

Pregnancy Over 35  
- Is It Really High Risk?

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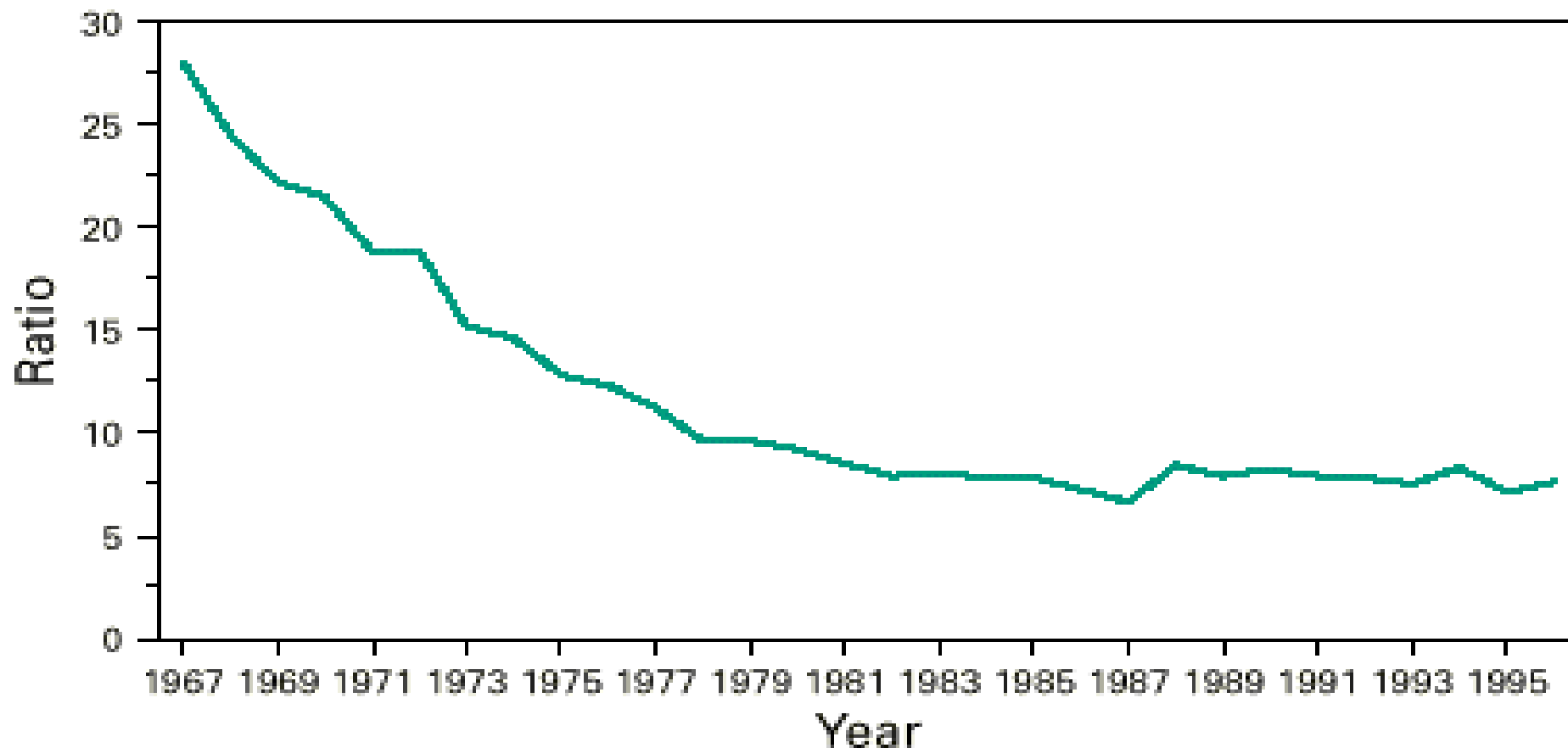
Evergreen Maternal Fetal Medicine

# Conditions Associated With Increasing Age:

- Hypertension
- Diabetes
- Vascular disease
- Aneuploidy
- Infertility
- Multiparity

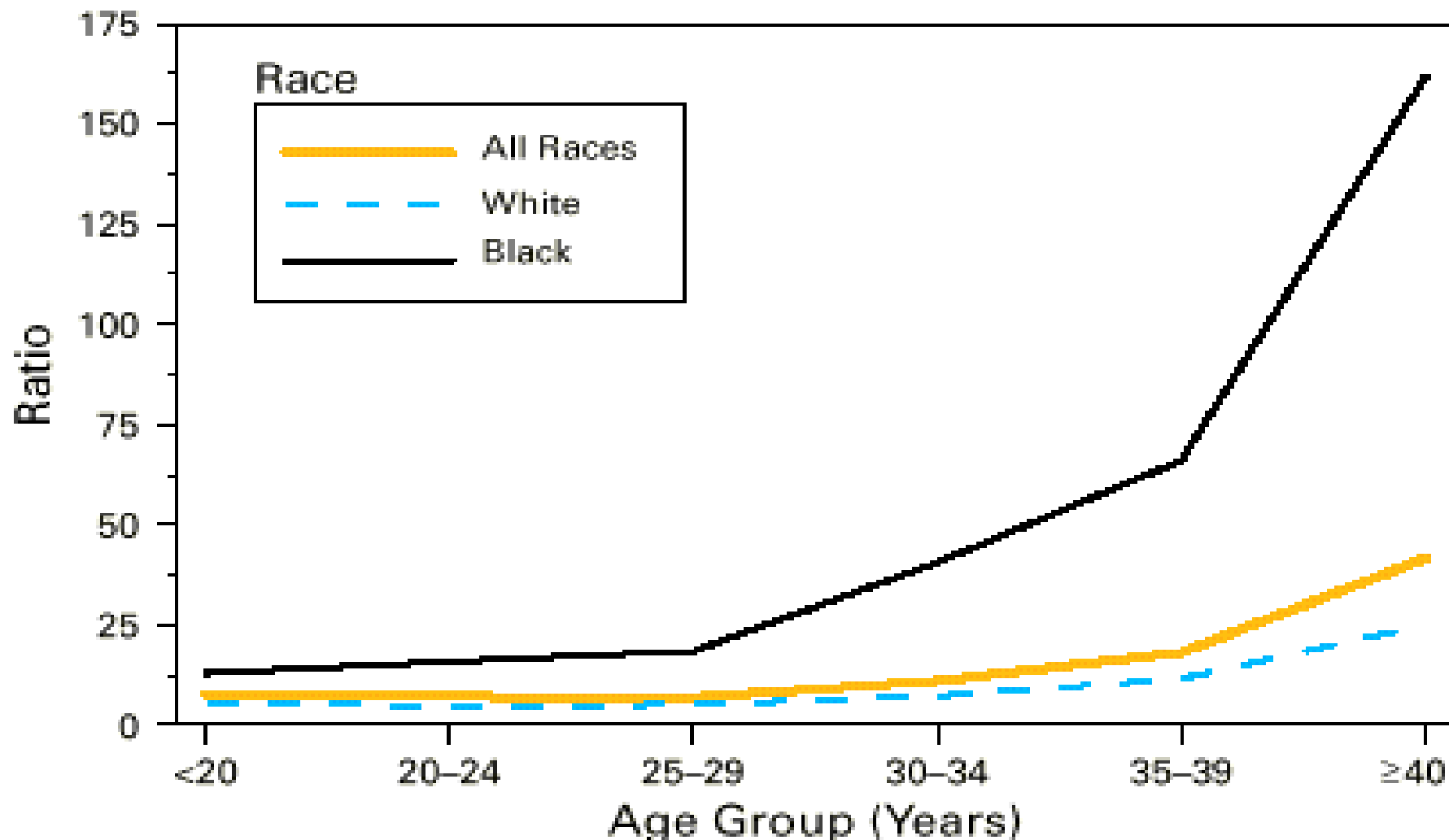
<b>Risk Factor</b>	<b>Odds of Unsatisfactory Outcome</b>
<b>Age &lt;18</b>	<b>1.2</b>
<b>Nullipara Age &gt;36</b>	<b>3.3</b>
<b>Bleeding Since LMP</b>	<b>1.4</b>
<b>Baby &gt;4 Kg</b>	<b>&lt;1.0</b>
<b>Hypertension</b>	<b>1.3</b>
<b>Labor &lt;2 Hours</b>	<b>1.6</b>
<b>Cesarean Section</b>	<b>1.1</b>
<b>Manual Removal of Placenta</b>	<b>2.2</b>
<b>Smoking &gt;10/day</b>	<b>1.7</b>
<b>Social Problems</b>	<b>1.3</b>
<b>No English</b>	<b>&lt;1.0</b>

**FIGURE 1. Maternal mortality ratio\*, by year — United States, 1967–1996**



\*Number of maternal deaths per 100,000 live births The term "ratio" is used instead of rate because the numerator includes some maternal deaths that were not related to live births and thus were not included in the denominator.

**FIGURE 1. Pregnancy-related mortality ratio,\* by age group and race — United States, 1987–1990**



# Maternal Age Specific Concerns

- Births to 35-49 yr. Olds increased 72% from 1982 to 2000
- Increase in maternal mortality
- Increased rate of placenta previa
- Increased risk of stillbirth

Why?

# Maternal Mortality

- Usually felt to be due to associated medical conditions
- Recent studies do not show increased risk of death - all small

# Perinatal Mortality

- Is PNM increase in AMA due to associated conditions or is it independent?

**511  $\geq$  40 yr. old compared to 26759 women 20-30 yr. old**

	<b>40+</b>	<b>20-30</b>
<b>Hypertension</b>	<b>9.65</b>	<b>2.7%</b>
<b>Previa</b>	<b>2.4%</b>	<b>0.6%</b>
<b>GDM</b>	<b>6.7%</b>	<b>1.6%</b>
<b>Fetal death</b>	<b>15.4%</b>	<b>5.1%</b>
<b>NND</b>	<b>9.6%</b>	<b>5.9%</b>
<b>CS</b>	<b>29.4%</b>	<b>18.7%</b>

**When corrected for parity and weight - all differences disappeared**

# Delayed childbearing and the outcome of pregnancy

Berkowitz et al 1990. NEJM

Data from 3917 private patients 20+ years old in their first pregnancy with a singleton gestation.

682 patients aged 35-39

117 patients aged 40+

## RESULTS;

**NO** independent association of age with:

**Low birthweight**

**Preterm delivery**

**Perinatal mortality**

**POSITIVE** independent association with CS (OR 1.9) and antepartum complications (OR 2.0)

# Perinatal Death (Berkowitz et al 1990)

<b>Maternal age</b>	<b>Frequency (%)</b>	<b>OR (95% CI)</b>
20-29	1.3	1.0
30-34	1.2	1.0 (0.5-2.0)
35-39	0.9	
40+	0.9	0.7 (0.3-1.6)

# Pregnancy outcome in nulliparous women

## 35 years or older

Prysack et al. 1995 Obstet Gynecol

Retrospective study of 890 women 35+ compared to 1054 women 25-29 yr.

### **RESULTS:**

- Increased GDM (6.9% vs 2.8%)
- Increased APH (2.8% vs 1.2%)
- Increased PTL (8.9% vs 4.6%)
- Increased PIH (14.3% vs 8.3%)
- **BUT** - More Obesity, Chronic hypertension, Fibroids

### **INDEPENDENT RISK FACTORS PREDICTING PNM:**

- Fibroids
- Preterm Birth
- Infection

• **NOT** age

# What About the Over 40's?

Vercellini et al 1993, Eur J Obstet Gynecol Reprod Biol

- Case control study of 327 women 40+ compared to matched controls 20-30 yr.
- Increased rates of GDM and PIH.
- Increased CS rate.
- Increased LBW.
- No difference in perinatal mortality.

**Conclusion: More complications but comparable results**

# Pregnancy Outcome at age 40 and older

Bianco et al, 1996 Obstet Gynecol

- Retrospective cohort study comparing 1404 40+ women with 6978 20-29 yr. Controls.
- Stratified by parity.
- Multiple logistic regression to allow for confounding factors.

# Results

## Odds Ratios Comparing 40+ to 20-29 Yr.

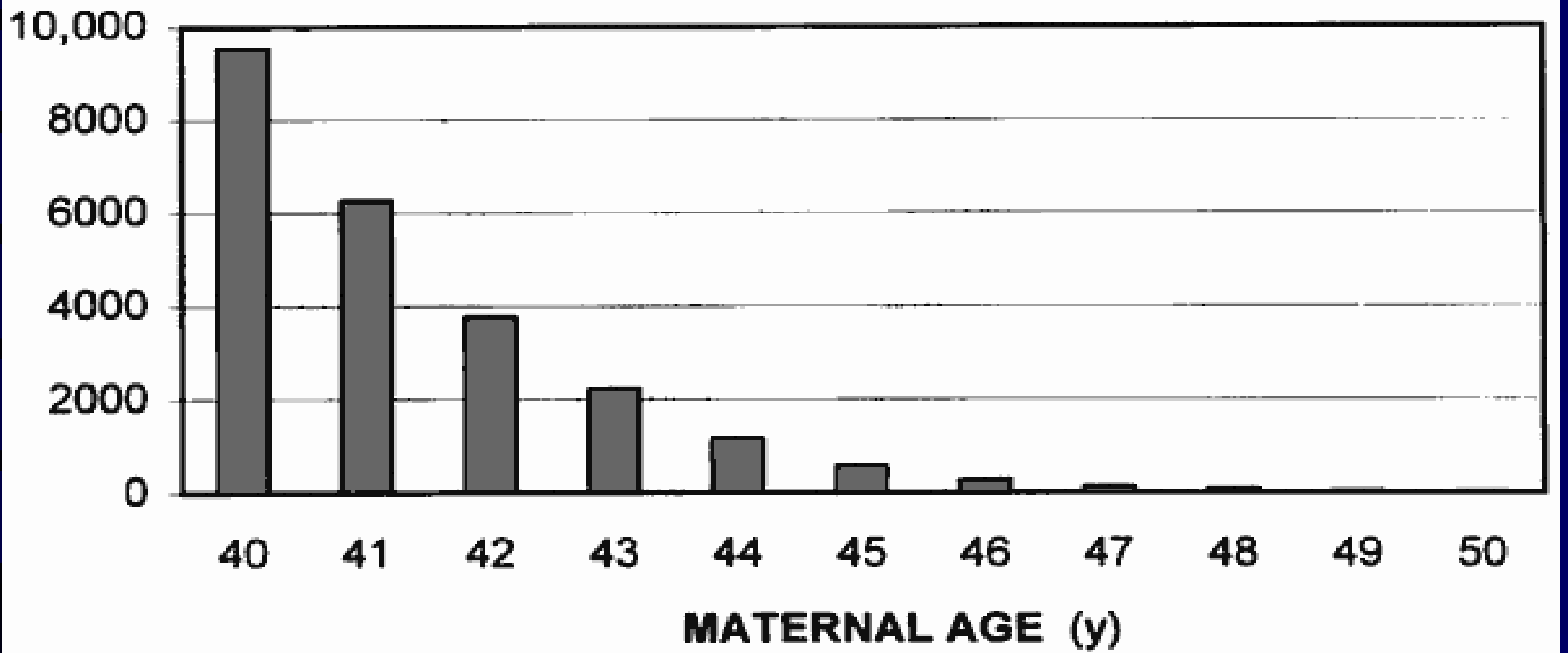
	<b>Nullips</b>	<b>Multips</b>
<b>GDM</b>	2.7 (1.9-3.7)	3.8 (2.7-5.4)
<b>PIH</b>	1.8 (1.3-2.6)	1.9 (1.2-2.9)
<b>Previa</b>	13 (4.8-35)	6.4 (2.6-15.6)
<b>Cesarean del.</b>	3.1 (2.6-3.7)	3.3 (2.6-4.1)

**No increase in PNM or overall neonatal outcome**

# Childbearing Beyond Age 40: Pregnancy Outcome in 24,032 Cases

Gilbert Et Al 1999, Obstet Gynecol

- **1,160,000 deliveries in California Health Information for Policy Project database**
- **2% 40+ = 24,032 compared to 642,525 women aged 20-29**
- **Retrospective analysis with adjusted odds ratios allowing for parity, race and payer status**



Number of women (age 40-50) delivering between January 1, 1992, and December 31, 1993.

# Results

Diagnosis	Nullips (%)		OR	Multips (%)		OR
	40+	20-29		40+	20-29	
Birth trauma	6.6	8.2	0.8	4.3	4.2	1.1
Birth asphyxia	6.0	4.0	1.6*	3.4	2.4	1.5*
IUGR	2.5	1.4	1.9*	1.4	1.0	1.6*
IVH	0.2	0.1	1.9*	0.14	0.08	1.9*
NND	0.4	0.35	1.4	0.6	0.39	1.7*

\* = significant

Largely explained by other pregnancy complications

# Over 45

Dildy et al 1996, Am J O&G

- **Descriptive study of 79 women aged 45-53**
- **0.63 per 1000 births**
- **46.8% had obstetric complications**
  - **GDM (12.7%)**
  - **PIH (10.1%)**
  - **PTD (15.2%)**
- **CS rate - 31.7%**
- **PNM rate - 1.3%**

# Conclusion:

Age confers an increased risk of specific antepartum complications but no increase in perinatal mortality or morbidity

# The Alternative View

Advancing age confers  
pregnancy risks  
**independently** of associated  
medical conditions or  
complications

# Maternal Age at First Childbirth and Risk of Low Birth Weight and Preterm Delivery in Washington State

Aldous & Edmonson 1993 JAMA

- Birth certificate study 1984-1988
- Singleton 1st born of women aged at least 20 yr.
- Analyzed for **independent risk factors** resulting in:
  - Low birth weight
  - Very low birth weight
  - Preterm delivery

# Results

Age	Preterm delivery (OR)	LBW (OR)	VLBW (OR)
20-24	reference	reference	reference
25-29	1.0	1.1	0.88
30-34	1.4*	1.5*	1.1
35-39	1.6*	1.7*	1.4
>40	1.8*	2.3*	1.8

# Effects of Maternal Age, Parity, and Smoking on the Risk of Stillbirth

Raymond Et Al, 1994, Br J O&G

- Cohort study 1983-89 N=638,242
- Singletons 28 weeks + at least 20 years old

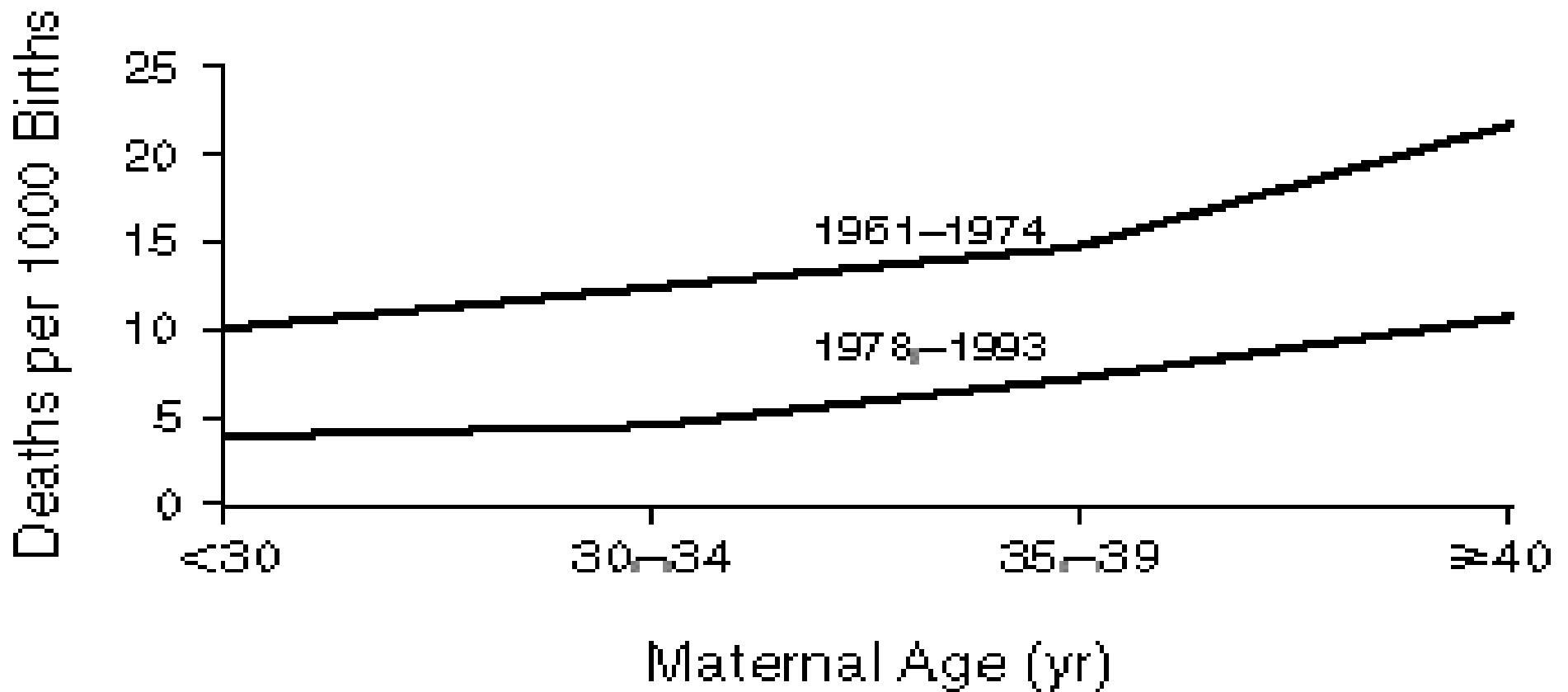
## RESULTS:

- Stillbirth rate increased in AMA and smokers
- Smokers increased rate related solely to IUGR
- **Even when adjusted for PIH, DM, previa elevated risk persisted for AMA**
- The AMA related risk of SB increased with gestational age.

# Increased Maternal Age and the Risk of Fetal Death

**Fretts Et Al, 1995, NEJM**

- McGill obstetrical database, N=94,346 1961 to 1993
- Logistic regression analysis allowing for parity, year of delivery, history of fetal death, race, marital status, DM, hypertension, previa and abruption
- Odds ratios calculated comparing to “low risk” group of <30 yr. Multiparas



**Fetal Deaths per 1000 Total Births, According to Maternal Age and Study Period.**

Table 4. Odds Ratios for Fetal Death According to Maternal Variables and Time Period.\*

VARIABLE	1961–1974	1978–1993
Total births	39,666	54,680
	<i>odds ratio (95% confidence interval)</i>	
Age <30 yr, parity 1–2	1.0 (—)	1.0 (—)
Age 30–34 yr	1.2 (0.9–1.6)	1.3 (0.9–1.7)
Age 35–39 yr	1.2 (0.9–1.7)	<u>1.9 (1.3–2.7)</u>
Age ≥40 yr	1.8 (1.1–3.1)	<u>2.4 (1.3–4.5)</u>
Pregnant with first child	<u>1.9 (1.5–2.4)</u>	1.2 (0.9–1.6)
Pregnant with fourth or subsequent child	<u>1.7 (1.3–2.3)</u>	<u>1.8 (1.1–2.9)</u>
Previous abortion	1.2 (0.9–1.5)	1.1 (0.8–1.4)
Married	0.7 (0.5–0.9)	0.7 (0.5–0.97)
Diabetes mellitus		
Treated with diet	2.1 (0.6–6.8)	1.2 (0.4–3.2)
Treated with insulin	<u>3.5 (1.9–6.8)</u>	1.7 (0.7–3.9)
Hypertension	<u>2.9 (1.6–5.5)</u>	<u>1.8 (1.2–2.8)</u>
Previous stillbirth	<u>3.1 (2.0–4.8)</u>	1.4 (0.6–3.6)
Multiple gestation	1.5 (1.0–2.6)	<u>3.4 (2.1–5.2)</u>
Placental abruption	<u>10.8 (8.1–14.5)</u>	<u>18.7 (13.4–26.0)</u>
Placenta previa	<u>4.3 (2.0–9.3)</u>	3.6 (1.1–11.5)

\*Odds ratios have been adjusted for the date of delivery with a period-appropriate reference group (women less than 30 years of age having their second or third child, with no medical risk factors).

After controlling for maternal characteristics, women 35 years of age or older continued to have a **significantly higher rate of fetal death** than their younger counterparts (odds ratio for women 35 to 39 years of age as compared with women <30 years of age, 1.9; 95 percent confidence interval, 1.3 to 2.7; for those 40 or older, 2.4; 95 percent confidence interval, 1.3 to 4.5).

***Conclusions.*** Changes in maternal health and obstetrical practice have resulted in a 70 percent decline in the rate of fetal death among pregnant women of all ages since the 1960s.

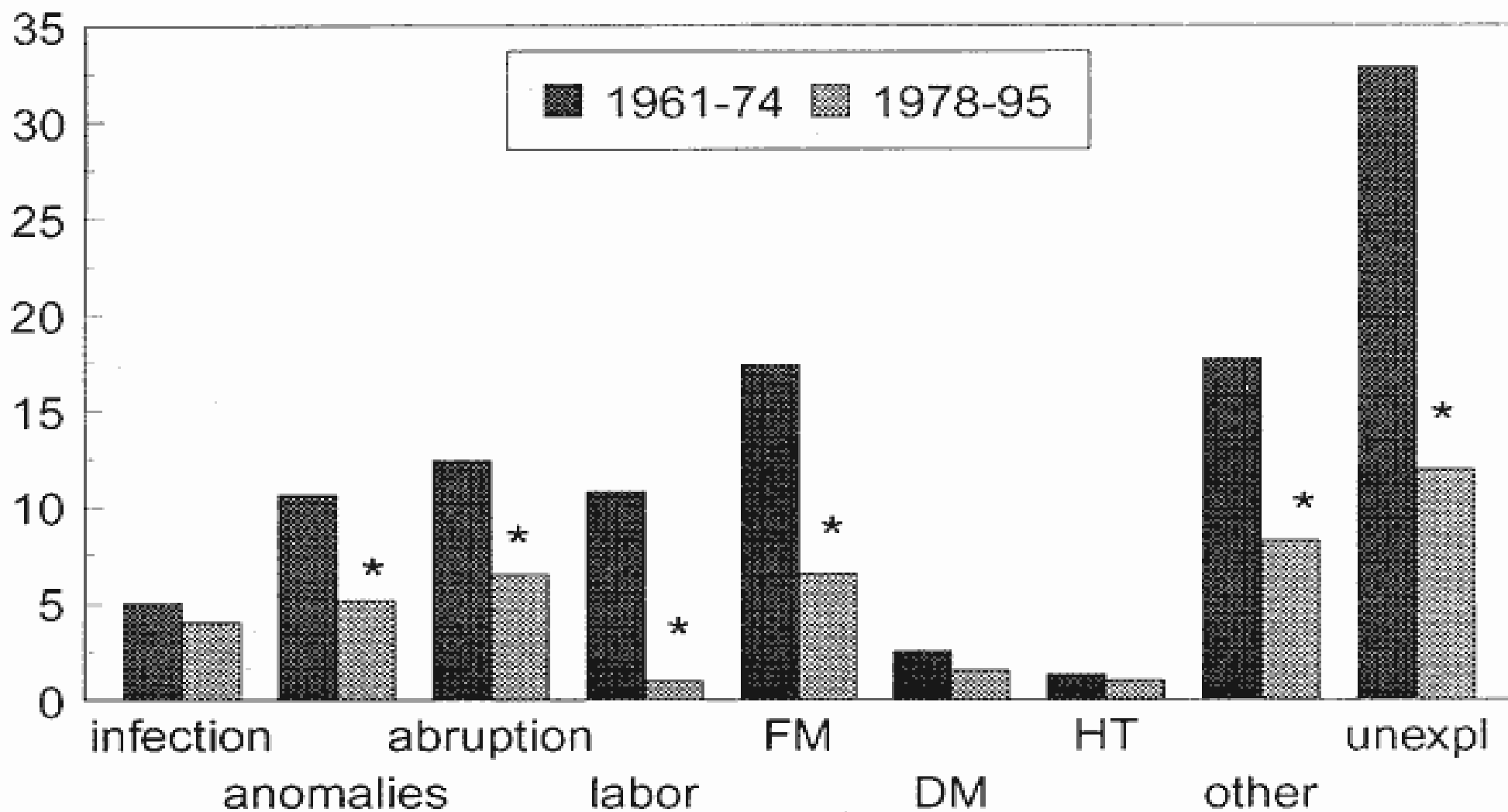
**Advancing maternal age, however, continues to be a risk factor for fetal death.**

# Causes of Fetal Death

Fretts & Usher 1997 Obstet Gynecol

- <35 yr. Compared to >35 yr,
- 715 SB, 822 NND
- 97% autopsy rate
- 101,640 births from 1961 to 1995

Rate/10,000



## Specific causes of fetal death in 1978-1995 (rate per 10,000 births)

Age	<35	35+	OR
Infection	3.2	9.1	2.8 (1.1-6.9)
Anomalies	5.5	1.1	0.2 (0.03-1.5)
Abruption	5.5	10.2	1.9 (0.8-4.0)
Labor	1.1	0	NS
Fetal malnutrition	5.6	11.3	2.0 (0.9-4.2)
Diabetes	0.9	3.4	3.6 (0.8-15.1)
Hypertension	1.1	0	NS
Unexplained	10.2	22.7	2.2 (1.3-3.8)*

# Fetal or Uterine Factors?

Wolff Et Al, 1997 Obstet Gynecol

- Perinatal outcome compared in AMA women with spontaneous and oocyte donation pregnancies
- Retrospective cohort study
- 46 egg recipients cv 49 spontaneous pregnancies  
38+

**Table 3. Obstetric Outcome in Oocyte Recipients Compared With Women of Advanced Age Who Conceived Without Assisted Reproductive Technologies: Singleton Pregnancies**

Outcome	Oocyte recipients (n = 23) (%)	Natural conception (n = 48) (%)	Adjusted RR* (95% CI)
Placenta previa	13.0	2.1	12.2 (0.6, 240.5)
Preterm PROM	8.7	4.2	0.9 (0.8, 9.8)
Glucose intolerance of pregnancy	13.0	6.3	0.3 (0.0, 5.2)
Pregnancy-induced hypertension	13.0	2.1	64.0 (1.0, 4102.6)

Abbreviations as in Table 2.

\* Adjusted relative risks were calculated controlling for maternal age, gravidity, parity, previous spontaneous or induced abortion(s), race, alcohol use, tobacco use, and relevant past medical history.

# Conclusions

**Comparable complication rates in AMA oocyte recipients and spontaneous conceptions (with the exclusion of multiples) suggest that it is maternal rather than fetal factors responsible for the high complication rates.**

**Caveat: Small numbers**

# Placenta Previa

- All studies have identified a significantly increased rate of placenta previa

# Placenta Previa

- Age 34+ confers a **2-3 fold** increased risk of previa independent of:

↓ **Race**

↓ **Gravidity**

↓ **Parity**

↓ **Prior abortion**

↓ **Prior cesarean**

# Labor

- Many studies describe an increased rate of cesarean section with advancing maternal age
- Causes?
  - Physician factors
  - Dystocia
  - Patient complications

# Advanced maternal age as a risk factor for cesarean delivery

Gordon et al 1991, Obstet Gynecol

- King County vital statistics
- 2985 singleton births to women 35+ compared to 6140 20-29 yr olds
- **RESULTS:**
  - Primips with no recorded complications
  - Age 35+ increased risk of CS by RR **2.5** (1.8-3.5)
- **CONCLUSION:**
  - AMA may lead physicians to do unnecessary CS

# **Maternal age: An independent risk factor for cesarean delivery**

**Peipert et al 1993, Obstet Gynecol**

- **Primips 1988-1991 Yale Health and Pregnancy Study**
- **At least 20 yr. of age**
- **N=735**
- **Multivariate stepwise logistic regression analysis**
  
- **Comparisons between:**
  - **20-29 yr.**
  - **30-34 yr.**
  - **35+**

# Results

- **Adjusted odds ratio for CS**

- **1.6 (0.9-2.7) in 30-34 yr olds**

- **2.3 (1.1-4.8) in 35+**

- **Independent of pregnancy or labor complications**

**Conclusion: The increased rate of CS may be due more to provider attitude than obstetric indication**

# Contributing Factors - ?Dystocia

- Adashek et al 1993 am J ob Gyn.
- Prospective study of nullips in spontaneous labor with singleton vertex pregnancies.
- 35+ yr. C.V. 20-29 yr.
- **Results:**
  - Cs or 2.4 for AMA.
  - AMA patients had more oxytocin for longer at higher doses.

# Second Stage

- **Rasmussen et al 1994 - Acta Obstet Gynecol Scand**
- **7214 deliveries 1987-1991 - Norway**
- **Age is one of the most influential independent maternal characteristics of the duration of the second stage of labor**

# Conclusion

- Increased risk of previa
- Increased risk of fetal death
- Increased risk of dystocia
- Increased risk of cesarean section

# Suggested Approach

- Women over the age of 40 should be considered “high risk” despite otherwise good health
- Fetal monitoring in the third trimester
- Consider induction at term if cervix favorable
- Educate patients about the potential for dystocia and cesarean section