Late Preterm Birth: Etiology, Outcomes & Prevention

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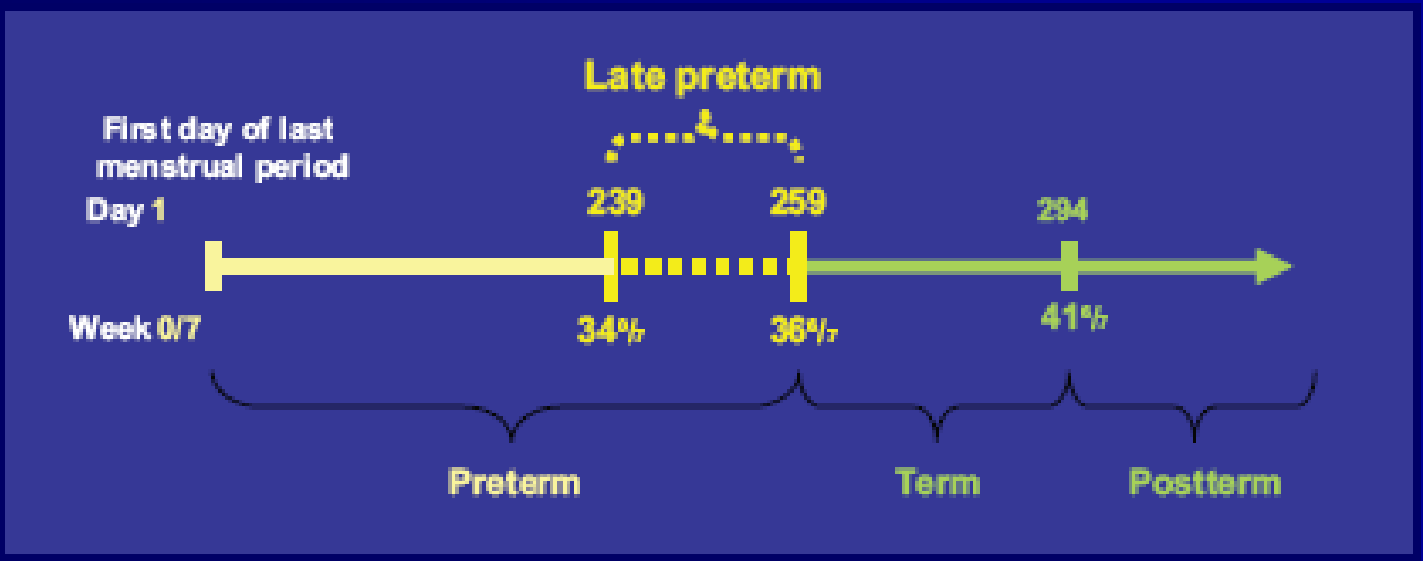
Late PTB definition

- Neonates born between 34 0/7 and 36 6/7 gestational weeks



ACOG Committee Opinion No. 404, 2008
Engle WA et al Pediatrics 2007

Late preterm neonates

- A population that is at risk for adversity but often overlooked in research & clinical practice because of mistaken perceptions that these babies are physiologically mature

ACOG Committee Opinion No. 404, 2008

Late PTB epidemiology

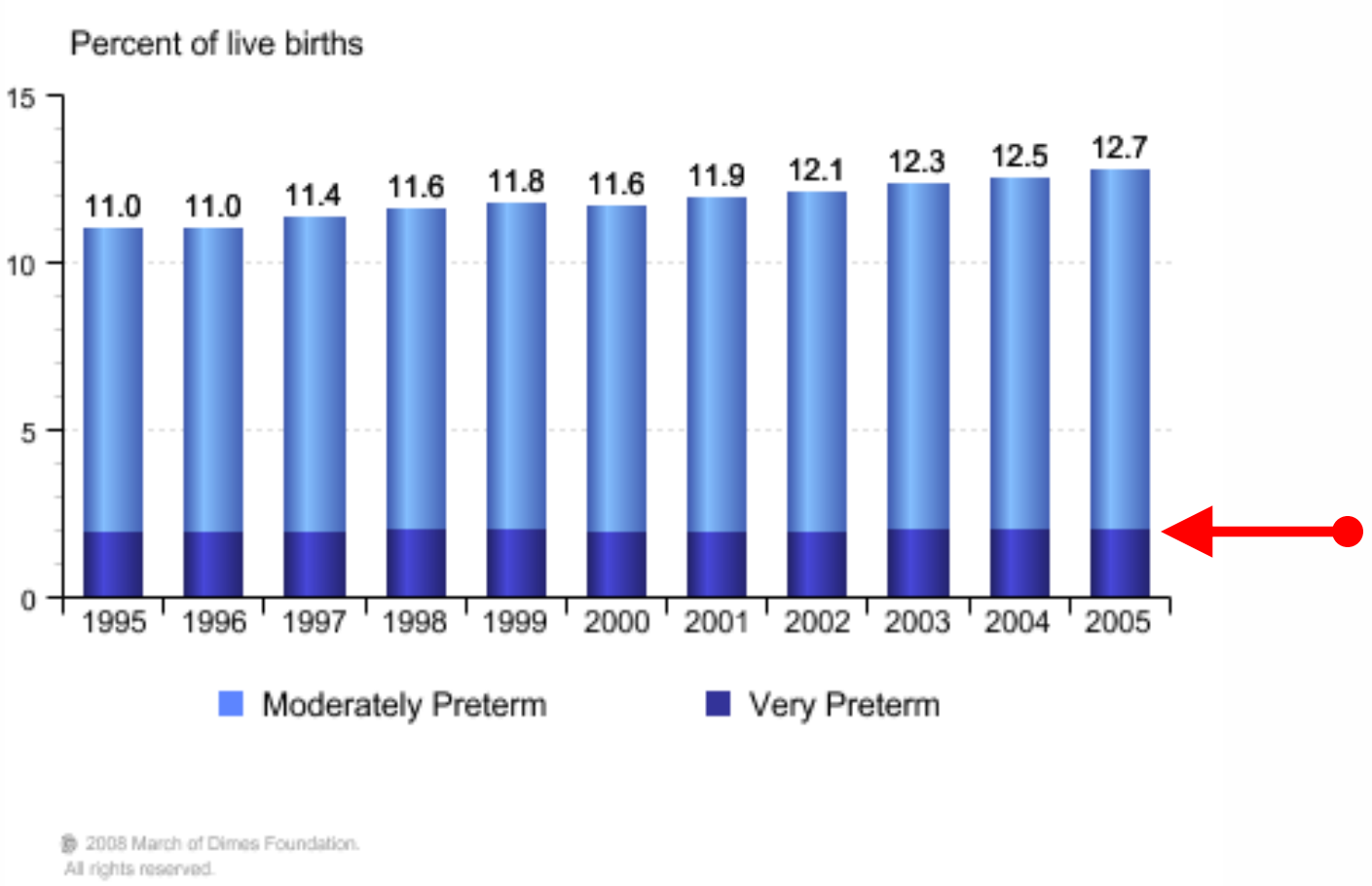
- Most of the recent rise in preterm birth rate in the US is attributed to late PTB
  - Very PTB rate has been fairly stable since 1990
- Late PTB accounts for over 71% of preterm birth in the US
- Leading cause of death in the 1st month of life

Davidoff MJ et al Semin Perinatol 2006

NCHS final natality data 2008

Preterm births

US, 1995-2005



Preterm is less than 37 completed weeks gestation. Very preterm is less than 32 completed weeks gestation. Moderately preterm is 32-36 completed weeks of gestation.
Source: National Center for Health Statistics, final natality data. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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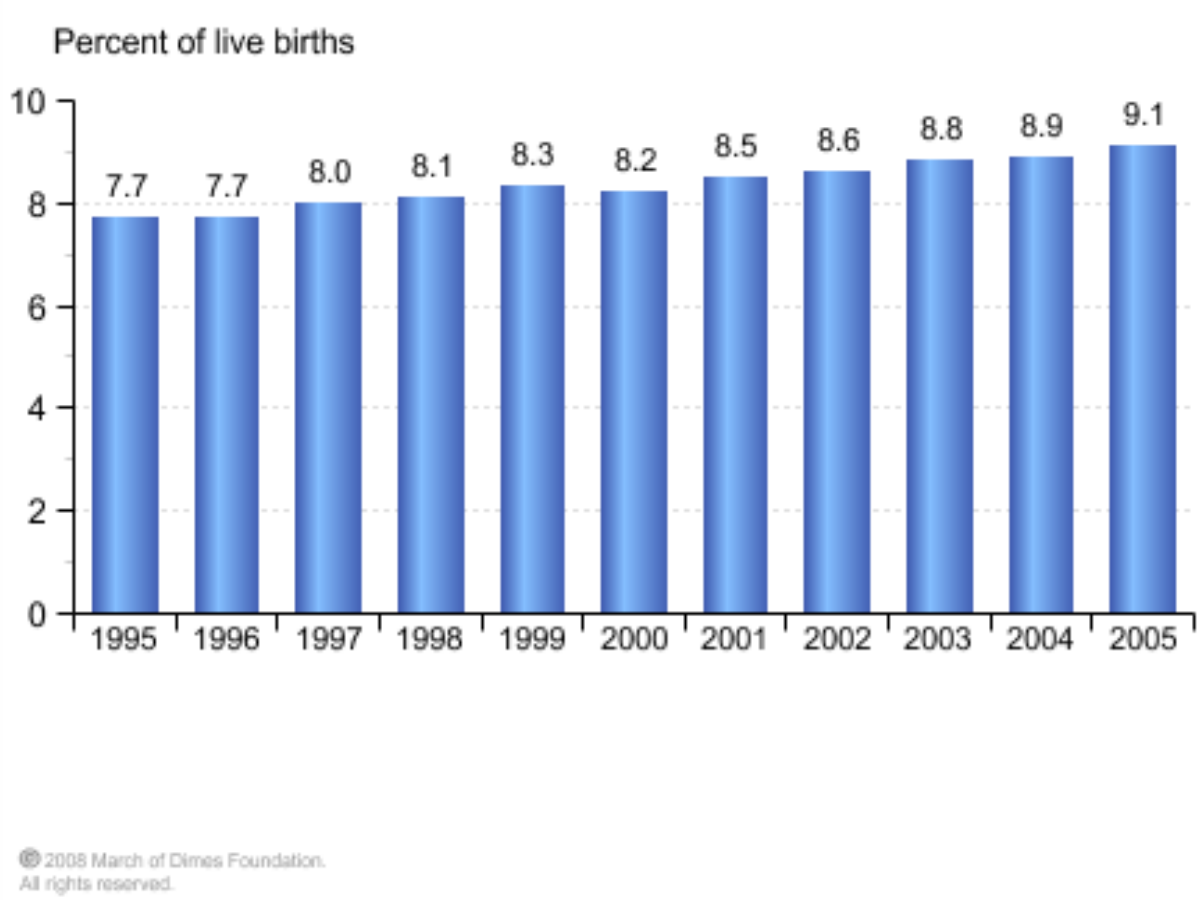
Late preterm births

US, 1995-2005



Late preterm is between 34 and 36 completed weeks gestation.
Source: National Center for Health Statistics, final natality data. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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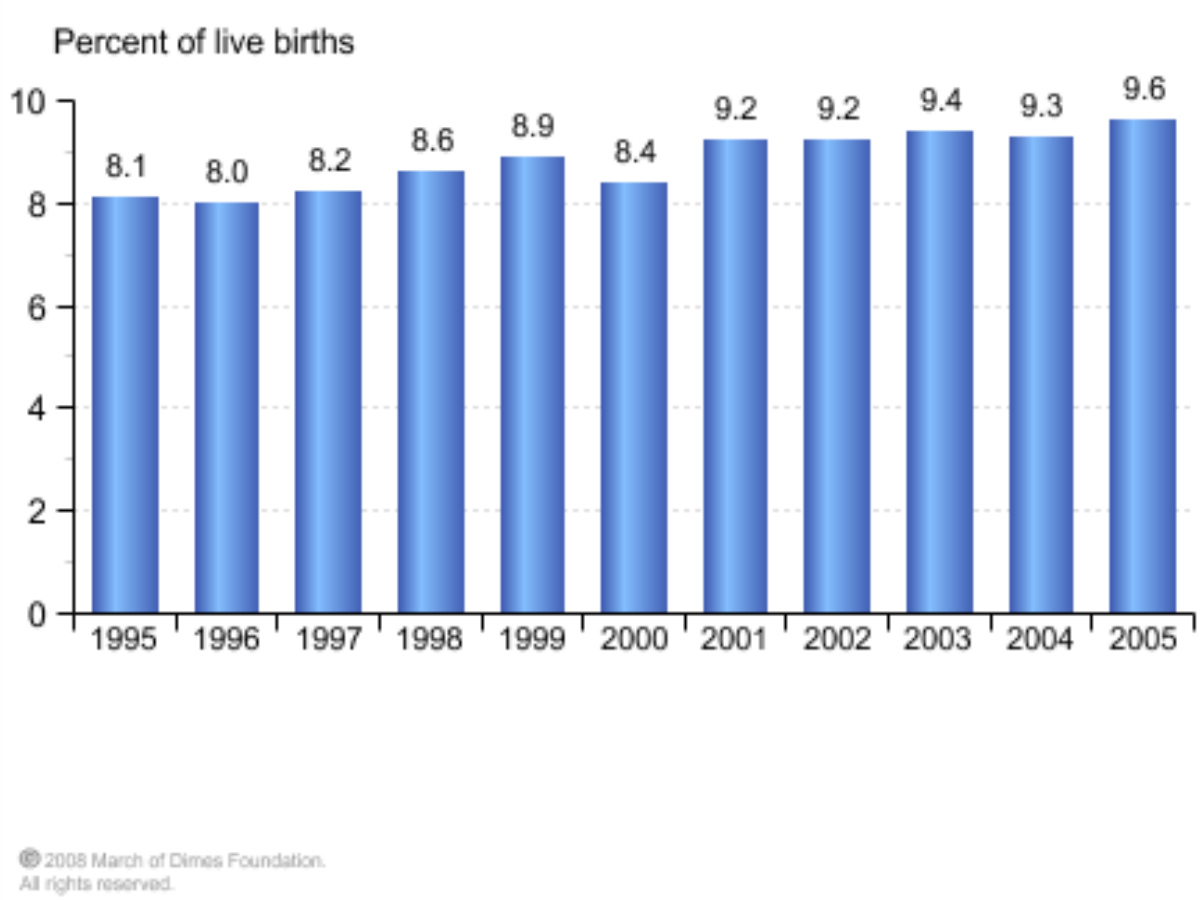
Late preterm births

Missouri, 1995-2005



Late preterm is between 34 and 36 completed weeks gestation.
Source: National Center for Health Statistics, final natality data. Retrieved September 16, 2008, from www.marchofdimes.com/peristats.

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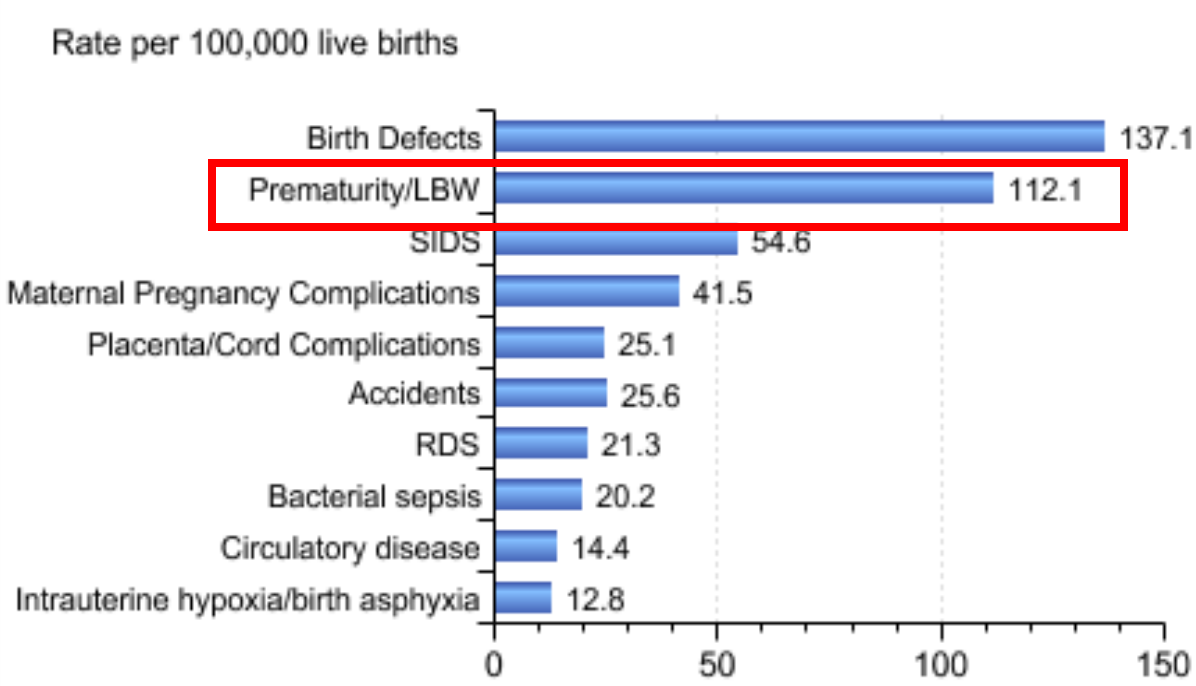
Ten leading causes of infant mortality

US, 2004



An infant death occurs within the first year of life. SIDS is Sudden Infant Death Syndrome. RDS is Respiratory Distress Syndrome.
Source: National Center for Health Statistics, period linked birth/infant death data. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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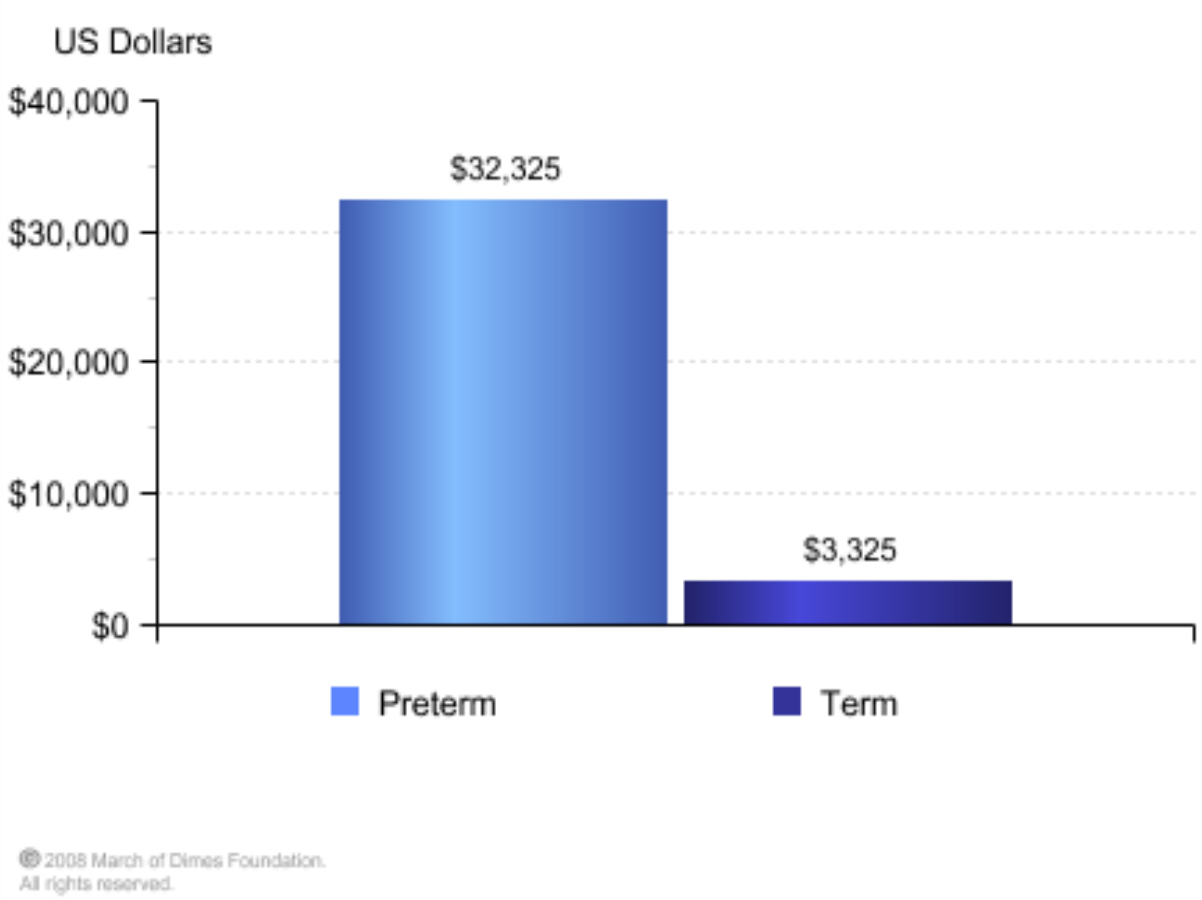
Average medical costs among preterm and term births

US, 2005



Preterm is less than 37 completed weeks gestation.
Source: Institute of Medicine. 2006. Preterm Birth: Causes, Consequences, and Prevention. National Academy Press, Washington, D.C.
Published and unpublished analyses. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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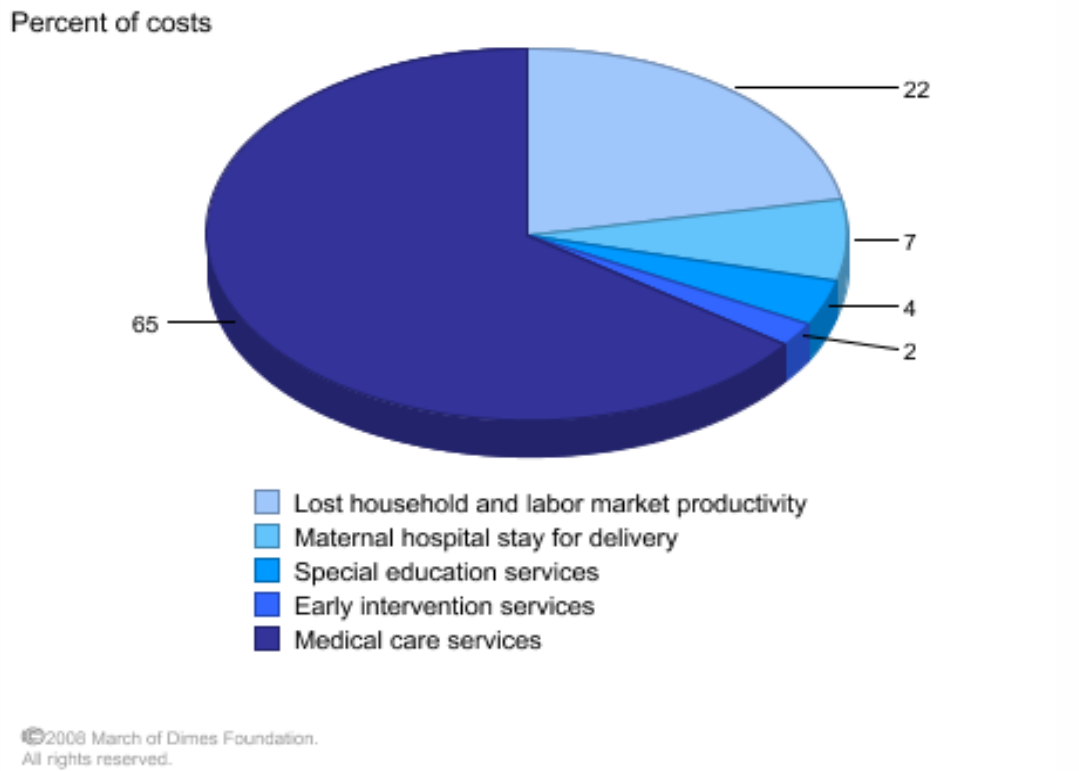
Distribution of $26 billion societal economic costs of preterm birth

US, 2005



Source: Institute of Medicine. 2006. Preterm Birth: Causes, Consequences, and Prevention. National Academy Press, Washington, D.C. Published and unpublished analyses. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

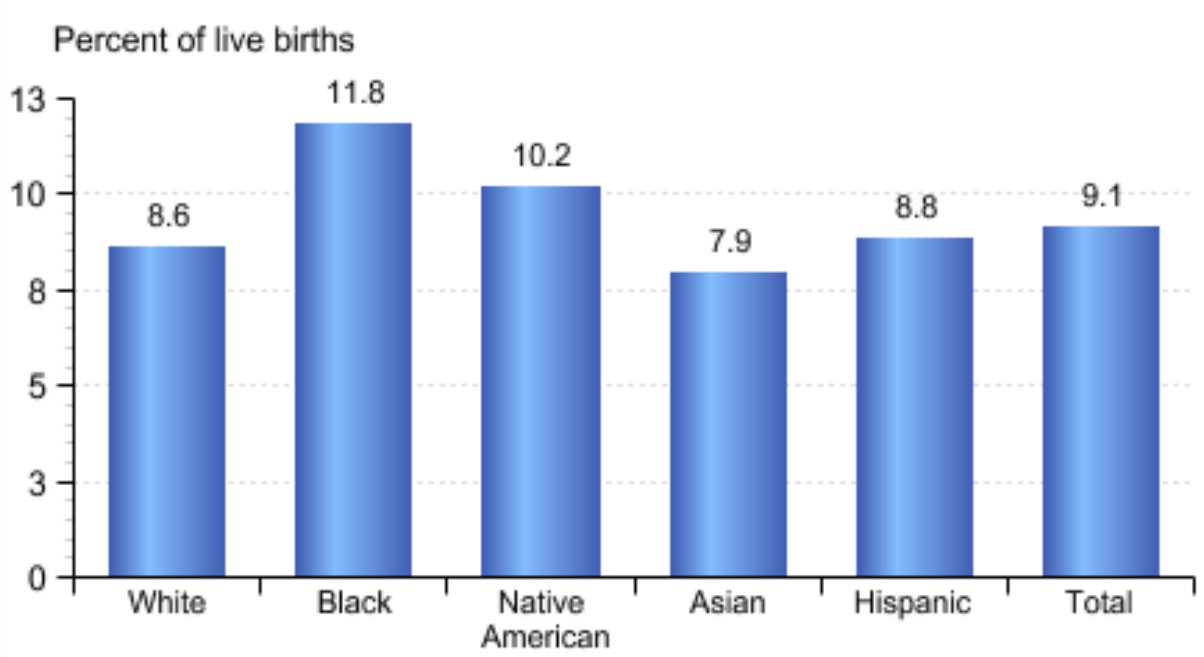
Late PTB epidemiology

- Some of the major risk factors
  - Prior PTB
  - Race
  - Maternal age
  - Tobacco (21% mothers in US) or drugs
  - Infection
  - Maternal chronic disease or pregnancy complications
  - Multifetal pregnancies & ART

Iams JD Clin Perinatol 2003.
CDC

Late preterm births by maternal race/ethnicity

US, 2005



Rates for all races except Black have been trending upward

All race categories exclude Hispanics. Late preterm is between 34 and 36 completed weeks gestation.
Source: National Center for Health Statistics, final natality data. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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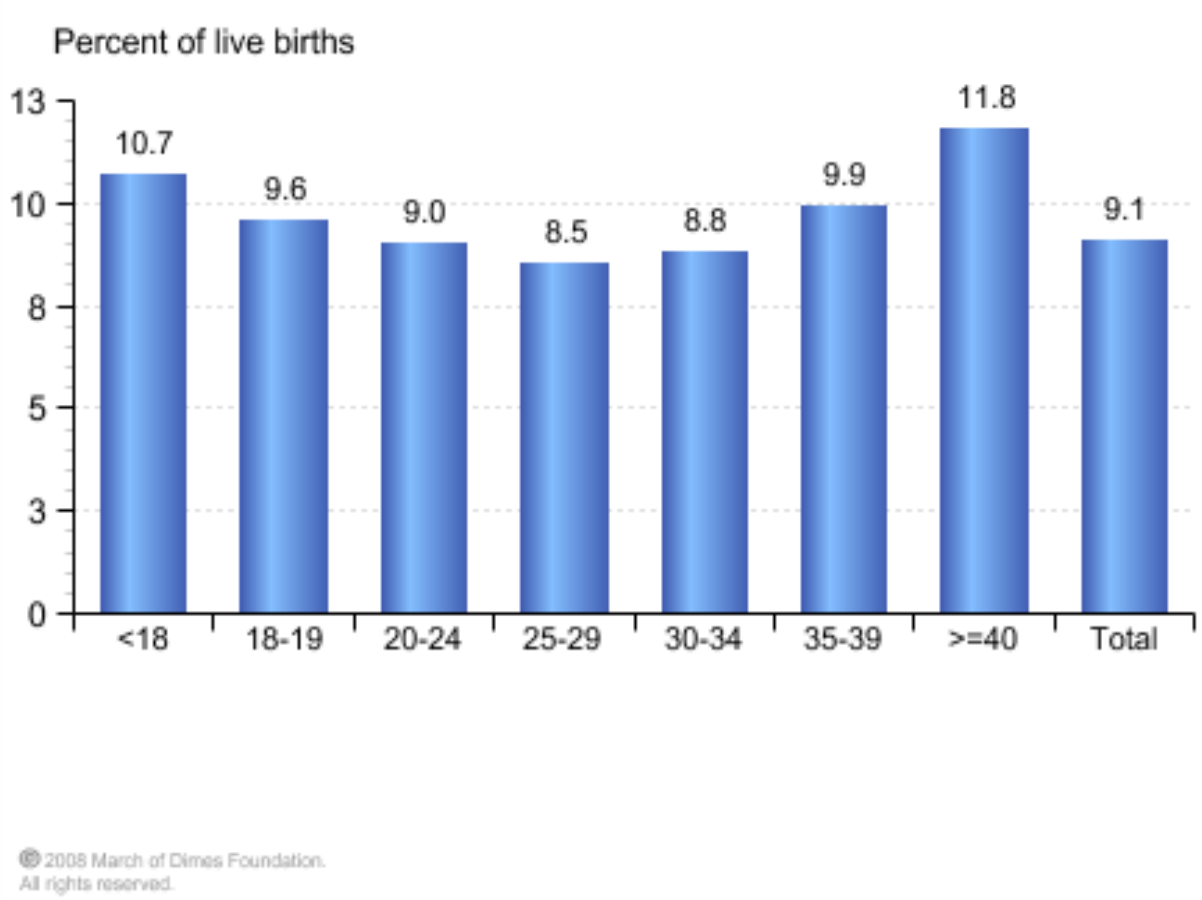
Late preterm births by maternal age

US, 2005



Late preterm is between 34 and 36 completed weeks gestation.
Source: National Center for Health Statistics, final natality data. Retrieved June 18, 2008, from www.marchofdimes.com/peristats.

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Late PTB epidemiology

- >26,000 MI death/birth certificate data
- 75% spontaneous & 25% indicated PTB
- Maternal morbidities in late PTB (v term)
  - Hypertension (15% vs 7%)
  - Diabetes (8% vs 5%)
  - Lung disease (6% vs 4%)
  - Cardiac disease (2% vs 1.8%)
  - Renal disease (1% vs 0.5%)

Shapiro-Mendoza et al Pediatrics 2008

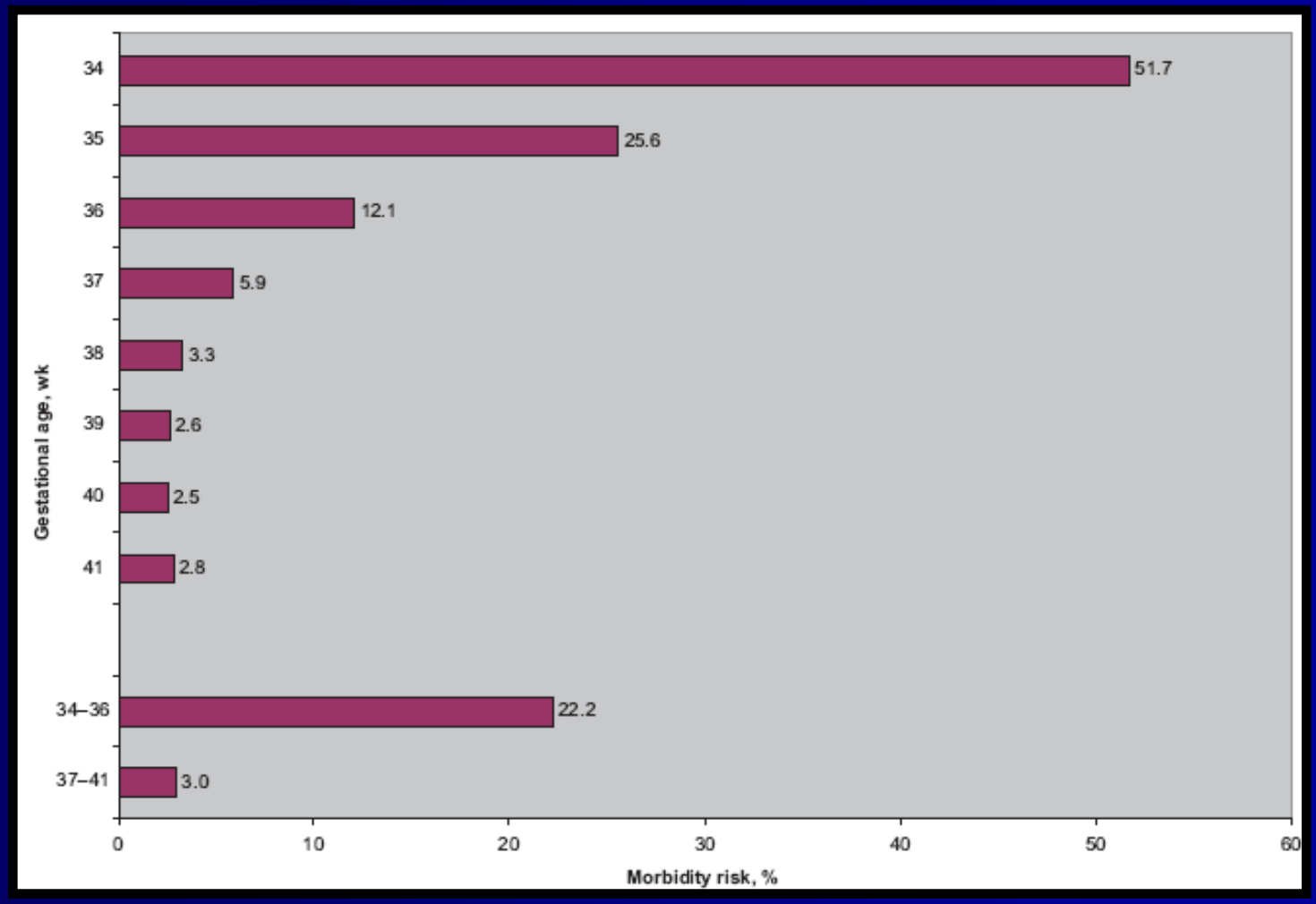
Late PTB epidemiology

- Synergy between late PTB & maternal disease for risk of newborn morbidity
  - Morbidity 7x more likely in late PTB than term (22% vs 3%)
  - Morbidity rate doubled for each week earlier than 38 weeks
  - OR for morbidity 9-12 when both late PTB & maternal disease present

Shapiro-Mendoza et al Pediatrics 2008

Late PTB neonatal morbidity

Shapiro-Mendoza et al Pediatrics 2008



Late PTB neonatal outcomes

- Late PTB newborns 4-7 times more likely to have a least 1 medical condition
  - Temperature instability (10% vs 0%)
  - Hypoglycemia (16% vs 5%)
  - RDS (29% vs 4%)
  - Apnea (6% vs <0.1%)
  - Jaundice (54% vs 38%)
  - Feeding difficulties (32% vs 7%)
  - ICN (88% at 34 weeks vs 2.6%)

ACOG Committee Opinion No. 404, 2008
Engle W & Kominiarek MA. Clin Perinatol 2008
Shapiro-Mendoza et al Pediatrics 2008

Late PTB neonatal outcomes

- Neonatal mortality 4.6 times higher
  - 4.1 vs 0.9/1000 live births
- Infant mortality 3.1 times higher
  - 7.7 vs 2.5/1000 live births

Engle W & Kominiarek MA. Clin Perinatol 2008

Late PTB neonatal outcomes

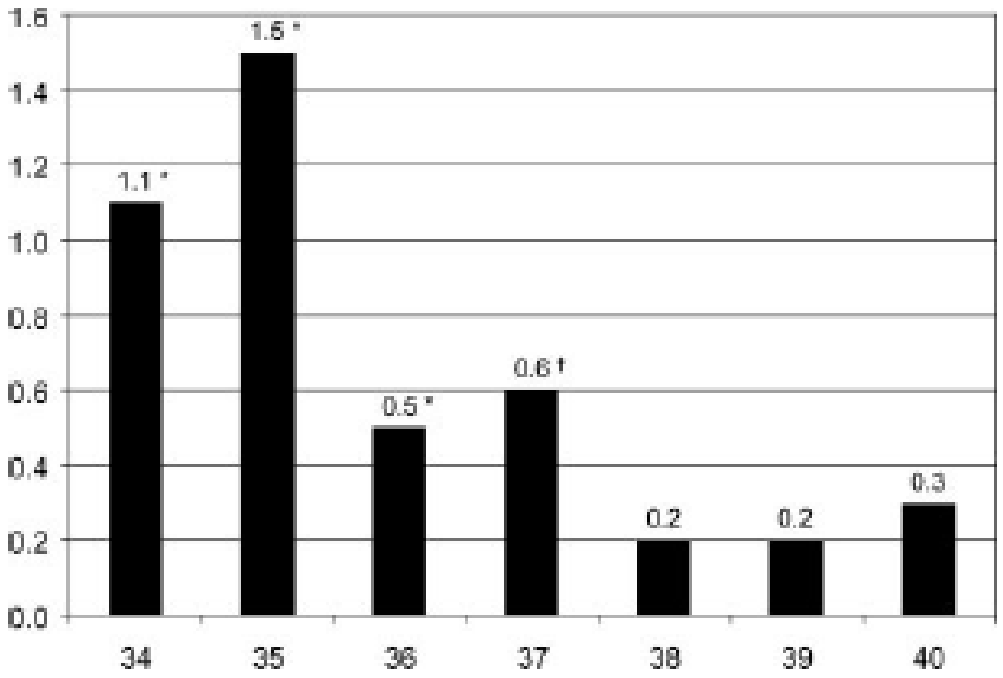


Fig. 2. Neonatal death rates from 34 to 40 weeks of gestation in singleton infants without malformations. *$P<.001$ compared with 39 weeks as the referent. †$P=.02$ compared with 39 weeks as the referent.

McIntire. Late Preterm Births and Neonatal Morbidity. Obstet Gynecol 2008.

- 18-yr single center cohort (N=241,000)
- M & M increased at 36, 35 & 34 weeks

Late PTB neonatal outcomes

- Long term outcomes: developmental delay, ADHD & behavior problems, respiratory disorders

Table 3
School age outcome of healthy late preterm (n = 22,552) versus healthy term (n = 164,628) infants in Florida

Outcome	Age (years)	Relative risk (95% confidence interval)
Developmental delay or disability	0–3	1.46 (1.42–1.50)
Special education	5	1.13 (1.11–1.15)
Grade retention	5	1.11 (1.08–1.14)

Data from Adams-Chapman I. Neurodevelopmental outcome of the late preterm infant. Clin Perinatol 2006;30:947–64; with permission, and Morse SB, Tang Y, Roth J. School-age outcomes of healthy near-term infants (34–37 weeks) versus healthy term infants (38–42 weeks). Pediatr Res 2006;1(Suppl):158.

“Early term” neonates

- 37-38 gestational weeks
- Increased risk for:
  - RDS 1.8% (3-fold increase)
  - Pulmonary hypertension
  - ICN admission or prolonged admission
  - Asthma
  - Food allergies

Engle W & Kominiarek MA. Clin Perinatol 2008

Implicated factors for increased rate of late PTB

- Increased surveillance
- Inaccurate gestational age
- Increased multifetal pregnancies
- Worsening maternal demographics
- Presumption of maturity at 34 wks
- Fear of fetal risks

- Maternal autonomy
- Physician practice patterns
  - Convenience
  - Delivery w/o indication
  - Planned delivery
  - Delivery mode

A rise in medically indicated PTB

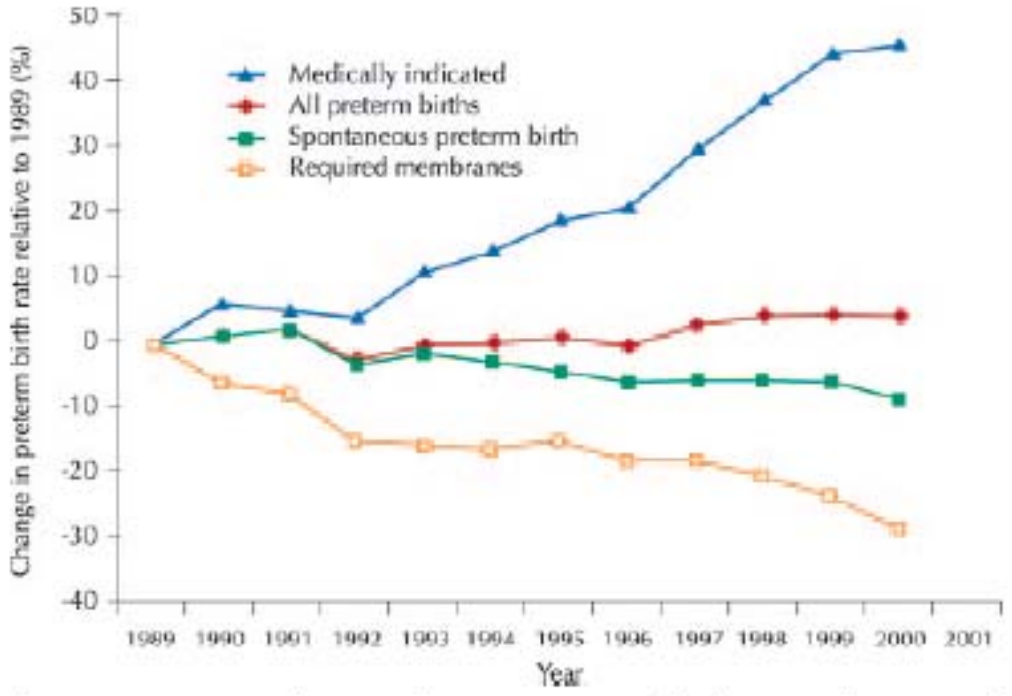
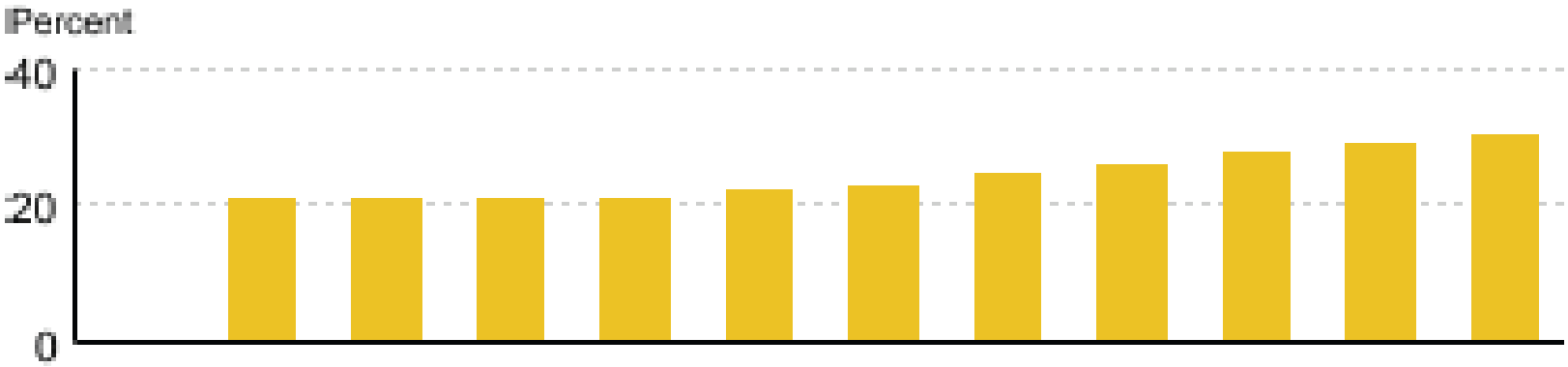


Fig. 2. Reasons for singleton preterm births in the United States, 1989–2000. Ananth CV, Joseph KS, Oyelese Y, Demissie K, Vintzileos AM. Trends in preterm birth and perinatal mortality among singletons: United States, 1989 through 2000. Obstet Gynecol 2005;105:1084–91.

Leveno. Rising Cesarean Delivery and Preterm Birth Rates. Obstet Gynecol 2008.

- Shifting rates of morbidity or lower threshold for delivery?

Rise in cesarean rate



Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
US Rate	20.8	20.7	20.8	21.2	22.0	22.9	24.4	26.1	27.5	29.1	30.3

- Between 1995 and 2005, the percent of live births delivered by cesarean section in the United States increased nearly 46%.

NCHS final natality data, March of Dimes

Rise in cesarean rate: related to increase in PTB?

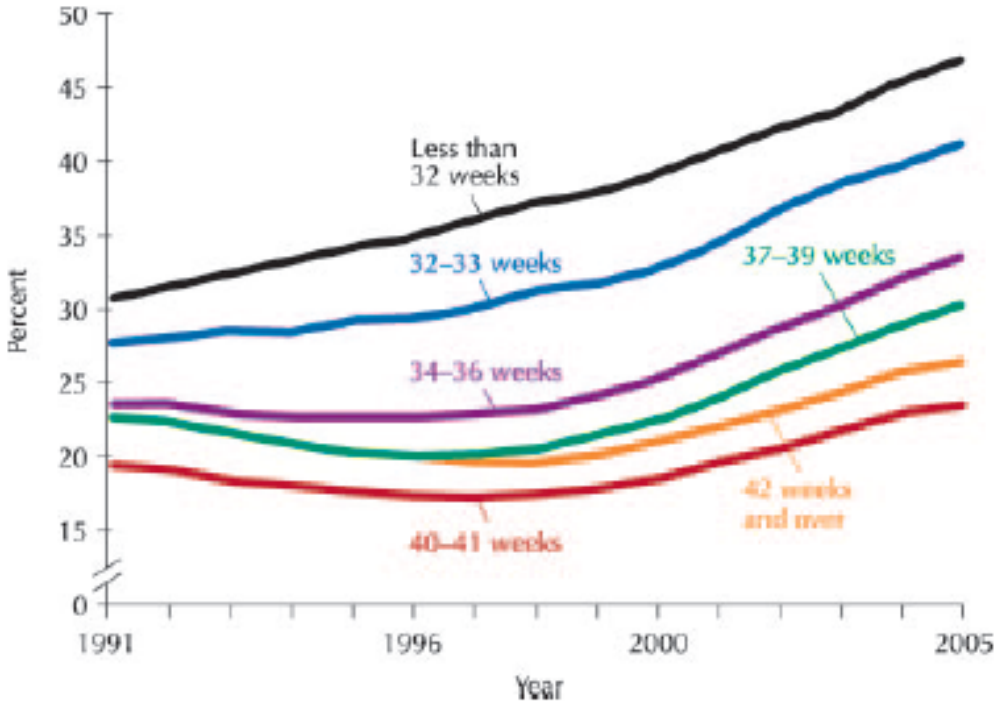


Fig. 1. Rise in cesarean rates according to gestational age for live births in the United States, 1991–2005. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S et al. Births: final data for 2005. Natl Vital Stat Rep 2007;56:1–202.

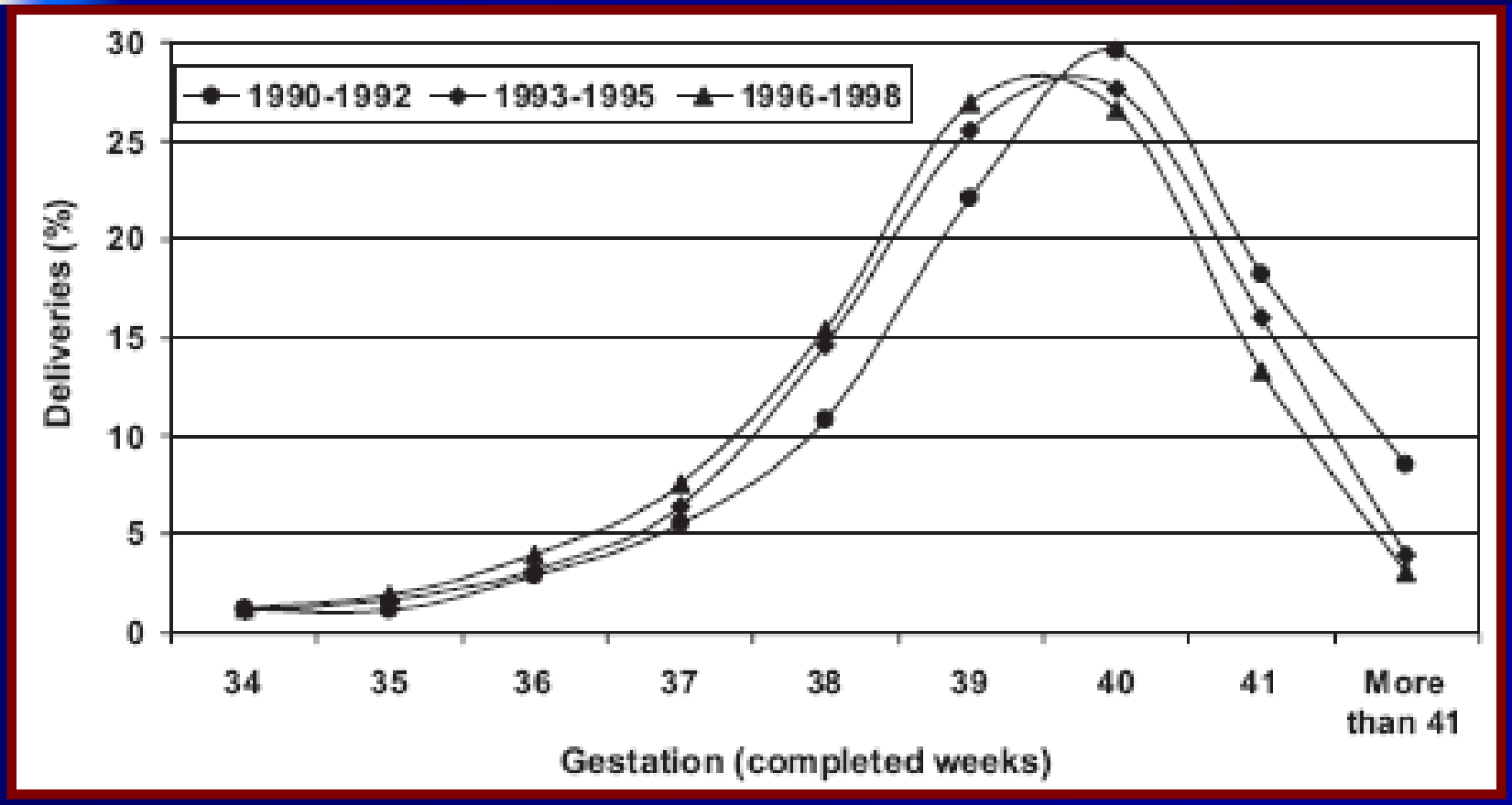
Leveno. Rising Cesarean Delivery and Preterm Birth Rates. Obstet Gynecol 2008.

Late PTB, cesarean & pregnancy complications

- Over a 9-year period at 1 tertiary center: increased rates of cesarean & late PTB
  - Both associated with increased neonatal respiratory complications
- Increase in DM, HTN, maternal weight, nonreassuring FHR, fetal sonography, scant prenatal care
- Shift downward in delivery gestational age distribution

Yoder BA et al. Obstet Gynecol 2008

Late PTB, cesarean & pregnancy complications



Yoder BA et al. Obstet Gynecol 2008

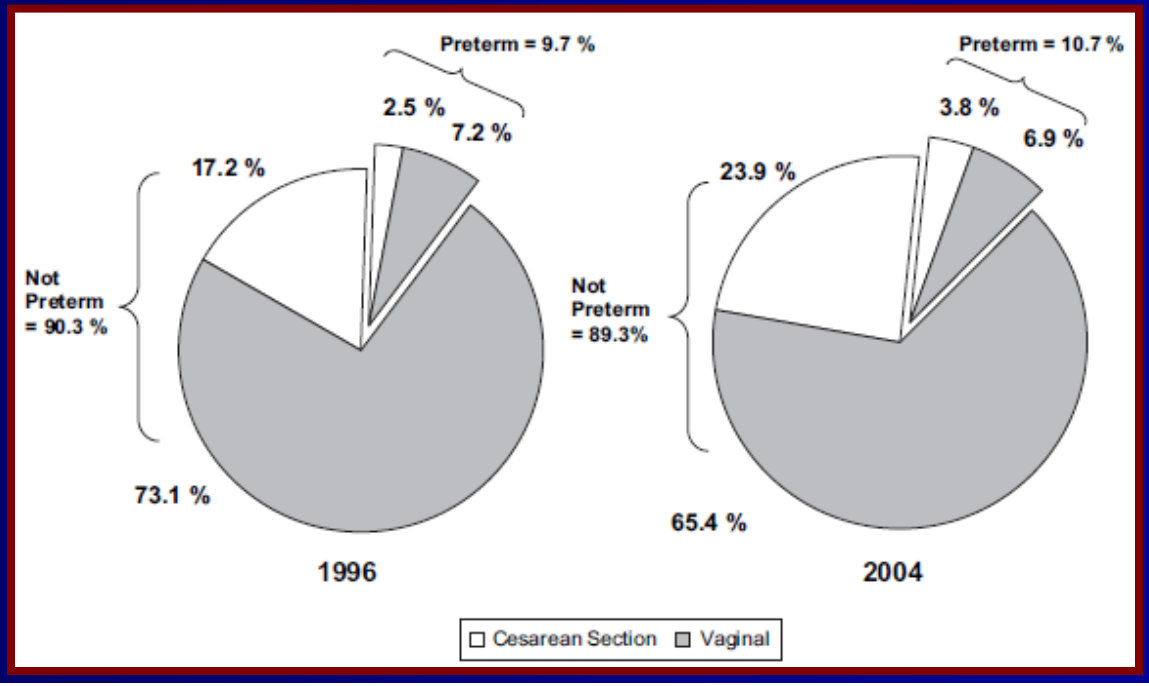
Late PTB, cesarean & pregnancy complications

- Yee & colleagues *Obstet Gynecol* 2008
  - Canadian cohort
  - Elective cesarean at 36-38 4/7 weeks associated with increased neonatal respiratory morbidity

Rise in cesarean rate: related to increase in PTB?

(Bettegowda VR et al. Clin Perinatol 2008)

- Increase in US singleton PTB rate from 1996 to 2004 occurred primarily among those delivered by cesarean with the largest % increase in late PTB
  - Almost no increase in late PTB via vaginal delivery & 92% of late PTB increase attributed to cesarean



Rise in cesarean rate: related to increase in PTB?

(Bettegowda VR et al. Clin Perinatol 2008)

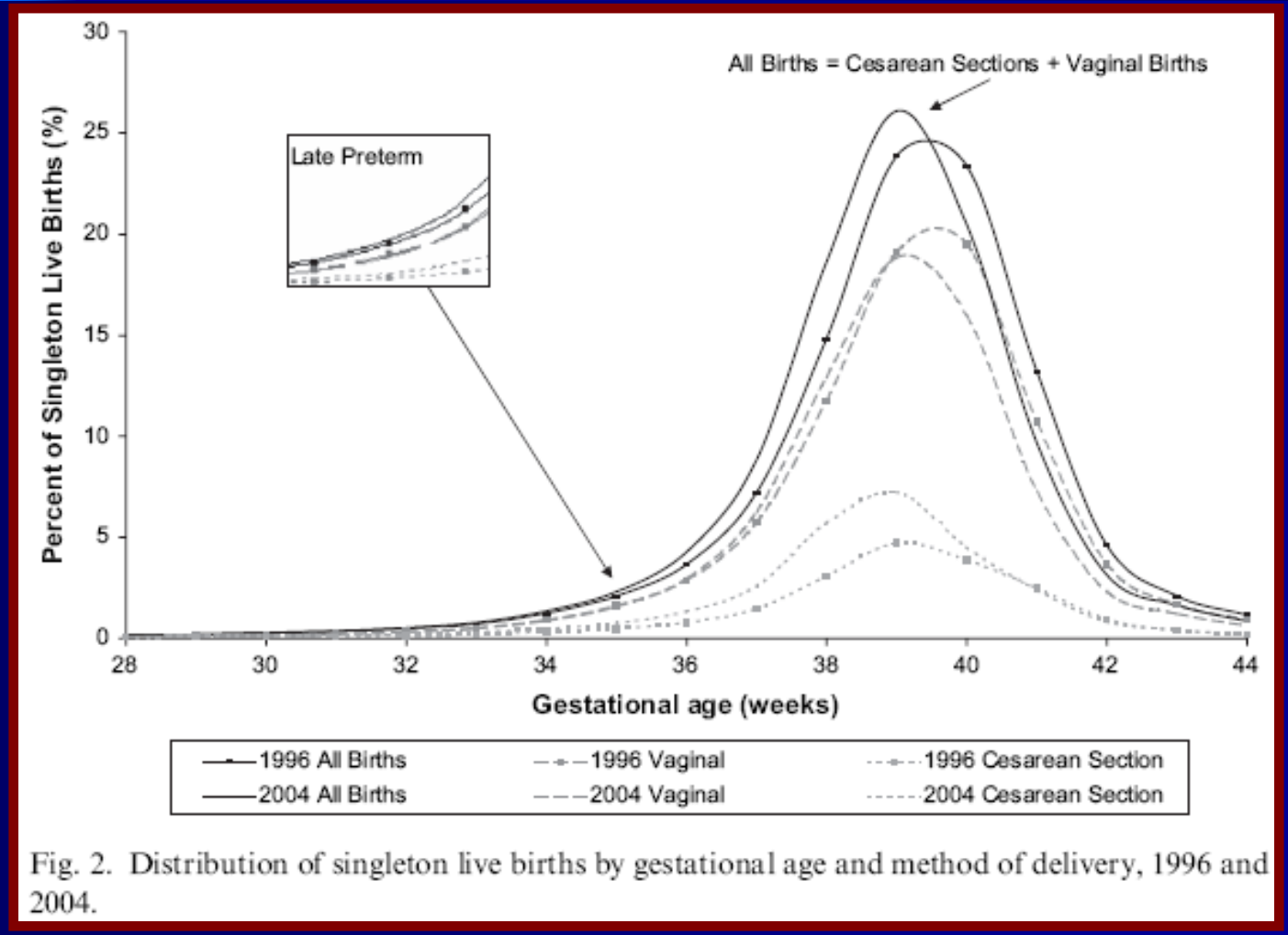


Fig. 2. Distribution of singleton live births by gestational age and method of delivery, 1996 and 2004.

Rise in labor induction rate: related to increase in PTB?

- Left shift in delivery gestational age
- Rise in labor induction & cesarean rates - not explained by changing maternal demographics or risk factors
  - Davidoff & colleagues, Semin Perinatal 2006
- Several studies show increasing rates of labor induction in general
- Several studies show increasing rates of medically indicated PTB by induction or cesarean

Prevention of late PTB

- Accurate gestational dating
- Prudent use of antenatal fetal testing
- Prudent use of labor induction & cesarean, targeting significant medical indications
- ART strategies to minimize multifetal gestations

Prevention of late PTB

- Fetal lung maturity testing prior to 39 wks for elective deliveries.
- Criteria for inferring 39 wks:
  - FHT on Doppler for 30 wks
  - 36 wks since +hCG
  - CRL at 6-11 wks
  - Ultrasound fetal biometry at 12-20 wks confirms LMP

ACOG Practice Bulletin No. 230. 1996

Prevention of late PTB

- Weekly 250 mg 17-OH progesterone IM (16-36 wks) in pts with a prior preterm birth
  - Reduces PTB risk by 33%
  - Has not been shown to reduce risk in multifetal pregnancies
- Daily 200mg vaginal progesterone 24-34 wks for short cervix (<16mm @ 20-25 wks)
  - Reduces PTB risk by 40%

Meis et al. NEJM 2003
Rouse et al. NEJM 2007
Fonseca et al. NEJM 2007

PTL at 34-36 wks: should it be arrested?

- Labor should not be induced at 34-35 wks
- Tocolysis & steroids "may be considered"
  - Arnon S, et al. Paediatric & Perinatal Epidemiol 2001

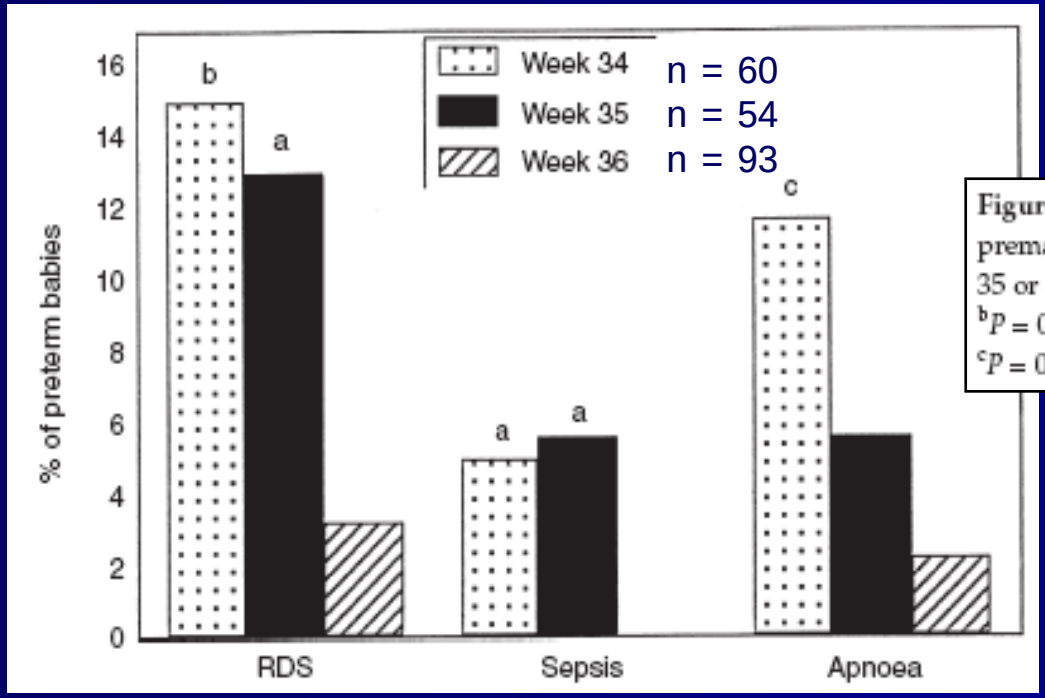


Figure 1. Frequency of RDS, sepsis and apnoea of prematurity (%) of babies born preterm after 34, 35 or 36 weeks of gestation. [a]$P = 0.02$, and [b]$P = 0.008$ compared with the 36-week group, [c]$P = 0.015$ compared with the 36-week group.

Areas in need of research

- Corticosteroid use beyond 34 0/7 wks
- Short term tocolysis beyond 34 wks
- Critical evaluation of OB practices leading to late PTB: possible expectant management of some pregnancy complications
  - E.g. PPROM >34wks, oligohydramnios, IUGR, preeclampsia
- Association between late PTB & cesarean or labor induction

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Thank you …

stamiliod@wustl.edu

Short-term outcomes of late preterm birth: a single center study

Table 3. Outcomes of Babies Admitted to the Special Care Nursery (n = 697)

Gestational age, weeks	34	35	36
Number of babies	252	205	240
Median weight, grams (range)	2277 (1338-3400)	2509 (1416-4658)	2793 (1692-4526)
Median length of stay, days (range)	11 (1, 28)	6 (1, 28)	4 (1, 22)
Median age at full feeds by mouth, days (range)	10 (1, 23)	6 (1, 25)	3 (1, 16)
Received total parenteral nutrition, n (%)	60 (23)	22 (10)	13 (5)
Received surfactant, n (%)	43 (16)	43 (20)	35(14)
Received mechanical ventilation, n (%)	62 (24)	58 (28)	41 (17)
Received nasal cannula oxygen, n (%)	16 (6)	12 (5)	16 (6)
Air leaks, n (%)	8 (3)	7 (3)	11(4.5)
Received antibiotics, n (%)			
None	152 (60)	105 (51)	142 (59)
48 hours	100 (38)	88 (42)	75 (31)
7 days	7 (2)	12 (5)	23 (9.5)
Received phototherapy, n (%)			
Yes	70 (27)	63 (30)	28 (11)
None	182 (72)	142 (69)	212 (88)
Admitted for hypothermia, n (%)	6 (2.3)	19 (9.2)	11 (4.5)
Admitted for hypoglycemia, n (%)	0	15 (7.3)	17 (7)
Admitted for poor feeding	4 (1.5)	15 (7.3)	8 (3)
Admitted for jaundice	1 (0.3)	4 (1.9)	9 (3)

Vachharajani et al. Clin Pediatr 2008

Late PTB & preeclampsia

Habli M et al. AJOG 2007

TABLE 2
Delivery characteristics and neonatal outcomes for women who had experienced preeclampsia or GH and for women who had had normotensive pregnancies

	Gestational age (wk)					
	35		36		37	
Variable	Normotensive	Preeclampsia/GH	Normotensive	Preeclampsia/GH	Normotensive	Preeclampsia/GH
N	59	28	124	42	196	86
SGA (n)*	1 (1.7%)	5 (17.9%)†	15 (12.2%)	14 (33.3%)‡	21 (10.8%)	11 (12.8%)
Admission to NICU (n)	20 (34.5%)	16 (57.1%)†	13 (10.7%)	14 (33.3%)§	17 (8.7%)	22 (25.6%)§
NICU stay (d)‖	6.0 ± 6.4	5.3 ± 4.0	11.2 ± 10.3	10.3 ± 8.6	2.5 ± 2.7	5.7 ± 5.0*
Total neonatal stay (d)‖	5.0 ± 5.3	4.9 ± 4.9	2.8 ± 4.2	5.5 ± 4.8‡	2.0 ± 2.1	3.9 ± 3.6§
Respiratory distress syndrome (n)	3 (5.2%)	1 (3.6%)	2 (1.6%)	4 (9.5%)†	4 (2.1%)	6 (7.0%)
Respiratory support (n)						
None	47 (81.0%)	20 (71.4%)	108 (89.3%)	34 (81.0%)	182 (93.8%)	73 (84.9%)†
Oxygen/continuous positive airway pressure/mechanical ventilation	11 (19.0%)	8 (28.6%)	13 (10.7%)	8 (19.1%)	12 (6.2%)	13 (15.1%)†
Induced labor/cesarean section (n)	15 (25.4%)	15 (53.6%)‡	33 (26.6%)	28 (66.7%)§	50 (25.5%)	58 (67.4%)§
Cesarean delivery (n)	9 (15.3%)	4 (14.3%)	13 (10.5%)	8 (19.2%)	18 (9.2%)	22 (25.6%)§

* Ascertained among women with delivery of a live infant.

† $P < .05$.

‡ $P < .01$.

§ $P < .001$.

‖ Data are presented as mean ± SD.