Gestational dietary intakes, metabolic abnormalities and human milk hormones

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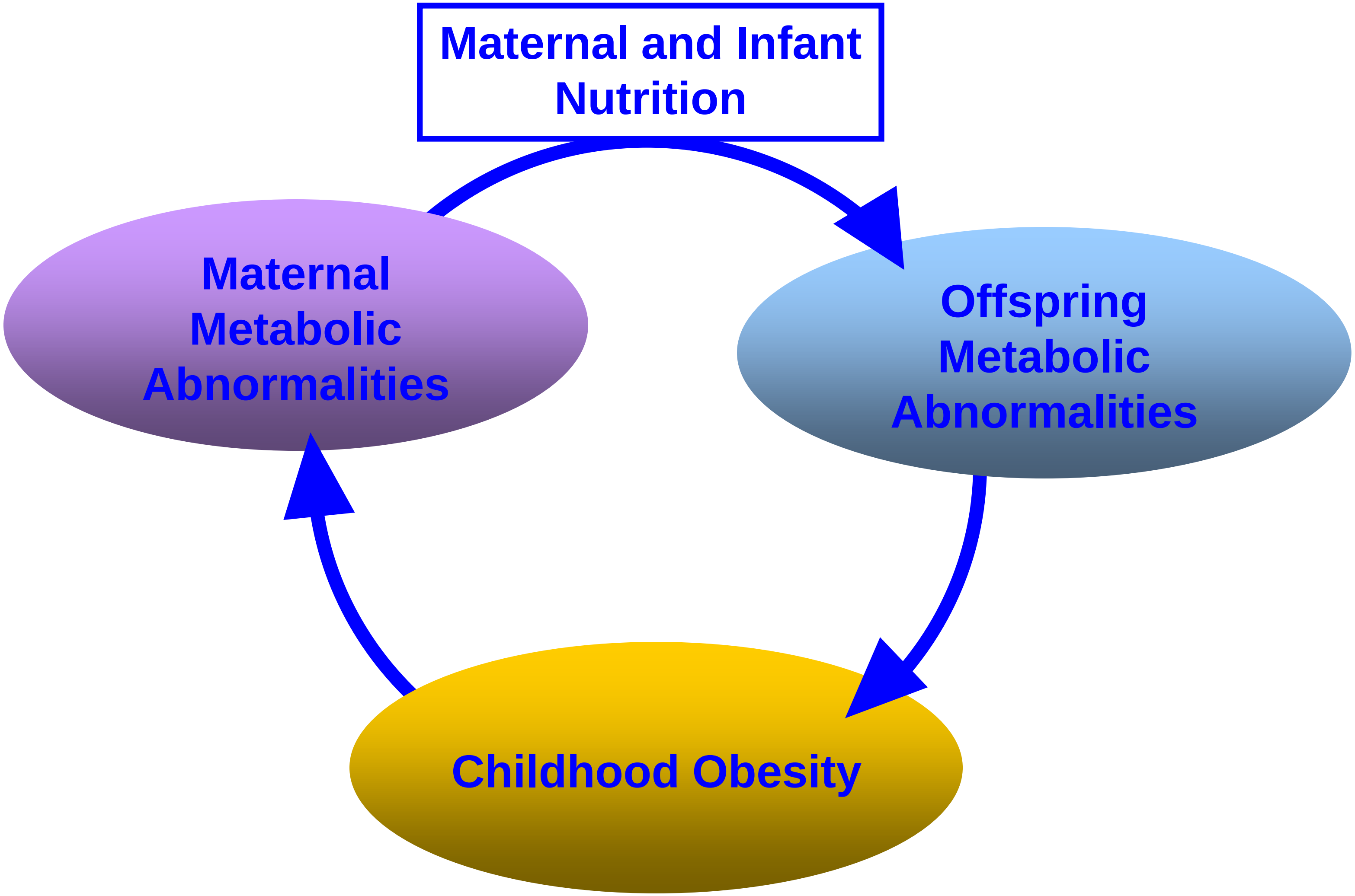
CFDR Breakfast and Research Showcase

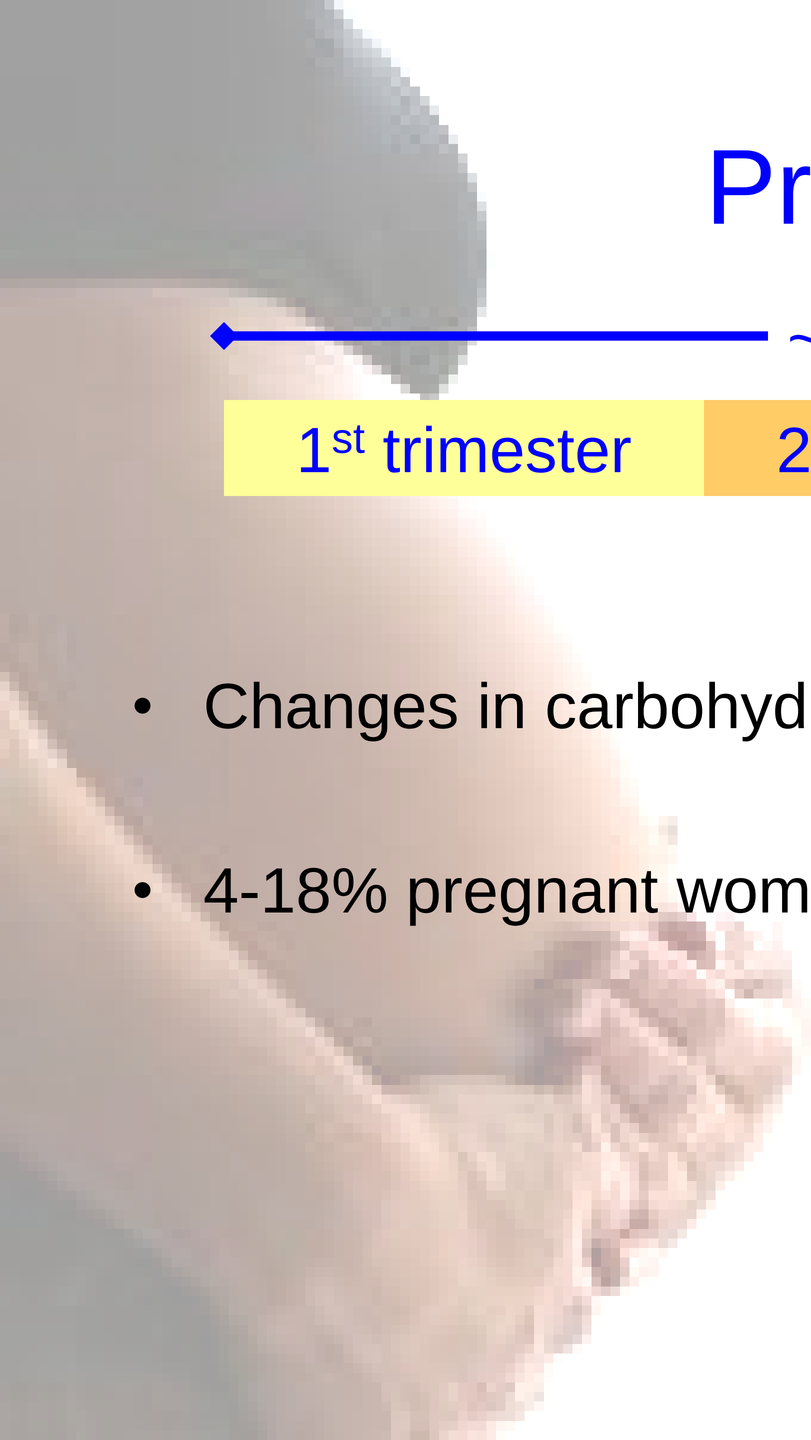
May 2012

SickKids

MOUNT SINAI HOSPITAL
Joseph and Wolf Lebovic Health Complex


Maternal and Infant Nutrition
Maternal Metabolic Abnormalities
Offspring Metabolic Abnormalities
Childhood Obesity

Pregnancy



~40 weeks

1st trimester	2nd trimester	3rd trimester

- Changes in carbohydrate and lipid metabolism
- 4-18% pregnant women develop gestational diabetes

Butte *Am J Clin Nutr* 2000; 71:1256S
CDA *Can J Diabetes* 2008; 32:S1

Consequences of Gestational Diabetes

	Mom	Offspring
pregnancy outcome	•c-section	•macrosomic infant
early postpartum / early life	•lactation performance	•compromised nutrition
long-term	•type 2 diabetes •vascular disease	•obesity •type 2 diabetes

Reece et al *Lancet* 2009;373:1789
Hilson et al *J Hum Lact* 2004;20:18

Dietary Intake and Glucose Metabolism

- Large prospective cohort studies
  - ↑total fat intake and ↑glucose intolerance
  - ↑*trans* fat, ↓polyunsaturated fat and ↑type 2 diabetes

- Clinical studies
  - ↑dietary fiber and ↑insulin sensitivity, ↓type 2 diabetes

Hu *et al. Diabetologia* 2001; 44:805
Weickert *et al. J Nutr* 2008; 138:439

Diet during 2nd Trimester of Pregnancy and Risk of Gestational Diabetes

	RR (95% CI)	p
Substituting 1% fat for CHO	1.1 (1.02-1.10)	0.002

Adjusted for BMI, maternal age, and ethnicity

Saldana *et al. Am J Clin Nutr* 2004; 79:479

Diet during 1st Trimester of Pregnancy and Risk of Gestational Diabetes

PROJECT Viva

A Study of Health for the Next Generation

	OR (95% CI)
Substituting 1% fat for CHO	1.00 (0.96-1.05)

Adjusted for maternal age, pre-pregnancy BMI, ethnicity, previous GDM, history of diabetes in participant’s mother, smoking during pregnancy

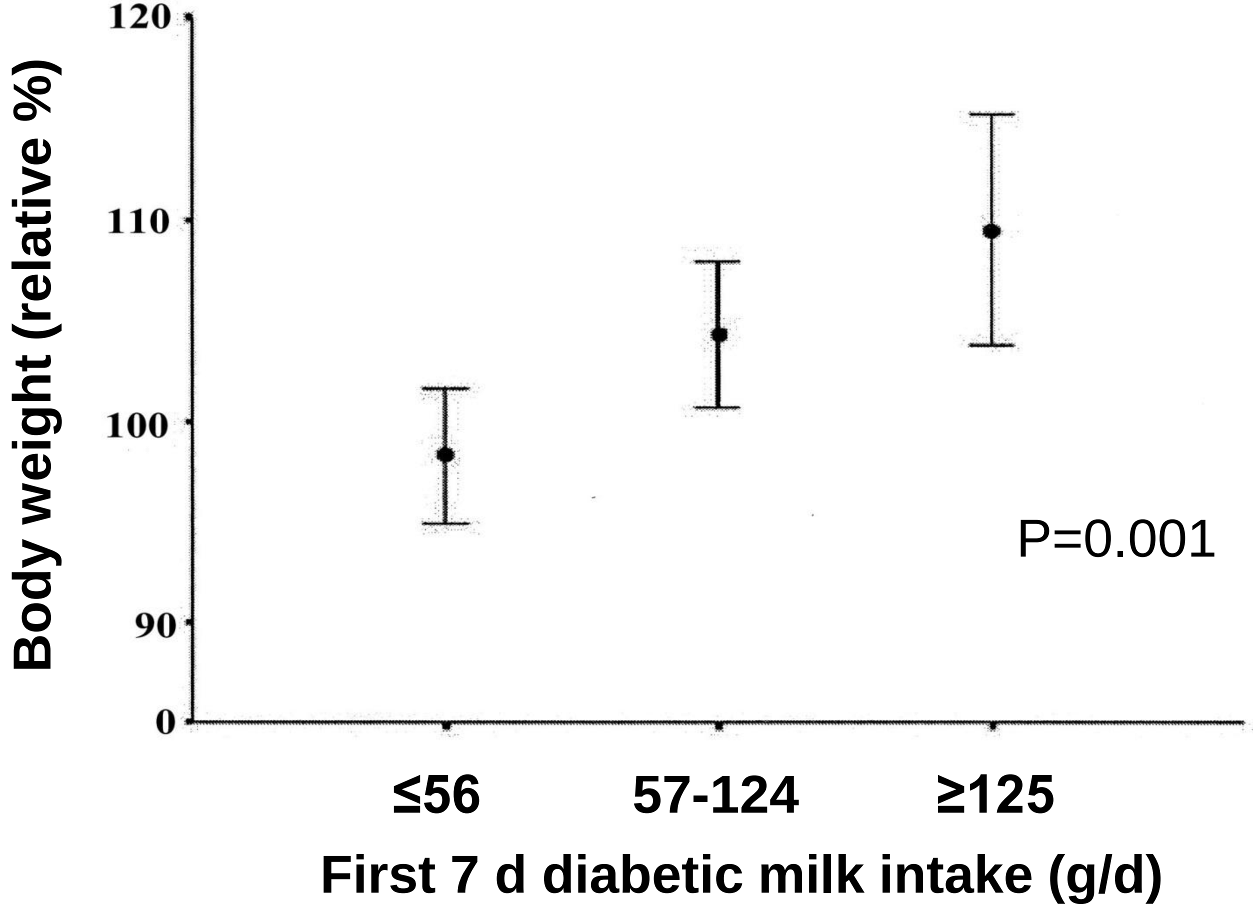
Radesky *et al. Paediatr Perinat Epidemiol* 2008; 22:47

Consequences of Gestational Diabetes

	Mom	Offspring
pregnancy outcome	•c-section	•macrosomic infant
early postpartum / early life	•lactation performance	•compromised nutrition
long-term	•type 2 diabetes •vascular disease	•obesity •type 2 diabetes

Reece *et al. Lancet* 2009; 373:1789
Hilson *et al. J Hum Lact* 2004; 20:18

Milk from women with diabetes and offspring body weight at 2 years



Plagemann *et al. Diabetes Care* 2002; 25:16

Detection of Metabolic Hormones in Human Milk

- Insulin
  - Kulski *et al. Endocrinol Exp* 1983; 17:317
  - Read *et al. Pediatr Res* 1984; 18:133
  - Hamosh *et al. Pediatr Clin North Am* 2001; 48:69

- Adiponectin
  - Martin *et al. Am J Clin Nutr* 2006; 83:1106
  - Bronsky *et al. Clin Chem* 2006; 52:1763
  - Weyermann *et al. Clin Chem* 2006; 52:2095

Knowledge Gaps

1. Only a few reports have investigated the impact of diet during pregnancy on risk of gestational diabetes, and none have studied this question using comprehensive glucose homeostasis profile

2. A number of studies have detected insulin and adiponectin in human milk, but none have investigated the impact of maternal metabolic status assessed during pregnancy on these hormones in milk

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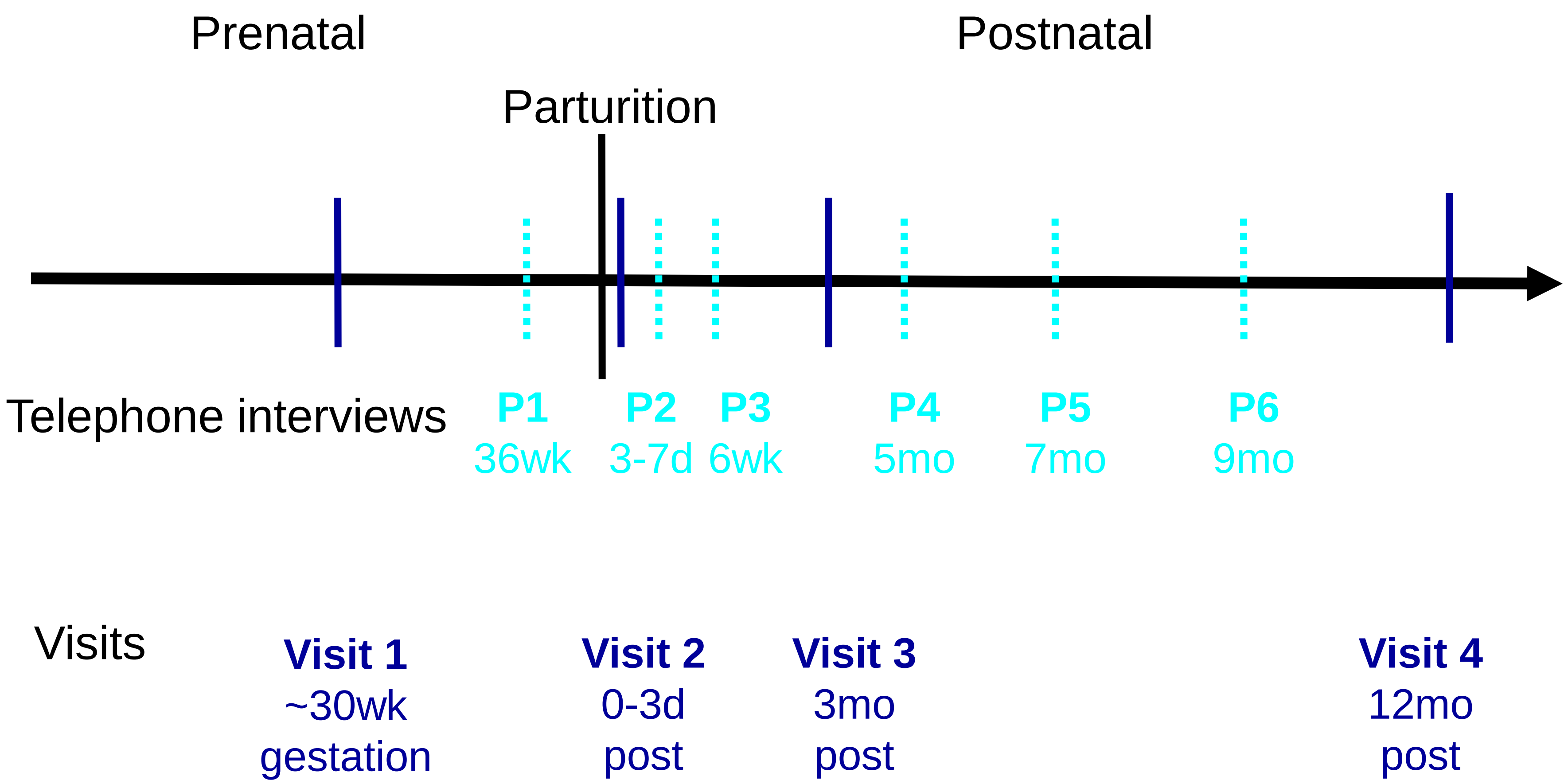
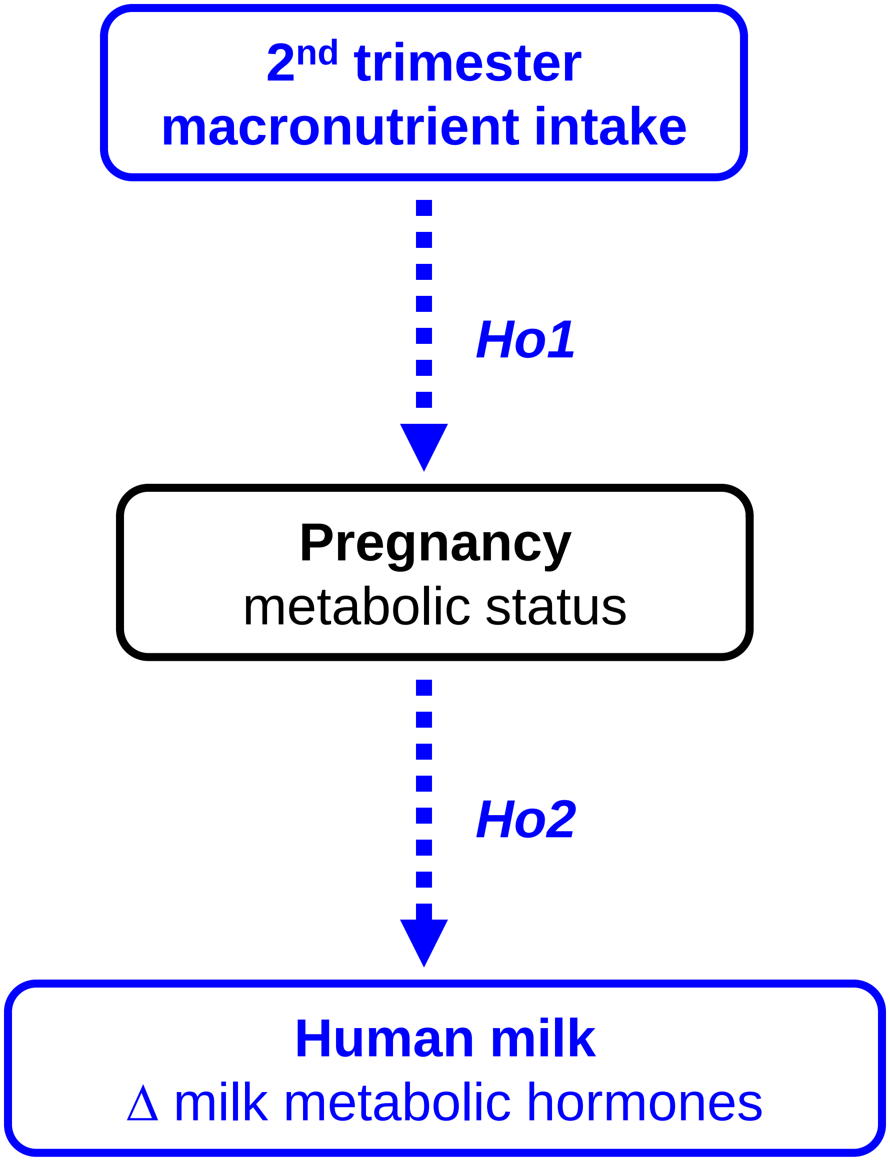
Maternal and Infant Nutrition Study

Scheduled Visits and Interim Interviews



Ley *et al. BMC Public Health* 2010;10:590


2nd trimester
macronutrient intake
Ho1
Pregnancy
metabolic status
Ho2
Human milk
Δ milk metabolic hormones

Methods: Study Participants

March 2009 – July 2010
n=271 pregnant women recruited
≥20 y.o. without diabetes

↓

n=66 excluded

n=56 incomplete 3-h OGTT data at ≥20 wks gestation
n=10 twin pregnancies

↓

n=205
included in the current analysis

Results: Characteristics of participants by GDM status at 30±2.6 wks gestation

	No GDM (n=158)	**GDM (n=47)**
Age (years)	34.3 ± 4.2	35.5 ± 4.5
Ethnicity*		
White	**100 (62.9)**	**22 (47.8)**
Non-White	**58 (36.7)**	**25 (53.2)**
Family history of type 2 diabetes*	**79 (50.0)**	**33 (70.2)**
Pregravid BMI (kg/m^2)	24.7 ± 4.8	26.5 ± 6.6
Nulliparous	90 (57.3)	21 (44.7)

*P<0.05; mean ± SD or n (%)

Ley *et al. Am J Clin Nutr* 2011; 94:1232

Results: Dietary composition and insulin resistance among those with a family history of diabetes[1]

	beta ± SE	p
Energy	-0.0001 ± 0.0002	0.63
% carbohydrate	-0.038 ± 0.023	0.10
% total fat	0.023 ± 0.026	0.37
% saturated fat	0.104 ± 0.057	0.07
% *trans* fat	0.295 ± 0.361	0.42
P : S fat ratio	-0.938 ± 0.551	0.09
Total fibre[2]	-0.031 ± 0.024	0.20
Veggie&fruit fiber[2]	**-0.100 ± 0.029**	**0.0008**

[1]Adjusted for age, ethnicity, pregravid BMI, parity, previous GDM, pregnancy weight gain up to the OGTT, and gestational weeks at the time of OGTT; [2]Additionally for energy intake

Ley *et al. Am J Clin Nutr* 2011; 94:1232

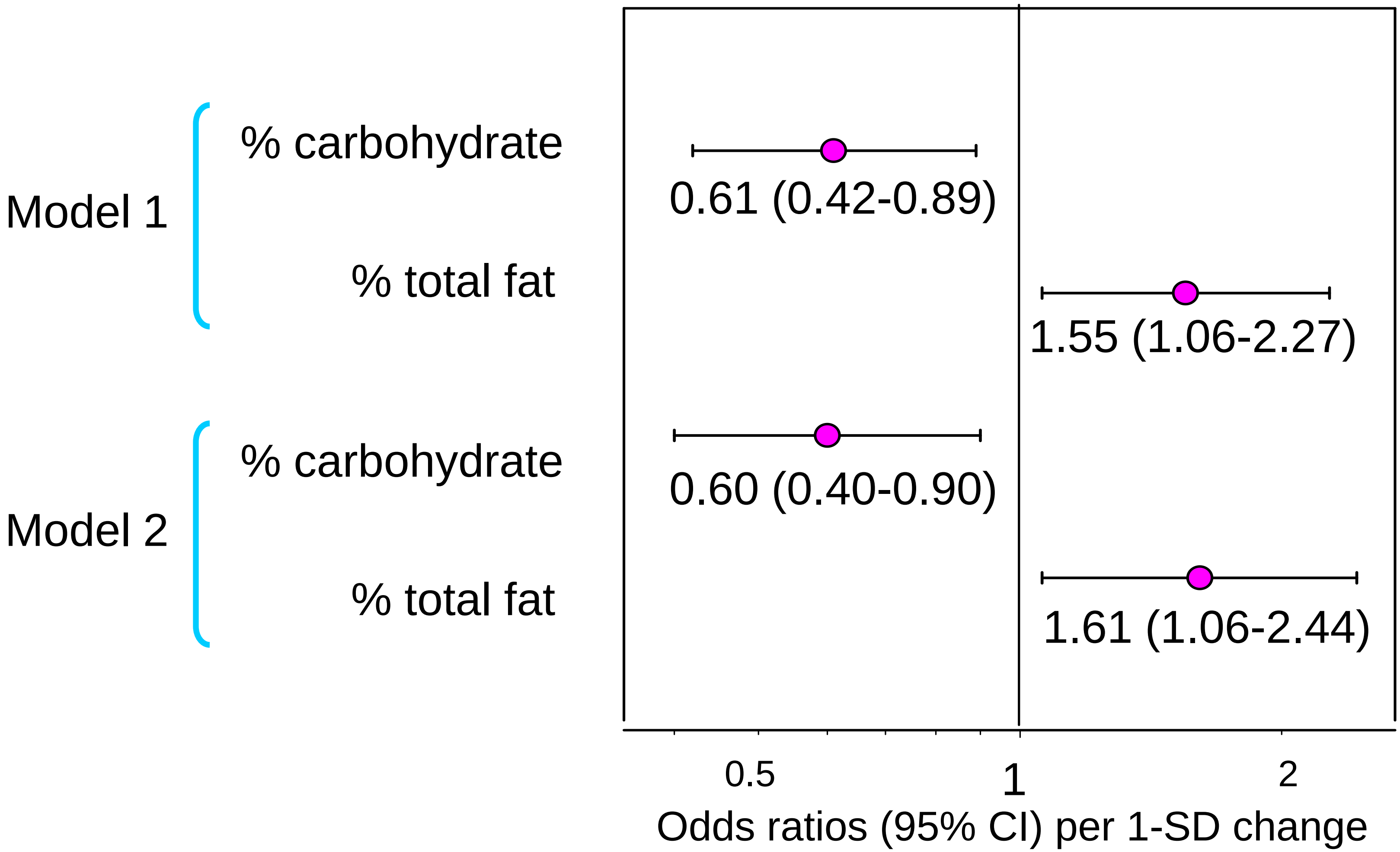
Results: Dietary composition and insulin sensitivity among those with a family history of diabetes[1]

	beta ± SE	p
Energy	0.00003 ± 0.00008	0.73
%carbohydrate	0.010 ± 0.009	0.28
% total fat	-0.0004 ± 0.010	0.97
% saturated fat	-0.020 ± 0.023	0.39
% *trans* fat	0.022 ± 0.143	0.88
P : S fat ratio	0.206 ± 0.220	0.35
Total fibre[2]	0.003 ± 0.009	0.78
Veggie&fruit fiber[2]	**0.029 ± 0.012**	**0.01**

[1]Adjusted for age, ethnicity, pregravid BMI, parity, previous GDM, pregnancy weight gain up to the OGTT, and gestational weeks at the time of OGTT; [2]Additionally for energy intake

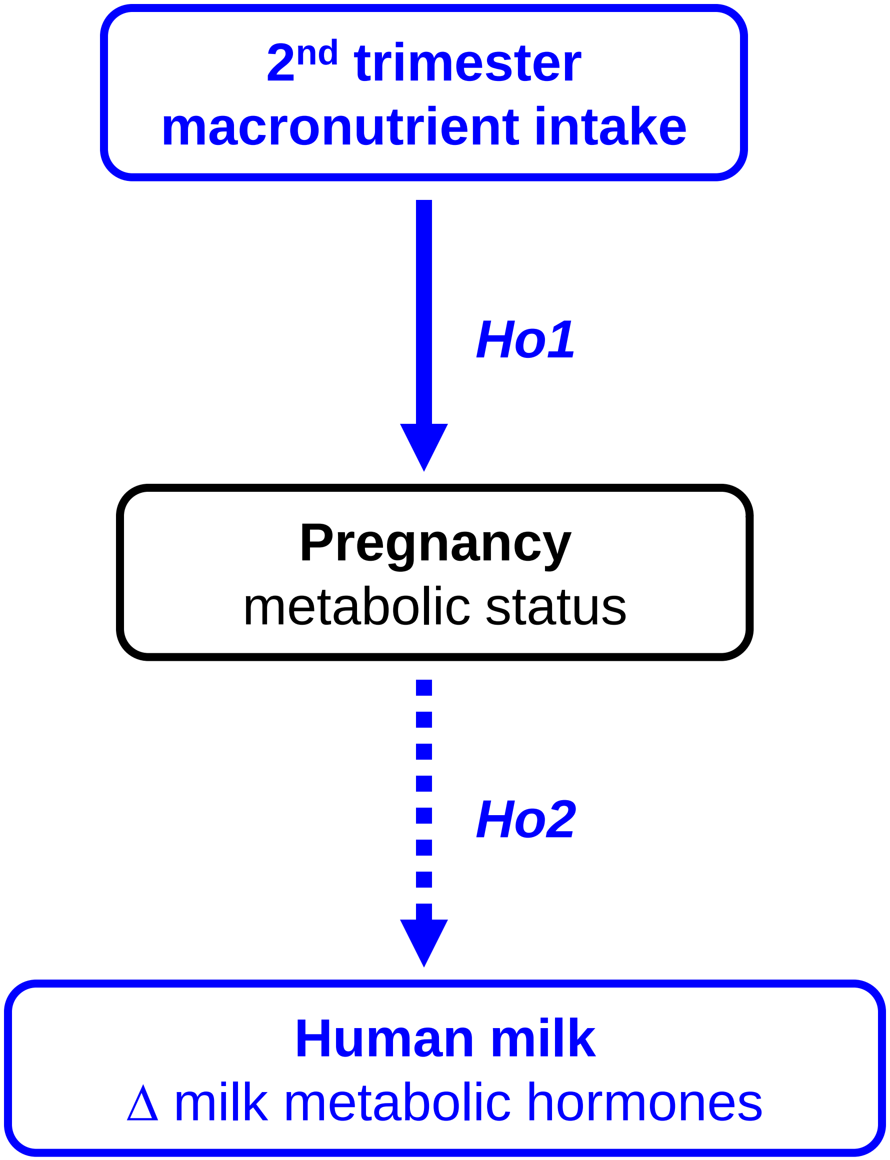
Ley *et al. Am J Clin Nutr* 2011; 94:1232

Results: Macronutrient Intake and Risk for GDM



1. adjusted for age, ethnicity, family history of diabetes, pregravid BMI; 2. additionally for parity, previous GDM, pregnancy weight gain up to the OGTT, and gestational weeks at the OGTT

Ley *et al. Am J Clin Nutr* 2011; 94:1232


2nd trimester
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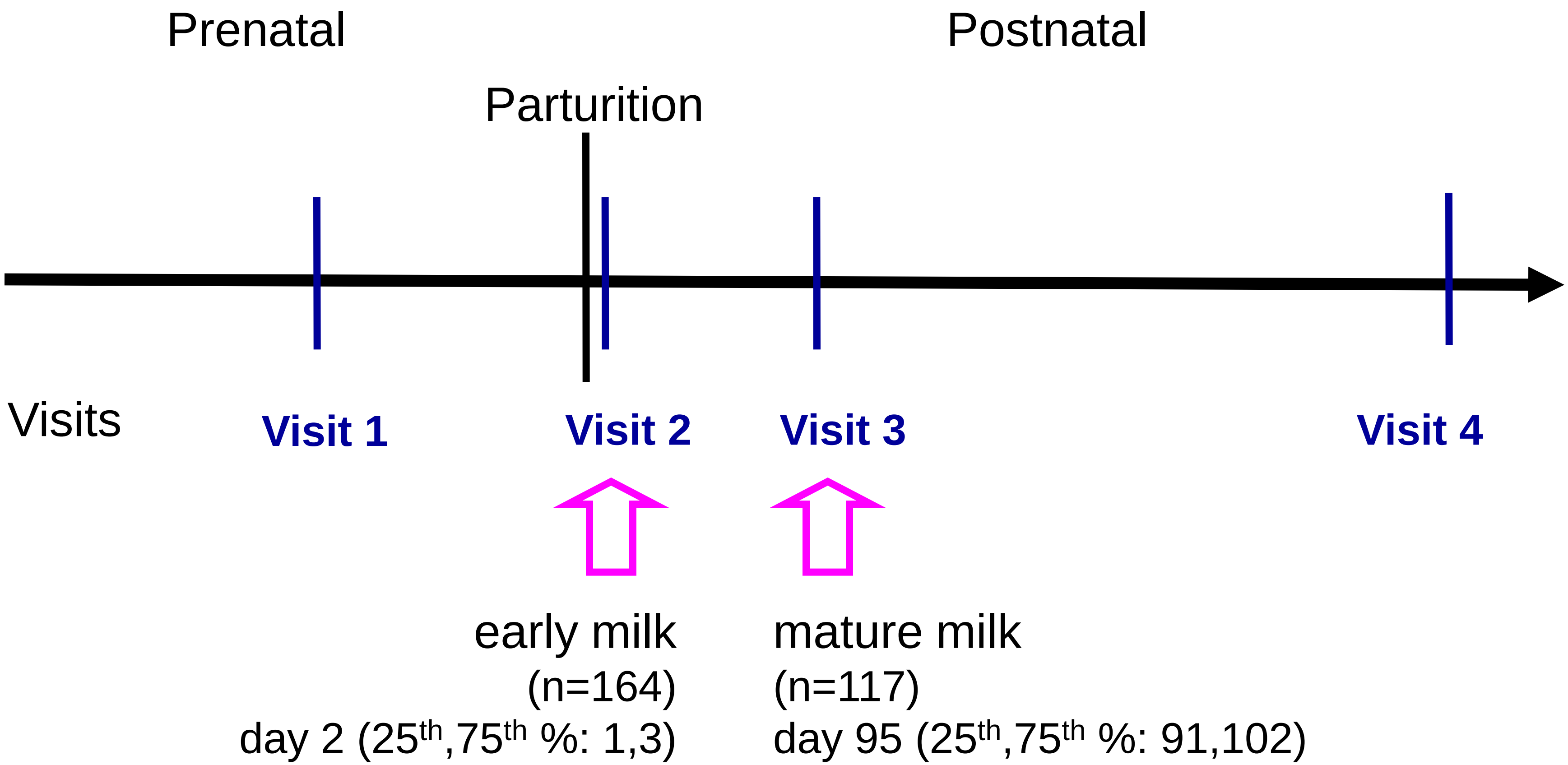
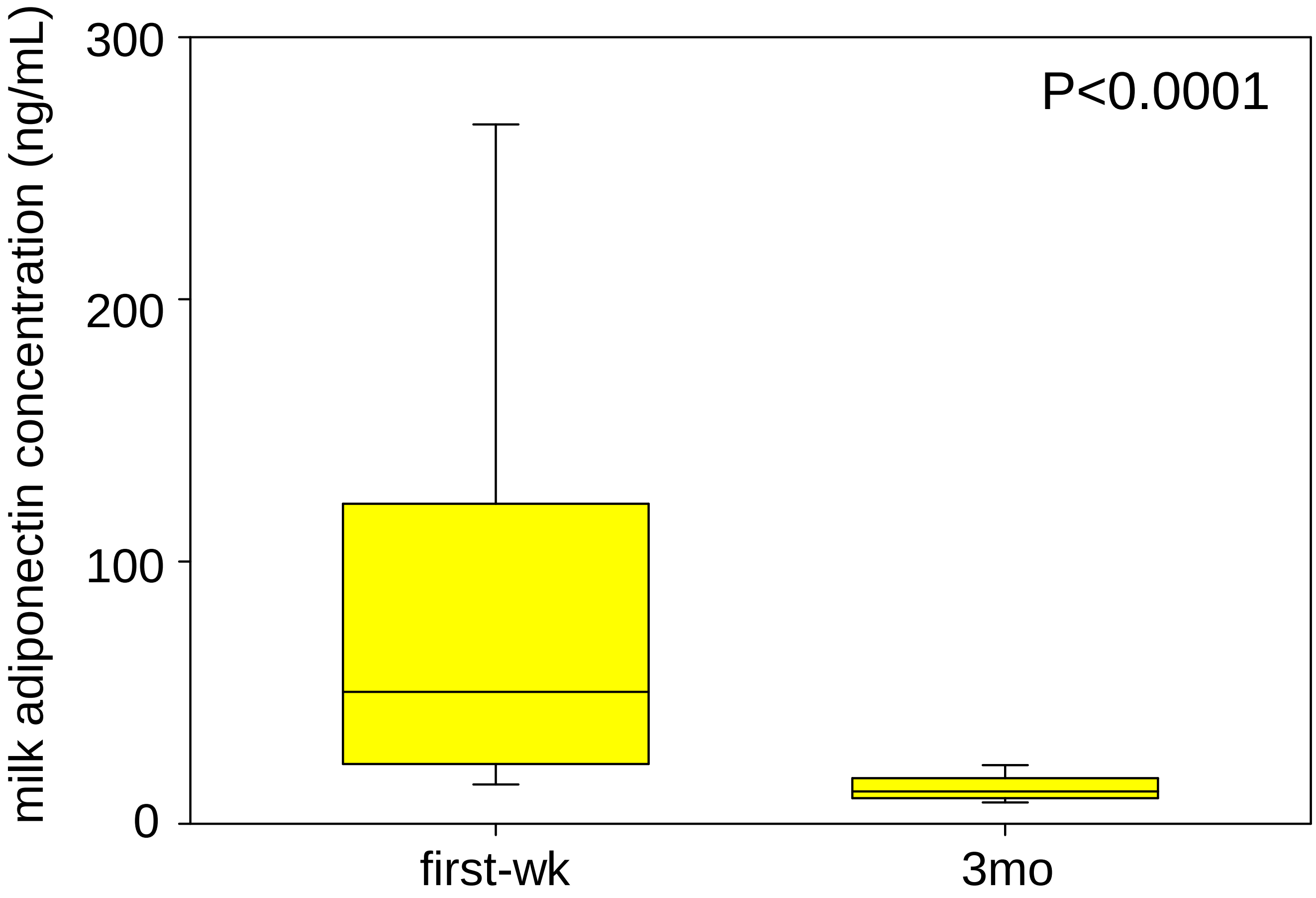
Scheduled Visits



Ley *et al. BMC Public Health* 2010; 10:590

Results: Milk adiponectin concentrations in first-week v. 3-month postpartum

(n=111; paired t test)



Ley *et al. Am J Clin Nutr* 2012; 95:867

Results: Milk insulin concentrations in first-week v. 3-month postpartum

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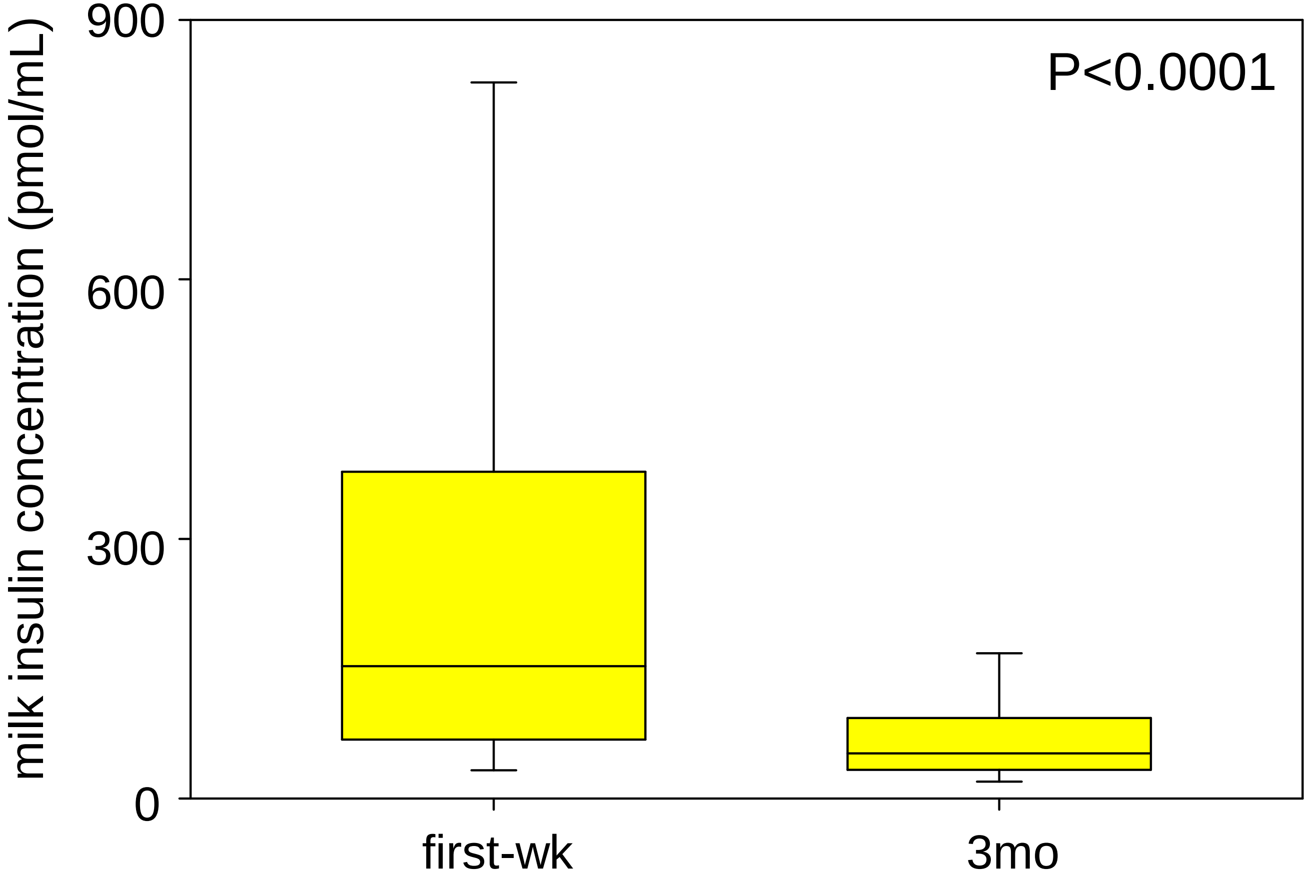


Ley *et al. Am J Clin Nutr* 2012; 95:867

Results: Maternal prenatal metabolic measures and milk adiponectin[1]

	1st week		3mo	
	beta±SE	p	beta±SE	p
Pregravid BMI	0.003±0.014	0.81	-0.019±0.010	0.06
Serum Fasting Glucose	-0.048±0.139	0.73	-0.036±0.060	0.55
Serum HOMA-IR	0.027±0.053	0.61	-0.056±0.035	0.12
Serum ISogtt	-0.088±0.125	0.48	0.071±0.079	0.37
Serum adiponectin	**0.102±0.032**	**0.002**	**0.045±0.020**	**0.03**
Gestational diabetes	-0.129±0.180	0.47	-0.081±0.117	0.49

[1]General linear model analyses were used with adjustment for maternal age, ethnicity, and postpartum time

Ley *et al. Am J Clin Nutr* 2012; 95:867

Results: Maternal obstetrical measures and milk adiponectin[1]

	1st week		3mo	
	beta±SE	**p**	**beta±SE**	**p**
Nulliparous	**0.546±0.146**	**0.0002**	0.138±0.098	0.16
Scheduled C-section[2]	**-0.422±0.186**	**0.02**	-0.231±0.120	0.06
Unscheduled C-section[2]	**0.387±0.162**	**0.02**	-0.158±0.107	0.14
Length of gestation	**0.171±0.058**	**0.004**	-0.027±0.040	0.50

[1]General linear model analyses were used with adjustment for maternal age, ethnicity, and postpartum time
[2]v. spontaneous delivery

Ley *et al. Am J Clin Nutr* 2012; 95:867

Results: Maternal prenatal metabolic measures and milk insulin[1]

	1st week		3mo	
	beta±SE	p	beta±SE	p
Pregravid BMI	-0.002±0.020	0.91	**0.053±0.014**	**0.0003**
Serum Fasting Glucose	-0.185±0.200	0.36	**0.218±0.087**	**0.01**
Serum HOMA-IR	0.015±0.077	0.85	**0.255±0.047**	**<0.0001**
Serum ISogtt	-0.217±0.180	0.23	**-0.521±0.108**	**<0.0001**
Serum adiponectin	-0.022±0.048	0.65	**-0.116±0.029**	**<0.0001**
Gestational diabetes	-0.200±0.259	0.44	0.102±0.174	0.56

[1]General linear model analyses were used with adjustment for maternal age, ethnicity, and postpartum time

Ley *et al. Am J Clin Nutr* 2012; 95:867

Results: Maternal obstetrical measures and milk insulin[1]

	1st week		3mo	
	beta±SE	p	beta±SE	p
Nulliparous	-0.191±0.219	0.38	**-0.310±0.144**	**0.03**
Scheduled C-section[2]	-0.178±0.279	0.53	0.301±0.180	0.10
Unscheduled C-section[2]	0.099±0.246	0.69	0.144±0.160	0.37
Length of gestation	-0.074±0.086	0.39	0.056±0.059	0.34

[1]General linear model analyses were used with adjustment for maternal age, ethnicity, and postpartum time
[2]v. spontaneous delivery

Ley *et al. Am J Clin Nutr* 2012; 95:867

Conclusions

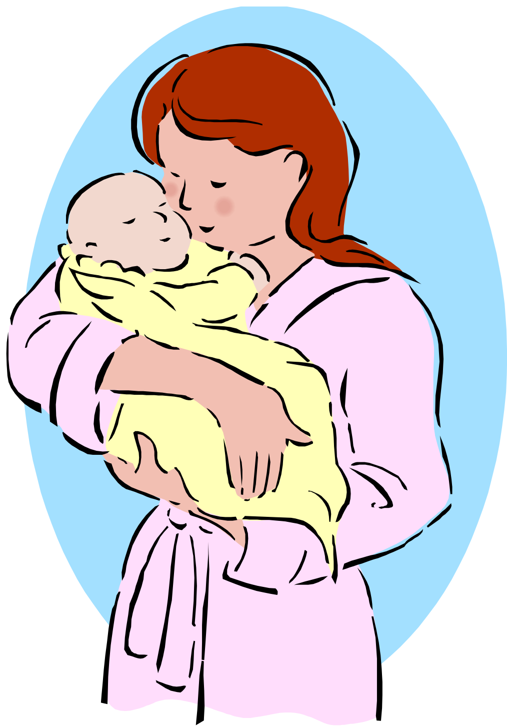
- Prenatal metabolic abnormalities are associated with higher insulin in mature milk
- Obstetrical parameters are associated with higher adiponectin in early milk

Discussion

- <u>animal models</u>
  - oral insulin stimulated gut maturation/ function and attenuated atherosclerosis progression
- <u>preterm infants</u>
  - tube-fed insulin enhanced intestinal function and reduced feeding intolerance

- milk metabolic hormones might have a role through local and/or systemic mechanisms regulating infant development

Shehadeh *et al. J Pediatr Gastroenterol Nutr* 2006; 43:276



Donor Human Milk Experimental Study

Donor Human Milk

- There are increasing demands for donor milk when mother’s own milk is not available
- Donor milk is pasteurized at 62.5°C for 30 min (Holder method) in North America
- Limited data are available on its impact on milk metabolic hormones

Tully *et al. J Hum Lact* 2000; 16:235
Human Milk Banking Association of North America 2005

Methods: Pasteurization Effects

Human Milk Bank Association of North America guidelines

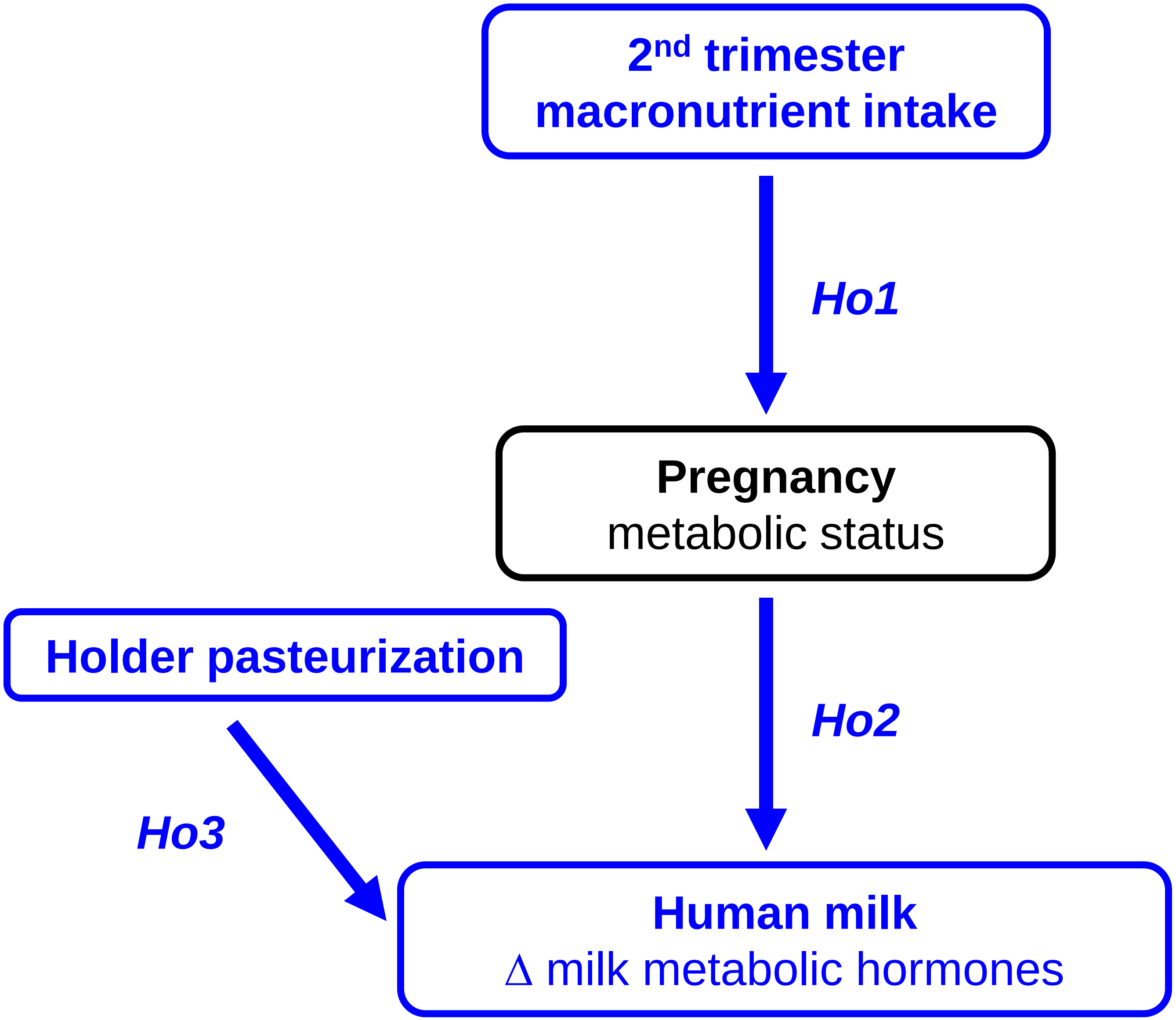
- Milk samples from 34 mothers were pooled to produce 17 distinct batches (4 mothers / batch)
- Holder pasteurized (62.5°C for 30 min)
- Adiponectin, insulin, energy, fat, glucose and total protein concentrations were measured pre- and post-pasteurization

Results: Concentrations (Mean ± SD) of milk components pre- and post-pasteurization

	Pre	Post	% Δ
Adiponectin, ng/mL	**13.91 ± 4.84**	**9.34 ± 2.96**	**-32.8****
Insulin, pmol/L	**162.8 ± 64.2**	**87.8 ±26.3**	**-46.1****
Energy, Kcal/dL	71.5 ± 9.9	69.4 ± 8.8	-2.9
Fat, g/L	4.29 ± 0.95	3.91 ± 0.81	-8.9*
Glucose, mmol/L	0.97 ± 0.25	1.11 ± 0.22	1.4*
Protein, g/L	14.8 ± 1.5	14.8 ± 1.1	<1.0

*<0.05; **<0.0001

Ley *et al. Pediatr Res* 2011; 70:278


2nd trimester macronutrient intake
Ho1
Pregnancy
metabolic status
Holder pasteurization
Ho2
Ho3
Human milk
Δ milk metabolic hormones

Limitations and future directions

- Observed association of vegetable and fruit fiber intake with insulin sensitivity might have been confounded by other components
- Impact of variations in milk hormones on infant development and subsequent risk for type 2 diabetes warrants further investigation

Take Home Messages

Our findings support continued work to develop

1. prenatal nutritional strategies to prevent maternal metabolic abnormalities and

2. postnatal strategies to improve development of nutritionally vulnerable offspring exposed to maternal metabolic abnormalities

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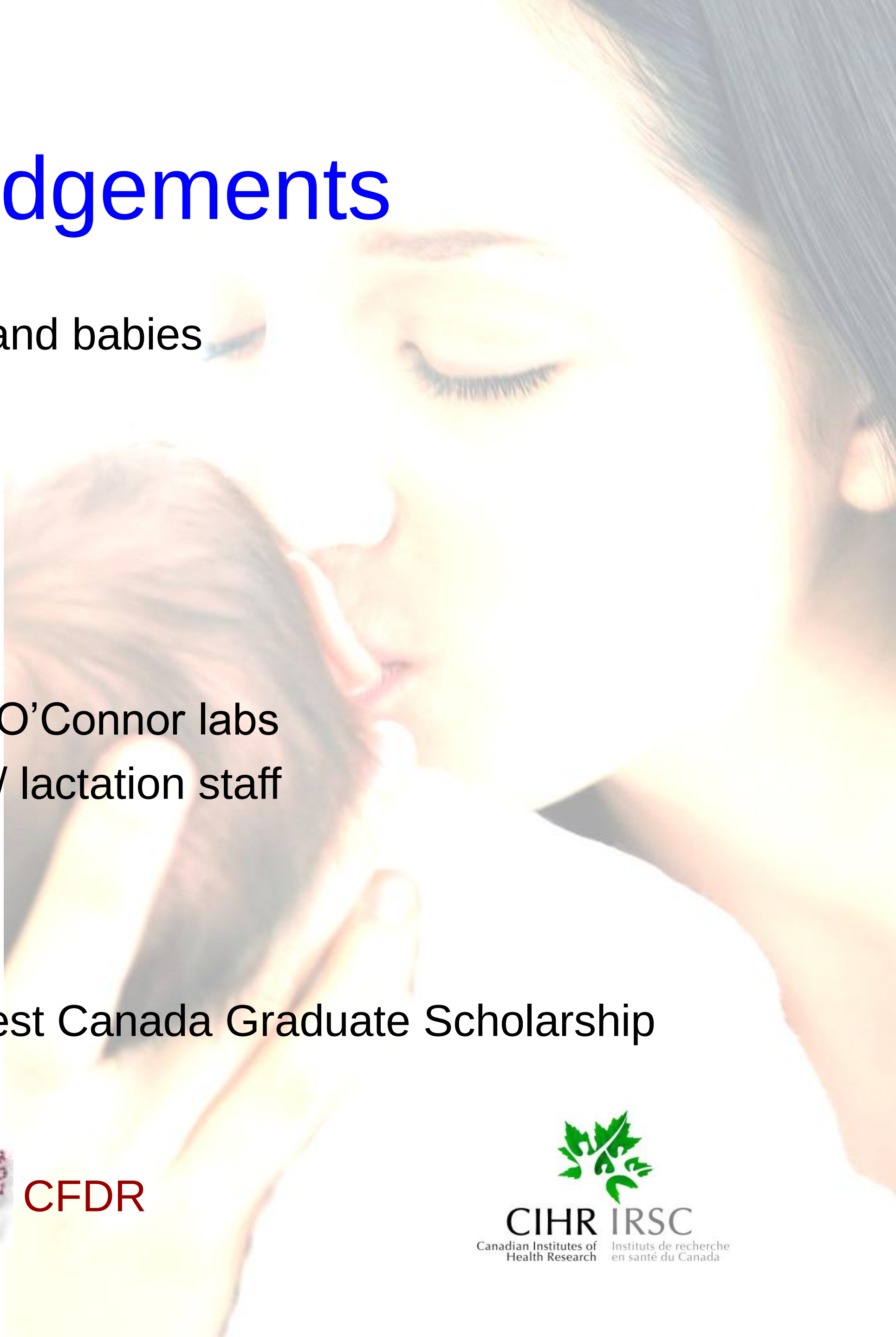
CIHR Frederick Banting and Charles Best Canada Graduate Scholarship

Canadian Diabetes Association

TOGETHER ADVANCING NUTRITION CFDR

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



Q and A