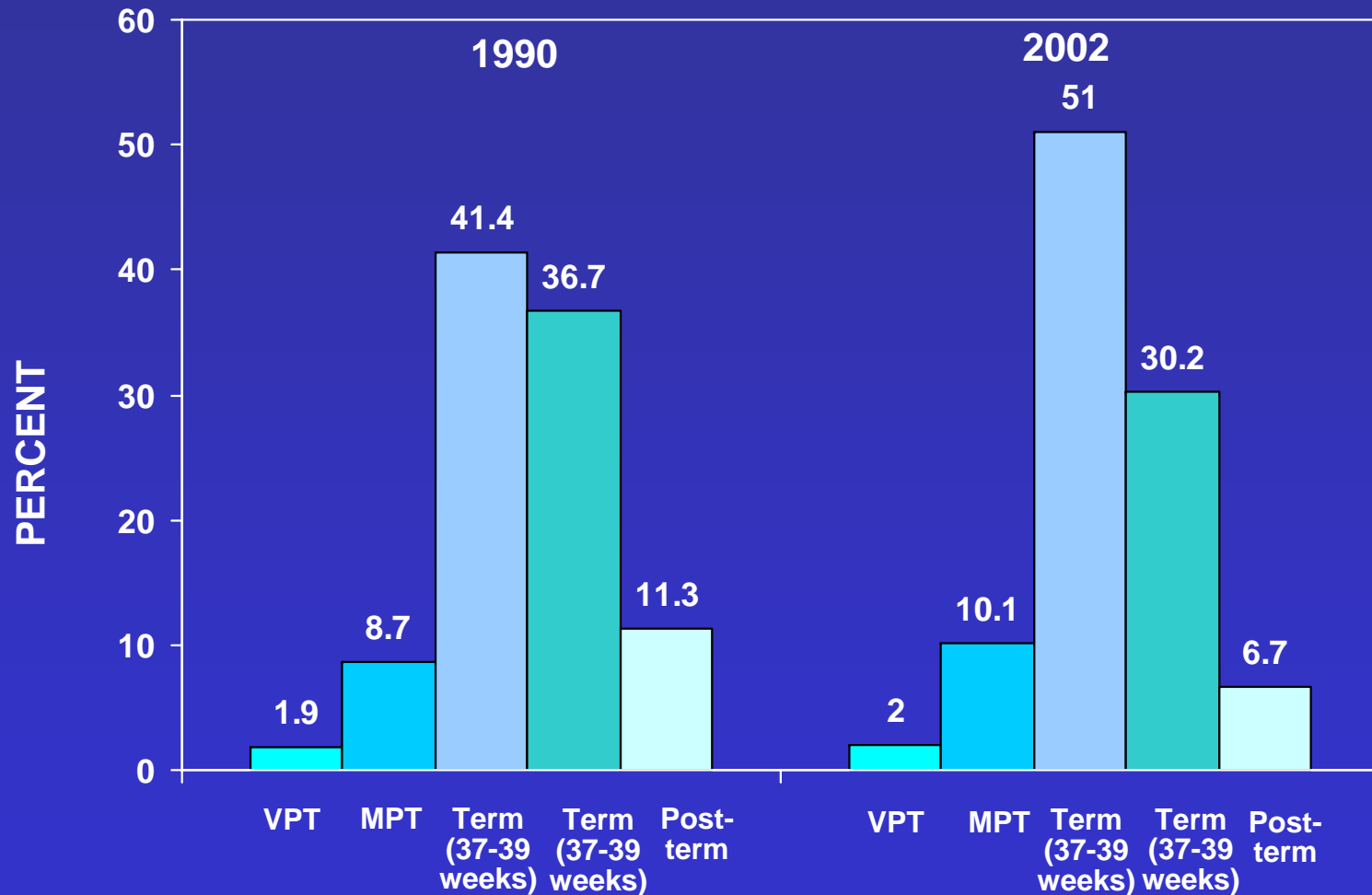# Heterogeneity of the pre-term delivery syndrome

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Distribution of births by gestational age: United States, 1990 and 2002

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Why are we unable to reduce preterm delivery, when much progress has been made in other areas of medicine ?

- Mechanisms of initiation of labour yet to be elucidated

- Preterm delivery is a multifactorial syndrome

Factors associated with an increase in preterm deliveries

- Increase in obstetric interventions

- Multiple births related to higher maternal age

- Assisted reproduction techniques

- Gestational age under estimation

- Other socio-economic factors

Hypothesis

Is there different morbidity and mortality among clinical presentations and mechanisms of preterm delivery ?

Villar J. et al;Obstet. and Gynecol 2004;104:(July)

Populations enrolled in the WHO multicentre randomized trial for the evaluation of a new, evidence based, routine antenatal care model (1996-1998)

Argentina, Cuba, Saudi Arabia, Thailand

Cluster randomization study design

Villar J. et al; Lancet 2001;357:1551-64

Preterm delivery

- Gestational age at birth of less than 37 completed weeks

- Gestational age based on best obstetric estimate

- Early ultrasound examination for dating

- Description of study population and methodology in:

Villar J. et al; Paediatric and Perinatal Epidemiology 1998;12:27-58

Villar J. et al; Lancet 2001;357:1551-64

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Pre-term delivery classified by:

1. Clinical presentations

- Spontaneous initiation of labour
- Labour after prelabour spontaneous rupture of membranes (PROM)
- Medically indicated (induced labour or elective caesarean delivery)

2. Obstetric and medical complications

- At least one of the following:
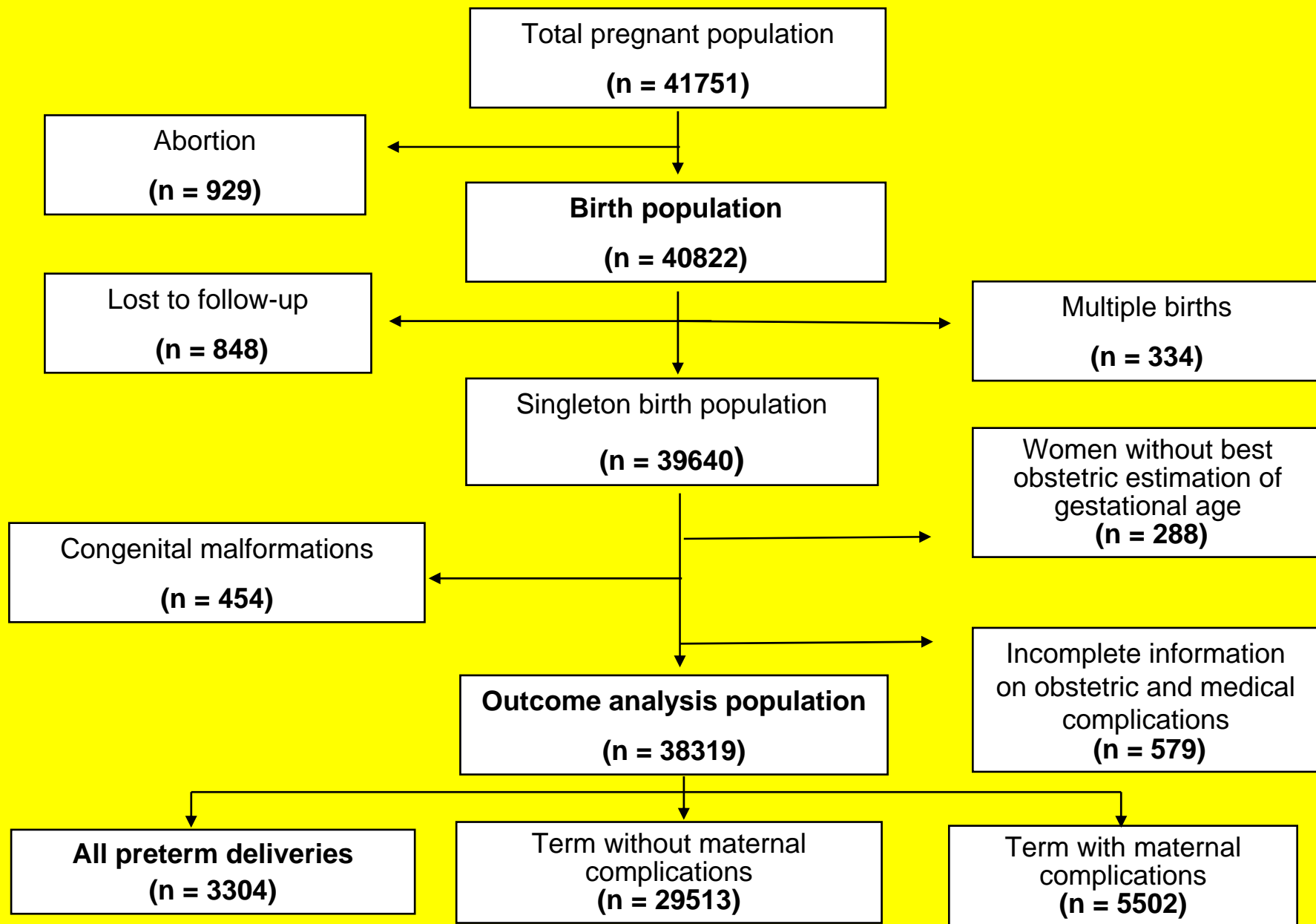
Obstetric and medical complications

- Chronic hypertension or antihypertension treatment

- Hypertension in the present pregnancy after the 20th week

- Preeclampsia or eclampsia

- Hemorrhage during pregnancy but before labour

Obstetric and medical complications

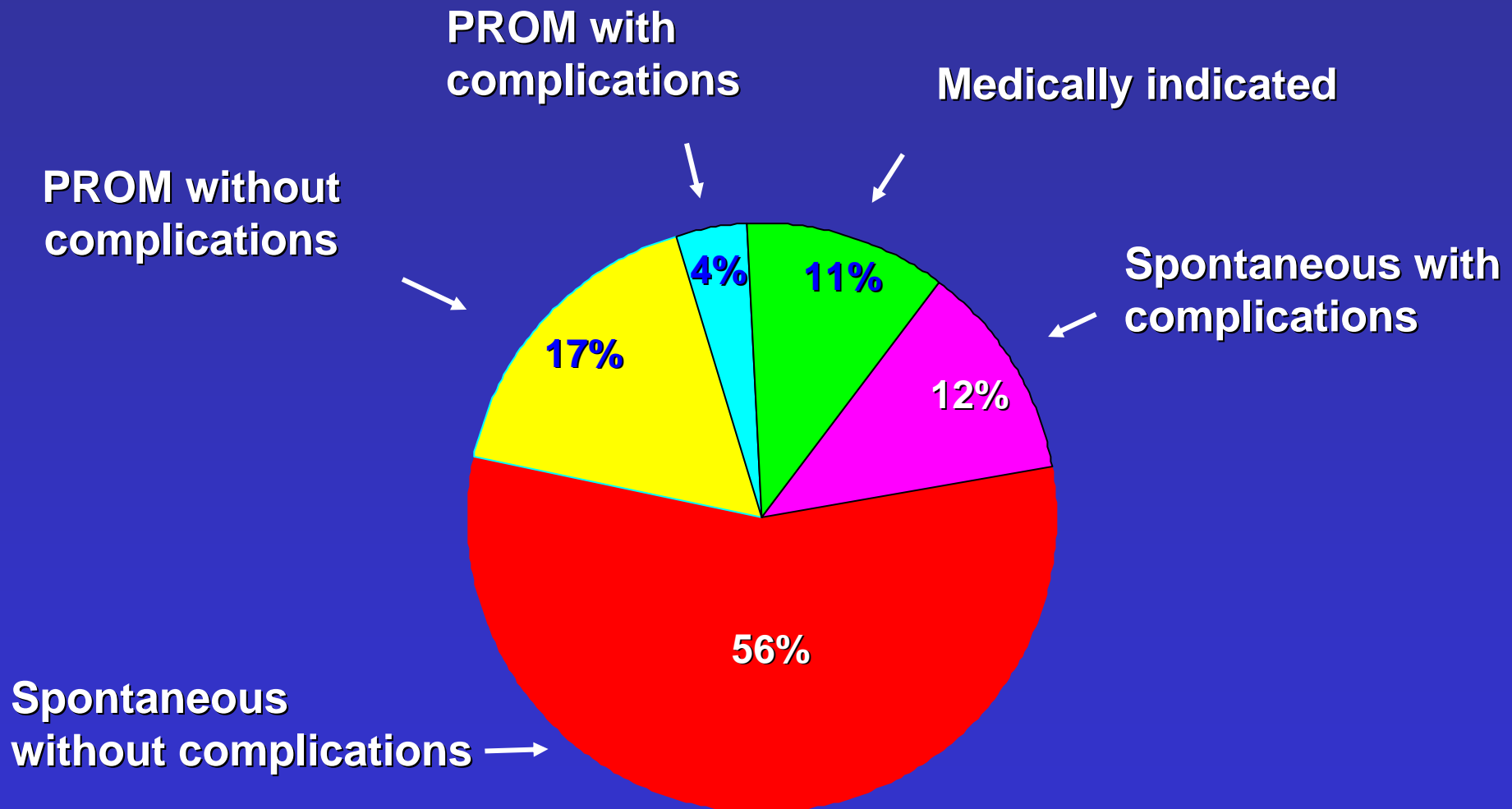- Any cardiopathy, renal disease or any other severe medical complications

- Severe anemia (Hb less than 90 g/L), or hemolytic disease in the present pregnancy (rhesus-isoimmunization)

Agreement between observers for preterm delivery diagnostic

- Kappa statistics = 0.88 (95% CI 0.84 – 0.94) for "preterm delivery" status

- Intra-class correlation coefficient for gestational age at birth = 0.93% (95% lower CI 0.92%)

Total pregnant population

(n = 41751)

Abortion

(n = 929)

Birth population

(n = 40822)

Lost to follow-up

(n = 848)

Multiple births

(n = 334)

Singleton birth population

(n = 39640)

Women without best obstetric estimation of gestational age
(n = 288)

Congenital malformations

(n = 454)

Incomplete information on obstetric and medical complications
(n = 579)

Outcome analysis population

(n = 38319)

**All preterm deliveries
(n = 3304)**

Term without maternal complications
(n = 29513)

Term with maternal complications
(n = 5502)

Distribution of the 3,304 preterm deliveries (8.6%)

PROM with complications

Medically indicated

PROM without complications

Spontaneous with complications

4%

11%

17%

12%

56%

Spontaneous without complications

Socio-demographic characteristics according to preterm delivery sub-group

	Spontaneous without complications (%) (n = 1773)	Spontaneous with complications (%) (n = 394)	Medically Indicated (%) (n = 365)	PROM Without complications (%) (n = 530)	PROM with complications (%) (n = 134)
Age <16 years	5.8	4.1	3.6	5.9	4.5
Age >40 years	1.0	2.5	**4.9**	1.7	2.2
Married/stable union	84.3	86.0	84.4	78.1	83.6
Education: incomplete primary	**41.3**	34.4	29.1	31.4	27.6
Smokers	13.6	15.8	13.7	**22.3**	**18.1**
Any substance abuse	0.5	0.8	0.6	0.9	**3.0**
Crowded house	37.9	38.1	35.9	37.0	35.8
Primiparous	37.6	34.5	37.5	40.9	33.6

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Birth weight and gestational age according to preterm delivery subgroup

Group			N	Birth weight (g) Mean	Std Dev.	Gestational age (weeks) Mean	Std Dev.
Preterm delivery	Spontaneous	Without complications	1751	(*) 2509	698	34.2	2.7
		With complications	381	2307	812	33.3	3.7
	Medically Indicated	With complications	364	2168	780	33.9	2.8
	PROM	Without complications	529	2232	680	33.4	3.1
		With complications	134	2092	823	32.6	3.7
Term – Without complications			29396	3251	453	39.4	1.3

(*) P <0.01 compared to all PTD groups

Incidence of very preterm delivery (<32 weeks) according to preterm delivery sub-group

- PROM with complications   **37% (*)**
- Spontaneous without complications   **17% (*)**
- Spontaneous with complications   **25%**
- PROM without complications   **24%**
- Medically indicated   **26%**

(*) $p < 0.01$

Small for Gestational Age according to preterm delivery subgroup

Group		N	%
Preterm delivery / **Spontaneous**	Without complications	1745	7.3
	With complications	376	11.2
Medically Indicated	With complications	364	**22.3**
PROM	Without complications	528	8.7
	With complications	133	8.3
Term – Without complications		**29376**	**13.2**

(*) < 10th percentile

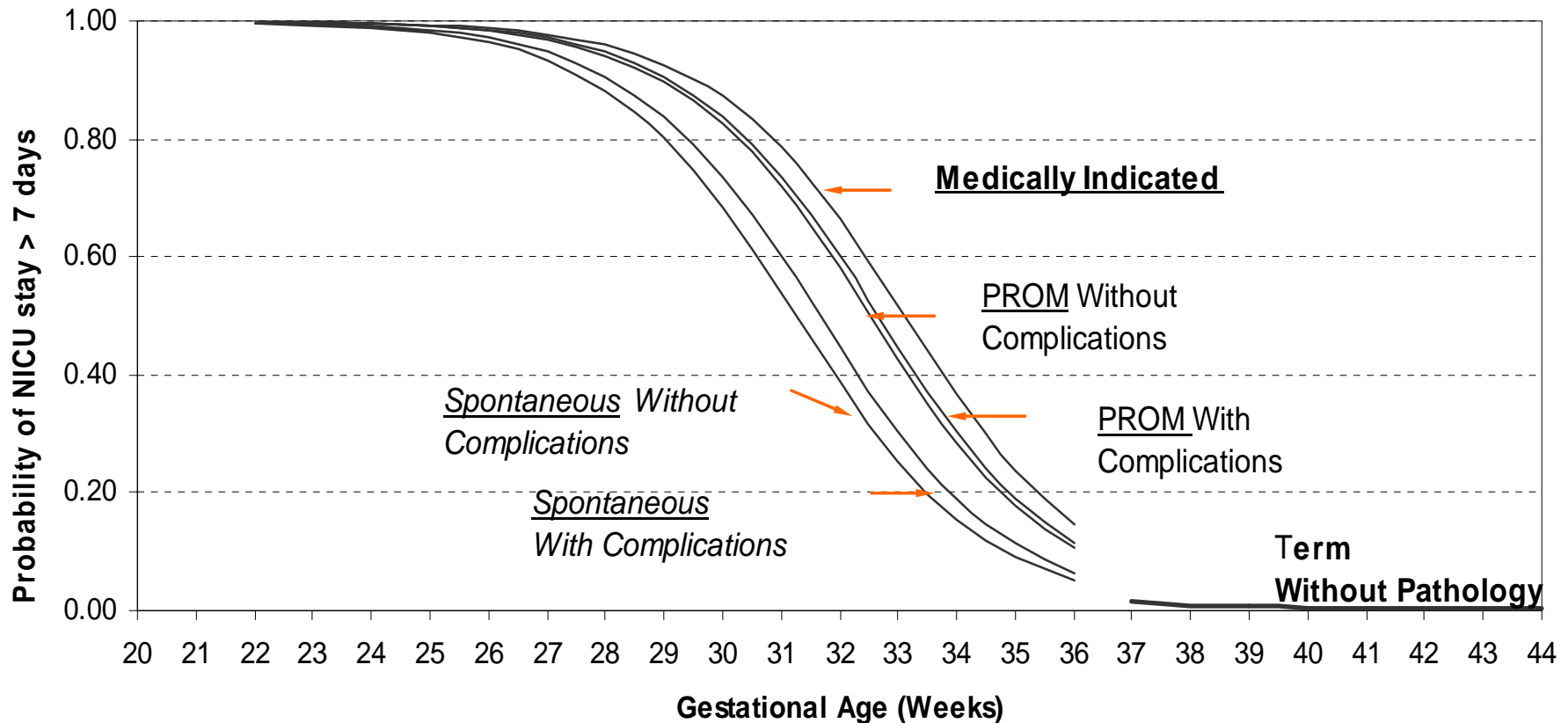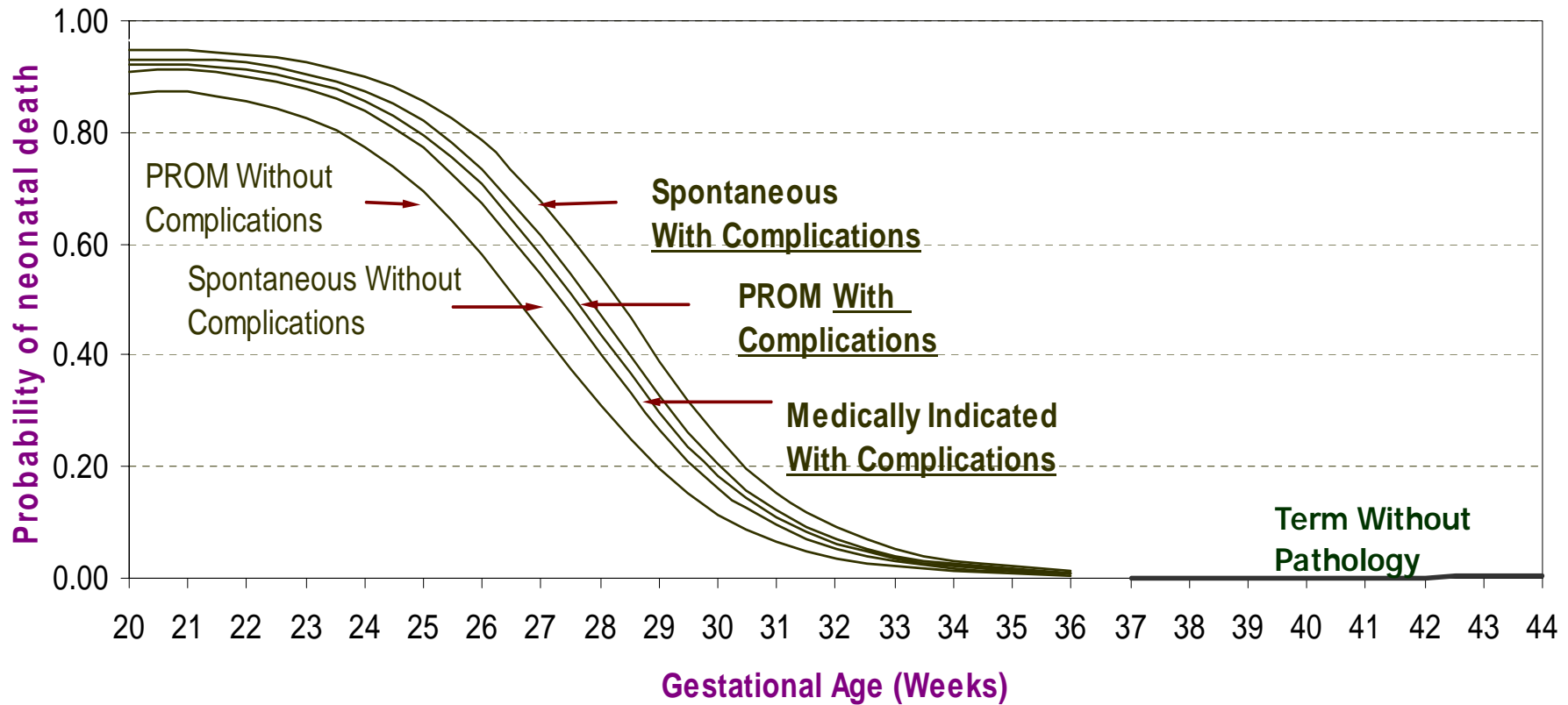# Probability of intrapartum death
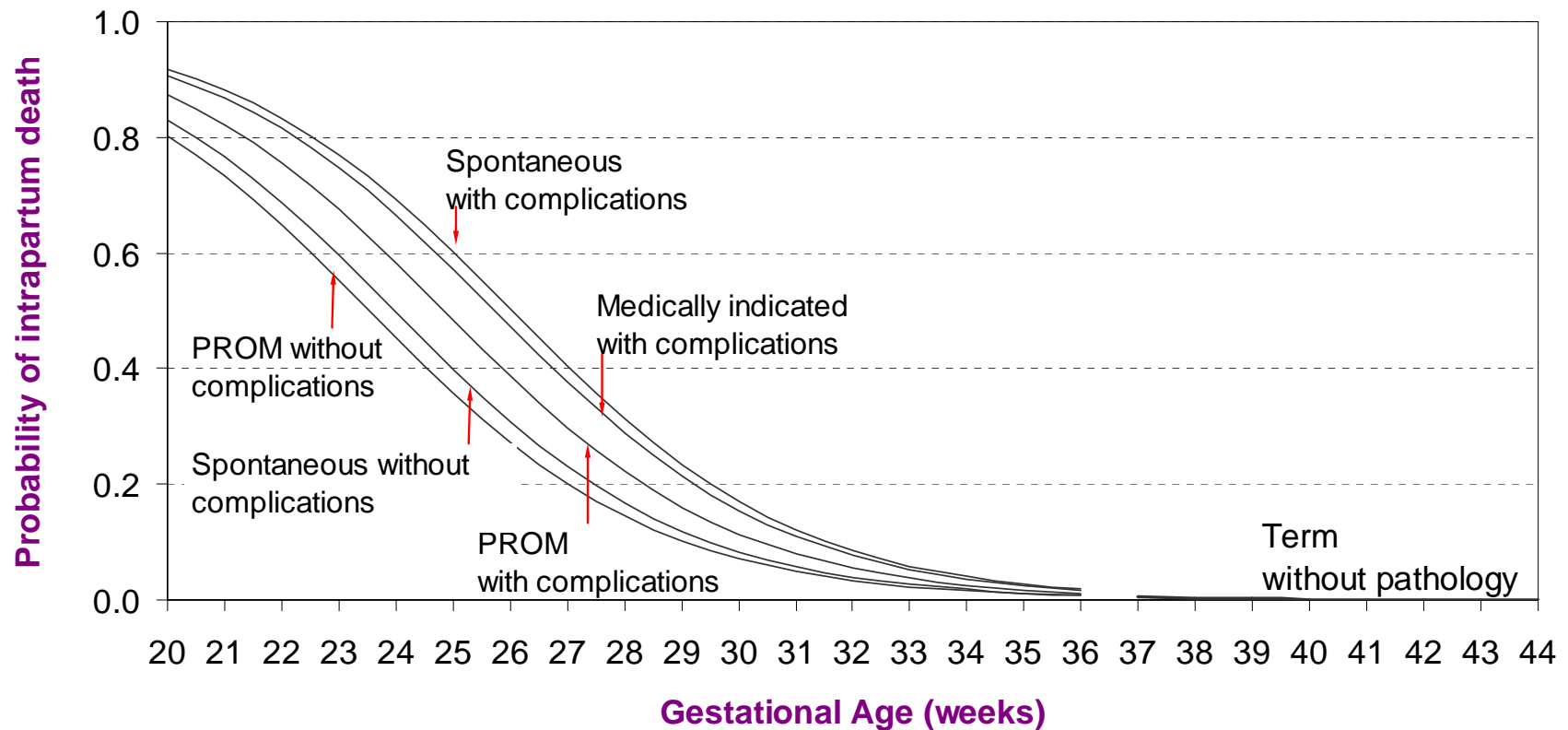
Villar J et al. 2003

Probability of NICU stay >7 days by preterm delivery subgroups

Villar J et al. 2003

Probability of neonatal death by preterm delivery subgroups

PROM Without Complications

Spontaneous With Complications

Spontaneous Without Complications

PROM With Complications

Medically Indicated With Complications

Term Without Pathology

Probability of neonatal death

Gestational Age (Weeks)

Villar J et al. 2003

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Conclusions

There are differential neonatal outcomes among preterm deliveries, adjusted by birth weight and gestational age, according to:

- Clinical presentation (PROM, spontaneous …)

- Timing of delivery (< 32 weeks)

- Pregnancy complications

- Small for gestational age

The syndromic nature of preterm delivery should be fully understood to achieve its prevention.