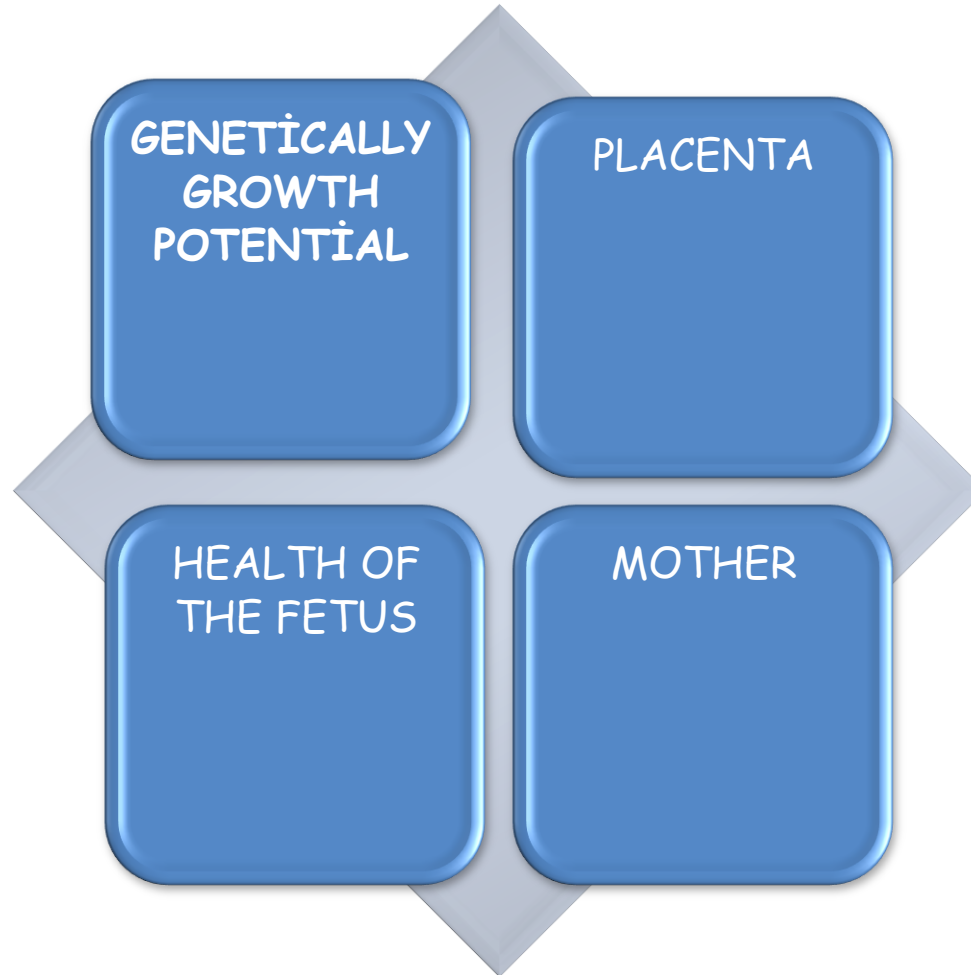# Late Onset FGR: Fetal Monitoring, Delivery Time

Özlem Pata
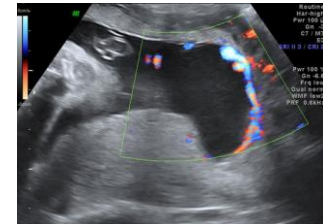Acıbadem University Obstetric And Gynecology Department

Neonatal Weight, Size and Condition
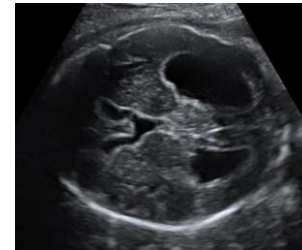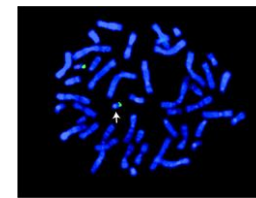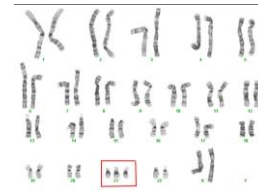
FGR-Etiology

Placenta / umbilical Cord:
velamentous cord. ins., Single Umblical Artery

Perinatal infections:
TORCH, Parvovirus, Syphilis

Genetic:
anoploidy, single gen disease

Structural:
Cardiac, GIS anomaly

FGR
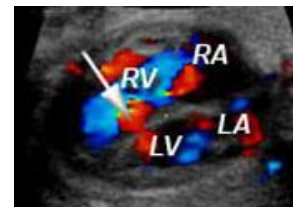
o **Sonographic estimated fetal weight <10th percentile**
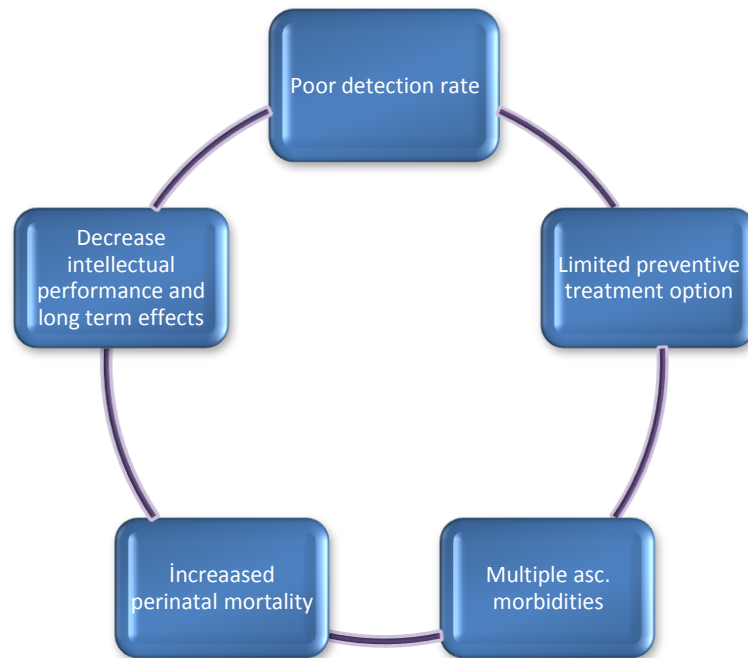
Early Onset FGR
Easy to identify, Difficult to treatment

Placental insufficiency in second trimester- early onset FGR-preterm labor

Delivery Time ?

First Option Early
neonatal mortalitity - prematurity

Second Option Wait
I.U. hypoxia, acidosis, stillbirth, asphyxia

Long term and Adult affects

Early Onset FGR

Baschat, High risk pregnancy

Early Onset FGR

Normal umbilical artery | Elevated Doppler index | Absent/reversed end-diastolic velocity

Normal middle cerebral artery | 'Brain sparing'

Normal ductus venosus | Elevated Doppler index | Absent / reversed a- wave

FHR variation loss
Late decelerations
Declining amniotic fluid volume
Loss of breathing
Loss of movement
Loss of tone

4-6 Weeks

Baschat, UOG, 2011

Late Onset FGR

○ Half of stillbirths occur > 37 weeks

○ 60-65 % of unexplaine stillbirth are (customized) FGR and small placenta

○ In >60% of all stillbirt significantt placental cord pathology is present

96% of Births

Detection For SGA
Why So İmportant ?

ncreased Perinatal Mortality

Detection antenataly decrease mortality

Vashevnik et al., 2007
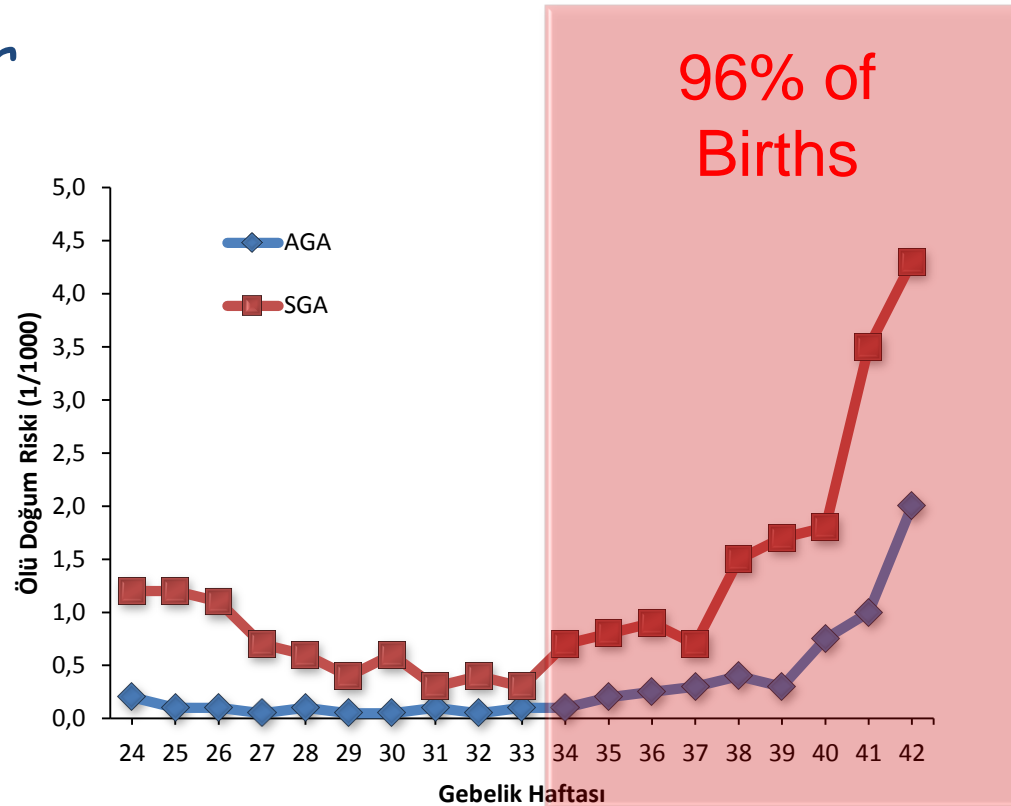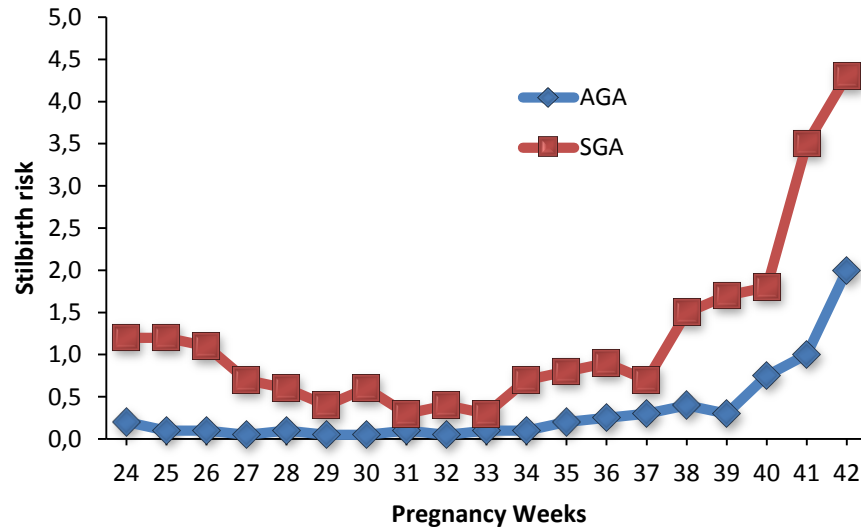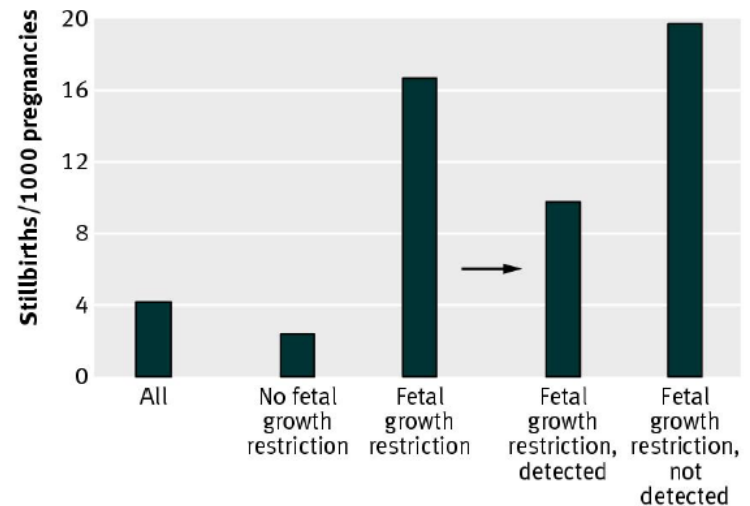
Gardosi et al., BMJ, 2013

Perinatal Mortality Risk
Birth Weight percentile at term

BW centile	PND(n)	%	Adj OR*	95% CI	p-value
<1st %ile	77	1.78	15.61	(11.52, 21.14)	<0.001
1-3rd %ile	63	0.62	5.51	(4.01, 7.59)	<0.001
3-5th %ile	46	0.47	4.13	(2.90, 5.89)	<0.001
5-10th %ile	90	0.34	3.11	(2.33, 4.15)	<0.001
10-25th %ile	185	0.23	2.10	(1.64, 2.69)	<0.001
25-50th %ile	244	0.17	1.58	(1.25, 2.01)	<0.001
50-75th %ile	166	0.11	1.06	(0.82, 1.36)	0.655
75th-90%ile	99	0.11	1.00	reference category	
90-95th %ile	40	0.13	1.28	(0.88, 1.85)	0.193
95th-97th %ile	18	0.14	1.33	(0.81, 2.21)	0.263
97-99th %ile	17	0.13	1.14	(0.67, 1.95)	0.615
>99th %ile	26	0.3	2.79	(1.81, 4.30)	<0.001

614.000 birth, 1999-2008

Francis, 2012

Other neonatal morbidities...

Table 3 Outcomes of >72,000 Live-Born Singleton Term Infants Born at ≥37 Weeks of Gestation in Relation to Birth-Weight Percentile

Outcome	Birth-Weight Percentile					
	≤3rd (n = 3184)	4th-5th (n = 2065)	6th-10th (n = 5254)	11th-15th (n = 5400)	16th-25th (n = 10,857)	26th-75th (n = 55,601)
Apgar score ≤3 at 5 min	7 (0.2)*	1 (<0.1)	6 (0.1)	5 (0.1)	9 (0.1)	38 (0.1)
Umbilical-artery blood pH ≤7.0	28 (0.9)*	12 (0.6)	28 (0.5)	27 (0.5)	37 (0.3)	212 (0.4)
Intubation in delivery room	70 (2.2)*	11 (0.5)	39 (0.7)	39 (0.7)	70 (0.6)	317 (0.6)
Seizures during first 24 h after birth	14 (0.4)*	4 (0.2)	14 (0.3)*	9 (0.2)	16 (0.1)	68 (0.1)
Sepsis (positive blood culture)	15 (0.5)*	6 (0.3)	12 (0.2)	15 (0.3)	28 (0.3)	125 (0.2)
Death in first 28 days	9 (0.3)*	2 (0.1)	2 (<0.1)	3 (0.1)	3 (<0.1)	18 (<0.1)

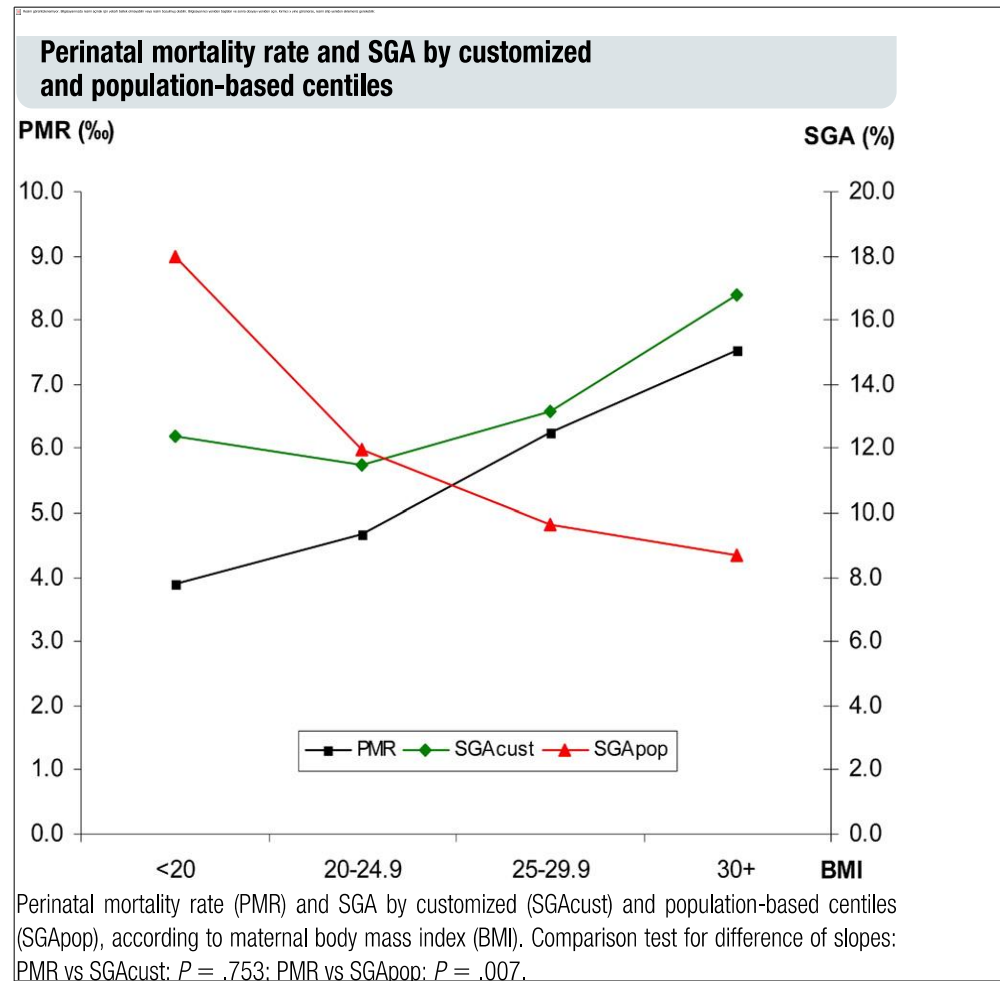Values are n (%).
Reprinted with permission from McIntire et al.[5]
*P < 0.05 for the comparison with the infants with birth weights in the 26th through 75th percentiles for gestational age.

McIntyre et al., NEJM, 1999

Customized Charts

Estimated Birth weight should be adjusted or customized

- Sex
- Maternal characteristics.
  - Height
  - Weight
  - Parity
  - Ethnic

Perinatal mortality rate and SGA by customized and population-based centiles

PMR (‰) SGA (%)

Perinatal mortality rate (PMR) and SGA by customized (SGAcust) and population-based centiles (SGApop), according to maternal body mass index (BMI). Comparison test for difference of slopes: PMR vs SGAcust: $P = .753$; PMR vs SGApop: $P = .007$.

Customized Growth Chart

Mrs. Small

Mrs. Large
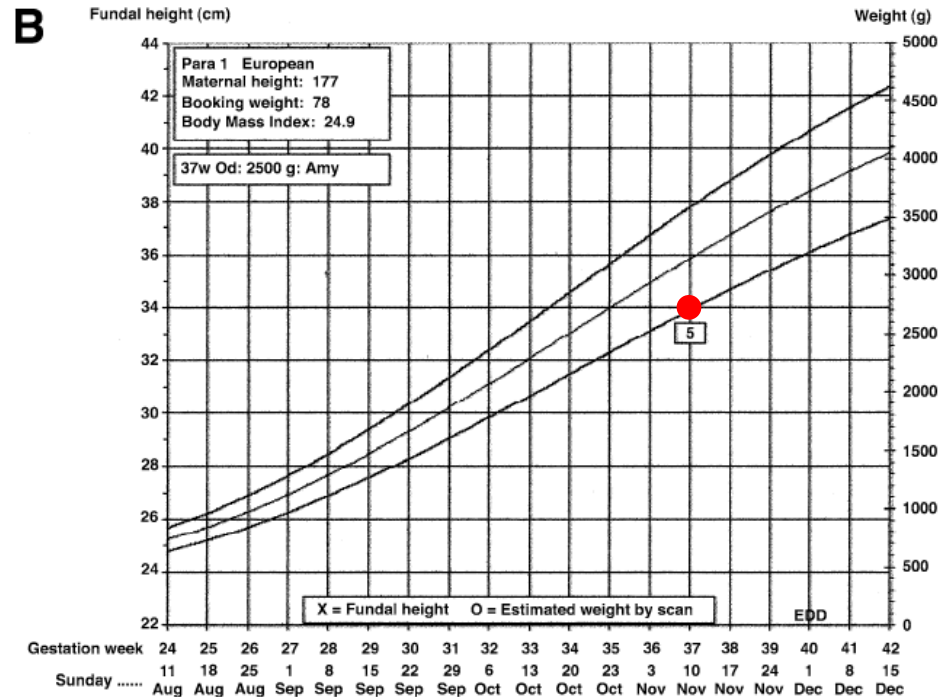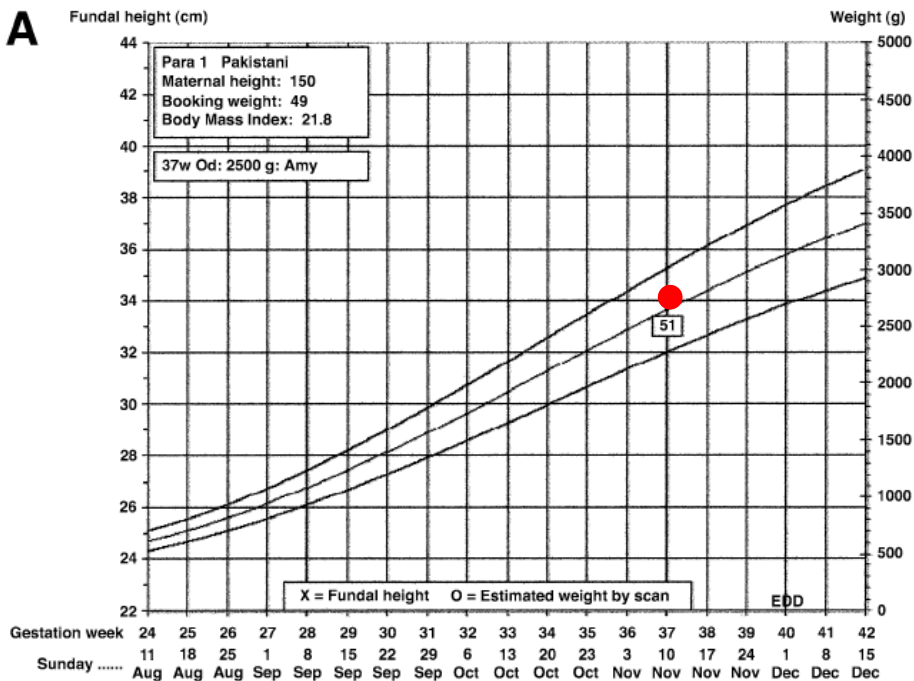
"Customized growth standards"

Customized Grow	Etnicity, Maternal weight (before pregnancy), Maternal height, Fetal gender, Parity

* GROW = Gestation Related Optimal Weight
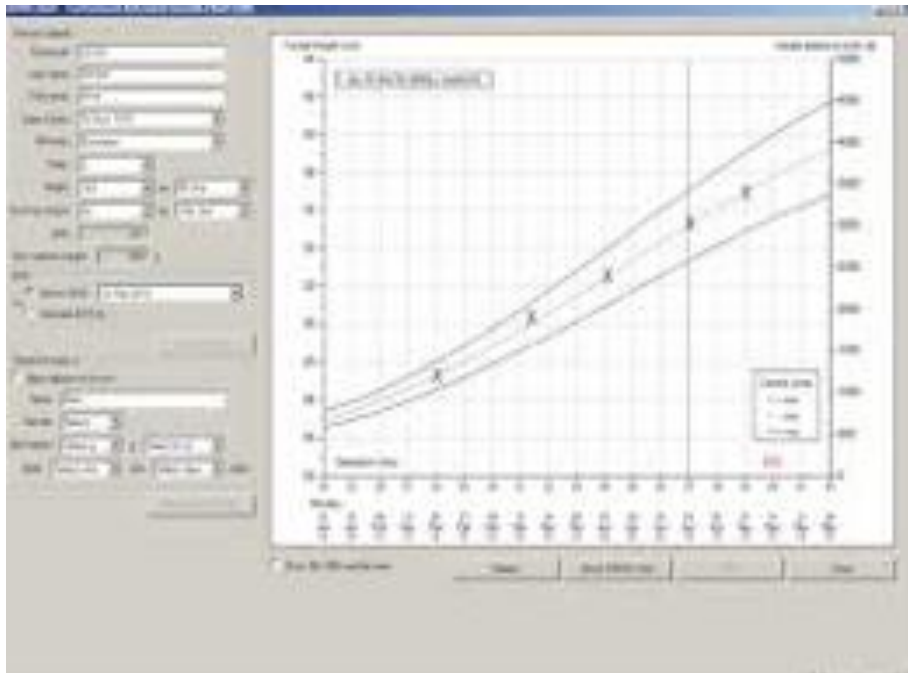
improve the ability of
fetal biometry to detect high-risk
fetuses.

Decrease false negative
SGA (<10.p) fetuses 28% normal
LGA (>90.p.) fetuses 22% normal
İncrease spesificity

Decrease unnecessary advanced
care and maternal anxiety

Gardosi et al., Lancet, 1992

Late Onset FGR
Difficult to diagnosis

1- Perinatal mortality high

2- Diagnosis is diffucult

:
Fundal height measurement sensitivity %17,
PPD %20
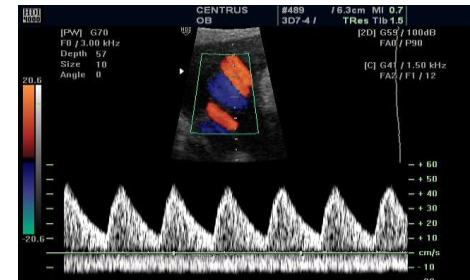
Sparks, 2011

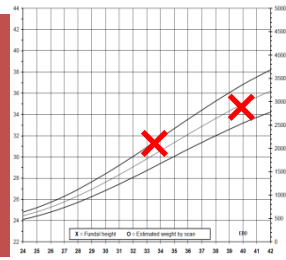**Estimated fetal weight by US:**
+/-15 %failure, at the edge accuracy low

Scioscia, 2008

Umbilical artery Doppler:
Almost normal (cant be used for"screening"

Does slow growth mean that placental insufficiency ?

Fetal adaptation:
At the advanced pregnacy weeks with slow grow MCA PI decrease ("brain sparing")

Operative delivery: *P= 0.02
suspected fetal compromise
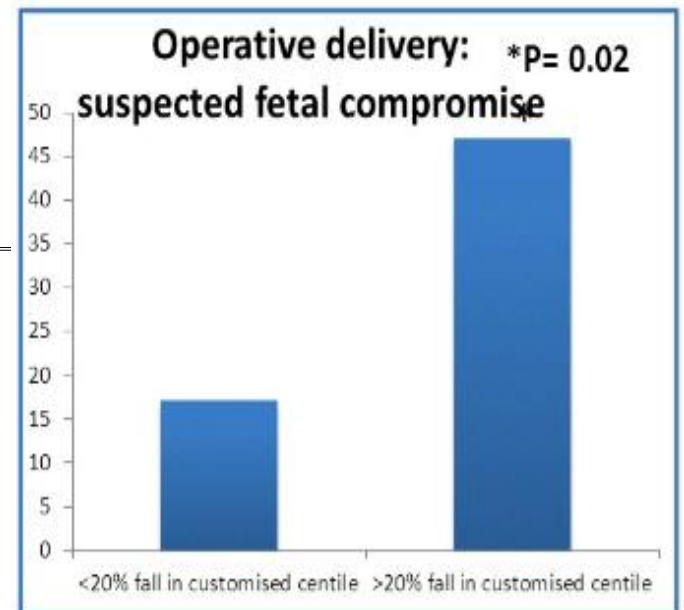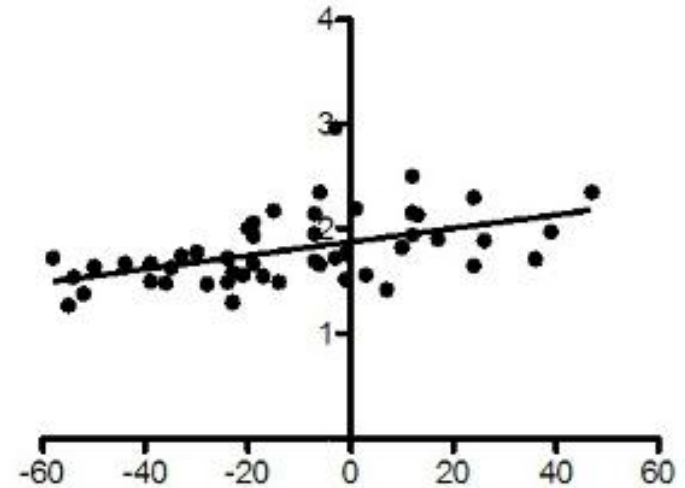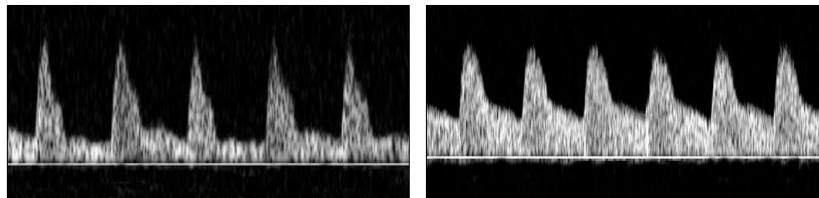
	SGA	AGA
Weight <3 percentile	54.2%	9.9% i
Histological abnormalities	78.2%	25.4%
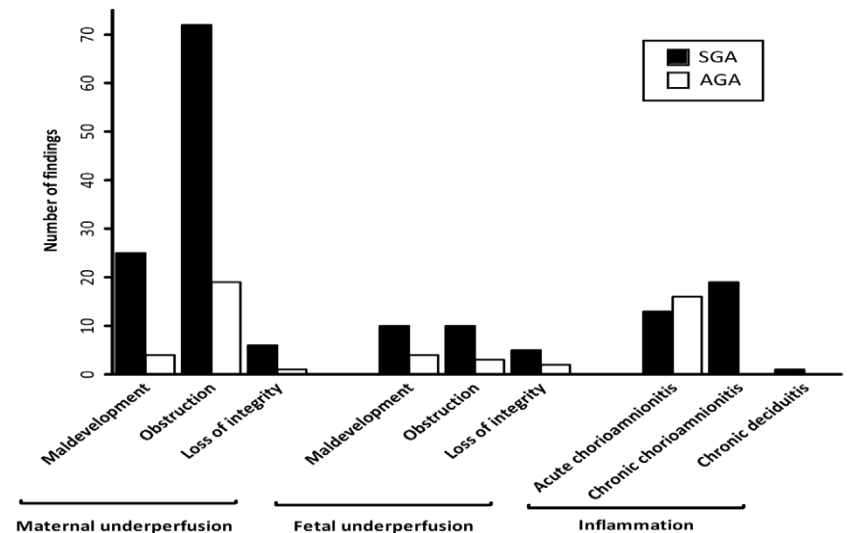
. **1.** Distribution of placental findings in small-for-gestational age births (S
: 161) and adequate-for-gestational age births (AGA, $n = 46$), grouped by category
ions.

Latent insufficiency in uteroplacental blood supply. Need for new markers of placental disease.

Parra-Saavedra. et al Placenta 2013:34
1136-1141

Late Onset FGR

o Abnormal Doppler's in umblical artery only occur in case of 30-50 % reduction of placental function/capacity

o Late in pegnancy fetus can not live just only %50 percent capacity of placenta

Risk Factors For 3rd Trimester Stillbirth

	OR Multivariate multivariate
FGR	7 (3.3-15.7)
Age>35	4.1 (1.0-16.5)
BMD >25	4.7(1.1-10.2)
Education <10 years	3.4(1.2-9.6)
FGR+ >BMD 25	71 (14-350)

Froen, Gardosi. Et al. 2004
Acta Obstet Gynecol Scan.
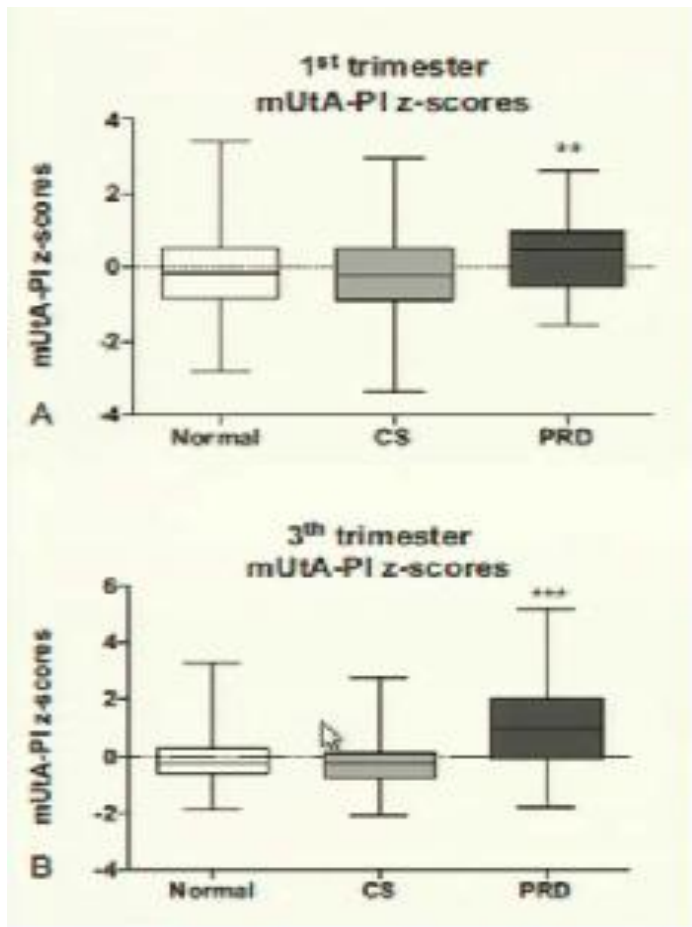
Table 4 Concordance between first- and third-trimester abnormal mUtA-PI z-scores.

mUtA-PI z-scores	Third trimester	
	normal (<2 SD)	abnormal (≥2 SD)
First trimester, normal (<2 SD)	878	31
First trimester, abnormal (≥ 2SD)	31	5

mUtA-PI, mean uterine artery pulsatility index: SD, standard deviation.

Llurba E, 2013 AJPerinatol
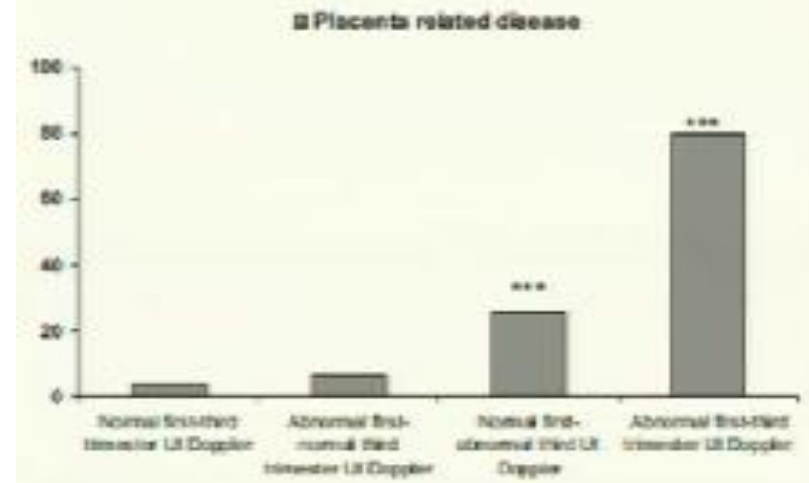
Late Onset FGR

Perinatal complications and long-term neurodevelopmental outcome of infants with intrauterine growth restriction

Anne-Karen von Beckerath; Martina Kollmann, MD; Christa Rotky-Fast, MD;

Long-term outcomes

Long-term outcome	IUGR (n = 146)		SGA (n = 215)		P value	OR	95% CI
	n	%	n	%			
Neurodevelopmental outcome							
Normal	110	75.34	203	94.42			
Abnormal	36	24.66	12	5.58	< .0001	5.54	2.77–11.08
Grade of disability							
Mild	22	15.07	7	3.26	< .0001	5.27	2.19–12.70
Moderate	8	5.48	5	2.33	ns		
Severe	6	4.11	0	0	.004	19.94	1.11–357.0
Impaired domain							
Motor	20	13.70	8	3.72	.001	4.11	1.76–9.61
Speech	22	15.07	8	3.72	.0002	4.60	1.98–10.63
Cognition	17	11.64	3	1.40	< .0001	9.31	2.67–32.41
Hearing	1	0.68	1	0.47	ns		
Vision	13	8.90	2	0.93	.0002	10.41	2.31–46.88
Cerebral palsy							
Diplegia	2	1.37	0	0	ns		
Hemiplegia	1	0.68	0	0	ns		
Infant growth							
Appropriate	115	78.77	199	92.56			
Dystrophic	31	21.23	16	7.44	.0002	3.35	1.76–6.40

Long-term outcome of infants with IUGR compared with constitutionally SGA fetuses.
CI, confidence interval; *IUGR*, intrauterine growth restriction; *ns*, not significant; *OR*, odds ratio; *SGA*, small for gestational age.

von Beckerath. Perinatal and long-term outcome after intrauterine growth restriction. Am J Obstet Gynecol 2013.

AJOG 2013

Cerebral Palsy and restricted growth status at birth: population based study: 334 infants with CP

		OR	
Early preterm	<34	0.8	(0.4-1.4
Late preterm	34-37	1.1	0.4-3.4
Term	>37	5.2	2.7-10.1

- Severely SGA birthweights had a 5- to 7-fold risk of CP

- Combination of malnutrition and fetal hypoxia

Jacobsson L BJOG 2008

Pathways of neuronal and cognitive development in children born SGA or late preterm

Neurological assessment	Control	Late Pretem	SGA
Abnormal Bender test	6.3%	16.7%	27.3
RNFL (μm)	97	100	89.7
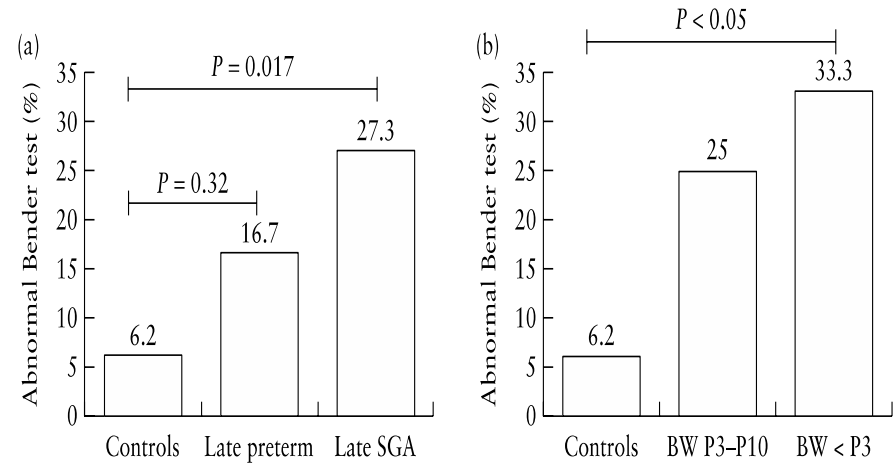
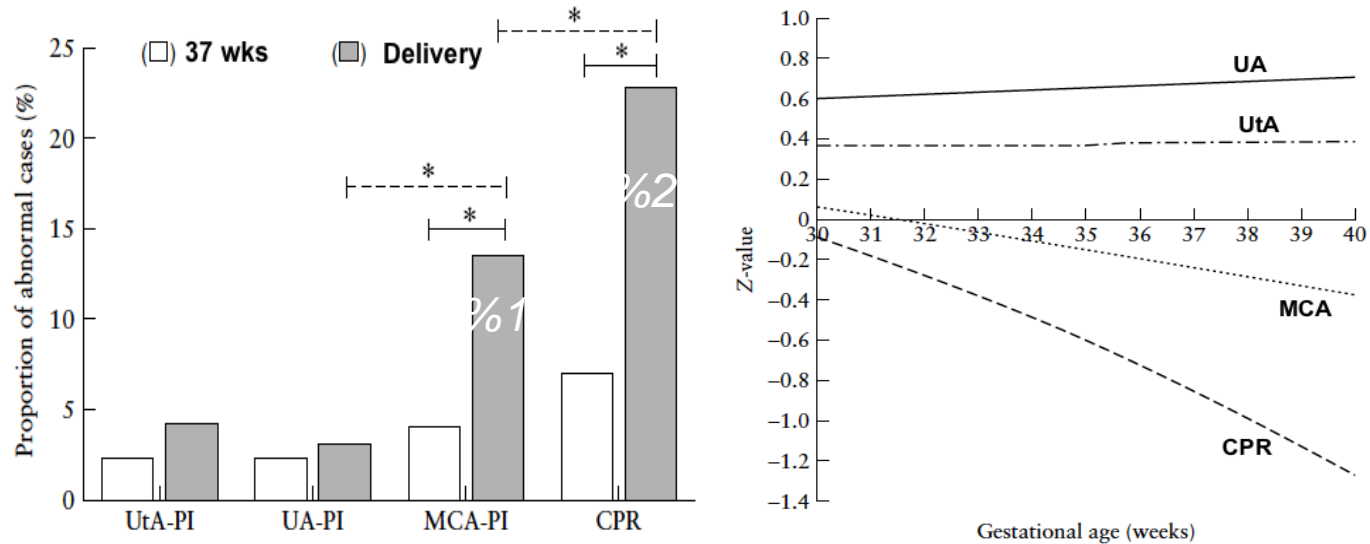*347 children aged 6–13years,*

Late-onset SGA infants are at increased risk for axonal loss in the retina and present specific visuomotor difficulties.

Oros D P. UOG. 2014
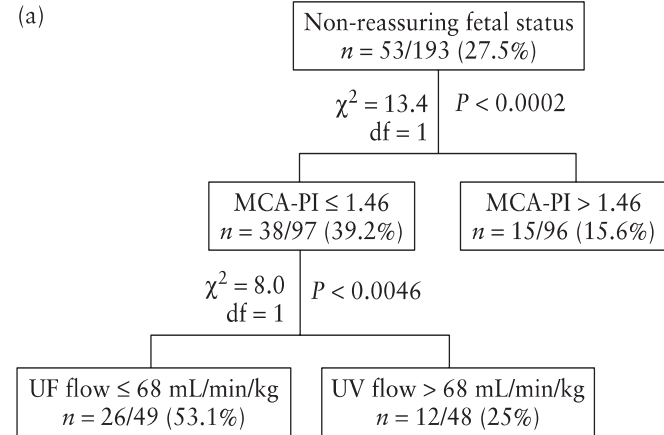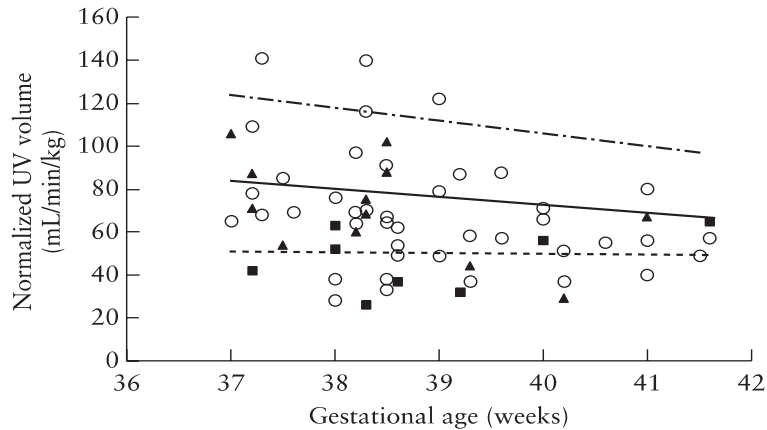
- CPR becomes abnormal earlier than MCA-PI
- UtA and UA Doppler do not deteriorate
- progression from 37 weeks with worsening CPR and MCA

$$CPR = \frac{MCA\ PI}{Umbilical\ artery\ PI}$$

Oros et al., UOG, 2011

TAJEV 2014

Late Onset FGR And Doppler
Umblical Blood Flow

(a)

```
                    ┌──────────────────────────┐
                    │ Non-reassuring fetal status│
                    │   n = 53/193 (27.5%)      │
                    └──────────────────────────┘
                    χ² = 13.4    P < 0.0002
                    df = 1
        ┌───────────────────┐        ┌───────────────────┐
        │  MCA-PI ≤ 1.46    │        │  MCA-PI > 1.46    │
        │ n = 38/97 (39.2%) │        │ n = 15/96 (15.6%) │
        └───────────────────┘        └───────────────────┘
        χ² = 8.0    P < 0.0046
        df = 1
  ┌─────────────────────┐    ┌─────────────────────┐
  │ UF flow ≤ 68 mL/min/kg│  │ UV flow > 68 mL/min/kg│
  │  n = 26/49 (53.1%)  │    │  n = 12/48 (25%)    │
  └─────────────────────┘    └─────────────────────┘
```

ଚ more direct and physiological measurement of vascular placental function

ଚ   UV blood flow with spectral brain Doppler allows better identification late-onset IUGR at risk of non-reassuring fetal status during labor and of neonatal metabolic acidosis.

- PARRA-SAAVEDRA *Ultrasound Obstet Gynecol* 2013; **42:** 189–195
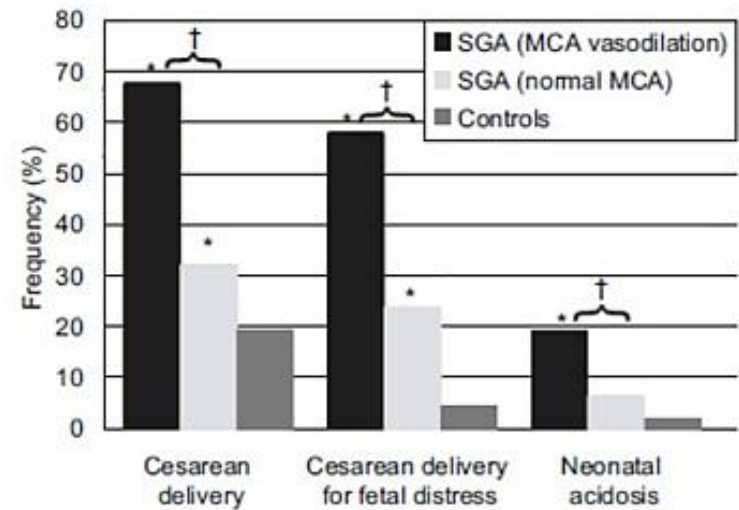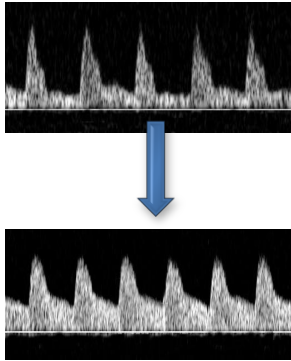
Murata et al., J Obstet Gynaecol Res., 2011

ಐ Associations between UA Doppler and neurodevelopment manifest differently across patterns of fetal growth delay

ಐ Abnormal UA Doppler is a less prominent feature and developmental abnormalities

Cerebral redistribution

REDV > AEDV

Gestational age

Body size

Head size

24   28   32   36   40

Gestational week

Baschat UOG 2011
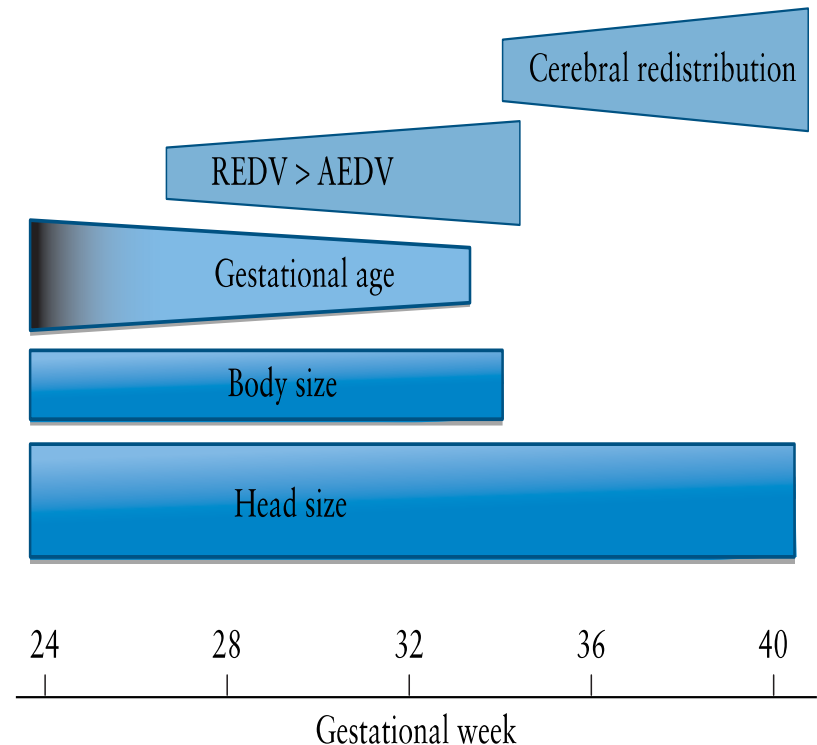
Identification of Late FGR

Table 1. Summary of the main differences between early- and late-onset forms of FGR

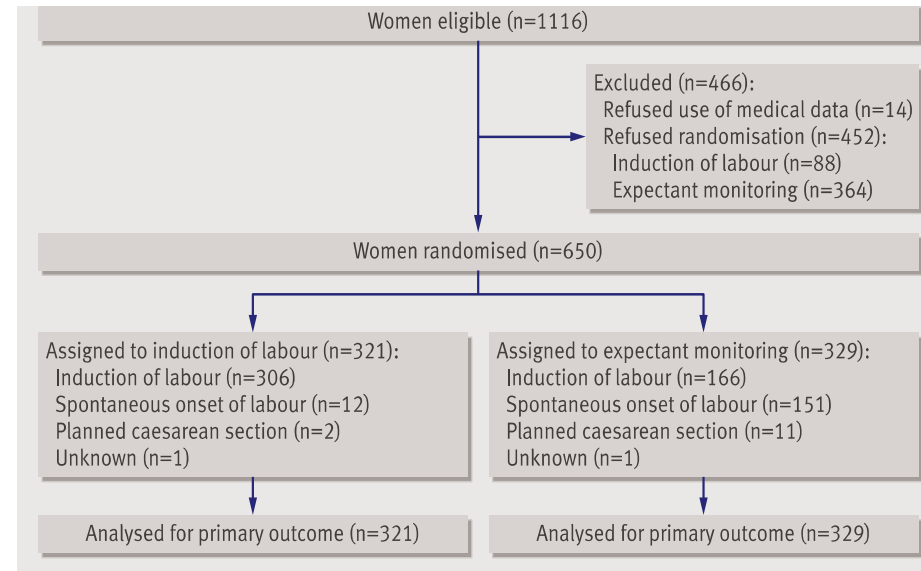| Early-onset FGR (1–2%)	Late-onset FGR (3–5%)
Problem: management	Problem: diagnosis
Placental disease: severe (UA Doppler abnormal, high association with preeclampsia)	Placental disease: mild (UA Doppler normal, low association with preeclampsia)
Hypoxia ++: systemic cardiovascular adaptation	Hypoxia +/–: central cardiovascular adaptation
Immature fetus = higher tolerance to hypoxia = natural history	Mature fetus = lower tolerance to hypoxia = no (or very short) natural history
High mortality and morbidity; lower prevalence	Lower mortality (but common cause of late stillbirth); poor long-term outcome; affects large fraction of pregnancies

Respiratory Morbidity
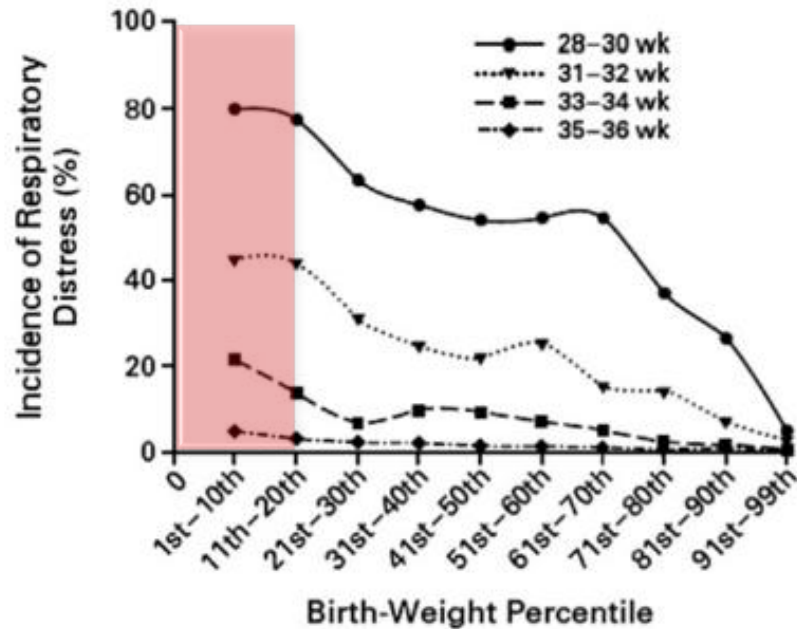
McIntyre et al., NEJM, 1999

Late FGR: Induction versus Expectant Management: DIGITAT

	İnduction	Expectant Manegment
N	321	329
C/S	14%	13.7%
BW<3 per	12.5%	36,7%
PN mortality	-	-
Composite Morbidity	5.3%	6.1%

Women eligible (n=1116)

Excluded (n=466):
Refused use of medical data (n=14)
Refused randomisation (n=452):
Induction of labour (n=88)
Expectant monitoring (n=364)

Women randomised (n=650)

Assigned to induction of labour (n=321):
Induction of labour (n=306)
Spontaneous onset of labour (n=12)
Planned caesarean section (n=2)
Unknown (n=1)

Assigned to expectant monitoring (n=329):
Induction of labour (n=166)
Spontaneous onset of labour (n=151)
Planned caesarean section (n=11)
Unknown (n=1)

Analysed for primary outcome (n=321)

Analysed for primary outcome (n=329)

abour induction affects neither the rate of adverse neonatal outcomes nor the rates of instru- mental vaginal delivery or caesarean section.

Boers et al BMJ 2010

However, neonatal admissions are lower after 38 weeks of pregnancy

Boers et al. AJOG 2012

Late Onset FGR
DIGITAT: 2 years Fallow

neither a policy of induction of labor nor expectant management affect developmental and behavioral outcome when compared to expectant management

the Ages and Stages Questionnaire (ASQ) and Child Behavior Checklist (CBCL)

NO DİFFERENCE

van Wyk L. AJOG 2012

Where are we?

TAJEV, 2014

Diagnostic markers
Weeks

UtA PI >p95

CPR <p5

MCA PI <p5

AoI PI >p95

Acute deterioration
Hours

AoI reverse

CTG decelerations

Late Onset FGR

Repeat in 1 week

No

Repeat in 2 weeks

Stage I: EFW <3rd centile or CPR <5th centile or MCA pulsatility index <5th centile (both persisting 12 h apart) or mean UtA pulsatility index >95th centile

Yes

≥37 weeks

Yes

No

SGA: ≥40 weeks

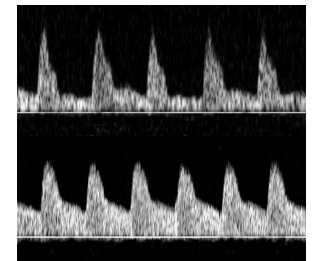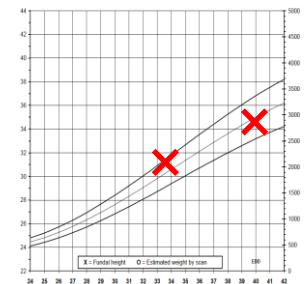No

Yes

Labor induction
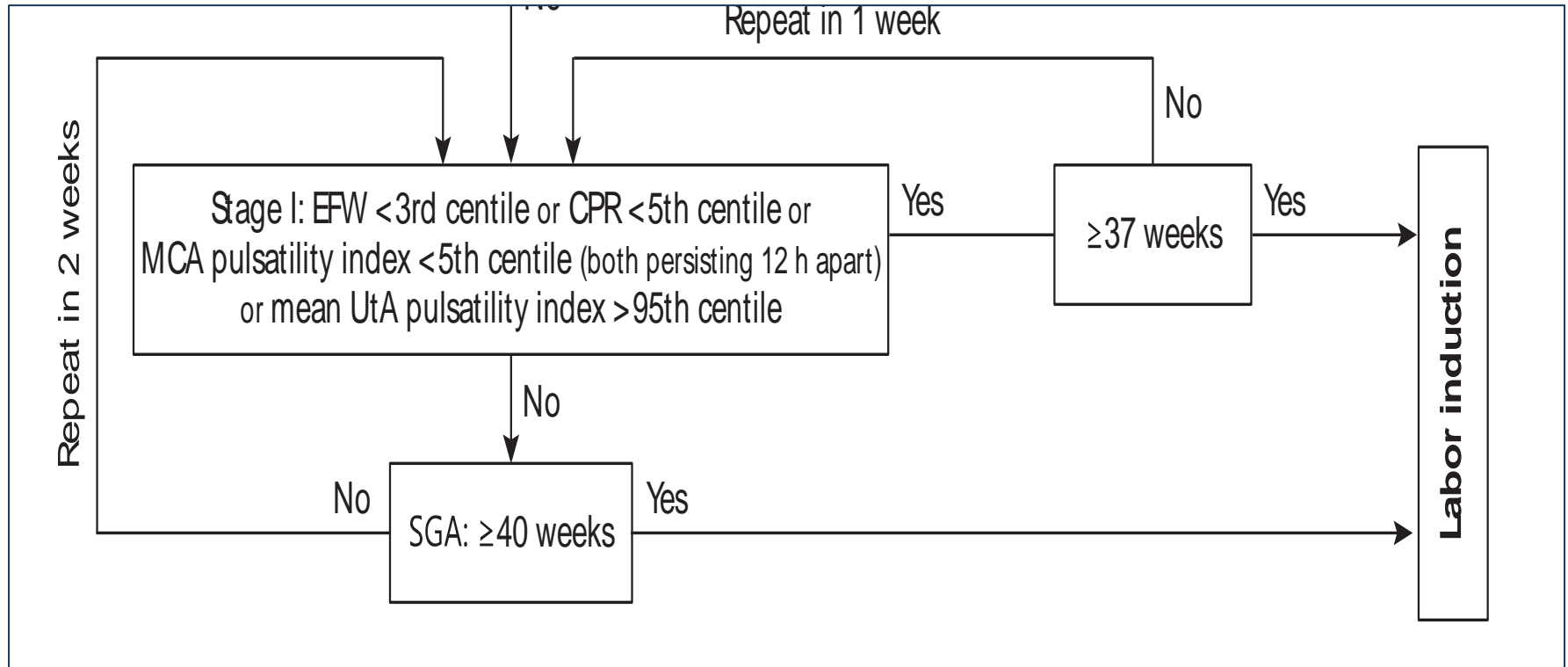
Conclusions

"customisation":

ଙ improve the ability of fetal biometry to detect high-risk fetuses

- First Trimester risk assesment
- 30 wks uterine artery Doppler(+ plasma proteins)
- Longitudinal growth assesment
- 30 wks if growth <25 percentile
  - CPR
  - Umblical vein
  - FHR acceleration capacity

Conclusions

If you have any doubt take your baby out