

# Global Maternal and Perinatal Research: the next 25 years

**José Villar M.D.**

**Department of Department of Reproductive  
Health and Research**

**World Health Organization  
Geneva**

**Boston, June 2004**

The same evidence of  
effectiveness and safety  
should be required for both  
drugs and non-drugs forms of care  
including health policies  
and service administration

- **Summarising evidence**
- **Generating evidence**
  - **Research priorities**
    - **Outcomes**
- **Utilisation of research**

# **Summarising evidence: the future of literature review**

# Systematic reviews of **trials**: challenging issues

- **up-dating**
- **Heterogeneity - to pool or not to pool?**
- **publication bias**
- **combining individual and cluster  
randomisation trials**
- **meta-analysis of small trials: over  
optimistic ?**

# Systematic reviews **beyond trials!**

## **Incidence/prevalence**

WHO systematic review,  
maternal morbidity  
(completed 2003)

## **Effectiveness of screening**

WHO systematic review,  
screening for pre- eclampsia  
(completed 2004)

## **Pathophysiology/aetiology**

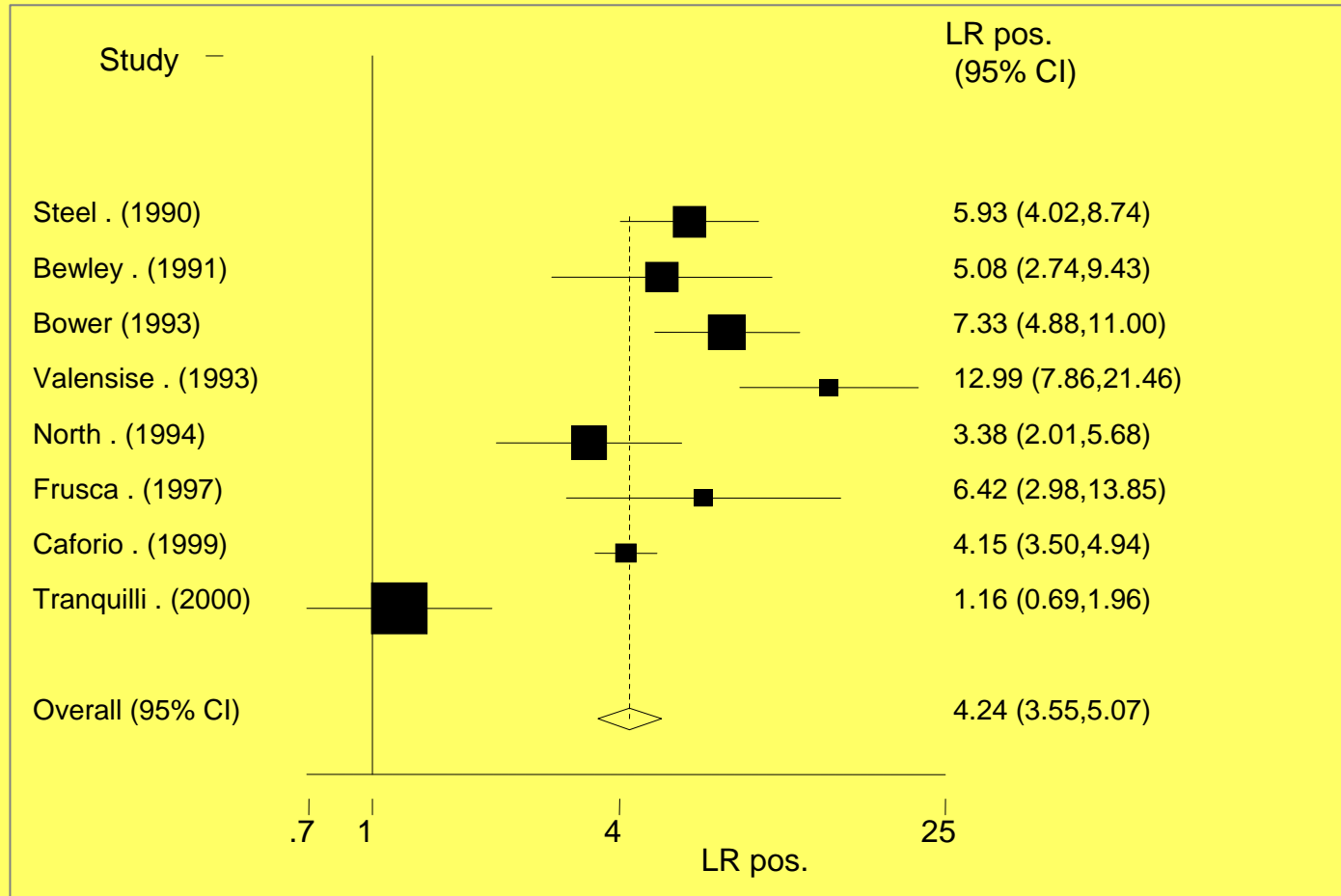
WHO systematic review of  
aetiology of pre-eclampsia :  
1) Homocysteine in pre- eclampsia  
(completed 2004)

# WHO systematic review of screening for preeclampsia , 2003

- Reports from electronic search 7191
- Detailed evaluation 214
- Included in data set 88

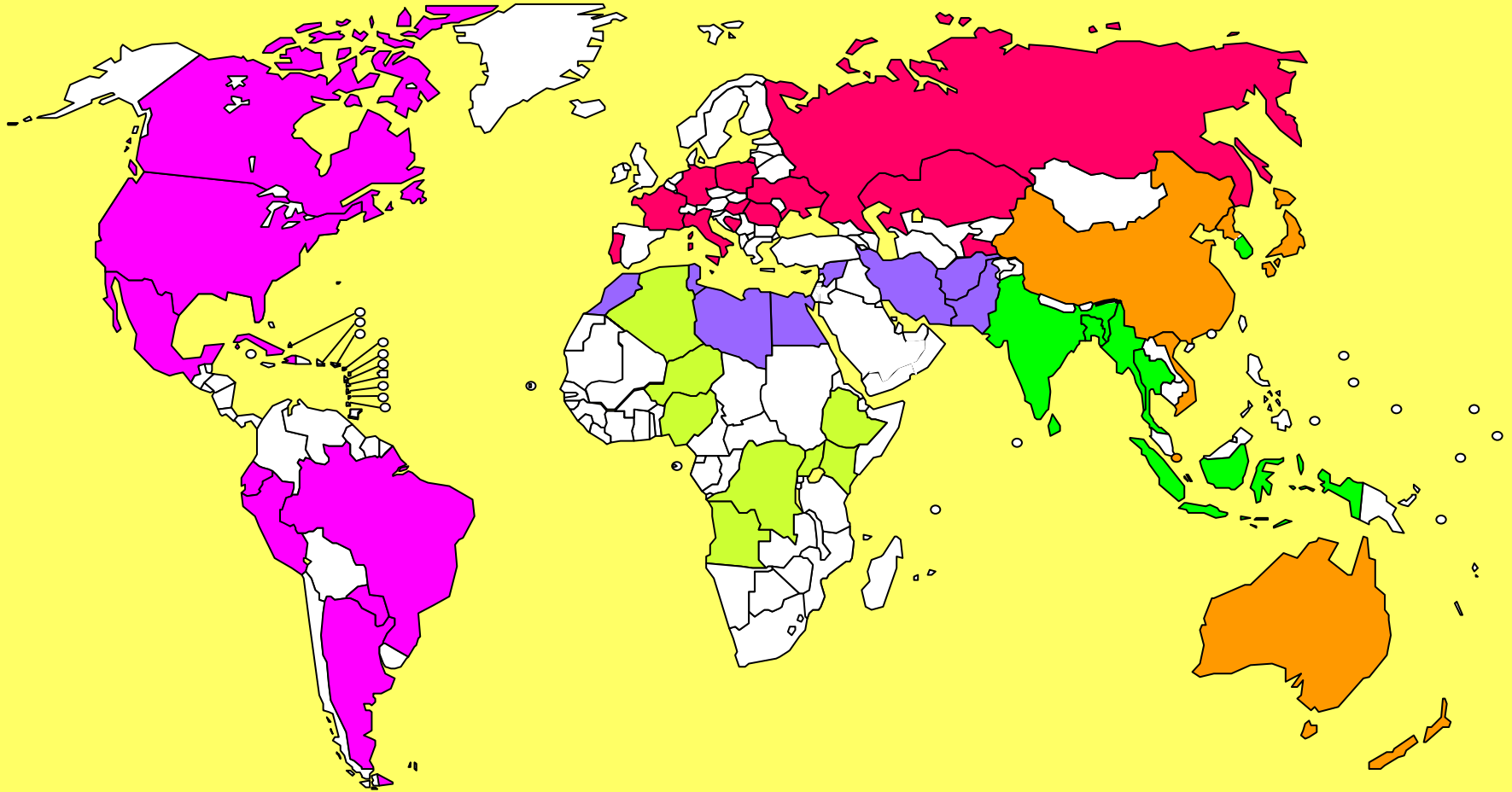
# WHO systematic review of screening for pre-eclampsia

## Abnormal waveform ratio in low-risk women





**We still need large, focused epidemiological studies :  
the WHO 500,000 women survey of mode of delivery**



# **GENERATING EVIDENCE**

# Knowledge Available For Pregnancy-specific Conditions

	ETIOLOGY	PRIMARY PREVENTION	TREATMENT	EMERGENCY
<b>Pre-eclampsia and Eclampsia</b>	No	No	some	Yes
<b>Preterm delivery</b>	No	No	No	Yes
<b>PROM</b>	No	No	No	Yes
<b>Miscarriage</b>	Some	No	No	Yes
<b>Postpartum haemorrhage</b>	some	~ 4% > 1,000 ml	Yes	Yes
<b>IUGR</b>	some	No	No	Yes
<b>Postpartum depression</b>	No	No	Yes ?	Yes
<b>Obstructed labour</b>	Yes ?	Yes ?	Yes	Yes
<b>Rh (-) Isoimmunization</b>	Yes	Yes	Yes	Yes

The molecular and genetic  
revolution should  
provide the basis for new  
preventive  
and therapeutic strategies.....

# Global Program to Conquer Preeclampsia / Eclampsia



From basic science to implementation



The Global Preeclampsia / Eclampsia Collaboration and  
Department of Reproductive Health and Research, World Health Organization  
2002

British Journal of Obstetrics and Gynaecology  
December 1998, Vol. 105, pp. 1244–1247

# **Randomised trials in maternal and perinatal medicine: global partnerships are the way forward**

# Recent Multicentre Trials and Follow-ups

	<i>CENTRES</i>	<i>PARTICIPANTS</i>	<i>STATUS</i>
<b>Antenatal care</b>	5	24,678	Published
<b>Prevention Postpartum Haemorrhage</b>	9	18,530	Published
<b>Treatment preeclampsia (Magpie Trial)</b>	28	10,141	Published
<b>Reduction of unnecessary caesarean section</b>	5	149,206	In press
<b>Evaluation of Reproductive Health Library</b>	2	76,053	Completed
<b>Primary prevention of preeclampsia (calcium)</b>	7	8400	Completed
<b>Primary prevention of preeclampsia (antioxidants)</b>	4	3,500	On going
<b>Secondary prevention of preeclampsia (treatment moderate hypertension)</b>	6	1,600	In preparation
<b>Treatment of postpartum haemorrhage</b>	4	1,000	In preparation
<b>Screening and treatment asymptomatic bacteriuria</b>	4	18,000	On going

# **First, Do the Trials Then, Do No Harm**

By David Brown

Sunday, August 4, 2002;  
Page B01, The Washington  
Post

O N L I N E



What are the research  
priorities?

# Estimated pre-eclampsia and eclampsia cases per year

	Developing countries (n=179)	Industrialised countries (n=44)
<b>Births/year*</b>	118 766 000	13 227 000
<b>Incidence of pre-eclampsia (range % )</b>	1.3 – 6.7	0.4 – 2.8
<b>Estimated N of pre-eclampsia /year</b>	1 543 958 – 7 957 322	52 908 – 370 356
<b>Incidence of eclampsia among women with pre-eclampsia** (%)</b>	2.3	0.8
<b>Estimated N of eclampsia /year</b>	35 511 – 183 018	423 – 2963

\* Source:World Population Prospects: 2000 Revision

\*\* Magpie Trial, 2002

# Obstetric morbidities in the South East Thames Region (48,865 deliveries)

- **Severe obstetric morbidity 1.2%**
- **Severe haemorrhage 0.8%**
- **Severe preeclampsia ,  
sepsis, uterine rupture 0.4%**

# Intrauterine growth retardation in developing countries, 2000

Indicator	Rate (%) <sup>(*)</sup>	number of newborns / year ( 2000) <sup>**</sup>
LBW <2500 g; all gestational age)	16.4 (5.8-28.3)	19,477,000
IUGR (<10 <sup>th</sup> percentile all gestational age)	23.8 (9.4-54.2)	28,266,000

\* Adapted from de Onis M, Blössner M, Villar J. EJCN; 1998

\*\* UN World Population Prospects; 1995-2000

# Population based Perinatal mortality according to birth weight percentile: Chile, all 262681 deliveries in 1999

<b>Gestational age (weeks)</b>	<b>&lt;p5</b>	<b>&lt;p10</b>	<b>p10-90</b>	<b>Ratio &lt;p10 / p10-90</b>
22-25	1000	1000	679	1.5
26-29	616	519	288	1.8
30-33	372	357	116	3.1
34-36	168	128	30	4.3
37-40	19	12	2	6.0
41-43	14	10	2	5.0
<b>Total</b>	<b>110</b>	<b>62</b>	<b>3</b>	<b>20.7</b>

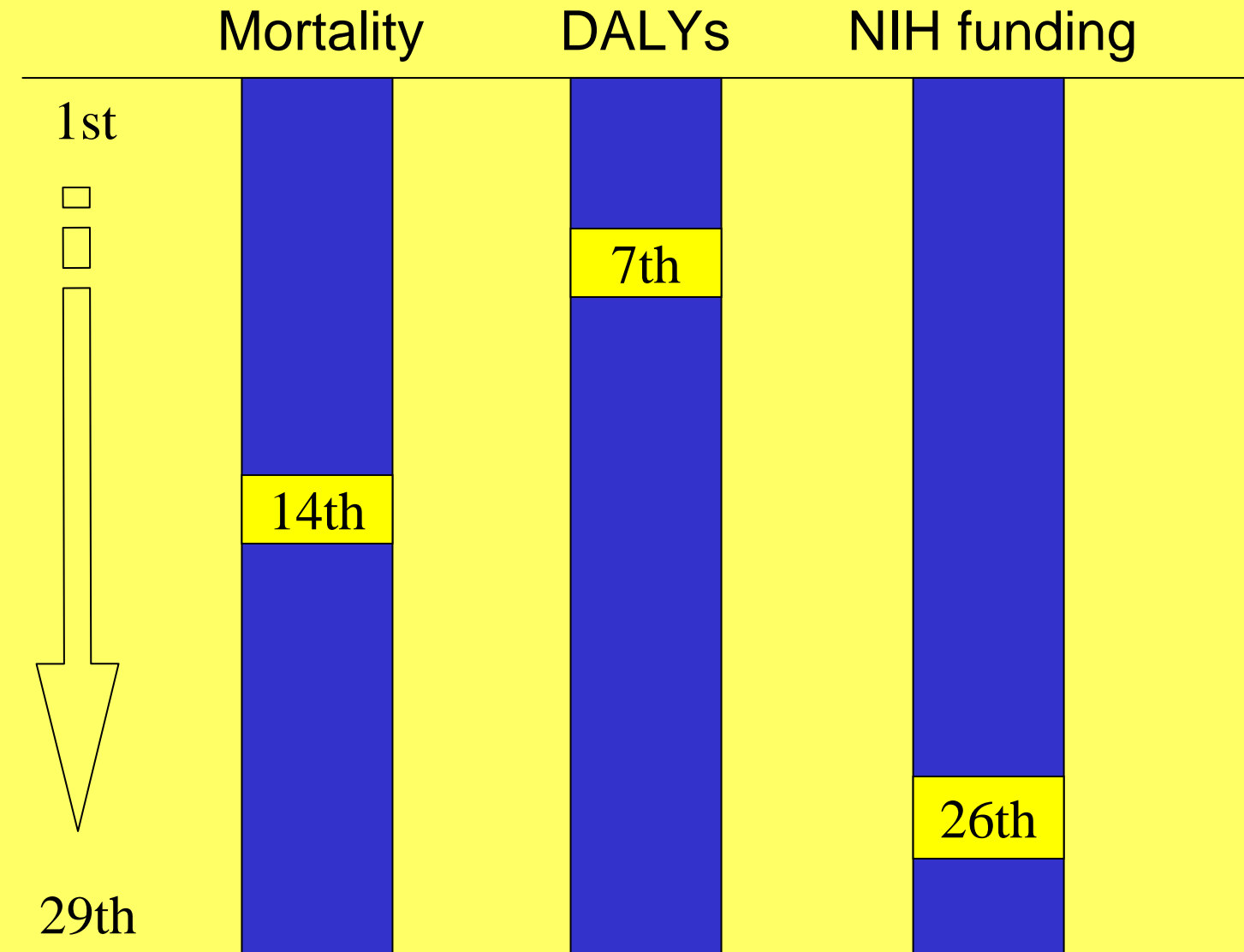
Gonzalez R. personal communication (2003)

# Pregnancy and Childbirth Trials in the *Cochrane Library*, 2000 *according to primary outcome*

	N = 9014	%
P.P.Haemorrhage	45	0.5
Pre-eclampsia	156	1.7
IUGR/SGA	111	1.2



# Ranking of maternal and perinatal conditions among 29 medical conditions



Gross CP, et al. NEJM, 1999;340:1881-7

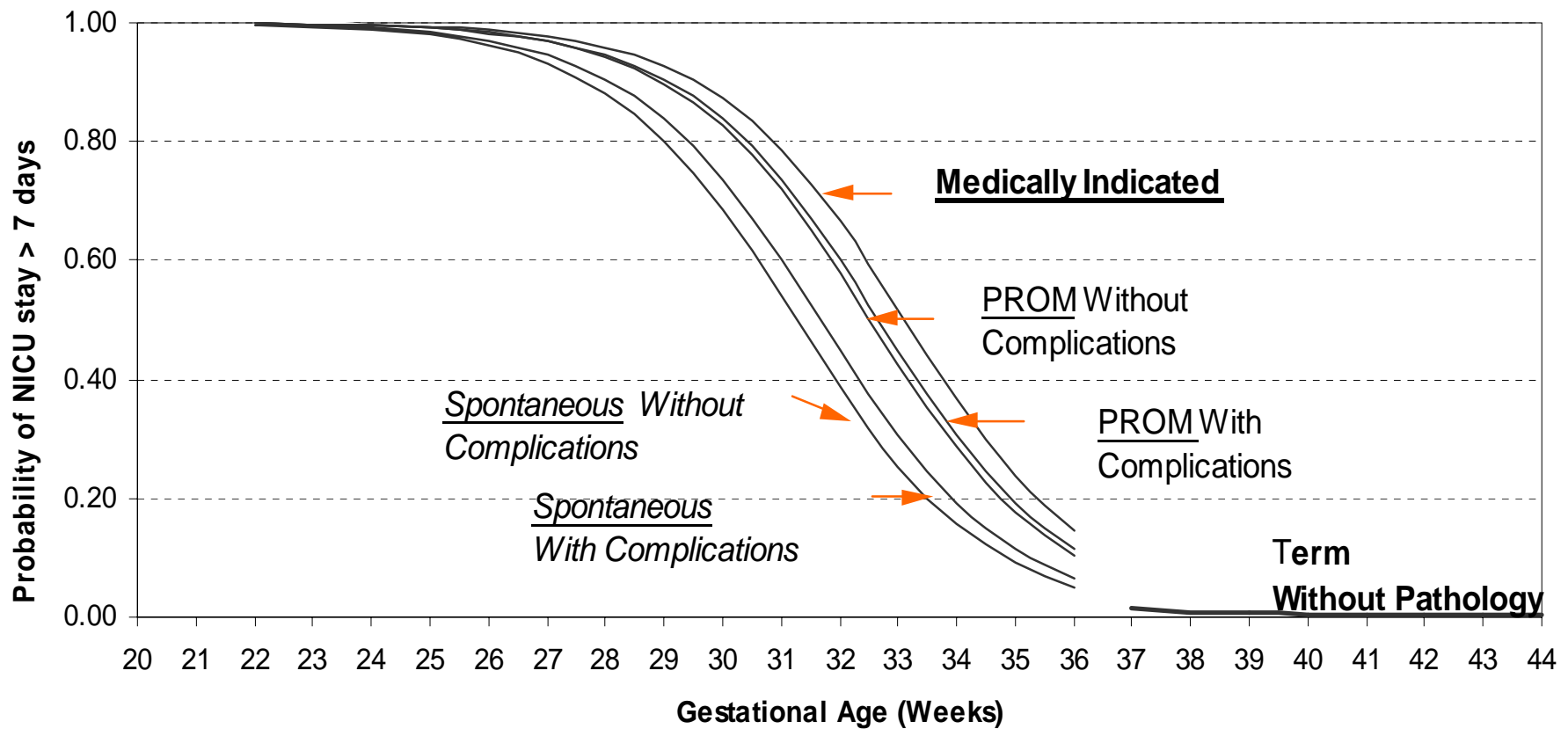
# Emerging topics

- After the evidences , ...the quality of care
- Personal choices : cloning
- Demographic changes : a new baby boom?
- Migrations and high risk pregnancies
- Caesarean sections for all deliveries ?

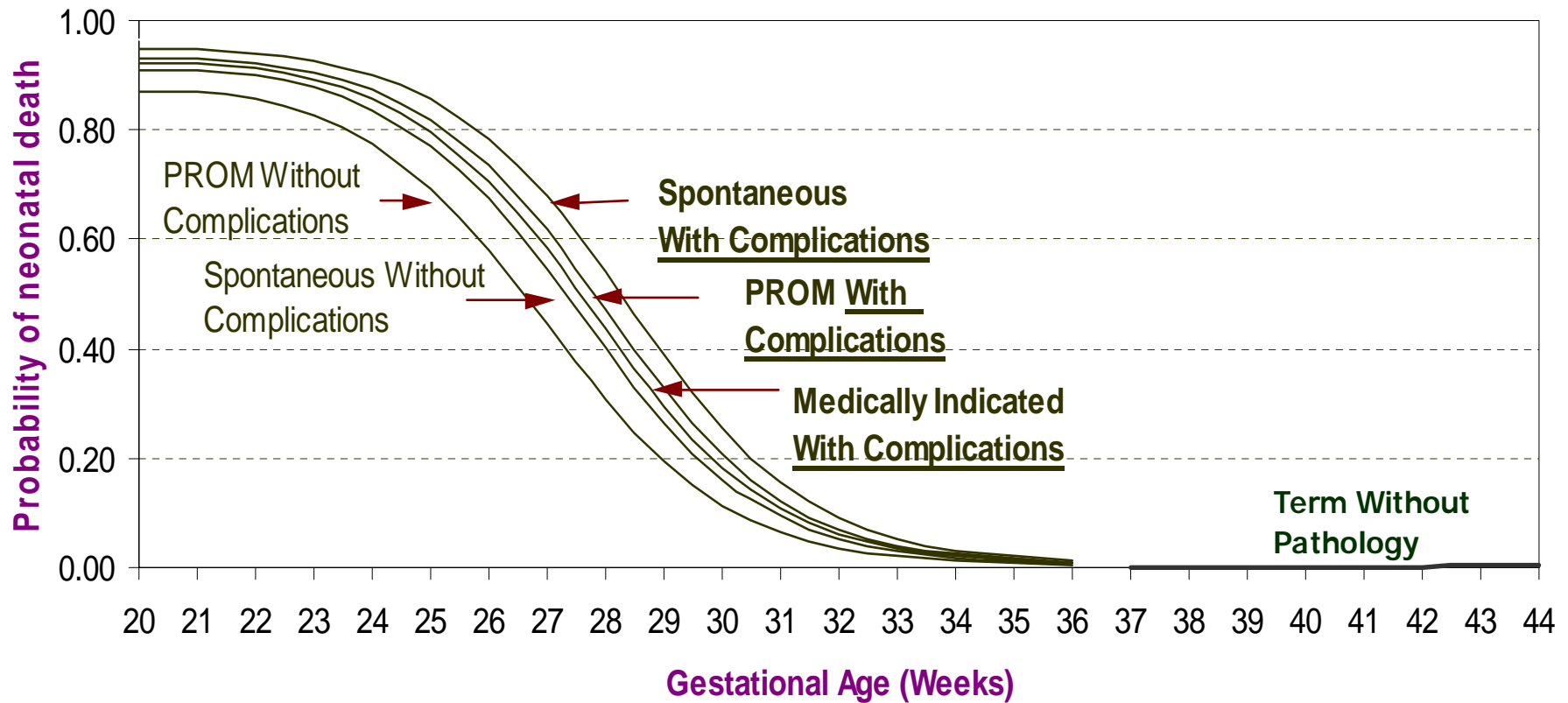


What are the most  
appropriate outcomes ?

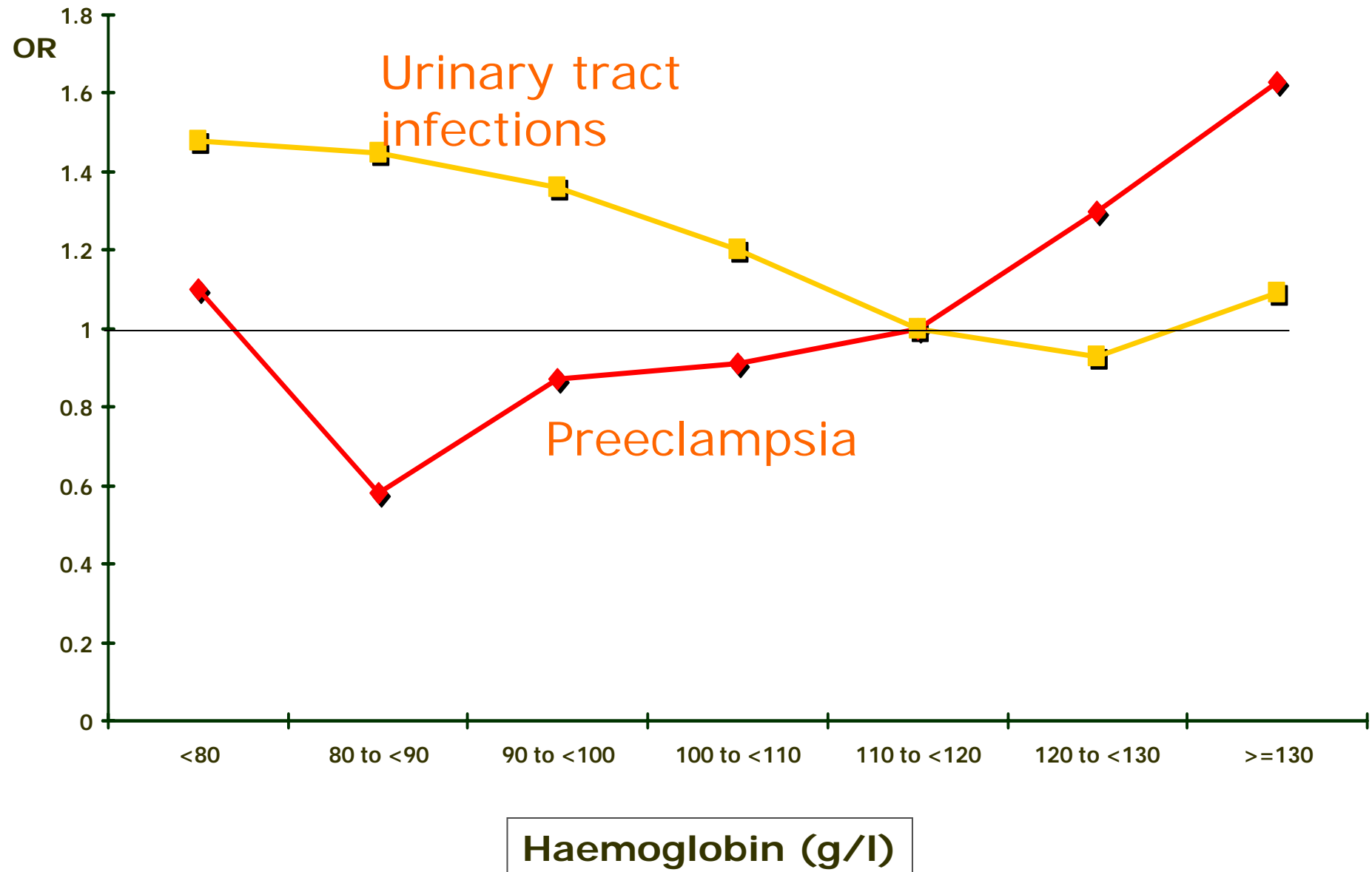
# Probability of NICU stay >7 days by preterm delivery subgroups



# Probability of neonatal death by preterm delivery subgroups



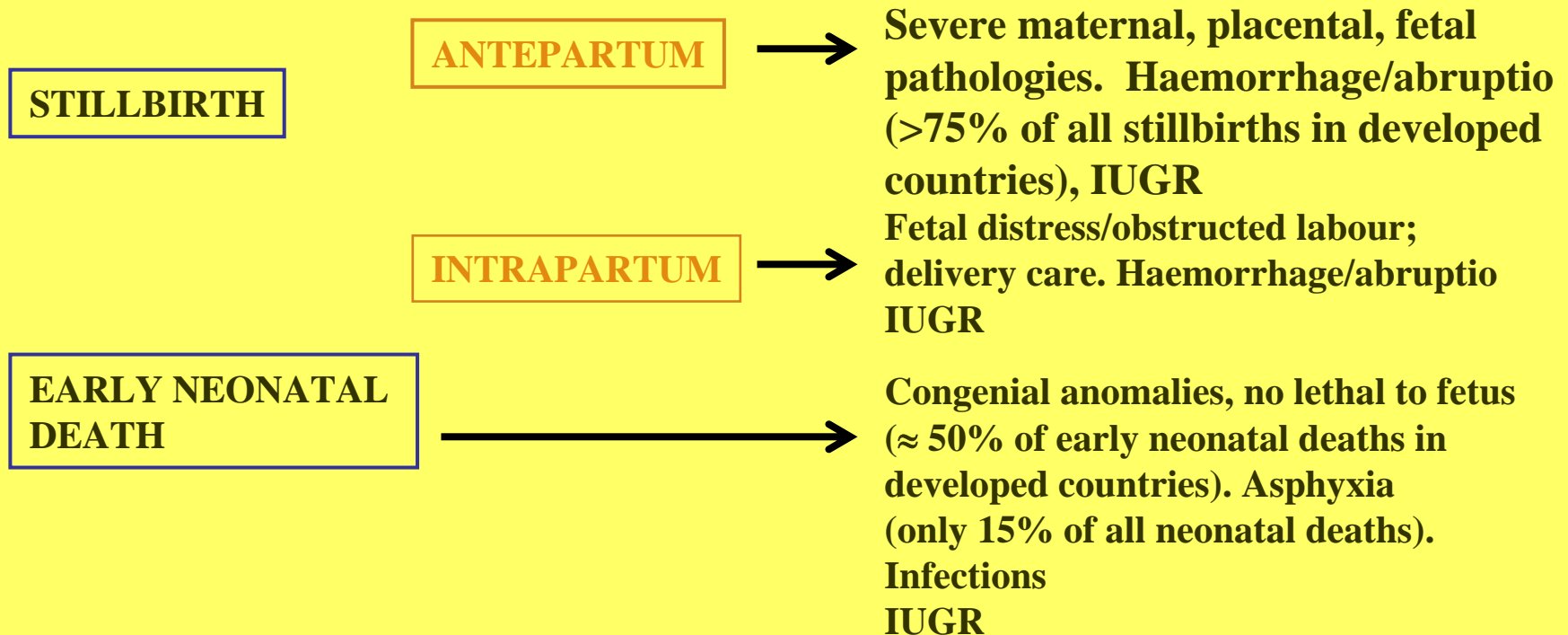
# Pregnancy outcomes according to Hb values



# Aetiological differences in perinatal mortality

## Outcome

## Aetiological factors



# **Major pregnancy and perinatal entities are heterogeneous**

- **Preeclampsia /eclampsia**
  - **IUGR**
  - **Preterm delivery**
  - **PROM**
- 
- **Stillbirth**
  - **Perinatal mortality**
  - **Maternal Mortality**

# **Identifying better continuous medical education and research utilisation strategies**



Cartoon published in Latin America