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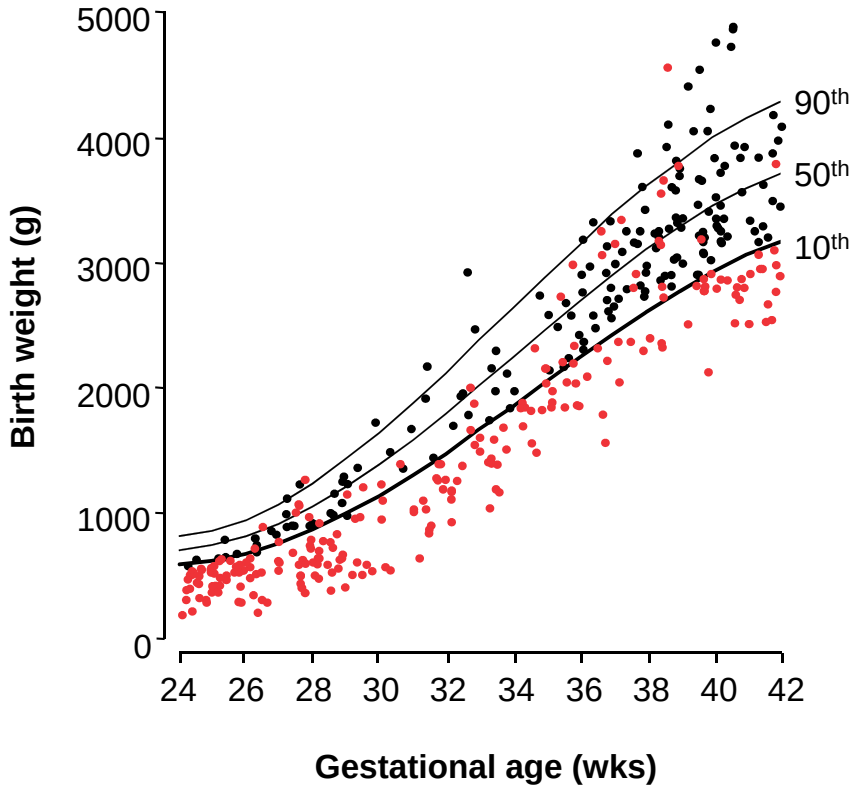
Prediction of stillbirth



Stillbirth

Impaired placentation
- **Small for gestation**
- **Preeclampsia**
- **Abruption**

Unexplained

The Fetal Medicine Foundation

Stillbirth

Definitions and questions

Frida Kahlo, 1932

Proportion of all stillbirths:

- Term vs preterm
- Antepartum vs intrapartum
- SGA vs AGA

Prediction / prevention of impaired placentation:

- PE and SGA
- Maternal factors & SFH
- Universal vs customised charts
- Strategy for identification

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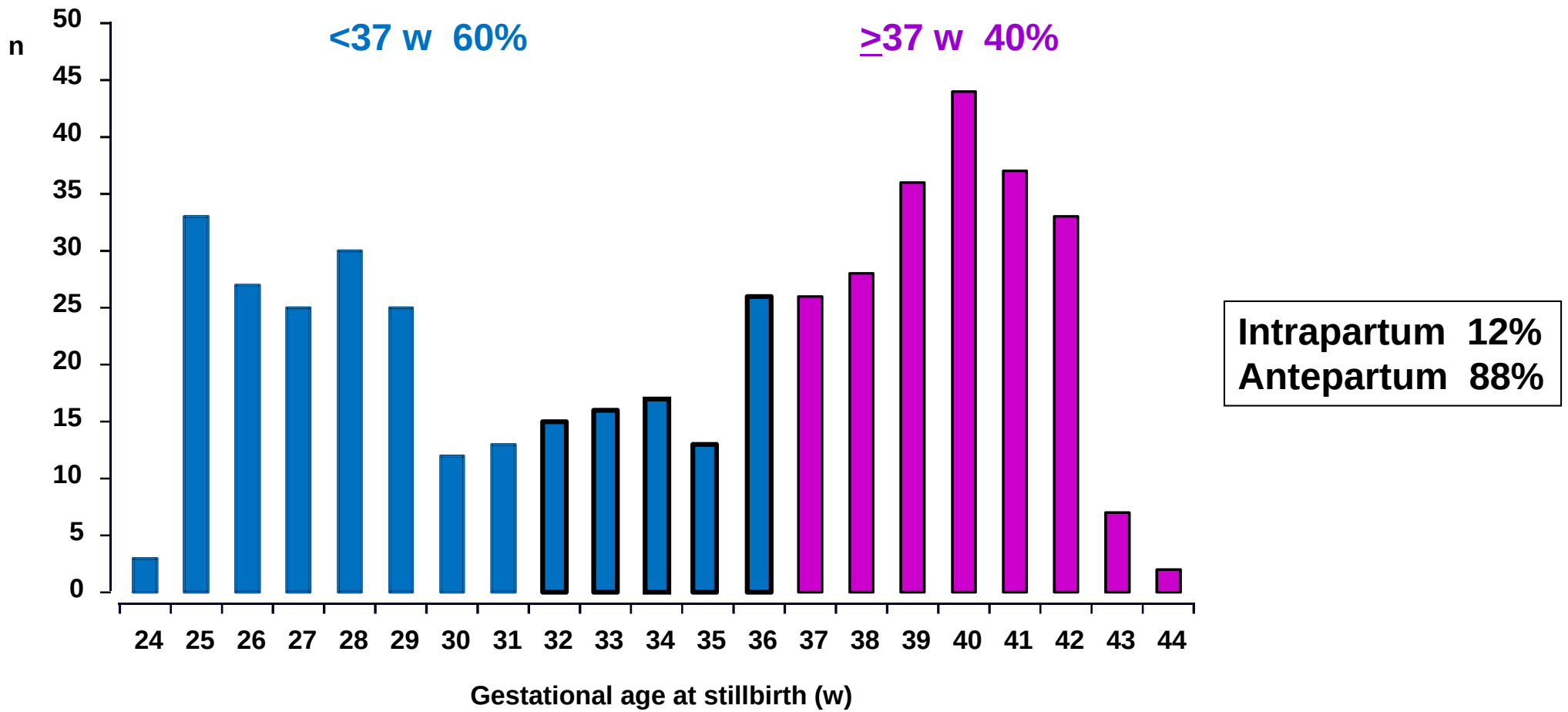
Stillbirth

Preterm vs term



Stillbirth KCH, MMH, UCLH (2006-2014): 468 / 121,774 (3.8 / 1,000 births)

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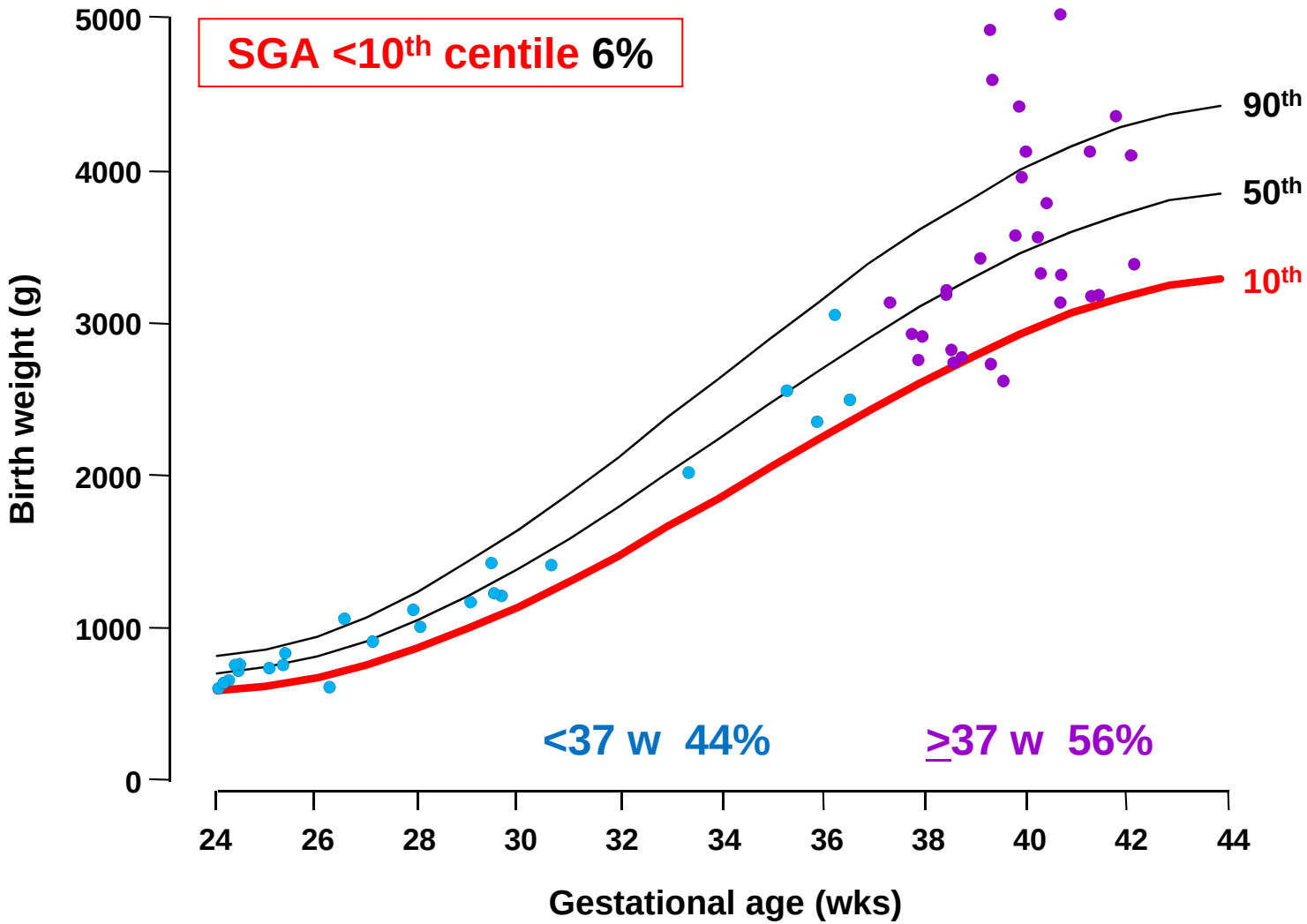
Stillbirth : intrapartum (12% of total)

SGA vs non-SGA



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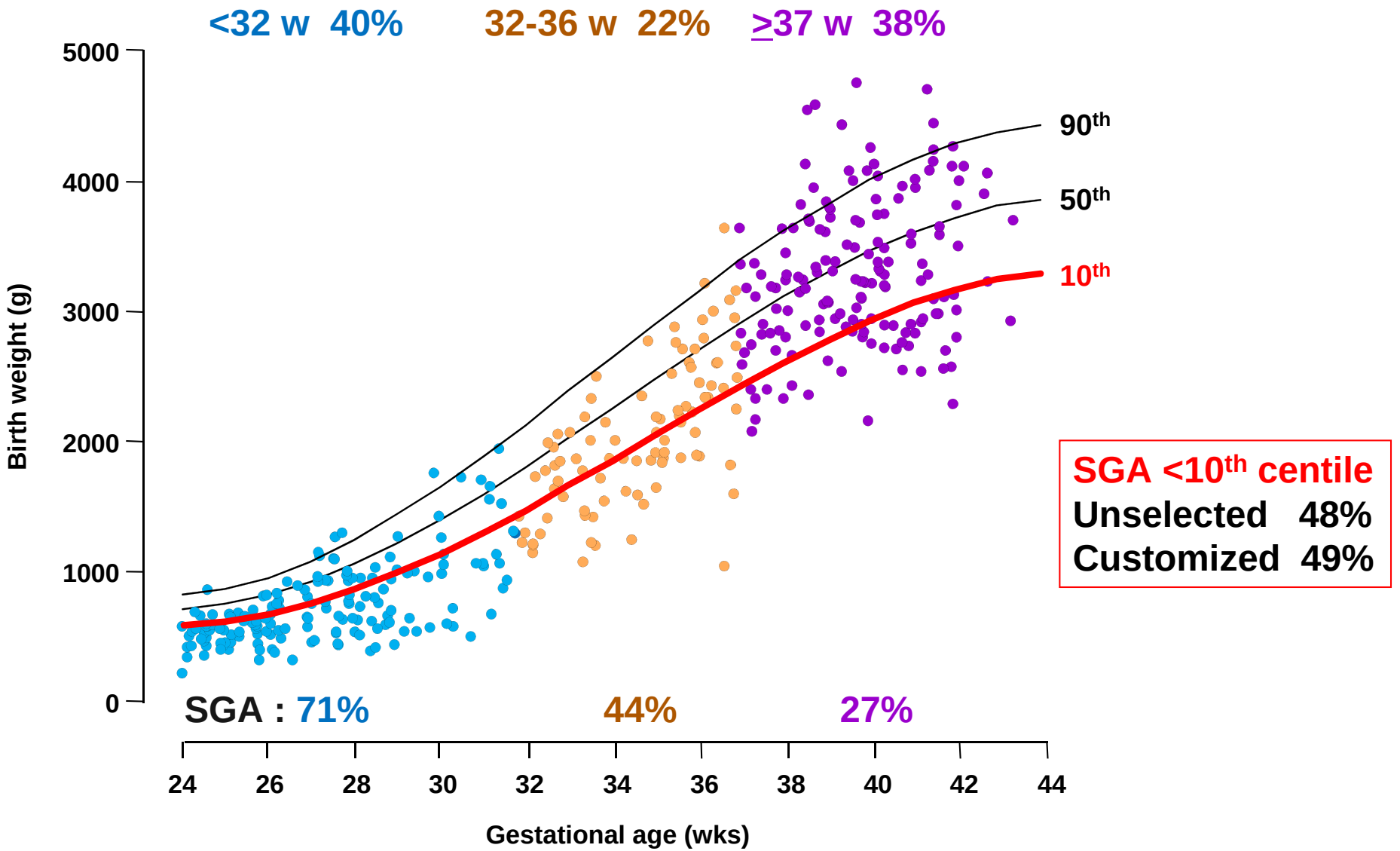
Stillbirth : antepartum (88% of total)

SGA vs non-SGA



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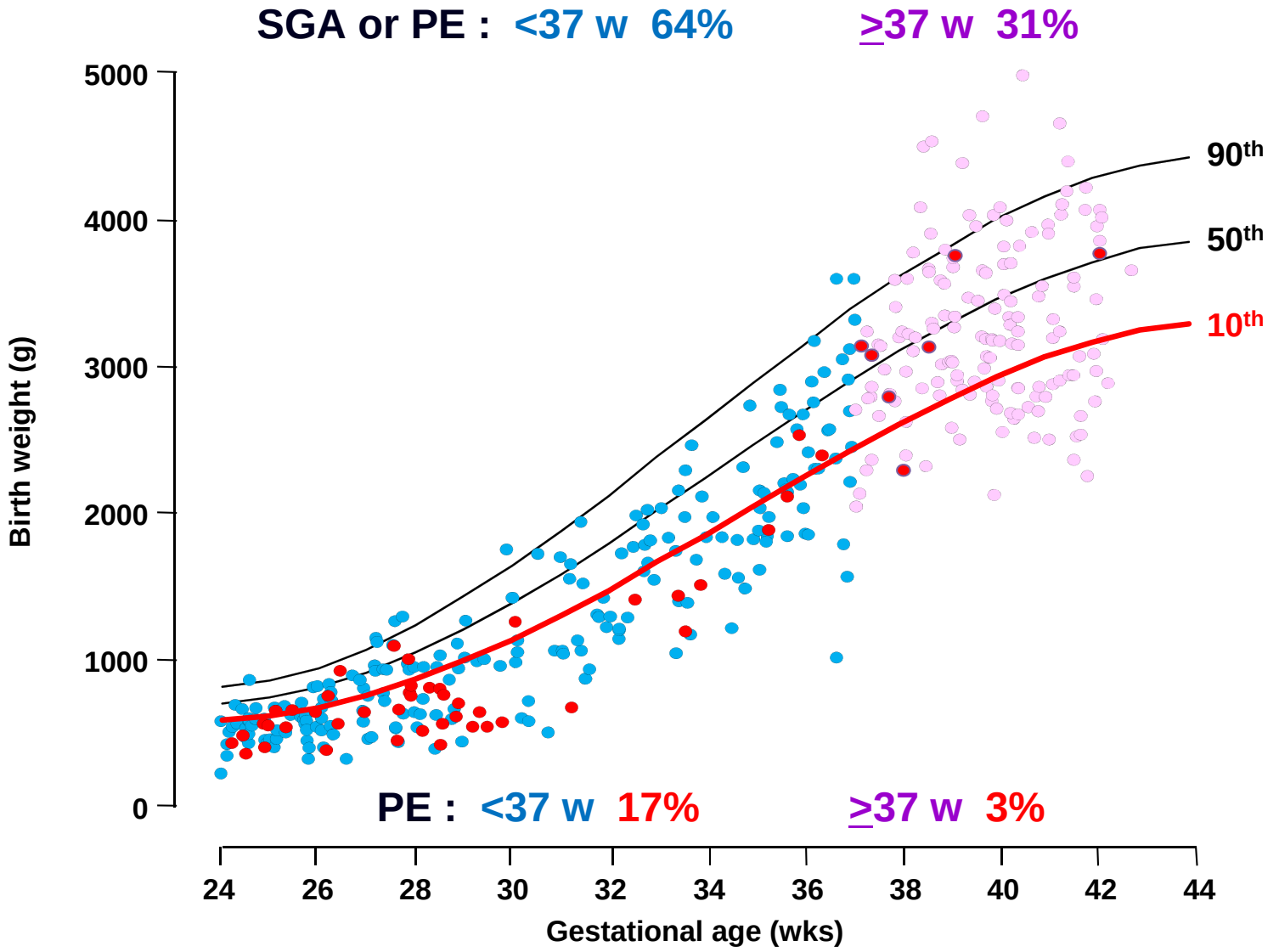
Stillbirth : antepartum

PE vs no PE



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Policy to reduce stillbirth in England

Saving Babies' Lives

A care bundle for reducing stillbirths

NHS England

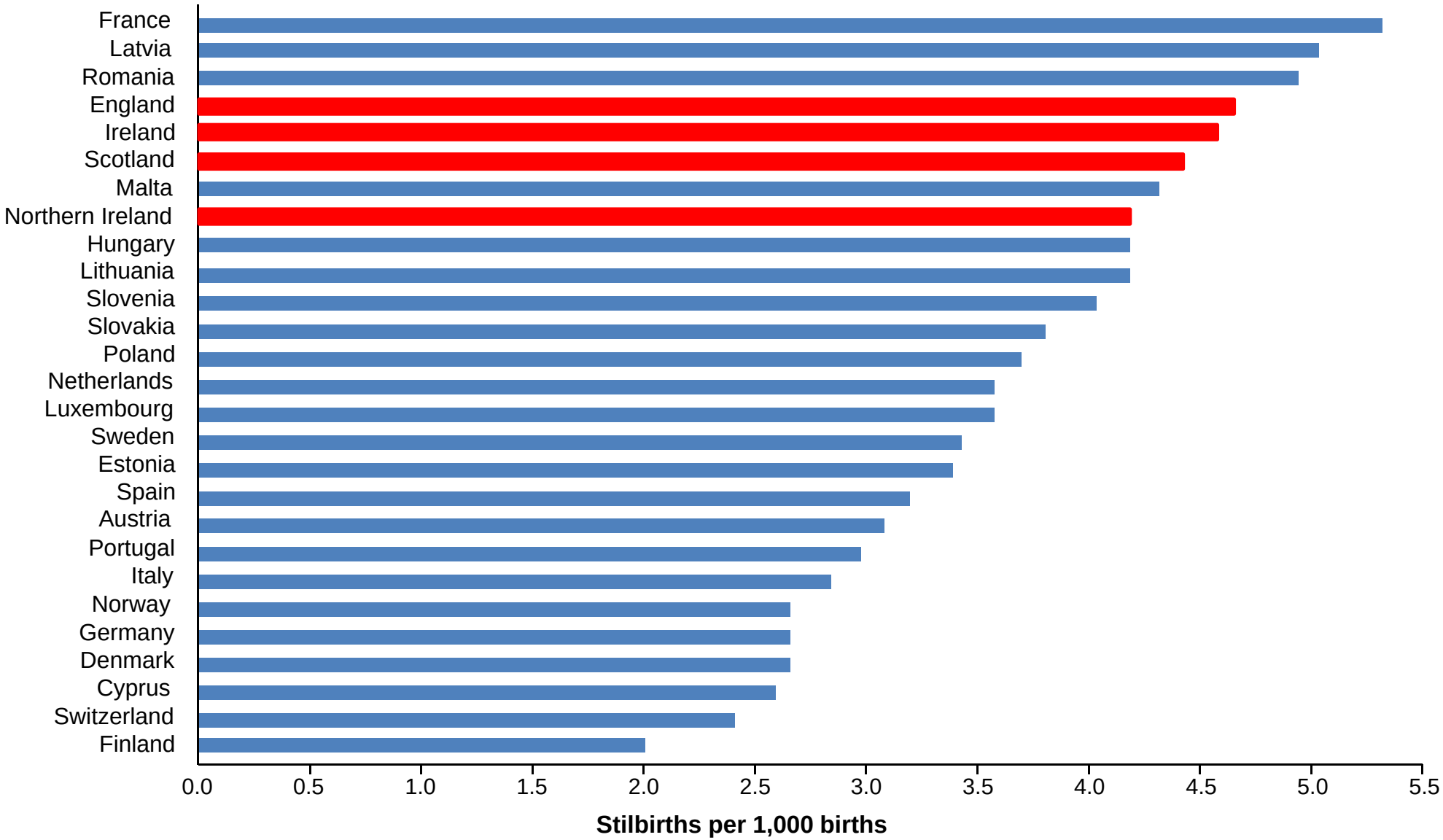
- Reduction of smoking in pregnancy
- Risk assessment for growth restriction
- Raising awareness of reduced movements
- Effective monitoring in labour

Royal College of Obstetricians & Gynaecologists

The Royal College of Midwives

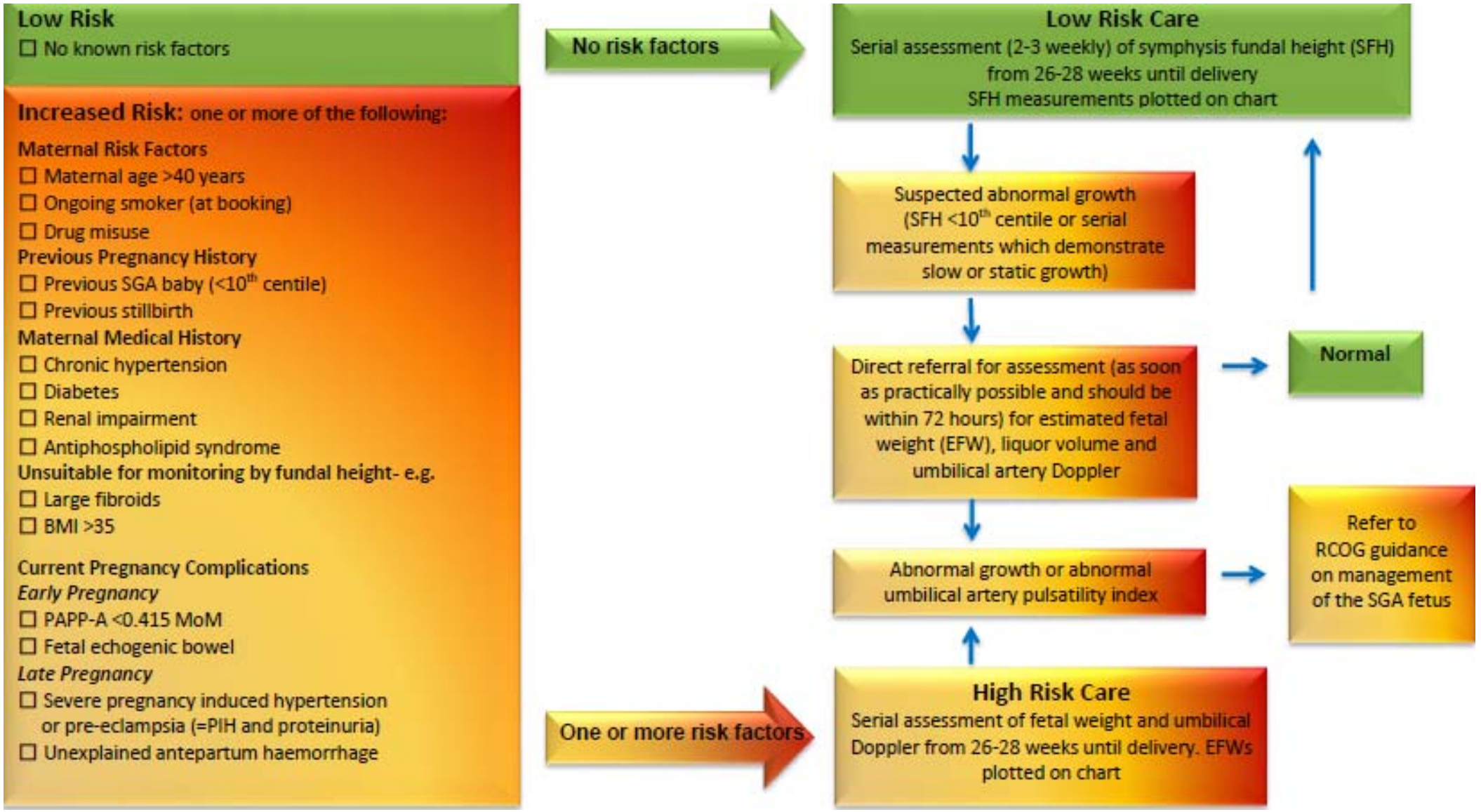
The Fetal Medicine Foundation

Stilbirth rates in Europe in 2014



NHS England

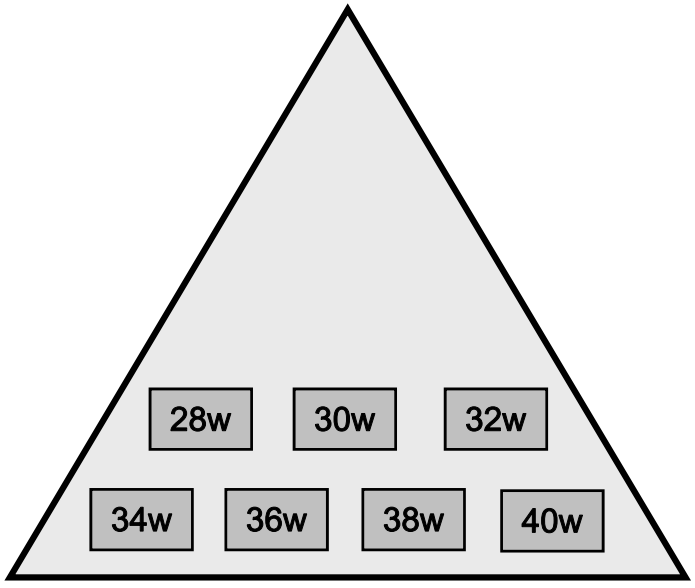
Risk assessment for growth restriction

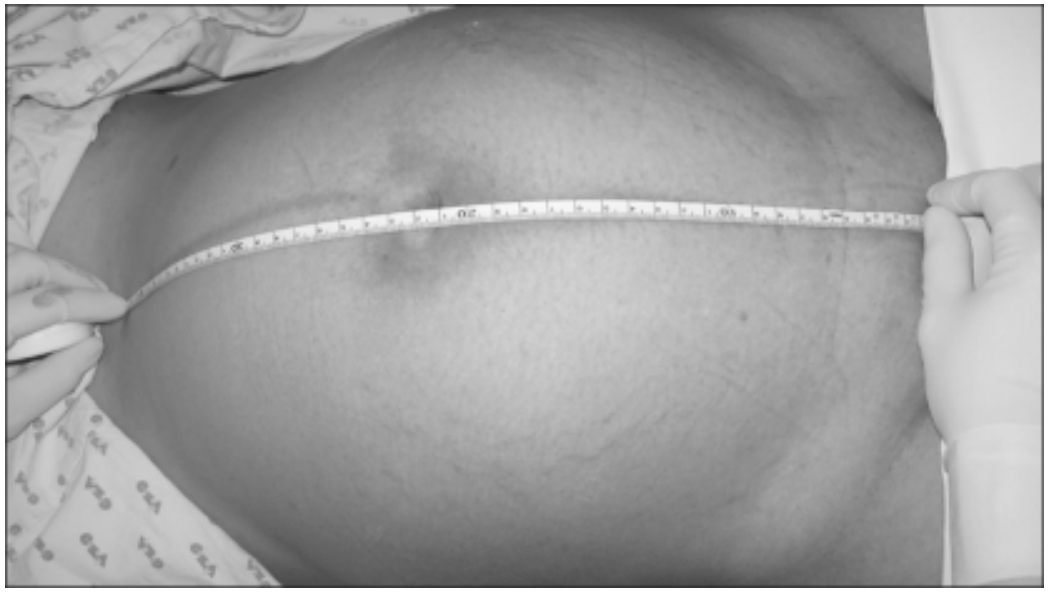


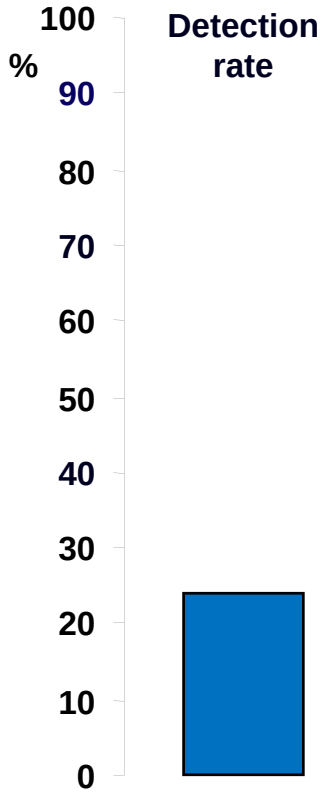
NHS England

Risk assessment for growth restriction

Strategy for Group with no risk factors







Bais *et al.,* Effectiveness of detection of intrauterine retardation by abdominal palpation as screening test in a low-risk population: an observational study. Eur J Obstet Gynecol Reprod Biol **2004**; 116: 164-169.

Lindhart *et al.,* The implications of introducing the symphyseal-fundal height-measurement. A prospective randomized controlled trial. BJOG **1990**; 97: 675-680.

NHS England

Risk assessment for growth restriction

Strategy for Group with risk factors

RISK FACTORS

- Age >40 years
- Smoking
- Drug misuse

- Previous SGA (<10th)
- Previous stillbirth

- Chronic hypertension
- Diabetes mellitus
- Renal impairment
- Anti-phospholipid syndrome

- Large fibroids
- BMI >35 kg/m^2

- PAPP-A <0.415 MoM (7th)
- Fetal echogenic bowel

- Preeclampsia or PIH
- Unexplained haemorrhage

NO RISK FACTORS

- SFH <10th percentile
- SFH showing static growth

8 extra scans for ?45% of pregnancies

Ultrasound scans every 2 wks from 26 wks until delivery: EFW and UA Doppler

If EFW <10th

Delivery:

<32 w	DV abnormal
32 w	UA ARED
33-36 w	UA high PI
37 w	MCA low PI

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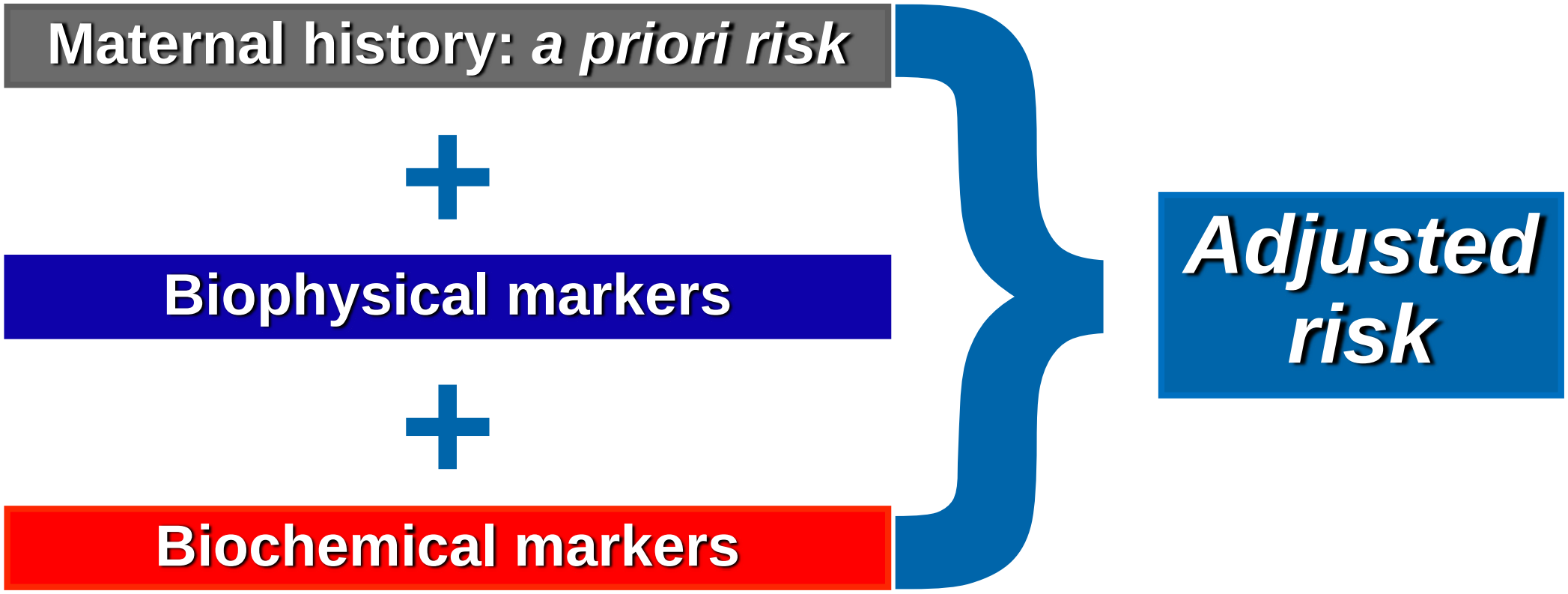
Prediction of stillbirth



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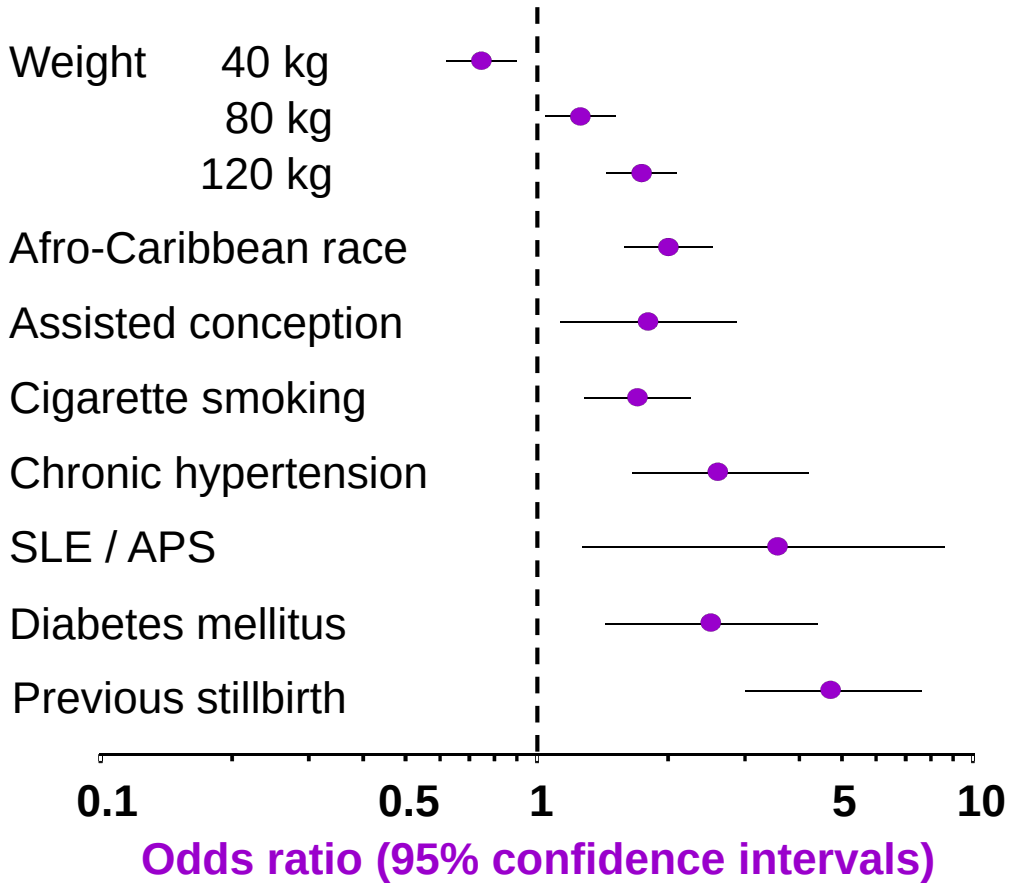
Prediction of stillbirth

a priori risk: maternal factors

Screening study
March 2006 – Oct 2015

Study population (n=113,415)
Antepartum stillbirths (n=396)

Impaired placentation (n=230)
Unexplained + other (n=166)



Yerlikaya G, Akolekar R, McPherson K, Syngelaki A, Nicolaides KH: Prediction of stillbirth from maternal demographic and pregnancy characteristics. Ultrasound Obstet Gynaecol 2016; 48:607-612.

The Fetal Medicine Foundation

Prediction of stillbirth

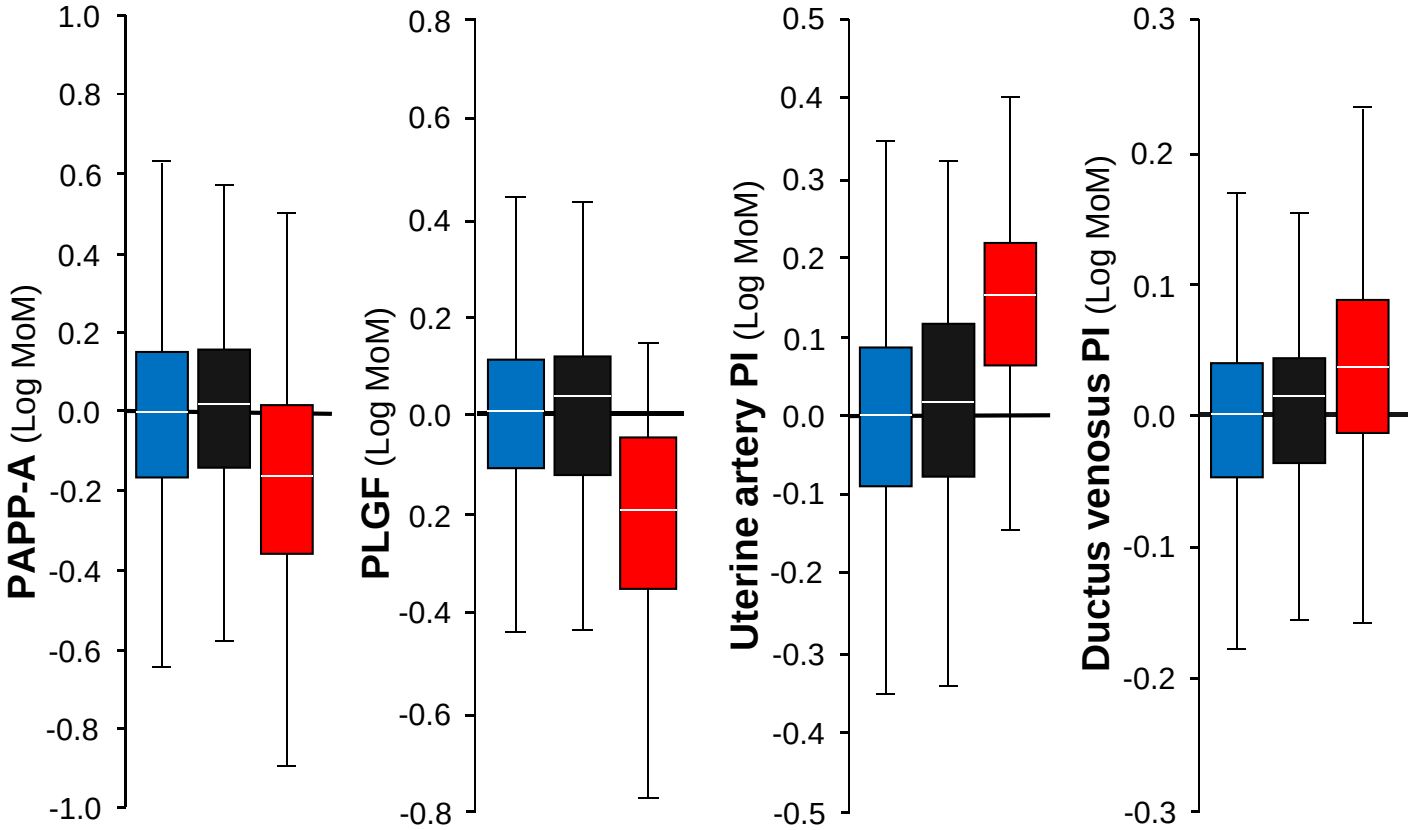
Biomarkers at 11-13 weeks

Screening study

Study population (n=76,897)
Antepartum stillbirths (n=268)

Impaired placentation (n=157)
Unexplained + other (n=111)

Livebirth
Stillbirth - unexplained
Stillbirth - impaired placentation



Mastrodima S, Akolekar R, Yerelika G, Tzelepis T, Nicolaides KH: Prediction of stillbirth from biophysical and biochemical markers at 11-13 weeks. Ultrasound Obstet Gynaecol 2016; 48:613-617.

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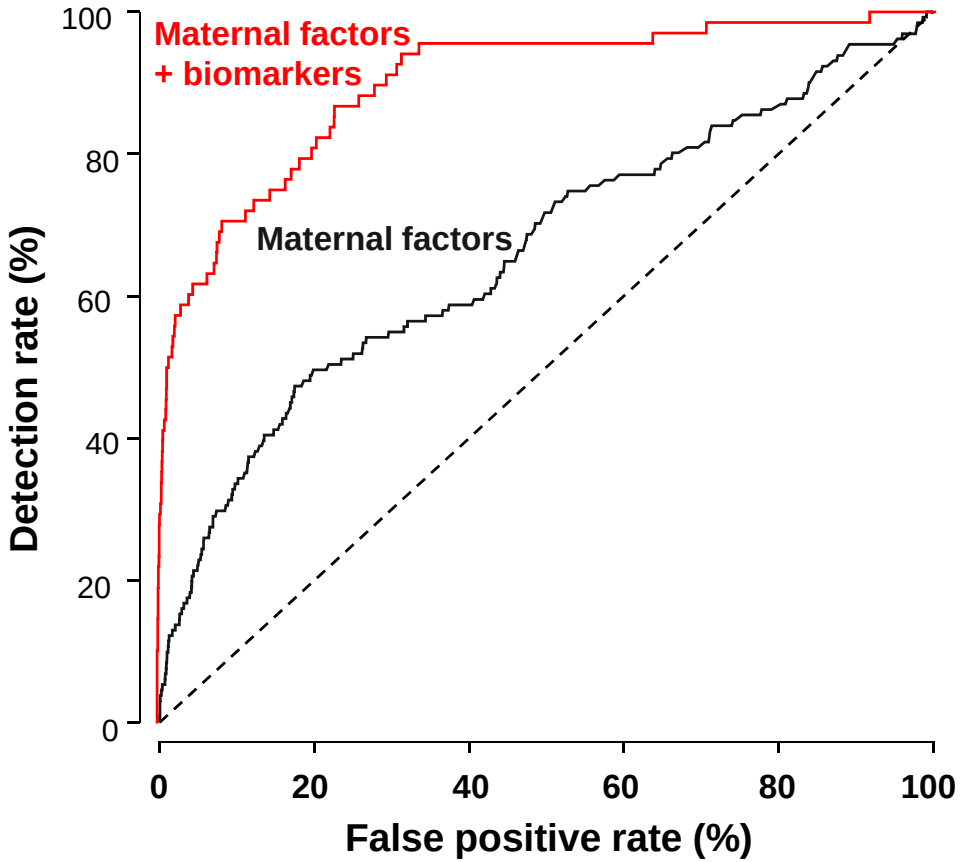
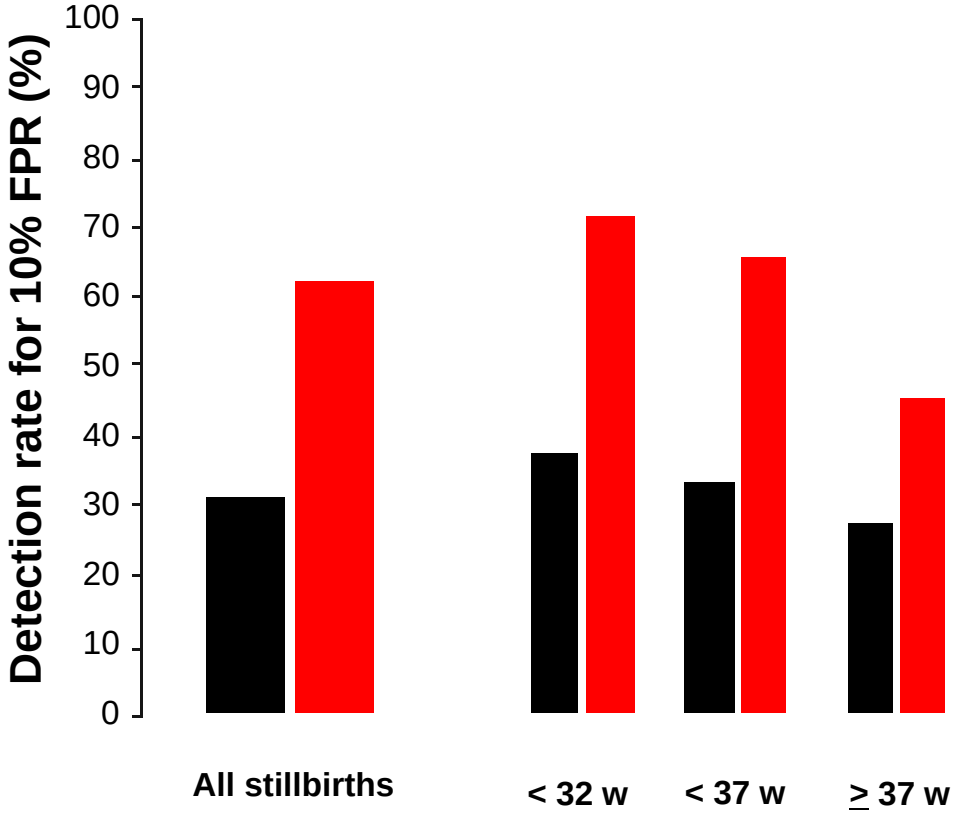
Prediction of stillbirth

Biomarkers at 11-13 weeks





Akolekar R, Machuca M, Mendes M, Paschos V, Nicolaides KH: Prediction of stillbirth from placental growth factor at 11-13 weeks. Ultrasound Obstet Gynaecol 2016; 48:618-623.

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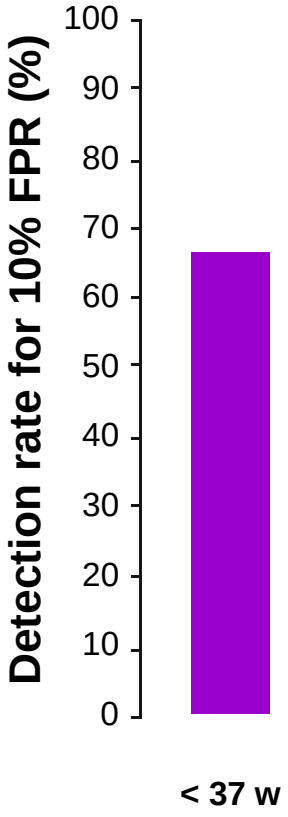
Prediction of stillbirth

Biomarkers at 11-13 weeks



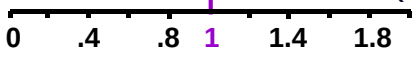
Low-dose aspirin

Preeclampsia

≤ 16 w (n=1,479)		**0.47** (0.36-0.62)
> 16 w (n=10,673)		**0.78** (0.61-0.99)

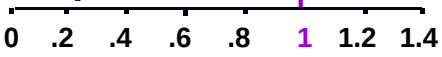
Fetal growth restriction

≤ 16 w (n=1,064)		**0.46** (0.33-0.64)
> 16 w (n=7,196)		**0.98** (0.88-1.08)



Perinatal death

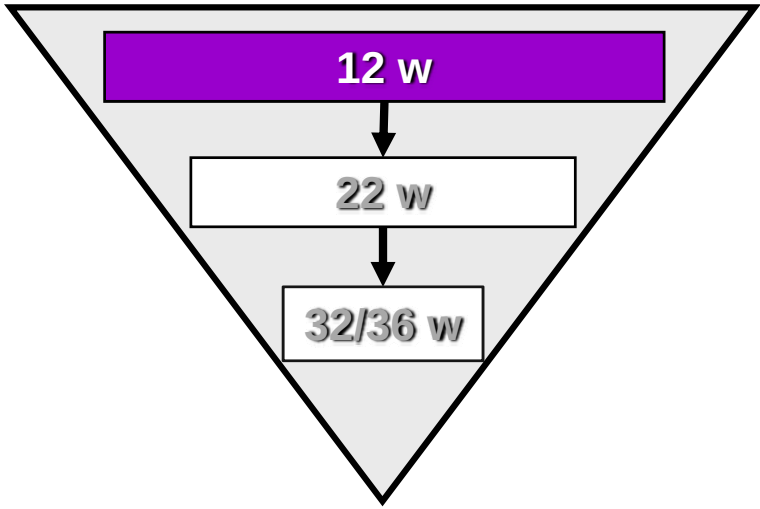
≤ 16 w (n=1,308)		**0.41** (0.19-0.92)
> 16 w (n=9,557)		**0.93** (0.73-1.19)



Bujold *et al.,* 2010; Roberge *et al.,* 2013

funded by EU FP7 ASPRE project

SEVENTH FRAMEWORK PROGRAMME



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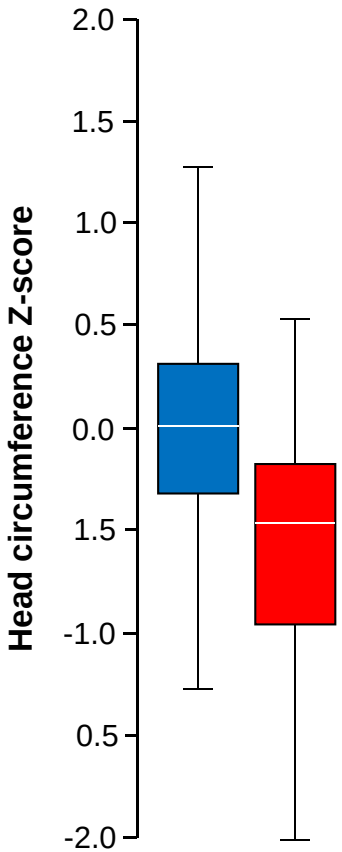
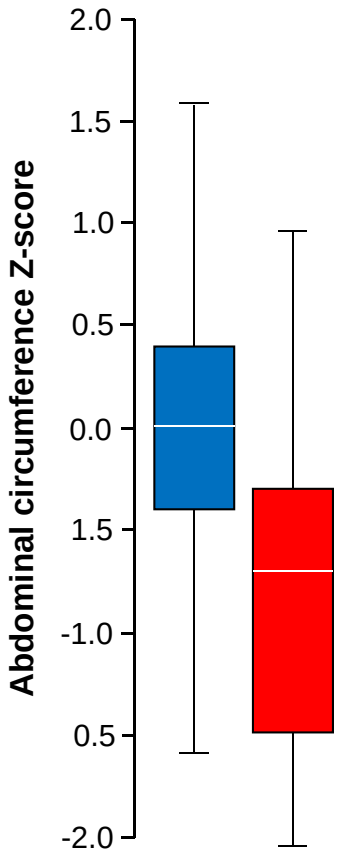
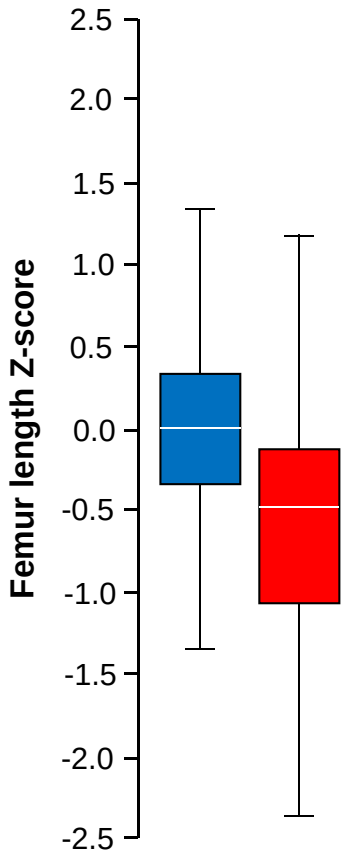
Prediction of stillbirth

Biometry at 20-24 weeks







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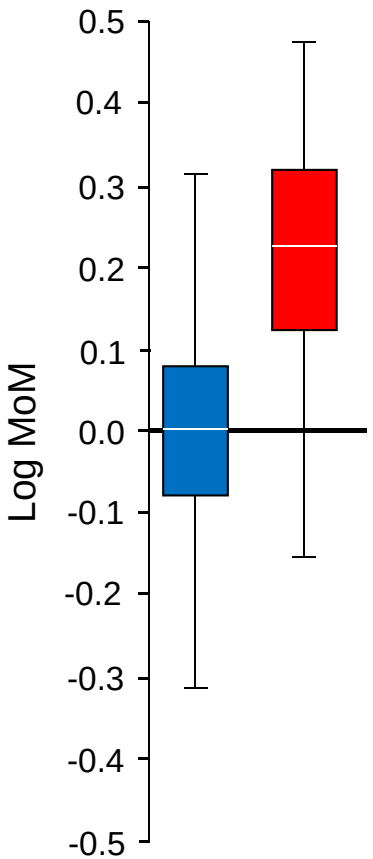
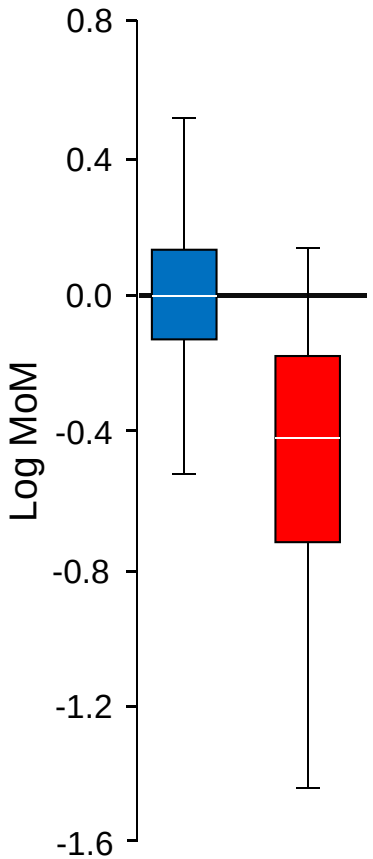
Prediction of stillbirth

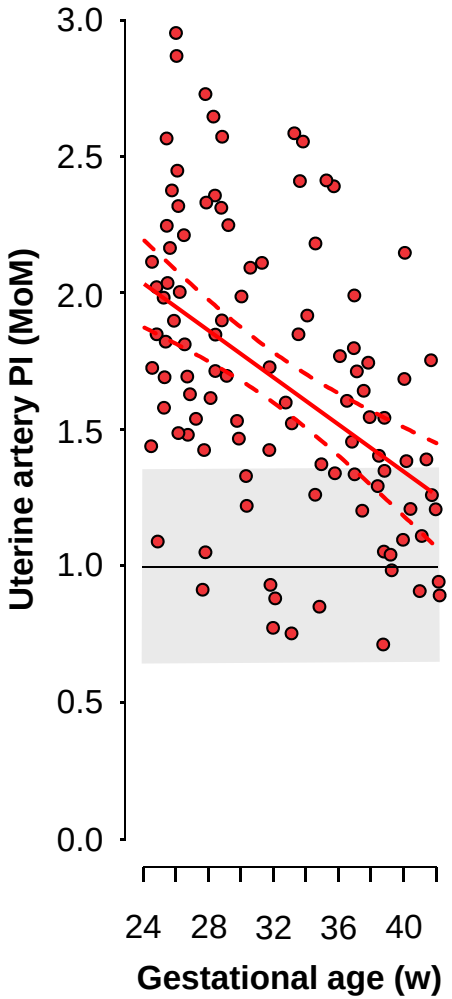
Biomarkers at 20-24 weeks

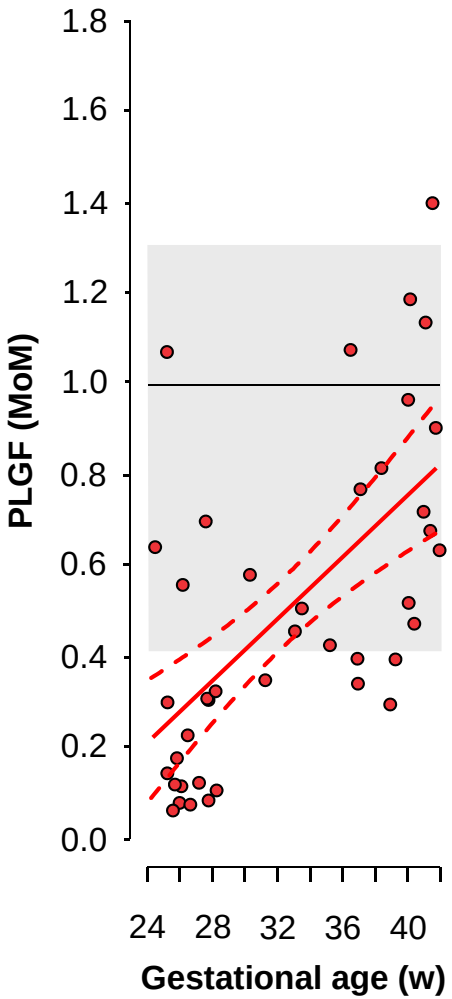
Uterine artery PI



Serum PLGF







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Prediction of stillbirth

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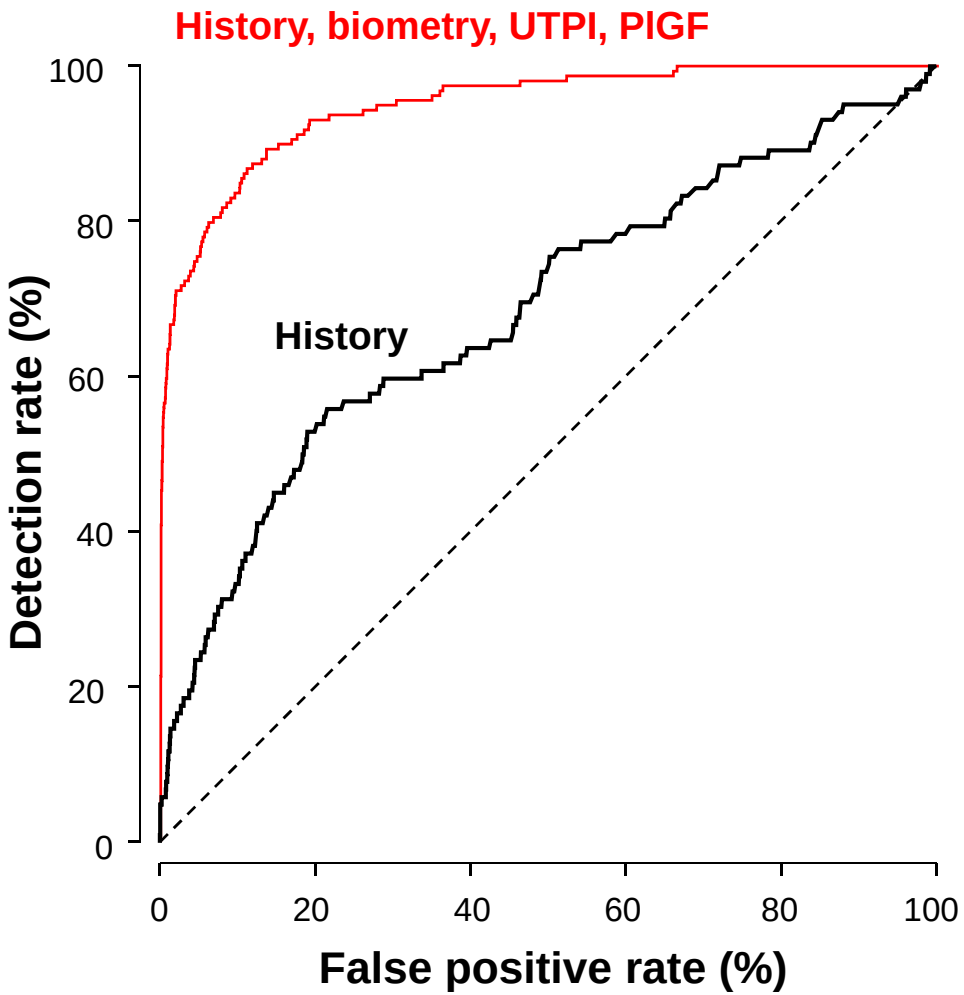

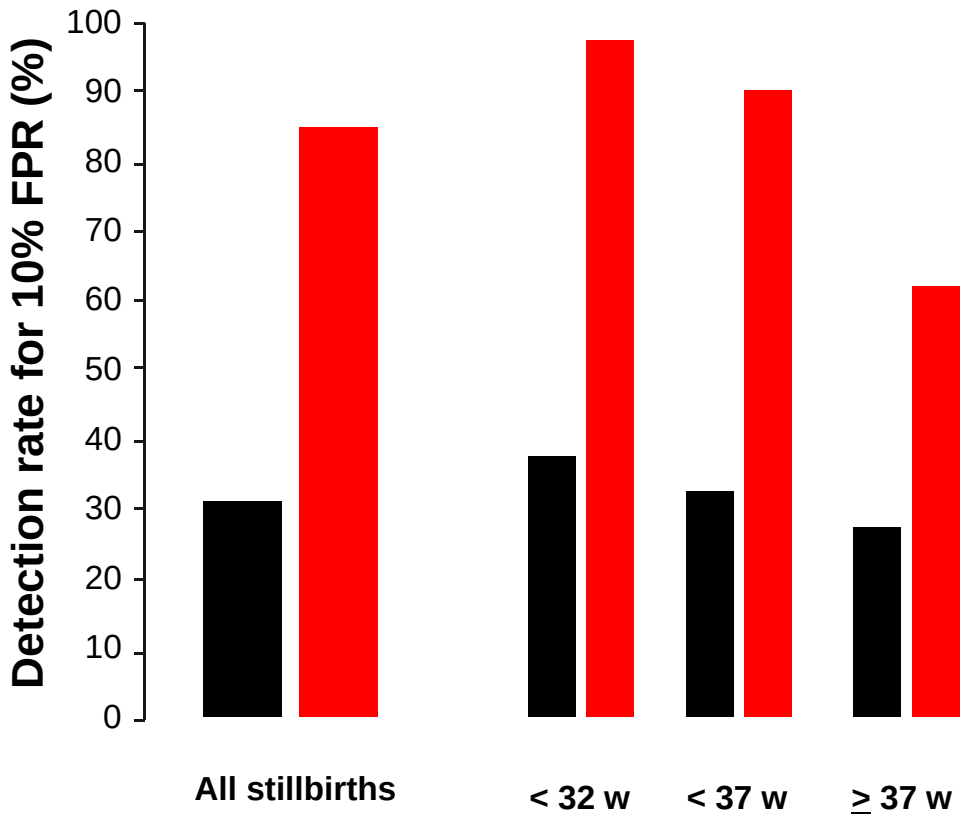

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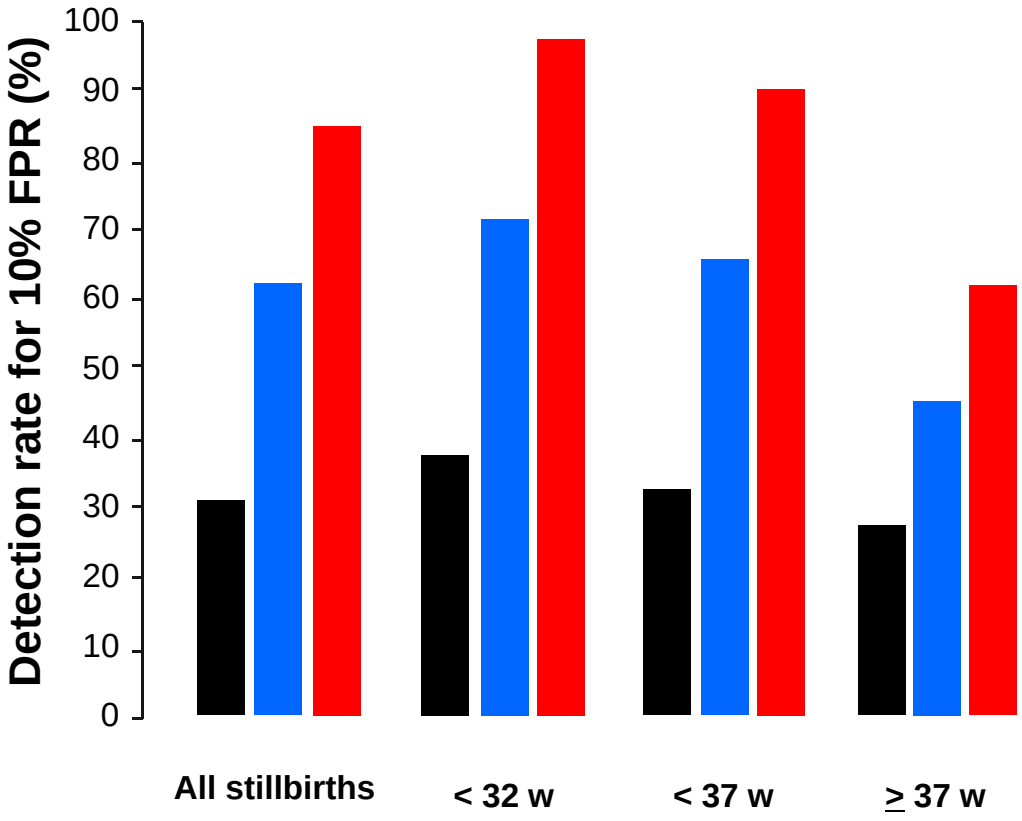
Prediction of stillbirth

Conclusions

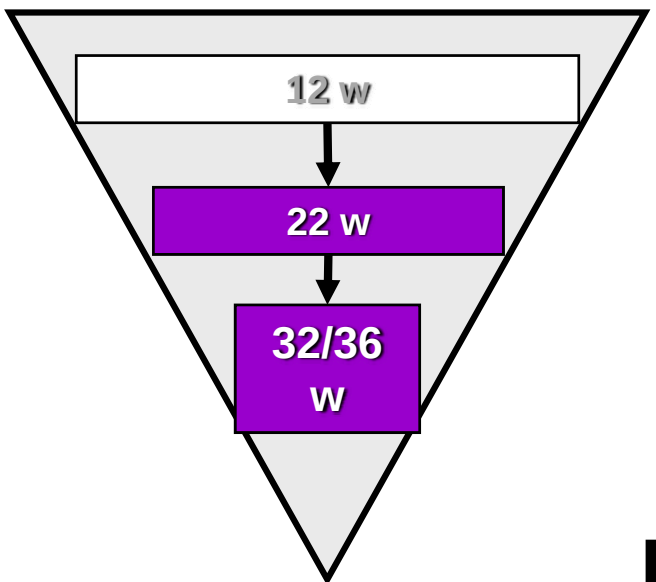


- **High proportion of stillbirths due to impaired placentation are predictable**
- **Best biomarkers at 11-13 w: UTPI, PLGF, PAPP-A, DVPI**
- **Best biomarkers at 20-24 w: BIOMETRY, UTPI, PLGF**

The Fetal Medicine Foundation

Prediction of stillbirth

Combined test at 22, 32 and 36 w



Assessment at 22 w

Low-risk

Moderate-risk

High-risk

Follow-up 24-32 w

Assessment at 32 w

High-risk

Follow-up 32-36 w

Assessment at 36 w

High-risk

No further scan

Follow-up / delivery 38 w

The Fetal Medicine Foundation

Prediction of stillbirth

Biometry at 20-24 weeks

Fetal responses to hypoxia

Placental dysfunction

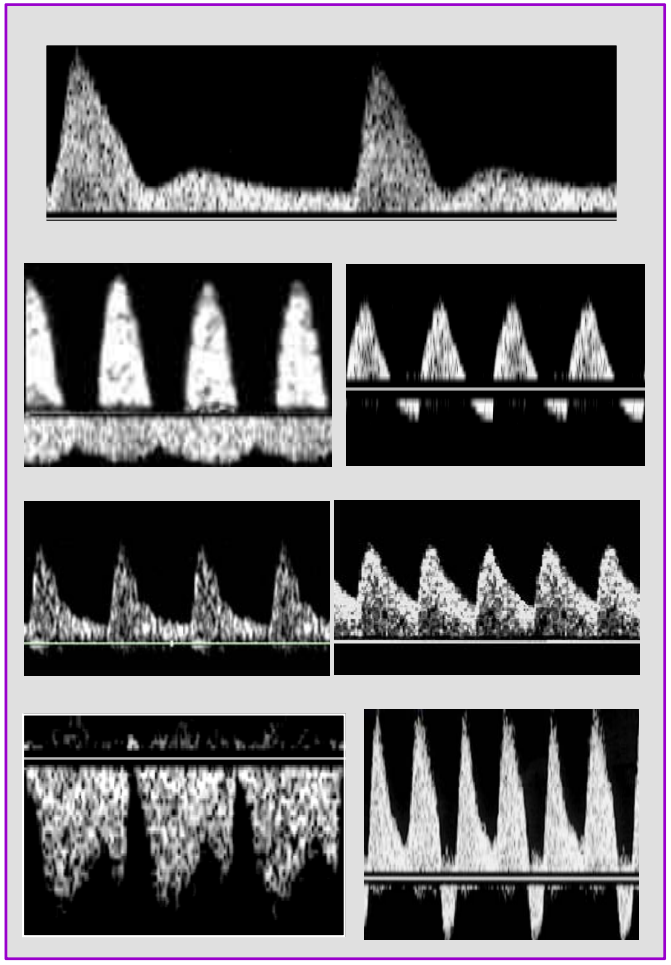
Abnormal umbilical artery

Abnormal MCA Doppler
Brain sparing effect

Abnormal venous Doppler

Loss of fetal movement/
Abnormal cCTG

Stillbirth



Hypoxia

↓

Acidemia

↓

CNS damage

↓

Stillbirth

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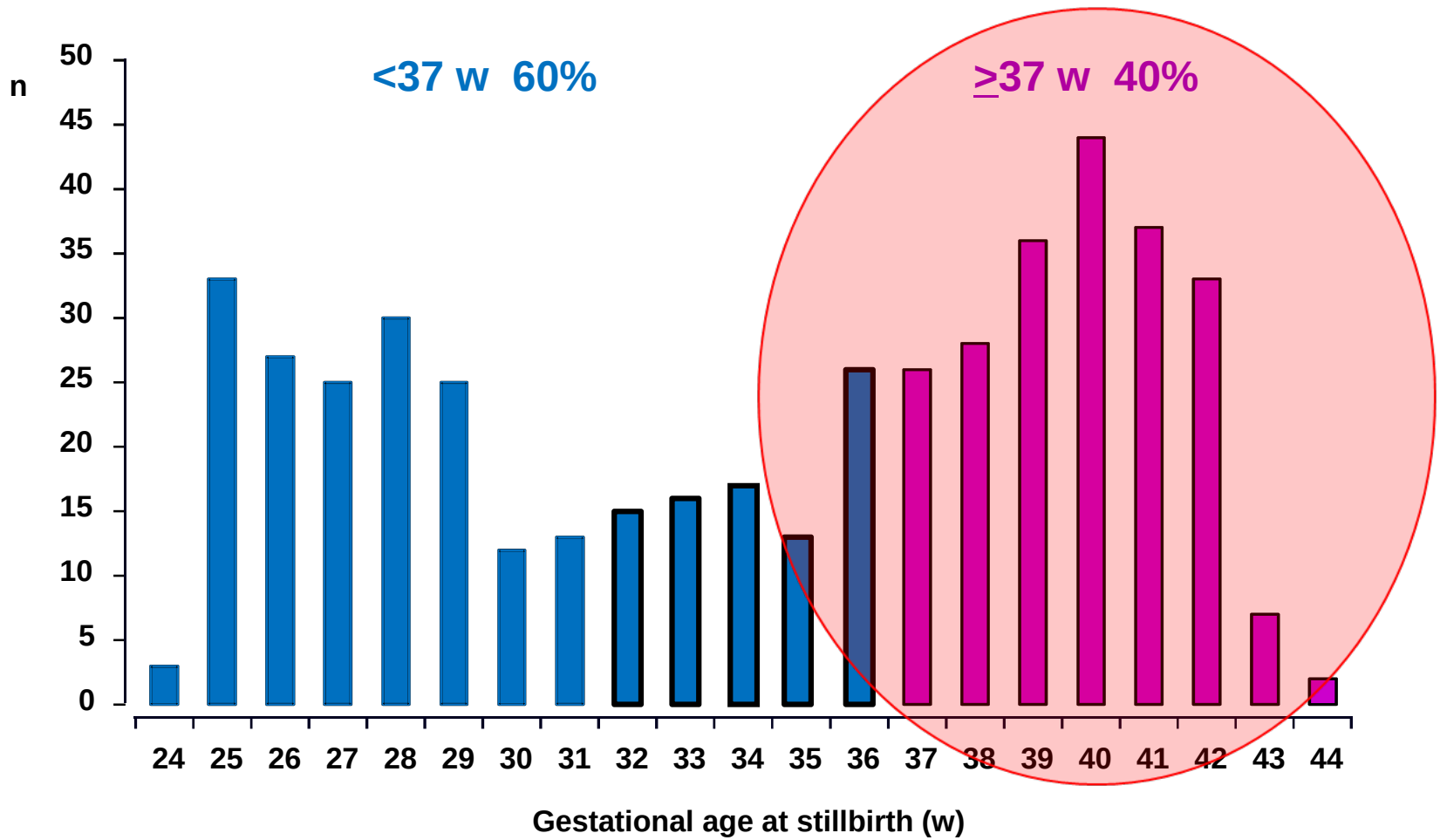
Stillbirth

Preterm vs term



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The Fetal Medicine Foundation

Stillbirth : antepartum (88% of total)

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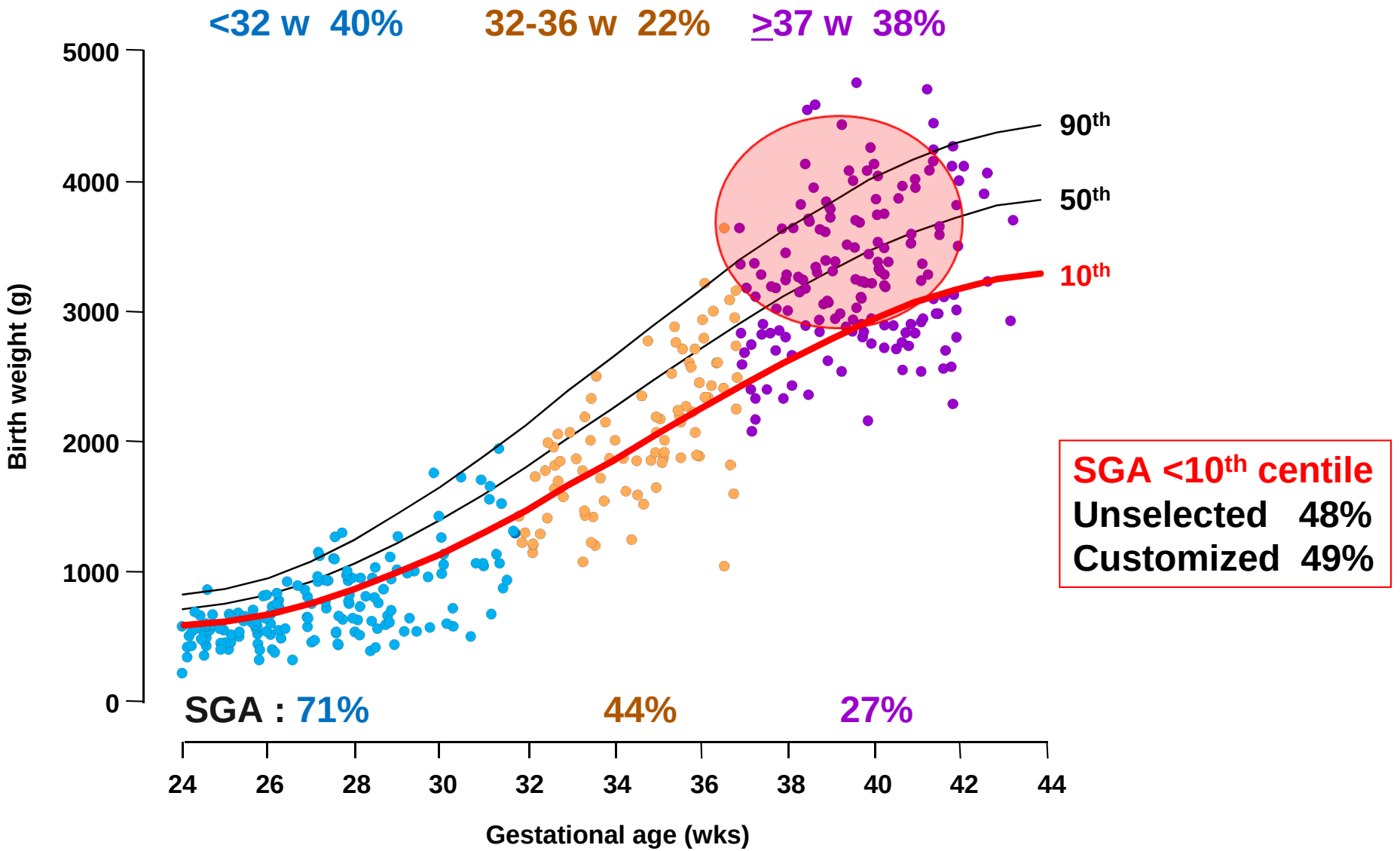

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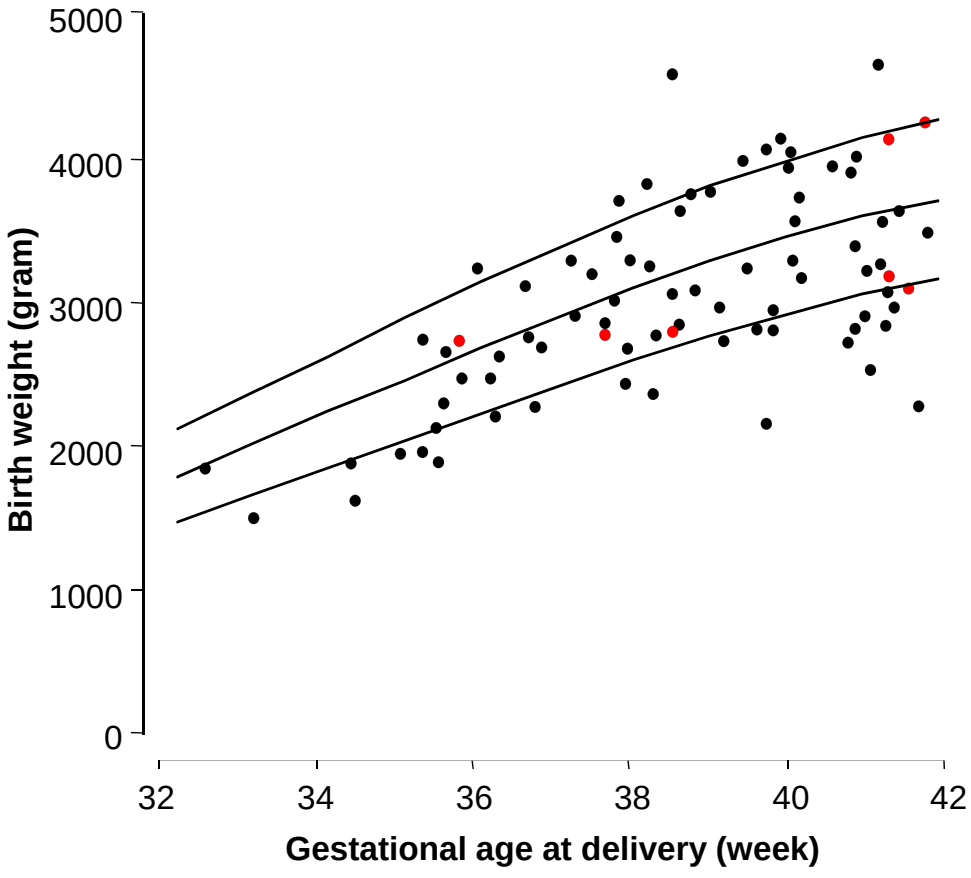
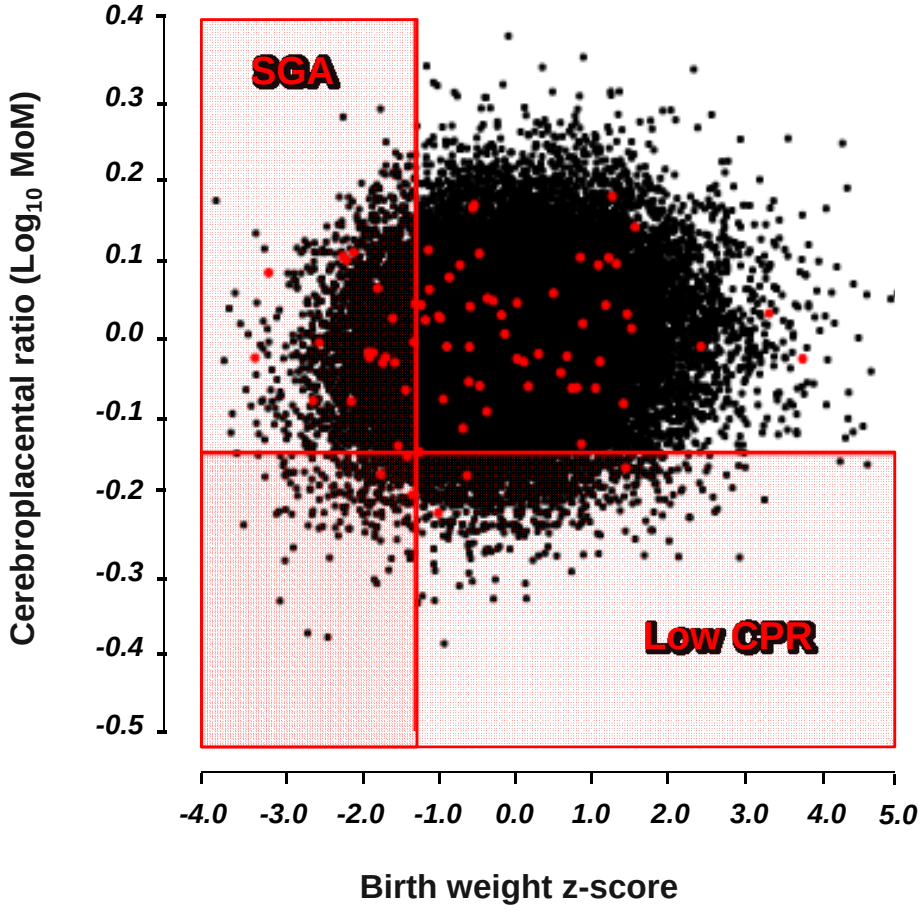
Prenatal prediction at 32 w

Stillbirths





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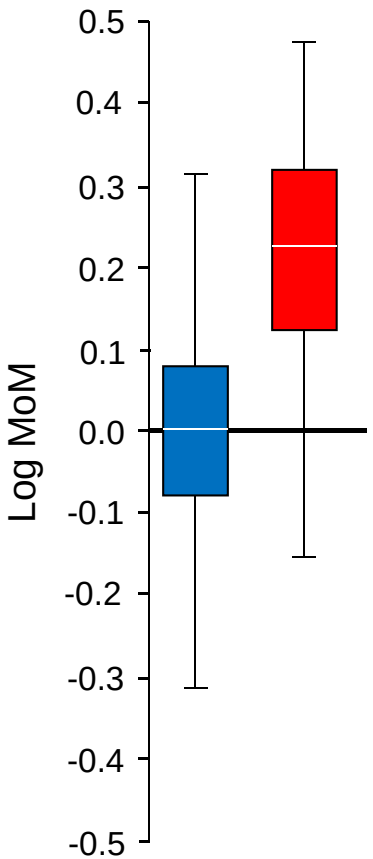
Prediction of stillbirth

Biomarkers at 20-24 weeks

Uterine artery PI



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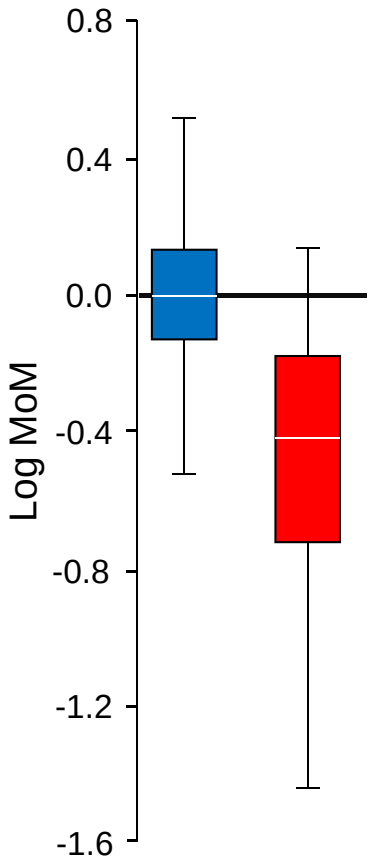

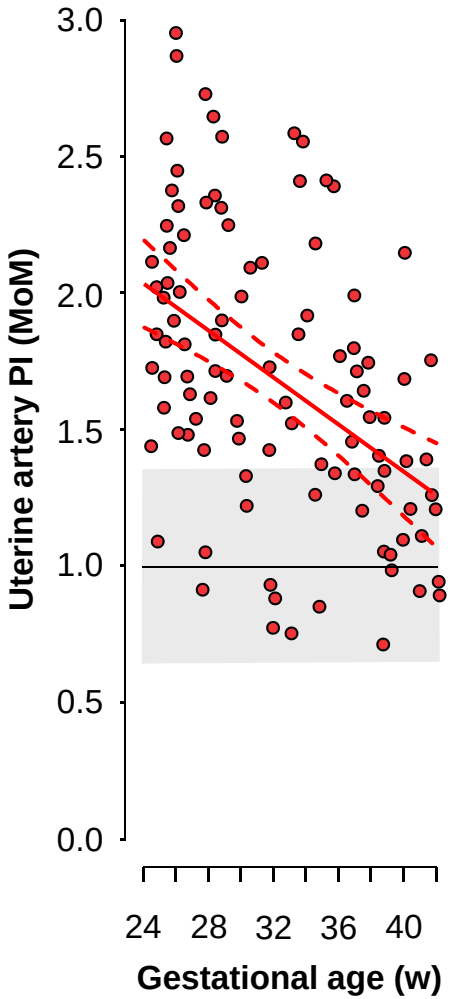

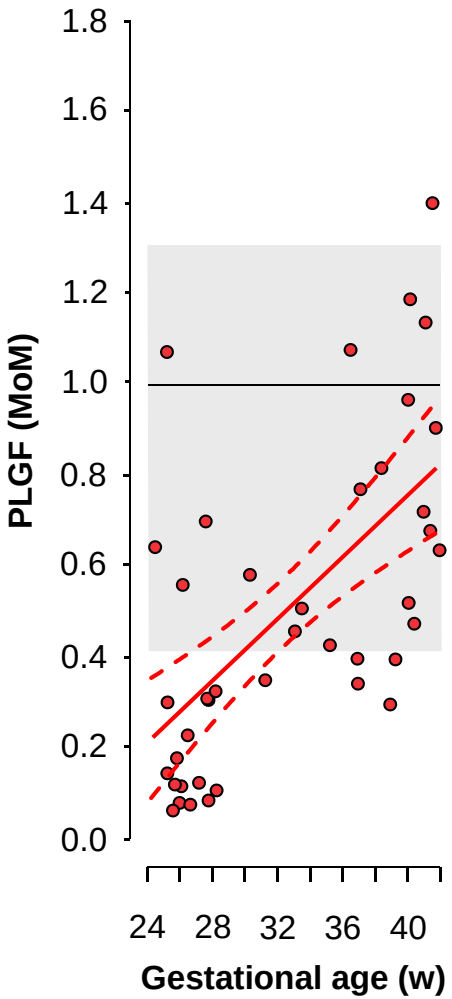

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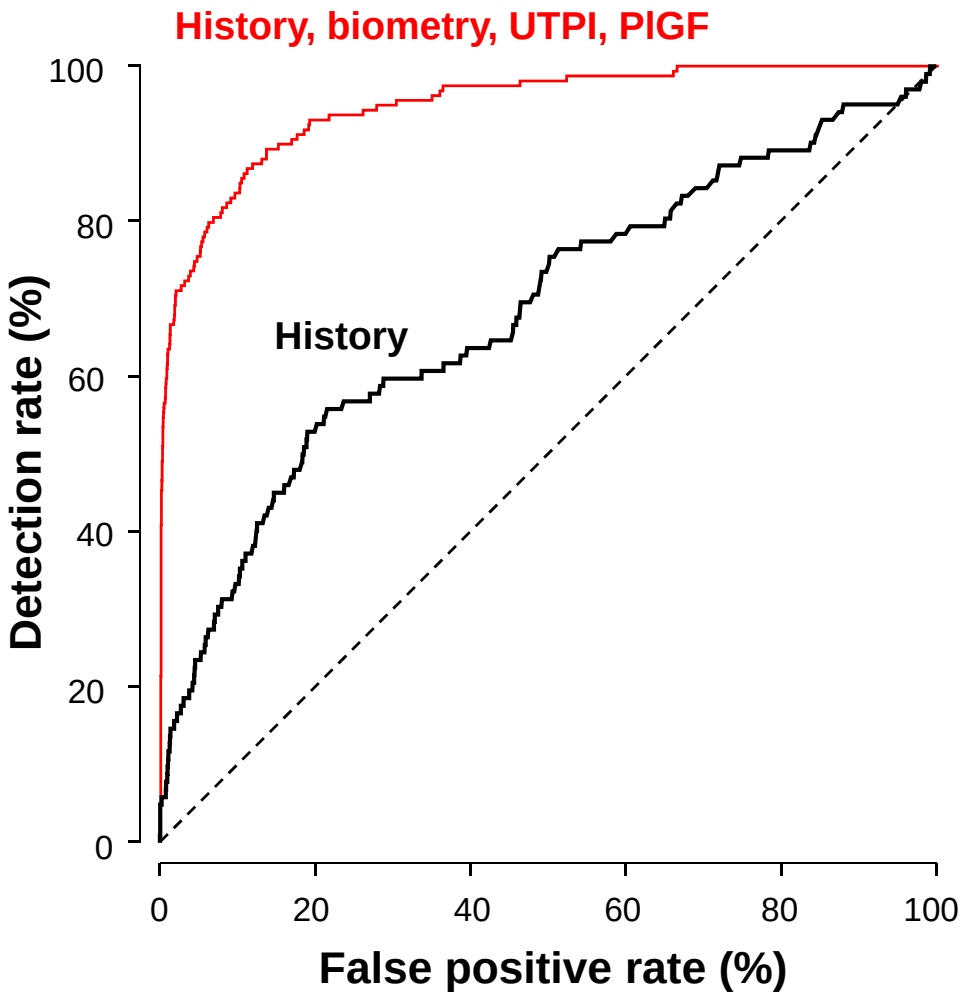
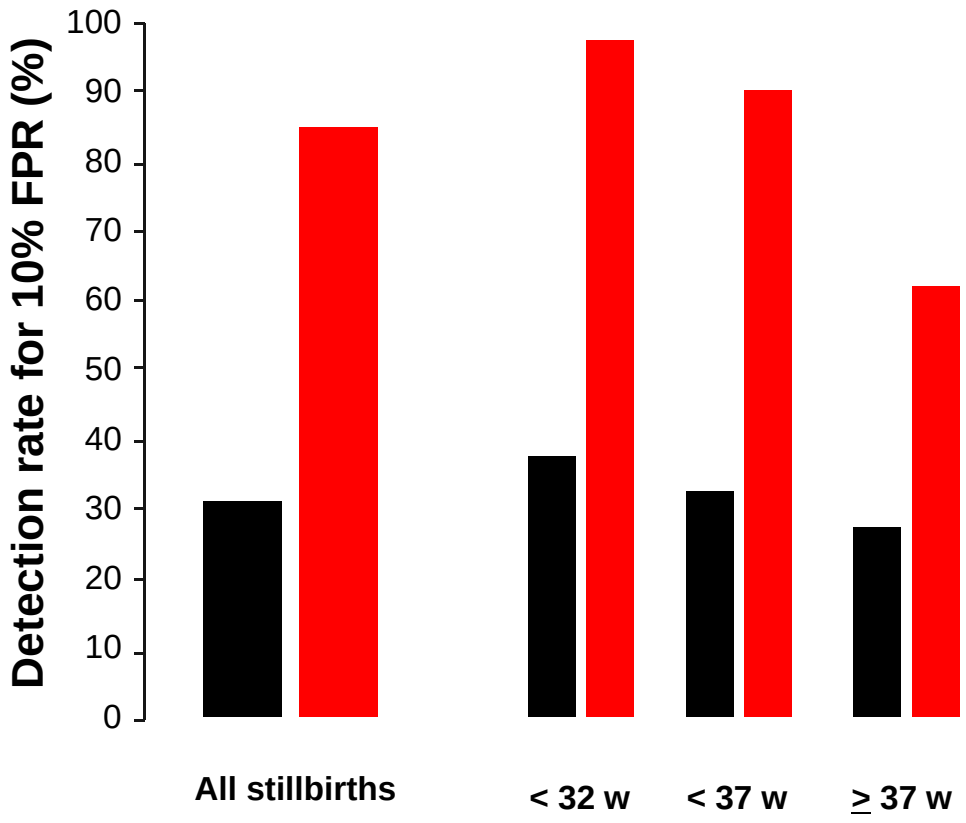
Prediction of stillbirth

Biomarkers at 20-24 weeks





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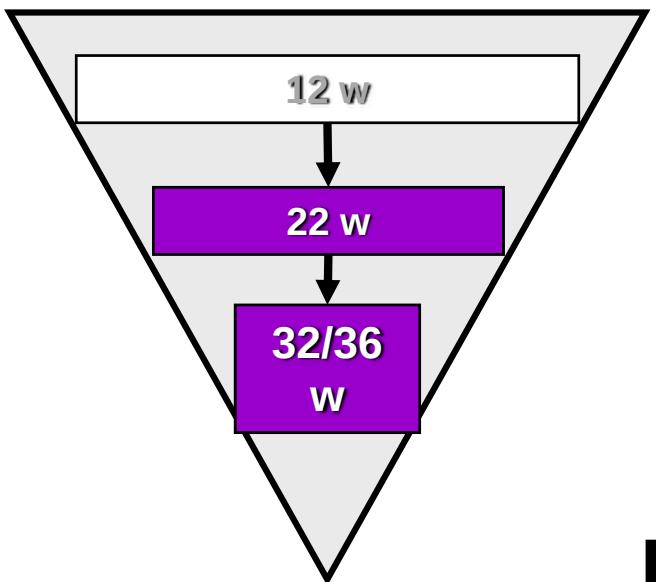
Prediction of stillbirth

Combined test at 22, 32 and 36 w



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Low-risk

Moderate-risk

High-risk

Follow-up 24-32 w

Assessment at 32 w

High-risk

Follow-up 32-36 w

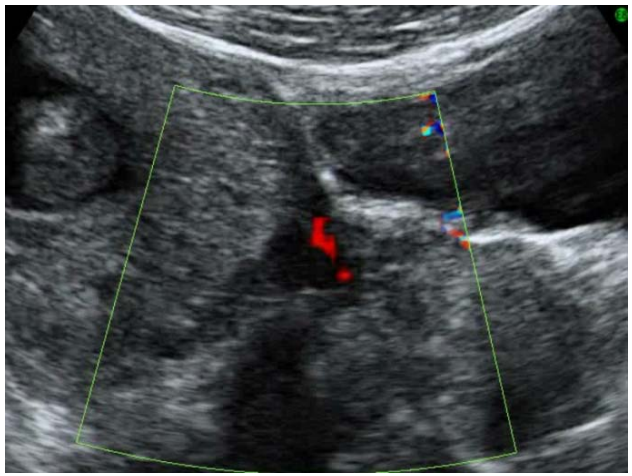
Assessment at 36 w

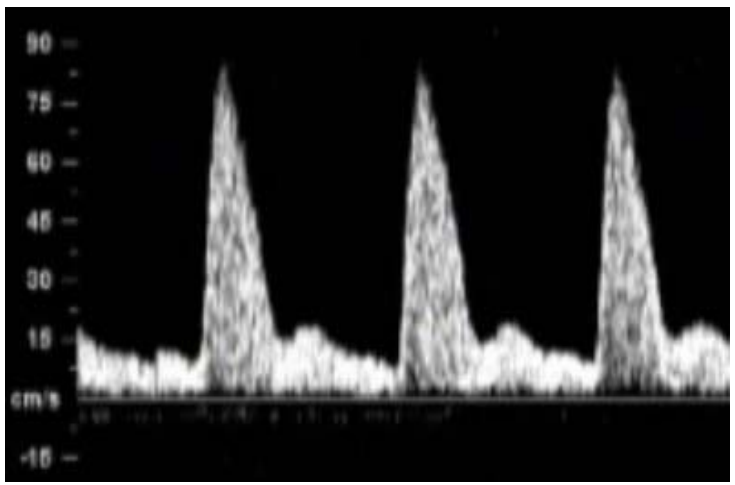
High-risk

No further scan

Follow-up / delivery 38 w

Uterine artery pulsatility index





Transabdominal ultrasound

- **Identify uterine arteries:**
  - Sagittal section of the cervix
  - Color flow mapping
  - Move transducer from side to side
  - Arteries are at the level of the internal os
- **Sampling gate:** 2 mm to cover whole vessel
- **Angle of insonation:** less than 30º
- **Peak systolic velocity:** more than 60 cm/s
- **Mean PI:** average PI (left + right / 2)

The Fetal Medicine Foundation

Prediction of stillbirth

Are the markers of impaired placentation and fetoplacental hypoxia observed in SGA STARVED fetuses also present in AGA STARVED fetuses?

Unfortunately NOT because:

- **AGA STARVED fetuses are not hypoxic**
- **Measures of hypoxic morbidity are mainly the consequence of 'unpredictable' events in labor than prelabor fetal hypoxia**
- **Assessment at 32 and 36 weeks is too insensitive or too remote from the event it aims to predict**