Increasing Obstetric Intervention

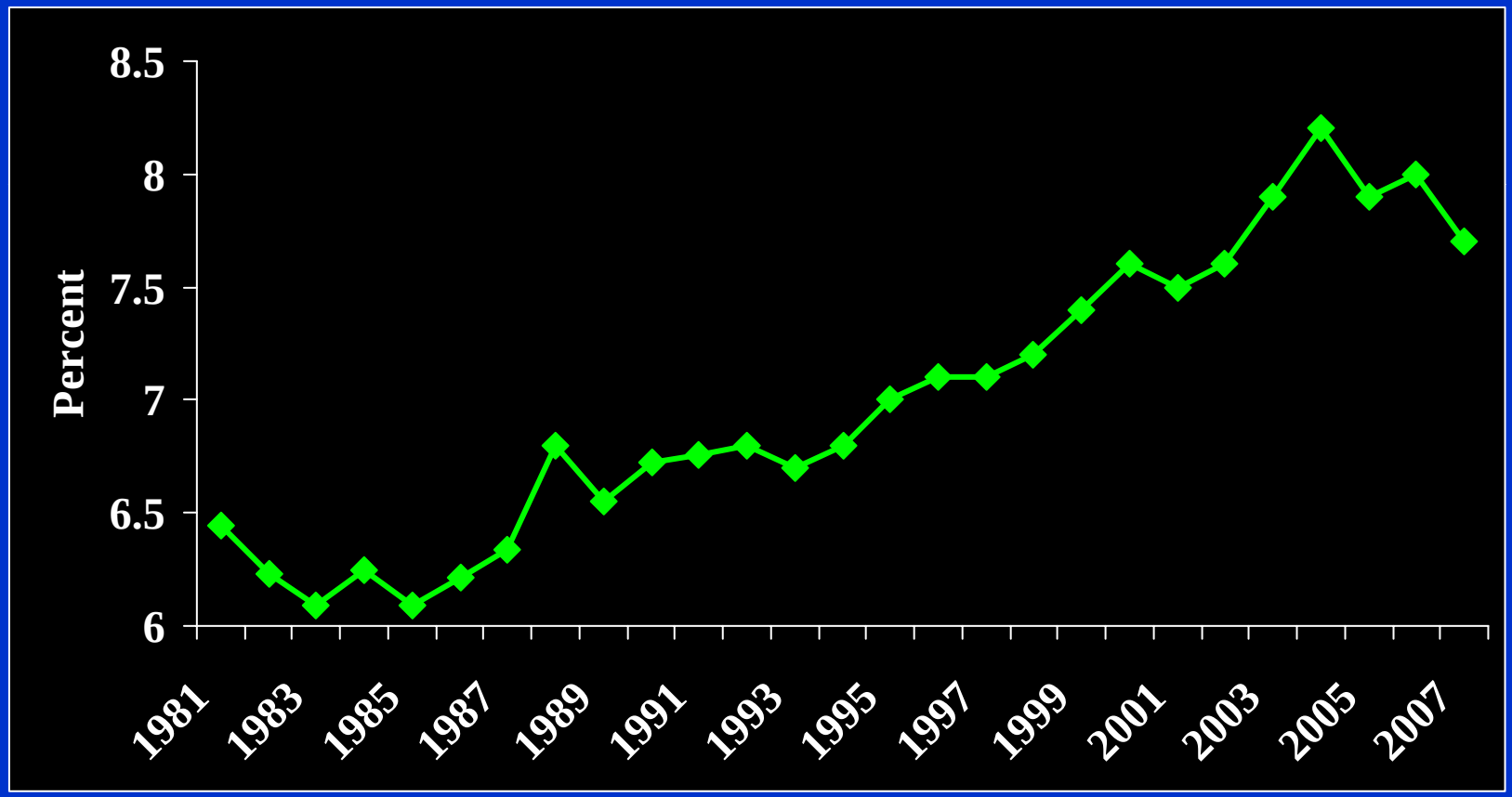
- Infertility treatment
  - IVF/ICSI
  - Ovulation stimulation
- Prenatal diagnosis & pregnancy termination
- Labor induction
- Cesarean delivery

Impacts on Pregnancy Outcomes

- Preterm birth
- Multiple birth
- Postterm birth
- Stillbirth
- Gestational age & birth weight at term
- Infant mortality
- Amniotic fluid embolism (AFE)
- Postpartum hemorrhage (PPH)

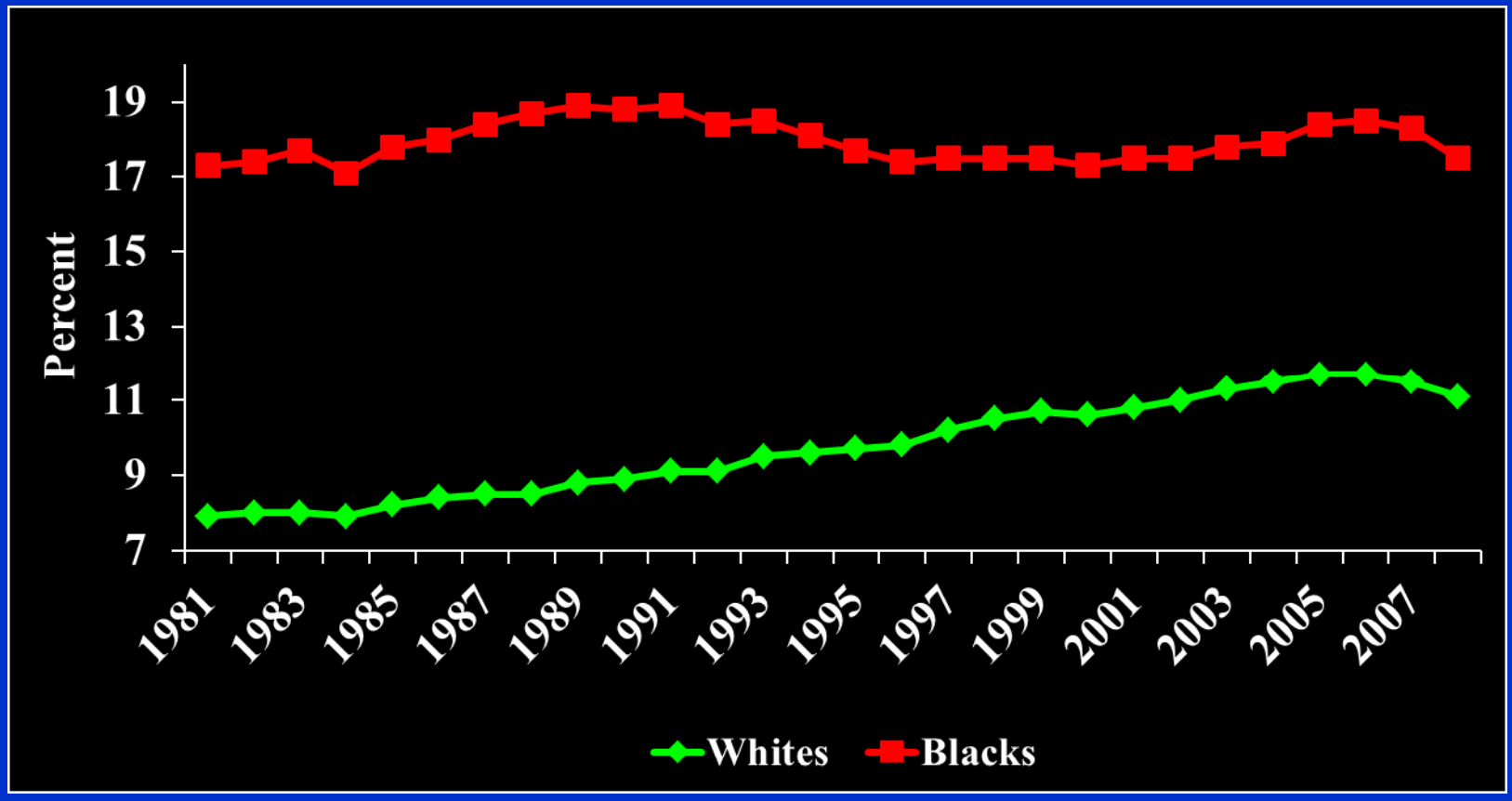
The Preterm Birth Epidemic

Canada, 1981-2007



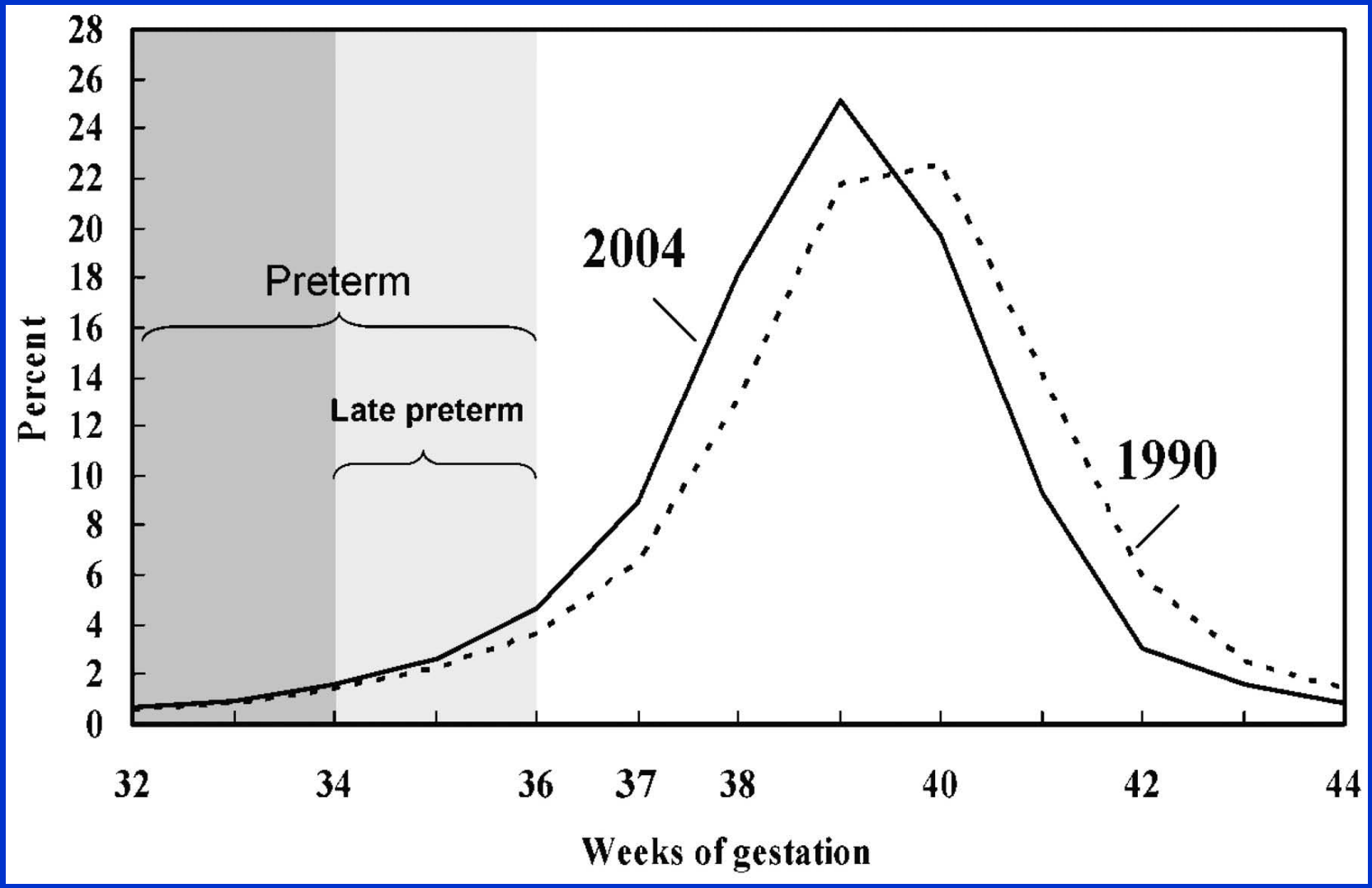
U.S. Trends in Preterm Birth

Non-Hispanic Whites and Blacks, 1981-2008



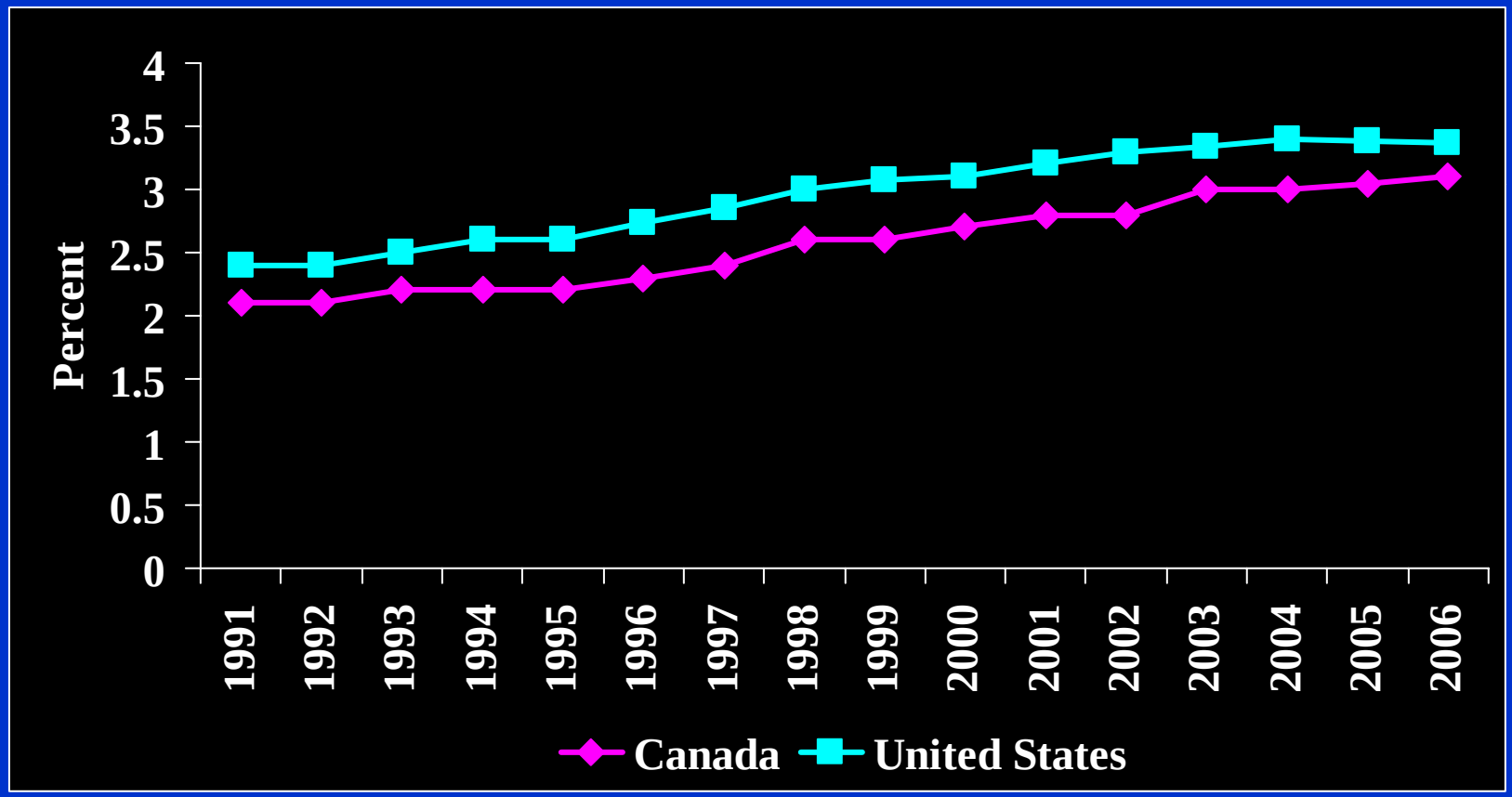
GA Distribution

U.S., 2004 vs 1990



Trends in Multiple Births

U.S. and Canada, 1991-2006



Twin Births in Sweden, 1971-95

Figure 2: **Risk ratio of twin births in Sweden**
1971 set at 1·0. IVF=in-vitro fertilisation.

Source: Bergh et al, Lancet 1999;354:1579-1585

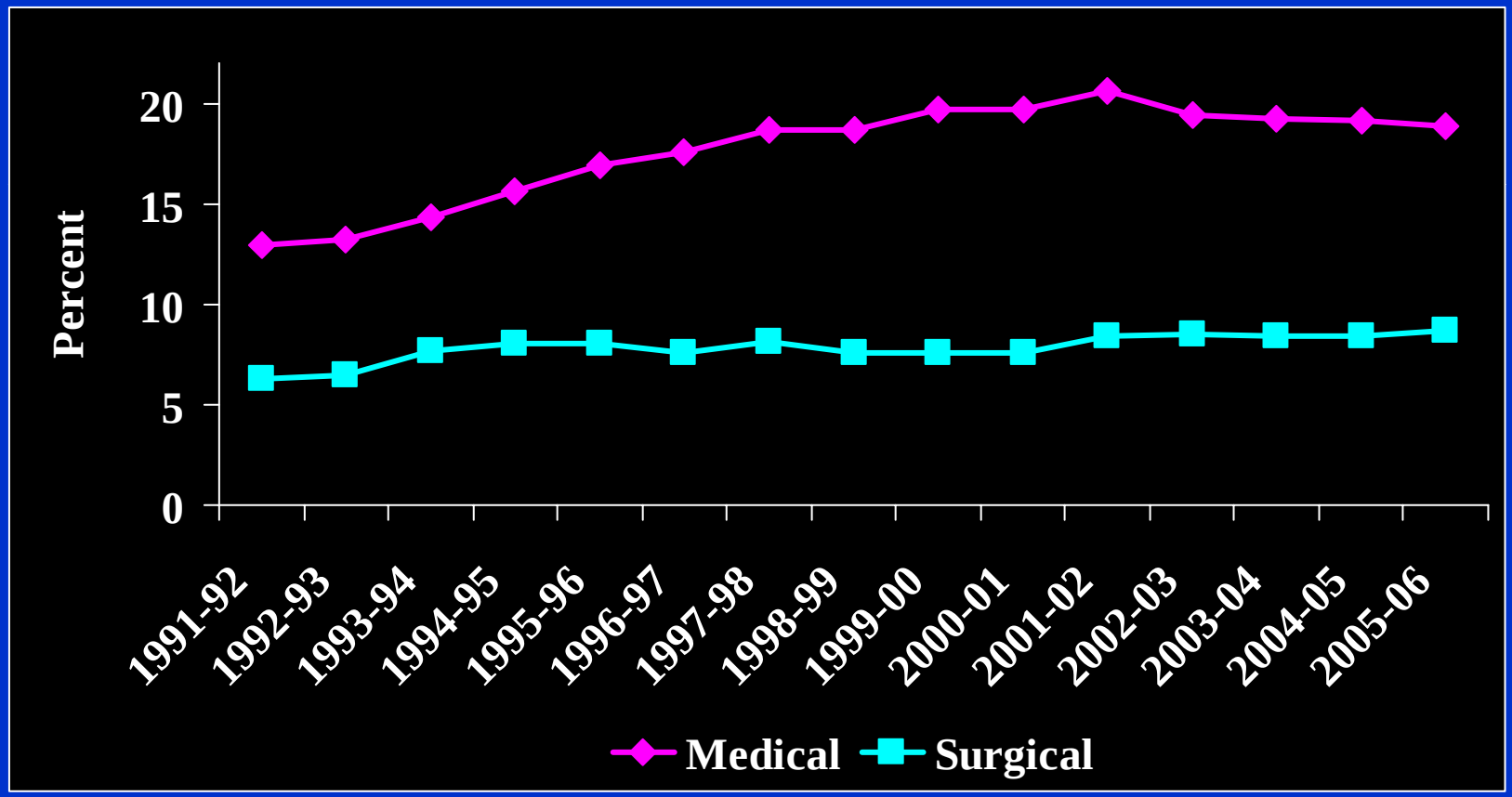
Ovulation Stimulation & Multiple Births
U.S., 2005

- Estimates based on Bayesian meta-analysis
  - Age-adjusted multiple rates in 2005 vs 1971
  - Risk of multiple gestation given ovulation stimulation and successful pregnancy
    - Clomiphene, other anti-estrogens: 8.9%
    - Gonadotropins: 14.3%
- Fraction of all 2005 multiples: 22.8%

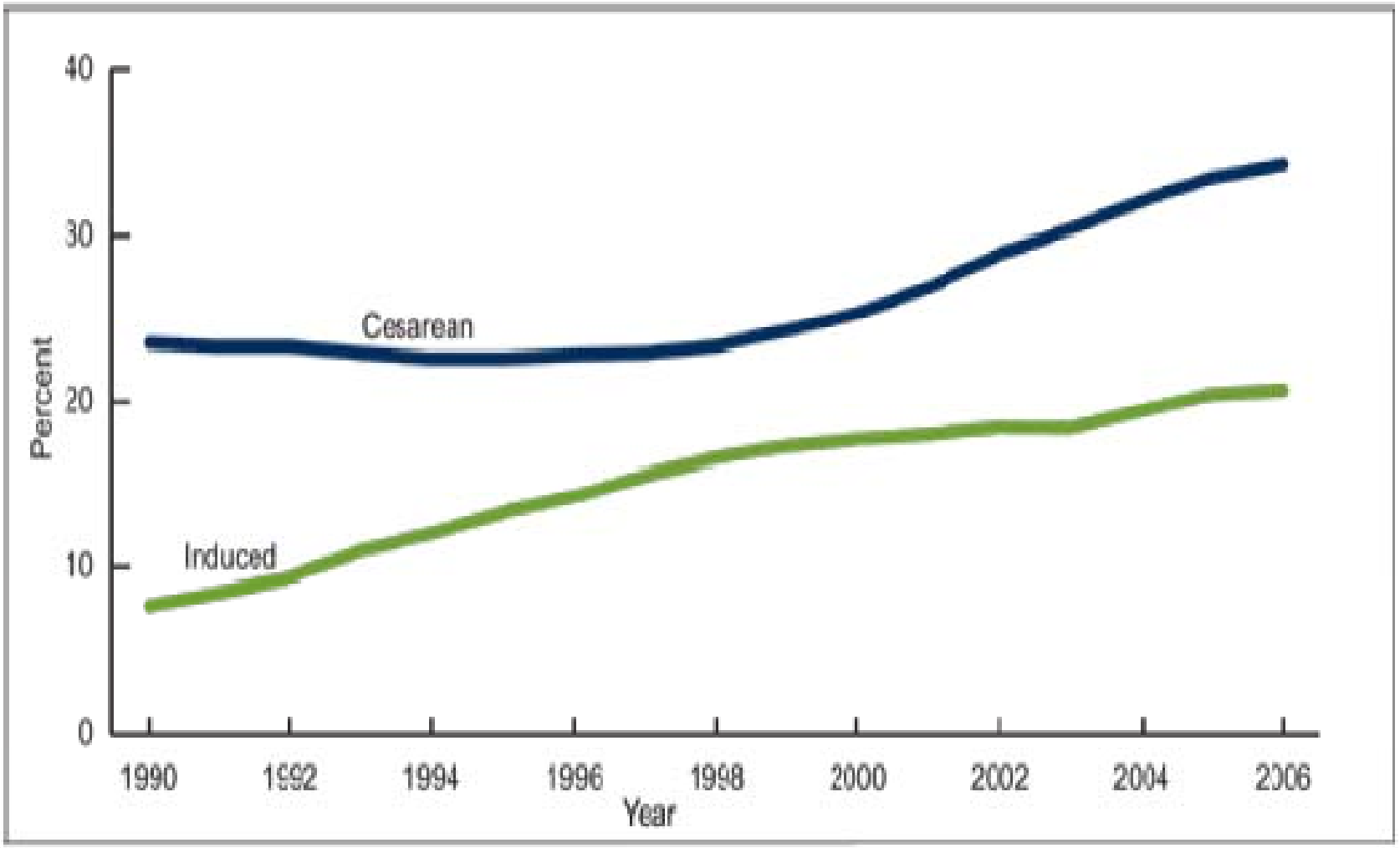
Source: Schieve et al, Am J Epidemiol 2009;170:1396-1407

Trends in Labor Induction

Canada, 1991-2006



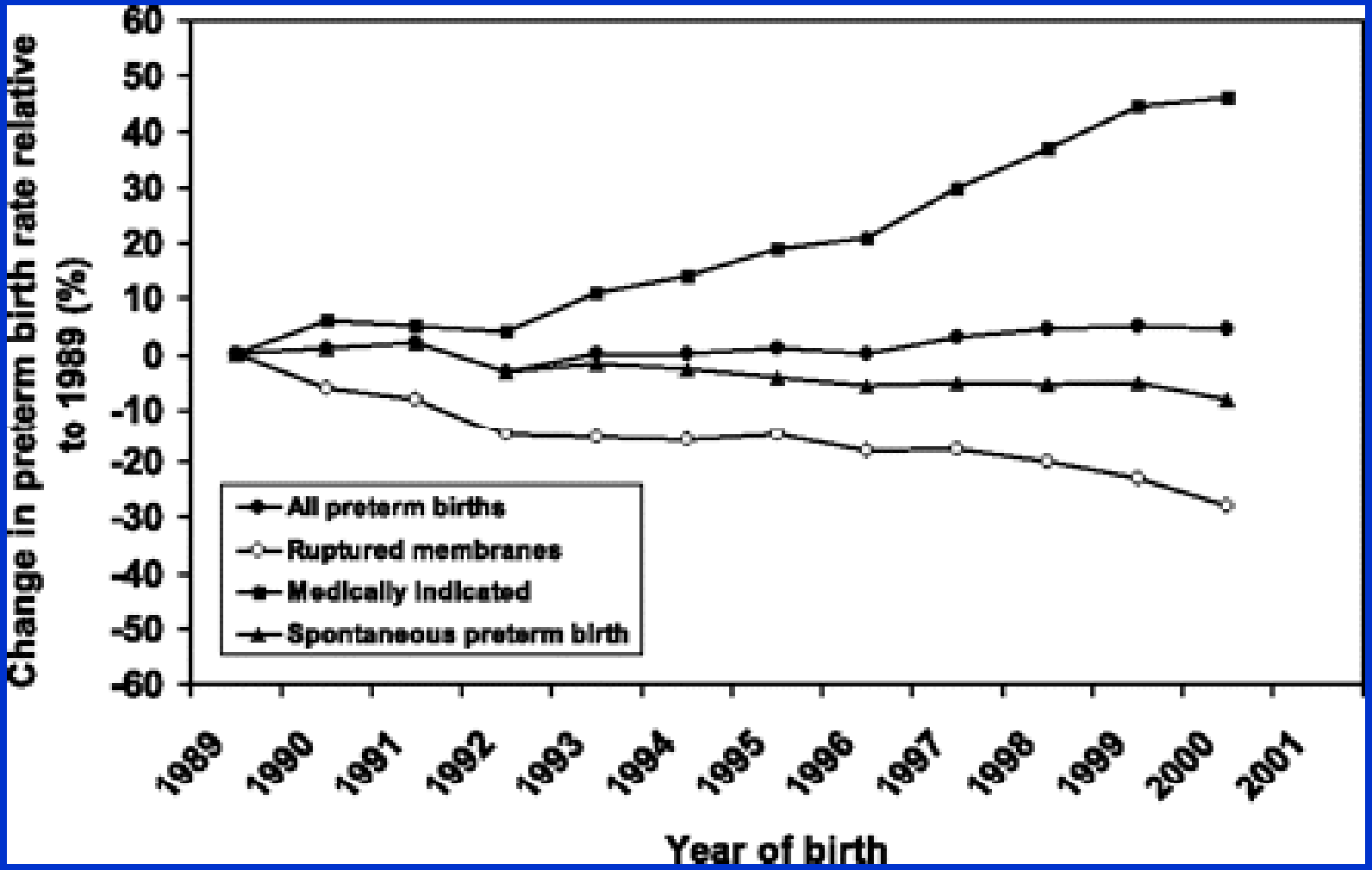
Trends in Induction & Cesarean
34-36 Weeks, U.S. 1990-2006



Source: Martin et al, NCHS Data Brief 24, 2009

Trend in Preterm Birth Subtypes

U.S. Singleton Births, 1989-2000



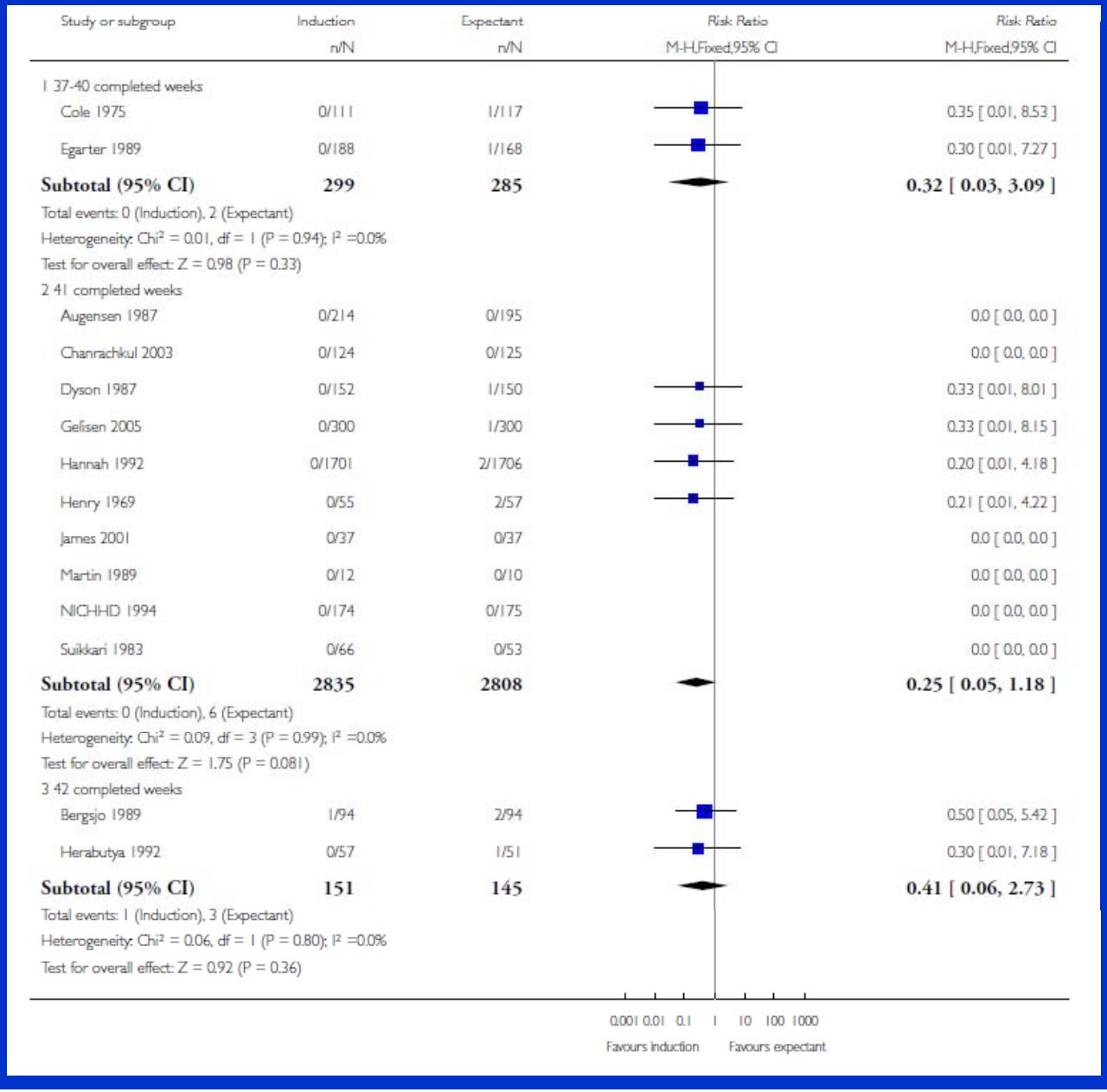
Source: Ananth et al, Obstet Gynecol 2005;105:1084-1091

Change in PTB Subtype by Race
RR (95% CI) in 2000 vs 1989, Singletons

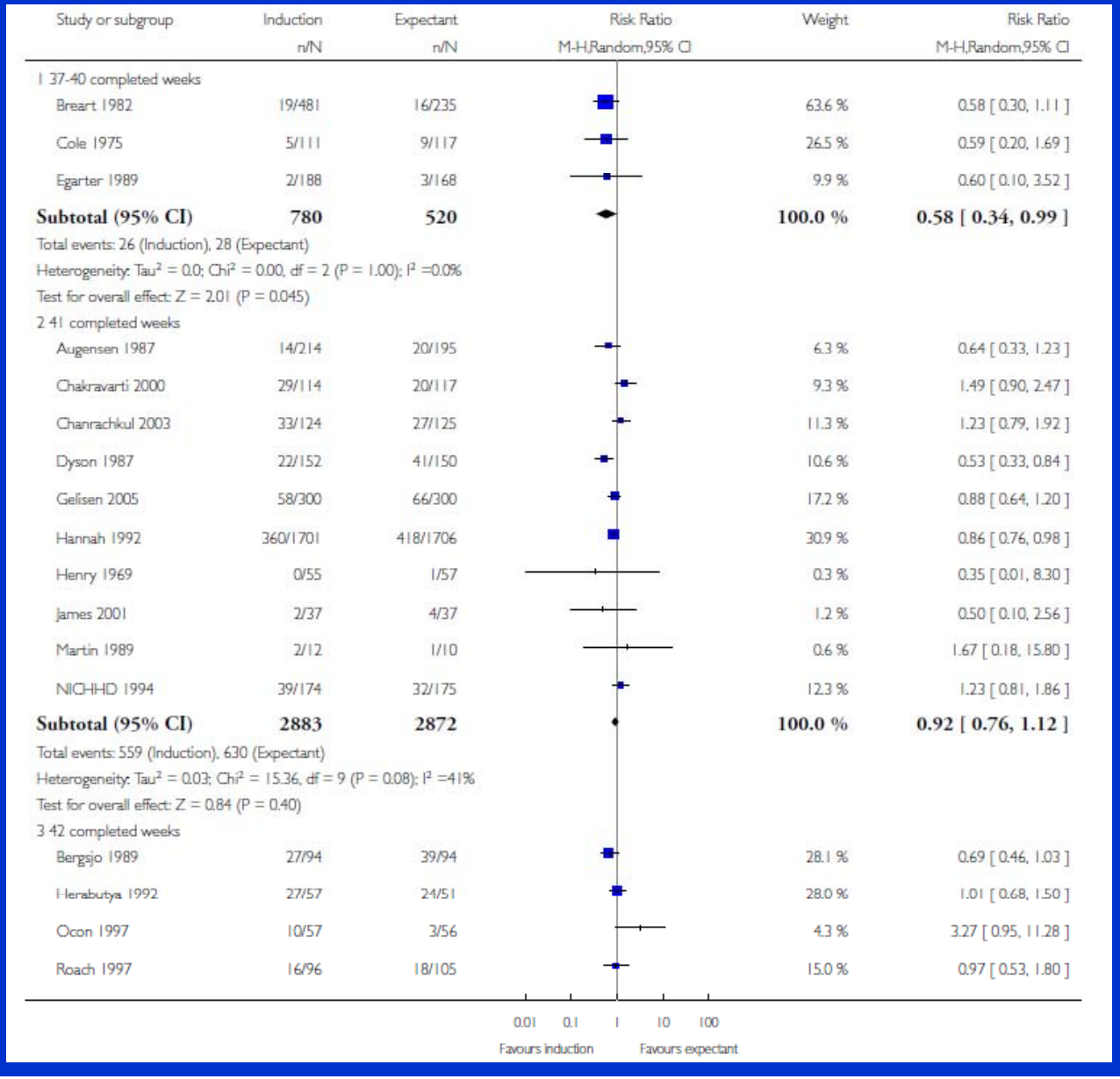
PTB Subtype	Whites	Blacks
Spontaneous PTL	1.03 (1.02-1.04)	0.73 (0.70-0.76)
PPROM	0.77 (0.76-0.78)	0.63 (0.62-0.65)
"Indicated"	1.55 (1.53-1.56)	1.32 (1.29-1.34)

Source: Ananth et al, Obstet Gynecol 2005;105:1084-1091

Routine Induction & Perinatal Death



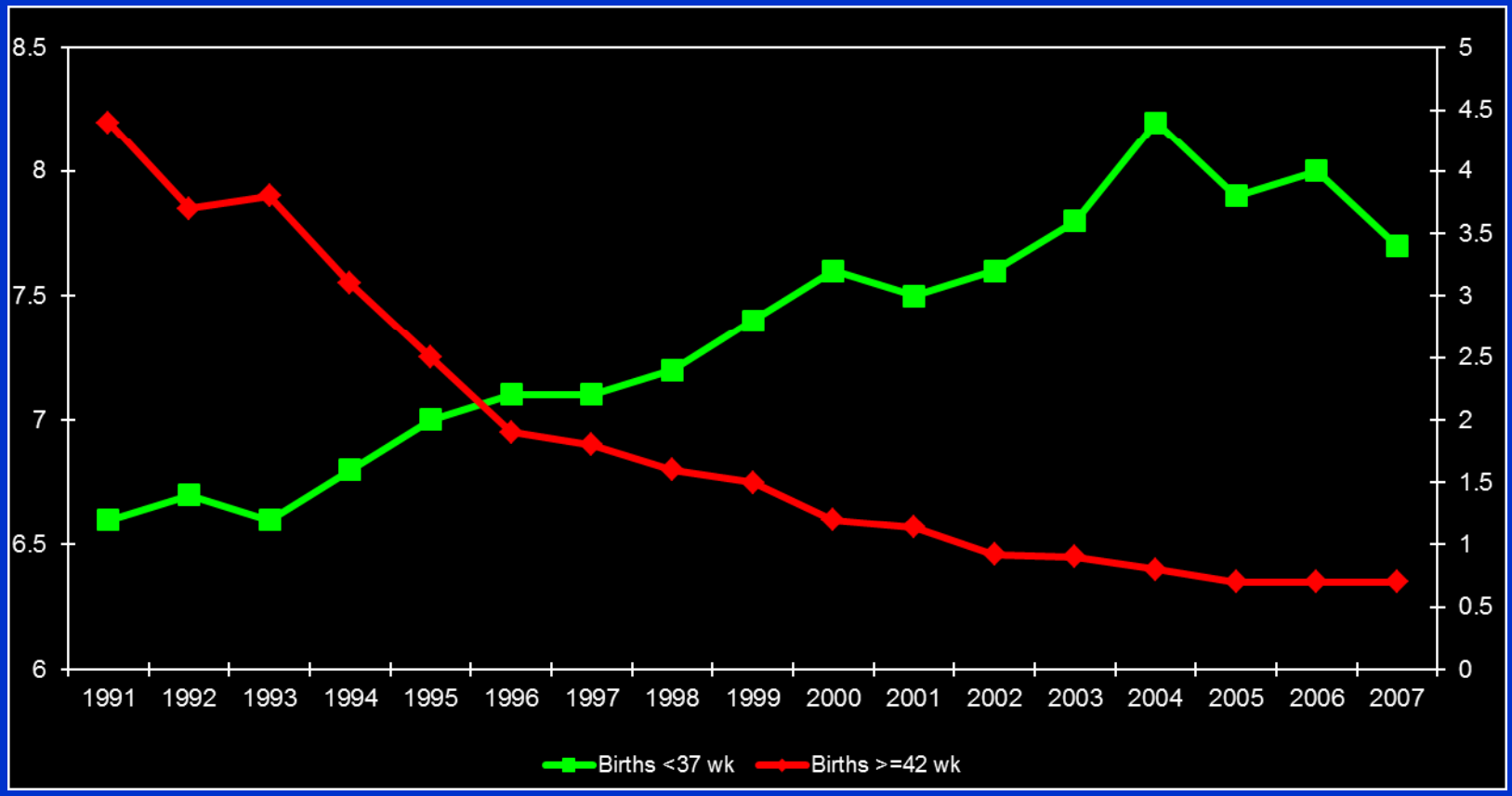
Routine Induction & Cesarean



Study or subgroup	Induction n/N	Expectant n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 37-40 completed weeks					
Breart 1982	19/481	16/235		63.6 %	0.58 [0.30, 1.11]
Cole 1975	5/111	9/117		26.5 %	0.59 [0.20, 1.69]
Egarter 1989	2/188	3/168		9.9 %	0.60 [0.10, 3.52]
Subtotal (95% CI)	**780**	**520**		**100.0 %**	**0.58 [0.34, 0.99]**
Total events: 26 (Induction), 28 (Expectant)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 2 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.01 (P = 0.045)					
2 41 completed weeks					
Augensen 1987	14/214	20/195		6.3 %	0.64 [0.33, 1.23]
Chakravarti 2000	29/114	20/117		9.3 %	1.49 [0.90, 2.47]
Chanrachkul 2003	33/124	27/125		11.3 %	1.23 [0.79, 1.92]
Dyson 1987	22/152	41/150		10.6 %	0.53 [0.33, 0.84]
Gelisen 2005	58/300	66/300		17.2 %	0.88 [0.64, 1.20]
Hannah 1992	360/1701	418/1706		30.9 %	0.86 [0.76, 0.98]
Henry 1969	0/55	1/57		0.3 %	0.35 [0.01, 8.30]
James 2001	2/37	4/37		1.2 %	0.50 [0.10, 2.56]
Martin 1989	2/12	1/10		0.6 %	1.67 [0.18, 15.80]
NICHHD 1994	39/174	32/175		12.3 %	1.23 [0.81, 1.86]
Subtotal (95% CI)	**2883**	**2872**		**100.0 %**	**0.92 [0.76, 1.12]**
Total events: 559 (Induction), 630 (Expectant)					
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 15.36$, df = 9 (P = 0.08); $I^2 = 41\%$					
Test for overall effect: Z = 0.84 (P = 0.40)					
3 42 completed weeks					
Bergsjo 1989	27/94	39/94		28.1 %	0.69 [0.46, 1.03]
Herabutya 1992	27/57	24/51		28.0 %	1.01 [0.68, 1.50]
Ocon 1997	10/57	3/56		4.3 %	3.27 [0.95, 11.28]
Roach 1997	16/96	18/105		15.0 %	0.97 [0.53, 1.80]

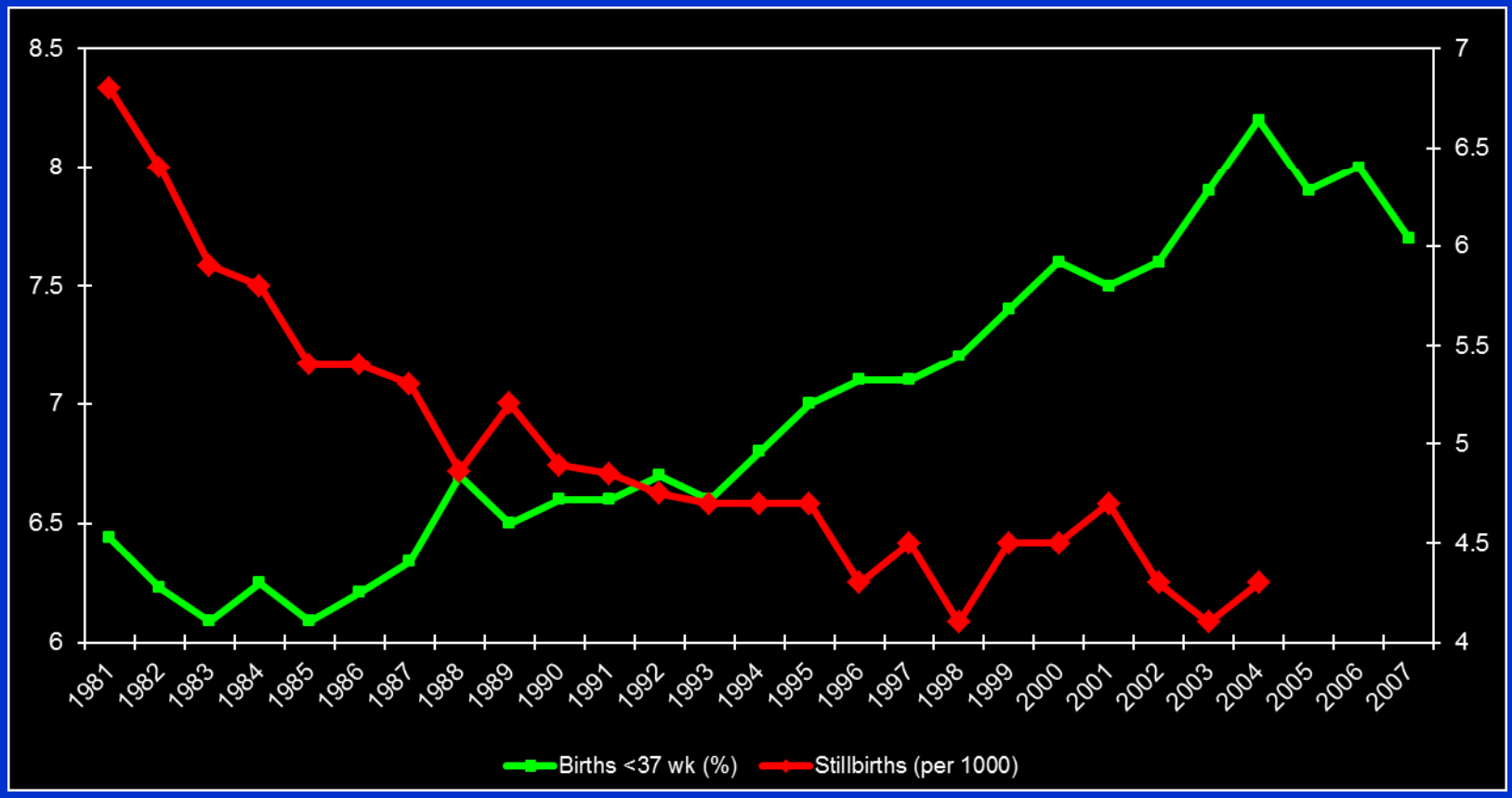
Trends in Preterm & Postterm Birth

Canada, 1991-2007



Trends in Preterm Birth & Stillbirth*

Canada, 1981-2007

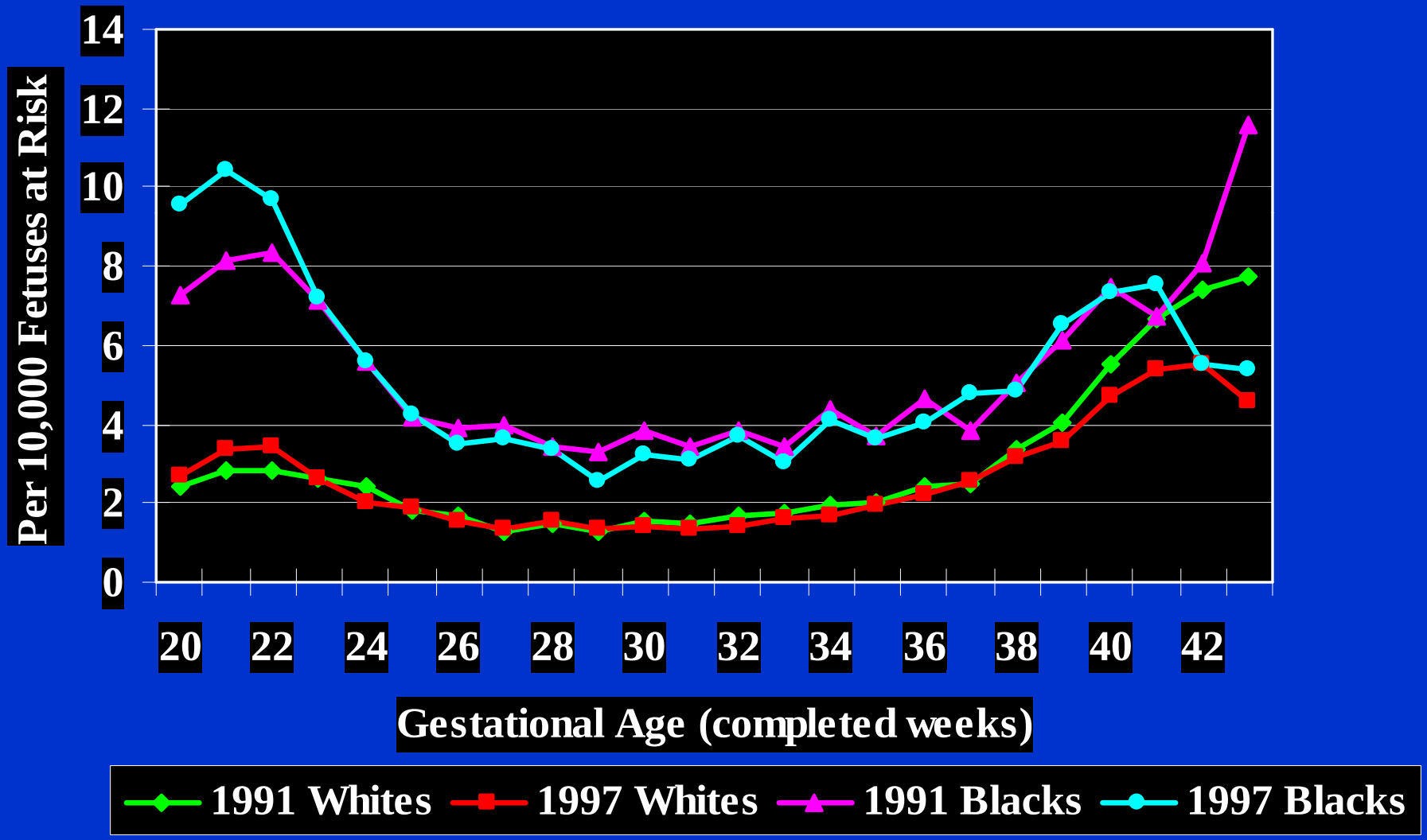


*Stillbirth ≥500 g

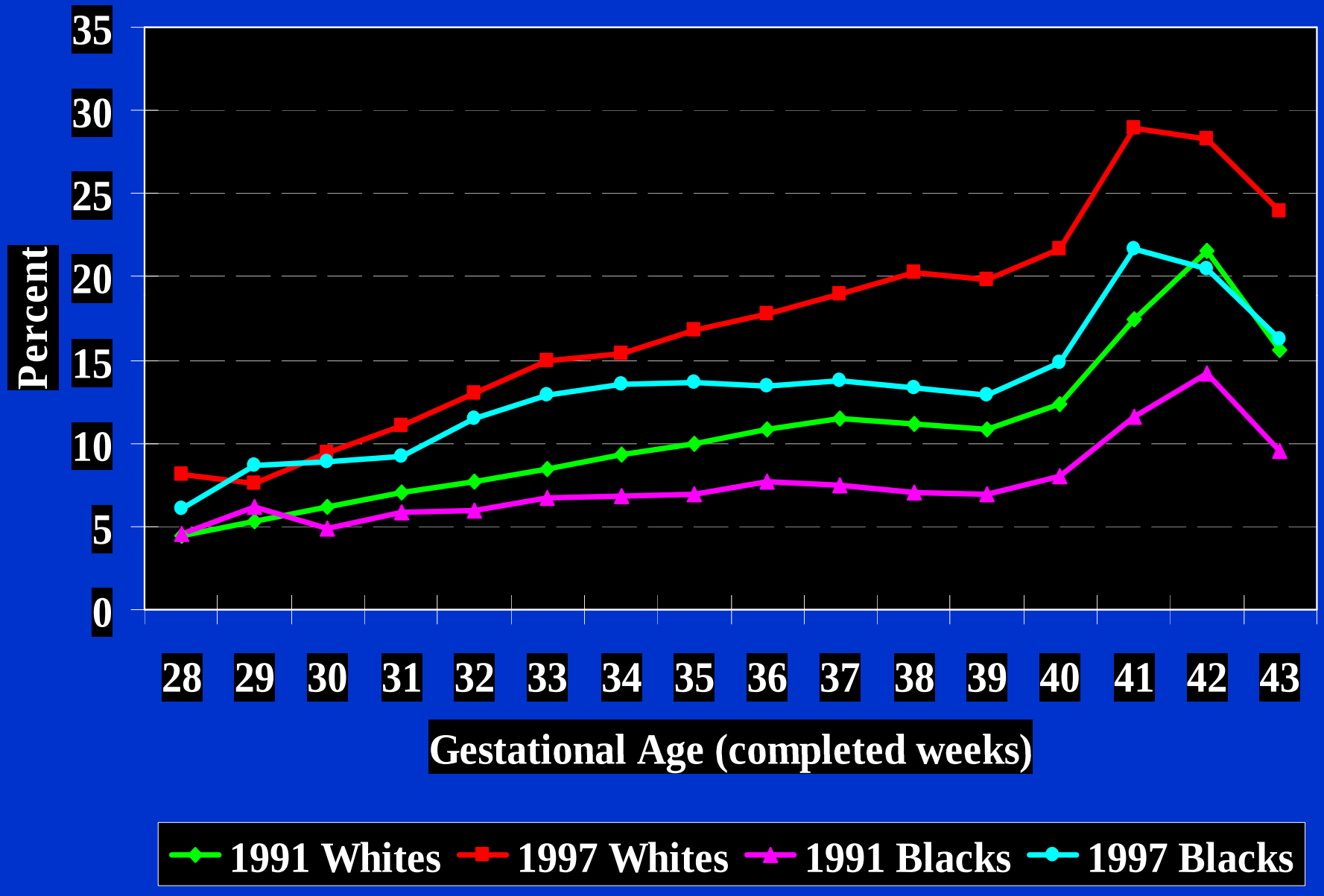
Studying Effects of Induction

- Best approach: RCT
- Observational studies of induction
  - Confounded by indication for induction
  - No data on indication: cannot be controlled
  - Temporality: antepartum stillbirths often induced
- Ecologic analysis less likely to be biased
  - Large variations among states
  - Largely due to practice style rather than indication
  - Differences in practice style create a quasi-experiment across the geographic areas

Stillbirth in U.S., 1997 vs 1991



Induction in U.S., 1997 vs 1991



Adjustment for Induction

Poisson Regression, 1997 vs 1991, 40-43 Weeks

	White	White	Black	Black
	Crude	Adjusted	Crude	Adjusted
Total	0.79 (0.74-0.84)	0.98 (0.82-1.16)	0.76 (0.67-0.87)	0.67 (0.50-0.88)
Low-Risk	0.82 (0.75-0.90)	1.19 (0.95-1.49)	0.70 (0.58-0.85)	0.63 (0.44-0.93)
High-Risk	0.78 (0.70-0.87)	0.96 (0.71-1.27)	0.84 (0.68-1.03)	0.77 (0.49-1.17)

Adjustment for Induction

Poisson Regression: Blacks, 42-43 Weeks

	Crude	Adjusted
Total	0.69 (0.56-0.84)	0.69 (0.51-0.94)
Low-Risk	0.58 (0.43-0.79)	0.58 (0.39-0.88)
High-Risk	0.81 (0.58-1.13)	1.06 (0.64-1.73)

Increase in Infant Mortality, 2002

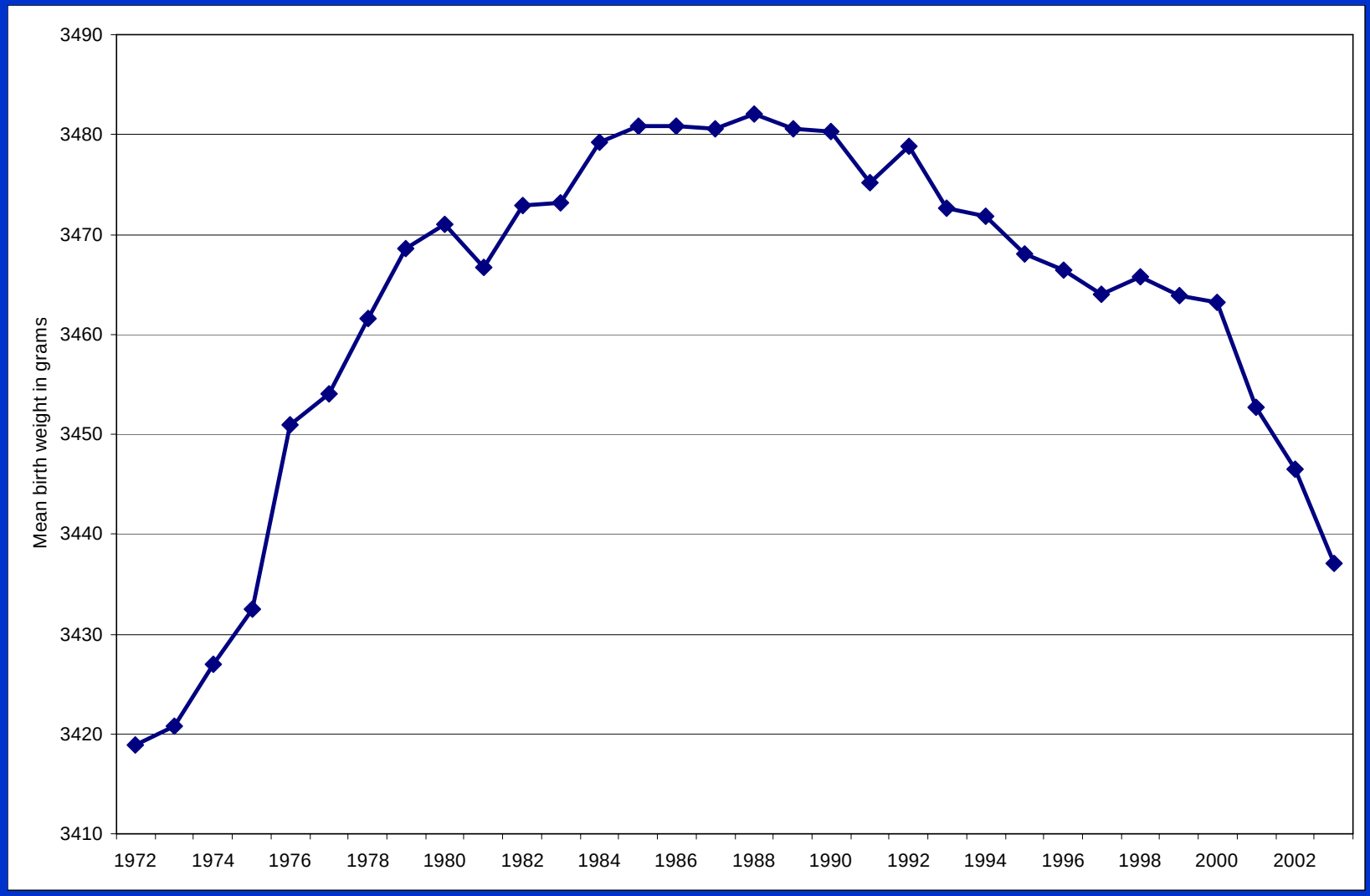
Table 1: Numbers and rates of infant deaths and live births with birth weight less than 500 g or gestational age less than 24 weeks in Alberta and all of Canada[2,7,8]

			Live births < 500 g		Live births < 24 wk	
Year	No. of infant deaths	Infant mortality rate (per 1000 live births)	No.	Rate (per 10 000 live births)	No.	Rate (per 10 000 live births)
Alberta						
2000	244	6.6	48	13.0	81	21.9
2001	210	5.6	43	11.4	66	17.5
2002	283	7.3	62	16.0	103	26.6
Canada						
1992	2431	6.1	202	5.1	339	8.5
1993	2448	6.3	329	8.5	411	10.6
2000	1737	5.3	261	8.0	423	12.9
2001	1739	5.2	266	8.0	445	13.4
2002	1762	5.4	327	10.0	502	15.3

Source: Joseph et al, CMAJ 2005;172:856-7

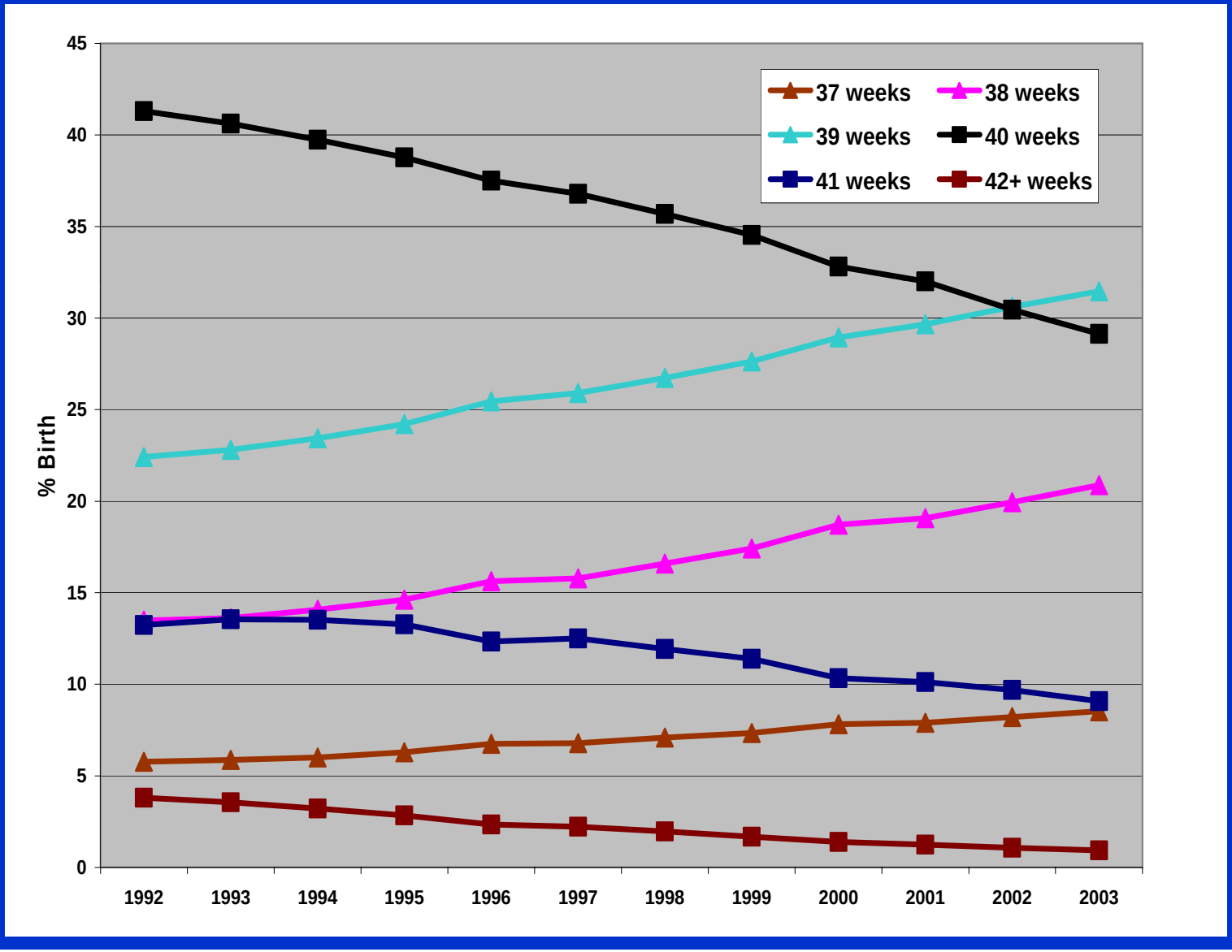
Trend in Mean BW ≥37 Weeks

U.S. Whites, 1972-2003



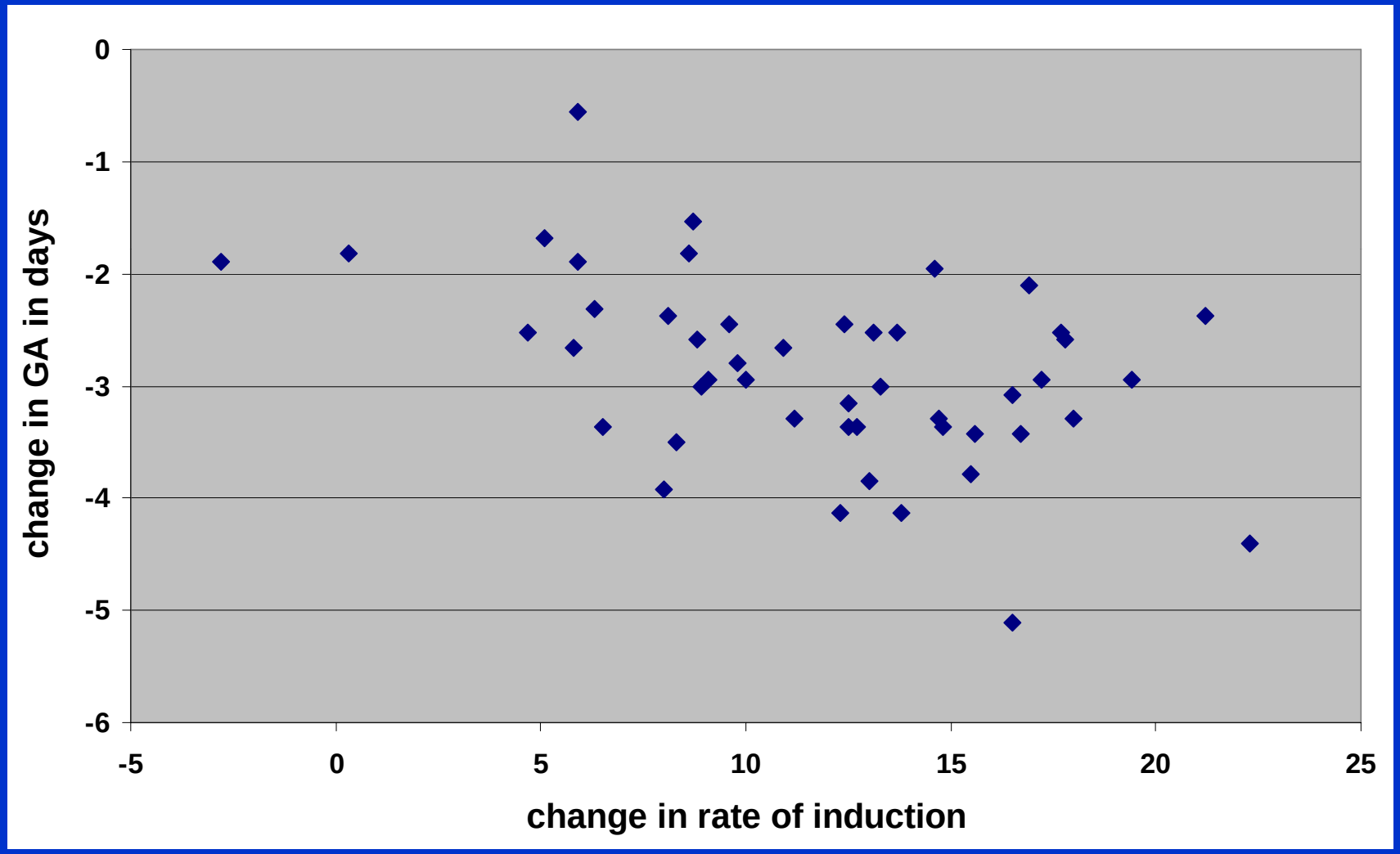
GA Distribution ≥37 Weeks

U.S. Non-Hispanic Whites, 1992-2003



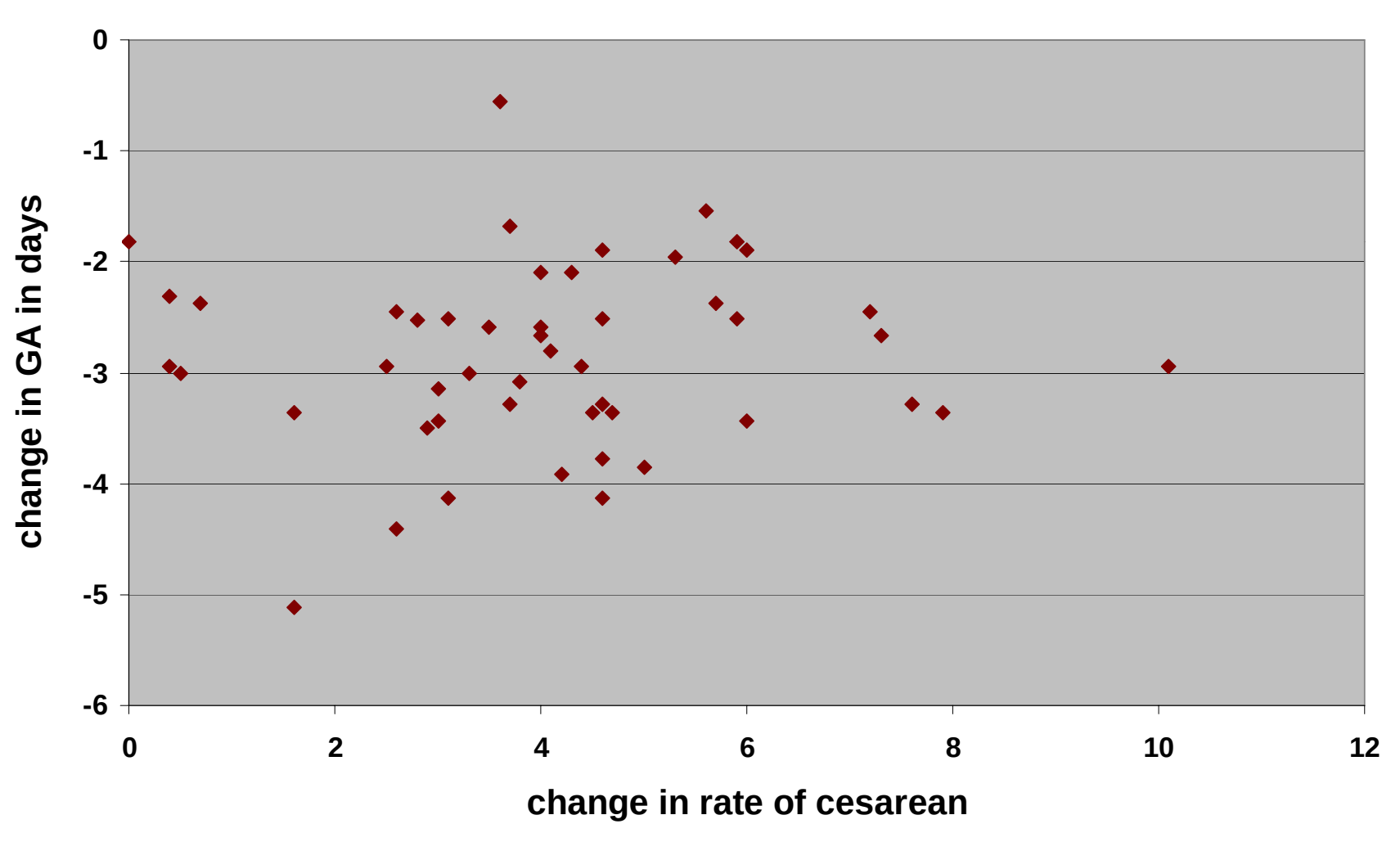
Change in GA vs Change in Induction Rate

State Level, 1992-2003 (r=-0.41, p=0.009)



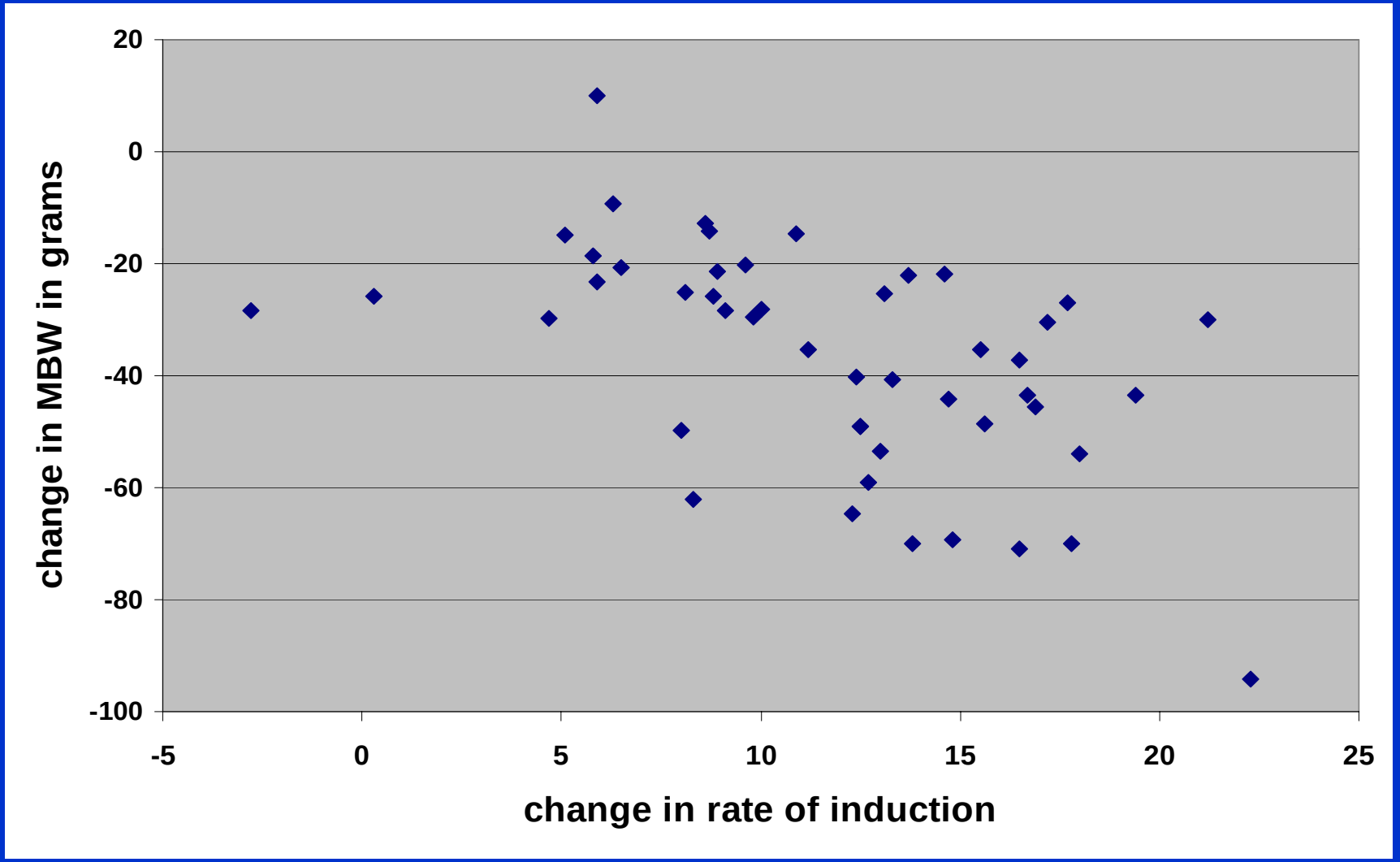
Change in GA vs Change in Cesarean Rate

State Level, 1992-2003 (r=-0.17, p=0.30)



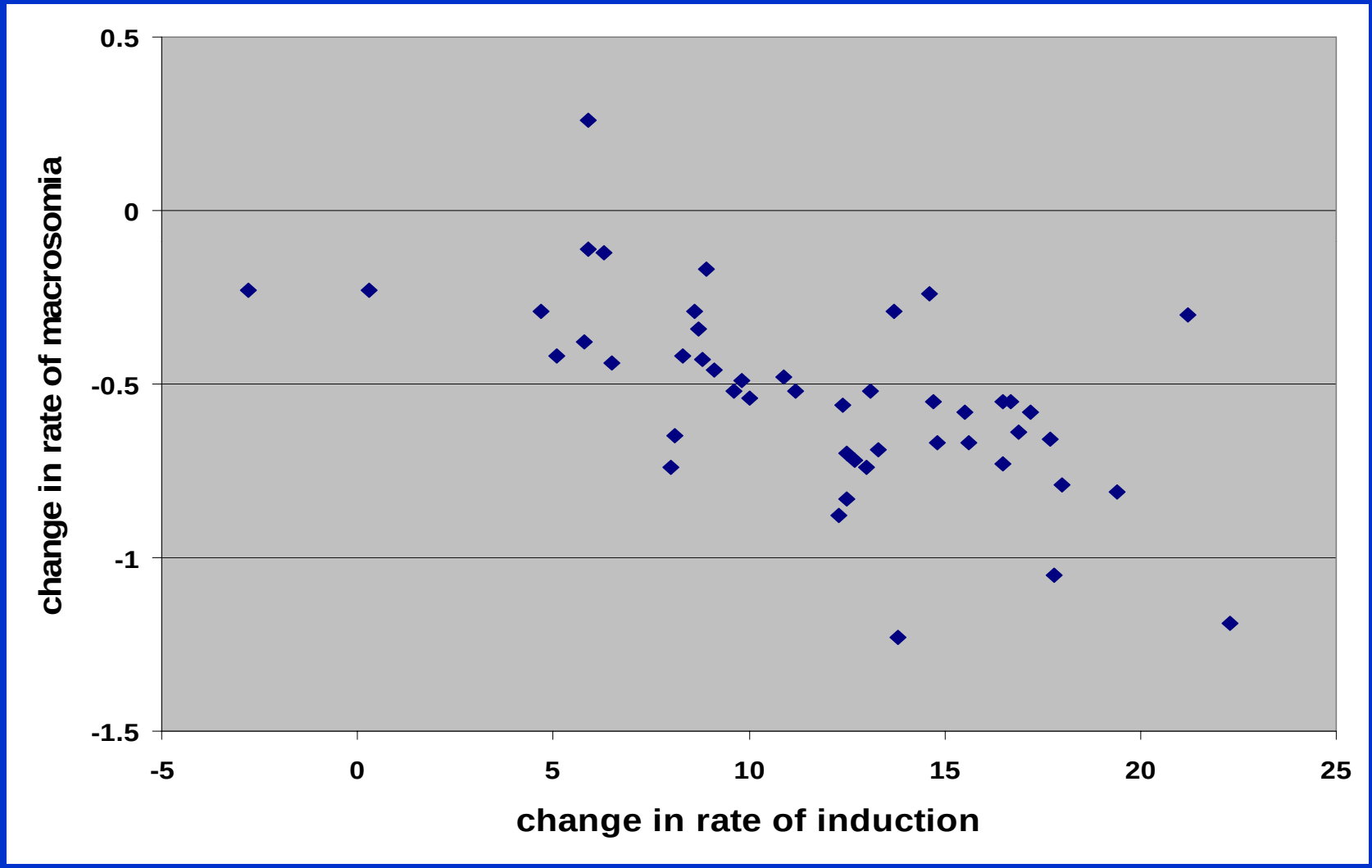
Change in BW vs Change in Induction Rate

State Level, 1992-2003 ($r=-0.56$, $p<0.001$)



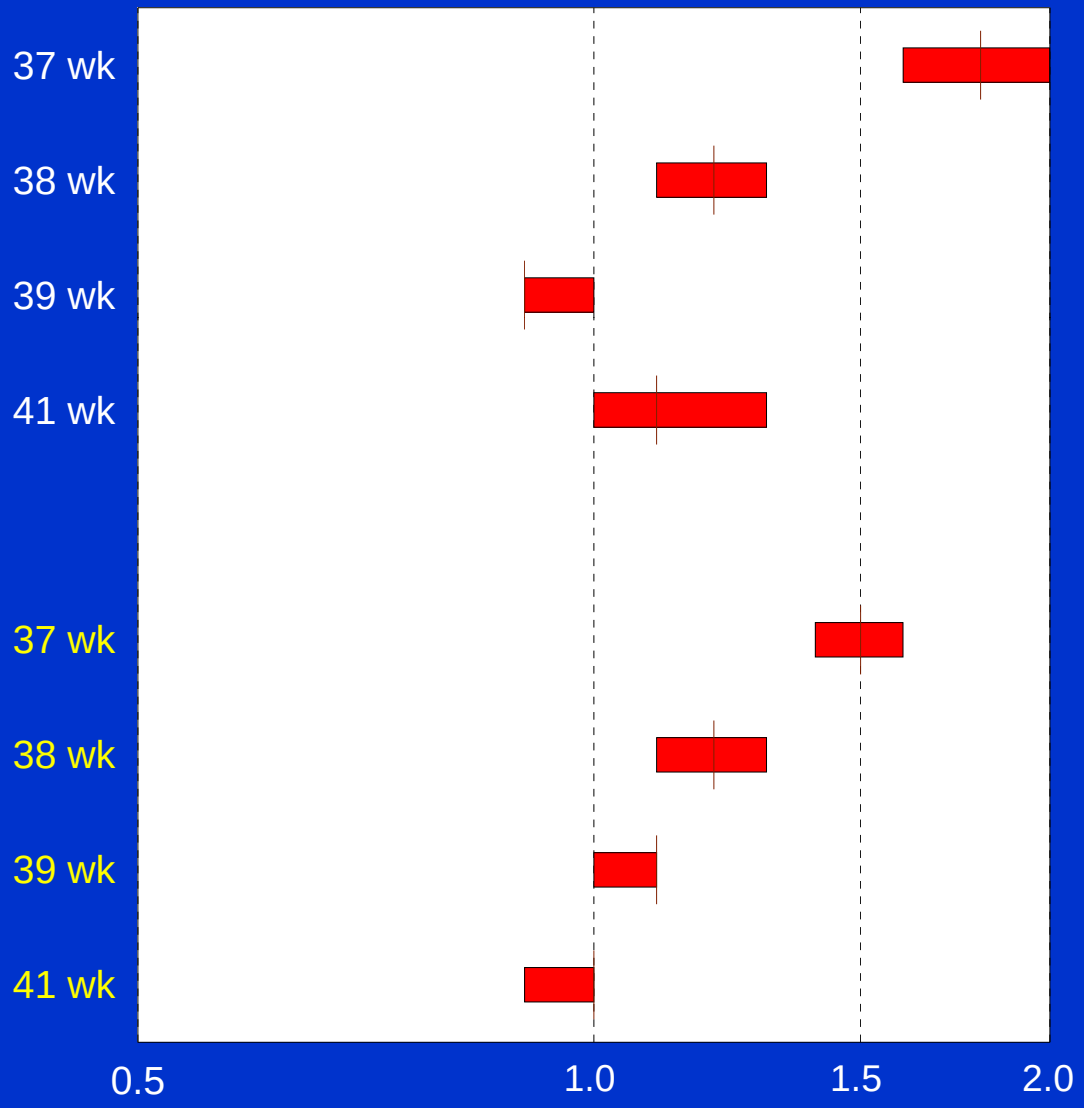
Change in Macrosomia vs Induction Rates

State Level, 1992-2003 (r=-0.46, p=0.003)



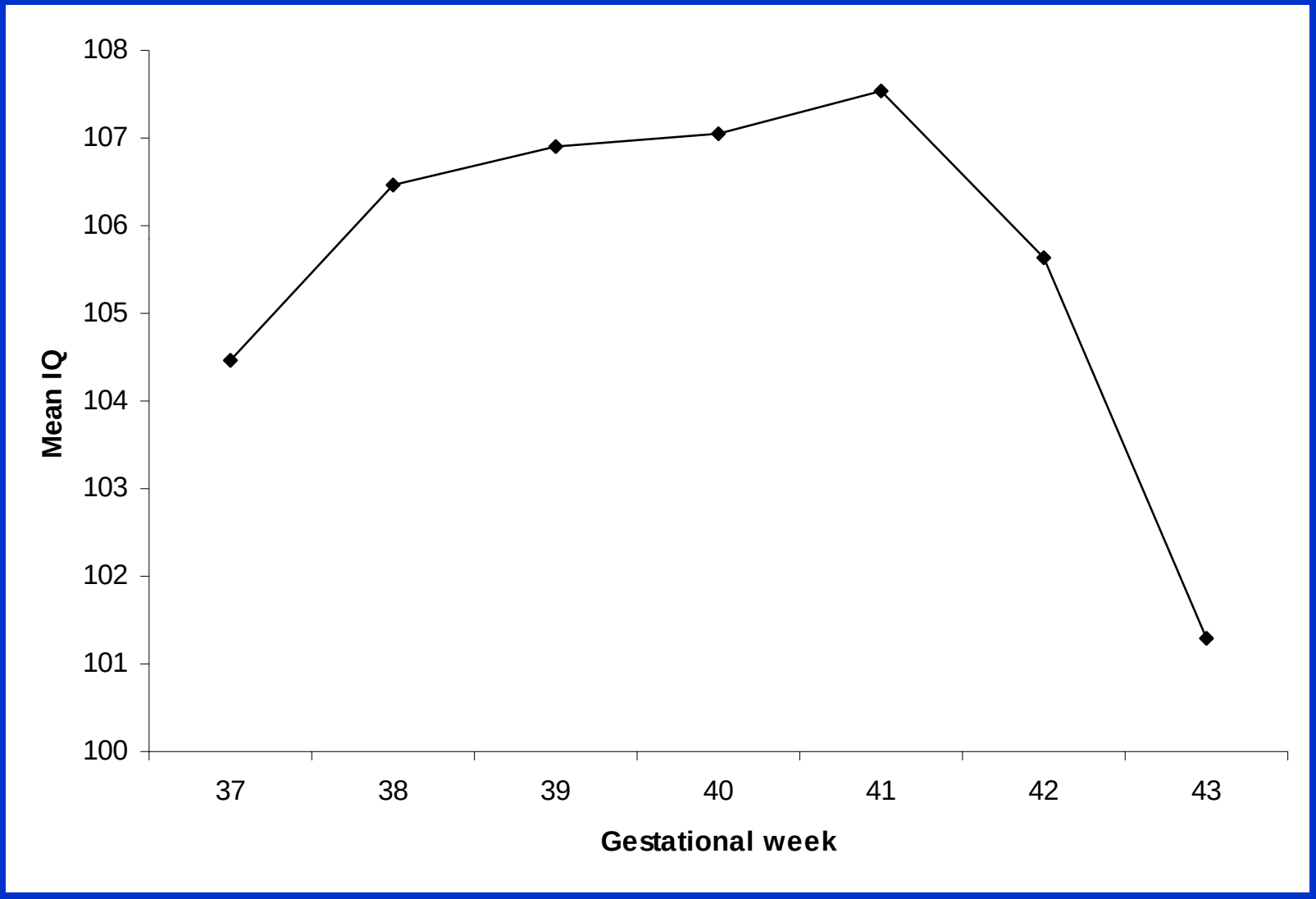
Variation in NMR/PNMR by Term GA

U.S., Non-Hispanic Whites, 1995-2001



Full-Scale IQ vs GA

PROBIT Trial, Belarus, 1996-97



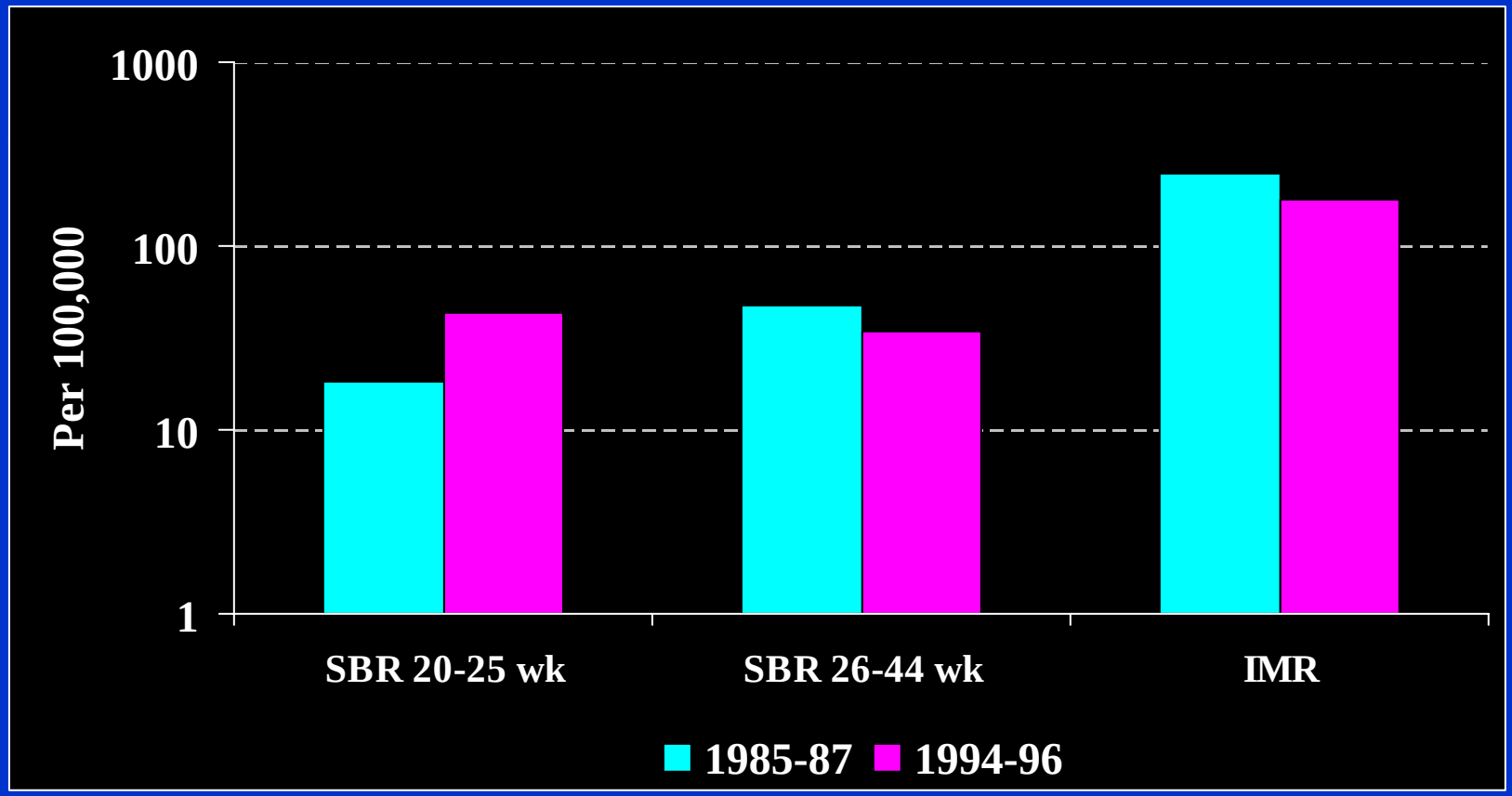
WASI Full-Scale IQ vs GA

Completed wks (n)	Crude Diff (95% CI)	Adjusted* (95% CI)
37 (n=469)	-2.6 (-3.7 to -1.4)	-1.7 (-2.7 to -0.7)
38 (n=2,100)	-0.6 (-1.1 to -0.01)	-0.4 (-1.1 to +0.2)
39-41 (n=11,074)	0.0 (reference)	0.0 (reference)
42 (n=171)	-1.4 (-3.5 to +0.6)	-0.5 (-2.6 to +1.6)
43 (n=10)	-5.8 (-14.0 to +2.5)	-6.0 (-15.0 to +3.1)

*Adjusted for clustering, marital status, number of other children, and parental education & occupation

Stillbirth and Infant Mortality Due to Congenital Anomalies

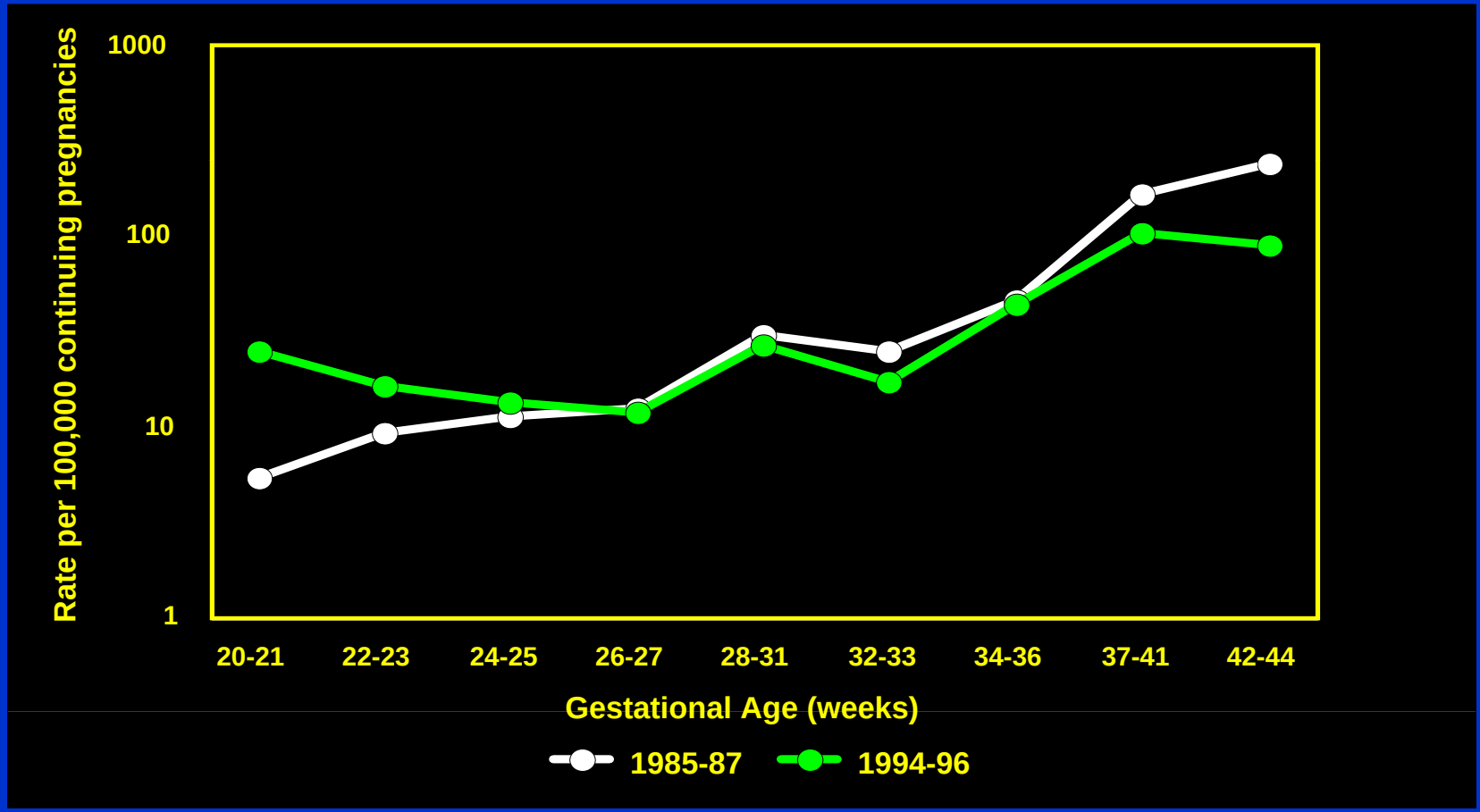
Canada, 1985-96



Source: Liu et al, Am J Med Gen 2001;104:7-13

Canadian Infant Mortality Due to Congenital Anomalies

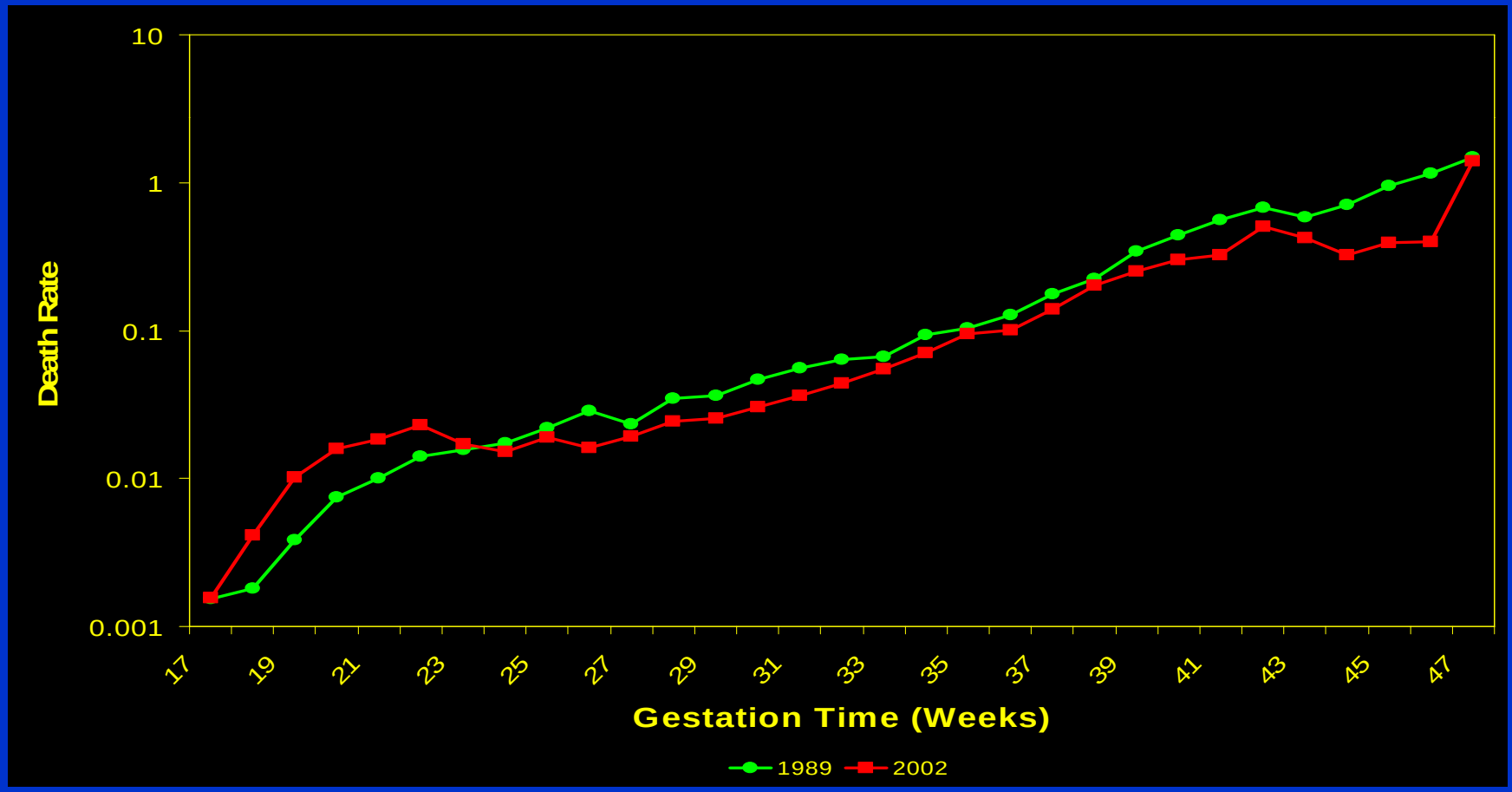
1994-96 vs 1985-87



Source: Liu et al, Am J Med Gen 2001;104:7-13

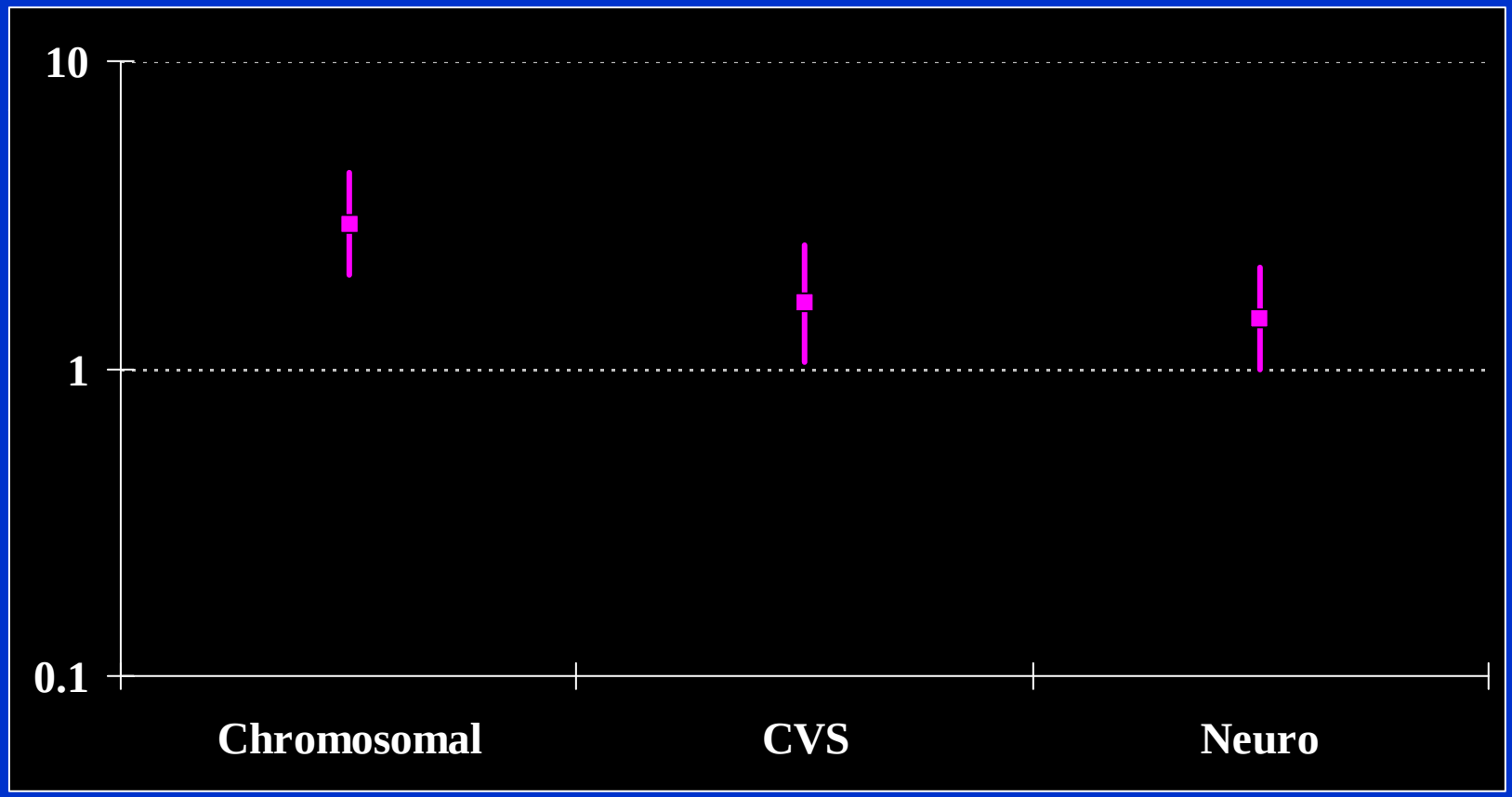
U.S. Infant Mortality Due to Congenital Anomalies

2002 vs 1989



U.S. Infant Mortality Due to Congenital Anomalies ≤24 Wk

RR in 2002 vs 1989 (By Type)



Importance of AFE

- AFE is one of the leading causes of maternal mortality in developed countries
- In Canada
  - 1988-1992: 13 of 99 direct maternal deaths
  - 1997-2000: 7 of 44 direct maternal deaths
  - Ranks 3rd behind cerebrovascular and hypertensive disorders
  - Ranks ahead of postpartum hemorrhage and other pulmonary embolisms

Etiology

- Believed to arise from simultaneous tears in fetal membranes and uterine vessels
  - Permits amniotic fluid to enter uterine vein
  - Hence to pulmonary arterial circulation
- Sudden dyspnea and cardiopulmonary collapse
  - Mechanism unclear, but resembles anaphylaxis
    - Prostaglandins?
    - Leukotrienes?
    - Histamine?
    - Bradykinin?
  - Probably involves genetic susceptibility

Methods

- Population-based cohort of 3,018,781 hospital deliveries in Canada, FYs 1991-2002
  - Hospital records collected by Canadian Institute for Health Information (CIHI)
  - Quebec, Manitoba, Nova Scotia excluded
  - Includes ~70% of all Canadian deliveries
- Diagnoses: ICD-9 (673.1) and ICD-10 (O88.1)
- Procedures
  - Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (1991-2001)
  - Canadian Classification of Interventions (2001-02)

Risk Factors Studied

- Plurality (singleton vs multiple)
- Maternal age
- Medical and surgical induction of labour
- Presentation (cephalic vs noncephalic)
- Delivery method (cesarean, vacuum, forceps, SVD)
- Previous cesarean delivery
- Pregnancy complications (hypertensive disorders, placenta previa/abruption, diabetes, polyhydramnios, amniotic infection)
- Labor complications (prelabour membrane rupture, cervical laceration or rupture, fetal distress, dystocia)
- Fetal macrosomia and fetal growth restriction
- Elderly primigravidity and grand multiparity (parity not coded)

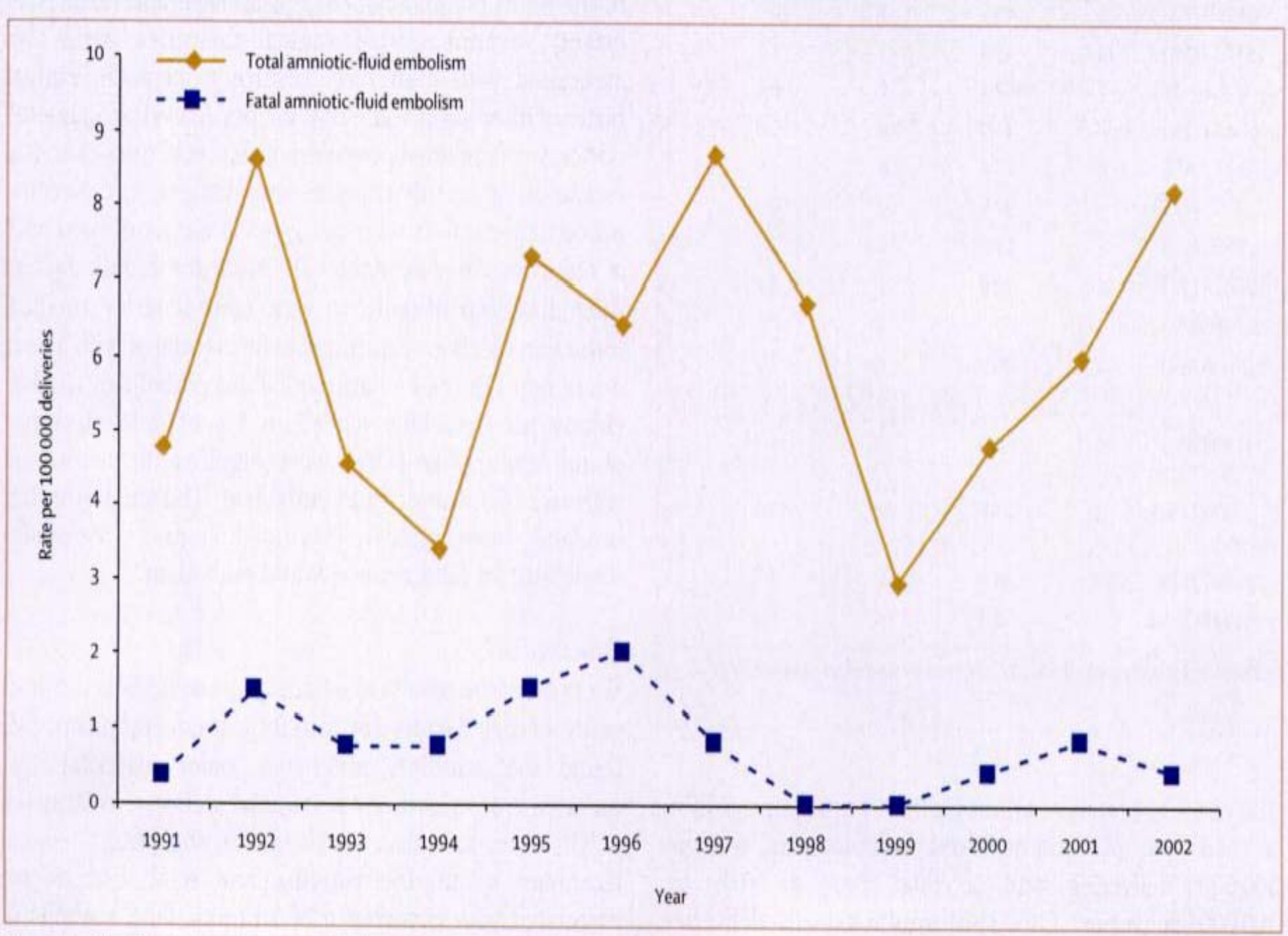


Figure: **Total and fatal rates of amniotic-fluid embolism in singleton deliveries per year in Canada, 1991–2002**

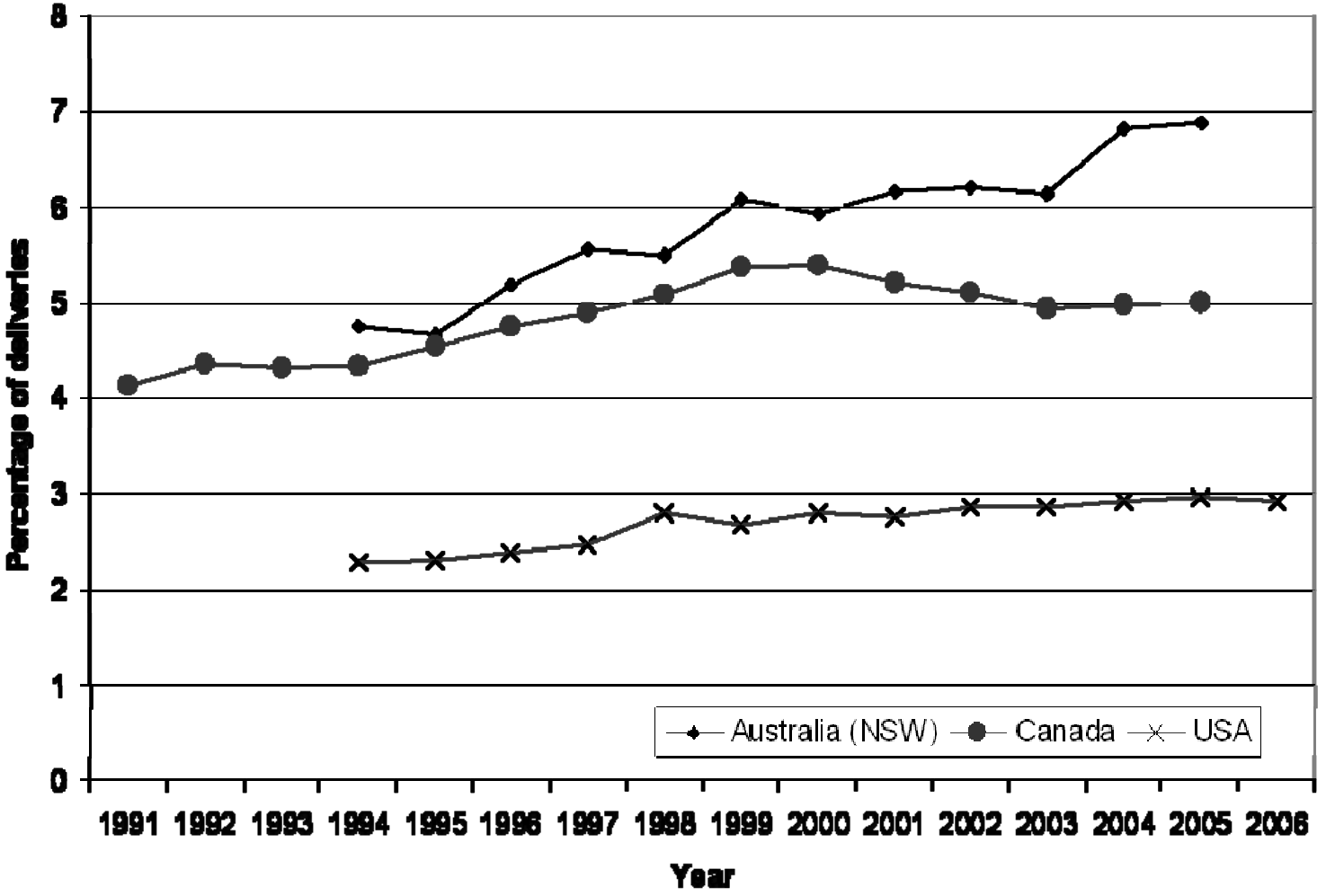
Results

- Risk among singletons (n = 2,984,977)
  - Total AFE (n = 180): 6.0 per 100,000
  - Fatal AFE (n = 24): 0.8 per 100,000
- Risk among multiples (n = 33,804)
  - AFE (total n = 5; 0 fatal): 14.8 per 100,000
  - RR (vs singletons) = 2.5 (95% CI = 1.0-6.0)
- Multiple logistic regression: singletons only
- Adj OR = 1.8 (1.3-2.7) for medical induction

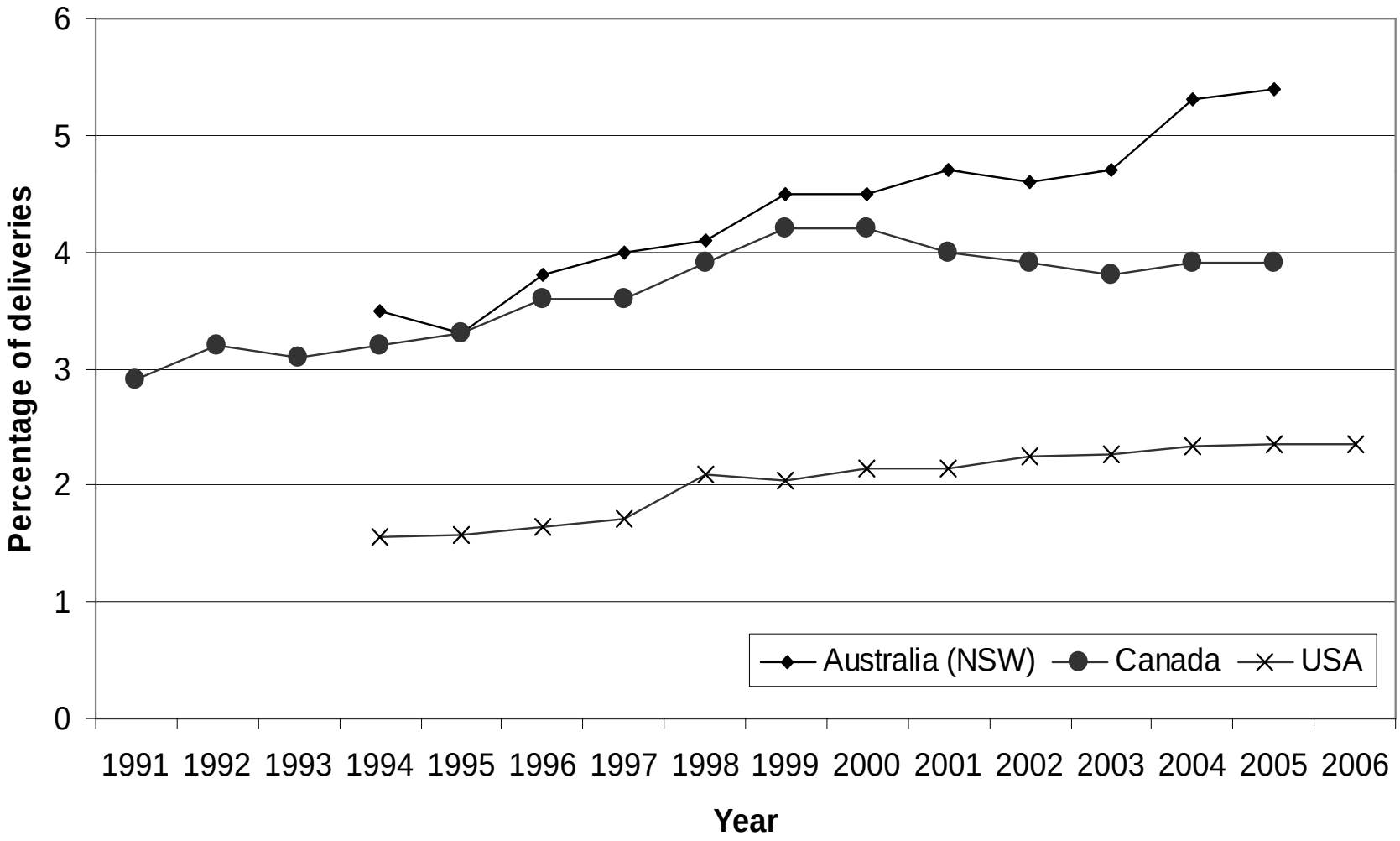
Labor Induction and AFE

Country	Adjusted OR (95% CI)
Canada	1.8 (1.3-2.7)
U.S.	1.5 (0.9-2.3)
U.K.	3.9 (2.0-7.3)
Australia (NSW)	1.9 (0.8-4.9)

Temporal Trends in Total PPH



Temporal Trends in Atonic PPH



Objectives

- Examine risk factors for PPH
- Describe temporal trends in risk factors
- Assess extent to which trends in risk factors account for trend in PPH

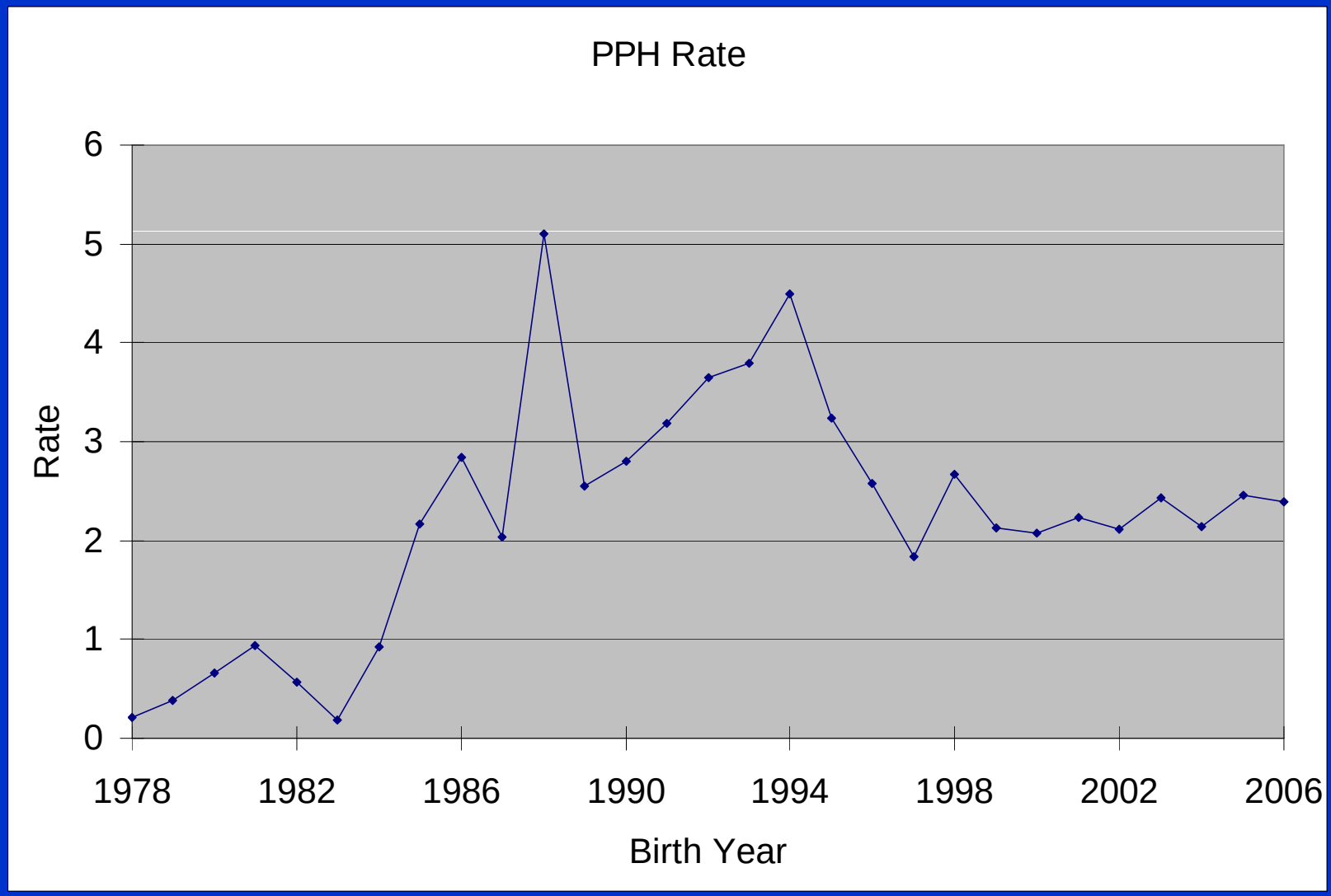
Data Source

- McGill Obstetric and Neonatal Database
- Consecutive singleton deliveries, Royal Victoria Hospital, Montreal
  - January 1, 1978-January 31, 2007
  - N = 103,726
- Standardized medical records abstraction
  - Any PPH (>500 ml vaginal, >1000 ml CD)
  - Severe PPH (>1500 ml, available since 2001)
  - PPH + blood transfusion and/or hysterectomy

Methods

- Potential risk factors & covariates
  - Sociodemographic
  - Pre-pregnancy
  - Pregnancy
  - Labor
  - Delivery
- Crude and adjusted associations
- Temporal trends in PPH and risk factors

Temporal Trend in PPH



Factors Not Associated with PPH

- Maternal education
- Maternal smoking
- Diabetes or impaired glucose tolerance
- Duration of labor >12 hours
- Maternal height
- Maternal pre-pregnancy BMI
- Labor analgesia
- Labor anesthesia (including epidural)

Sequential Logistic Regression for Yearly Trend in PPH

Model	OR (95% CI)
Year only	1.029 (1.024-1.034)
Plus maternal age	1.028 (1.023-1.033)
Plus parity	1.027 (1.022-1.033)
Plus prior cesarean	1.006 (1.000-1.012)
Plus labor induction	1.005 (0.999-1.011)
Plus augmentation	0.998 (0.992-1.004)
Plus placenta previa	0.997 (0.991-1.004)
Plus abnormal placenta	0.995 (0.988-1.001)

Increasing Obstetric Intervention
Changing the Landscape

- Infertility treatment: ↑ multiples, preterm birth
- Prenatal diagnosis, TOP: ↑ infant mortality
- Labor induction
  - ↑ preterm birth, PPH; ↑ risk for AFE
  - ↓ postterm stillbirth, but also GA and BW at term
- Cesarean delivery
  - ↑ maternal morbidity in index pregnancy
  - ↑ risk of PPH in later pregnancies

Increased Obstetric Intervention:
More Good Than Harm?

- Benefits
  - Children for infertile couples
  - TOP for birth defects
  - ↓ postterm stillbirths
- Harms
  - ↑ late preterm and early term births
  - ↑ maternal morbidity (index, future pregnancies)
- Time for a large RCT of early induction?