



**VIETNAM
2010**

**PATHOPHYSIOLOGY OF
DIABETES IN PREGNANCY**

G.C. Di Renzo, MD, PhD

University of Perugia, Perugia, Italy

Gestational diabetes

- **Defined as any degree of glucose intolerance of varying severity with onset or first recognition during pregnancy**
- **With obesity, it is the most common metabolic abnormality during pregnancy**
- **7% of all pregnancies, range of prevalence 1-14%**

SHOULD WE EXPECT AN INCREASE IN DIABETIC PREGNANTS?

INCREASE OF BMI & OBESITY
INCREASE IN CHILDREN OBESITY
INCREASED MEAN AGE AT 1°
PREGNANCY

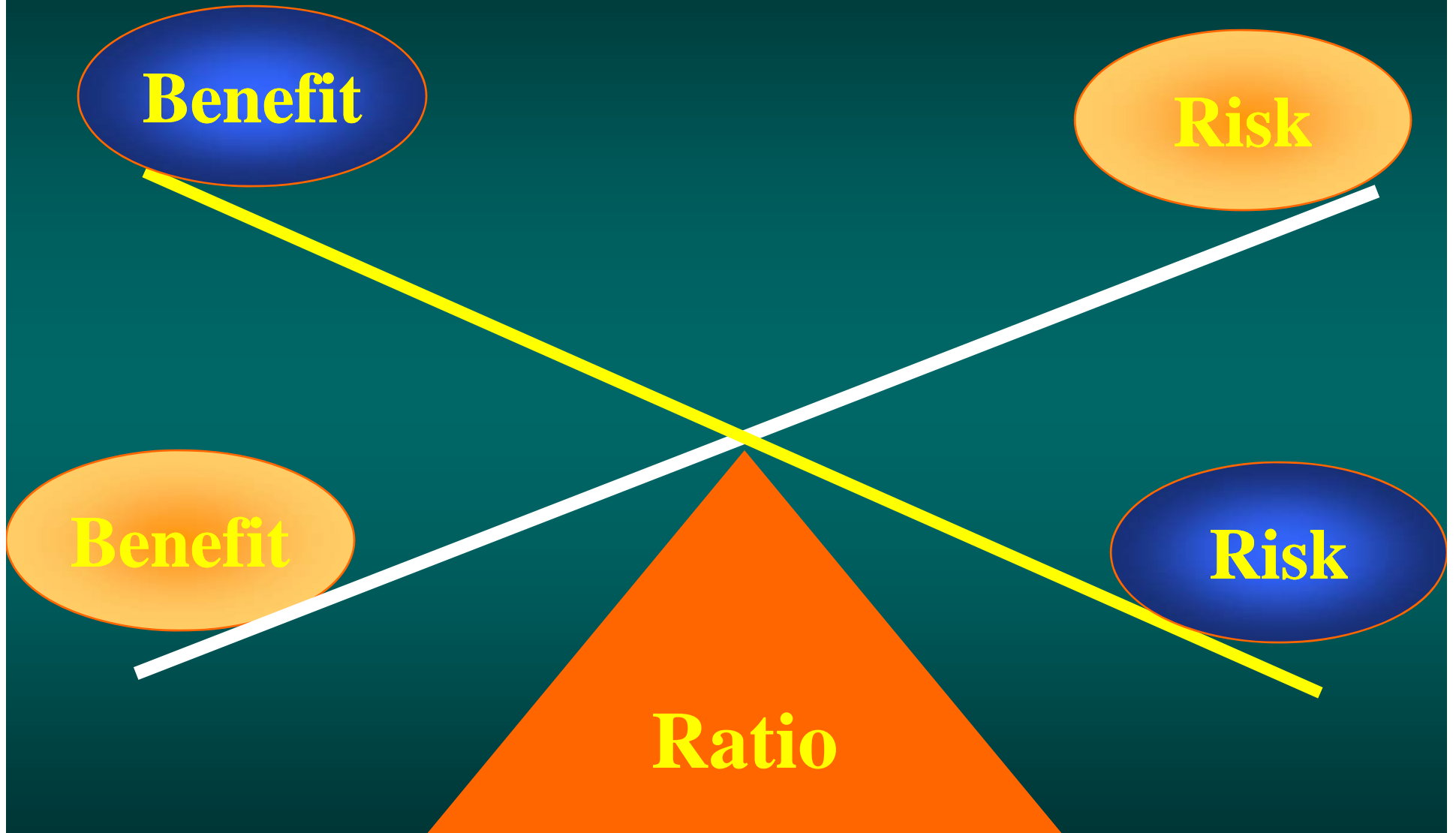
YES

**ELECTIVE DELIVERY IN
DIABETIC PREGNANCY ?**

TIMING OF DELIVERY OF THE DIABETIC PATIENT IS A BALANCING ACT BETWEEN:

- **POTENTIAL INTRAUTERINE DEATH**
- **SHOULDER DYSTOCIA**
- **CESAREAN SECTION and**
- **THE CONSEQUENCES OF PREMATURE DELIVERY.**

TO DELIVER OR NOT TO DELIVER??



Cesarean Section – Adverse Outcome

Immediate

Risk of anesthesia

Blood loss

Bowel and bladder injury

Amniotic or air embolism

Scalp damage to baby 1-2%

Post-op Risks

Infection

Bleeding

Neonatal RDS/wet lungs

Relative Risk for Rehospitalization C/S vs VD

Washington state 54,074 CS, 142,765 SVD

Lndon-Rochelle et al JAMA 2000

	Incidence / 1000 high risk women		
	SVD	CS	RR
Uterine infection	2.9	5.2	2.0
Wound infection	0.1	3.9	30.2
PPH	2.4	2.9	1.2
Genitourinary	1.3	1.7	1.5
Thromboembolism	0.3	0.9	2.5
Total	10.0	17.0	1.8

Stillbirth

Association Between Diabetes & SB's US, '95-'97

Mondestin, Am J Ob Gyn 2002;187:922-6

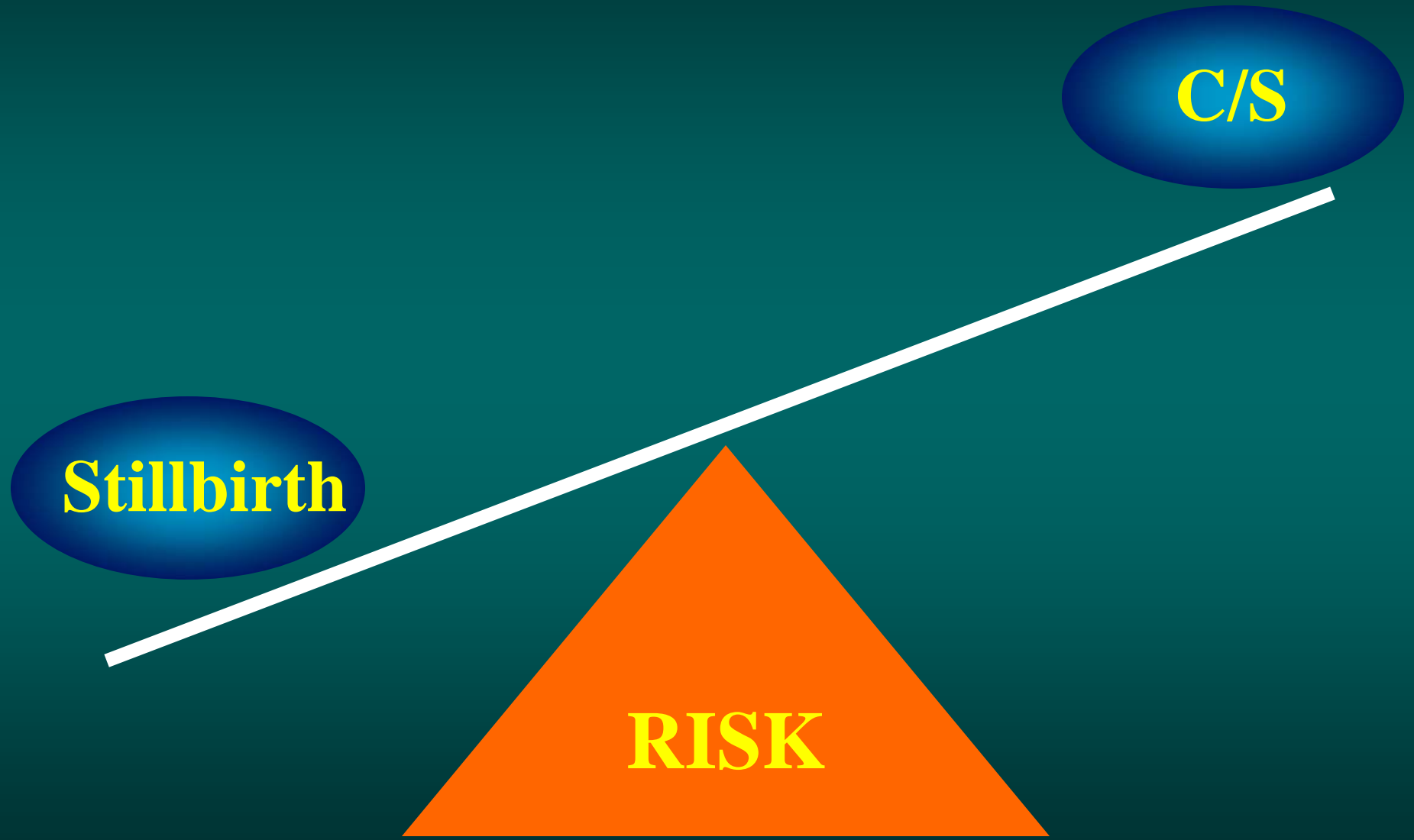
<i>Birth weight (g)</i>	<i>Fetal death rate</i>		<i>RR</i>	<i>(95% CI)</i>
	<i>Non-diabetic</i>	<i>Diabetic</i>		
	<i>N=10,733,983</i>	<i>N=271,691</i>		
2,250-2,499	7.2	13.6	1.8	(1.4-2.2)
2,500-2,749	3.3	8.3	2.3	(1.8-2.8)
2,750-2,999	1.8	3.4	1.6	(1.3-2.6)
3,000-3,249	1.1	2.6	1.7	(1.4-2.2)
3,250-3,499	0.7	2.4	2.9	(2.4-3.5)
3,500-3,749	0.6	2.4	3.2	(2.6-3.6)
3,750-3999	0.6	2.3	3.2	(2.5-4.1)

Association Between Diabetes & SB's US, '95-'97

Mondestin, Am J Ob Gyn 2002;187:922-6

<i>Birth weight (g)</i>	<i>Fetal death rate</i>		<i>RR</i>	<i>(95% CI)</i>
	<i>Non-diabetic</i>	<i>Diabetic</i>		
	<i>N=10,733,983</i>	<i>N=271,691</i>		
4,000-4,249	0.6	2.9	3.6	(2.7-5.1)
4,250-4,499	0.7	3.7	3.7	(2.7-5.1)
4,500-4,749	0.9	7.1	6.4	(4.4-9.3)
4,750-4,999	2.0	8.6	3.1	(1.9-5.1)
5,000-5,249	3.7	15.9	3.4	(1.9-6.1)
5,250-5,499	5.2	21.6	3.6	(1.5-8.6)
>5,500	18.3	38.9	1.8	(1.7-1.9)

TO DELIVER OR NOT TO DELIVER?

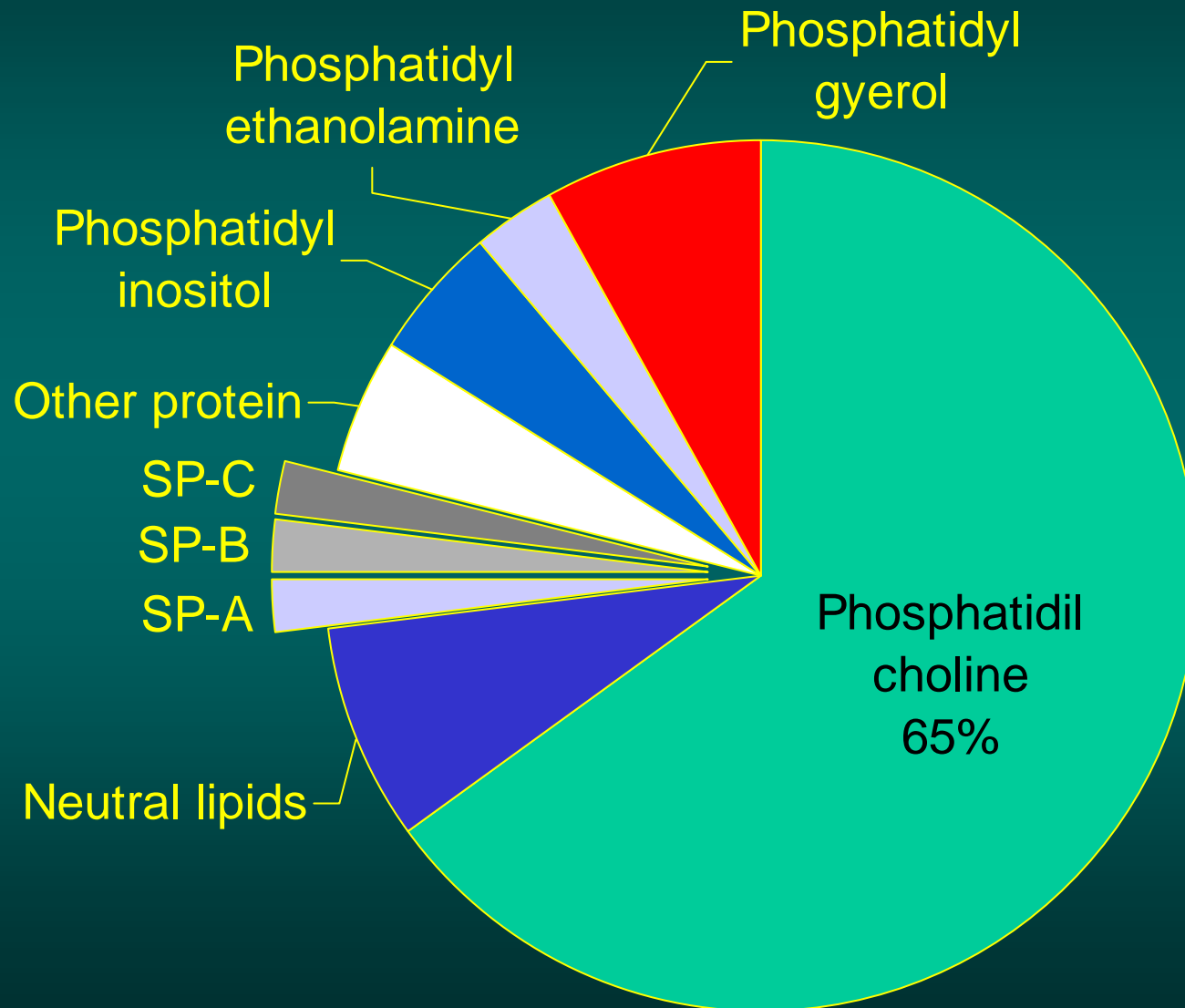


Lung Maturation

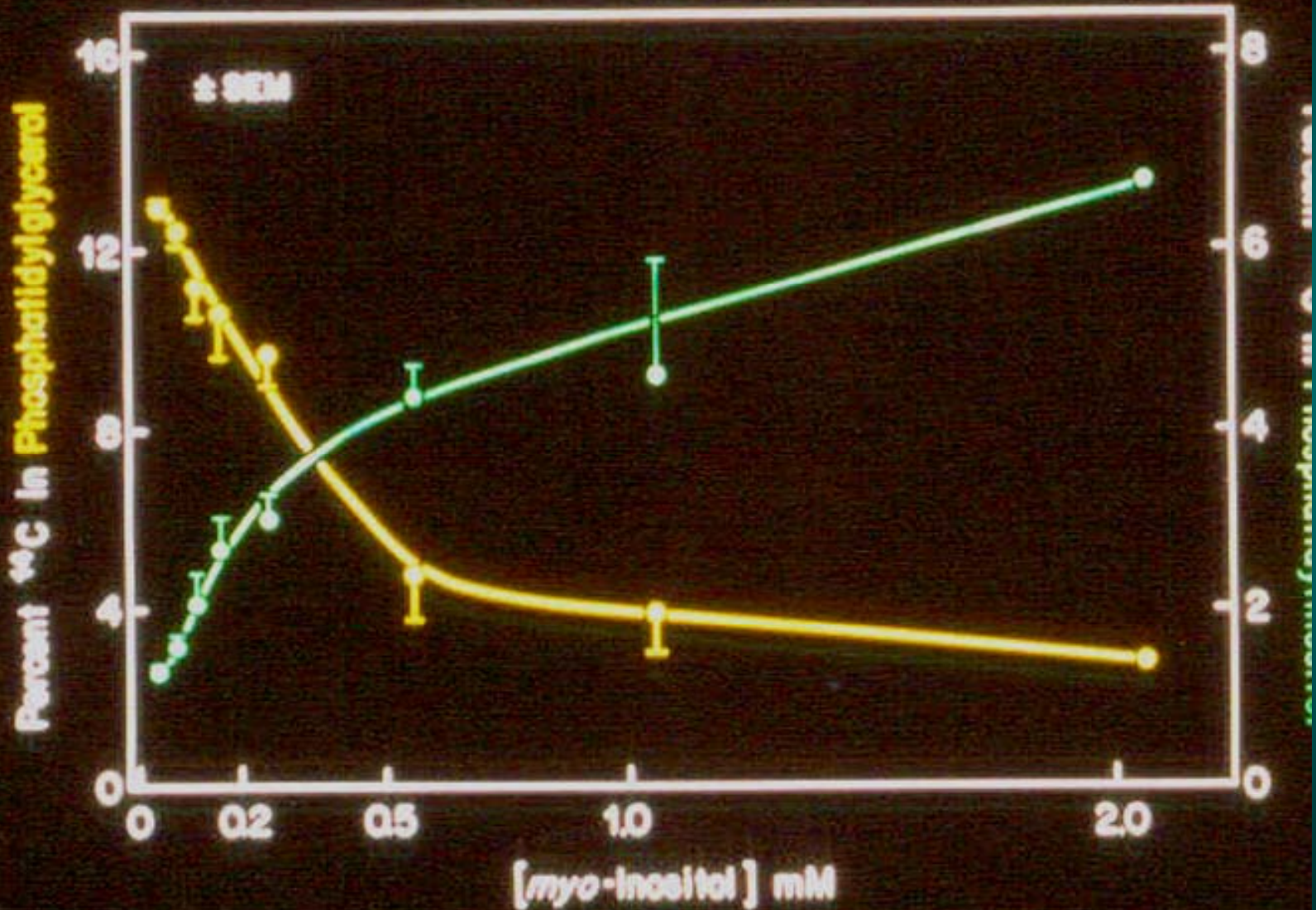
Diabetic pregnancy and fetal lung maturity

- Nondiabetic fetus achieves pulmonary maturity at a mean gestational age of 34-35 weeks
- By 37 weeks, more than 99% of normal newborns have mature lung profiles as assessed by phospholipid assays
- In a diabetic pregnancy, however, it is unwise to assume that the risk of respiratory distress has passed until after 38,5 gestational week have been completed

Composition of surfactant

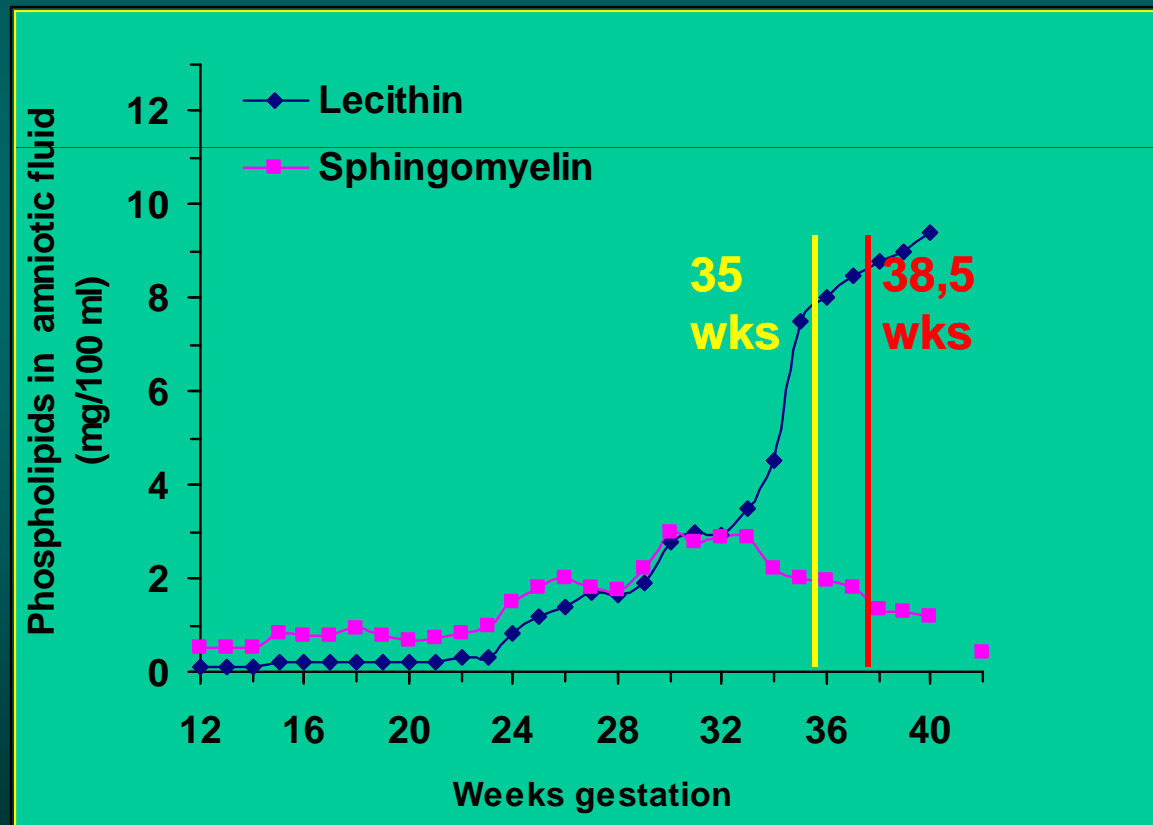


EFFECT OF MYO-INOSITOL ON INCORPORATION OF [¹⁴C] GLYCEROL INTO PHOSPHATIDYLGLYCEROL AND PHOSPHATIDYLINOSITOL



Changes in the concentrations of lecithin and sphingomyelin in the amniotic fluid.

The achieved pulmonary maturity in nondiabetic and diabetic pregnancy



LUNG IMMATURITY: POOR vs. WELL CONTROL

Piper, AJOG 1993
Langer, JMF 2002

	<u>R.R.</u>	<u>95% C.I.</u>
< 34 WEEKS 107	1.27	0.02 -
34-36.9 WEEKS 3.70	1.25	0.43 -
37-37.9 WEEKS 19.3	4.33	1.02 -
38-38.9 WEEKS 10.9	2.50	0.61 -
> 39.9 WEEKS	1.00	0.00 -

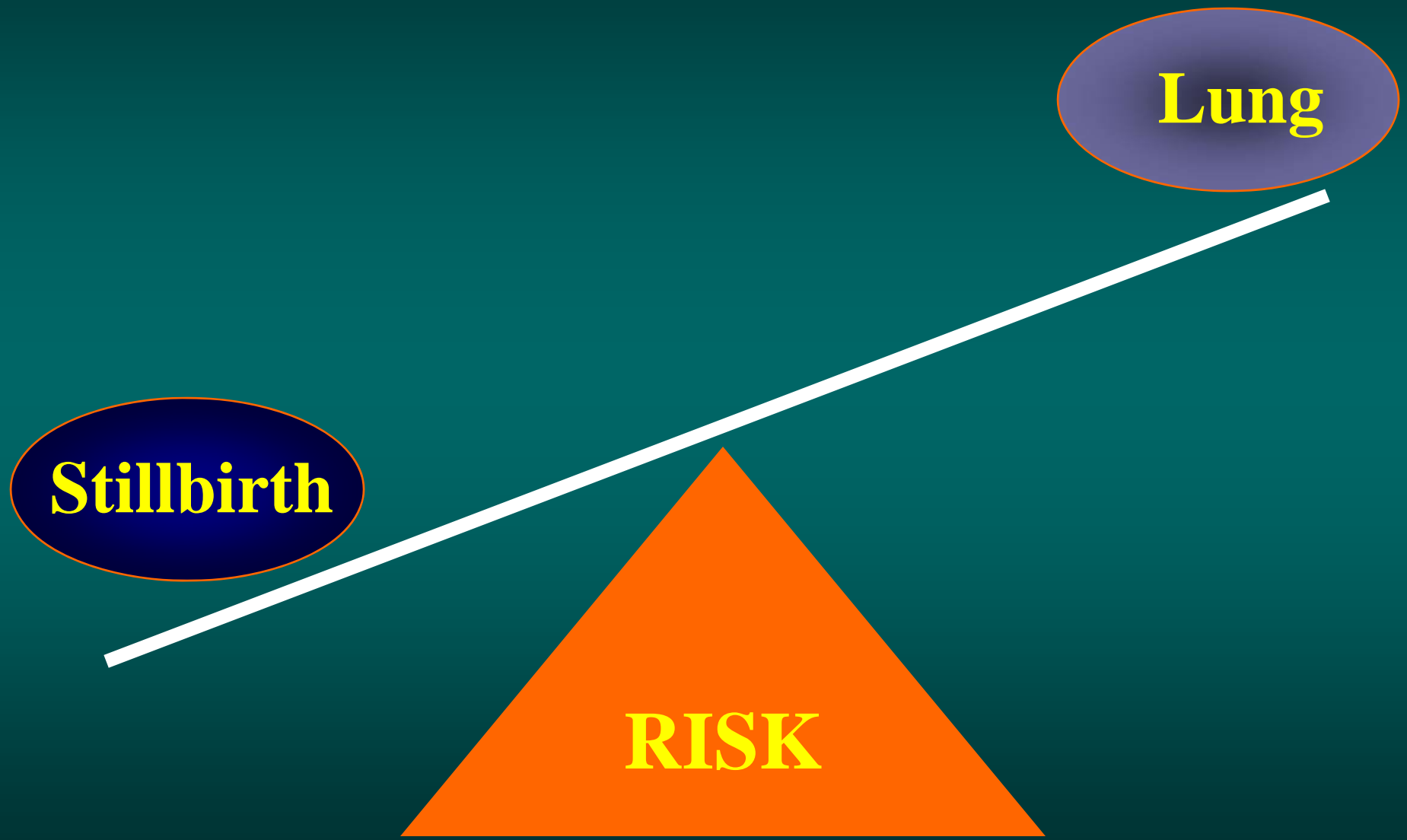
LUNG IMMATURITY: POOR CONTROL vs. NON-DIABETIC

	<u>R.R.</u>	<u>95% C.I.</u>
< 34 WEEKS 36.9	7.37	1.0 –
34–36.9 WEEKS 6.9	3.64	1.9 –
37–37.9 WEEKS 10.4	4.12	1.7 –
38–38.9 WEEKS 13.6	4.26	1.2 –
> 38.9 WEEKS	4.04	1.9 –

LUNG IMMATURITY: WELL CONTROL vs. NON-DIABETIC

	<u>R.R.</u>	<u>95% C.I.</u>
< 34 WEEKS 31.1	4.69	0.61 –
34–36.9 WEEKS 5.76	2.33	0.94 –
37–37.9 WEEKS 16.6	3.81	0.94 –
38–38.9 WEEKS 9.10	1.43	0.23 –
> 39.9 WEEKS 0.45	0.45	0.10 –

TO DELIVER OR NOT TO DELIVER?



Macrosomia





What is in the box ?



1. Unfortunately, the prenatal diagnosis of fetal macrosomia remains **imprecise**.

ACOG, 2000



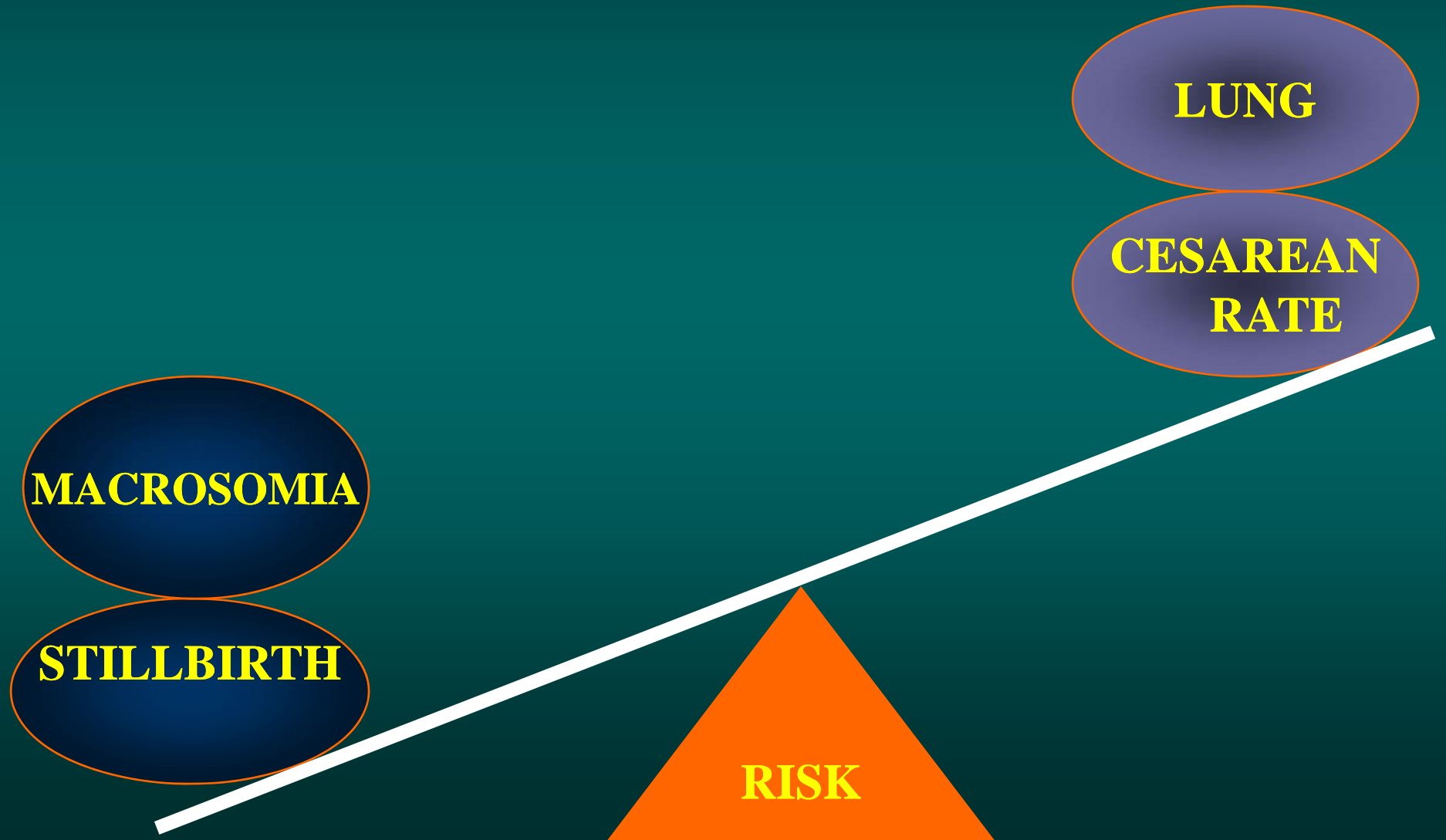
What is in the box ?



2. Although ultrasonography enables the direct measurement of various fetal body parts, its accuracy in predicting macrosomia has been **unreliable.**

ACOG, 2000

TO DELIVER OR NOT TO DELIVER?



Shoulder Dystocia

Prognosis for Brachial Plexus Injury

Of all cases of shoulder dystocia:

15% suffer brachial plexus injury

20% of these are permanent

Therefore,

**3% shoulder dystocia have
permanent injury**

In the USA - 54,000 infants >4500 g

19% SD in >4500 g = 10,260 infants

2/3 BPI = 6840 infants

80% full recovery = 5472 infants

20% permanent BPI = 1368 infants

The price:

**Estimates of unnecessary CSs
to prevent shoulder dystocia:**

50:1 – 1000:1

When there is uncertainty...

2. Elective CS

- Even more unnecessary CSs would be needed to prevent a **single case of BPI**

The price:

**Estimates of unnecessary CSs
to prevent brachial plexus
injury:**

100:1 – 3000:1

TO DELIVER OR NOT TO DELIVER?

LUNGS

US ERROR

C/S

STILLBIRTH

MACROSOMIA

SHOULDER
DYSTOCIA

RISK

OPTIMAL MANAGEMENT

What is critical in taking care of pregnant affected by diabetes?

GDM

...a new disease in a particular lifetime



Pregestational diabetes

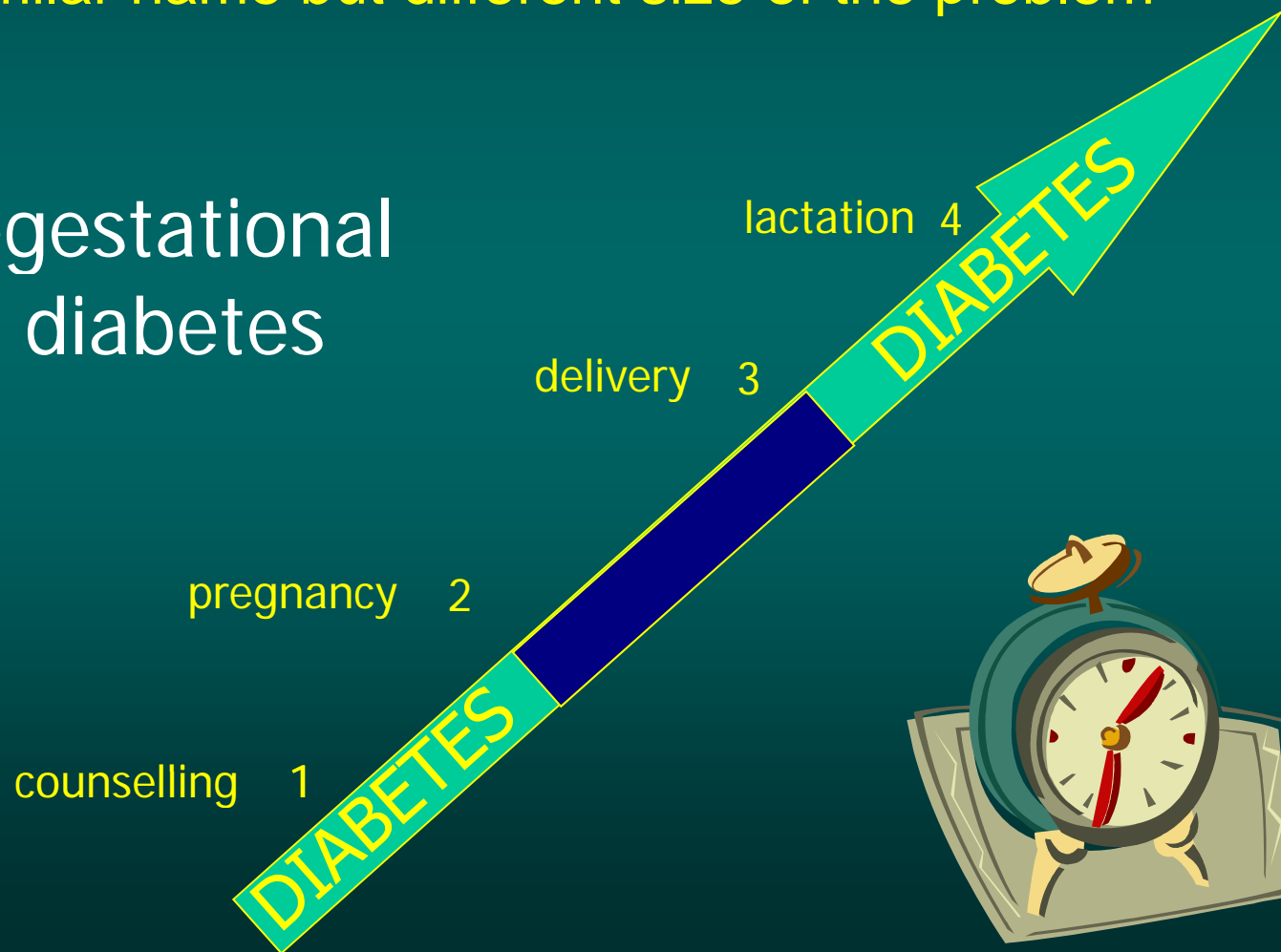
...to consider the impact of diabetes on foetus



What is critical in taking care of pregnant affected by diabetes?

.....similar name but different size of the problem

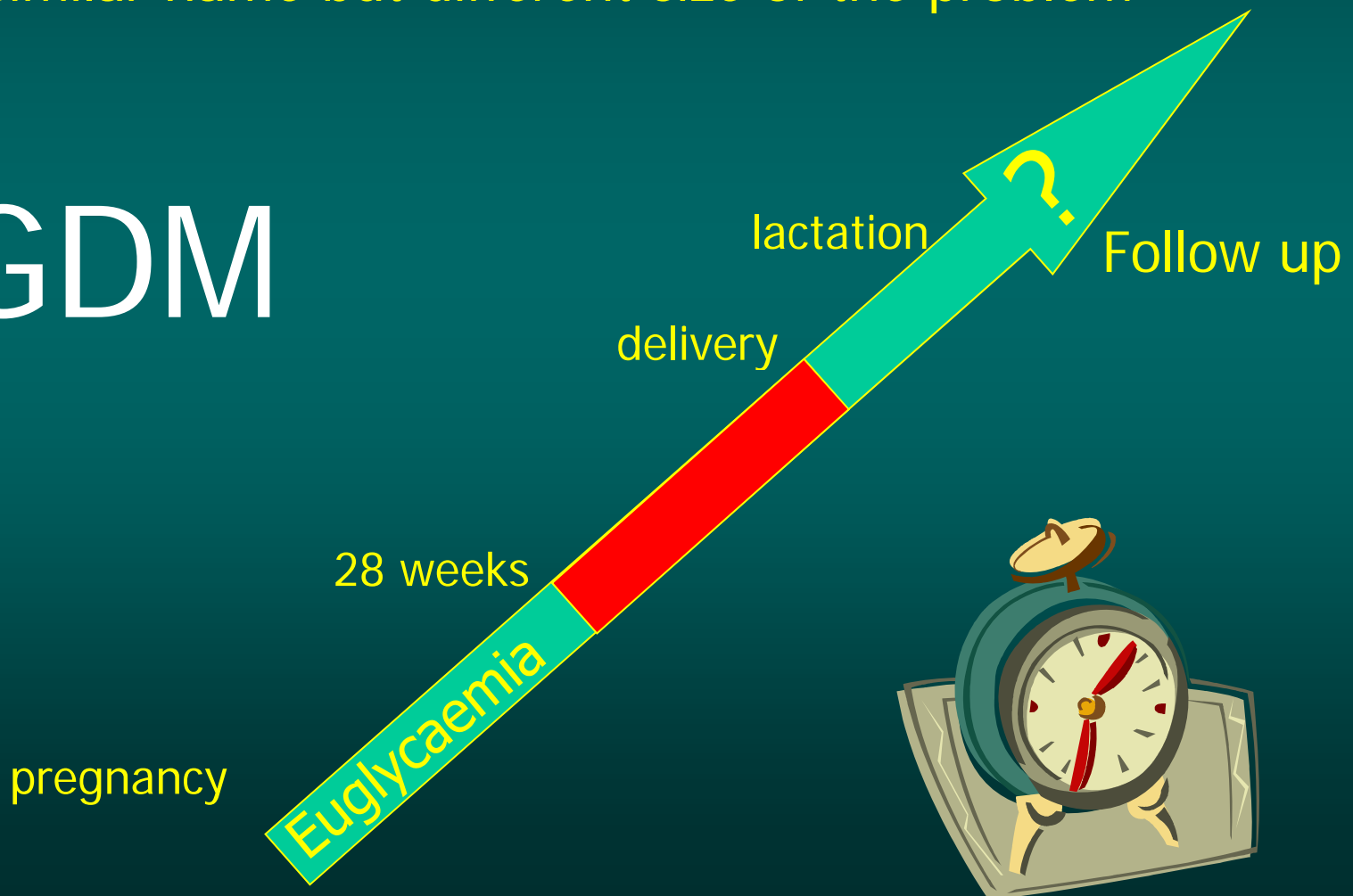
Pregestational diabetes



What is critical in taking care of pregnant affected by diabetes?

.....similar name but different size of the problem

GDM



What is critical in taking care of pregnant affected by diabetes?

GDM:

1. Few weeks for diagnosis and treatment
2. The psychologic impact with the disease
3. The actors involved in the diagnosis are the same as for pregestational diabetes?

?

Diabetologist

Obstetrician

Gynecologist

Midwives

Specialized Nurse

Dietitian

?

GDM: Primary care

- Information;
- To evaluate the risk factors;
- To promote the right behaviour (diet, physical activity, etc);
- To act as a filter for the secondary care (Diabetology Center, Perinatal Care).



Right information about planning of the pregnancy in obese and high risk women

Multidisciplinary TEAM

Diabetologist General Pract.

Gynecologist
Obstetrician



Metitian

Neonatologist Specialist
Nurse

Team work: Our experience

	Overall (167)	Obese (50)	Non Obese (117)
Pregestational BMI	27,6±6,6	34,9±4,6	23,5±2,8
GA at diagnosis	24,7±7,9	21.5±9.0	26.7±6.2

Team work: Our experience

Maternal – Obstetric Outcomes	Overall (167)	Obese (50)	Non Obese (117)
Caucasian (%)	54	31	66
Ponderal increments at delivery	10,8±5,3	7.2±5.6	12.6±4.2
Insulin therapy N (%)	75	83	72
Gestational Hypertension (%)	12,5	27	5
GA at delivery	38±1.9	37.4±2.3	38.3±1.7
Caesarean Section (%)	56	66	51

Team work: Our experience

Neonatal Outcomes	Overall (167)	Obese (50)	Non Obese (117)
Neonatal Transitory Tachipnea TTN (%)	7%	7%	7%
NICU admission (RDS)	2	2	0
Hypoglycemia (<30 mg%) (1 ^o h)(%)	7	5 (10)	2(1,7)
Ponderal Index	2.6\pm0.3	2.59\pm0.3	2.65\pm0.3
Hospital stay	4.3\pm2.9	5.2\pm4.2	4\pm2



Fetal or Maternal perspective?

Diabetes in pregnancy has evolved as a full-fledged subspecialty with integral components such as pre-existing diabetes, gestational diabetes, and metabolic syndrome in pregnancy and sub-classifications within each major category to address the growing epidemic proportions of women whose pregnancy is compromised by diabetes.

O. Langer 2005

CONCLUSIONS



PREGNANCY: stress test

metabolic syndrome

METABOLIC MONITORING

OXIDATIVE STRESS

TARGETS in preGDM: malformations

abortion, stillbirth

TARGETS in GDM: growth & maturity

TEAMWORK

PERICONCEPTIONAL COUNSELING

Textbook of

Diabetes and Pregnancy

Second Edition

Edited by

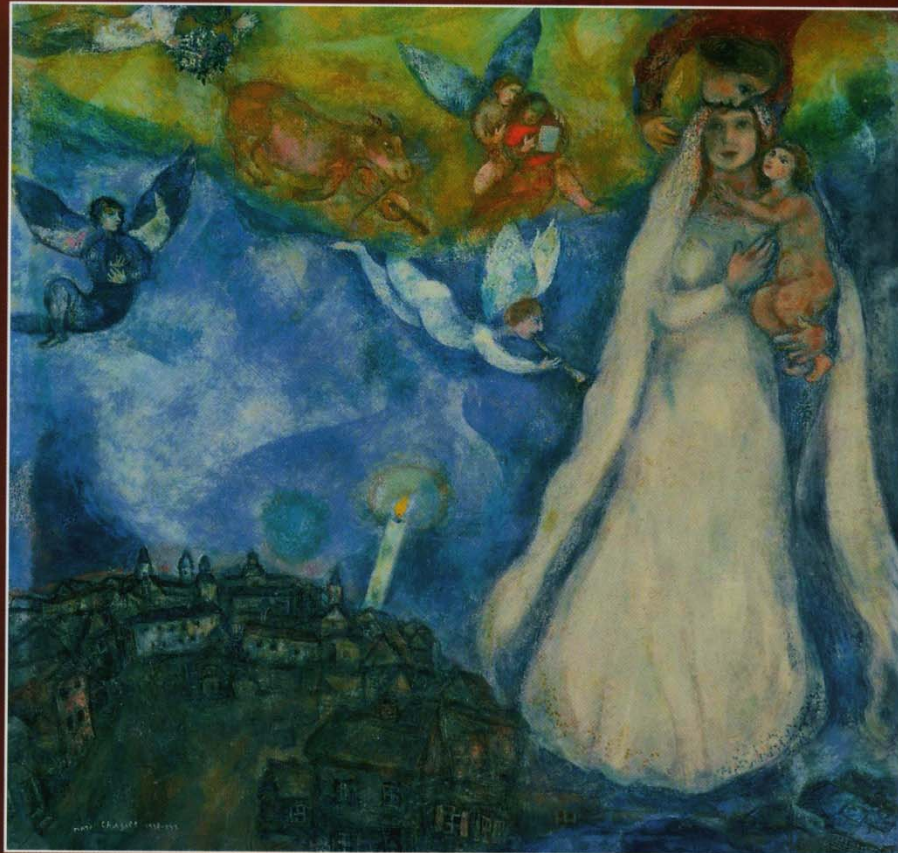
Moshe Hod

Lois Jovanovic

Gian Carlo Di Renzo

Alberto De Leiva

Oded Langer



informa
healthcare

Discovery consists of seeing what everyone has seen and thinking what nobody has thought.

Albert von Szent Gyorg



**GRAZIE
THANK YOU!**