

Advanced maternal age and obstetrical outcome

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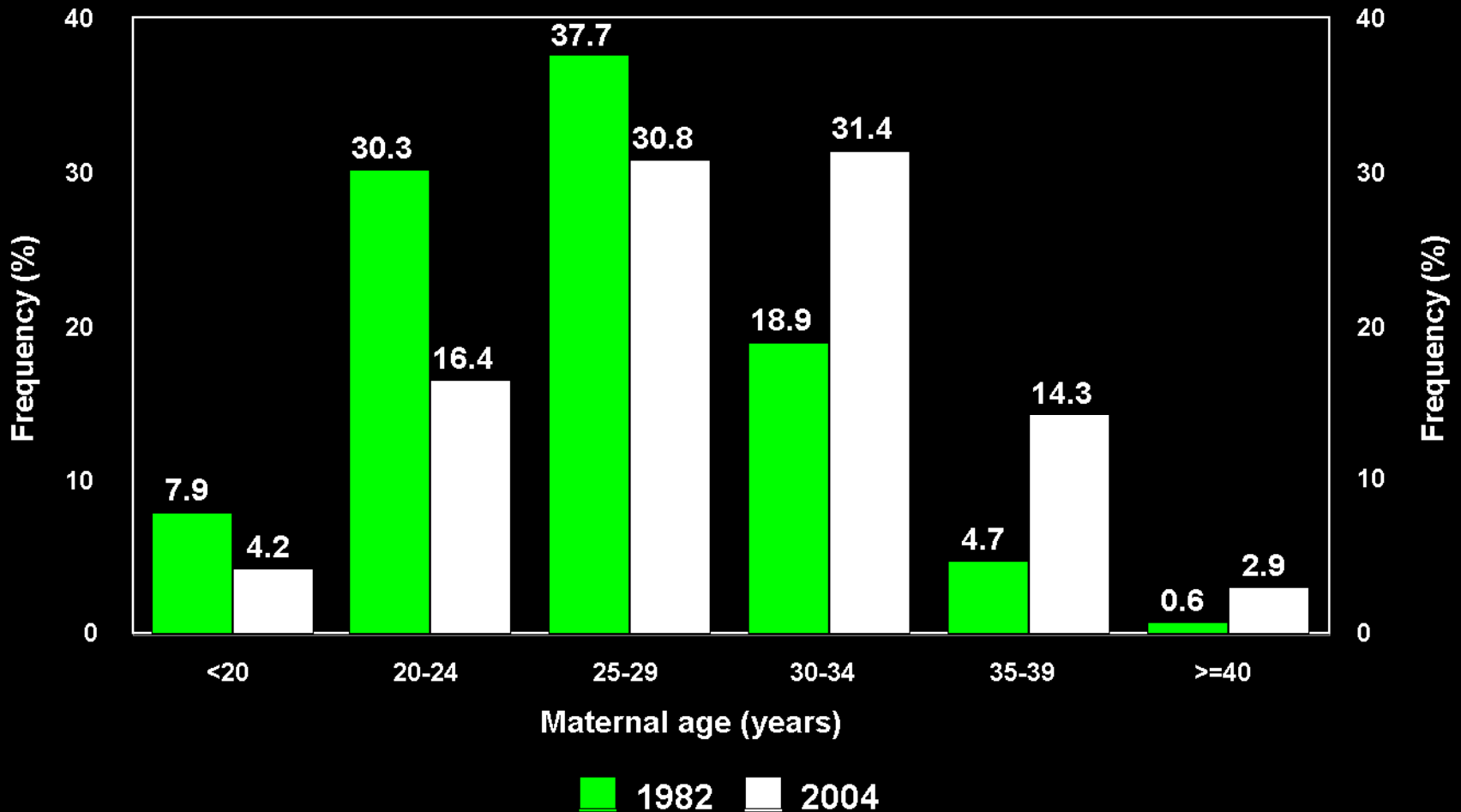
Dalhousie University and the IWK Health Centre

Conflict of interest statement and historical note

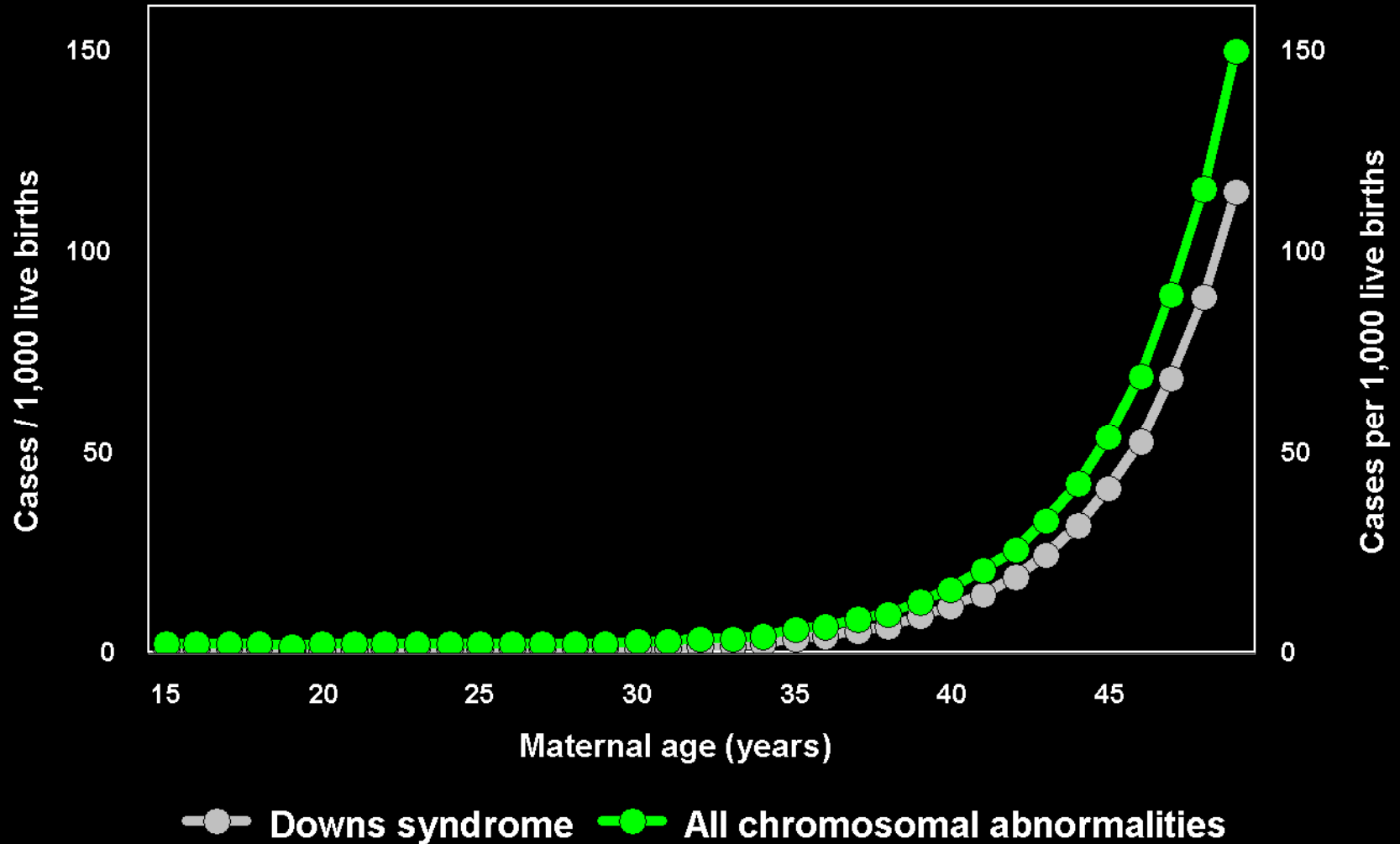
My mother was an “elderly primigravida”*

* Phrase coined by Waters and Wagner
(Am J Obstet Gynecol 1950;59:296-304.)

Proportion of live births by maternal age, Canada, 1982 and 2004

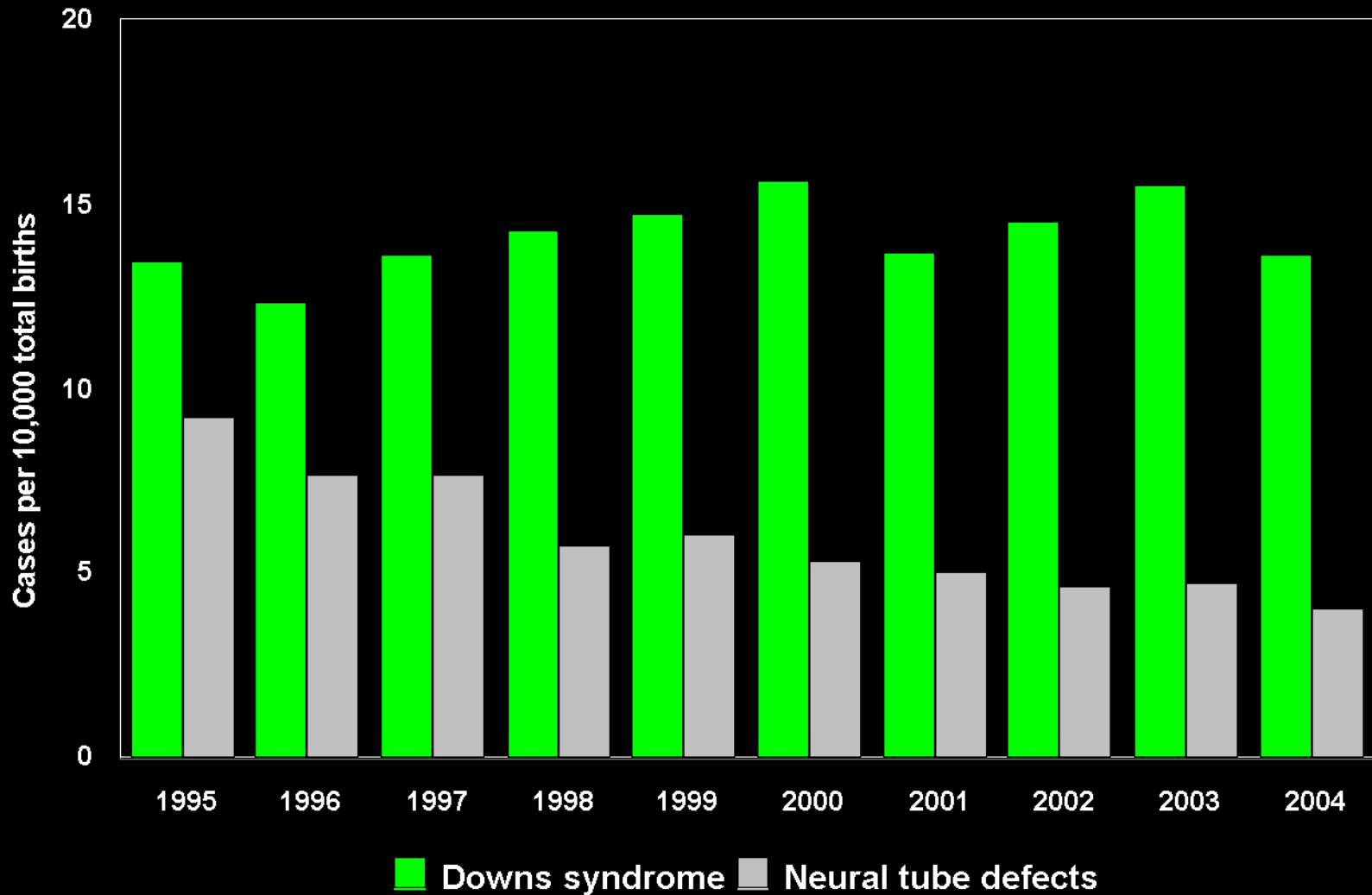


Maternal age and chromosomal abnormalities



(Hook EB. Obstet Gynecol 1981)

Downs syndrome and NTDs, Canada 1995-2004



Source: Canadian Perinatal Surveillance System

Older maternal age and PTB/SGA births

- Numerous studies
- E.g. recent Swedish study*
 - Rate ratio 40-44 years vs 20-29 years
 - PTB 1.54 (95% CI 1.47-1.60)
 - SGA 1.94 (95% CI 1.80-2.09)
- Majority of studies show an association between older maternal age and PTB/SGA

*Jacobsson et al. Obstet Gynecol 2004

Does older maternal age increase the risk
for perinatal mortality and serious
neonatal morbidity?

No increase in perinatal death!

	<u>Result Summary</u>
• Spellacy 1986	P>0.05
• Berkowitz al 1990	OR 0.7 (0.3-1.6)
• Leyland 1990	OR 1.28 (0.85-1.94)
• Roberts 1994	OR 1.1 (0.4-3.0)
• Prysak 1995	P>0.05
• Ezra 1995	OR 1.2 (0.6-2.3)
• Chan 1999	P>0.05
• Gilbert 1999	OR 1.4 (0.9-2.2)

Significant increase in perinatal death!

	<u>Result Summary</u>
• Cunningham 1990	P<0.05
• Cnattingius 1992	OR 1.4 (1.0-2.0)
• Cnattingius 1993	OR 2.0 (1.5-2.8)
• Cnattingius 1993	OR 1.8 (1.5-2.1)
• Raymond 1994	OR 1.5 (1.4-1.7)
• Fretts 1997	OR 2.4 (1.3-4.5)
• Andersen 2000	P<0.05
• Jolly 2000	OR 1.4 (1.2-1.7)

Older maternal age and perinatal mortality and serious neonatal morbidity

?Equivocal results regarding perinatal death

Few studies on serious neonatal morbidity

Do we need yet another study?

The Nova Scotia Atlee database is

- population-based
- clinical focused
- 160,000 births 1988-2002
- detailed information on confounders

Controlling for confounding

Parity Pre-pregnancy weight

Smoking Marital status

Prenatal class Period

Bad obstetric history

 Previous cesarean

 Previous low birth weight

 Previous perinatal death

SES missing - CIHR funding for linking Atlee
to income tax records at Stat Can (SAADD)

Details of the linkage

Data for 1988 to 1995 linked (n=76,300)

Confidential and secure

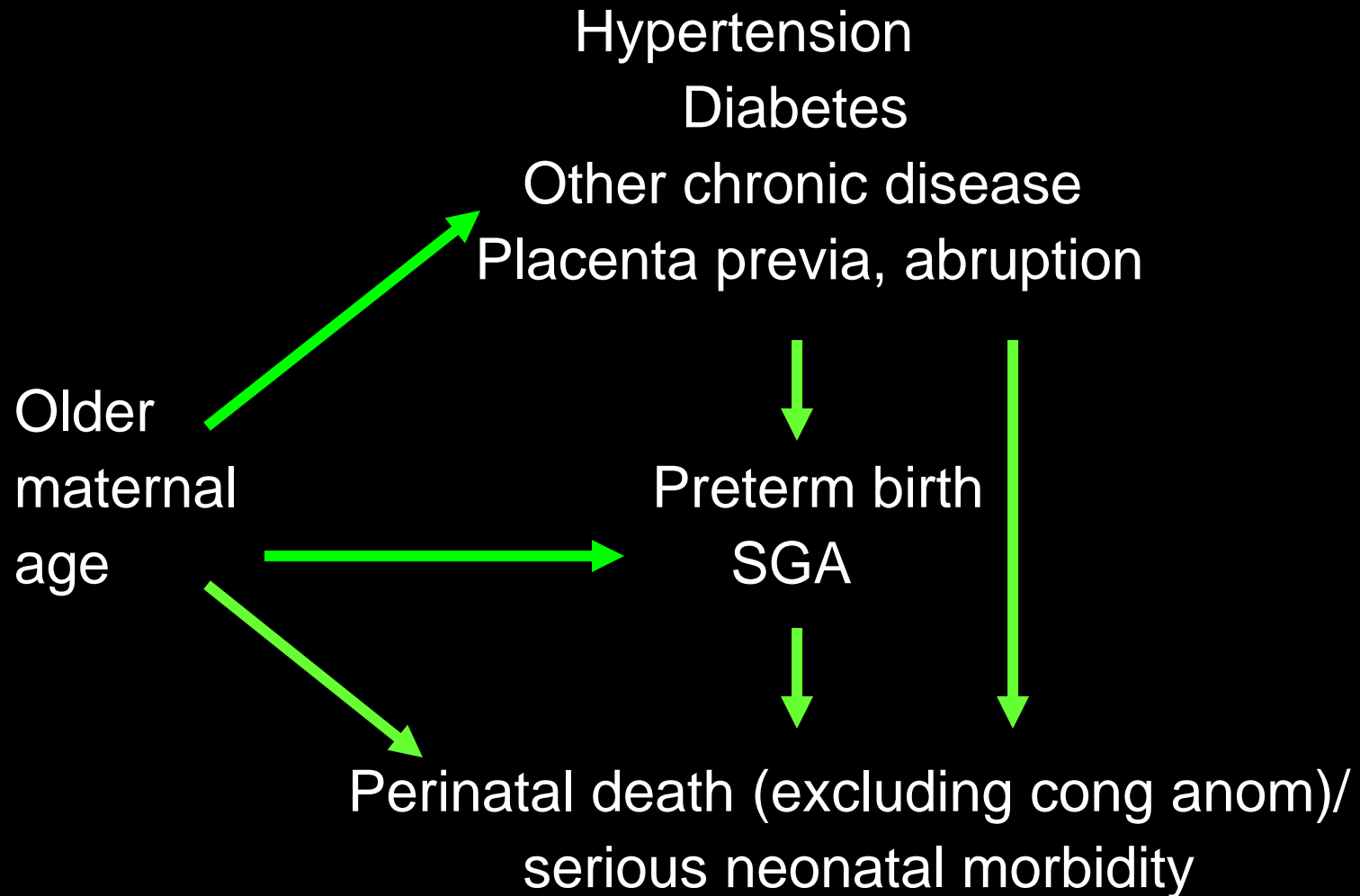
Linkage and analysis in SAAD offices

Investigators never saw tax records

Clinical confidentiality maintained

Approved by Dalhousie IRB, Stats Can

Clinical model (singleton pregnancy)



Primary outcome

Perinatal death

Stillbirths

Neonatal deaths

Serious neonatal morbidity including

Severe RDS

Severe ROP

BPD

NEC

IVH (grade 3 or 4)

Apgar \leq 3

PVL

Study population

Exclusion criteria, <20 weeks/<500g

Multiple births

Cong anomaly deaths

157,445 singleton deliveries, NS 1988-2002

Maternal age distribution

20-24 years	35,711
25-29 years	53,647
30-34 years	40,068
35-39 years	13,551
>=40 years	1,822

Analysis

Contrast between women 35-39 years and ≥ 40 years vs 20-24 years

Confounders modeled using indicators 0,1

Logistic models - GEE, with variance correction for non-independence of births to the same woman

Results

Older women were more likely to be

married

high income

attend prenatal classes

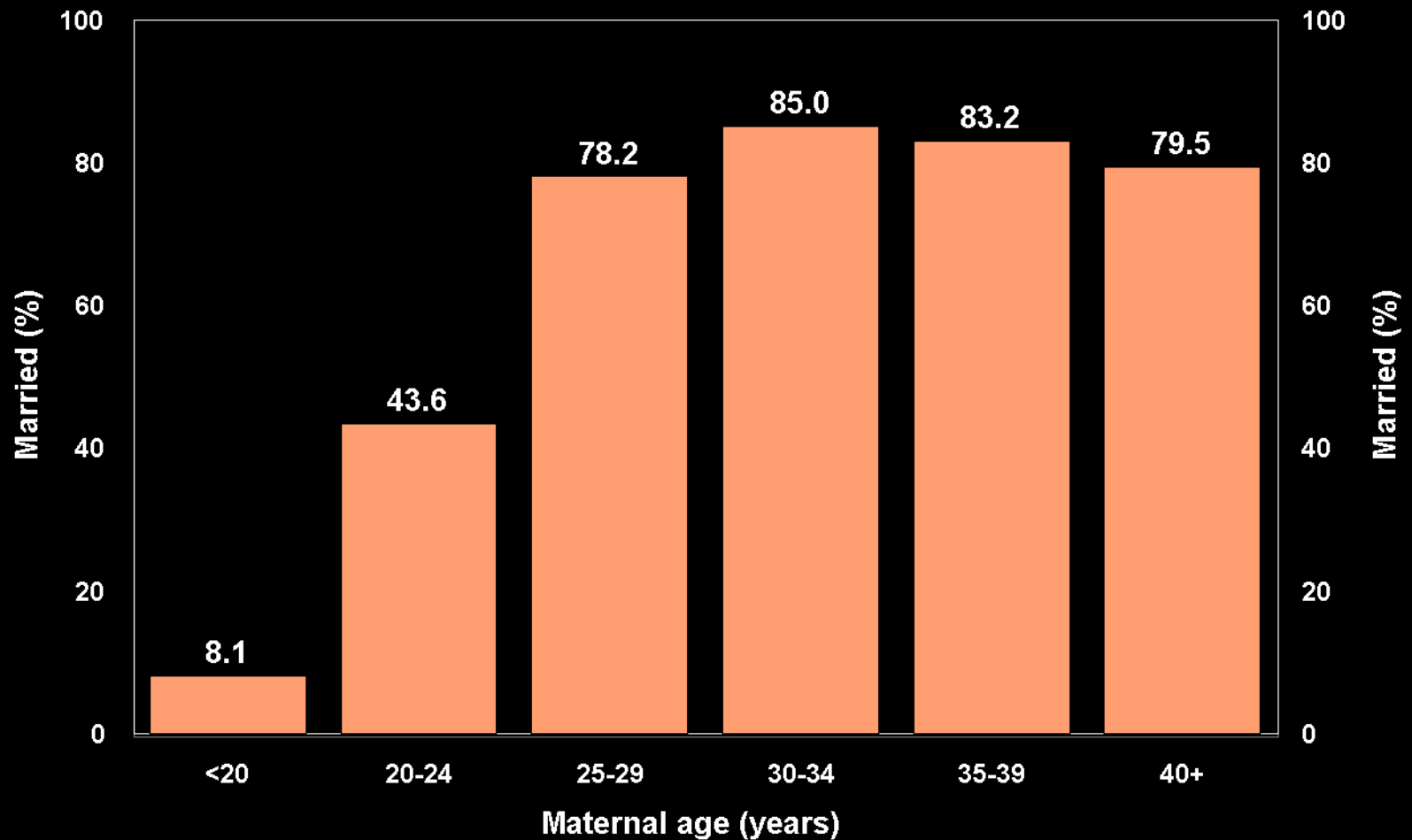
non-smokers

multiparous

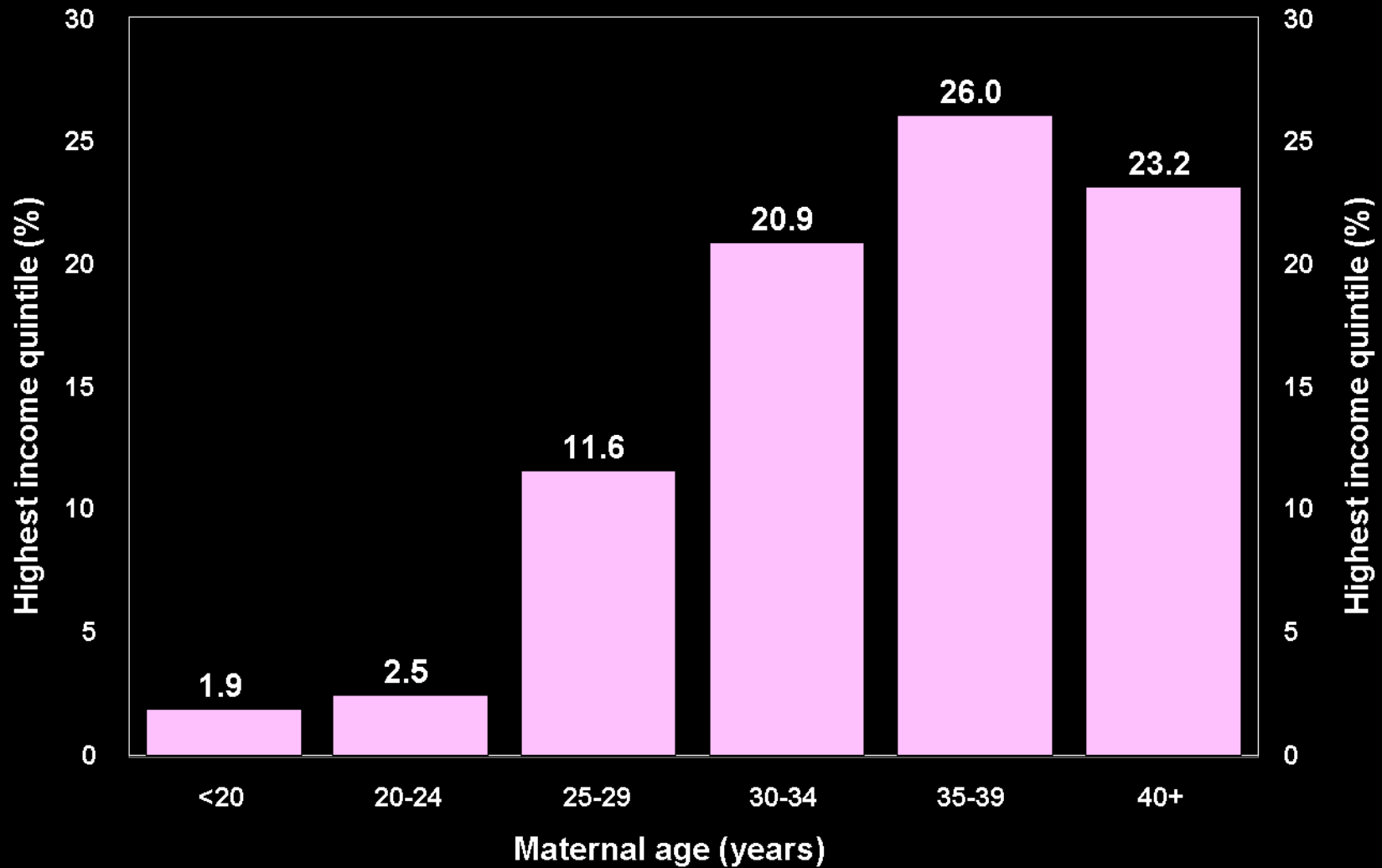
prepregnancy wt ≥ 70 kg

bad obstetric history

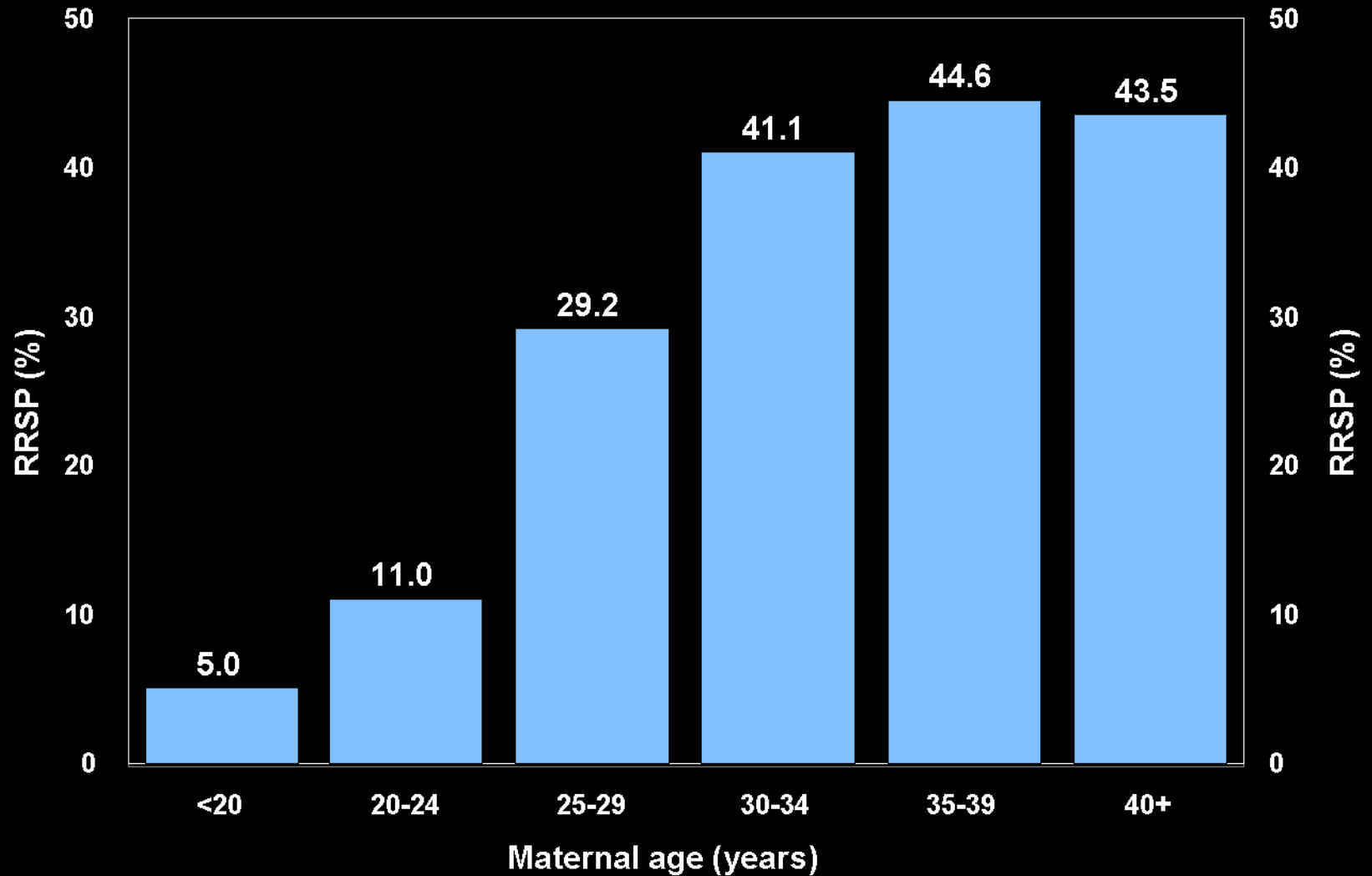
Marital status by maternal age



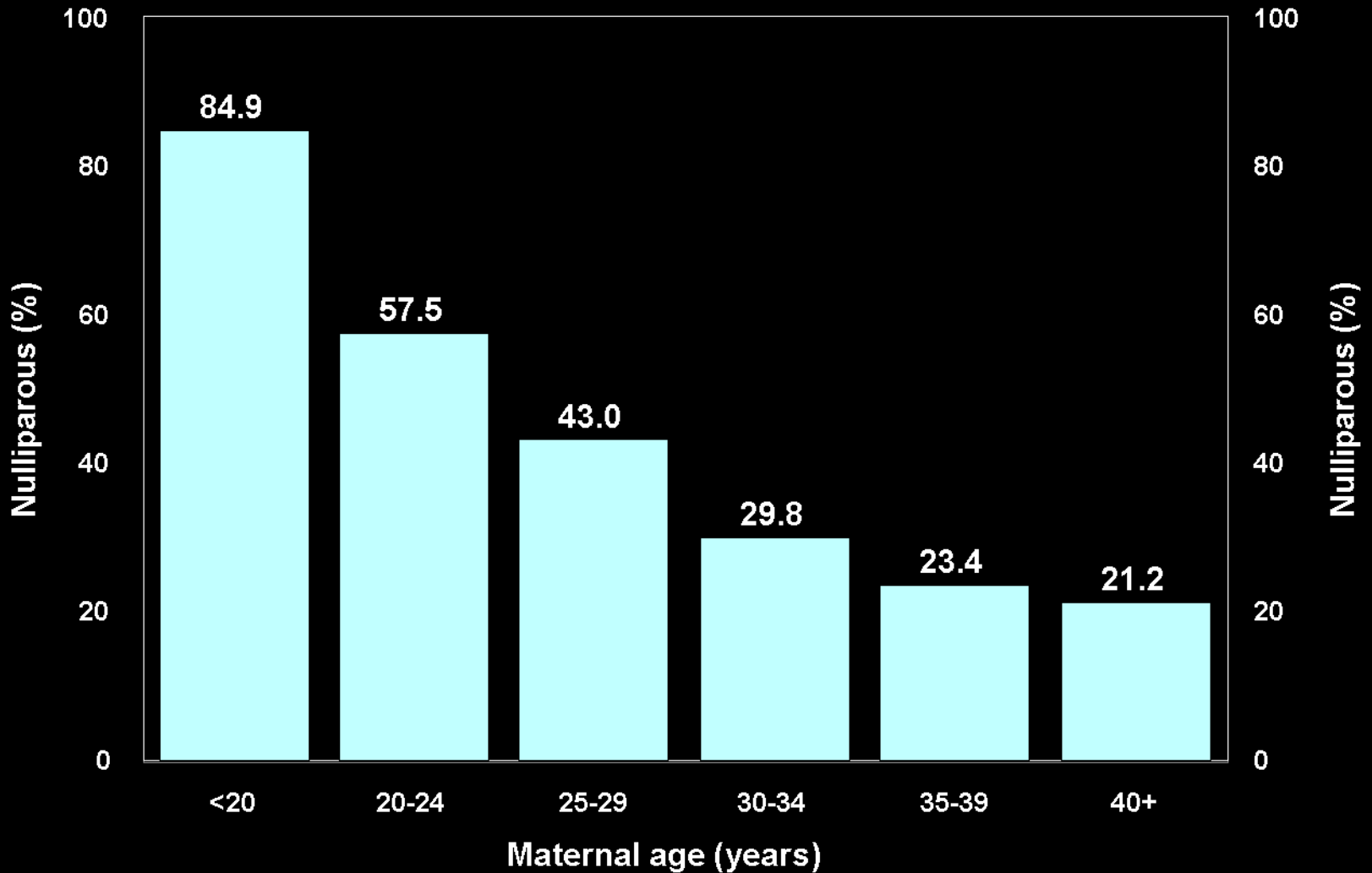
High family income by maternal age, (1988-95)



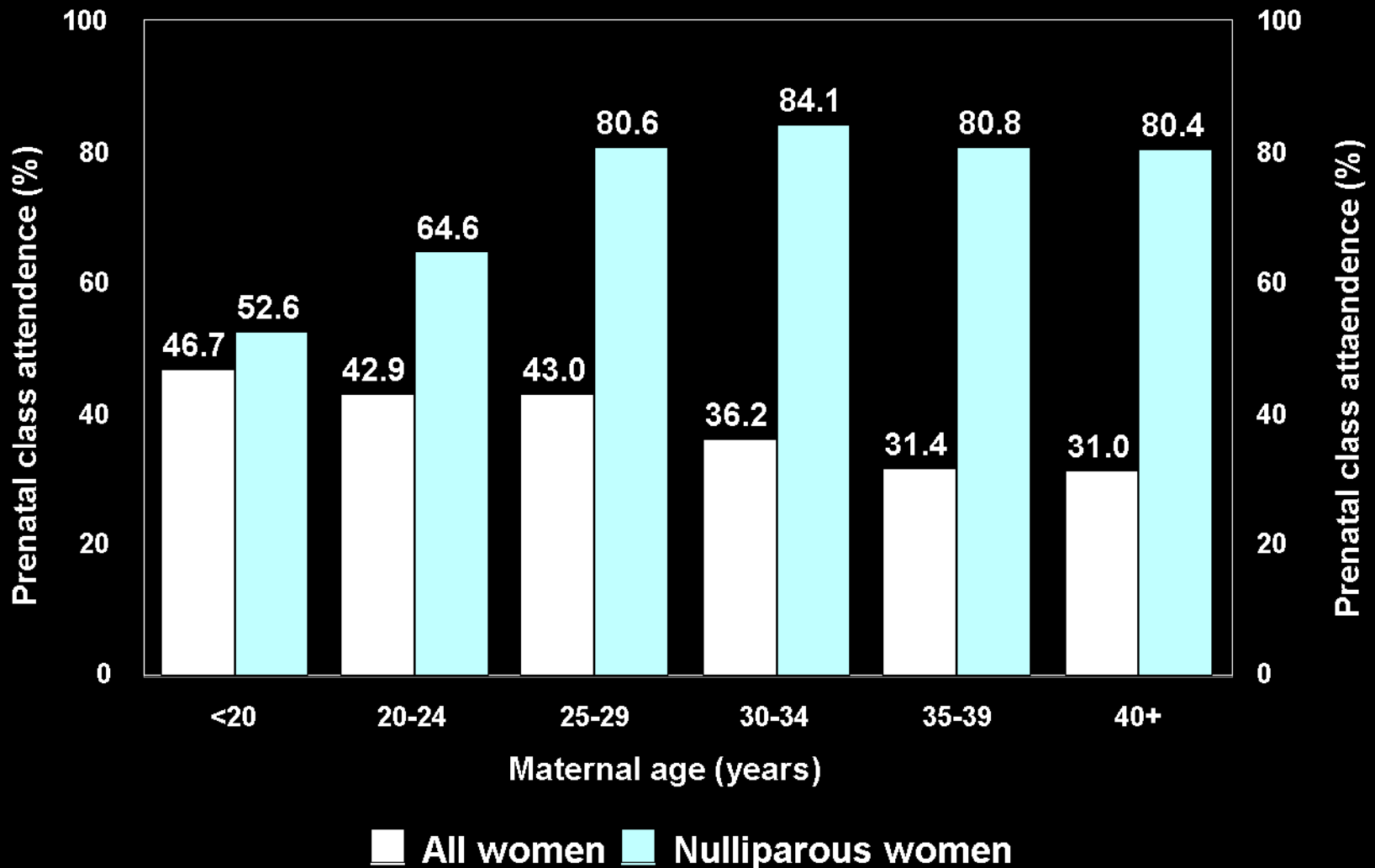
RRSP investment by maternal age, (1988-95)



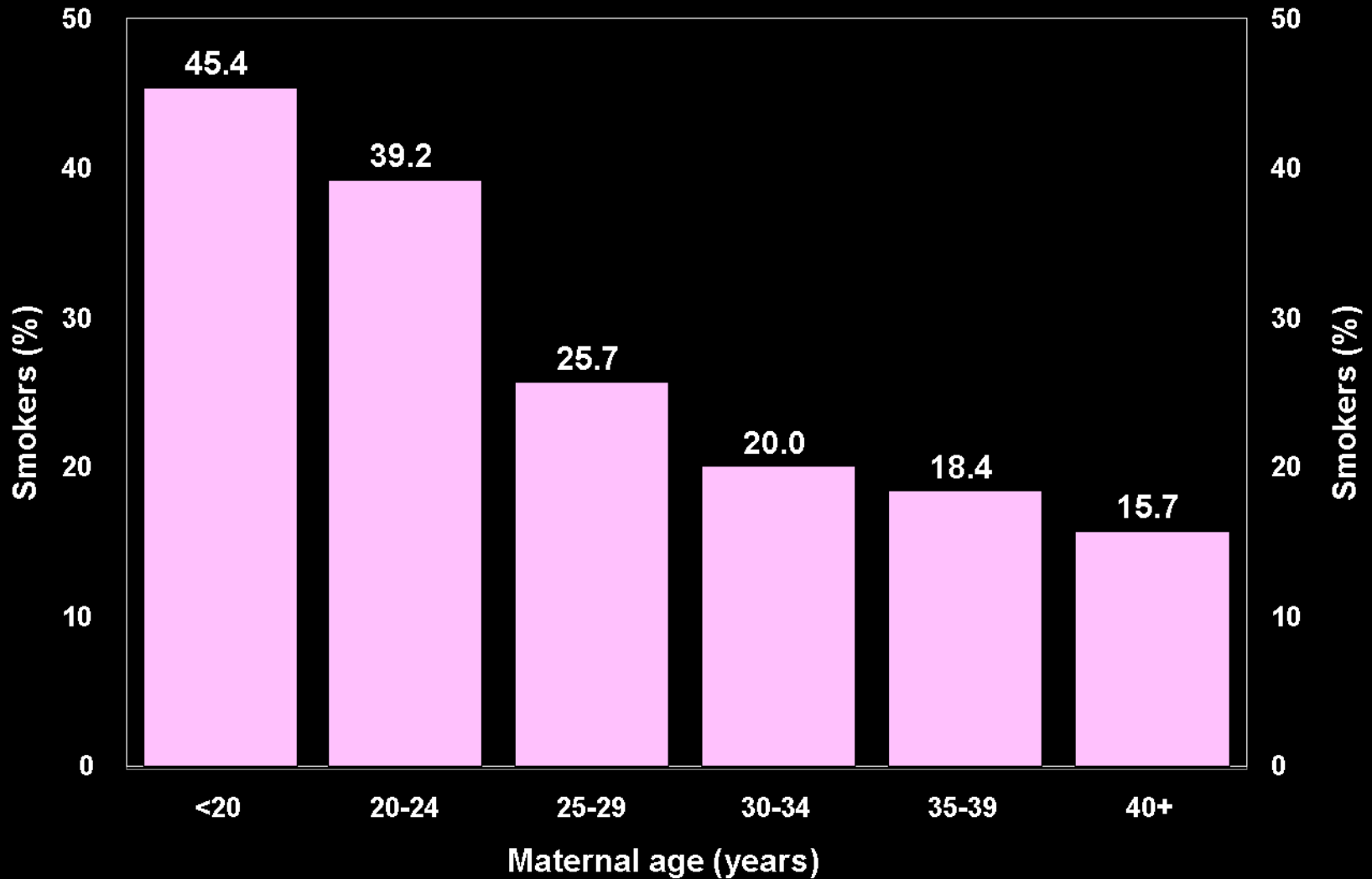
Proportion nulliparous by maternal age



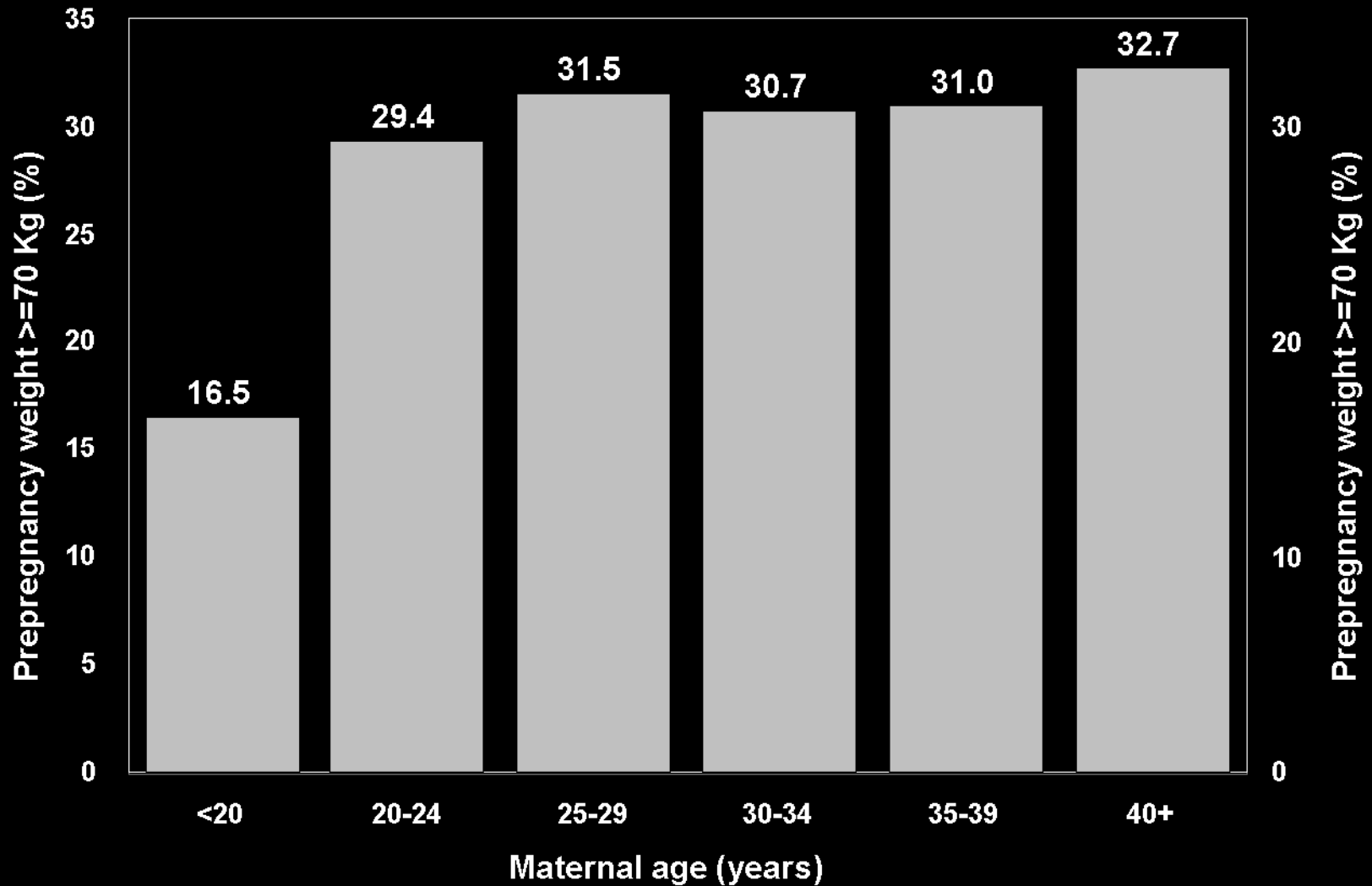
Prenatal class attendance by maternal age



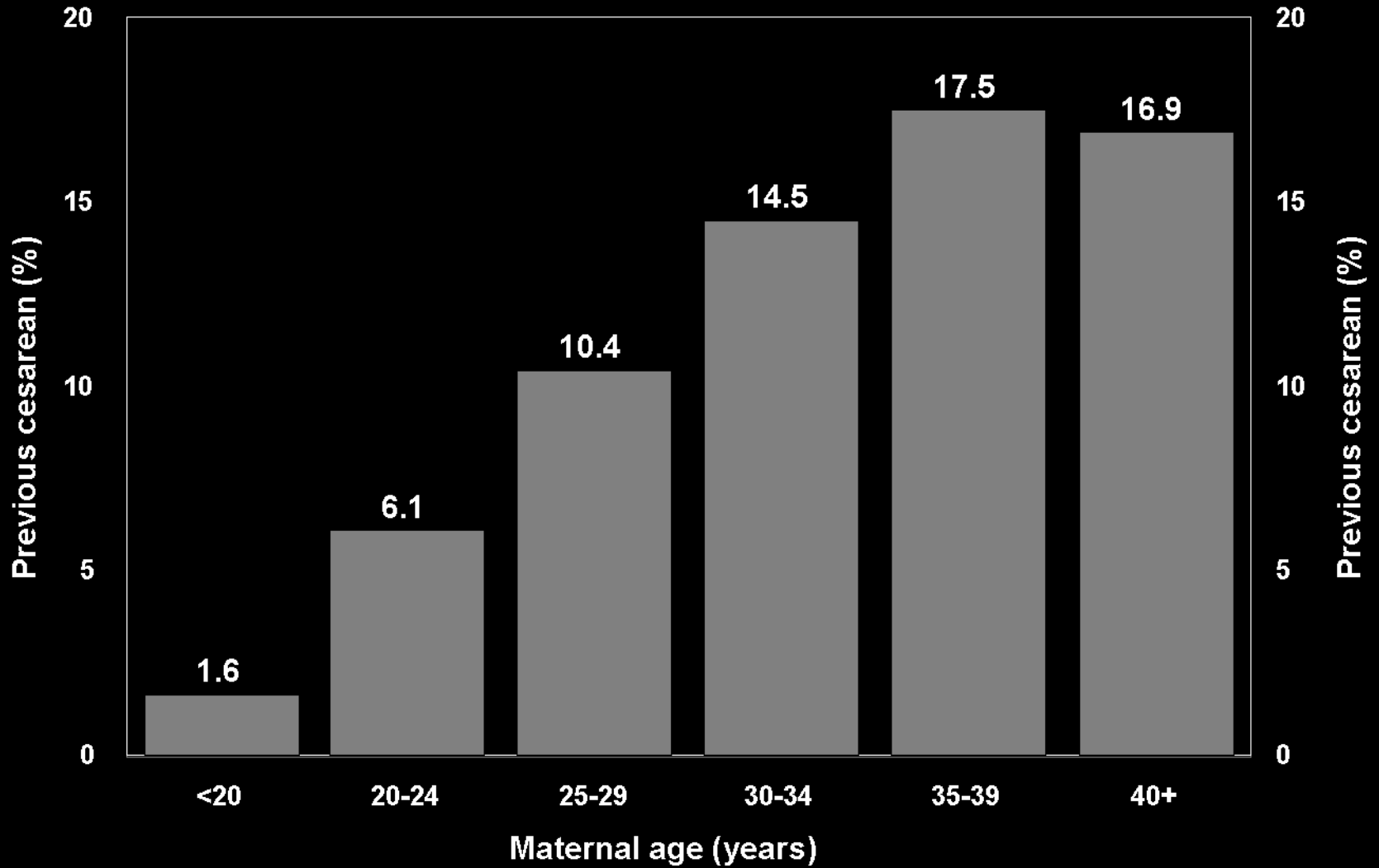
Smoking status by maternal age



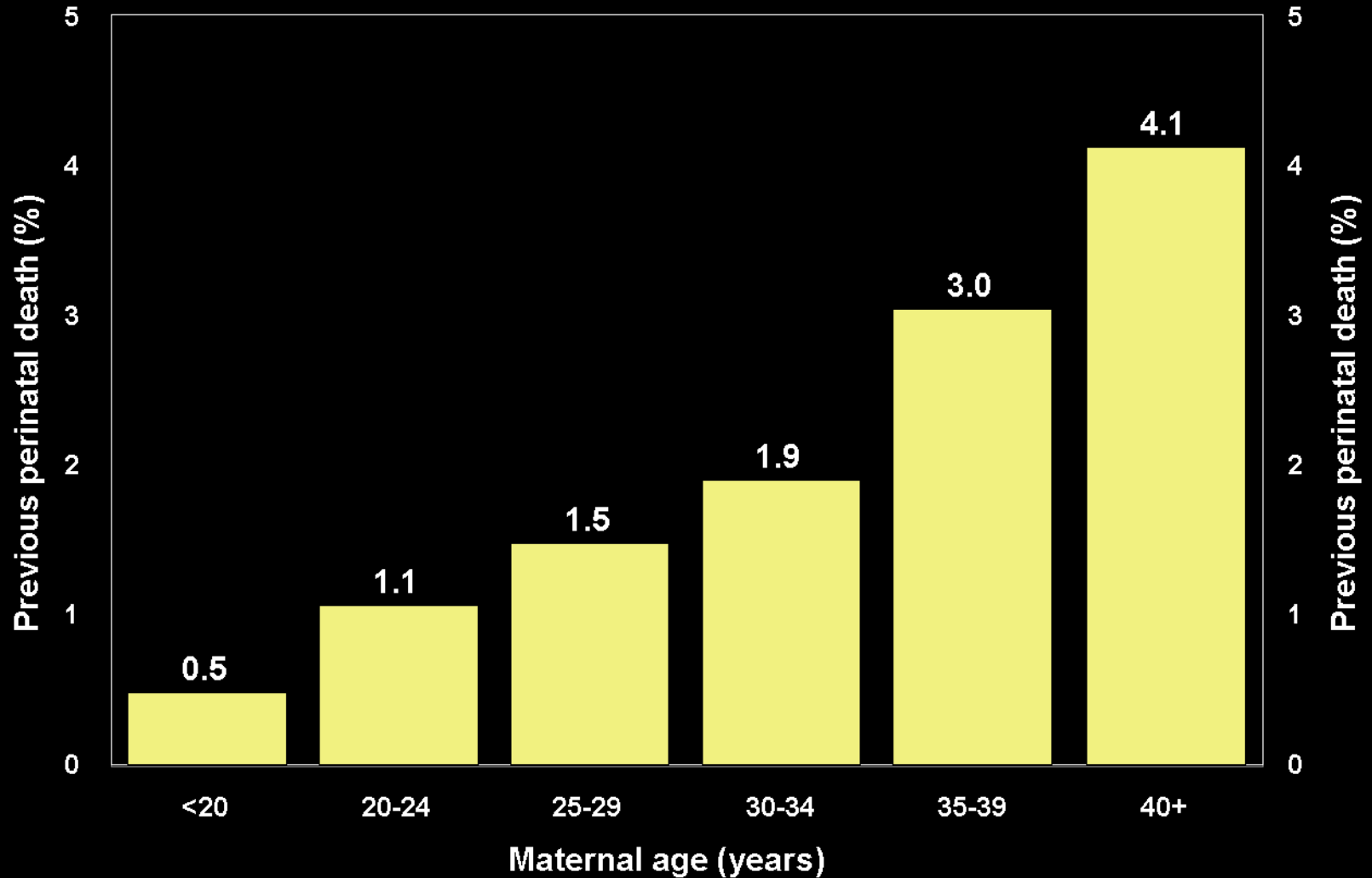
Prepregnancy weight ≥ 70 kg by maternal age



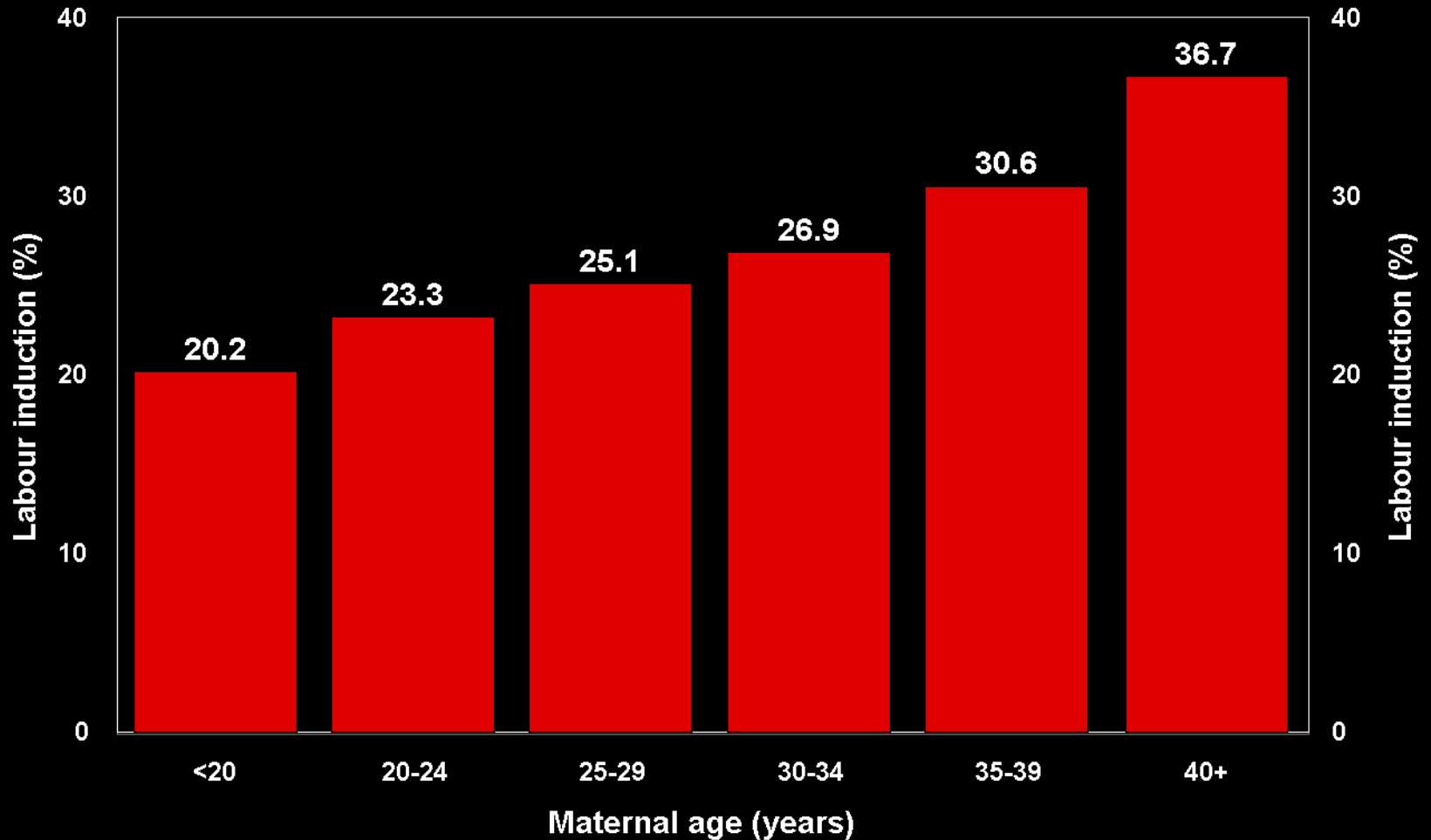
Previous cesarean delivery by maternal age



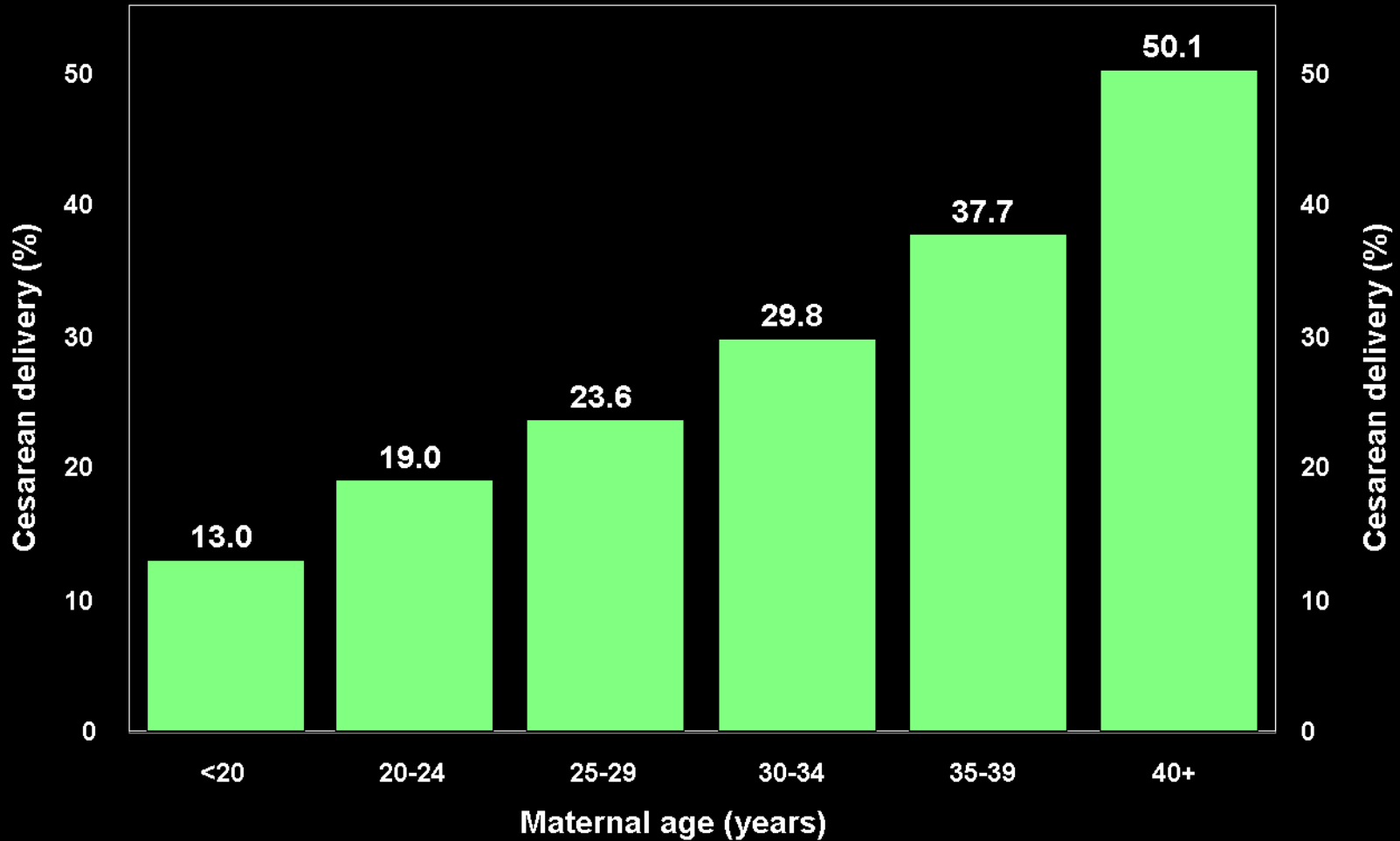
Previous perinatal death by maternal age



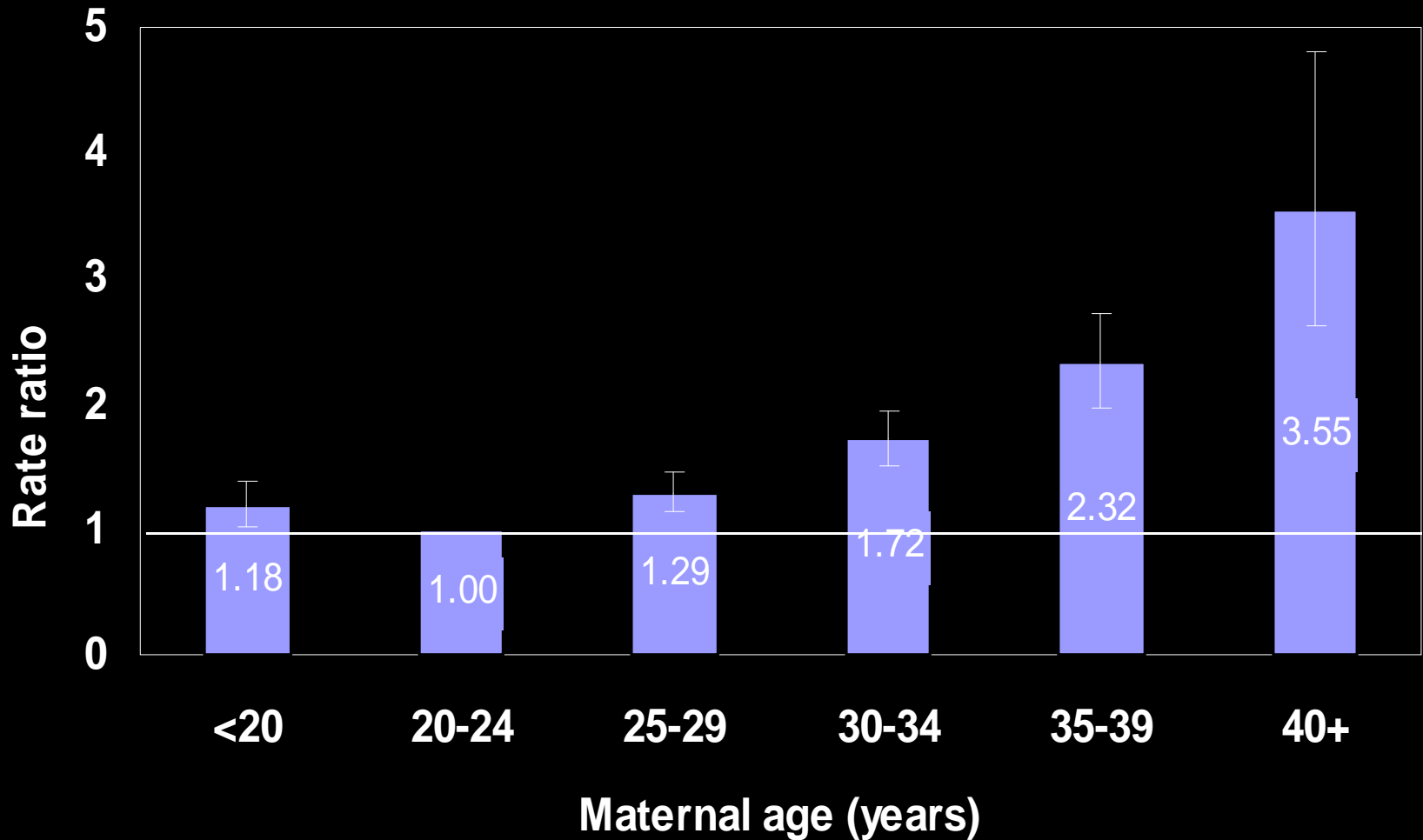
Labour induction by maternal age (nulliparous women)



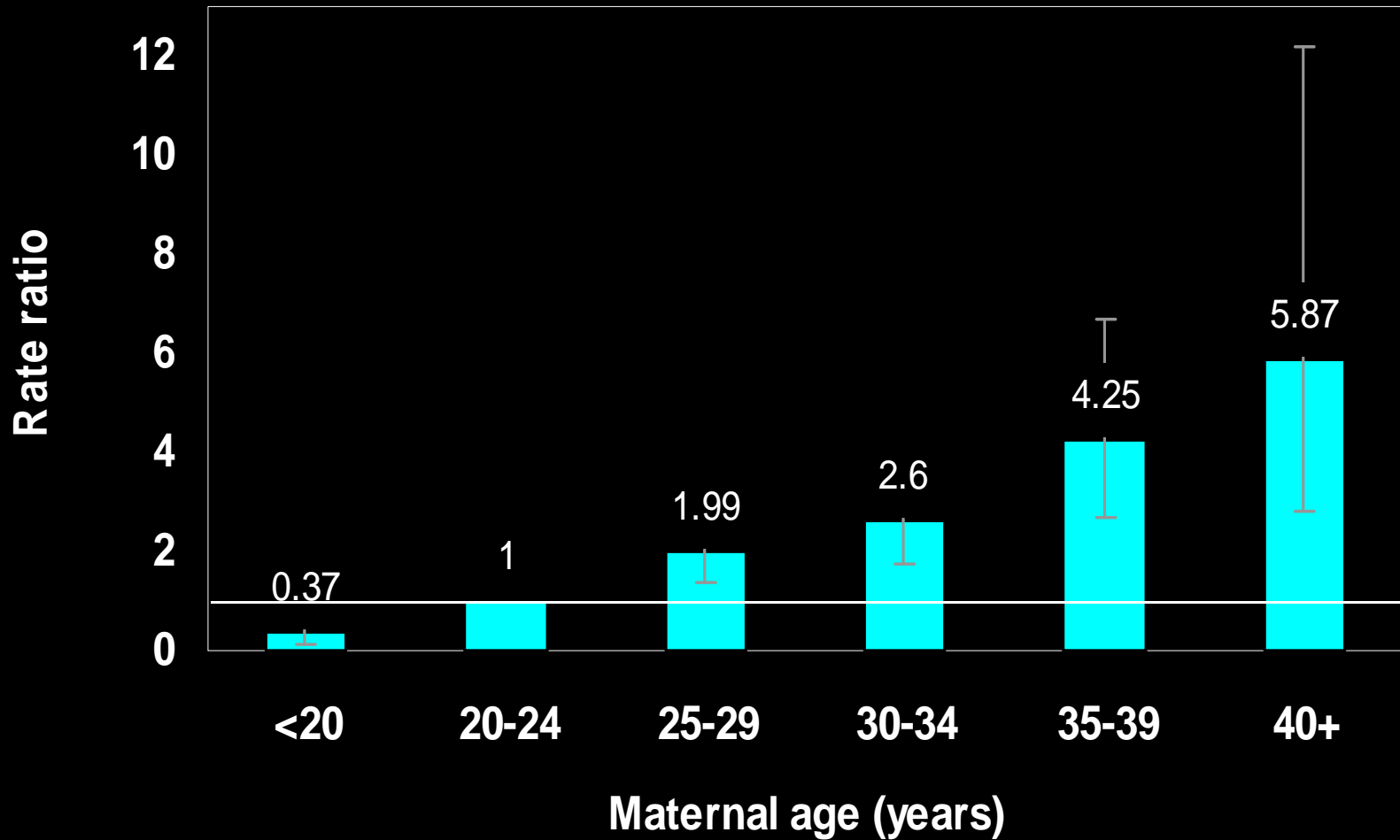
Cesarean delivery by maternal age (nulliparous women)



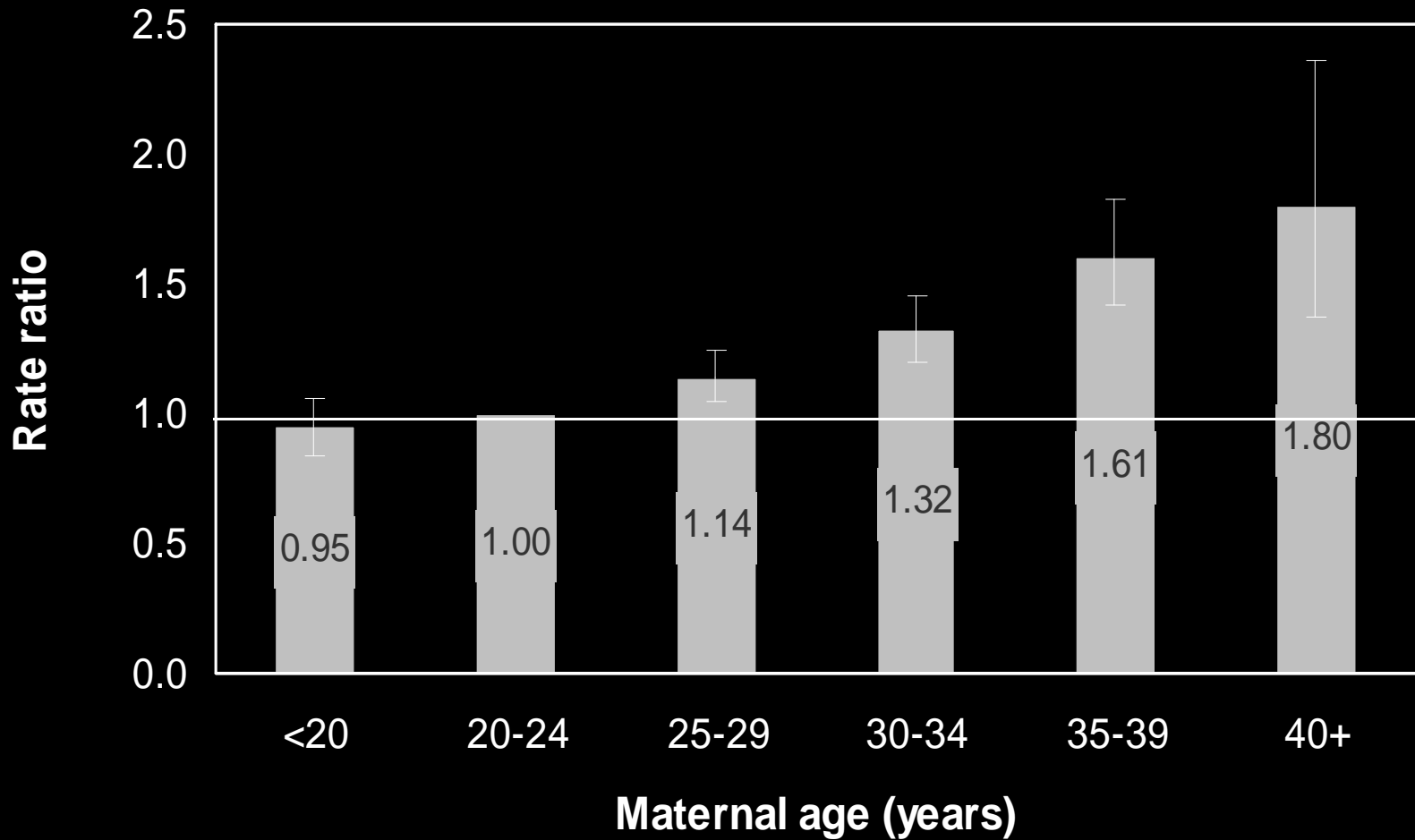
Hypertensive disorders and maternal age



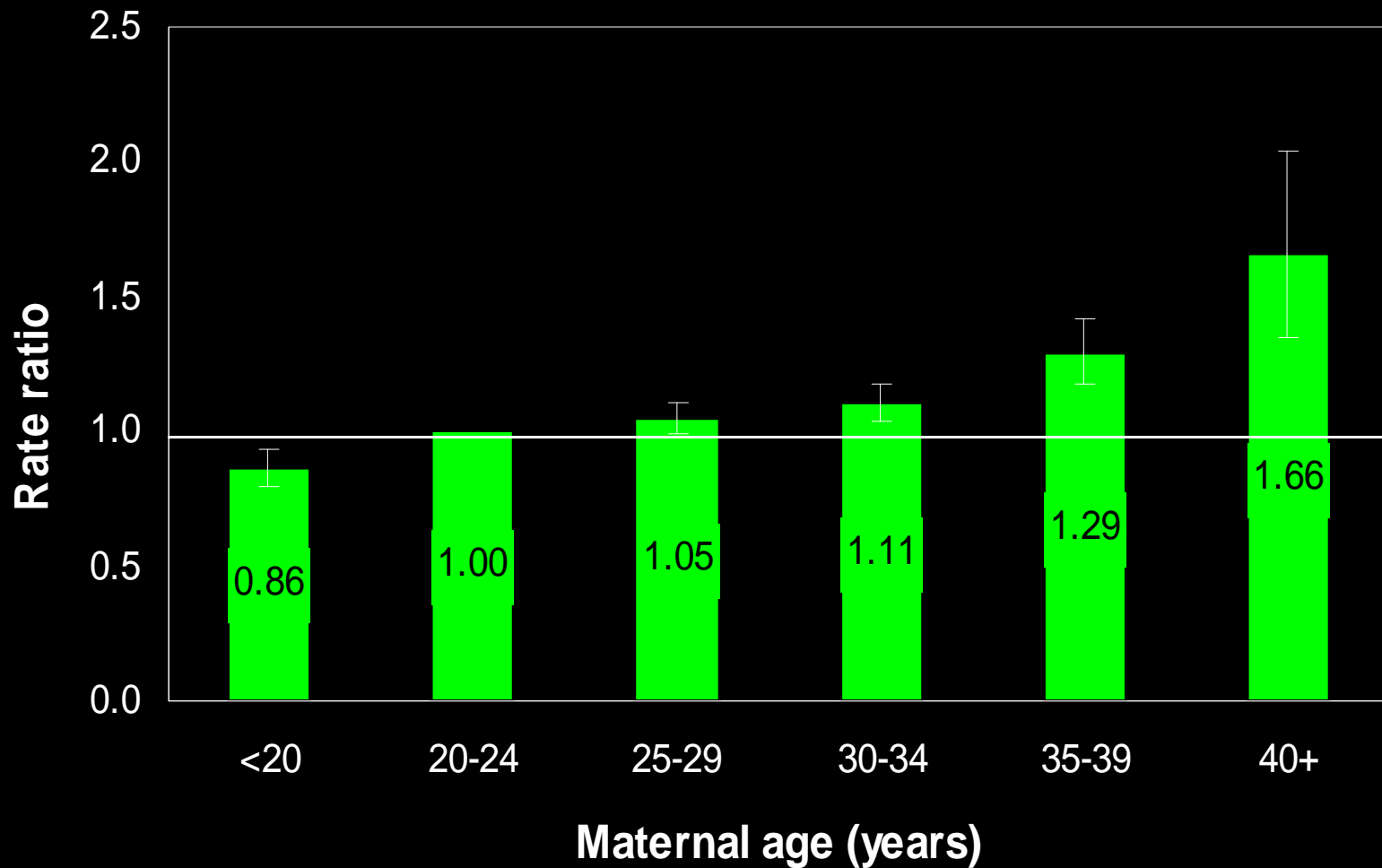
Placenta previa and maternal age



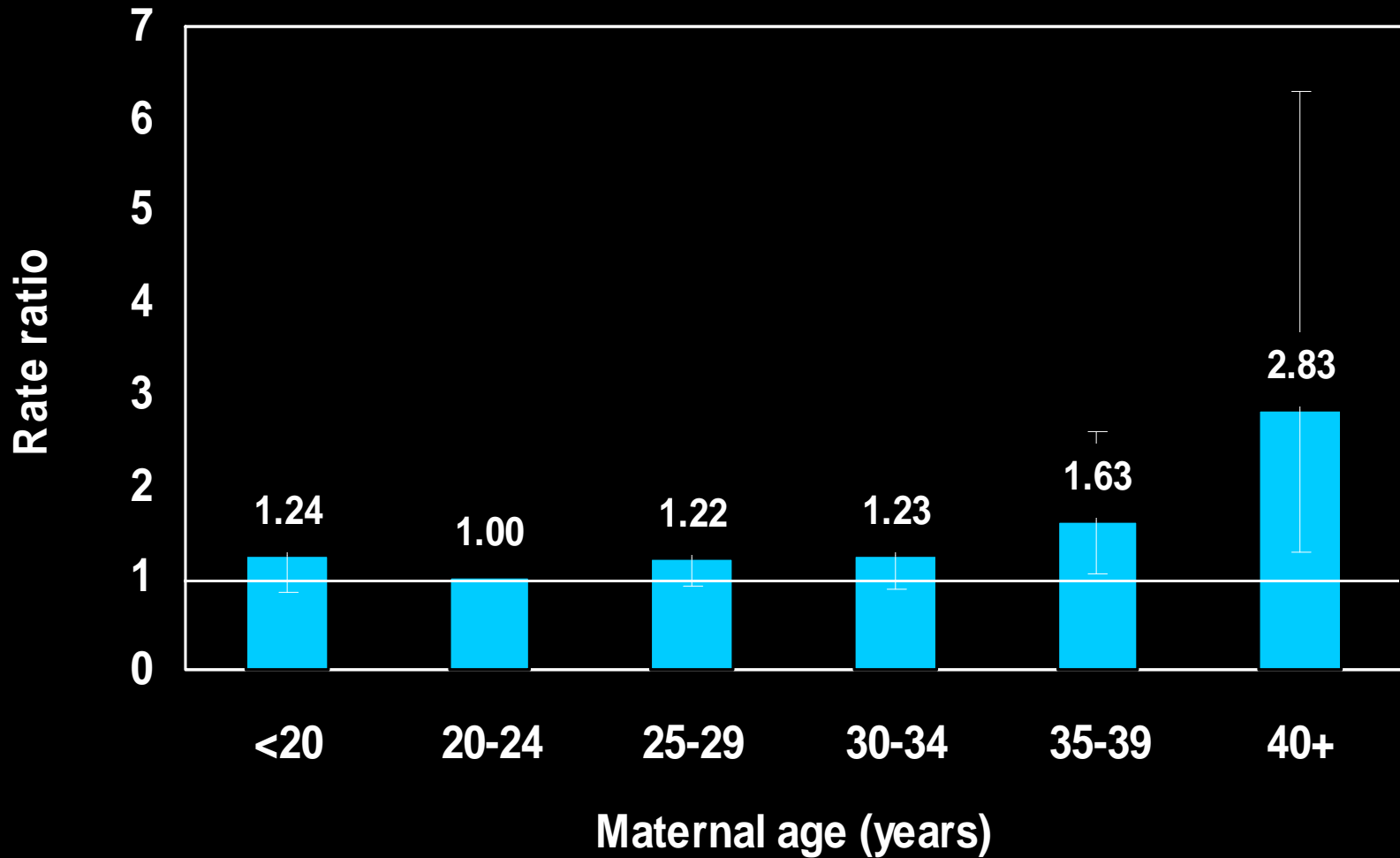
Maternal age and preterm birth



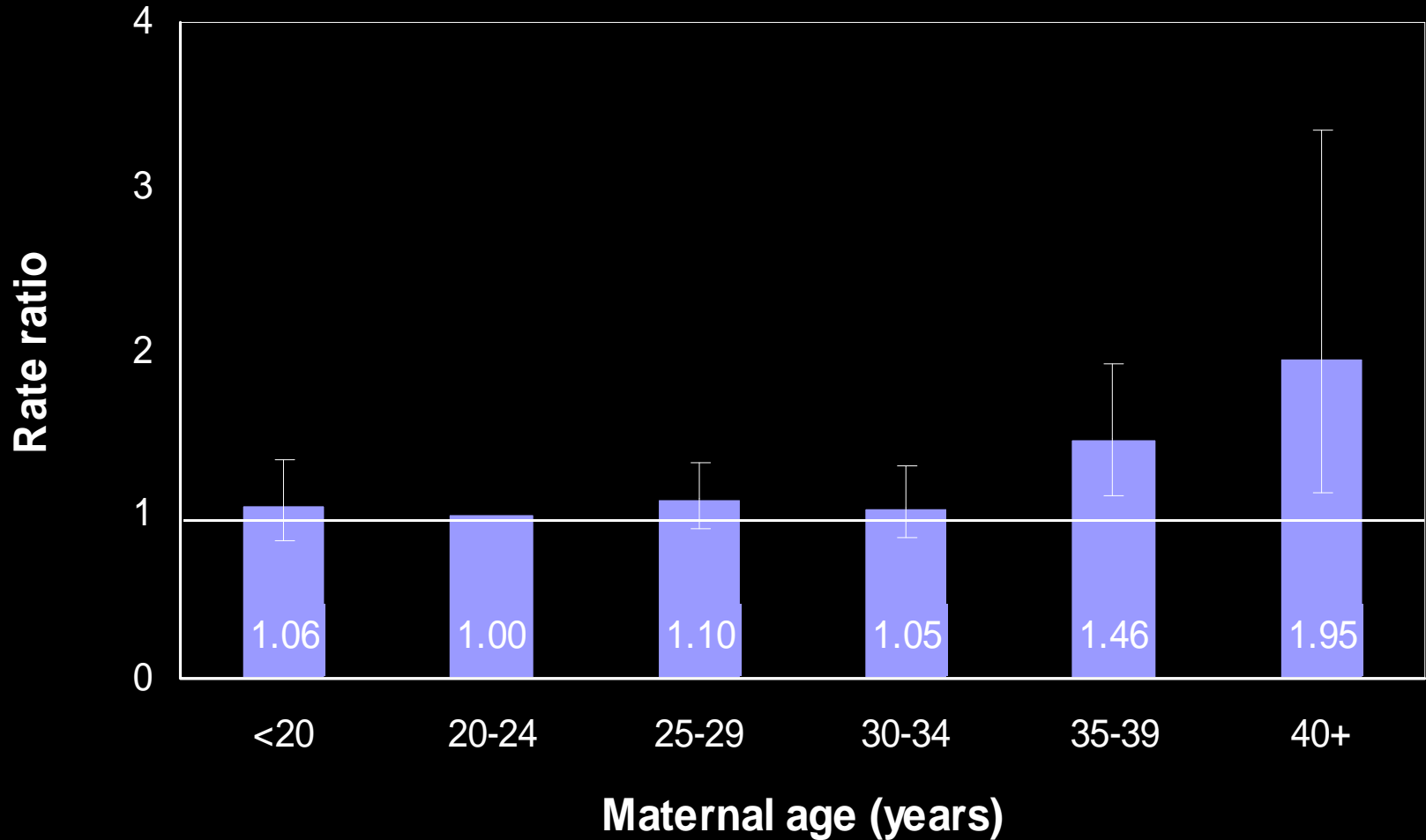
Maternal age and small for gestational age



Maternal age and perinatal mortality



Maternal age and perinatal death/serious neonatal morbidity



Discussion

Women without pregnancy complications – perinatal mortality/morbidity much lower but still associated with older age

Substantial period reductions in perinatal mortality but not mortality/morbidity

Discussion

Older women experience higher rates of

- Pregnancy complications
- Preterm birth
- Growth restriction
- Perinatal death
- Perinatal death/serious morbidity

despite higher rates of obstetric intervention

Discussion

Pregnancy complications 2 to 6 times higher

Preterm birth and SGA 50-100% higher

Perinatal mortality/morbidity increased by

46% for 35-39 years

95% for ≥ 40 years

Discussion

The excess risk is relative (to those 20-24)

Absolute rates of perinatal death are low (5 to 6 per 1,000) and falling. Rates of perinatal mortality/morbidity (10 to 15 per 1,000) also low but did not fall

- Older mothers can be “cautiously optimistic”

Other obstetric issues

Pregnancy in the sixth decade

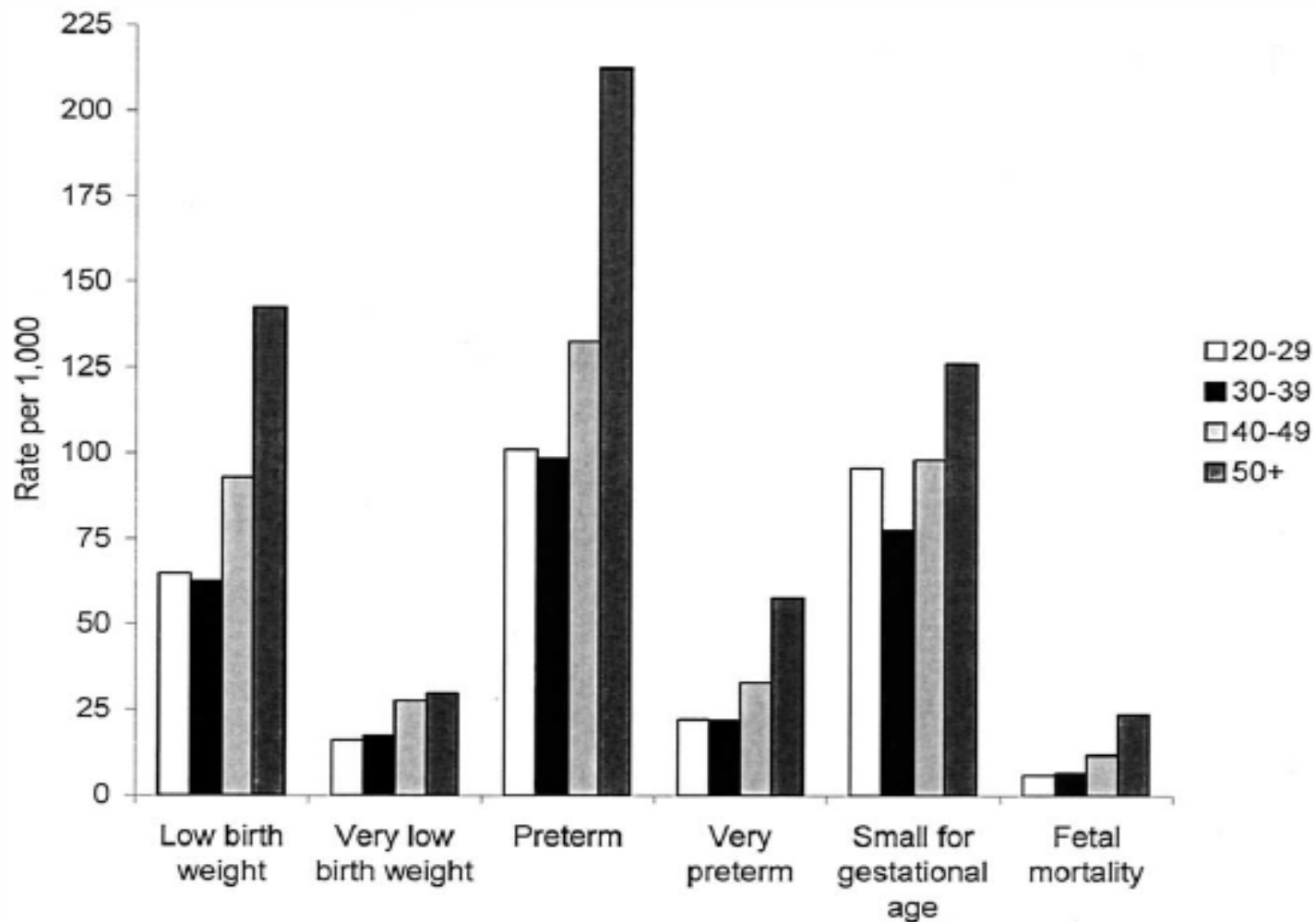


Figure 1. Crude rates for fetal morbidity and mortality among singletons by maternal age in the United States, 1997–1999.

Maternal mortality by maternal age, United Kingdom 1985-2002 (CEMACH)

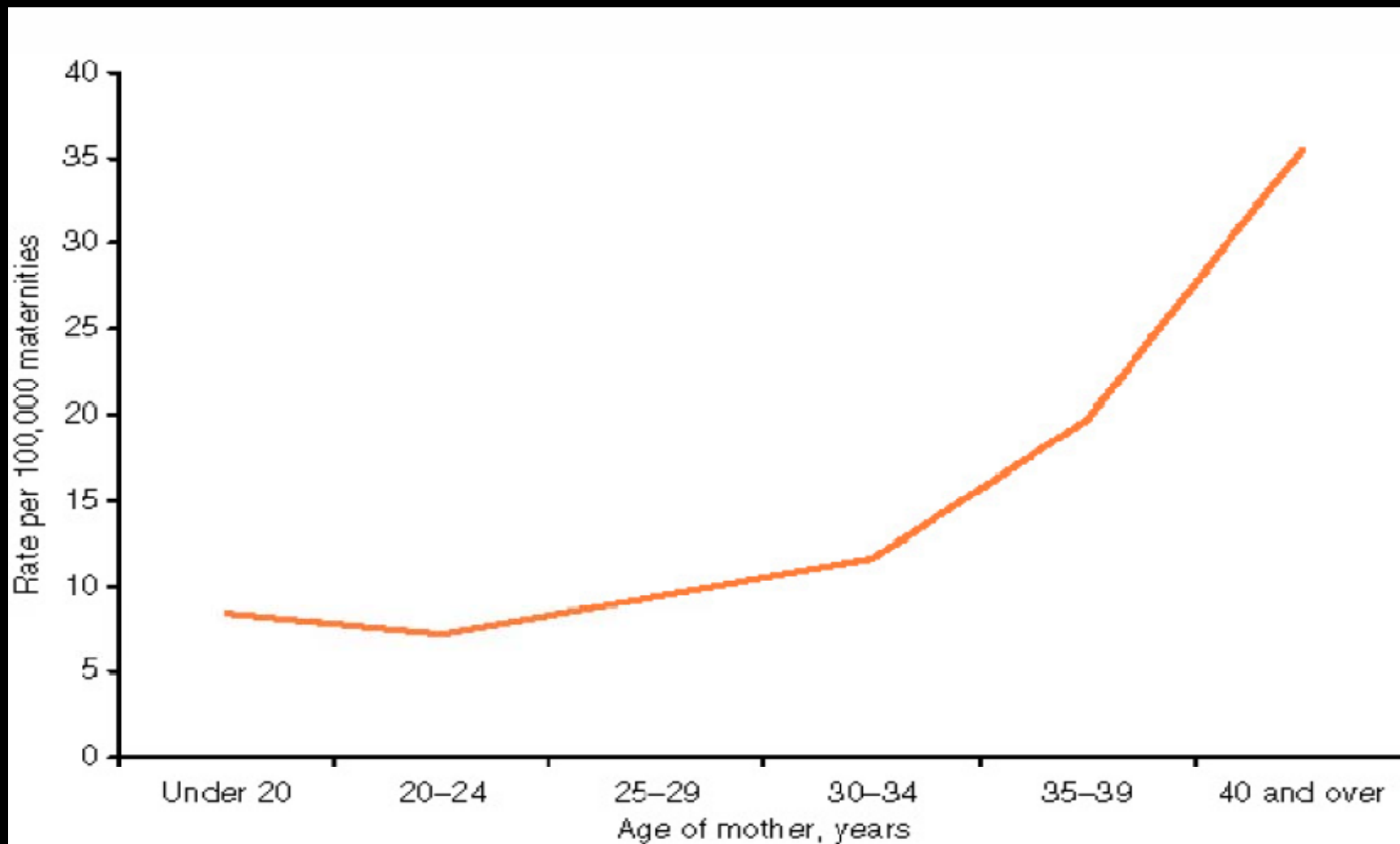


Figure 1.8 Maternal mortality rate, *Direct* and *Indirect* deaths, by maternal age; United Kingdom 1985-02

Maternal mortality by maternal age Canada 1997-2000

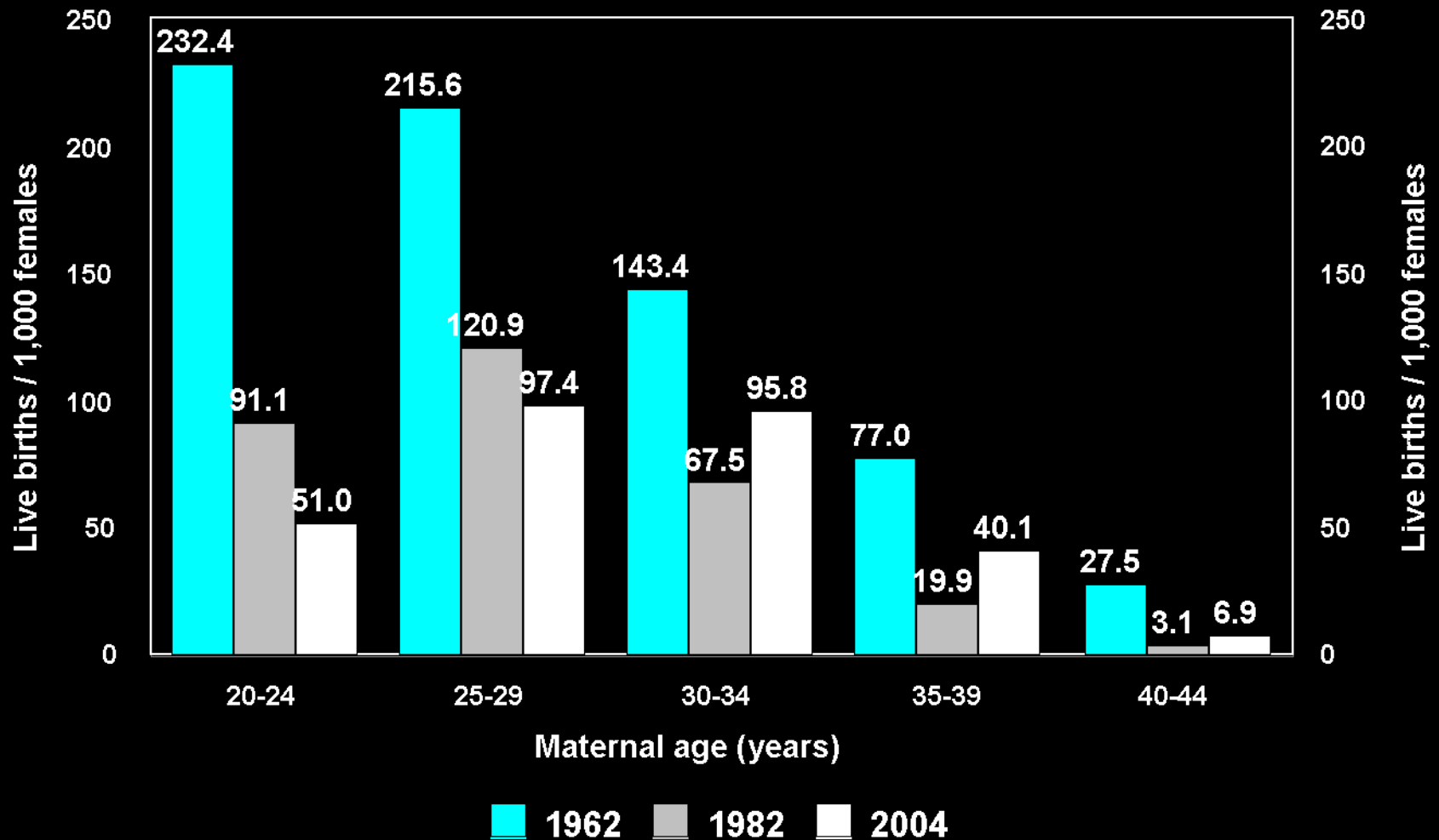
Table 4 Maternal mortality ratio (MMR) per 100,000 live births, by maternal age, Canada (excluding Quebec), 1997-2000

Age	Maternal deaths	Live births	MMR (95% CI)
< 20 years	2	62,236	3.2 (0.4-11.7)
20-24 years	4	187,062	2.1 (0.6-5.4)
25-29 years	16	321,753	5.0 (2.8-8.1)
30-34 years	24	316,588	7.6 (4.9-11.3)
35-39 years	15	142,968	10.5 (5.9-17.3)
40 years and older	3	24,221	12.4 (2.6-36.2)
Total	64	1,054,828	6.1 (4.7-7.7)

Source; Canadian Perinatal Surveillance System

On the other hand
(In praise of older women)

Age-specific live births by maternal age, Canada 1962, 1982, 2004



Maternal age and multiple births

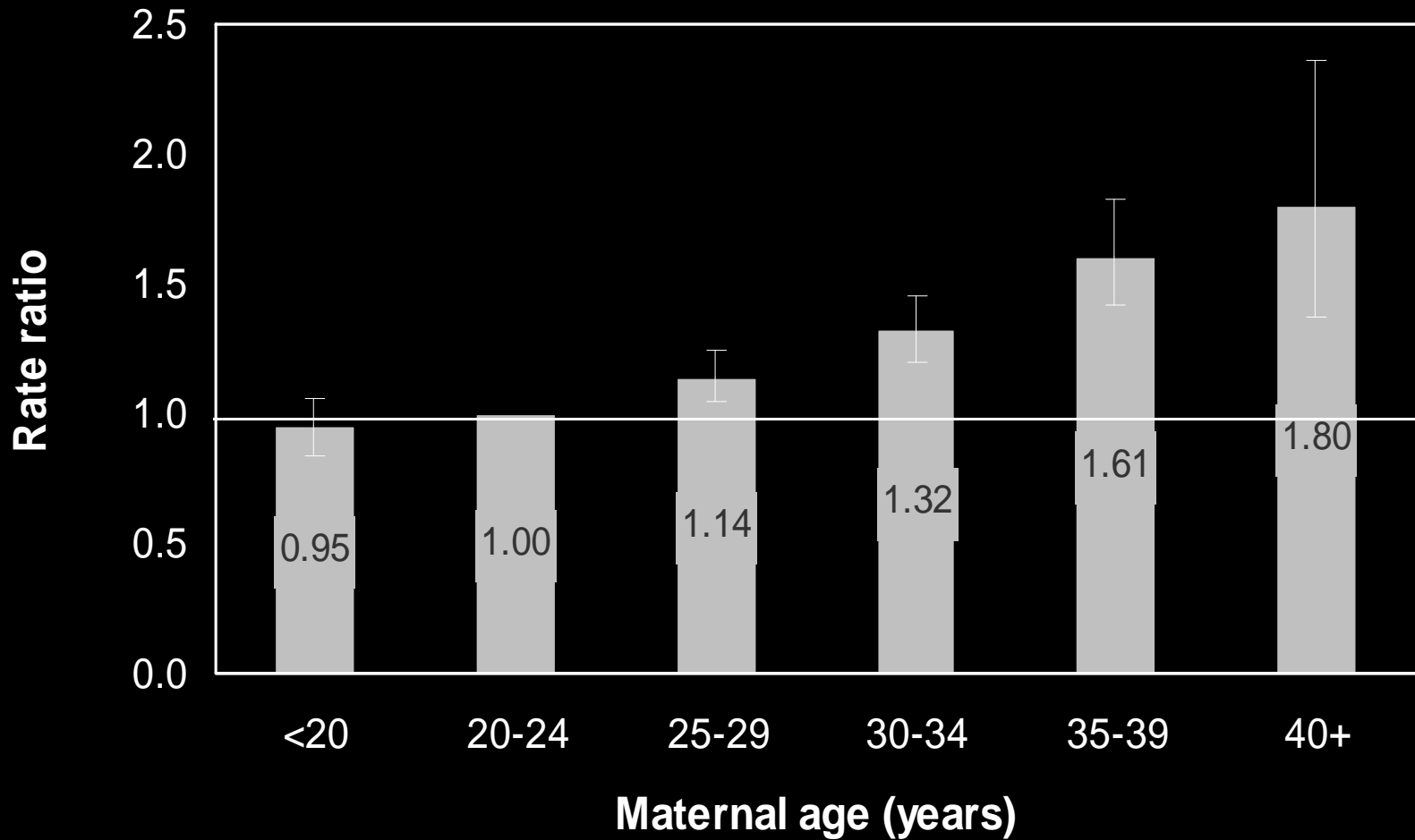
11,068 ART cycles in Canada in 2004

3,210 infants born (+ upto another 285 unborn)

1,286 twins and 120 triplets

<u>Maternal age</u>	<u>Cycles</u>	<u>Live births</u>
<35 years	4,634	1,311
35-39 years	4,056	822
>=40 years	1,924	229

Maternal age and preterm birth



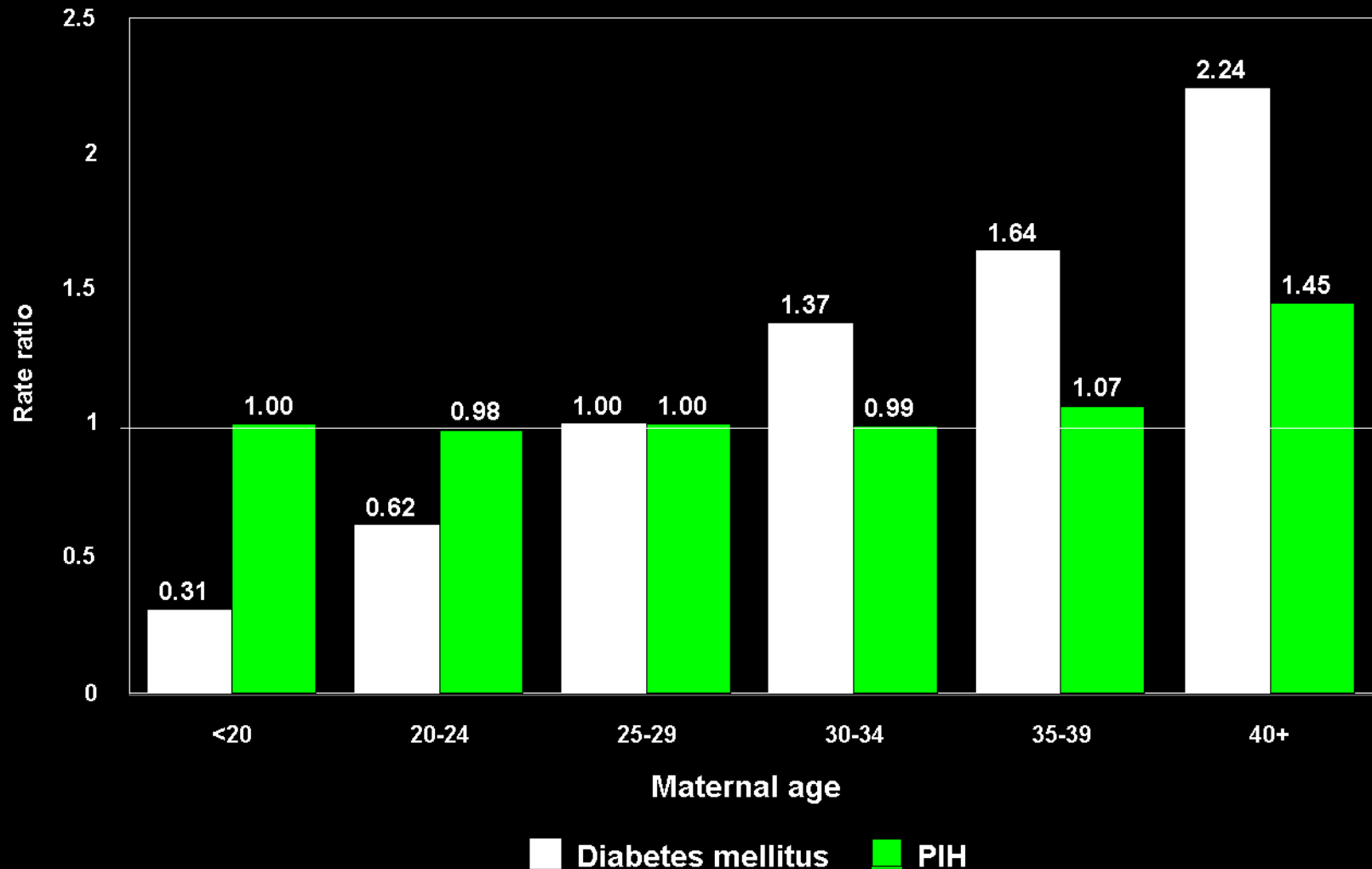
Impact of older maternal age

Individual impact: Risk of PTB/SGA increased by 50 to 100%
(Postneonatal mortality decreased)

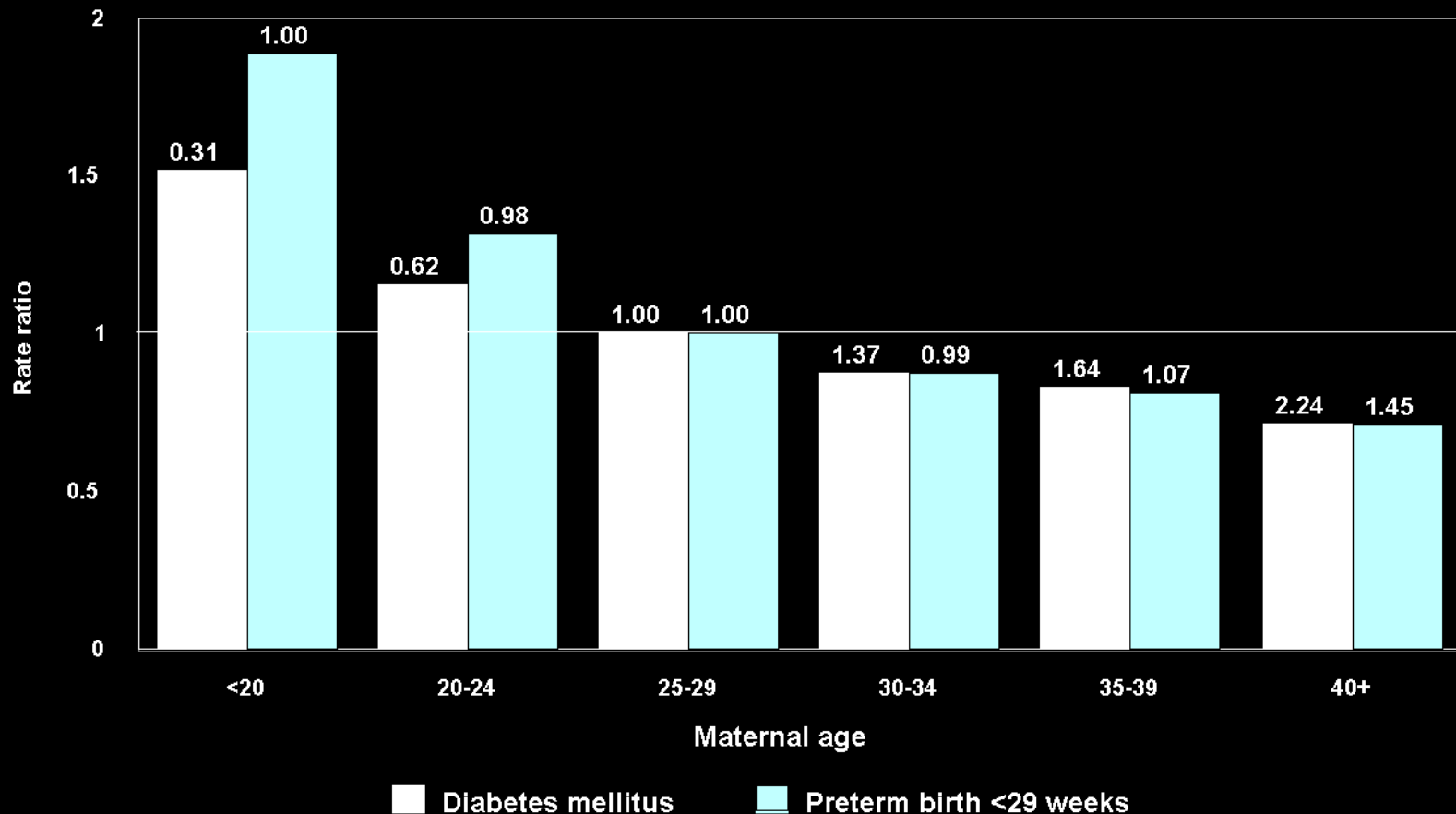
Population impact: If all women ≥ 35 years delivered at 20-24 years of age, this would prevent 9% of preterm birth and 5% of SGA

Social impact: Complex!

Paradoxical effect of older maternal age on twins and triplets



Paradoxical effect of older maternal age on twins and triplets



Explanations for the paradoxical effect

- US database studies
- Older women from higher SES backgrounds
- Better prenatal care, health coverage, etc
- More prenatal testing
- ART and ovulation induction lead to dichorionic diamniotic twins pregnancies
- Use of donor eggs

Summary

- Obstetric complications, perinatal outcomes higher among older women
- Delayed childbearing is a complex issue
 - better to avoid facile judgments

Acknowledgements

Small Area and Administrative Data Division
of Stats Can

Reproductive Care program of Nova Scotia

CIHR for funding study on
older maternal age



Pregnancy in the sixth decade

Table 3. Adjusted Estimates for Fetal Morbidity and Mortality Among Singletons by Maternal Age in the United States, 1997–1999*

	20–29 y		30–39 y		40–49 y		50+ y	
	<i>n</i>	AOR (95% CI)	<i>n</i>	AOR (95% CI)	<i>n</i>	AOR (95% CI)	<i>n</i>	AOR (95% CI)
Low birth weight	391,200	1.00	239,435	1.21 (1.15, 1.28)	22,650	1.82 (1.73, 1.91)	43	3.00 (2.10, 4.08)
Very low birth weight	100,316	1.00	66,021	1.33 (1.21, 1.47)	6704	2.03 (1.85, 2.22)	9	1.85 (0.92, 3.70)
Preterm	593,087	1.00	368,782	1.18 (1.13, 1.23)	31,414	1.62 (1.56, 1.69)	59	3.00 (2.14, 3.83)
Very preterm	129,562	1.00	81,954	1.27 (1.16, 1.39)	7821	1.86 (1.71, 2.02)	16	3.35 (2.0, 5.63)
Small size for gestational age	562,485	1.00	290,595	0.97 (0.93, 1.02)	23,221	1.20 (1.15, 1.25)	35	1.67 (1.16, 2.38)
Fetal mortality	34,634	1.00	24,614	1.13 (0.96, 1.34)	2982	1.94 (1.67, 2.26)	8	2.20 (1.01, 4.75)

AOR = adjusted odds ratio; CI = confidence interval.

Adjusted estimates were obtained by controlling for the effects of parity, marital status, maternal educational level, smoking, drinking during pregnancy, prenatal care utilization, and year of birth.

**P* for trend < .001 in all cases.

TABLE 3

Complications of pregnancy, delivery, and infant mortality by maternal age and plurality, all women.

Factor	Age	Singletons				Twins				Triplets			
		Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value
Diabetes	<20	0.87	0.30	0.30-0.30	<.0001	1.02	0.31	0.26-0.36	<.0001	3.36	0.60	0.25-1.43	.26
	20-24	1.70	0.61	0.61-0.62	<.0001	2.02	0.82	0.58-0.67	<.0001	3.81	0.69	0.45-1.06	.09
	25-29	2.68	1.00	—		3.23	1.00	—		5.56	1.00	—	
	30-34	3.57	1.37	1.36-1.38	<.0001	4.34	1.37	1.29-1.44	<.0001	6.22	1.13	0.91-1.40	.27
	35-39	4.87	1.89	1.87-1.91	<.0001	5.19	1.84	1.54-1.75	<.0001	7.81	1.42	1.13-1.80	.003
	≥40	6.69	2.64	2.60-2.68	<.0001	7.03	2.24	2.03-2.46	<.0001	7.28	1.32	0.91-1.92	.14
Chronic hypertension (<20 weeks)	<20	0.26	0.33	0.32-0.34	<.0001	0.48	0.46	0.36-0.59	<.0001	2.65	2.16	0.69-6.82	.21
	20-24	0.45	0.63	0.62-0.64	<.0001	0.72	0.76	0.67-0.87	<.0001	0.30	0.24	0.06-0.97	.045
	25-29	0.67	1.00	—		0.89	1.00	—		1.22	1.00	—	
	30-34	0.94	1.46	1.44-1.48	<.0001	1.16	1.39	1.25-1.54	<.0001	1.17	0.96	0.61-1.51	.85
	35-39	1.54	2.43	2.39-2.47	<.0001	1.62	1.94	1.73-2.17	<.0001	1.65	1.36	0.84-2.20	.21
	≥40	2.71	4.27	4.17-4.37	<.0001	2.67	3.24	2.77-3.80	<.0001	3.36	2.73	1.24-6.00	.01
Pregnancy-associated hypertension	<20	4.35	0.89	0.89-0.90	<.0001	9.37	1.00	0.94-1.07	.916	6.04	0.68	0.35-1.32	.26
	20-24	3.82	0.98	0.97-0.98	<.0001	7.72	0.98	0.94-1.03	.408	7.46	0.78	0.57-1.09	.15
	25-29	3.69	1.00	—		7.97	1.00	—		10.24	1.00	—	
	30-34	3.37	0.98	0.98-0.99	<.0001	7.86	0.99	0.95-1.03	.707	11.79	1.16	0.99-1.37	.07
	35-39	3.69	1.15	1.14-1.16	<.0001	8.19	1.07	1.02-1.12	.006	11.58	1.18	0.98-1.43	.07
	≥40	4.55	1.44	1.42-1.47	<.0001	11.35	1.45	1.34-1.56	<.0001	14.74	1.52	1.16-2.01	.003

TABLE 3

Continued.

Factor	Age	Singletons				Twins				Triplets			
		Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value
Delivery <29 weeks	<20	1.20	1.48	1.46-1.51	<.0001	10.50	1.57	1.47-1.66	<.0001	31.79	1.50	1.04-2.16	.03
	20-24	0.79	1.09	1.08-1.11	<.0001	6.93	1.16	1.11-1.22	<.0001	26.10	1.31	1.07-1.61	.009
	25-29	0.63	1.00	—		5.54	1.00	—		20.63	1.00	—	
	30-34	0.62	1.07	1.05-1.08	<.0001	4.49	0.85	0.81-0.89	<.0001	15.92	0.75	0.66-0.86	<.0001
	35-39	0.78	1.33	1.31-1.36	<.0001	4.14	0.80	0.76-0.85	<.0001	12.53	0.57	0.49-0.67	<.0001
	≥40	0.97	1.62	1.56-1.68	<.0001	3.82	0.72	0.64-0.81	<.0001	11.58	0.52	0.40-0.69	<.0001
Infant death of one or more babies	<20	0.91	1.67	1.64-1.70	<.0001	4.91	1.89	1.73-2.07	<.0001	13.38	1.36	0.80-2.31	.25
	20-24	0.69	1.26	1.24-1.28	<.0001	3.22	1.33	1.24-1.43	<.0001	13.18	1.58	1.20-2.09	.001
	25-29	0.51	1.00	—		2.30	1.00	—		8.11	1.00	—	
	30-34	0.74	0.96	0.94-0.97	<.0001	1.87	0.86	0.80-0.92	<.0001	5.49	0.69	0.57-0.85	.0003
	35-39	0.55	1.10	1.08-1.13	<.0001	1.68	0.77	0.71-0.85	<.0001	3.87	0.48	0.37-0.62	<.0001
	≥40	0.74	1.44	1.38-1.50	<.0001	1.51	0.69	0.57-0.83	<.0001	2.41	0.29	0.17-0.52	<.0001