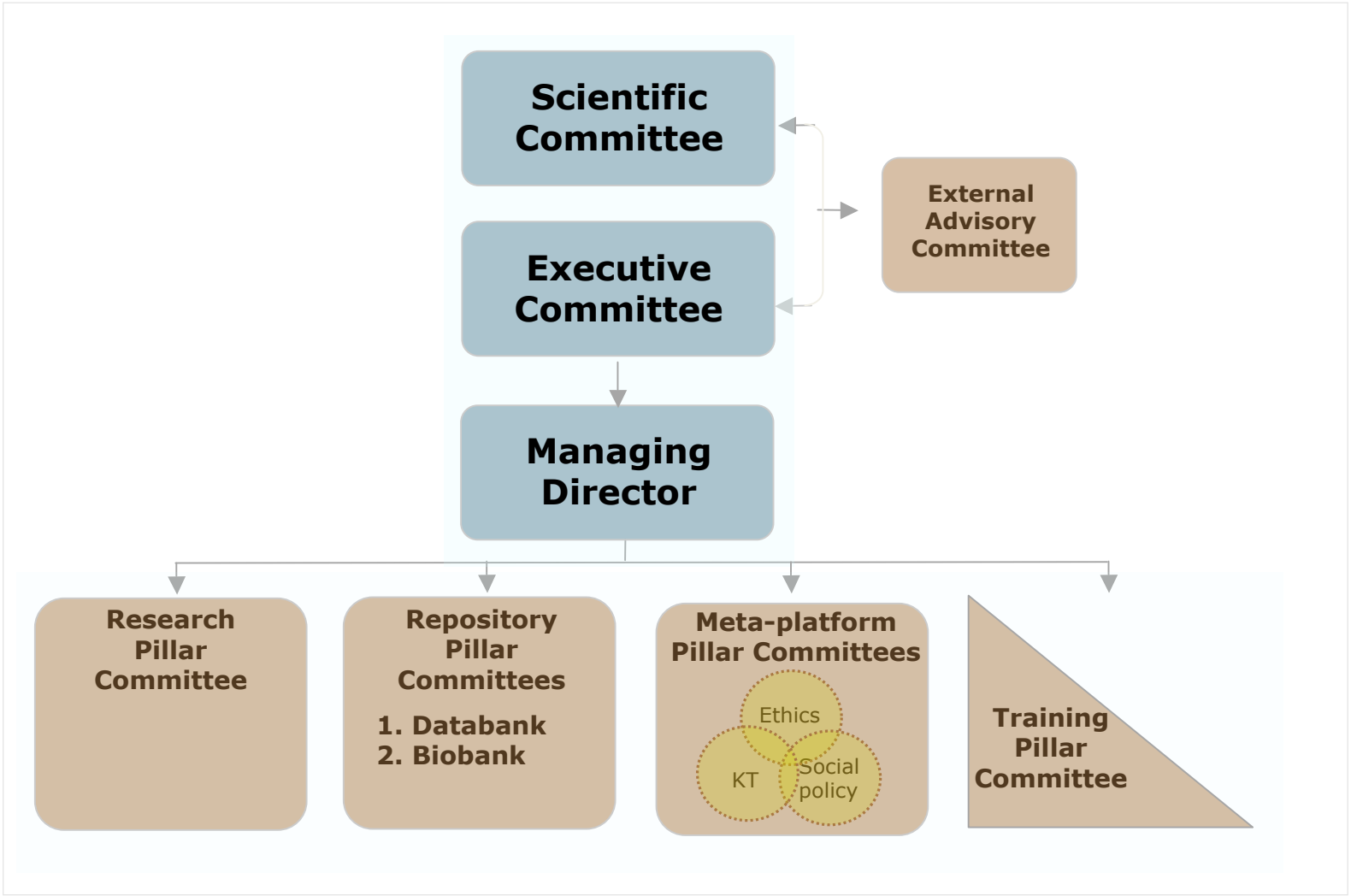
Methodology

- Creation of a cohort of 3000 femmes enceintes
  - From whence our sub cohorts.
  - That will provide our non-exposed patients
- Création of an ART cohort
- Creation of a cohorte of 1000 cases of congential anomalies

Structure of IRNPQ



Comités de l'IRNPQ



Challenges to MIREC and IRNPQEO

- **Governance Policy** : who 'owns' data and who is responsible for biospecimens; ensuring appropriate access to specimens: **NEED STRONG ETHICS**
- **Biobanking:** a complex challenge : start-up cost, space, equipment, technical expertise, maintenance

Lessons learned - Asking the right research questions is the most important

- Set stage (sufficient time, conviviality, key players) for serious and intense debates to identify are the most important scientific questions for the network – this is **the most important step**…..
- The research design solutions will follow….

Challenges for MIREC and IRNPQEO

- Ensuring funding for cohort : traditional funding agencies are not set up to ensure longitudnal follow-up of cohorts outside of the traditional funding cycle: 1 year to start up, 2 years to recruite, 3 years to 2 years of age, end of cycle!!!

Strategic Planning – the NICHD's Model under new Director Dr. Guttmacher

- Extensive Planning Exercize
- Horizon scanning – visioning the **most promising scientific opportunities** for the next decade.
- Set an **ambitious agenda** that inspires the research community
- Think **grandly** and not narrowly.
- Rely on **excellence** - internal and external – in developing vision.

Priority areas identified for visioning workshops:

- Plasticity
- Reproduction
- Development
- Developmental Origins
- Behaviour
- Pregnancy and Pregnancy Outcomes
- Diagnostics and Therapeutics
- Environment
- Cognition

Cross cutting areas:

- Analytic and measurement tools and methods.
- Animal and computational models
- Bioethics- Bioinformattics Bioengineering
- Biotechnology ad bioengineering
- Developmental Lens
- Differences- disparities across populations.

Cross cutting areas

- Epigenetics/meta-genomics
- Functional status
- Global health
- Implementation science, including health economics
- Nutrition
- Prevention/personalized medicine
- Stem cells
- Systems biology
- Training and mentoring

TRENDS

- Research, to be effective, must anticipate changing morbidity and mortality (SARS).
- Greater orientation toward **biological processes rather than disease** (study of precursor states) – **phenotype** will be a **'cloud of biological processes'** (Claude Laberge)
- Need to Take advantage of natural experiments to study Gene-Environment Interactions
- Importance of **behavior** as determinant of reproductive health.

Transdisciplinary approach

- Translational research requires fluency in three languages: clinical medicine, basic science and clinical epidemiology (M. Kramer)

Priorities for Institute Director

- Permanent mechanism for horizon scanning to find convergence of between knowledge generating capacity and public policy needs.
- Developing a strategic plan for getting from A (current) to B (research excellence) by international benchmarks, in 5-7 years

Priorities for Institute Director (2)

- Build cross-institute initiatives.
- Put in place a local, regional and provincial ‘Strategy for Patient Oriented Research’, in collaboration with other institutes.

Thank you! Merci!