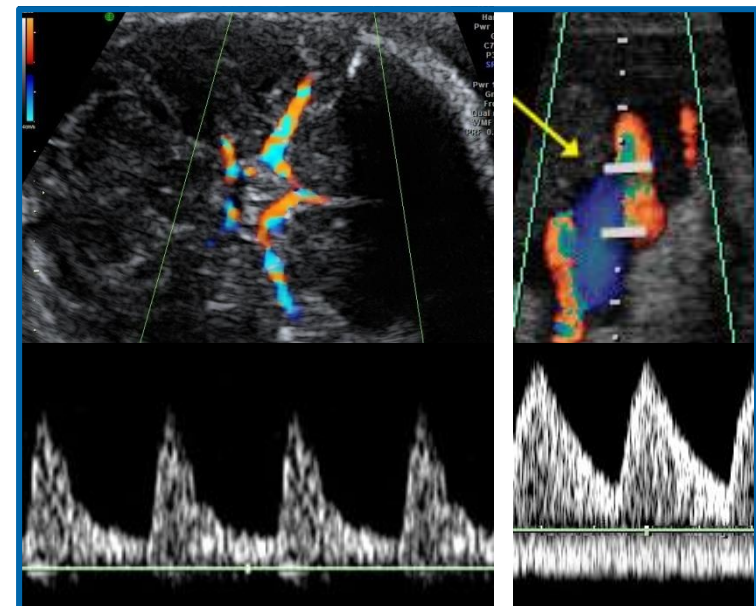


Fetal Well Being – Cerebroplacental ratio (CPR)

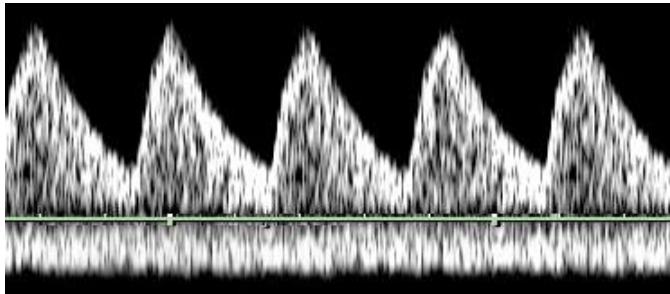
What is IT and How Should We Use It?

Asma Khalil
Professor in Fetal Medicine
St George's Hospital
London - UK

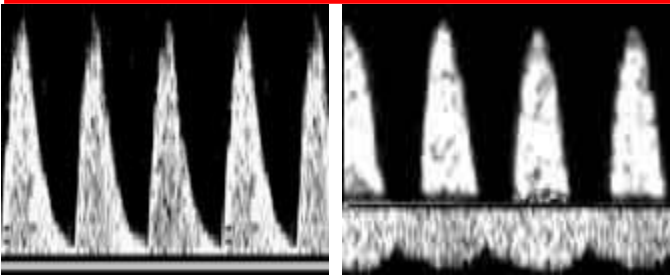


Fetal Doppler in FGR: Umbilical and Middle cerebral artery

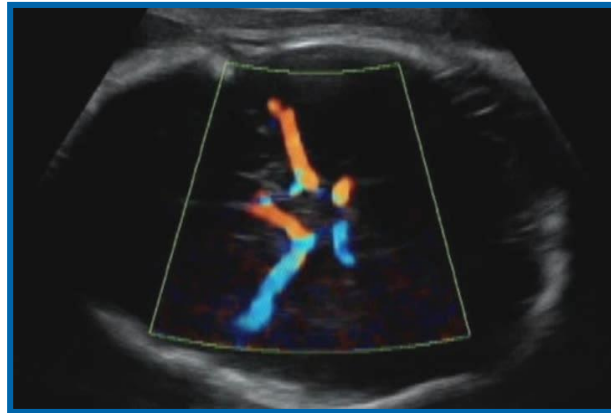
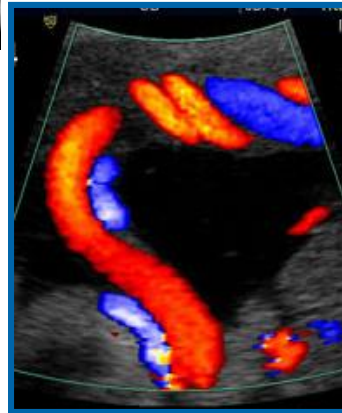
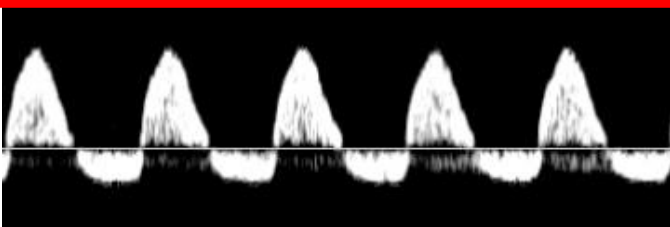
Normal



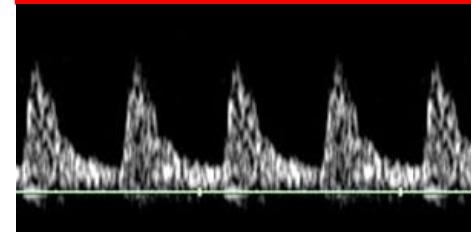
Hypoxia



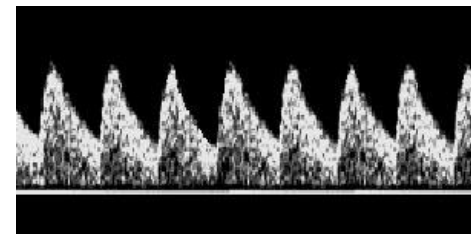
Acidosis



Normal

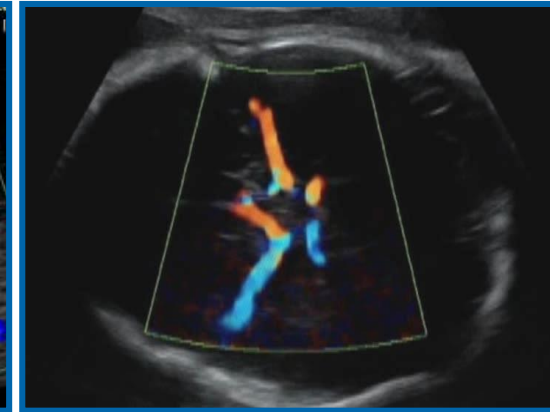
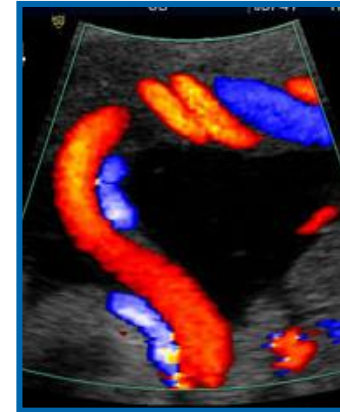


Hypoxia



Cerebroplacental Ratio

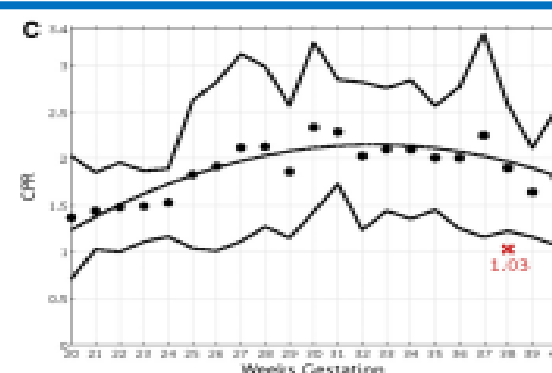
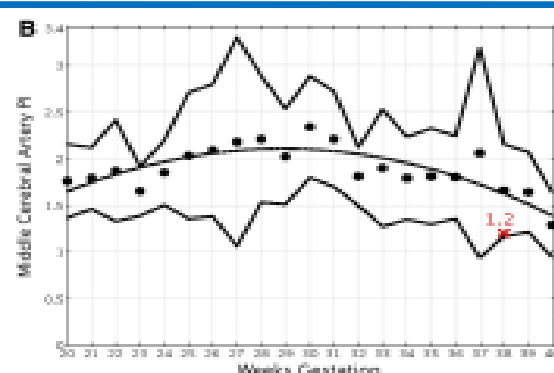
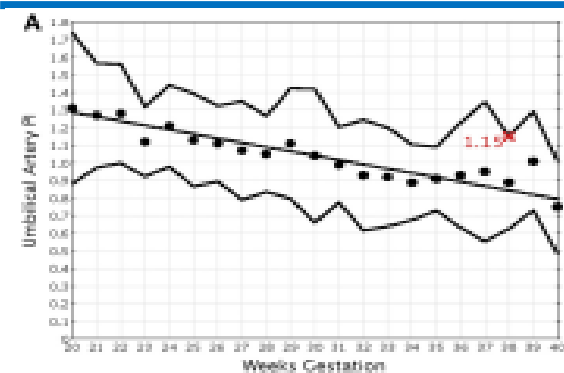
$$\text{Cerebroplacental Ratio (CPR)} = \frac{\text{MCA PI}}{\text{UA PI}}$$



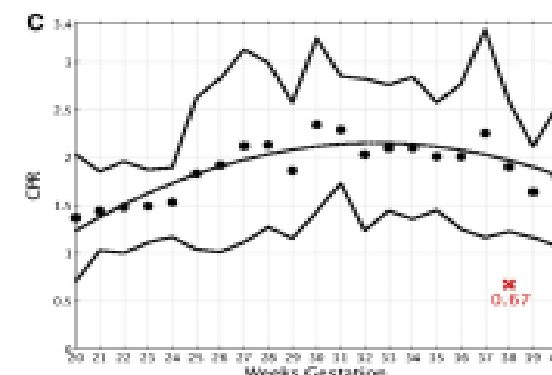
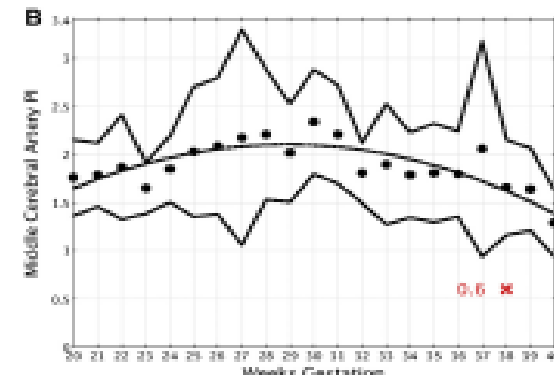
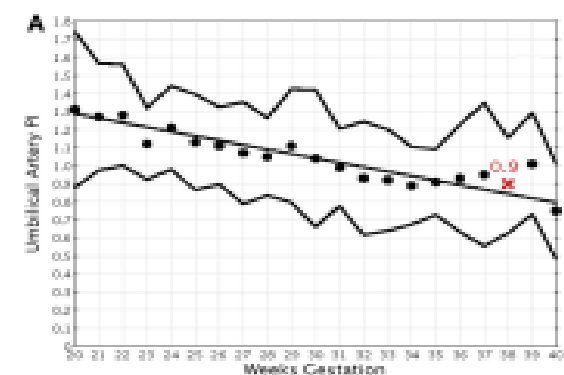
CPR is an earlier predictor of adverse pregnancy outcome at term than:

- **MCA PI**
- **UA PI alone**
- **Biophysical profile**

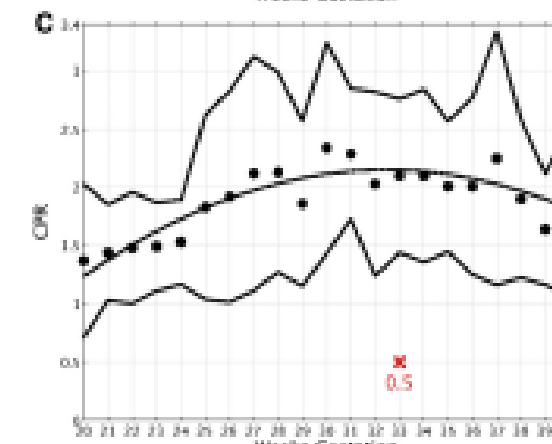
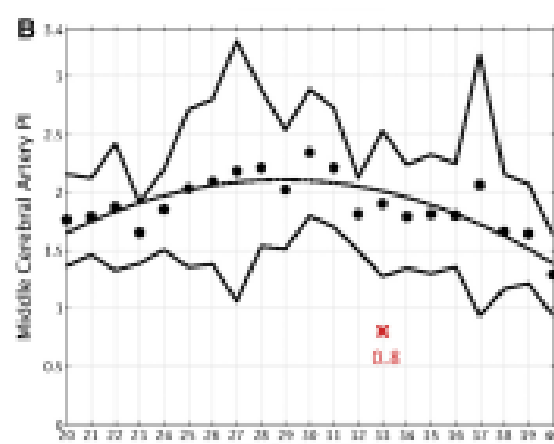
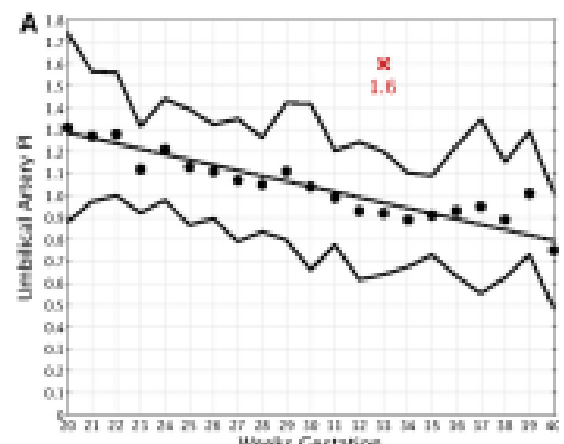
Abnormal CPR: 3 scenarios



↑UA PI
↓MCA PI
CPR <5th



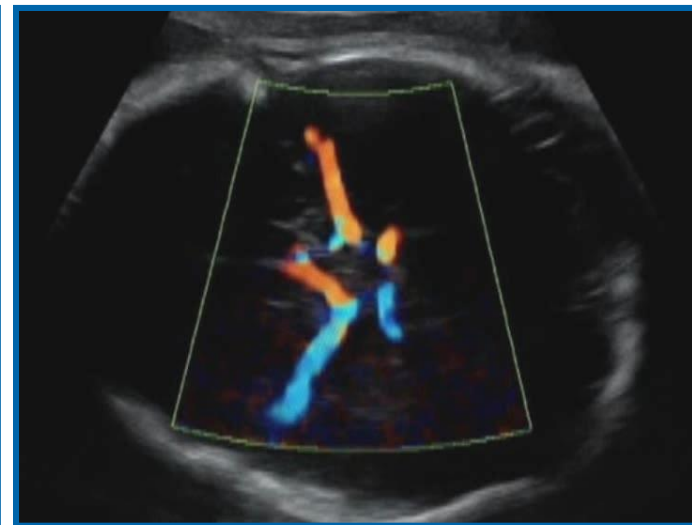
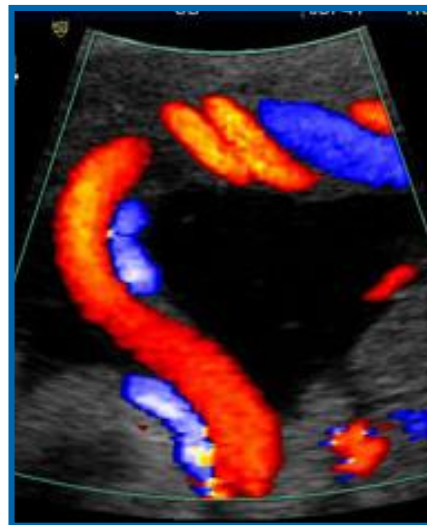
Normal UA PI
MCA PI <5th
CPR <5th



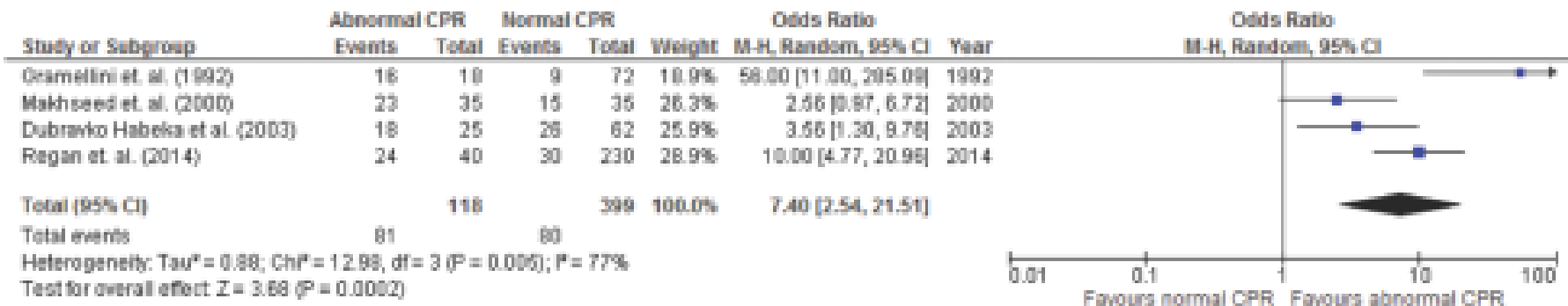
UA PI >90th
MCA PI <5th
CPR <5th

Cerebroplacental Ratio: when is it abnormal?

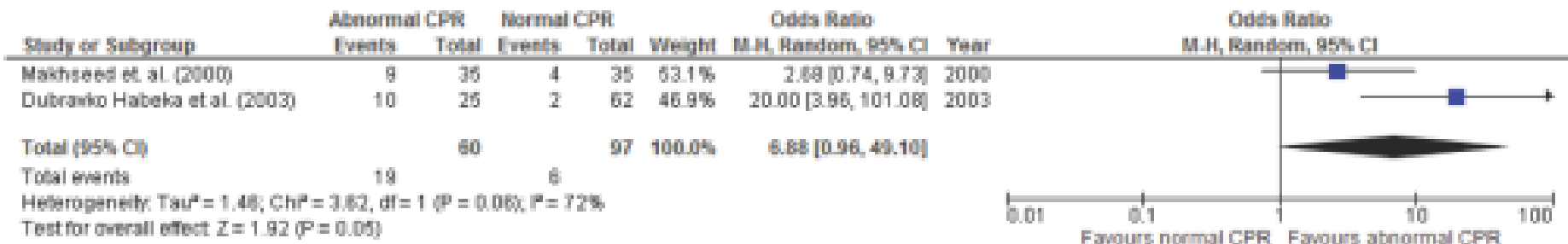
- **< 1**
- **< 1.08**
- **< 0.05 MoM**
- **< 5th centile**
- **< 2.5th centile**



CS for fetal distress: OR 7.4 (95% CI 2.5-21.5)

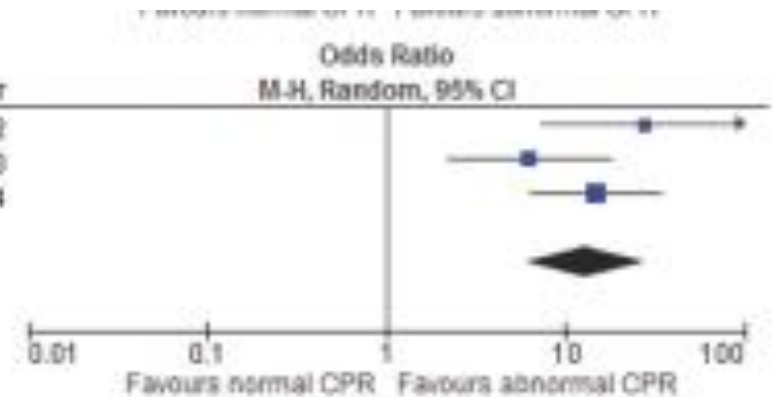


5-min APGAR scores: OR 6.9 (95% CI 0.96-49.1)



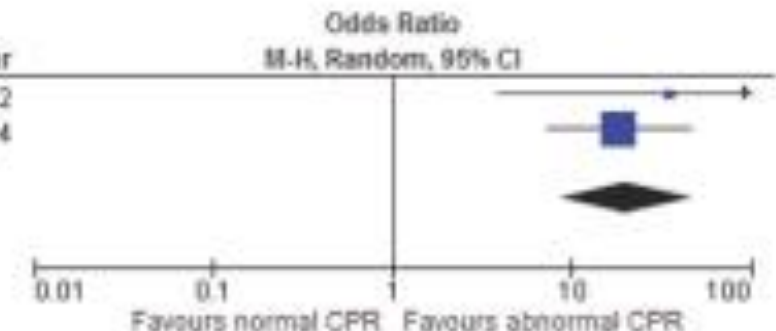
NICU admission: OR 13.0 (95% CI 6.03-27.9)

Study or Subgroup	Abnormal CPR		Normal CPR		Weight	Odds Ratio		Year
	Events	Total	Events	Total		M-H, Random, 95% CI		
Gramellini et. al. (1992)	14	18	8	72	23.9%	28.00 [7.39, 106.11]	1992	
Makhseed et. al. (2000)	26	35	11	35	33.4%	6.30 [2.23, 17.85]	2000	
Regan et. al. (2014)	32	40	49	230	42.7%	14.78 [6.40, 34.11]	2014	
Total (95% CI)		93		337	100.0%	12.96 [6.03, 27.87]		
Total events	72		68					
Heterogeneity: $\tau^2 = 0.18$; $\chi^2 = 3.22$, $df = 2$ ($P = 0.20$); $I^2 = 38\%$								
Test for overall effect: $Z = 6.56$ ($P < 0.00001$)								

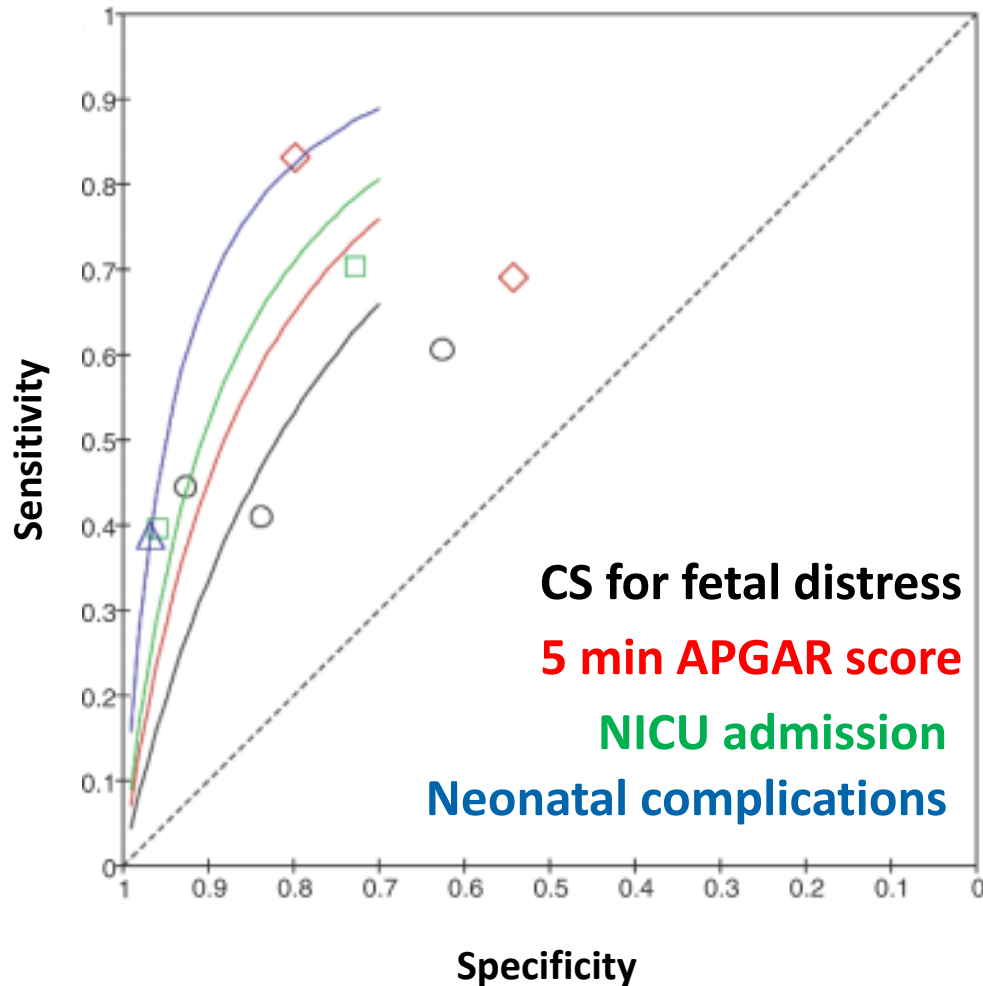


Neonatal complications: OR 20.4 (95% CI 8.7-47.6)

Study or Subgroup	Abnormal CPR		Normal CPR		Weight	Odds Ratio		Year
	Events	Total	Events	Total		M-H, Random, 95% CI		
Gramellini et. al. (1992)	6	18	1	72	14.6%	35.50 [3.92, 321.55]	1992	
Regan et. al. (2014)	34	40	54	230	85.2%	18.47 [7.36, 46.34]	2014	
Total (95% CI)		58		302	100.0%	20.35 [8.71, 47.56]		
Total events	40		55					
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.29$, $df = 1$ ($P = 0.59$); $I^2 = 0\%$								
Test for overall effect: $Z = 6.96$ ($P < 0.00001$)								



Brain Sparing in SGA/FGR



Sensitivity (%)	Specificity (%)
44-70	56-93
50-80	54-80
40-81	53-96
39-86	53-97

Consensus definition of placental FGR (2016)

Early FGR (<32 weeks)

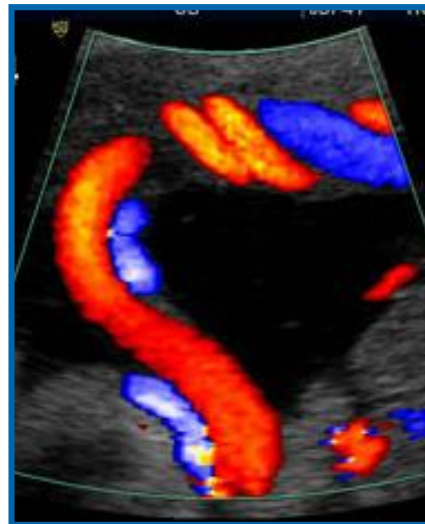
- AC <3rd centile
- EFW <3rd centile
- AEDF umbilical artery
- AC or EFW <10th centile + umbilical artery or uterine artery PI >95th centile

Late FGR (>32 weeks)

- AC <3rd centile
- EFW <3rd centile
- AC or EFW <10th centile or crossing centiles of >2 quartiles + CPR <5th centile

Early-onset (<34 wk) SGA + low CPR

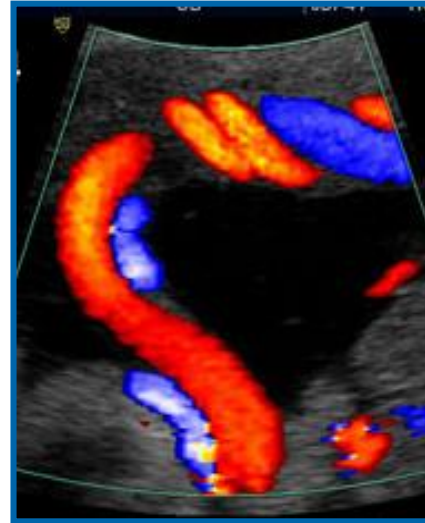
- ↓ GA at delivery
- ↓ Birthweight centile
- ↑ CS for fetal distress
- ↑ Apgar score at 5min <7
- ↑ neonatal acidosis
- ↑ NNU admission
- ↑ Neonatal morbidity
- ↑ Perinatal death



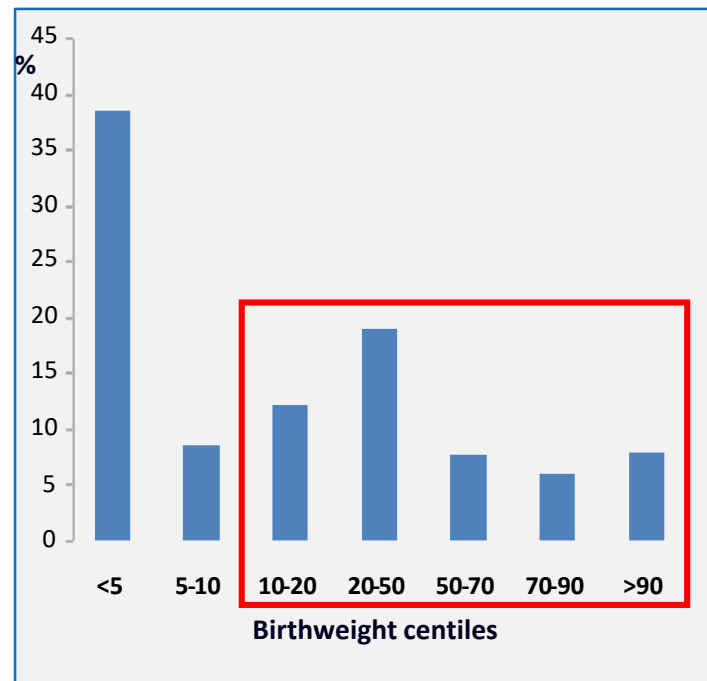
Brain Sparing in SGA/FGR

Late-onset (>34 wk) SGA or AGA + low CPR

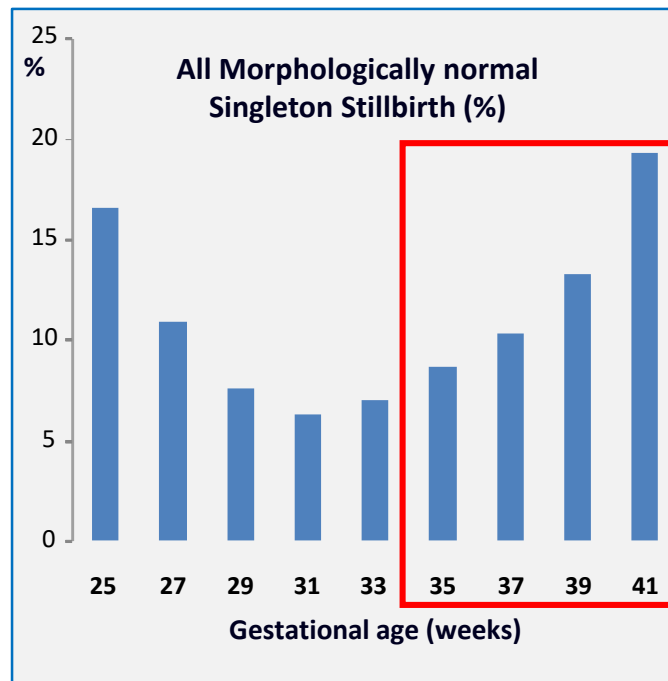
- **↑ CS for fetal distress**
- **↓ Umbilical cord pH**
- **↑ NNU admission**



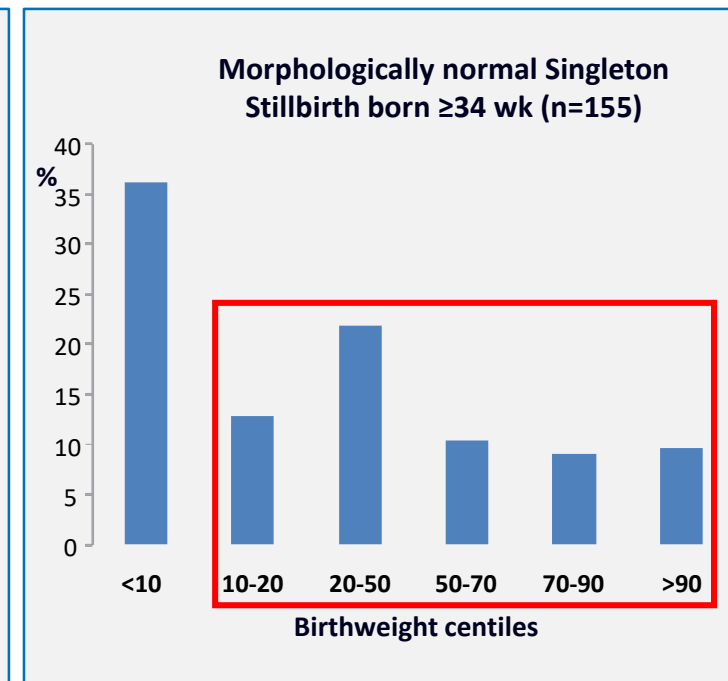
Morphologically normal singleton stillbirth and fetal size



53% of SB have BW $\geq 10^{\text{th}}$ centile



52% of SB ≥ 34 wk and 38% ≥ 37 wk



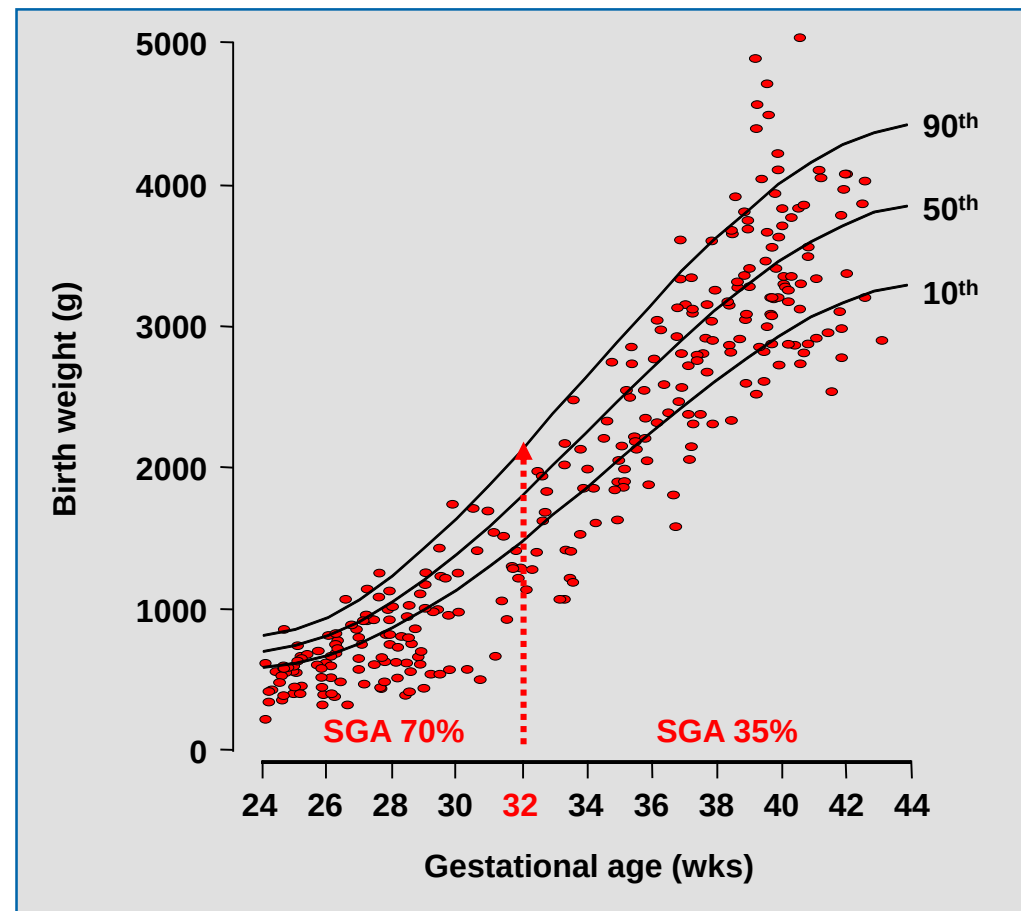
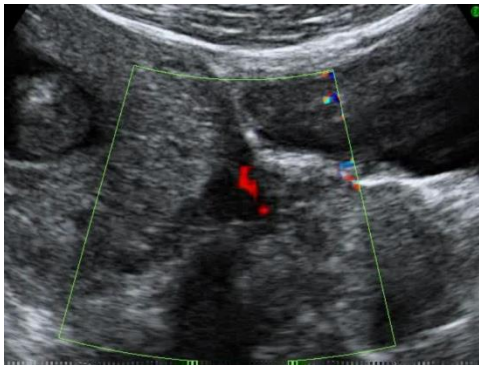
64% of SB have BW $\geq 10^{\text{th}}$ centile

Most studies investigating CPR focused on SGA (BW $< 10^{\text{th}}$ centile) pregnancies

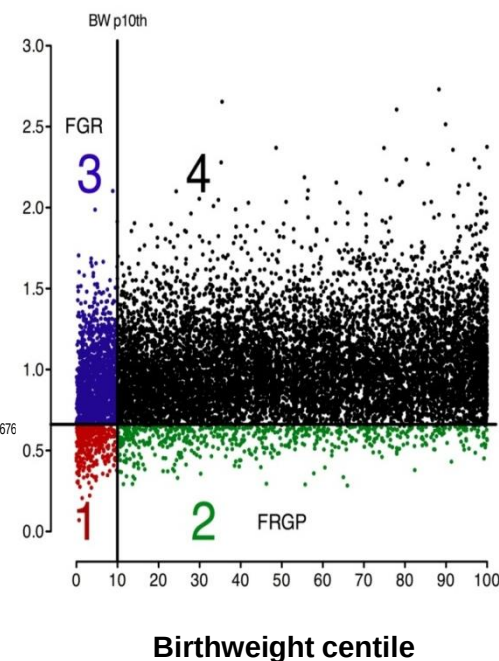
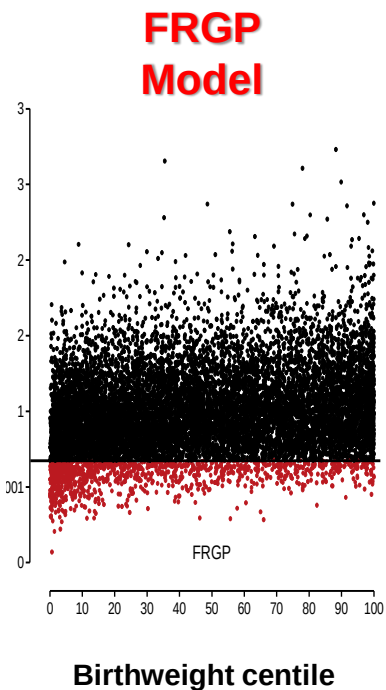
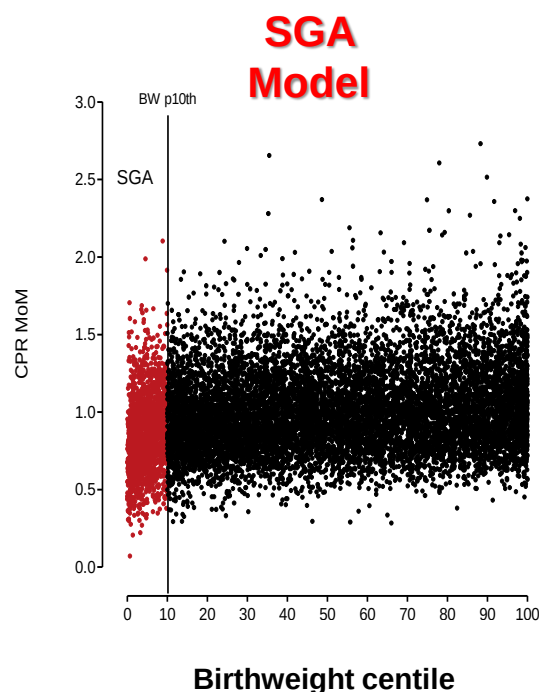
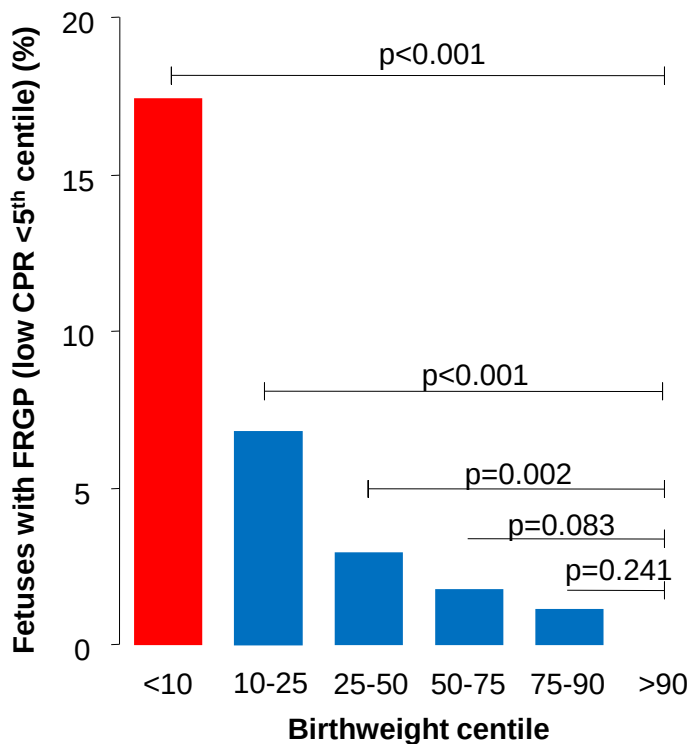
2-stage screening (12 and 32 wks)

OR (95% CI)

Black race	1.7 (1.2 - 2.5)
Smoking	1.9 (1.0 - 3.1)
Diabetes mellitus	2.9 (2.1 - 4.1)
Chronic hypertension	3.1 (1.4 - 7.0)
Assisted reproduction	2.7 (1.6 - 4.7)
Previous stillbirth	2.6 (1.5 - 4.6)
DV reversed a-wave	2.2 (1.1 - 4.4)

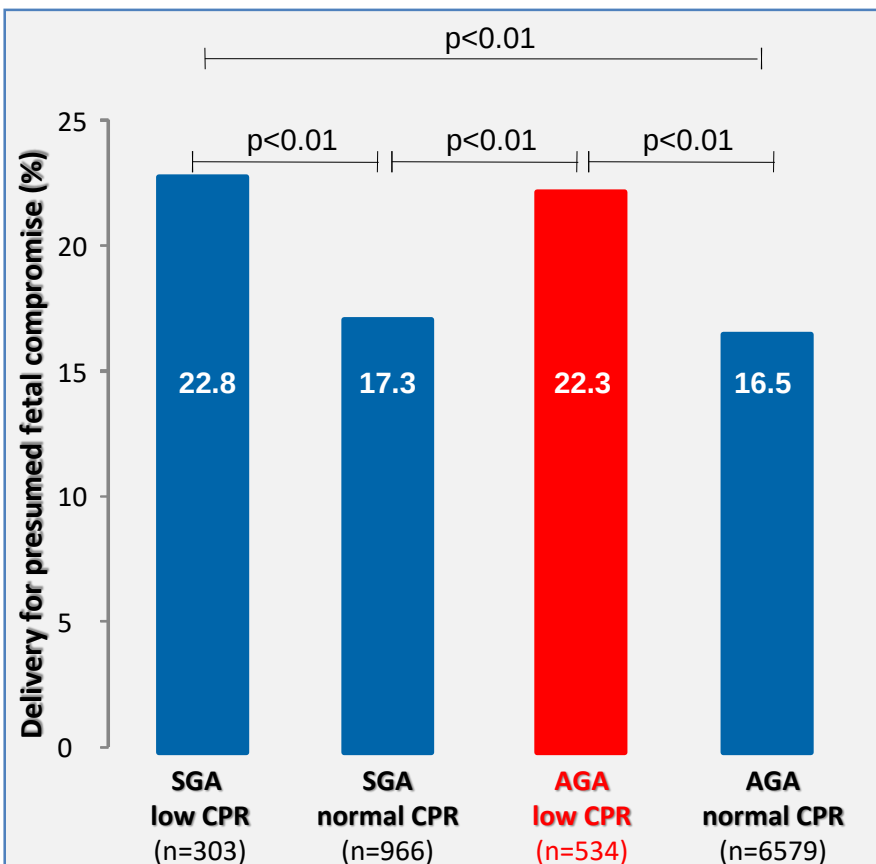
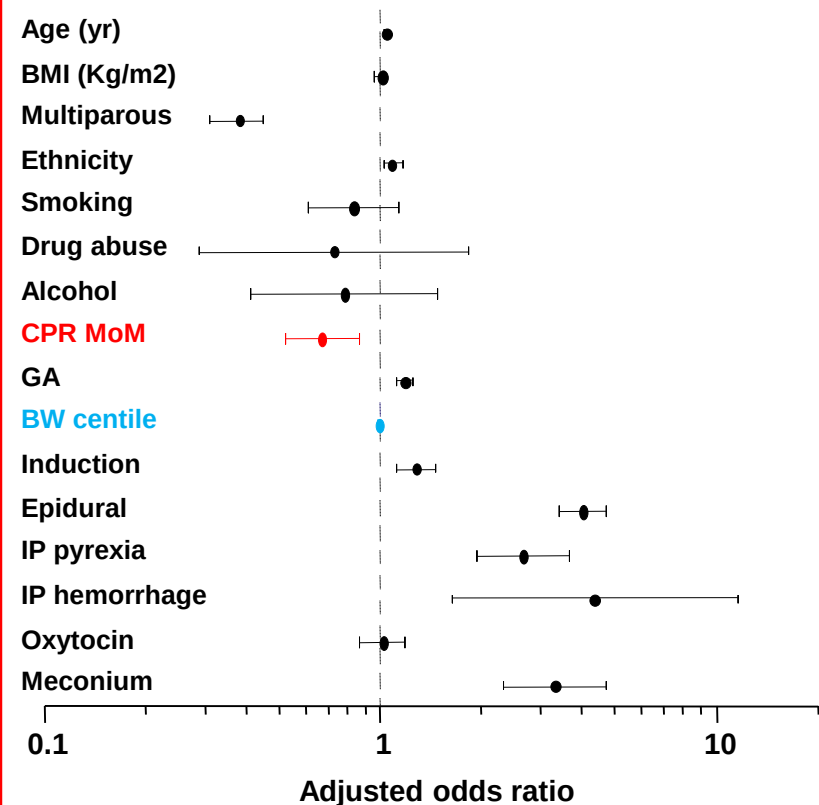


CPR and Birthweight



The lower the BW, the higher the proportion of fetuses showing redistribution

CPR at term and Delivery for presumed fetal compromise



AGA only (n=6786)

Factors	OR
Age (yr)	1.04
Multiparous	0.39
Race	1.08
CPR MoM	0.68
BW centile	0.996
GA at delivery	1.21
Induction	1.24
Epidural	4.03
IP pyrexia	2.67
IP hemorrhage	3.12
Meconium 2/3	2.87

n= 8,382 singleton pregnancies at term (≥37wk)

CPR and intrapartum fetal compromise

RESEARCH

ajog.org

OBSTETRICS

Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission?

Asma A. Khalil, MD, MRCOG; José Morales-Rosello, MD; Maddalena Morlando, MD; Hasina Hannan, MD; Amar Bhide, MD, MRCOG; Aris Papageorgiou, MD, MRCOG; Basky Thilaganathan, PhD, MRCOG

CPR and intrapartum fetal compromise

RESEARCH

www.AJOG.org

OBSTETRICS

Prediction of intrapartum fetal compromise using the cerebroumbilical ratio: a prospective observational study

Tomas Prior, BSc; Edward Mullins, BSc; Phillip Bennett, PhD; Sailesh Kumar, PhD

CPR and intrapartum fetal compromise



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journal homepage: www.elsevier.com/locate/placenta



Predicting intrapartum fetal compromise using the fetal cerebro-umbilical ratio

S. Sabdia ^{a, b}, R.M. Greer ^a, T. Prior ^a, S. Kumar ^{a, b, c, *}



AGA fetuses at term: 10% abnormal CPR

CPR

CS for intrapartum fetal distress

Abnormal

36%

Normal

10%

CPR >95th centile: No CS for fetal distress

Late-onset SGA fetuses: 39% abnormal CPR

CPR

CS for intrapartum fetal distress

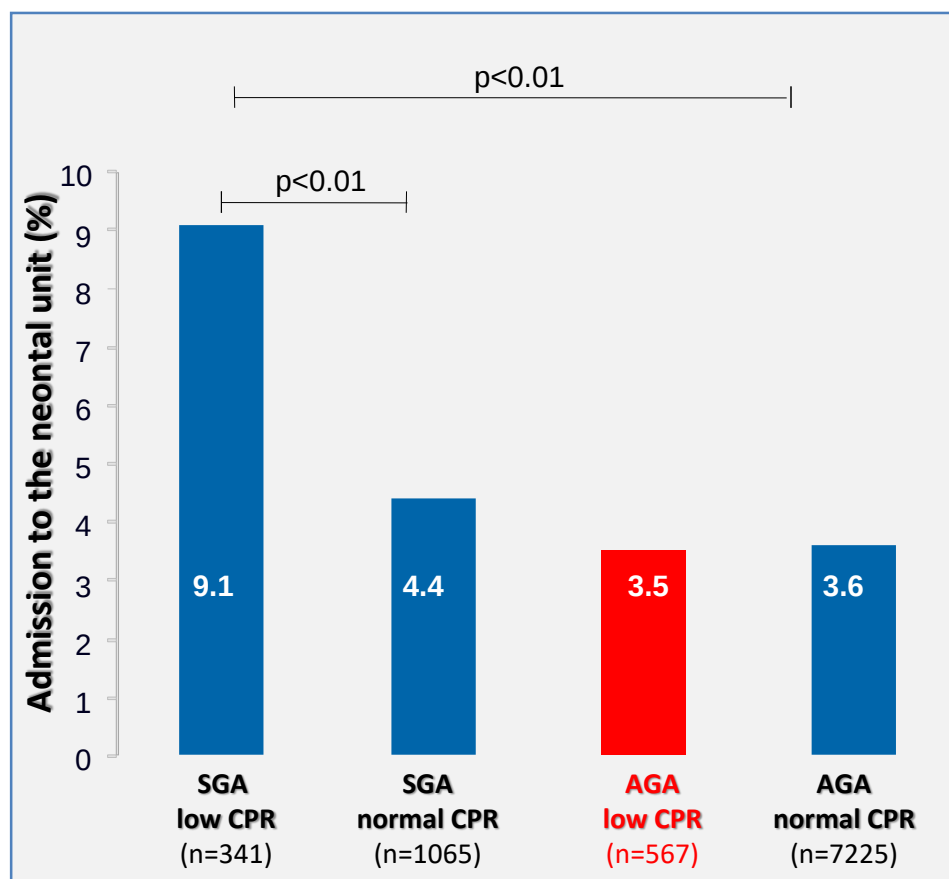
Abnormal

79%

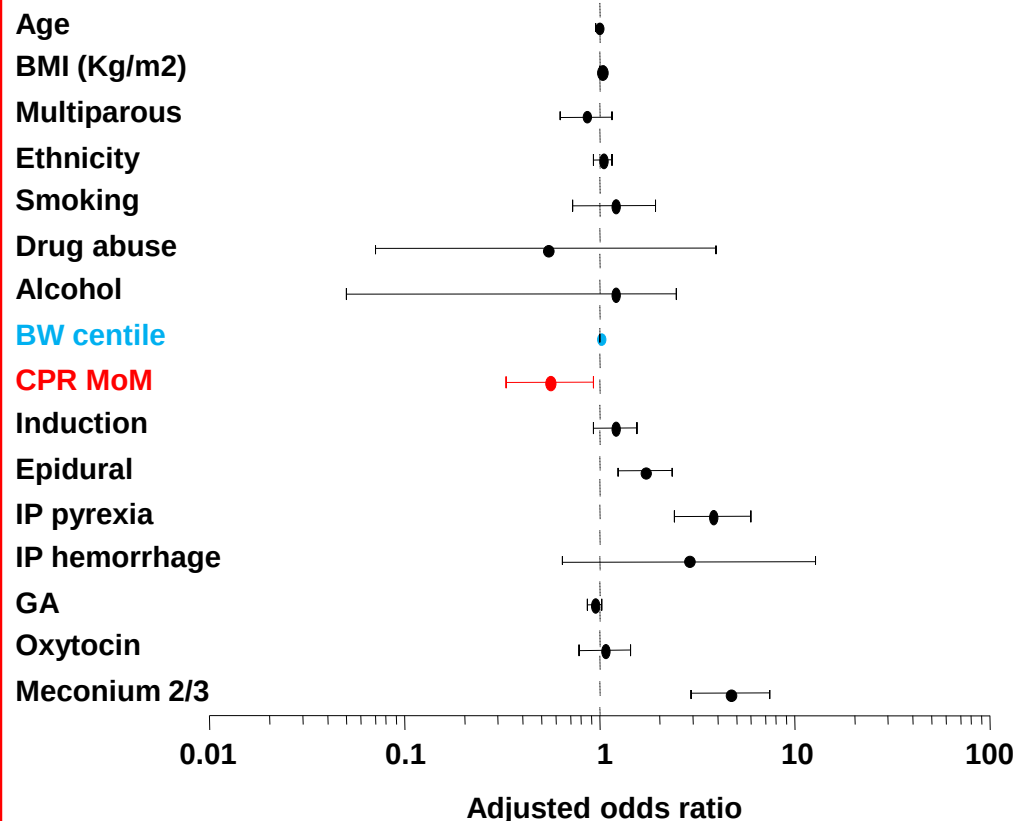
Normal

11%

CPR at term and NNU admission



n= 9,198 singleton pregnancies at term (≥37wk)



CPR at term and NNU admission

RESEARCH

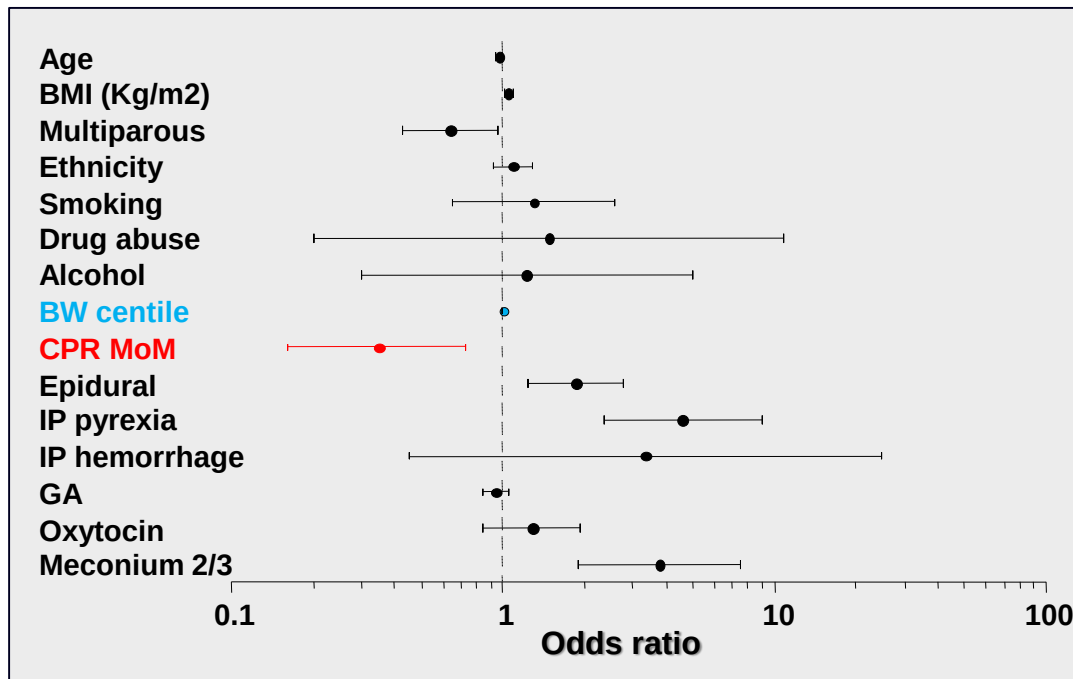
ajog.org

OBSTETRICS

The association between fetal Doppler and admission to neonatal unit at term

Asma A. Khalil, MD, MRCOG; José Morales-Rosello, MD; Malaz Elsadigg; Naila Khan;
Aris Papageorgiou, MD, MRCOG; Amar Bhide, MD, MRCOG; Basky Thilaganathan, PhD, MRCOG

CPR at term and Neonatal Morbidity



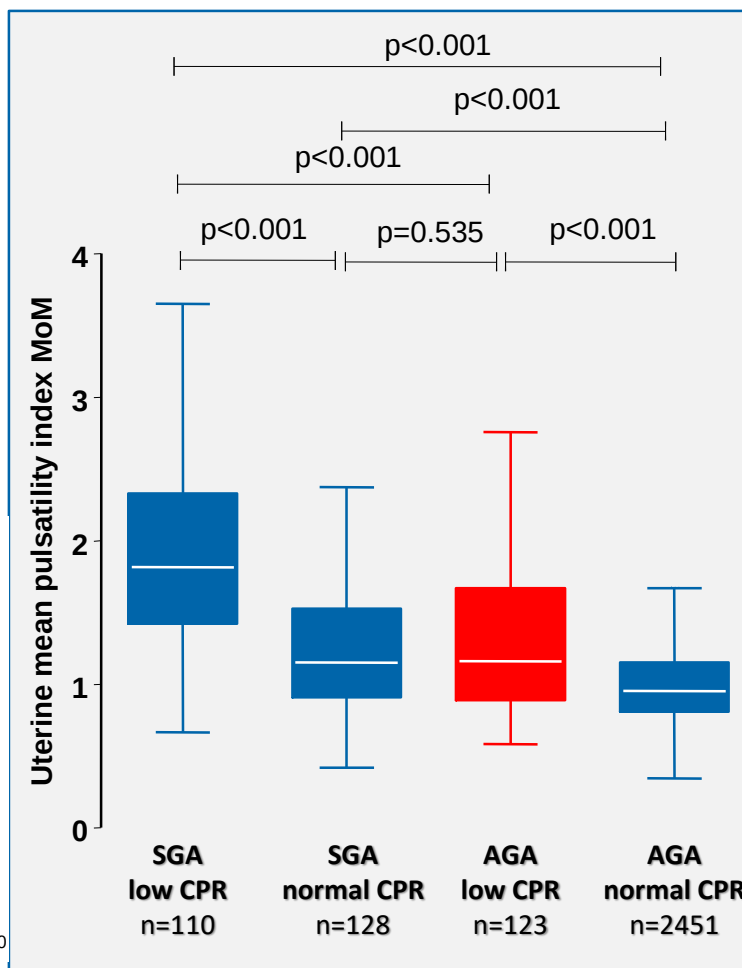
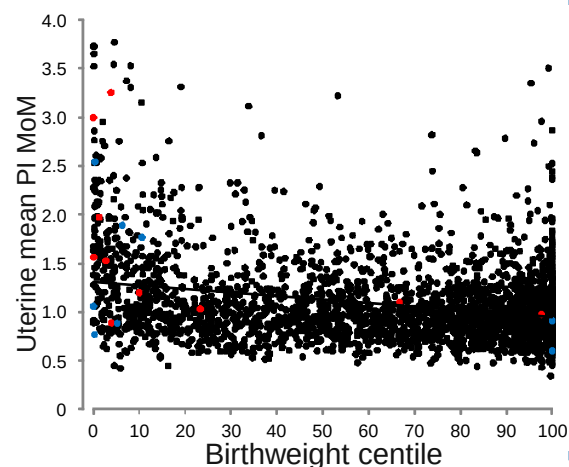
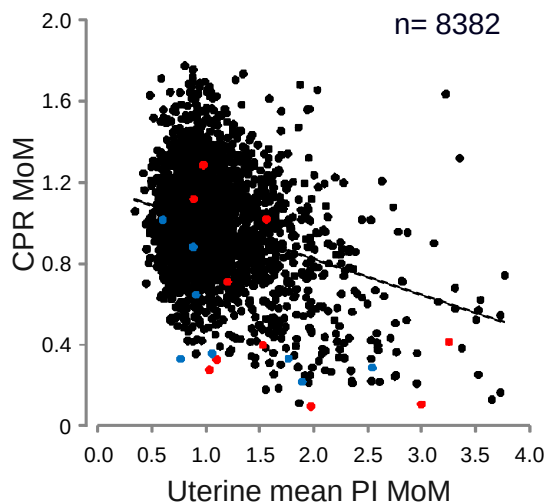
The outcome was a composite consisting of one or more of the following:

- NND
- RDS
- Culture-proven sepsis
- Stage 2 or 3 NEC
- Bronchopulmonary dysplasia
- Grade 3 or 4 IVH
- Periventricular leukomalacia

The incidence of neonatal morbidity was **1.2%**

n= 9,145 singleton pregnancies at term (≥37wk)

CPR and uterine artery Doppler >26wk



Stillbirth (n=10)

Factors	OR	P value	OR*	P value
BW centile	0.96	0.001	0.98	0.092
CPR MoM	0.004	<0.001	0.02	0.014
Uterine PI MoM	4.19	<0.001	1.09	0.87

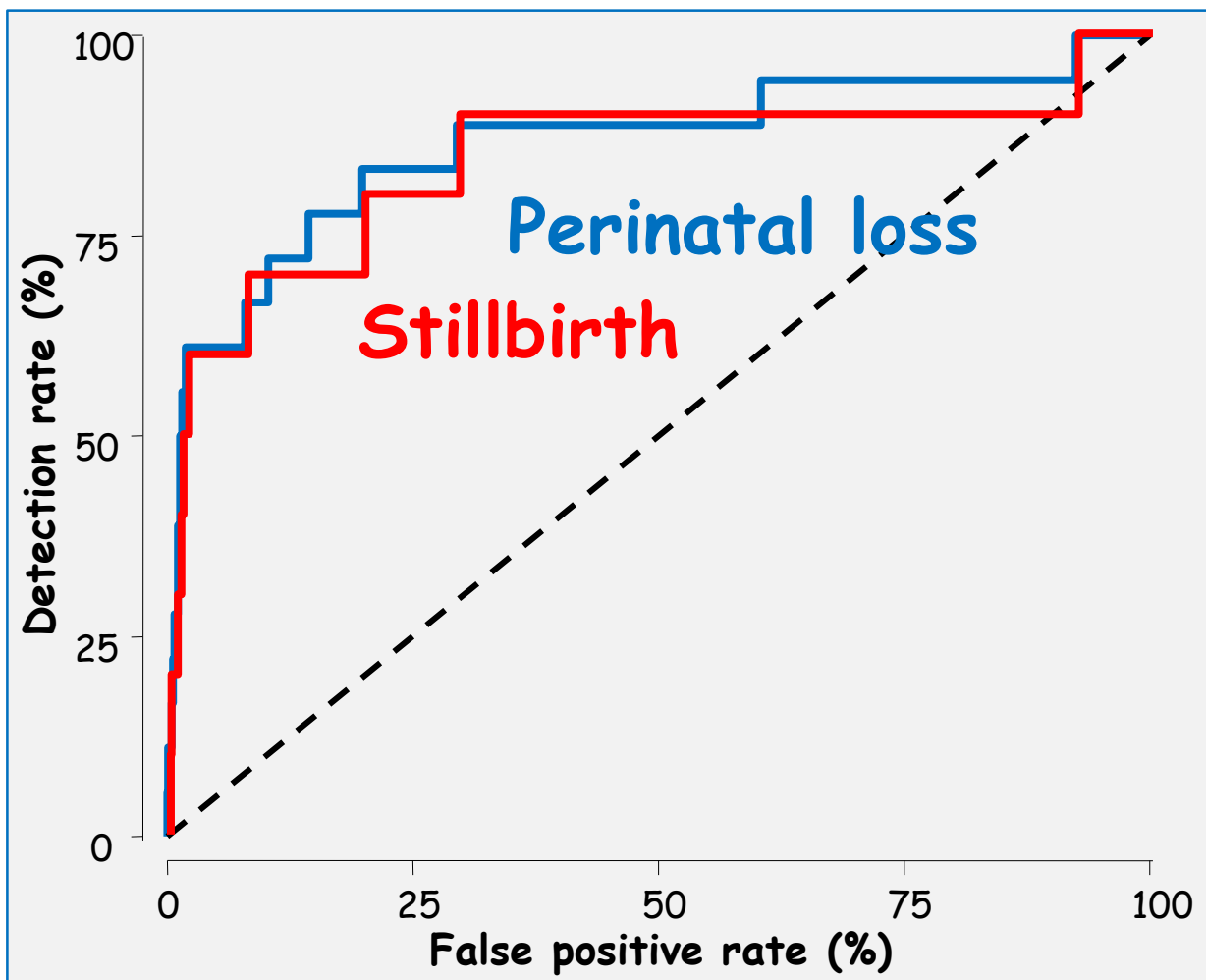
Perinatal death (n=18)

BW centile	0.96	<0.001	0.98	0.080
CPR MoM	0.003	<0.001	0.004	<0.001
Uterine PI MoM	3.36	<0.001	0.63	0.300

* adjusted

n= 2,812 singleton pregnancies

CPR and uterine artery Doppler >26wk



CPR + EFW + uterine mean PI

AUC

DR

FPR

+ LR

- LR

Stillbirth

0.85

70%

8%

8.89

0.33

Perinatal death

0.86

78%

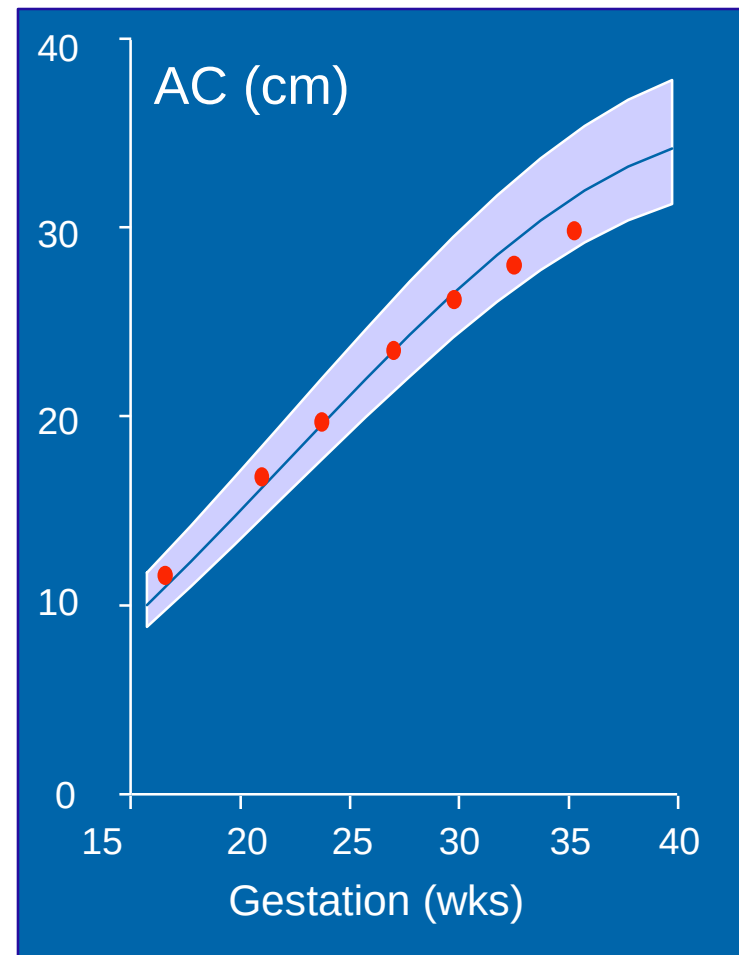
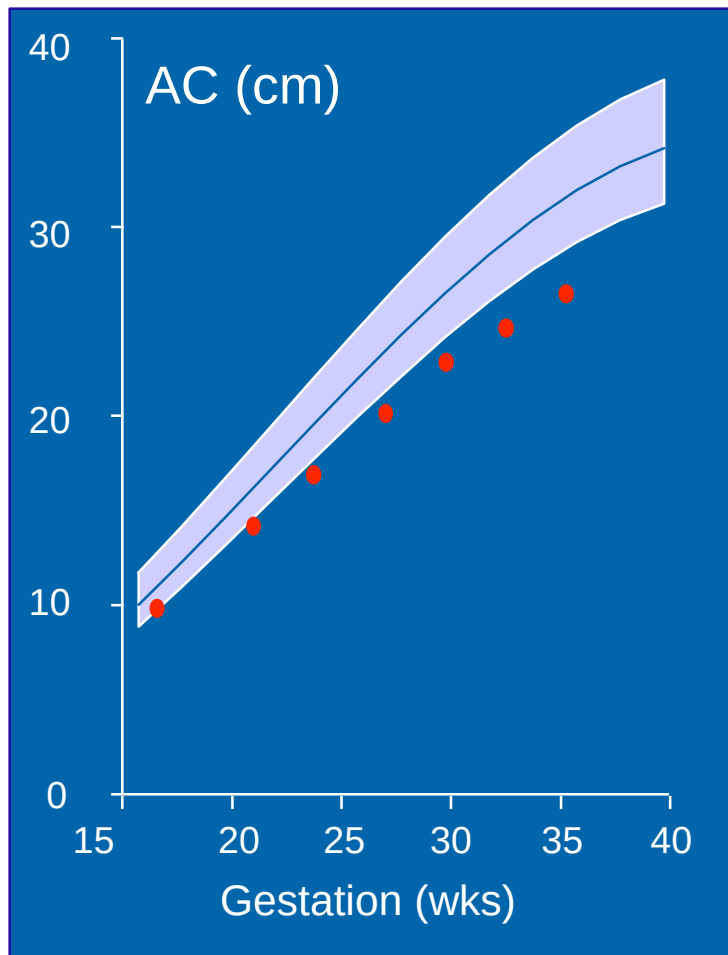
14%

5.42

0.26

n= 2,812 singleton pregnancies

Which fetus is at risk?



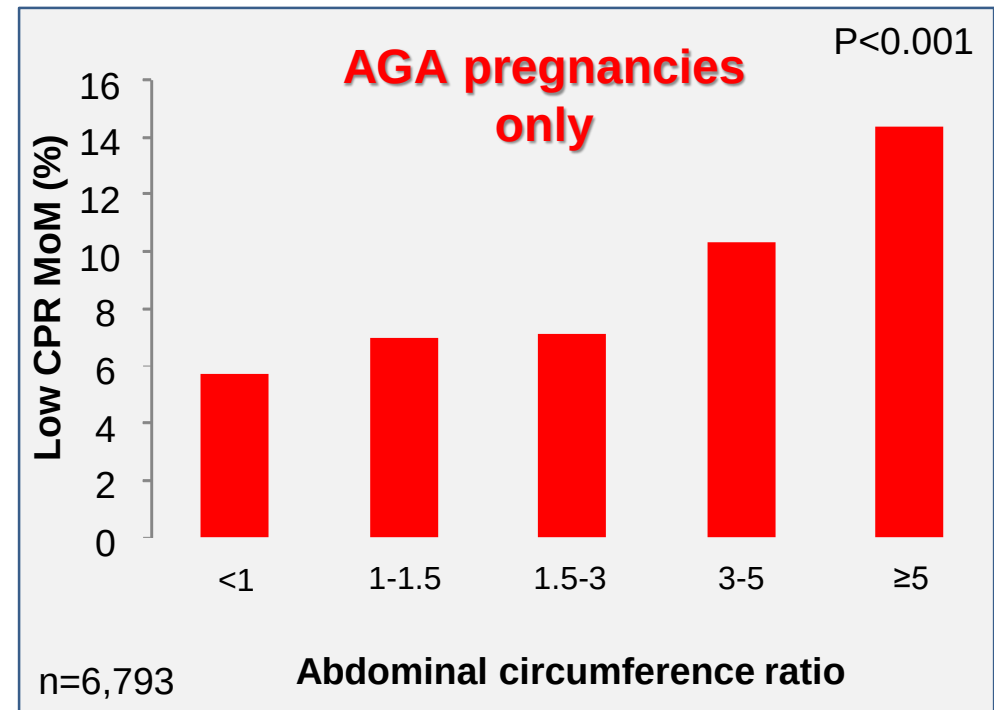
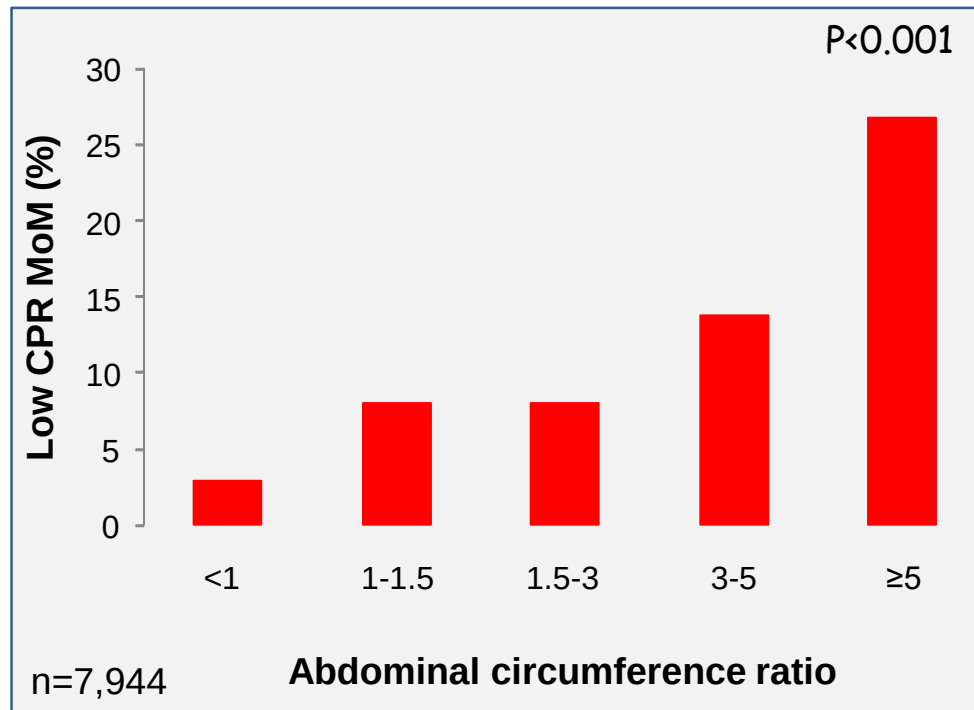
Screening for fetal growth restriction with universal third trimester ultrasonography in nulliparous women in the Pregnancy Outcome Prediction (POP) study: a prospective cohort study

Ulla Sovio, Ian R White, Alison Dacey, Dharmintra Pasupathy, Gordon C S Smith

EFW <10th centile + AC velocity in the lowest decile:

RR of SGA with neonatal morbidity 17·6 (95% CI 9·2-34·0, $p < 0·0001$)

AC ratio and CPR at term



Original Research

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OBSTETRICS

Is cerebroplacental ratio a marker of impaired fetal growth velocity and adverse pregnancy outcome?

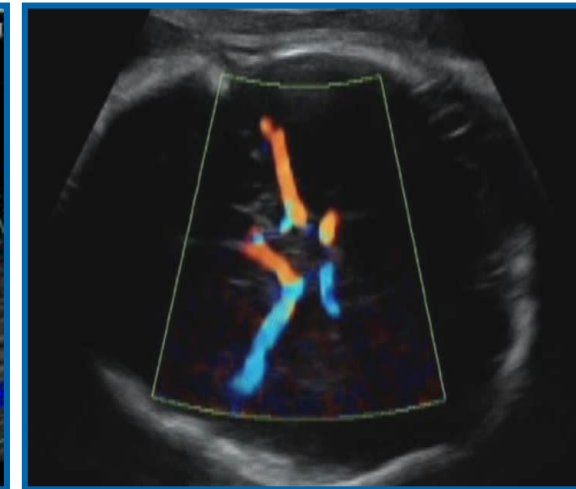
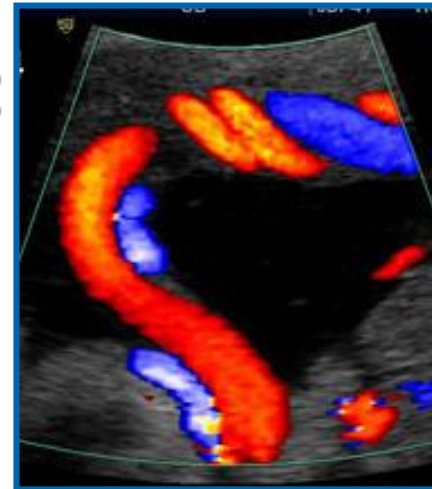


Asma Khalil, MD, MRCOG; José Morales-Rosello, MD; Naila Khan, MD; Mintu Nath, PhD; Priya Agarwal, BSc;
Amar Bhide, MD, MRCOG; Aris Papageorgiou, MD, MRCOG; Basky Thilaganathan, MD, PhD, FRCOG

When to measure the Cerebroplacental Ratio?

Third trimester US irrespective of:

- UA Doppler
- MCA Doppler
- EFW



Management Scenarios at term

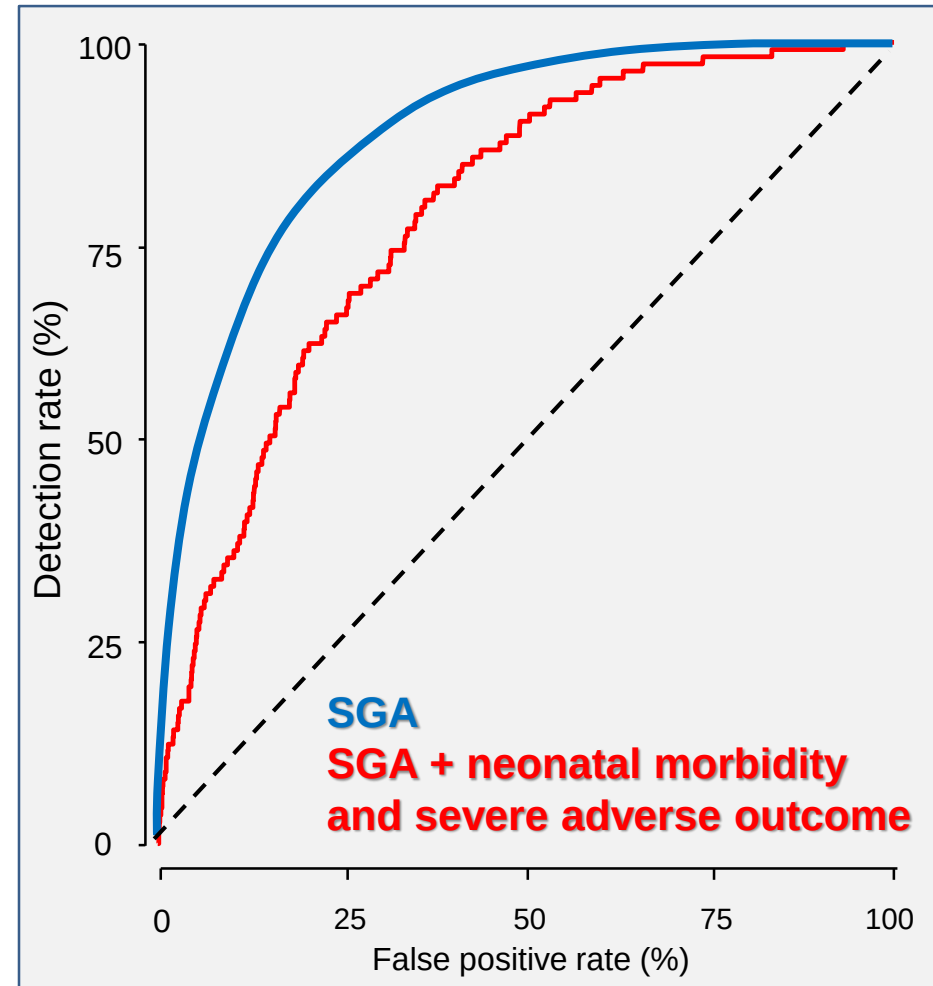
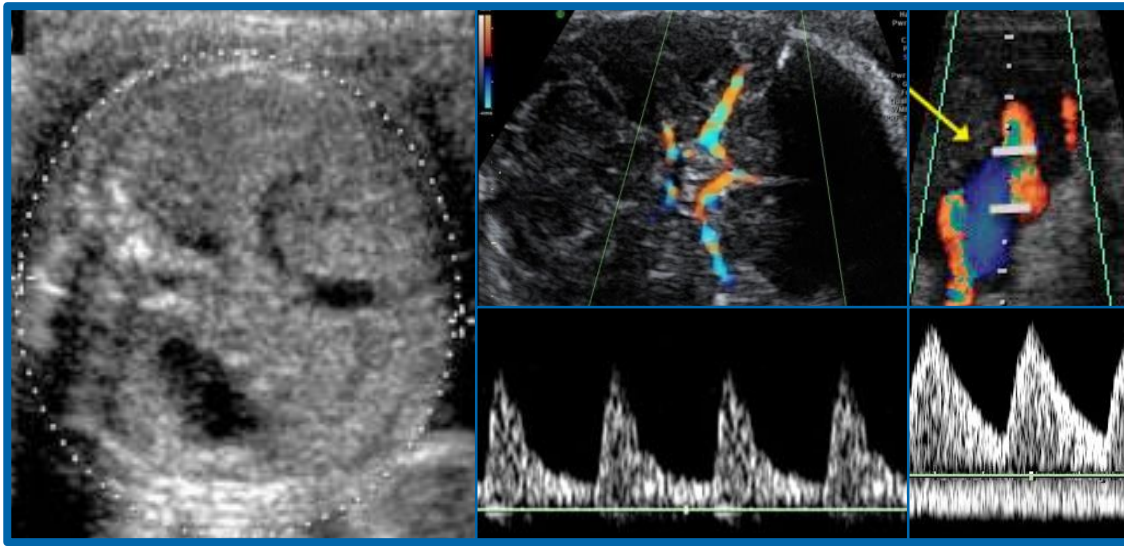
EFW centile	CPR	Growth velocity	Management
<10 th	Low	Normal or reduced	Delivery
<10 th	Normal	reduced	Delivery
<10 th	Normal	normal	Delivery ??
>10 th	Low	reduced	Delivery
>10 th	Low	normal	Delivery ??

Cerebroplacental Ratio in **Recurrent Reduced Fetal Movements**: Evidence for Worsening Fetal Hypoxaemia

	Controls (n= 1527)	Cases (RFM) (n=4500)	P-value
MCA PI MoM	0.97 (0.86-1.11)	0.95 (0.84-1.09)	<0.001
CPR MoM	0.99 (0.85-1.16)	0.97 (0.83-1.15)	0.018
CPR <5th centile (%)	60 (3.9)	272 (6)	0.002
BW centile	55.7 (30.6-79.5)	45.8 (23.7-70.3)	<0.001
SGA, n (%)	80 (5.2)	380 (8.4)	<0.001

EFW as predictor of adverse perinatal outcome

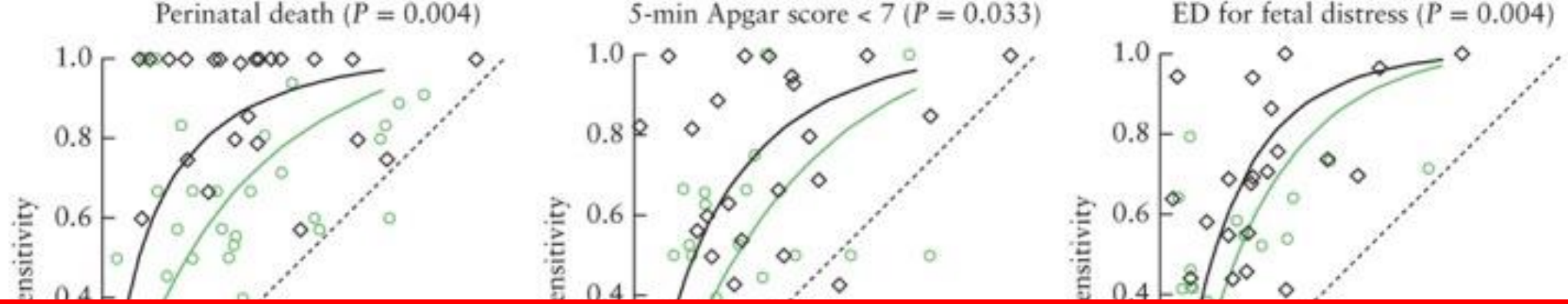
	DR (%)	FPR (%)
EFW centile: SGA	64	10
EFW: SGA + NN morbidity + severe adverse outcome	36	10



n=22,540 singleton pregnancies at term (>36wk)

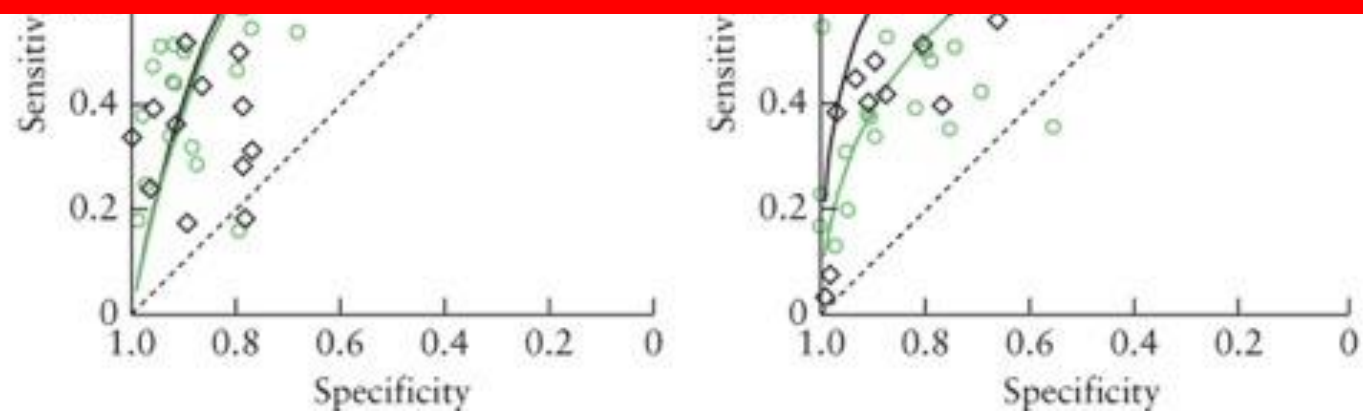
Prognostic accuracy of cerebroplacental ratio and middle cerebral artery Doppler for adverse perinatal outcome: systematic review and meta-analysis

C. A. VOLLGRAFF HEIDWEILLER-SCHREURS¹ , M. A. DE BOER¹, M. W. HEYMANS²,
L. J. SCHOONMADE³ , P. M. M. BOSSUYT⁴, B. W. J. MOL^{5,6} , C. J. M. DE GROOT¹
and C. J. BAX⁷



•CPR outperformed MCA Doppler in the prediction of composite adverse outcome ($P<0.001$) and emergency delivery for fetal distress ($P=0.013$)

•Calculating the CPR with MCA Doppler can add value to UA Doppler assessment in the prediction of adverse perinatal outcome in women with a singleton pregnancy



AGA fetuses

Utility of CPR

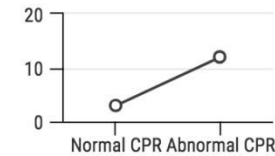


- Studies consistently report an association with increased rates of operative delivery due to presumed fetal compromise and abnormal FHR traces during labor.
- Lower CPR values correspond to lower birth weight percentiles albeit within ranges considered to be normal (>10%).
- A weak predictor of adverse outcomes in unselected populations.

Fetuses with low CPR are at increased risk of

~10%

lower birth-weight centile



○ Risk of intrapartum compromise

intrapartum compromise

SGA fetuses

Utility of CPR



- Better predictor for adverse outcome in late-FGR fetuses compared to other Doppler indices.
- Risk stratification is probable to determine the timing of delivery.
- Associated with adverse outcomes including abnormal FHR traces, operative delivery, admission to NICU, long-term neurocognitive impairment.
- Randomized trials are planned to determine clinical utility.

Fetuses with low CPR are at increased risk of



perinatal death



intrapartum compromise and NICU admission



long-term neurocognitive impairment

Management of suspected SGA fetuses

	≥37 weeks	≥38 weeks	≥39 weeks
Induce labor in the presence of	abnormal CPR and/or EFW ≤3 rd centile	EFW ≤3 rd centile Even with normal CPR	EFW ≤10 th centile Even with normal CPR
Intrapartum management	Cautious use of labor augmentation especially in nulliparous women	Use of labor augmentation should be individualized	Liberal use of labor augmentation especially in multiparous women
Risk of intrapartum Compromise	↑↑↑ in nulliparous women ↑ ↑ in multiparous women	↑↑ in nulliparous women ↑ in multiparous women	Variable ↑ to ↑↑
Risk of NICU admission	↑↑↑	↑↑	↑

Conclusions

Assessment of CPR could be more informative than standard fetal biometry in detecting late FGR

- **AGA fetuses with impaired growth velocity**
- **AGA fetuses subject to placental insufficiency**
- **Low Short term variation**
- **Need for operative delivery for fetal compromise at term**
- **NNU admission at term**
- **An independent predictor of stillbirth**

Thank you

