Thanks for coming!
Enjoy the faculty!

Jacky Nizard from Paris
For the Masterclass
He kindly helps to interact.

Stefano Faiola from Milano
For the hands-on workshop TOP 9
He kindly agreed to join the training.

Future Pre
EBCO

I thank Prof. Tullia Todros for asking patients to join the hands-on workshop.
Molte gracie a tutti patienti qui sono venuto.

In case of questions or comments: bino.clara.angela@gmail.com
The presentations will be seen on www.clara-angela.info

EBCOG 2016- Masterclass & Hands-on: Challenge of Twin Pregnancies

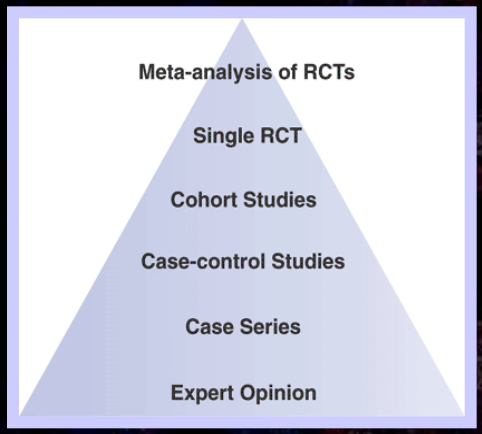
Twin birth rate from 19-32/1000 live births (70%).
Preterm birth< 37 wks in 60%, 65 vs 43 neon. deaths preterm.

Ultrasound Obstet Gynecol 2016; 47: 247–263
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.15821

isuog.org GUIDELINES

ISUOG Practice Guidelines: role of ultrasound in twin pregnancy

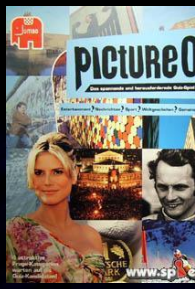
Experience/Eminance and Evidence



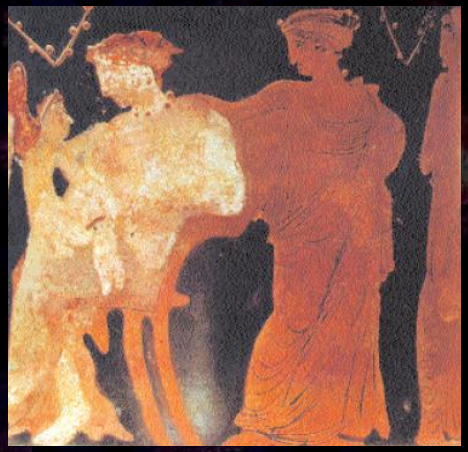
The discrepancy of judgement between teachers & residents is the most important break for progress in medical education *(Sir Arulkumaran, EBCOG Glasgow)*

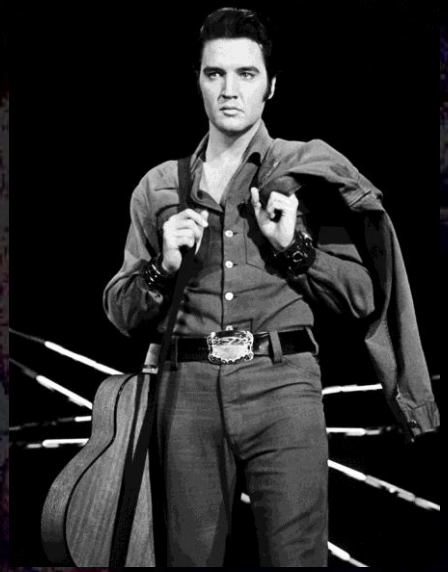
www.clara-angela.info

Historic / Present Twins



Which famous twin couples do you know?





Tia and Tamera Mowry

Biblical Twins

ESAU & JACOB

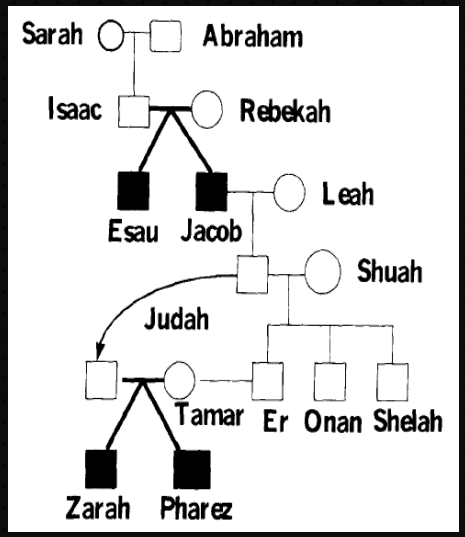
Fertility problems, premature labor,

Intensive fetal movements: „Two nations in the whomb“, 2 x vertex, short interval

Jacob gripped the feet of Esau: TTTS in MCMA twins(?) : Pseudo MA twins? PROM?

Metaphoric Interpretation?

Bennezzo Gozzoli, 1498, Sinopie Museum, Pisa



ZARAH & PHAREZ

Preterm labor, hand 2nd twin marked with red threat: transverse/vertex or vertex/transverse?

PROM 2nd twin or MA twins: „sunrise“

Genesis 25-27 Blickstein: Obstet Gynecl 1998

Devine twins deserve devine parents

Leda was together with Zeus (as a swan) and Tyndareos (her husband).

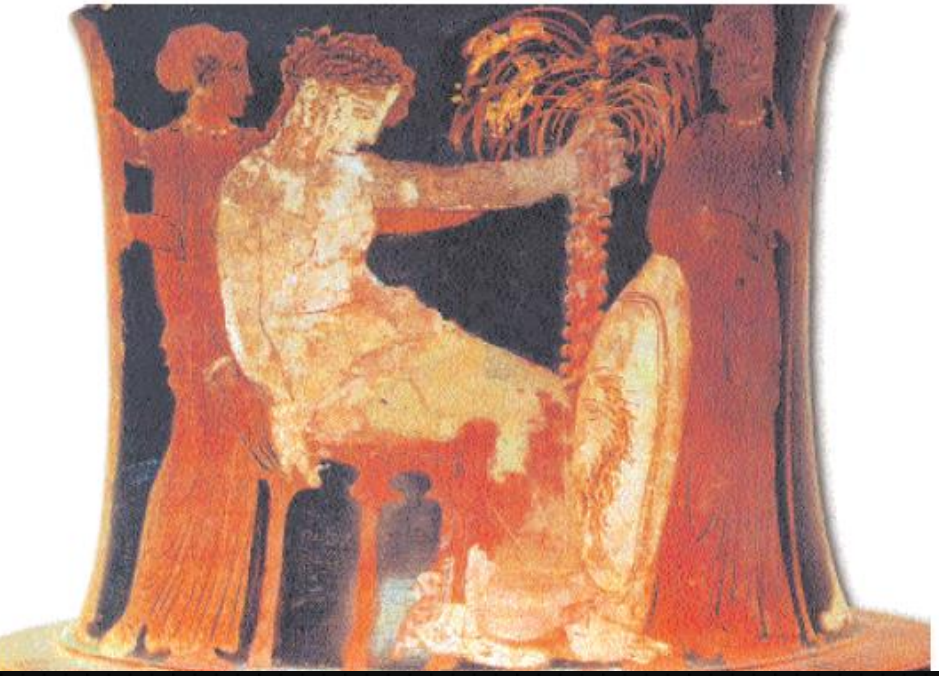
From two swan eggs two pairs of twins were born from two different fathers:

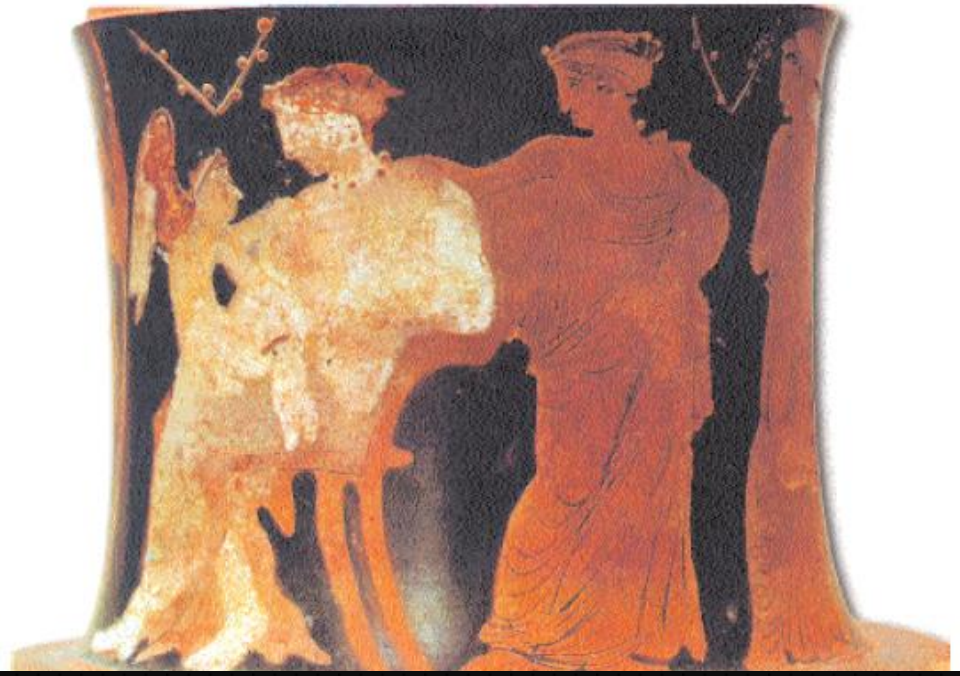
Castor & Polydeukes and Klytemnestra & Helena.

Greece

Devine twins deserve devine midwifes

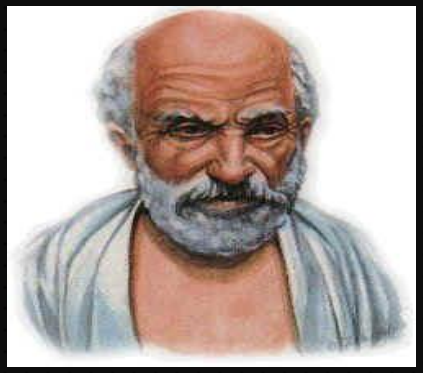
Hera as midwife of Alkmene:	Athene as midwife of Leto:
Hercules, 2nd twin in breech	Apollo & Artemis born vaginally





Twins deserve experienced obstetricians

Old Greece & Twin Birth Trial 2013



How and when to deliver twins ?

Hippocrates recommended 400 years a.C.:

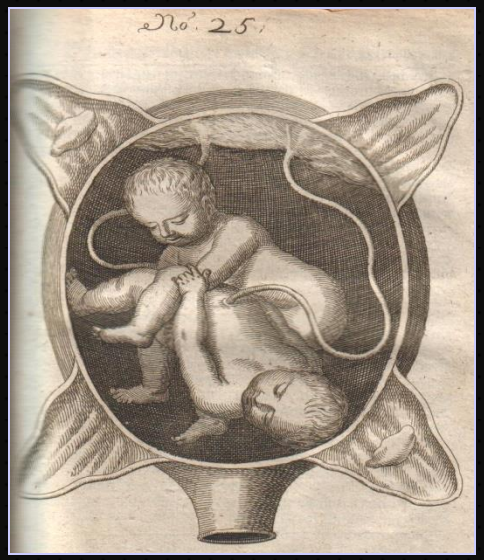
After a warm bath it is easier to perform internal or external versions.

Σείση της επιτόκου σε περίπτωση εγκαρσίου ή ισχιακού σχήματος του εμβρύου για τη μετατροπή του στο φυσιολογικό, η οποία γινόταν με αιώρηση της γυναίκας δεξιά-αριστερά πάνω στο κρεβάτι (οριζόντια σείση) ή με χτυπήματα του όρθιου κρεβατιού στο έδαφος (κάθετος σείση), αφού είχαν δέσει την επίτοκο. Τη μέθοδο αυτή παρέλαβε η λαϊκή ιατρική και στην Ελλάδα εκτελούνταν μέχρι και τον 18ο αιώνα από τις μαμές.[30] Σε κακοπαθημένα νεογνά δεν έκοβε αμέσως τον ομφάλιο λώρο, τον τοίο έκοβε η μαία που την ονόμαζε «ομφαλοτόμο».[31]

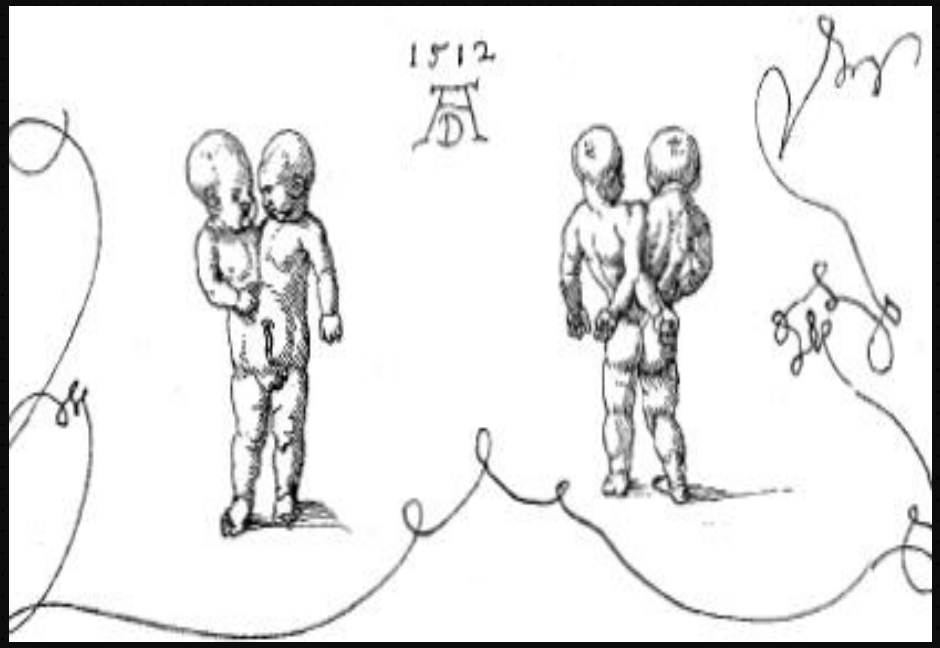
[31] Σέργιος Μανταλενάκης, «Η Μαιευτική μέχρι τον 19ο αιώνα», *Ελληνική Μαιευτική και Γυναικολογία* 2/14 (2002), σ. 83.

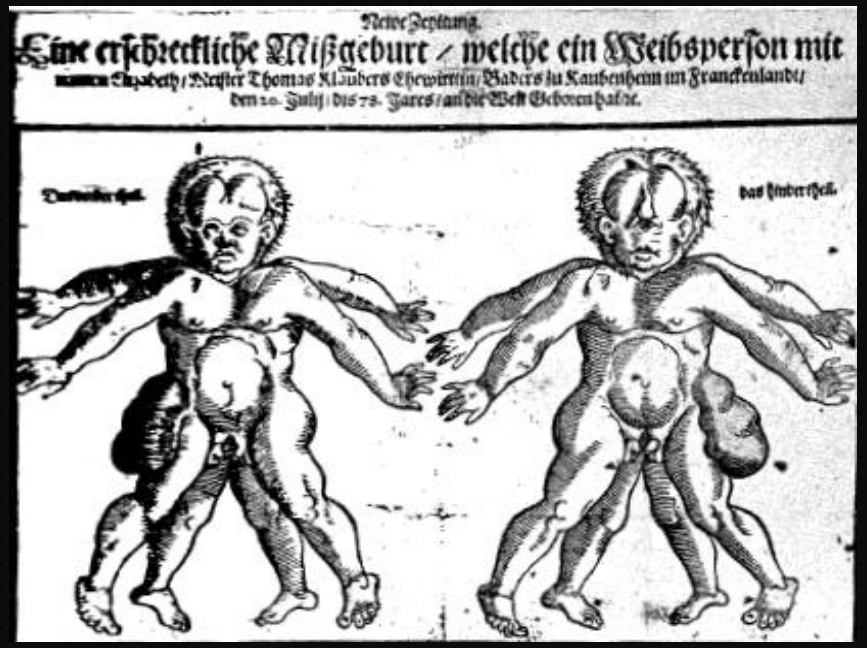
Delivery of Twins 16th-17th Century

Kindbarer frawen Rosengarten.
Von mancherley zufall vnd gebrechen so den Weibern vor/ nach/ vnd in der Geburt begegnen mögen.



“Monster Twins“(caused by devils?)



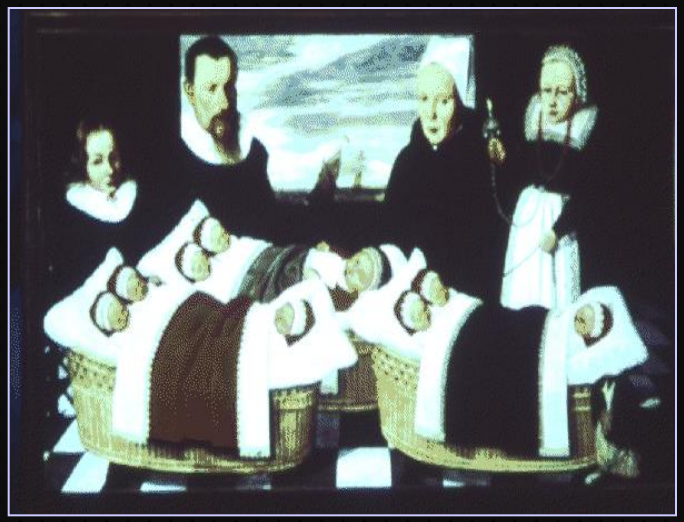


A. Dürer 1512, Oxford libary

Nürnberger Flugblatt 1578

Still a Challenge: Grief & Joy

Twins



Maria E Lämmerhirt (1644-1695)

Johann Ambrosius Bach (1645-1695)

Johann Christoph Bach (1645-93)

Johann Sebastian Bach (1685-1750)

Fam.Duke of Duesborg

17 th century

„How wonderful to have two sons in one bed“

(P 133)

Outline Masterclass Twins

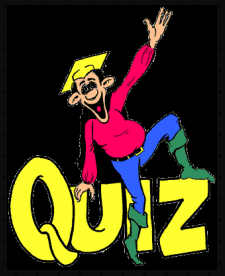
1st trimester: Dating, chorionicity & amnionicity, labelling, surveillance intervals, screening for aneuploidy, exclusion early malformations, discordancy of grwoth and malformations

2nd trimester: Prenatal diagnosis, screening for structural anomalies, fetal reduction/selective termination, screening preterm birth/growth, management of multiple pregnancy with single IUD

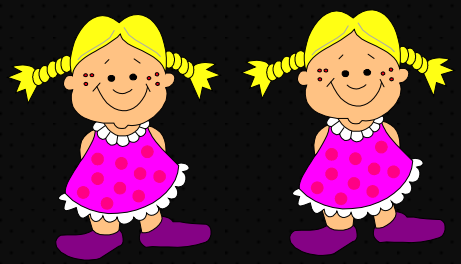
2nd & 3rd trimester: Screening, diagnosis & management of TTTS (TAPS & TOPS), TRAP sequence, MCMA twins, conjoined twins

Delivery of twins: Consider presentation, chorionicity, ges. age.
3rd stage of labor, cave hemmorhage, social support post partum

Post partum: Prevent hemorrhage, support breastfeeding & social care



First Trimester US



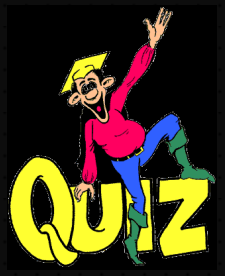
Dichorionic diamniotic twins….

a) Are characterized by a t-sign of the dividing membranes

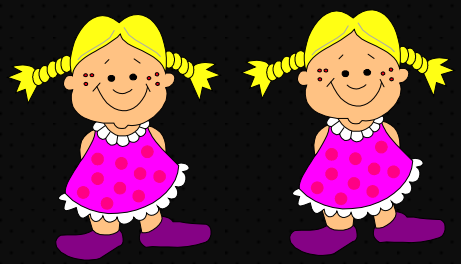
b) Are always dizygotic

c) Develop a twin-to twin transfusion syndrome in >5%

d) Have more discrepant early malformations than MC twins



First Trimester US



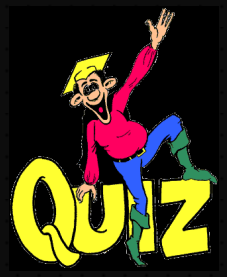
Monochorionic diamniotic twins….

a) Are seperated by only one chorion and two amnions

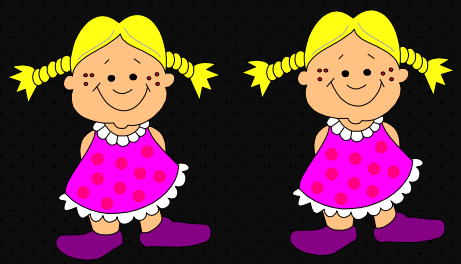
b) Are always monozygotic

c) >95% have the same structural abnormalities

d) > 95% have the same chromosomal abnormalities



First Trimester US



Monochorionic monoamniotic twins….

a) Contribute to 25% of all MC twins

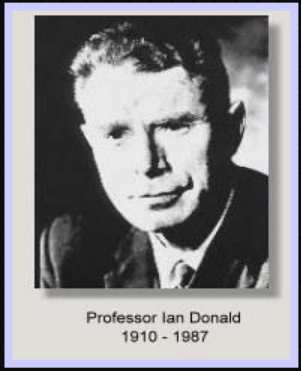
b) Share always one placenta and frequently one yolk sac

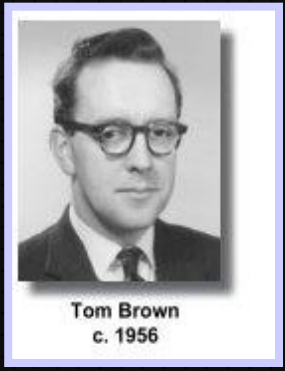
c) Show cord entanglement from ca. 18 weeks onwards

d) > 95% have the same chromosomal status.

From 1978 – today (my professional life)

From Eminence to Evidence





PubMed National Library of Medicine NLM

the cochrane library

30 years ago:
50 % of multiples
only diagnosed at birth

2016:
Ultrasound, RCTs
Meta-analyses
ISUOG Guideline

Key for EBM classification and grading of recommendations

using Task Force Preventive Health Criteria / GPP= Good Practice Point

Classification of evidence levels

1++	High-quality meta-analyses, SR of RCTs or RCTs with very low risk of bias
1+	Well-conducted meta-analyses, SR of RCTs or RCTs with low risk of bias
1–	Meta-analyses, SR of RCTs or RCTs with high risk of bias
2++	High-quality SR of CC or cohort studies or high-quality CC or cohort studies with very low risk of bias or chance and high probability that the relationship is causal
2+	Well-conducted CC or cohort studies with low risk of bias or chance and moderate probability that the relationship is causal
2–	Case–control or cohort studies with high risk of confounding, bias or chance and significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion

Key for EBM classification and grading of recommendations

using Task Force Preventive Health Criteria / GPP= Good Practice Point

Grades of recommendations

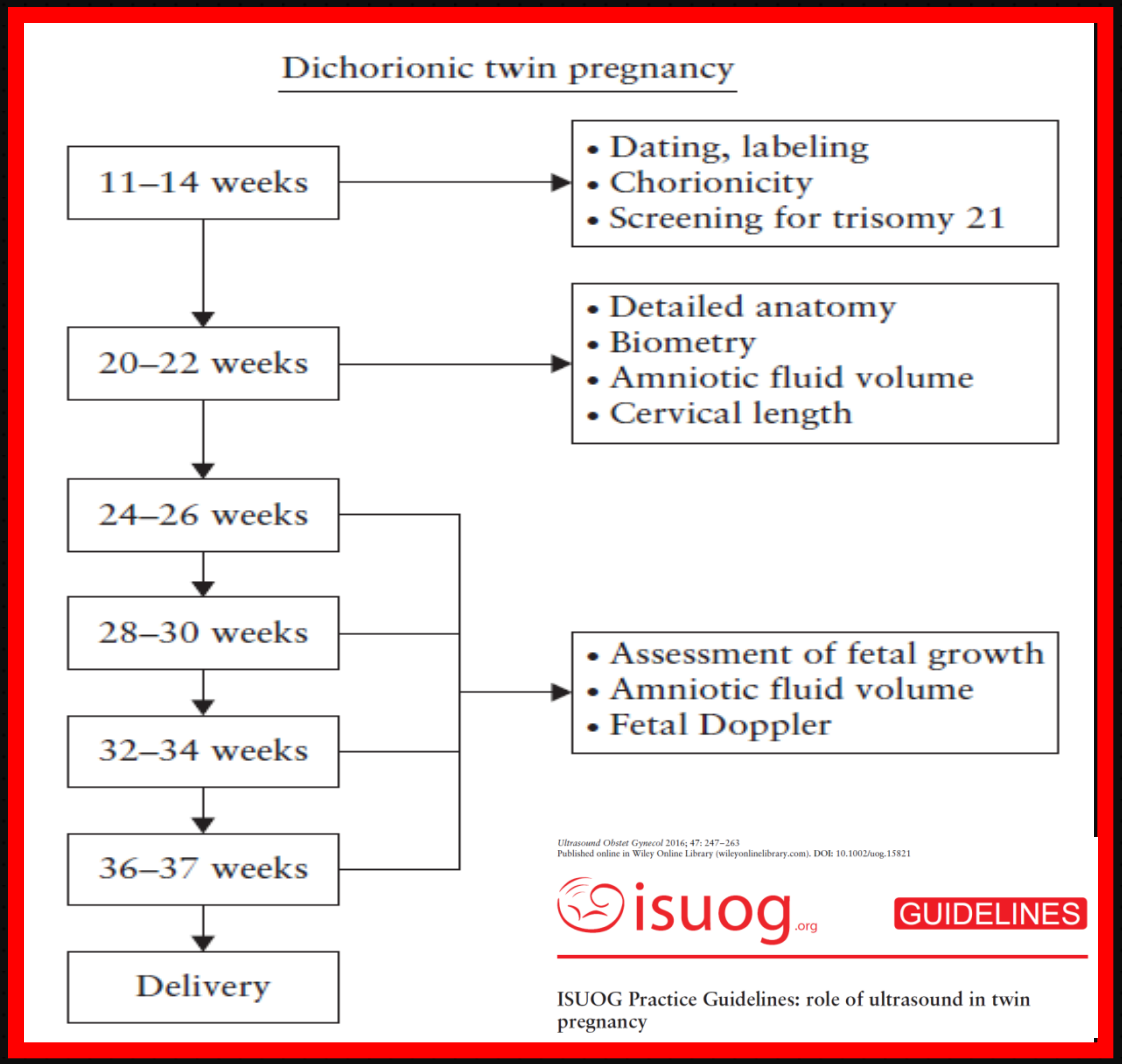
A	At least one meta-analysis, SR or RCT rated as 1++ and applicable directly to the target population; or SR of RCTs or a body of evidence of studies rated as 1+ applicable directly to the target population and demonstrating overall consistency of results
B	Body of evidence including studies rated as 2++ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	Body of evidence including studies rated as 2+ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence of level 3 or 4; or evidence from studies rated as 2+
GPP	Recommended best practice based on the clinical experience of the guideline development group

Surveillance by US in DC Twins

GPP

Scan @ first-trimester, scan in detail @ second-trimester including TVS of the cervix, scan every 4 weeks thereafter:

Fetal biometry, AFV, and UA Doppler from 20 wks' for both twins. Discordance in EFW should be documented.



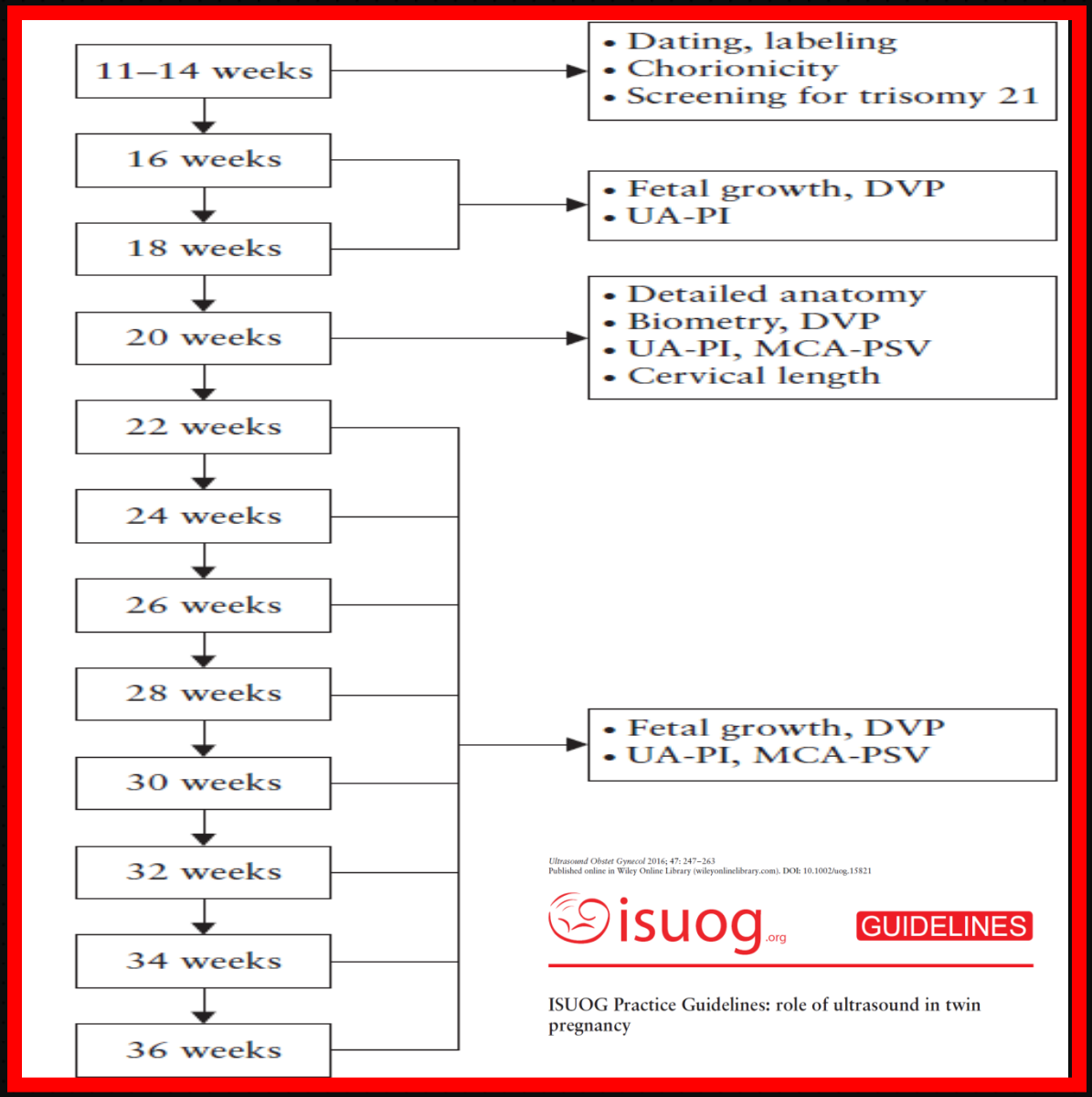
Surveillance by US in MC Twins

4 / C

Scan every 2 weeks from 16 wks onwards, as timely detection of TOPS/TAPS improves perinatal outcome.

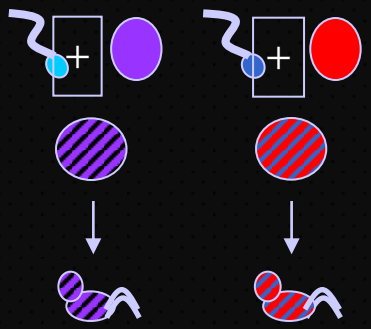
2+, 2++

Doppler UA & MCA from 20 wks, to screen for TAPS and the AFV (v. pocket) to screen for TTTS. CL @ to identify risks of SPTB.



Origin of DZ Twins

Genetic disposition / Ethnic differences / Hormone treatment



Always DICHORIONIC

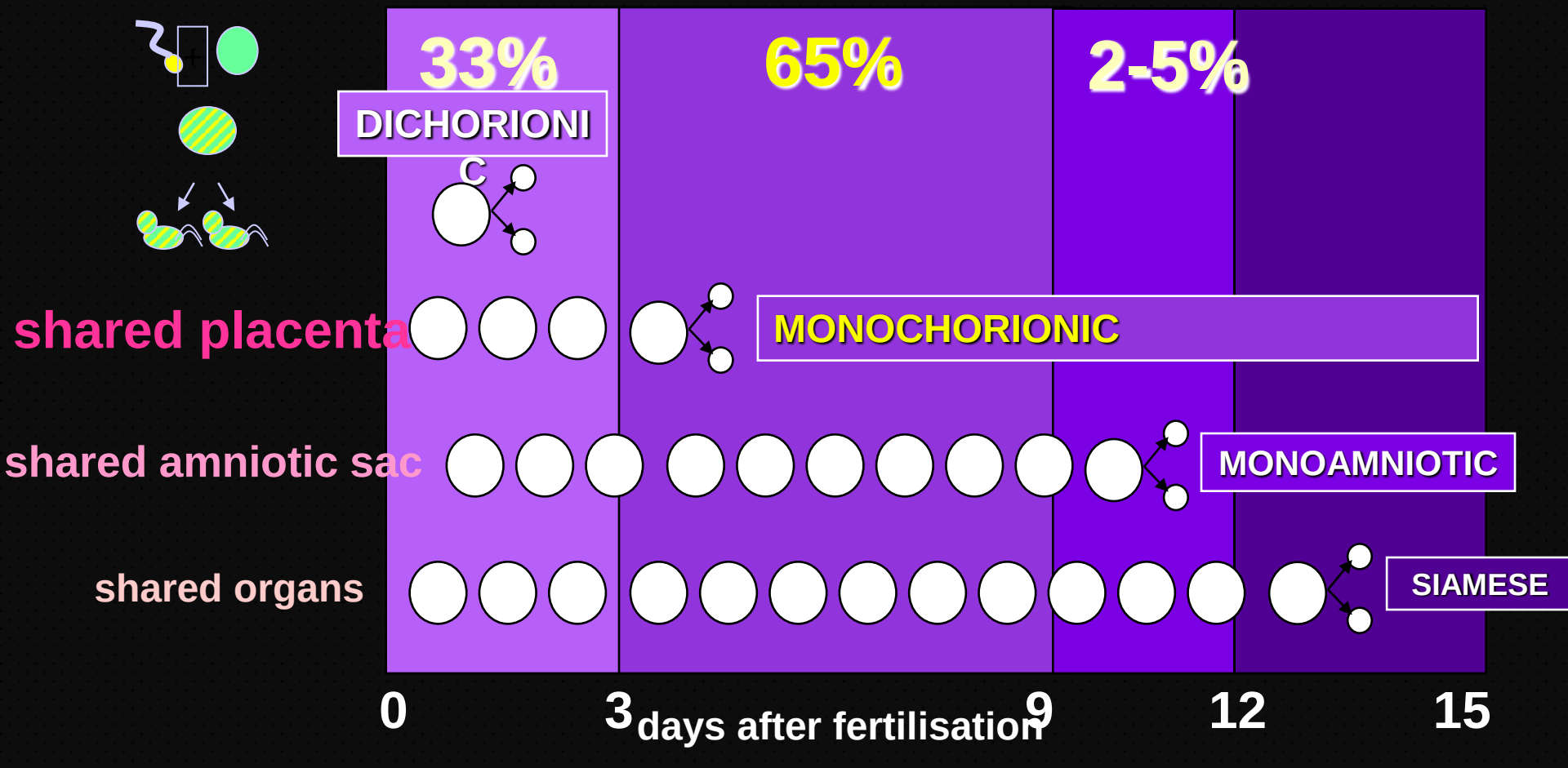
Two fetuses

Two placentas

Two chorionic sacs

Controversy: MZ Twins

Corner (AJOG 1956) versus Blickstein (2006)



Controversy: MZ Twins

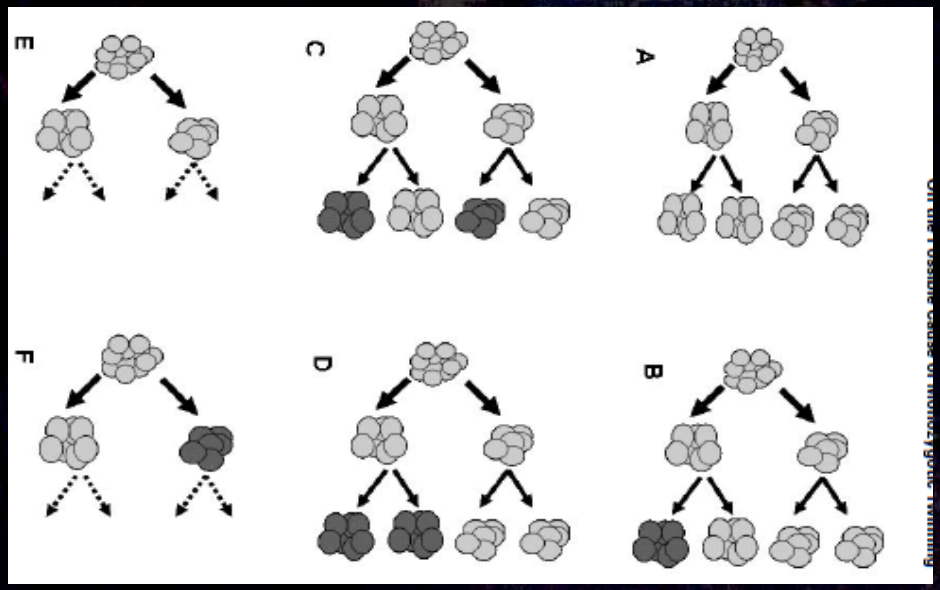
Corner (AJOG 1956) versus Blickstein (2006)

On the Possible Cause of Monozygotic Twinning: Lessons From the 9-Banded Armadillo and From Assisted Reproduction

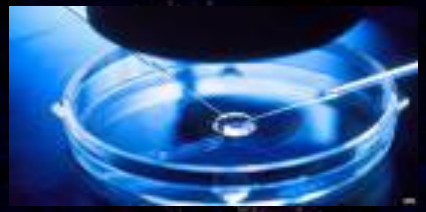
Isaac Blickstein[1] and Louis G. Keith[2]

[1] Department of Obstetrics and Gynecology, Kaplan Medical Center, Rehovot and the Hadassah-Hebrew University School of Medicine, Jerusalem, Israel

[2] Department of Obstetrics and Gynecology, The Feinberg School of Medicine, Northwestern University, and the Center for Study of Multiple Birth, Chicago, Illinois, United States of America



On the possible cause of monozygotic twinning



Various combinations of two binary fissions of a cell cluster form the zygote. The similarity of the cluster of cells to a morula is only for artistic purposes.

D/C

Chorionicity & Timing

•Chorionicity : 4 - 5 weeks

•Sensitivity >97%, Specificity:100%

•Should be determined< 14 weeks, document! Ask for help GPP/III

•Amnionicity: 7 - 8 weeks

•Sensitivity 100%, Specificity: > 98%

.Shetty & Smith: Prenat Diagn 2005; 25: 735–739

•Dating: CRL 45-84mm 11-13+6 weeks

•The larger should be used to estimate gestational age , some studies propose the mean.

•IN ART oocyte retrieval date/fertilization 2+

If uncertain about chorionicity it is safer to classify as MC! 3

•Labelling: Fix the description (Right/left) GPP

Membrane Status/Yolk sac & zygosity

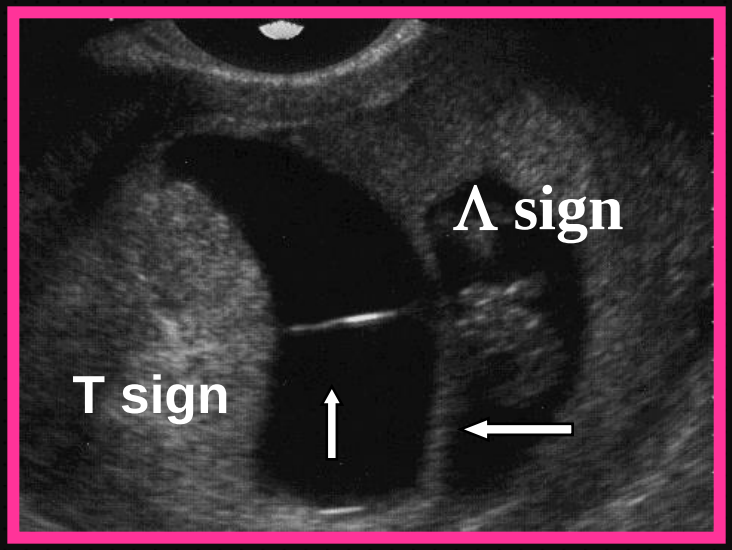
Monoamniotic Twins

amnion @ 6 –8 weeks

Always MZ

Dichorionic Triamniotic Triplets

chorion @ 4-5 weeks



100% MZ / 10% MZ - 90%DZ

Bromley B; Benacerraf B. J Ultrasound Med 1995; 14: 415-9

MCMA twins should always be transferred to a tertiary center! **GPP**

Twin Behavior

Joy of discovery

(when Prof. Nizard first met me in London in 1999)

Spontaneous / Evoked Activities (Video) Consider Testosterone

Male / male versus female / female (8-16 weeks)

Higher Incidence "fast" contacts in male pairs, early complex contacts in females

Arabin et al. UOG 1996; 8: 166-73

D: no chance

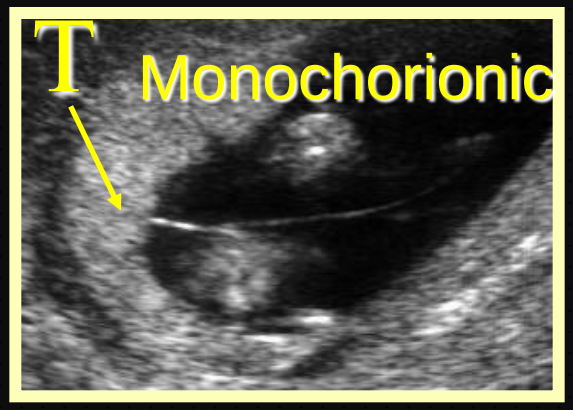
Spontaneous (!) MC 5-A Quintuplets

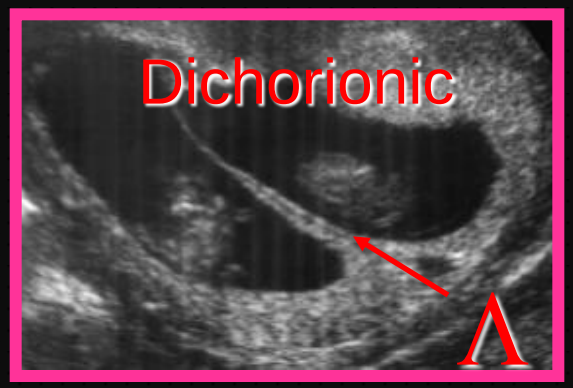
2D vs. 4D

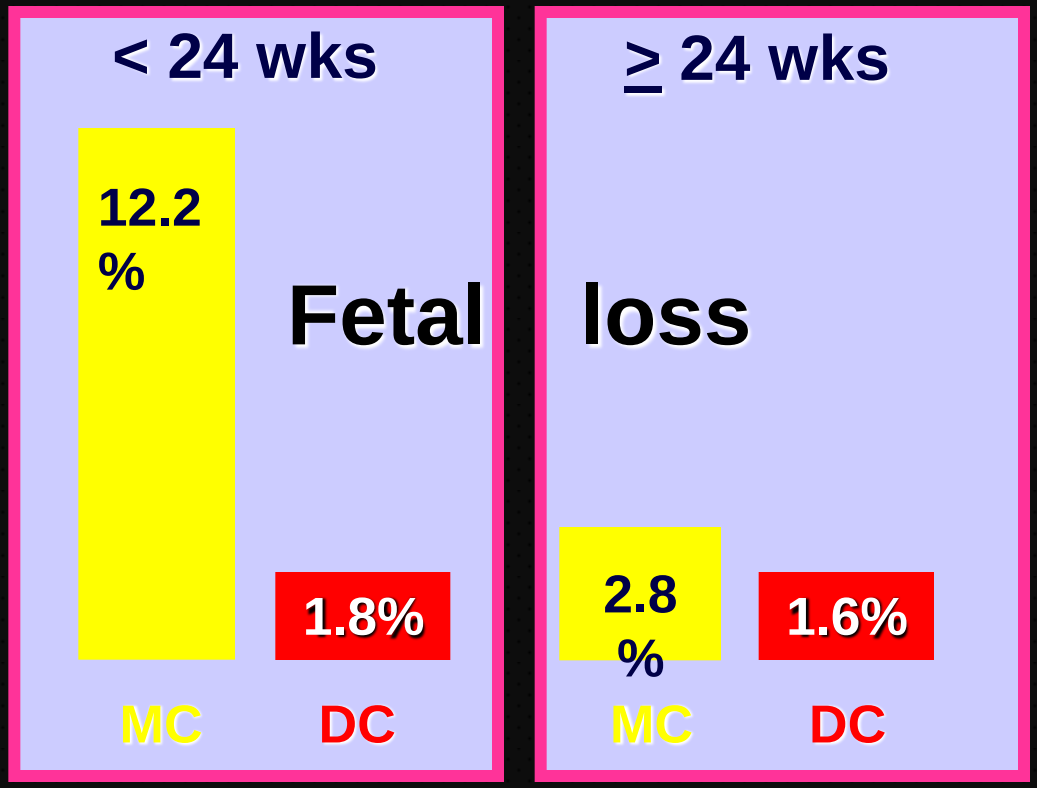
Arabin et al. Fetal Diagnosis and Therapy 2009; 11 : 222-6

2+

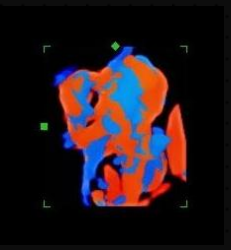
Early Informed Consent: Overall Prognosis







Perinatal Mortality: MCMA: up to 50% (85%)/ MCDA:10%/ DC=5%



Early Diagnosis umbilical cord

Velamentous insertion **: 7% in twins / > 50% in triplets**

>60% MC pregnancies with TTTS vs. 18.5% without TTTS.

Cord entanglement: **In MA pregnancies > 90% durng the 1st trimester.**

4

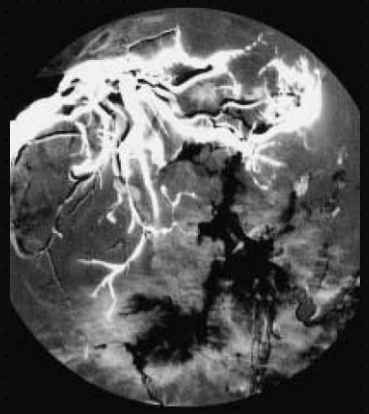
Benson CB & Doubilet PM. Semin Roent. 1991;1:50 ***Sebire NJ et al. U O G 2000; 16: 223-5***

Video

Ultrasound Obstet Gynecol 1999;13:181–186

Early prenatal diagnosis of cord entanglement in monoamniotic multiple pregnancies

B. Arabin†, R. N. Laurini†,‡ and J. van Eyck*,†*



Own series MA Twins , one center, 1994-2008

Arabin B, Hack K: UOG 2009

Study group MA Twins	Ante partum Death < 20 wks	Perinatal Death <7d.p.p.)	Neonatal Death up to 28 d.p.p.	Total loss
Umbilical entanglement (n=6)	5/6			5/6
Placental entanglement (n=30)	0/30	2/30 (from1 pair) Immature birth 23 weeks	2/30 (from 2 pairs) Fetal tumor Prematurity (26 weeks)	4/30
Total (n=36)	5/36 14%	2/36 5,5%	2/36 5,5%	9/36 25%

Monoamniotic Twins

2-

Early mortality to 16 wks high up to 50%.

Loss rate improved, from 40% to 10–15% in recent studies.

In a cohort study (n= 98) mortality > 20 wks to 28 d pp 19% and 17% after exclusion of fetuses with a lethal anomaly.

After 32 wks, 2 cases with perinatal mortality (4%).

The incidence of TTTS and cerebral injury was 6%.

Prefumo et al. Prenat Diagn 2015; 35: 274

Early Discrepancy

Discordancy ≥ 3 mm: Loss rate >50%.

Discordant CRL ≥5 Days: ↑ Rate of malformations, Indication for invasive and non-invasive examination. **3**

Dickey et al. Hum Reprod 1992; 7: 1170-2, Weissman et al. Obstet Gynecol 1994; 84:110

CRL discordance @ 11-13+6 wks > 10% associated with the risk of pregnancy loss (AUC 0.5), BW discordance (AUC 0.6), sFGR (AUC 0.6) & PB< 34 wks (AUC 0.5), (pooled predictive risk of 52%).

Risk of anomalies 4% vs. 25 %

D'Antonio et al. UOG 2014; 44: 138 *Kalish et al. A J O G 2004; 191: 1437*

CRL discordance @ 7+0 to 9+6 wks predicts single fetal demise in the first trimester (DR 74% for a FPR of 5%) **2++**

D'Antonio et al. Hum Reprod 2013; 28: 2621

OWN DATA CRL > 25% difference (n=15)

Triploidy, Vater syndrome, Trisomy 18,

Velamentous insertion, unequal sharing

Twin Reverse Arterial Perfusion (TRAP)

1% of MC twin pregnancies and 1 in 35 000 pregnancies overall,
through AA/ common cord insertion site: hyperdynamic circulation, CF pump T

Per. mortalitý pump twin up to >50%, now dependent on antenatal therapy
3 *Hecher et al. UOG 1997; 7: 170-2*

Survival might be improved by elective intervention @12–14 wks. **3**

PATHOPHYSIOLOGY?

1.Abnormal placental vasculature leading to subsequent alteration in cardiac development

Van Allen et al. (1983)

2. Abnormal primary cardiac embryogenesis

Severn and Holyoke (1973)

Group treatment acc.to acardiac twin size

Wong & Sepulveda, Prenat Diag.2005, 25, 796

Conjoined Twins (MCMA)

1/100 000 pregnancies (1% of MC twin pregnancies)

- **US: fixed apposition, fusion of the skin lines at some point.**
- **A series of 14 cases reported that 20% of parents opted for termination and 10% of fetuses died *in utero*.**
- **Among those opting to continue, survival to discharge was around 25%, and the majority of these had significant morbidity.**

Baken et al. Obstet Gynecol Surv 2013; 68: 743–752.

- **Congenital anomalies of organs in over 50% of conjoined twins, most common cardiac, neural tube defects & midline fusion defects.**
- **Most of them (40%) are stillborn or die after 24 hours after delivery.**
- **Prognosis depends on the type of conjunction, the involvement of shared organs and the presence of associated anomalies.**

Common liver & bowel outside the body, omphalocele.

Screening for aneuploidy+maternal age

Detection rate for a 5% false-positive rate

Cave: ß-HCG in ART!/ false+ / Complex informed consent!

	Combined test* (%)		Integrated Test** (%)
MC Twins (nearly always concordant for Down)	84	(88)	93
DC Twins (nearly always discordant for Down)	70	(87)	78
Singletons	85	(89)	95

- **NT, free β-hCG,PAPP-A at 10–13 weeks , Wald et al, 2003,*
- ***NT, PAPP-A at 10–13 weeks /AFP, uE3,β-hCG, inhibin-A at 14–22 weeks*
- *Praats et al. Prenat Diagn 2014; 34: 1077*

- **An alternative is a combination of maternal age and NT only.** **B**

In vanished twins with still measurable fetal pole, NT alone, in combination with maternal age, should be used for risk estimation. **B**

Screening for aneuploidy 3

MC Multiples: Increased NT:TTTS, malformations, "reverse flow" DV combined with ⬆ NT and ⬆ TTTS.

Sebire NJ et al. Br J Obstet Gynaecol 1996; 103: 999

Matias A et al. Twin Research 2000; 3: 65

Risk calculations in MC multiples are calculated per *pregnancy* based on the average risk of both fetuses.

CRL ≥10% or NT discordance ≥20%: discuss with a FMF expert. B

In spite of associations between discordance in NT, CRL, or reversed a-wave in the DV and TTTS, NT discordance of ≥20% (>25% in MC) had a sensitivity of 52–64% & a specificity of 78–80%, a PPV of 50% and a NPV of 86%. Risks of complications is < 10% if NT dis is <20%.

Kagan et al. UOG 2007; 29: 527

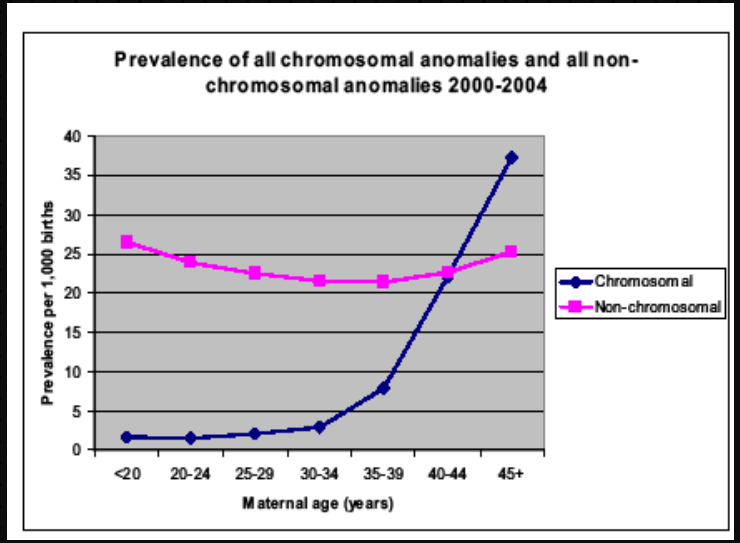
Cell-free DNA

2+

The weighted pooled DR for trisomy 21 in singleton pregnancy was 99% for a FPR of 0.1%. The corresponding values in twin pregnancy were 94.4% and 0%.

However, so far, the reported number of trisomy-21 cases in twin pregnancy diagnosed using cfDNA testing is small.

Gil et al. UOG 2015; 45: 249



Invasive Testing

Amniocentesis vs. Chorionic Sampling

Weisz and Rodeck, 2005

Fetal loss	No	Early (%)	Total (%)	
Tabsh and Theroux, 1995	53	—	9.4	All
post-MFPR				
Sebire *et al*., 1996	176	2.55	4.0	
Single needle				
McLean *et al*., 1998	79	5.06	—	All
post-MFPR				
Horger *et al*., 2001	71	—	7.6	
Yukobowich *et al*., 2001	476	2.73	2.73	0.63
(control) Antsaklis *et al*., 2002	347	—	8.77	

Early fetal loss, before 20 weeks / MFPR: multifetal pregn. reduction

Invasive Testing

D

Invasive testing should be carried out by a FMF expert.
CVS preferred in DC twin pregnancy, earlier than amniocentesis, lower risk of selective termination 1st compared with 2nd trimester (7% risk of loss of the entire pregnancy, 14%risk of PTB < 32 weeks).

Map position of twins. In concordant MC twins sample one amniotic sac, otherwise, both sacs because of rare discordant chromosomal anomalies in MC pregnancy.
CVS in MC pregnancy samples only a single placenta and may miss rare discordant chromosomal anomalies (trisomy 13,18,21, Turner, triploidy).
Machin. Semin Med Genet 2009; 151C: 110

In heterokaryotypic MC pregnancy, umbilical cord occlusion can be offered from 16 weeks onwards, with a SR> 80% for the healthy twin.
When MC twins are discordant for an abnormality, discuss the complexity of selective termination.

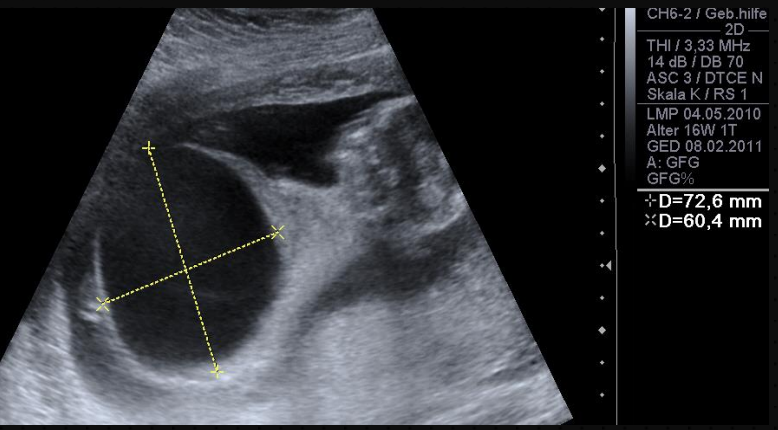
3

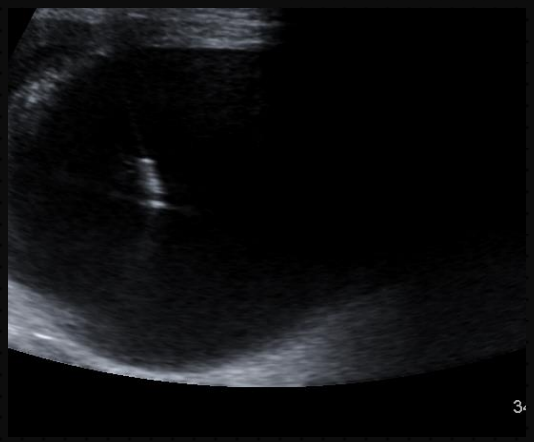
Lewi et al. Am J Med Genet A 2006; 140: 272, Lewi AJOG 2006; 194: 782

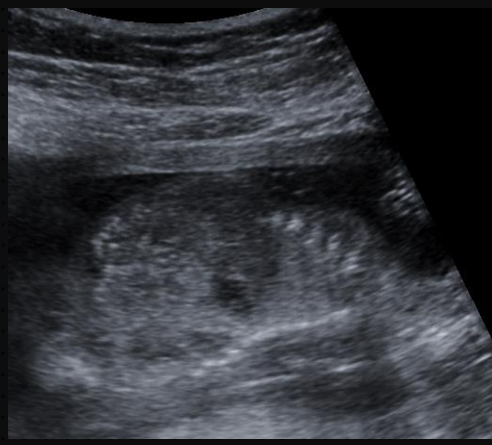
Early Discrepant malformations

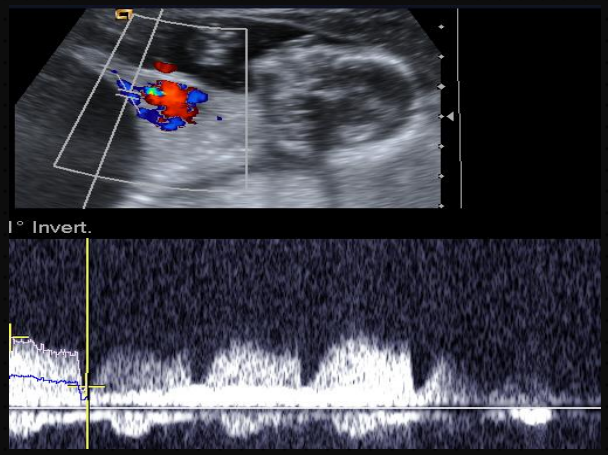
(> in MC twins) LUTO 2.2 / 10 000 Pregnancies

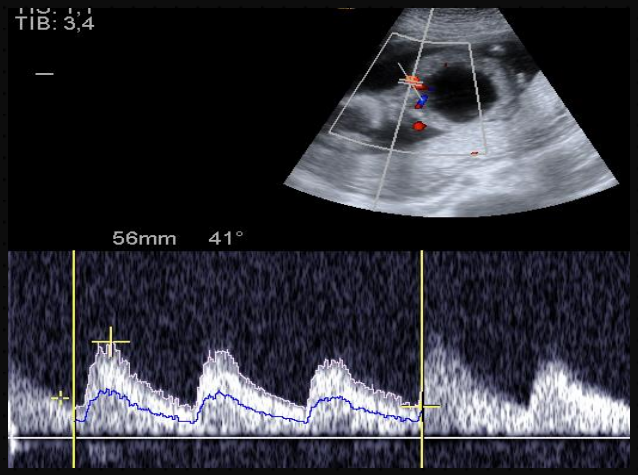
Cord occlusion before IUD of LUTO twin. Co-twin stayed healthy

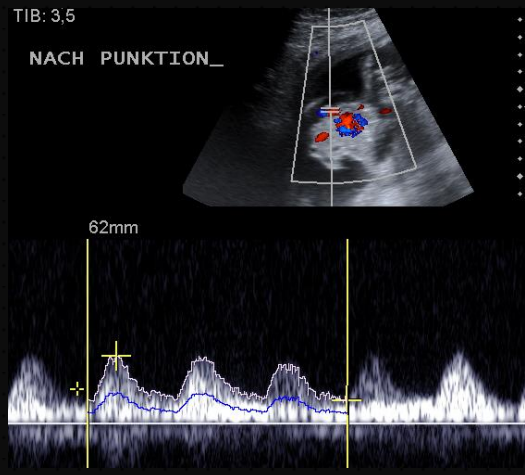






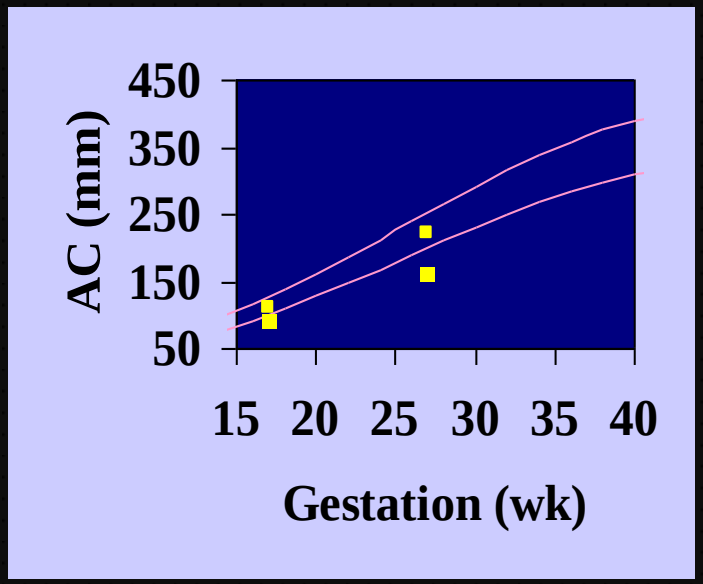


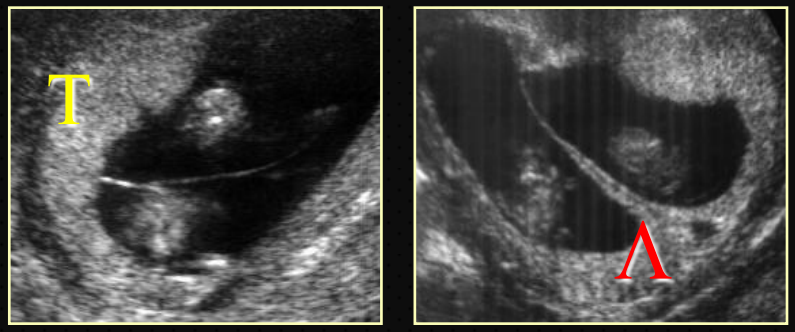


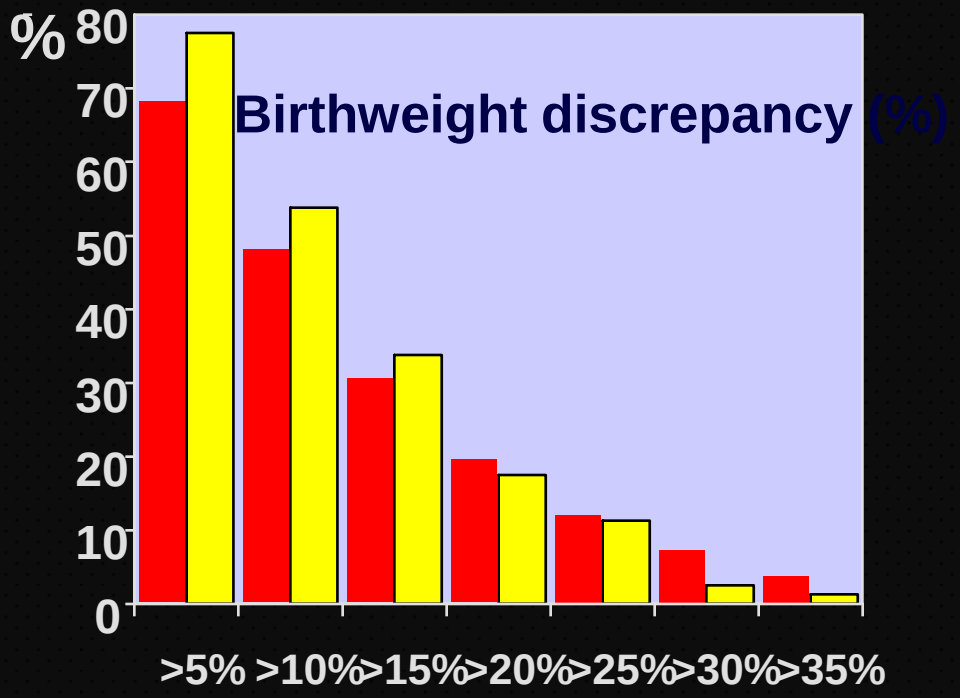


Fetal / Neonatal Weight

2-







	DC	MC
Discrepancy >25%	12%	11%
Weight <5%	12%	21%

N = 467 (FMF)

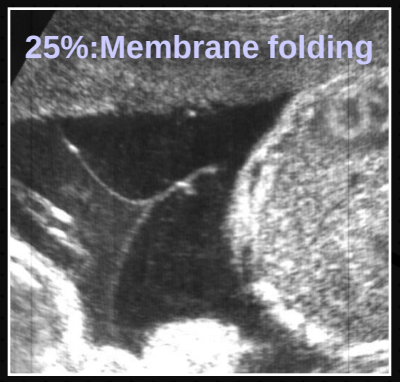
First Trimester „Markers“ Twin-Twin-Transfusion Syndrome

Angioarchitecture of vascular anastomoses determines the risk profile.
MC twins at risk if unequal hemodynamic and amniotic fluid balance.

Quintero. AJOG 2003; 188: 1333 Roberts et al. UOGynecol 2008; 31: 701–711. 85.
Roberts et al. Cochrane Database Syst Rev2014;1:CD002073.

11-14wks

15-17wks



First signs

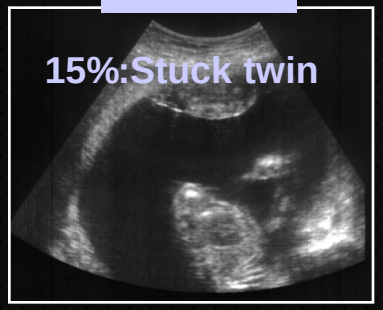
Membranes?

Insertion?

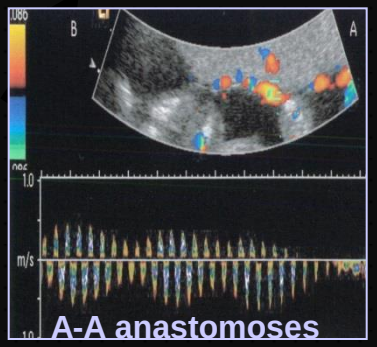
AAA?

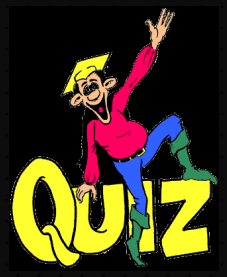
Cardiac performance?

14+ wks

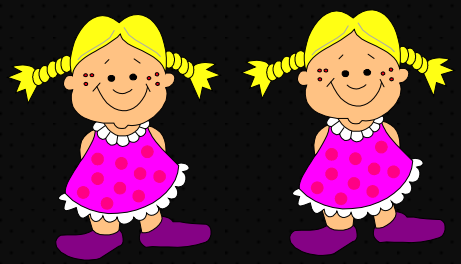


14+ wks





TTTS



Twin-to-Twin transfusion syndrome is classified as TOPS and TAPS

Which statement is right?

a) TAPS occurs ealier than TOPS

b) TAPS may occur in > 10% after TOPS and Laser

c) TOPS is always characterized by anemic donor & plethoric recipient

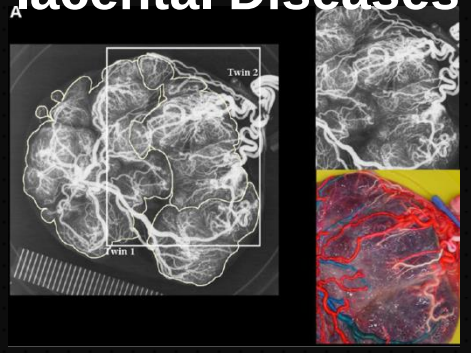
d) Selective fetocide may be an option in severe TTTS (TOPS) (3)

TOPS (6-8%), TAPS (4%), selective FGR

Placental sharing, birthweight discordance, and vascular anastomoses in monochorionic diamniotic twin placentas

Liesbeth Lewi, MD; Mieke Cannie, MD; Isaac Blickstein, MD; Jacques Jani, MD; Agnes Huber, MD; Kurt Hecher, MD, PhD; Steven Dymarkowski, MD, PhD; Eduard Gratacós, MD, PhD; Paul Lewi, PhD, Eng; Jan Deprest, MD, PhD

Placental Diseases



Live saving anastomoses

2nd Trimester

Several AV anastomoses

Twin-

Oligohydramnios-

Polyhydramnious-

Sequence

3rd Trimester

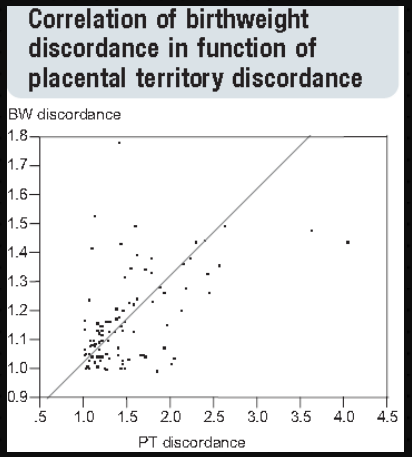
Few AA anastomoses

Twin-

Anemia-

Polycytemia-

Sequence



Upregulation of renin in donor, downregulation in recipient kidneys.

Renin and aldosterone elevated in the recipient and donor's plasma.

(Mahieu-Caputo et al., 2005) *(Kilby et al., 2001; Mahieu-Caputo et al., 2001).*

TOPS Staging and Prognosis

Progressive Imbalance: Unidirectional AV, Prevention: Bidirectional AA anastomoses

(Sebire et al., 2001)

In Europe, diagnosis of polyhydramnios is made when DVP ≥8cm @≤20 weeks & ≥10cm after 20 wks' gestation. Size discordance not essential.

STAGE I

- **Oligo-polyhydramnios (< 2 /> 8 cm)**

STAGE II

- **+ No visible bladder donor**

STAGE III

- **+ Abnormal Doppler (zero flow D)**

•STAGE IV

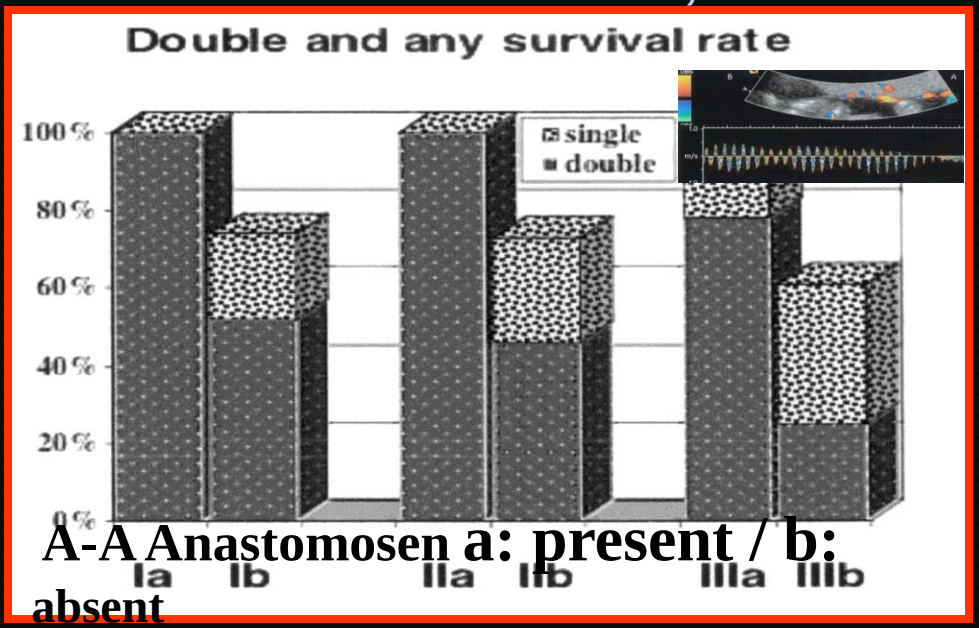
- **+ Hydrops recipient**

•STAGE V

- **+ Intrauterine death of one twin**

Quintero RA et al.. J Perin 1998; 19:550

Wee et al. Placenta 2005;26:19-24.



A-A Anastomosen a: present / b: absent

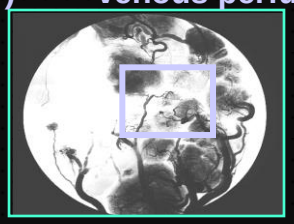
Tan et al. Obstet Gynecol 2004;103:1174

Chronic / Acute TTTS – does it exist?

TOPS (6-8%) vs. TAPS (4%)

Diagnosis @ 18 weeks, serial amniodrainage < 1000 ml/ week, delivery @ 36 weeks, 2 x normal outcome

arterial perfusion (donor) venous perfusion (recipient)

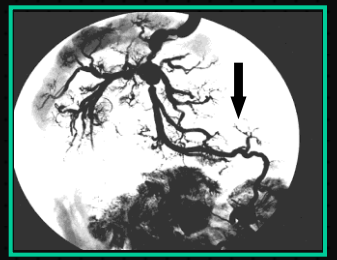




Magnification AV coteledonary anastomosis



Diagnosis

20 weeks	37 weeks
IUD	FD
after amniocentesis	3rd stage of labor

Outcome

2x IUD	2x uneventful

Laser - different techniques

Early fetoscopic laser ablation leads to 60–70% double survival / 80–90% survival of at least one twin. Following laser, the recurrence of TTTS is up to 14%, likely due to anastomoses missed at the time of the initial laser treatment.

2–

Recurrence of TTTS & occurrence of TAPS is reduced by use of the Solomon technique (equatorial laser dichorionization) compared with the highly-selective technique.

1+

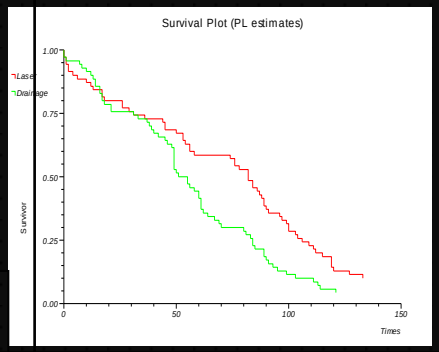
Roberts et al. Cochrane Syst Rev2014;1:CD002073. *Baschat et al. AJ OG 2013; 209: 234.e1*

LASER P<0.05 **AMNIODRAINAGE**

N=64 **N=63**

6/67 (8.9%) **10/43 (23.2%)**

Senat et al. N EJ M 2004; 351:136



Residual anastomoses in twin-twin transfusion syndrome after laser: the Solomon randomized trial

Prevalence, number, and size of residual anastomoses

Variable	Total			Laser complete (surgeon's opinion)		
	Solomon (n = 74)	Standard (n = 77)	*P* value	Solomon (n = 65)	Standard (n = 69)	*P* value
Placentas with residual anastomoses, n (%)	14 (19)	26 (34)	.04	8 (12)	22 (32)	< .01
Overall residual anastomoses per placenta, n[a]	2 (1–24)	2 (1–8)	.94	2 (1–4)	2 (1–5)	.90
Diameter of residual anastomoses, mm[b]	1.3 ± 1.8	0.8 ± 0.9	.07	2.1 ± 3.0	0.9 ± 1.0	.01
Placentas with arteriovenous residual anastomoses, n (%)	10 (71)	21 (91)	.11	6 (75)	17 (90)	.33
Placentas with arterioarterial residual anastomoses, n (%)	6 (43)	4 (17)	.09	3 (38)	2 (11)	.10
Placentas with venovenous residual anastomoses, n (%)	7 (50)	4 (17)	.04	4 (50)	3 (16)	.06

[a] Data are given as median (range); [b] Data are given as mean ± SD.

Slaghekke. Residual anastomoses in Solomon trial. Am J Obstet Gynecol 2014.

Slaghekke et al. Lancet 2014; 383: 2144

Following laser of TOPS or diagnosis of TAPS

Laser treatment should result in normalization of AF by 14 days.
Cardiac dysfunction normalizes in the recipient within 1 month, the donor suffers a temporary impairment of cardiac function.
Cave development of TAPS (anemia) after incomplete coagulation AV.

2+

Assaf et al. J Ultrasound Med 2010; 29: 1431
VanMieghem et al. Int J Pediatr 2010; Article ID 379792,

Prenatal diagnosis of TAPS based on discordant MCA Doppler. **D**
Treatment options still individualized. **GPP**

TAPS is due to small AV anastomoses (<1mm) leading to highly discordant hemoglobin concentrations at birth. **3**
Criteria for postnatal diagnosis include different Hb concentrations of > 8g/dL, reticulocyte conc.>1.7or small pl. anastomoses (<1mm).

Table 2 Antenatal and postnatal staging of twin anemia–polycythemia sequence (TAPS)[109,110]

Stage	*Antenatal staging*	*Postnatal staging: intertwin Hb diff (g/dL)*
1	Donor MCA-PSV > 1.5 MoM and recipient MCA-PSV < 1.0 MoM, without other signs of fetal compromise	> 8.0
2	Donor MCA-PSV > 1.7 MoM and recipient MCA-PSV < 0.8 MoM, without other signs of fetal compromise	> 11.0
3	Stage 1 or 2 and cardiac compromise in donor (UA-AREDF, UV pulsatile flow, or DV increased or reversed flow)	> 14.0
4	Hydrops of donor twin	> 17.0
5	Death of one or both fetuses, preceded by TAPS	> 20.0

AREDF, absent or reversed end-diastolic flow; DV, ductus venosus; Hb, hemoglobin; MCA, middle cerebral artery; MoM, multiples of median; PI, pulsatility index; PSV, peak systolic velocity; UA, umbilical artery; UV, umbilical vein.

Selective FGR in MC / FGR in DC Twins

Gratacos et al. UOG 2004; 24: 159

Classification depends on the pattern of umbilical artery Doppler. GPP

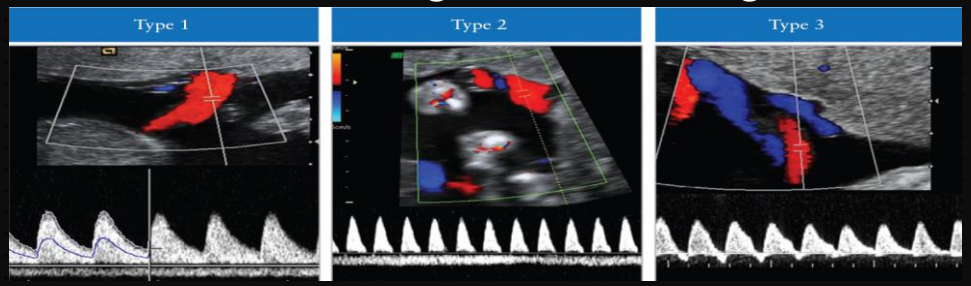
In **Type I**, positive end-diastolic flow, survival > 90%, in utero 4%.

In **Type II**, AREDF, high risk IUD of either twin in up to 29%, risk of neurol. sequelae in 15%.

In **Type III**, cyclical/intermittent pattern of AREDF, 10–20% risk of sudden death FGR twin, unpredictable. There is also (up to 20%) neurological morbidity in the surviving twin. 2++

In DC pregnancies, sFGR should be followed as in growth-restricted singletons. GPP

Limited evidence to guide the management of MC twins affected by sFGR. GPP



Management is complex & should be coordinated by FMF tert. center. 2–

Neonatal morbidity (38% *vs* 19%), RDS (32% *vs* 6%) and cerebral lesions, are higher in the larger than in the smaller twin. 2++

If there is a high risk of IUD of one twin < 26 wks, selective termination may be considered.

Lopriore et al. Twin Res Hum Genet 2012; 15: 541 D

In DC twin pregnancy with sFGR, fetal Doppler should be assessed ev. 2 weeks, depending on the severity. In MC twin pregnancy complicated by sFGR, fetal Doppler should be assessed at least weekly. GPP

Death of one DC or MC Twin

Implications: Intense Surveillance in case of MC twins at a level III center

Video

2++

COMPLICATIONS	MC	DC	TWINS
• Death of cotwin:	15%	3%	
• Preterm delivery:	68%	54%	
• Abnormal sonogram cotwin:	34%	16%	
• Neurod. impairment cotwin:	26%	2%	

Ong et al. BJOG 2006; 113: 992 Hillman et al. Obstet Gynecol 2011; 118: 928
Shek et al. Pract Res Clin Obstet Gynaecol 2014; 28: 249

In case of demise of one fetus (post-laser), brain imaging of the surviving cotwin should be considered 4–6 weeks later, neuro-developmental assessment should take place at 2 years of age.

GPP

Discrepant malformations in MC twins

Refer twin pregnancies discordant for fetal anomaly to FMF center (GPP).
Even in MZ twins,concordant structural anomalies are fewer than 20%.
Cardiac screening mainly essential in MC twins (GPP) .

Atrophy frontal parieto-occipital brain /
Atresia of duodenum and ileum:

Vascular lesions

Progression of hemi-hyper-throphy one twin. DNA:

Beckwith-Wiedeman syndrome both twins:

Different gene expression

Cranial / intestinal tumor
Infantile myofibromatosis (AD)

Different copy number variants?

Selective Fetocide

In DC twin pregnancy, selective feticide by intracardiac/ intrafunicular injection of potassium chloride or lignocaine, preferably 1st trimester. **B**

When diagnosis is made in the 2nd trimester, women might opt for late selective termination in the third trimester, if law permits. **(GPP)**

Selective feticide in MC twins is performed by cord occlusion, intrafetal laser ablation or radiofrequency ablation. **B**
Survival of the co-twin is ca. 80% and of PPROM & SPB < 32 wks 20%.
The risk of adverse neurological sequelae in the surviving twin may be increased compared with that in uncomplicated pregnancy. **2++**

Pros & cons should be considered (prematurity, loss, parental stress, availability of a FMF specialist to perform the procedure in case of pret. labor, and risk of complications associated with the anomaly). **2++**

Rossi et al. AJOG 2009; 200: 123 *Roman et al. UOG 2010;36:37*

Examples from Milano Study Group: BCC & Laser

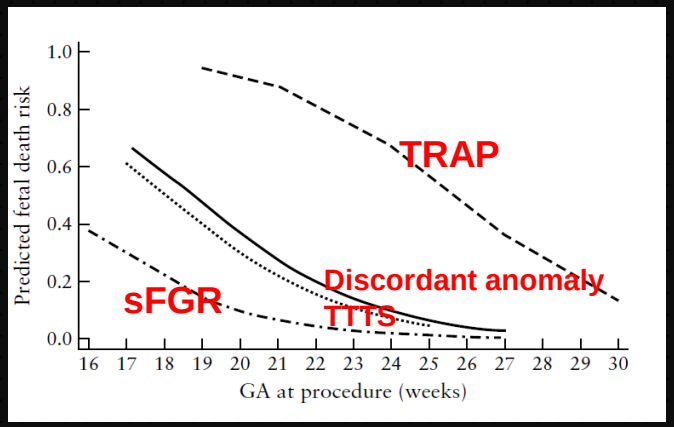
2-

Ultrasound Obstet Gynecol 2012; 39: 407–413
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.11073

Bipolar cord coagulation for selective feticide in complicated monochorionic twin pregnancies: 118 consecutive cases at a single center

M. M. LANNA*, M. A. RUSTICO*, M. DELL'AVANZO*, V. SCHENA*, S. FAIOLA*, D. CONSONNI†, A. RIGHINI‡, B. SCELSA§ and E. M. FERRAZZI*

To Umberto Nicolini, an unforgettable mentor and friend.



BCC < 19 weeks miscarriage 45%,
BCC > 19 weeks miscarriage 3% ***(P<0.001)***
PPROM in 45 (38%) cases.
Interval BCC & PPROM 4 (IR 2–9) wks.
In 15 (13%) cases, PPROM within 2wks.
Neonatal death:11 (9%), 2 (2%) children had severe neurologic morbidity.
Overall survival rate: 71% (84/118).

Fetal and Maternal Complications after Selective Fetoscopic Laser Surgery for Twin-to-Twin Transfusion Syndrome: A Single-Center Experience

M.A. Rustico[a] M.M. Lanna[a] S. Faiola[a] V. Schena[a] M. Dell'Avanzo[a] V. Mantegazza[a] C. Parazzini[c] G. Lista[d] B. Scelsa[e] D. Consonni[f] E. Ferrazzi[b]

Perinatal outcomes are similar to those of discordant MCDA twins treated with cord occlusion. However, the rate of PPROM is higher & GA @ delivery lower. 3

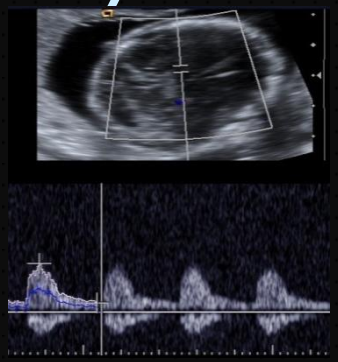
Table 5. Perinatal outcome in 150 pregnancies complicated by TTTS and treated by selective FLS

	Total	Period 1	Period 2	p value
Pregnancies treated	150	62	88	
With at least 1 survivor	111 (74.0)	41 (66.1)	70 (79.5)	0.06[1]
With 2 survivors	61 (40.7)	20 (32.3)	41 (46.6)	0.04[1]
With 1 survivor	50 (33.3)	21 (33.8)	29 (33.0)	0.27[1]
With 0 survivors	39 (26.0)	21 (33.9)	18 (20.4)	
Fetuses treated	300	124	176	
Perinatal survival	172 (57.3)	61 (49.2)	111 (63.1)	0.04[2]

Discrepant infections in MC twins

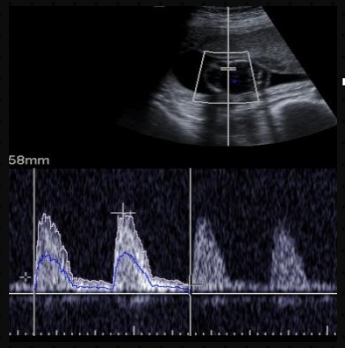
Sonographic examination (18+3 weeks)



Twin 1



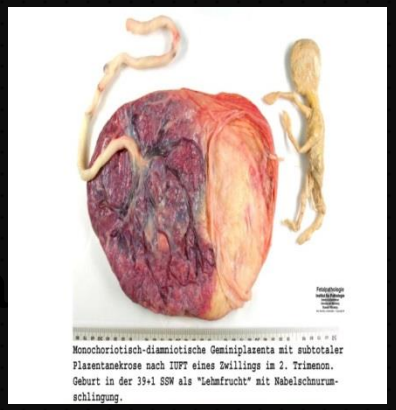



Twin 2

DD: Fetal Anemia Twin 2, Parvovirus B19?, TTTS ?

Discrepant Infections in MC twins 4

Material	Twin 1 (born @39 w)	Twin 2 (IUD19 w)
Placental villi	[a]1,4 x 10^1	2,5 x 10^4
Umbilical tissue	1,8 x 10^1	1,1 x 10^3
Fetal tissue	-	3,6 x 10^3



Monochoriotisch-diamniotische Geminiplazenta mit subtotaler Plazentanekrose nach IUFT eines Zwillings im 2. Trimenon. Geburt in der 39+1 SSW als "Lehmfrucht" mit Nabelschnurumschlingung.

Microbiology/Virology:

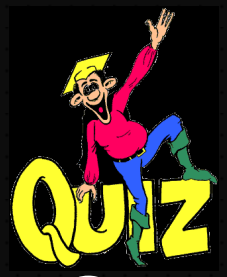
Twin 1: Umbilical cord — Parvovirus B19-DNA PCR +

Cord blood: — Parvovirus B19-IgG +, IgM – *

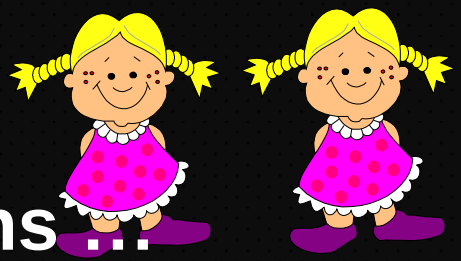
Twin 2 (Fetus papyraceus) CV: — Parvovirus B19-DNA PCR +

Interpretation:

- Maternal B19-Infection transferred to both fetuses
- Twin 1 IgG + possibly caused by matern. IgG/ Course until 12months
- Twin 1 IgM- does not exclude prenatal infection
- Twin 2 Fetal Hypoxia /Anemia / cardiac decompensation after IUT



Cervix in Twins



Cervical shortening in twin gestations …

a) **Follows a similar decrease as in singleton pregnancies, one cut-off (25mm) should be used.**

b) **Shortens faster because of a higher risk of microbial invasion.**

c) **Is an an indication for a cerclage**

d) **Should inidicate maternal hospitalization**

e) **Can be an indication for a cervical pessary**

Pathophysiology of Preterm Birth

More frequent in twins, most important reason for perinatal death

Romero et al. Ann N Y Acad Sci 1994; 734: 414-29

Friedman & Sachtleben
AJOG 1964;23:164-72

Stress / Hypoxia
CRH
Contractions/
Overdistension
Tocogram

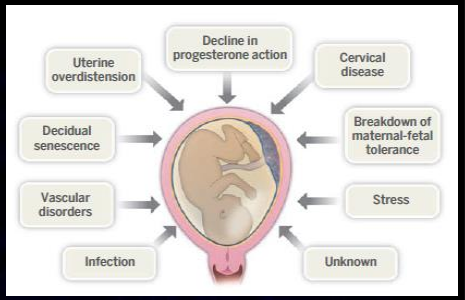
Membrane activation
Interleukines
Fibronectin

Cervical shortening
T V S

Smooth muscle < 8%, fibrous connective tissue: Proteoaminoglycans: collagen metabolism*

**Schwahn et al. AJOG 1966; 94: 391-404 Uldbjerg et al. AJOG 1982;147: 662-6*

State of the Art: Multicausal / The Microbiome has little impact on SPTB



Romero et al., Science 2014

RESEARCH Open Access

The vaginal microbiota of pregnant women who subsequently have spontaneous preterm labor and delivery and those with a normal delivery at term

Roberto Romero[1,2,3*], Sonia S Hassan[1,4], Pawel Gajer[5,6*], Adi L Tarca[1], Douglas W Fadrosh[5], Janine Bieda[1,7], Piya Chaemsaithong[1], Jezid Miranda[1], Tinnakorn Chaiworapongsa[1,4,7] and Jacques Ravel[5,6]

A longitudinal analysis of the vaginal microbiome in patients destined to deliver preterm failed to show any changes in bacterial taxa associated with SPTB.

SCIENTIFIC REPORTS /ABOUT /EDITORIAL BOARD /FOR AUTHORS

Sci Rep. 2015; 5: 8988. PMCID: PMC4355684
Published online 2015 Mar 11. doi: 10.1038/srep08988

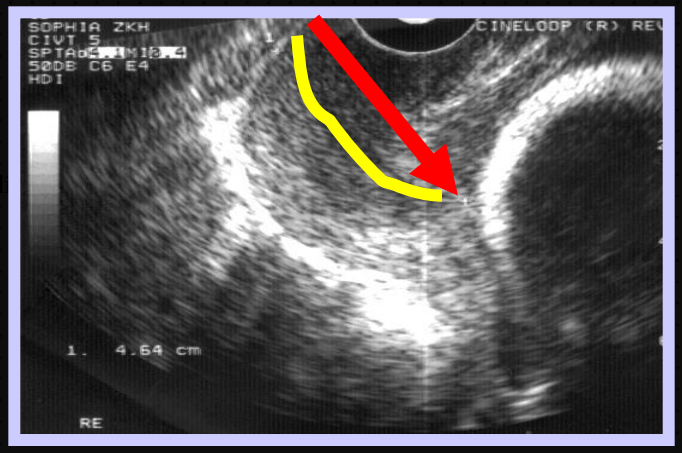
The vaginal microbiome during pregnancy and the postpartum period in a European population

David A. MacIntyre,[3,1] Manju Chandiramani,[1] Yun S. Lee,[1] Lindsay Kindinger,[1] Ann Smith,[2] Nicos Angelopoulos,[3] Benjamin Lehne,[4] Shankari Arulkumaran,[1] Richard Brown,[1] Tiong Ghee Teoh,[5] Elaine Holmes,[6] Jeremy K. Nicholson,[6,7] Julian R. Marchesi,[2,6] and Phillip R. Bennett[1]

This highlights the importance of patient-centred individualised treatment strategies designed to modulate the vaginal microbiome to promote health during pregnancy and beyond and the impact of interventions such as cerclage, pessary or progesterone.

Transvaginal Sonography

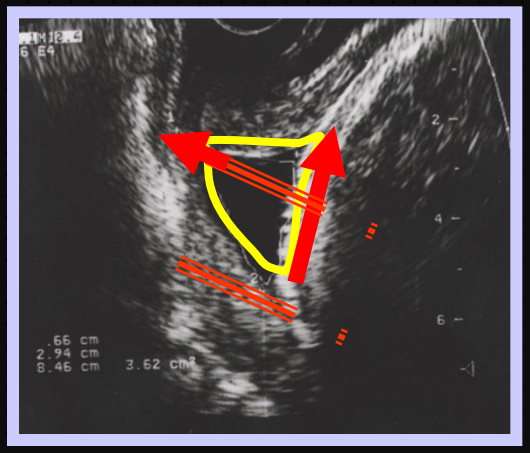
Cervical length



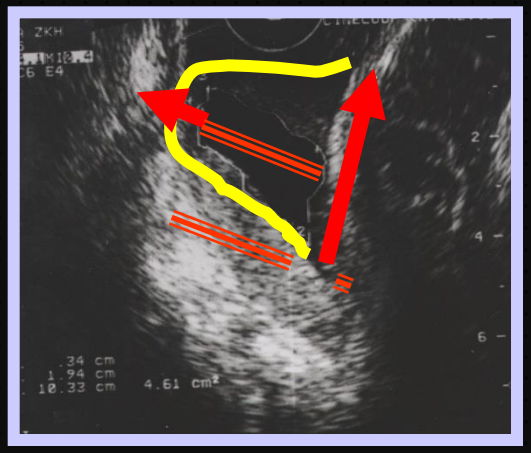
Anterior = posterior cervix
Internal - external os in 50% curved

Berghella et al. UOG 1997; 10: 161–6
Cock & Ellwood. UOG 2000; 15: 109-13
To et al. UOG 2001; 17: 217-9

Funneling width



V-shape



U-shape

SPTB on the basis of history and CL

A re-analysis of individual patient data

More than 50% (60%) of twins born < 37 wks, 12% < 32 weeks; these rates are 5.4 and 7.6 times the equivalent rates for singletons.

Cervix and Prematurity in Twin Pregnancy

At 24 weeks a CL ≤ 2.5 (≤2) cm was the best predictor of SPB but better in predicting its absence.

Goldenberg et al. AJOG 1996; 175: 1047-53, n=147 *Guzman et al. AJOG 2000; 183:1103-7, n=131*

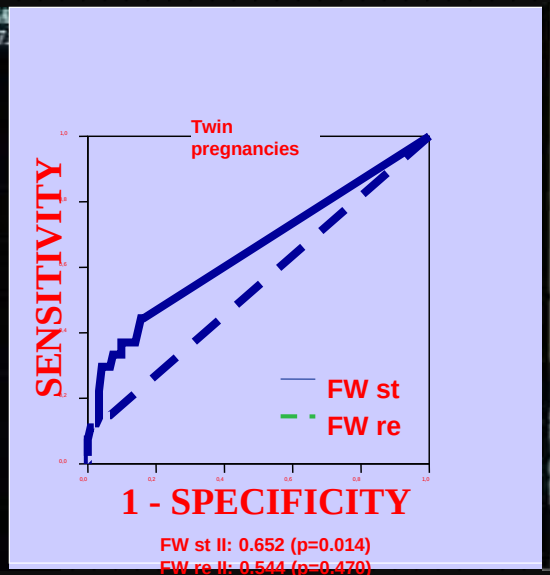
***Prediction** (not improved by maternal characteristics).*

CL 22-24 weeks	*Delivery < 32 weeks*
10 mm	*66%*
20 mm	*24%*
25 mm	***12 %***
>40 mm	*<1%*

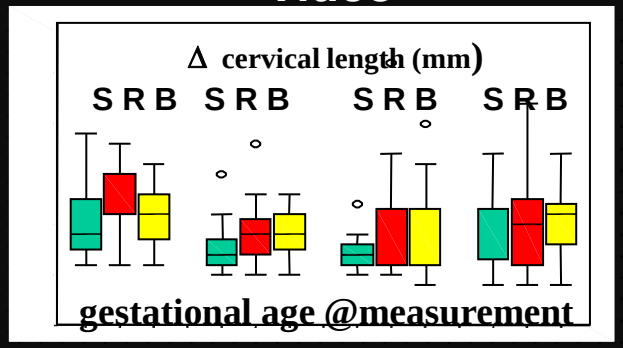
To et al. AJOG 2006 194:1360-5, n=1163

Cervix & Physical Stress

Video



Video



Arabin et al. J Reprod Med. 1997 ; 42 : 719-24

Arabin et al. U O G 2006; 27: 377-86

2++

Pooled Likelihood Ratios for a range of thresholds(CL)

Difference caused by symptoms / gestational age (twins)

Groups	SPB < 34 weeks	
Thresholds	+ LR (95% CI)	- LR (95% CI)
Asymptomatic		
<20 SSW		
20 mm	59.89 (3.46 – 103.48)	0.71 (0.52 – .96)
20-24 SSW		
20 mm	4.54 (1.46-14.14)	0.75 (0.64-0.90)
>24 SSW		
20 mm	3.44 (2.05-5.78)	0.41 (0.21-0.80)
30 mm	2.11 (1.43-3.12)	0.61 (0.42-0.87)
Symptomatic		
30 mm	2.33 (1.42-3.82)	0.15 (0.01-2.14)

Honest et al., Ultrasound Obstet Gynecol 2003; 22: 305

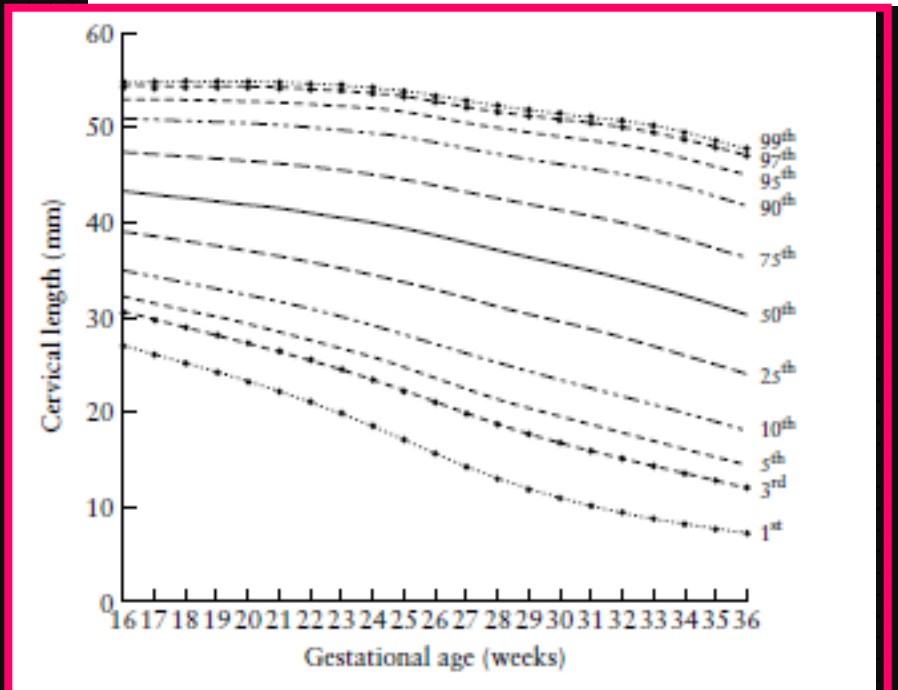
No Standard cut-offs, use Z-scores and centiles

Ultrasound Obstet Gynecol 2009; 33: 459–464
Published online 10 March 2009 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.6332

Reference range for cervical length throughout pregnancy: non-parametric LMS-based model applied to a large sample

L. J. SALOMON*, C. DIAZ-GARCIA†, J. P. BERNARD*‡ and Y. VILLE*

**Maternité, Hôpital Necker-Enfants Malades, Assistance Publique-Hôpitaux de Paris, Faculté de Médecine, Université Paris Descartes, Paris and Société Française pour l'Amélioration des Pratiques Echographiques (SFAPE) and ‡CEDEF, Le Chesnay, France and †Hospital Universitario Maternidad La Fe, Valencia, Spain*



Early stepwise (several TVS examinations in risk patients) secondary prevention is preferred to waiting until there is severe funneling, cervical shortening or dilatation.

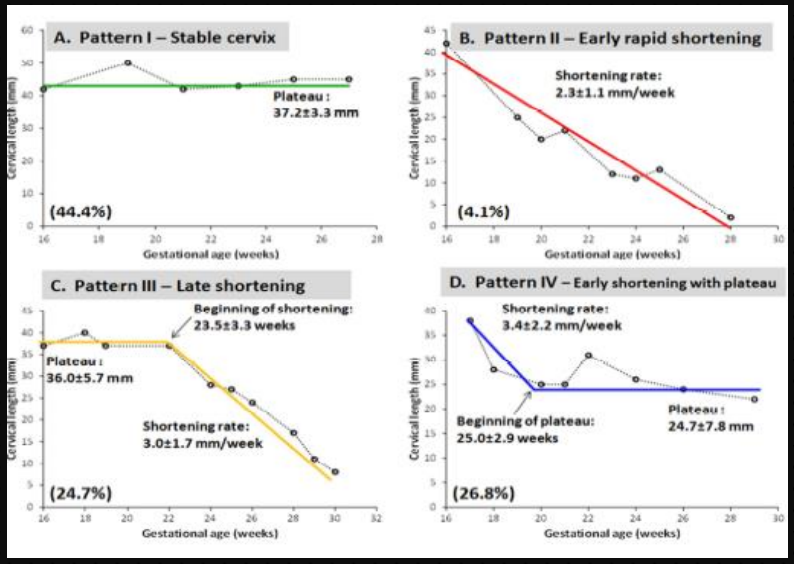
The Future:Consider different shortening patterns 2+

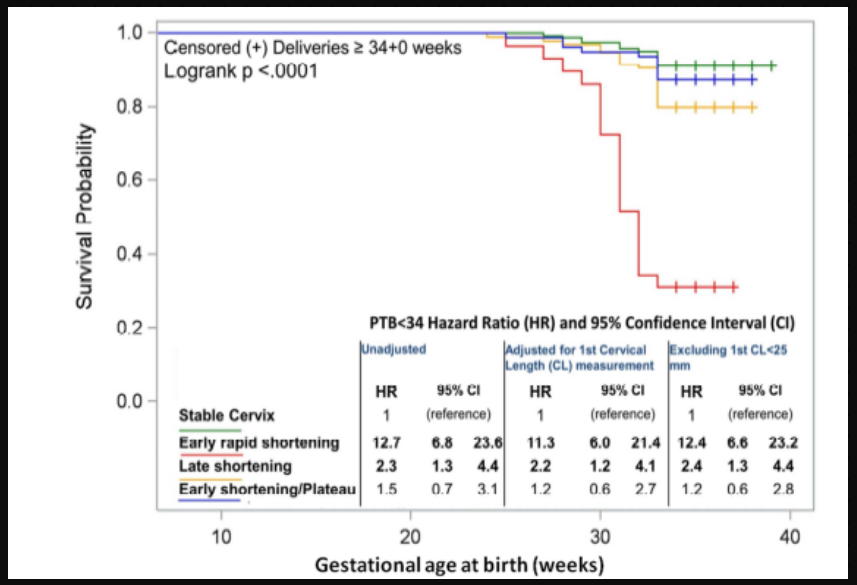
Accepted Manuscript **10th of May 2016**

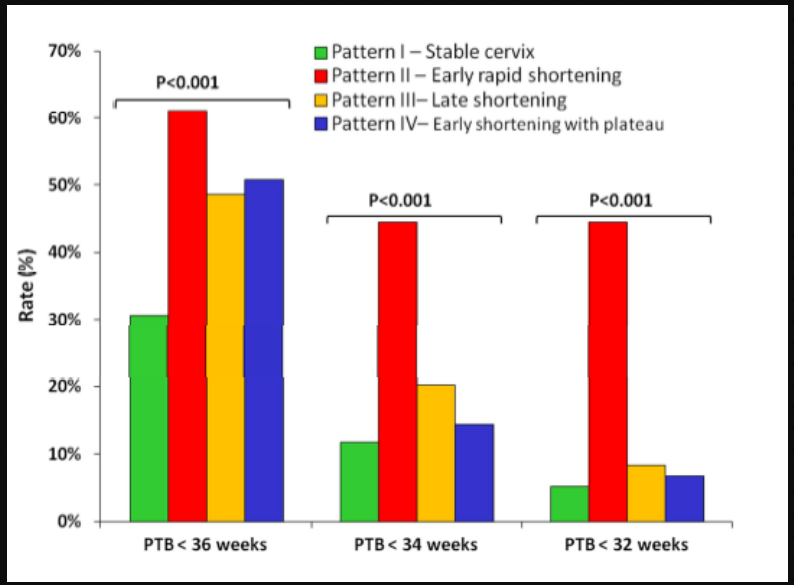
Serial Cervical Length Determination in Twin Pregnancies Reveals Four Distinct Patterns with Prognostic Significance for Preterm Birth

Nir Melamed, MD, MSc, Alex Pittini, Liran Hiersch, MD, Yariv Yogev, MD, Steven Korzeniewski, Ph.D., Roberto Romero, MD, D.Med.Sci, Jon Barrett, MD

Changes in CL in twins over time differ (related to the risk), but mostly that is only detectable after the standard examinations. Adapted therapy?







2++

The Future: Consider other diagnostic/therapeutic options

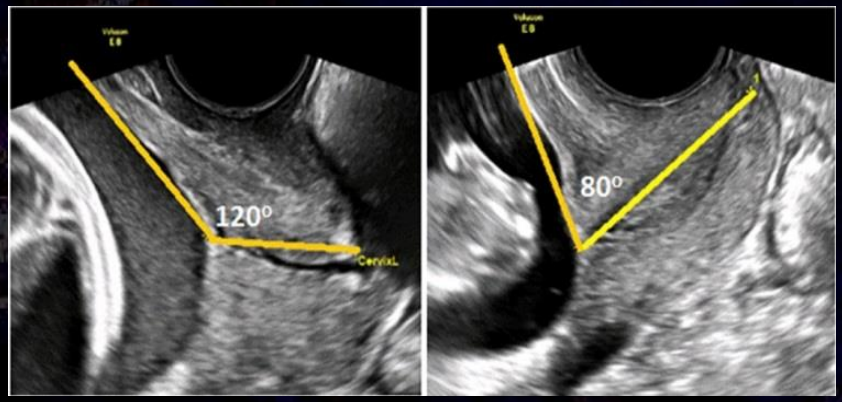
Uterocervical angle, a screening tool to predict SPB?
Results from a retrospective cohort of > 900 women

AJOG suppl. 1; 2016 abstract/ & accepted manuscript

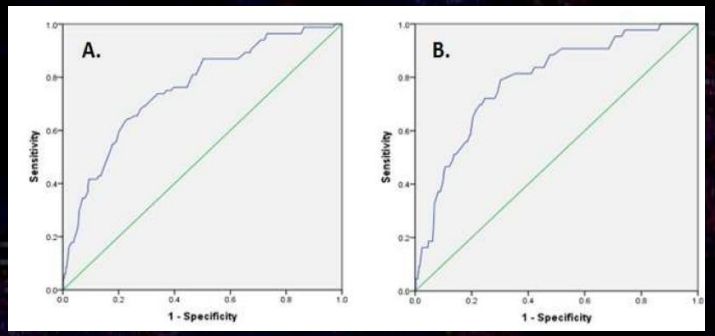
M. Dziadosz et al.

Parameters	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive likelihood ratio	Negative likelihood ratio
UCA >105°	81% (0.66 – 0.91)	65% (0.64 – 0.65)	10% (0.08 – 0.11)	99% (0.98 – 0.99)	2.3	0.29
CL ≤ 25mm	19% (0.093 – 0.31)	98% (0.97 – 0.98)	29% (0.14 – 0.47)	96% 0.96 – 0.97)	8.3	0.83
P value	<0.001	<0.001	<0.001	<0.001		
UCA >105° *or* CL≤ 25mm	63% (0.47 – 0.76)	65% (0.64 – 0.65)	7% (0.057 – 0.093)	97% (0.96 – 0.98)	1.8	0.57
UCA >105° *and* CL≤ 25mm	23% (0.13 – 0.33)	98% (0.98 – 0.99)	48% (0.27 – 0.68)	97% (0.96 – 0.97)	19	0.78

(95% Confidence Interval)



When TVU UCA is combined with CL, prediction of sPTB improves.



SPB< 37 weeks SPB< 34 weeks

2++

Cervix and Markers for PTB / infection in Twin Pregnancy

Cervical shortening is associated with histological signs of chorio-amniotnitis (45 twin placentas)

Guzman et al. AJOG 1999; 181: 793-7

Risk of SPB and Microbial Invasion of the amniotic cavity

Pregnancy (wks)	Clinical symptoms	Microbial invasion
Singleton (14-24)	Dilatation> 2cm, no PROM -	51,1%
Singleton < 34	Symptoms of SPB	21,6%
Twin < 34*	Symptoms of SPB	11,9%

* *Romero et al. AJOG 1990;163, 757-61*

C

Progressive Early Dilatation

Controversy: Delivery / expectant management

Ballooning ***Forelying cord***

Videos

10 twin pregnancies, -PPROM< 32wks: interval diagnosis to delivery:13 (1-29)d
8 twin pregnancies +PPROM <32 wks:interval UCP to delivery:4,5 (0-12)h

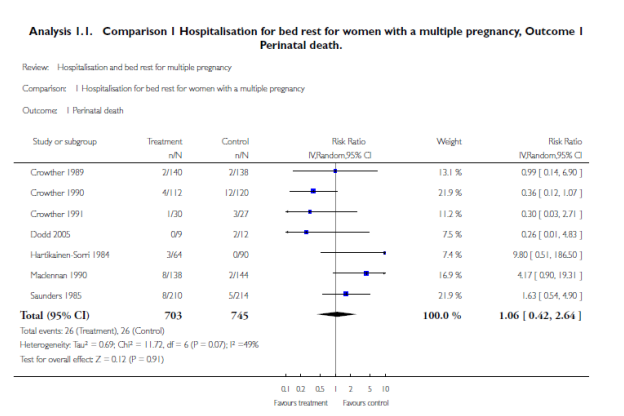
Nizard et al., BJ OG 2005, 112: 1-4 ***Arabin et al.J Perinat Med 2008; 36: 543-7***

Hospitalisation

1+

Crowthter et al. Cochrane Database of Systematic Reviews 2010, 7. Art. No.: CD000110.

Perinatal Death



Analysis 1.1. Comparison 1 Hospitalisation for bed rest for women with a multiple pregnancy, Outcome 1 Perinatal death.

Review: Hospitalisation and bed rest for multiple pregnancy

Comparison: 1 Hospitalisation for bed rest for women with a multiple pregnancy

Outcome: 1 Perinatal death

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Crowther 1989	2/140	2/138		13.1 %	0.99 [0.14, 6.90]
Crowther 1990	4/112	12/120		21.9 %	0.36 [0.12, 1.07]
Crowther 1991	1/30	3/27		11.2 %	0.30 [0.03, 2.71]
Dodd 2005	0/9	2/12		7.5 %	0.26 [0.01, 4.83]
Hartikainen-Sorri 1984	3/64	0/90		7.4 %	9.80 [0.51, 186.50]
Maclennan 1990	8/138	2/144		16.9 %	4.17 [0.90, 19.31]
Saunders 1985	8/210	5/214		21.9 %	1.63 [0.54, 4.90]
Total (95% CI)	**703**	**745**		**100.0 %**	**1.06 [0.42, 2.64]**

Total events: 26 (Treatment), 26 (Control)

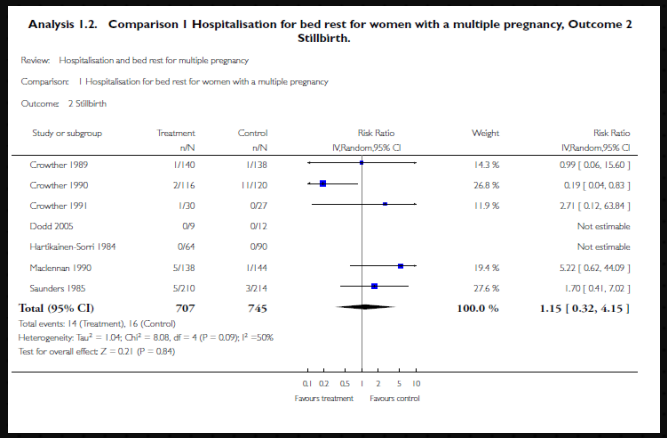
Heterogeneity: $Tau^2 = 0.69$; $Chi^2 = 11.72$, df = 6 (P = 0.07); $I^2 = 49\%$

Test for overall effect: Z = 0.12 (P = 0.91)

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

Stillborn



Analysis 1.2. Comparison 1 Hospitalisation for bed rest for women with a multiple pregnancy, Outcome 2 Stillbirth.

Review: Hospitalisation and bed rest for multiple pregnancy

Comparison: 1 Hospitalisation for bed rest for women with a multiple pregnancy

Outcome: 2 Stillbirth

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Crowther 1989	1/140	1/138		14.3 %	0.99 [0.06, 15.60]
Crowther 1990	2/116	11/120		26.8 %	0.19 [0.04, 0.83]
Crowther 1991	1/30	0/27		11.9 %	2.71 [0.12, 63.84]
Dodd 2005	0/9	0/12			Not estimable
Hartikainen-Sorri 1984	0/64	0/90			Not estimable
Maclennan 1990	5/138	1/144		19.4 %	5.22 [0.62, 44.09]
Saunders 1985	5/210	3/214		27.6 %	1.70 [0.41, 7.02]
Total (95% CI)	**707**	**745**		**100.0 %**	**1.15 [0.32, 4.15]**

Total events: 14 (Treatment), 16 (Control)

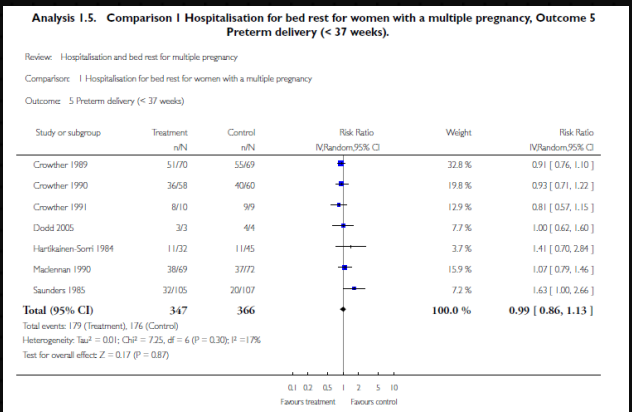
Heterogeneity: $Tau^2 = 1.04$; $Chi^2 = 8.08$, df = 4 (P = 0.09); $I^2 = 50\%$

Test for overall effect: Z = 0.21 (P = 0.84)

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

Preterm Birth < 37 weeks



Analysis 1.5. Comparison 1 Hospitalisation for bed rest for women with a multiple pregnancy, Outcome 5 Preterm delivery (< 37 weeks).

Review: Hospitalisation and bed rest for multiple pregnancy

Comparison: 1 Hospitalisation for bed rest for women with a multiple pregnancy

Outcome: 5 Preterm delivery (< 37 weeks)

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Crowther 1989	51/70	55/69		32.8 %	0.91 [0.76, 1.10]
Crowther 1990	36/58	40/60		19.8 %	0.93 [0.71, 1.22]
Crowther 1991	8/10	9/9		12.9 %	0.81 [0.57, 1.15]
Dodd 2005	3/3	4/4		7.7 %	1.00 [0.62, 1.60]
Hartikainen-Sorri 1984	11/32	11/45		3.7 %	1.41 [0.70, 2.84]
Maclennan 1990	38/69	37/72		15.9 %	1.07 [0.79, 1.46]
Saunders 1985	32/105	20/107		7.2 %	1.63 [1.00, 2.66]
Total (95% CI)	**347**	**366**		**100.0 %**	**0.99 [0.86, 1.13]**

Total events: 179 (Treatment), 176 (Control)

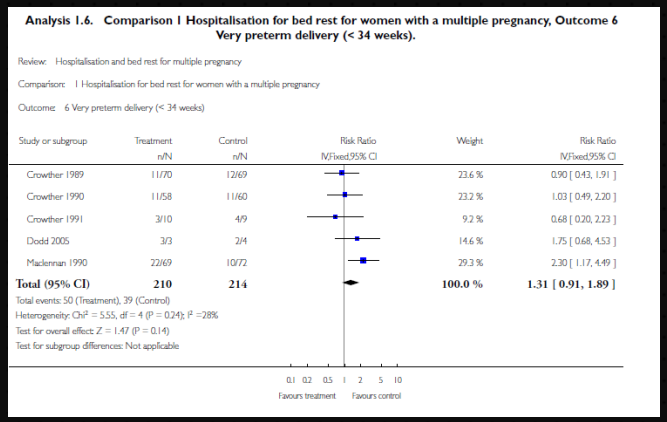
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 7.25$, df = 6 (P = 0.30); $I^2 = 17\%$

Test for overall effect: Z = 0.17 (P = 0.87)

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

Preterm Birth < 34 weeks



Analysis 1.6. Comparison 1 Hospitalisation for bed rest for women with a multiple pregnancy, Outcome 6 Very preterm delivery (< 34 weeks).

Review: Hospitalisation and bed rest for multiple pregnancy

Comparison: 1 Hospitalisation for bed rest for women with a multiple pregnancy

Outcome: 6 Very preterm delivery (< 34 weeks)

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Crowther 1989	11/70	12/69		23.6 %	0.90 [0.43, 1.91]
Crowther 1990	11/58	11/60		23.2 %	1.03 [0.49, 2.20]
Crowther 1991	3/10	4/9		9.2 %	0.68 [0.20, 2.23]
Dodd 2005	3/3	2/4		14.6 %	1.75 [0.68, 4.53]
Maclennan 1990	22/69	10/72		29.3 %	2.30 [1.17, 4.49]
Total (95% CI)	**210**	**214**		**100.0 %**	**1.31 [0.91, 1.89]**

Total events: 50 (Treatment), 39 (Control)

Heterogeneity: $Chi^2 = 5.55$, df = 4 (P = 0.24); $I^2 = 28\%$

Test for overall effect: Z = 1.47 (P = 0.14)

Test for subgroup differences: Not applicable

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

For women with an uncomplicated twin pregnancy the results show no benefit from routine hospitalisation. The policy cannot be recommended for routine clinical practice.

?

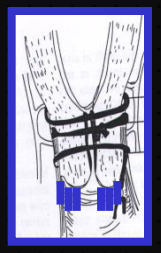
Cervix and tocolytics / indomethacin

Indomethacin for asymptomatic women with a CL<25 mm 14-27 weeks prevents SPB < 24 weeks, not in dilatation (singletons).

Berghella et al. AJOG 2006; 195: 809-13 / AJ Perinat 2009; 26: 13-9

"Although a lack of data prevents us from judging the efficiacy it seems logical to use atosiban or Ca-channel blockers as 1st line drugs because of the risk of pulmonary edema in twin gestations and beta-mimetics".

Vayssiere. J Gynecol Obstet Biol Reprod 2002; 31:114-23



1-

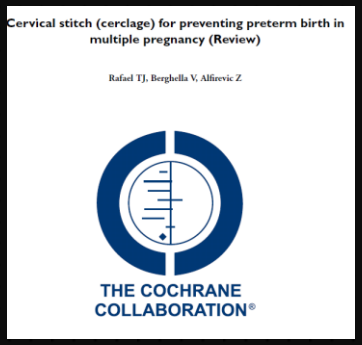
Cerclage In Twin Pregnancies ?

Meta-Analysis of Trials Using Individual Patient-Level Data

Increase of PTB after a cerclage

Twins	PTB < 35 wk	18/24 (75.0)	9/25 (36.0)	2.15 (1.15–4.01)
	Perin mort	11/48 (22.9)	3/50 (6.0)	2.66 (0.83–8.54)

Berghella et al. Obset Gynecol 2005 ; 106:181-89



Ultrasound-indicated cerclage associated with a risk of…

- **low birthweight** (RR 1.39, 95% CI 1.06 to 1.83/ 3 trials, n= 98)
- **very low birthweight** (RR 3.31, 95% CI 1.58 to 6.91/ 3 trials, n = 98)
- **RDS** (RR 5.07, 95% CI 1.75 to 14.70/ 3 trials, n = 98).

2014

Rise of morbidity after a cerclage

C/D

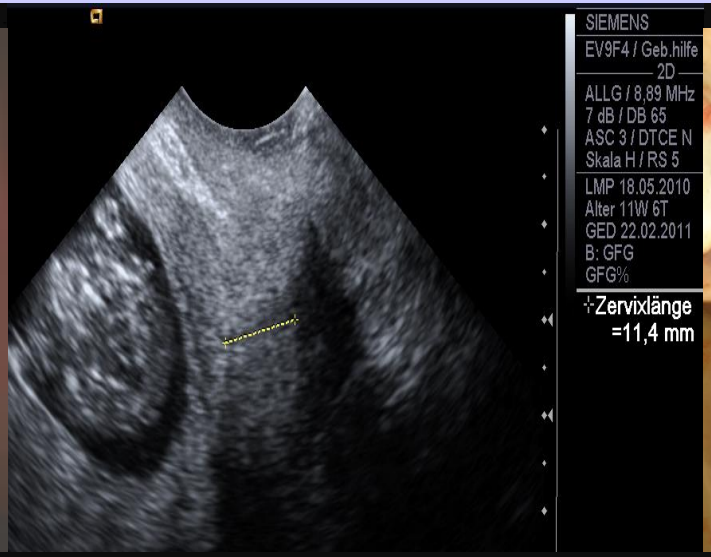
No cervix : Abdominal Cerclage

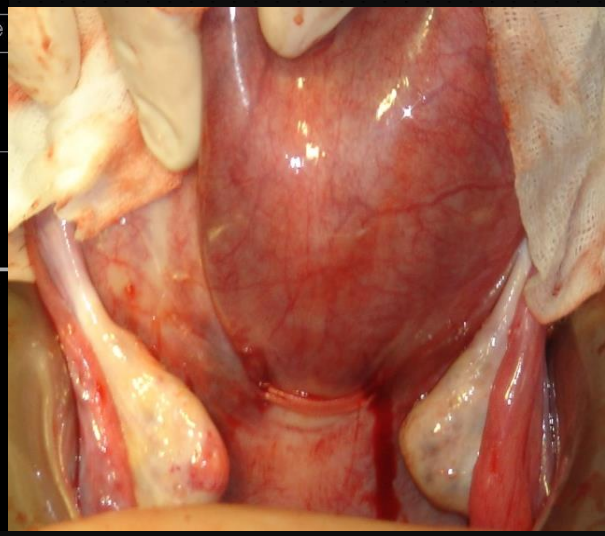
Outcome After Transabdominal Cervicoisthmic Cerclage

Frederik K. Lotgering, MD, PhD, Ingrid P. M. Gaugler-Senden, MD, Sabine F. Lotgering, and Henk C. S. Wallenburg, MD, PhD

Obstet Gynecol. 2006;107(4):779-84.

Example: Twin pregnancy after Trachelectomy. Abdominal cerclage at 13 weeks (after normal first-trimester screening), Cesarean at 35 weeks (preeclampsia)





Progestogens in twin pregnances: single RCTs

Study	N	Intervention	Outcome	Effect
Briery 2009	30	250mg17OHPC/Placebo	Delivery <35 wks	-
Cetingoz 2011	67	100mg vag.Prog/Placebo	Delivery <37 wks	Reduction Preterm birth
Lim 2011	654	250mg17OHPC/Placebo	Comp. outcome	-
Combs 2011	240	250mg17OHPC/Placebo	Comp. outcome	-
Nassar 2010	290	250mg17OHPC/Placebo	Delivery <37 wks	-
Norman 2009	500	90mg v.Prog.Gel/Placebo	Delivery <34 wks	Trend IUD!
Rode 2010	650	200mg vag.Prog/Placebo	Delivery <34 wks	-
Rouse 2007	661	250mg17OHPC/Placebo	Delivery <35 wks	Trend IUD
Rozenberg 2006	160	500mg17OHPC/Placebo	Interval Inclusion	-
Serra 2007/12 Caritis 2012	217 217	200-400mg v.Prog/Placebo 250mg17OHPC/Placebo	Delivery <37 wks Delivery <37 wks	- Increase preterm birth!

1-

Vaginal Progesterone in Twin Gestations: Retrospective meta-analysis

PF modulates gene expression in presence/ absence of inflammation. *Xu et al. AJOG 2008; 198: 314*

Effectiveness of progestogens to improve perinatal outcome in twin pregnancies: an individual participant data meta-analysis

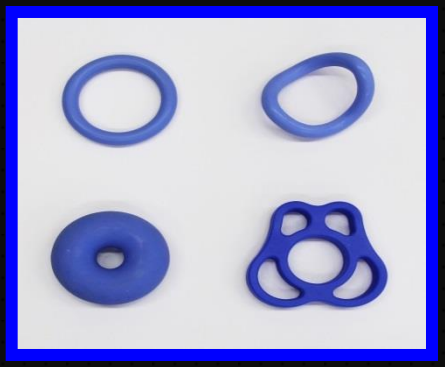
E Schuit,[a,b] S Stock,[c] L Rode,[d] DJ Rouse,[e] AC Lim,[b] JE Norman,[c] AH Nassar,[f] V Serra,[g] CA Combs,[h] C Vayssiere,[i] MM Aboulghar,[j] S Wood,[k] E Çetingöz,[l] CM Briery,[m] EB Fonseca,[n] K Worda,[o] A Tabor,[d] EA Thom,[p] SN Caritis,[q] J Awwad,[r] IM Usta,[s] A Perales,[r] J Meseguer,[t] K Maurel,[t] T Garite,[u] MA Aboulghar,[j] YM Amin,[j] S Ross,[k] C Cam,[l] A Karateke,[l] JC Morrison,[v] EF Magann,[w] KH Nicolaides,[x] NPA Zuithoff,[a] RHH Groenwold,[a] KGM Moons,[a] A Kwee,[y] BWJ Mol,[z] a Global Obstetrics Network (GONet) collaboration

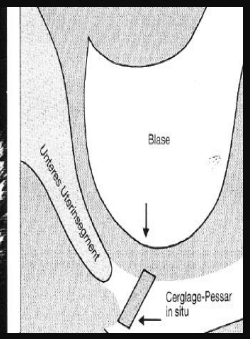
BJOG 2014; 528.13032.

13 trials included, 3768 women & 7536 babies.

Neither 17OH-PG (RR: 1.1; 95% CI: 0.97–1.4), nor vaginal PG (RR 0.97; 95% CI 0.77–1.2) reduced adverse perinatal outcome. In a subgroup with a CL of ≤25 mm, vaginal PG reduced adverse perinatal outcome (15/56 versus 22/60; RR 0.57; 95% CI 0.47–0.70), however, further research is warranted to confirm this finding.

Pessaries are thought to create an immunological barrier & change the inclination of the cervical canal, distributing pelvic force away from the cervix.





Kubli F, Arabin B., *Frühgeburt* , in *Praxis der Perinatalmedizin*, J.W. Dudenhausen, Editor. **1982**, Thieme: Stuttgart-new york. p. 148-84

Cross R. *Treatment of habitual abortion due to cervical incom-petence.* Lancet **1959**. 274: 127

Vitsky M. *The Incompetent Cervical Os and the Pessary.* AJOG **1963**. 87:144-7

Oster S, Javert CT. *Treatment of the incompetent cervix with the Hodge pessary.* Obstet Gynecol, **1966**. 28: 206-8

Jiratko K et al. *Useful treatment of imminent precocious delivery. Confrontation of the results gained by cerclage and by insertion of a pessary.* Cesk Gynekol, **1976**. 41: 184-6

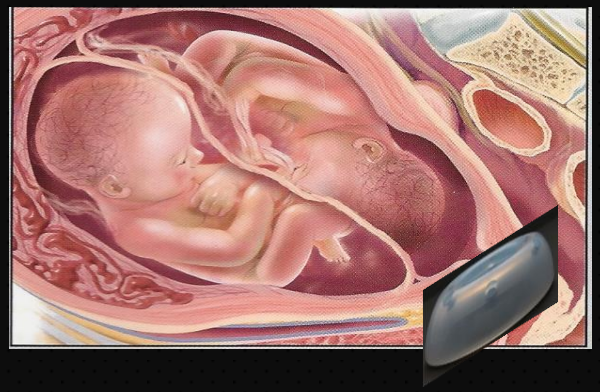
Arabin H. *Pessartherapie*, in *Gynäkologie*, G. Martius, Editor. **1991**, Thieme: Stuttgart-New York. p. 263-76.

Arabin B et al. *Is treatment with vaginal pessaries an option in patients with a sonographically detected short cervix?* J Perinat Med, **2003**. 31: p. 122-33.

Goya M et al. *Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial.* Lancet, **2012.**

Which Size? What do you observe?

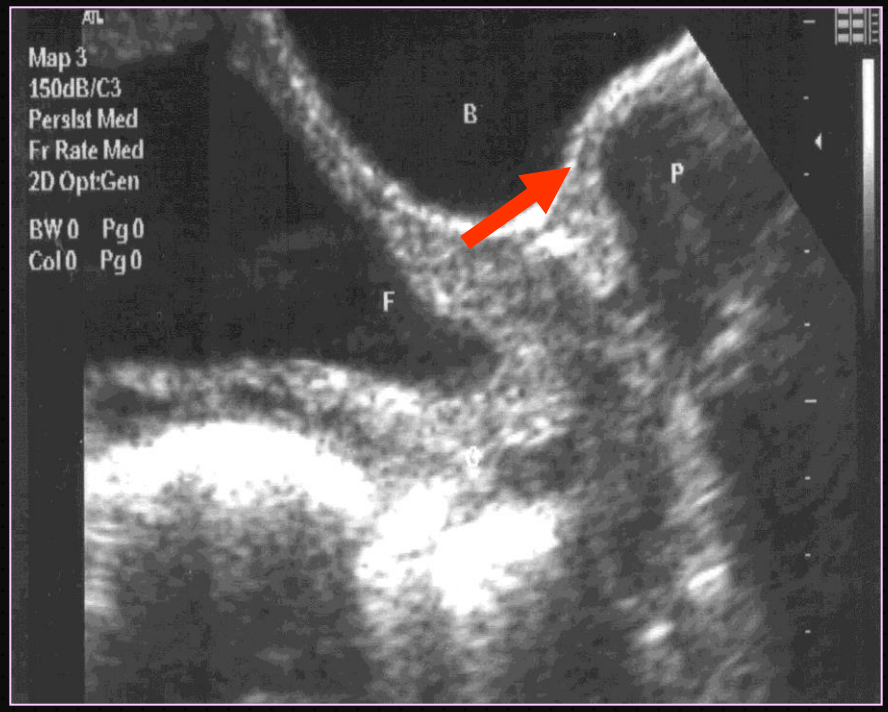
Upper diameter (32/35mm), Height (25mm) Lower diamater (65/70mm)



„Despair“

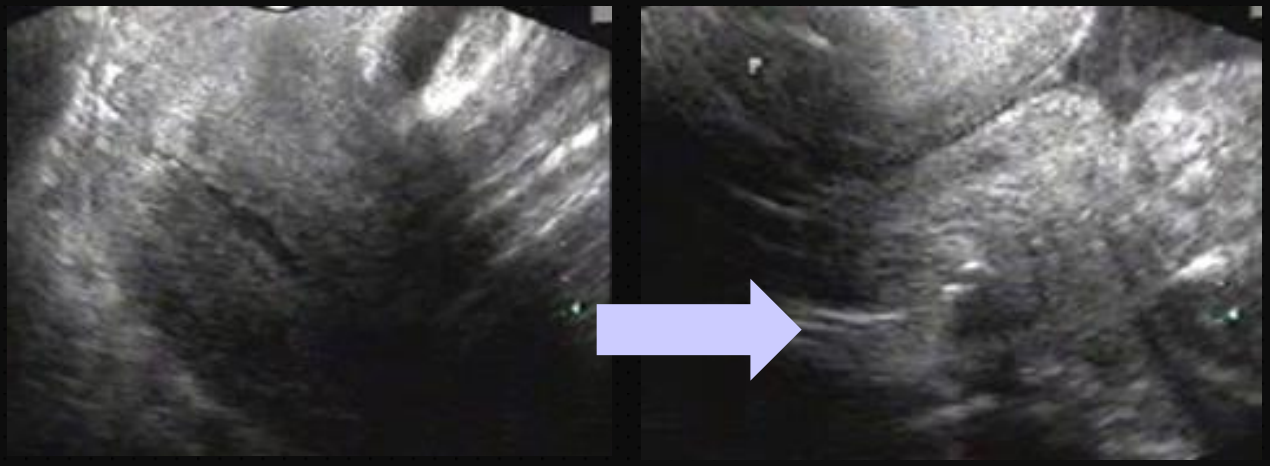
Combination Cerclage/Pessary, my first patient- a twin pregnancy

- Patient & 2 previous losses (cervical insufficiency)
- Now twin pregnancy
- In spite of cerclage opening of the internal os at 17 weeks
- Insertion of an Arabin Pessary with a CL of 3 mm.
- Delivery at 36 weeks



Cervix before / after Pessary

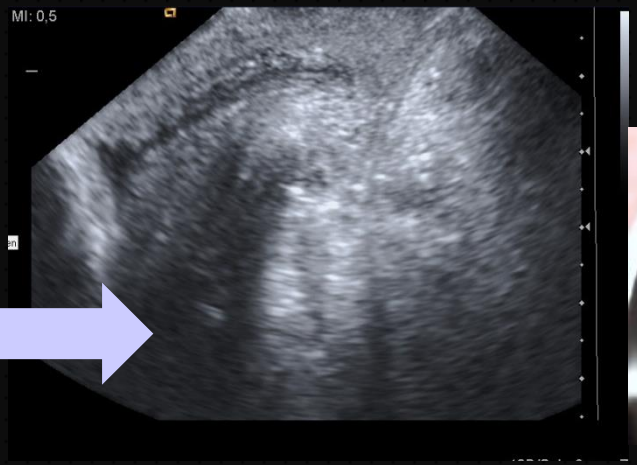
4/D



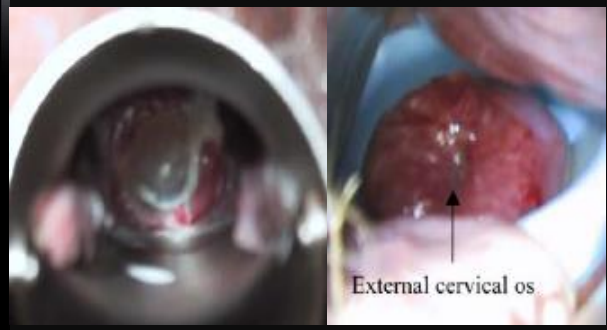
Secondary Prevention

Before pessary

After pessary



„Therapy“

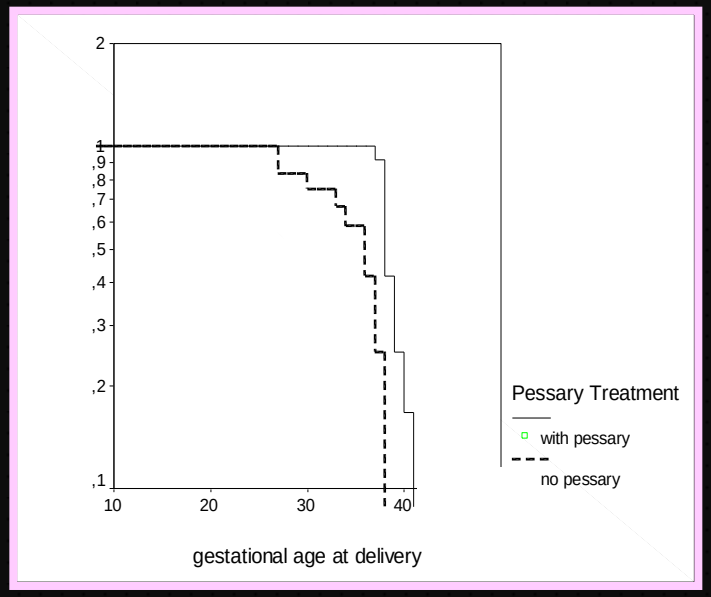


Cervical Pessary

2/ C

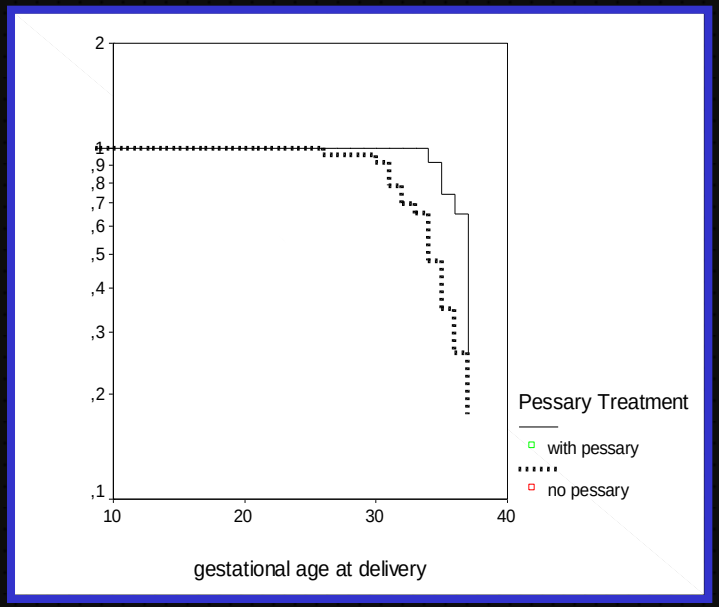
Case control study in CL < 10 th centile

n=24 singleton pregnancies, CL< 10th cent



J Perinat 2003; 31: 122

n=46 twin pregnancies, CL< 10th cent



Conclusion: RCTs needed!

D

Application

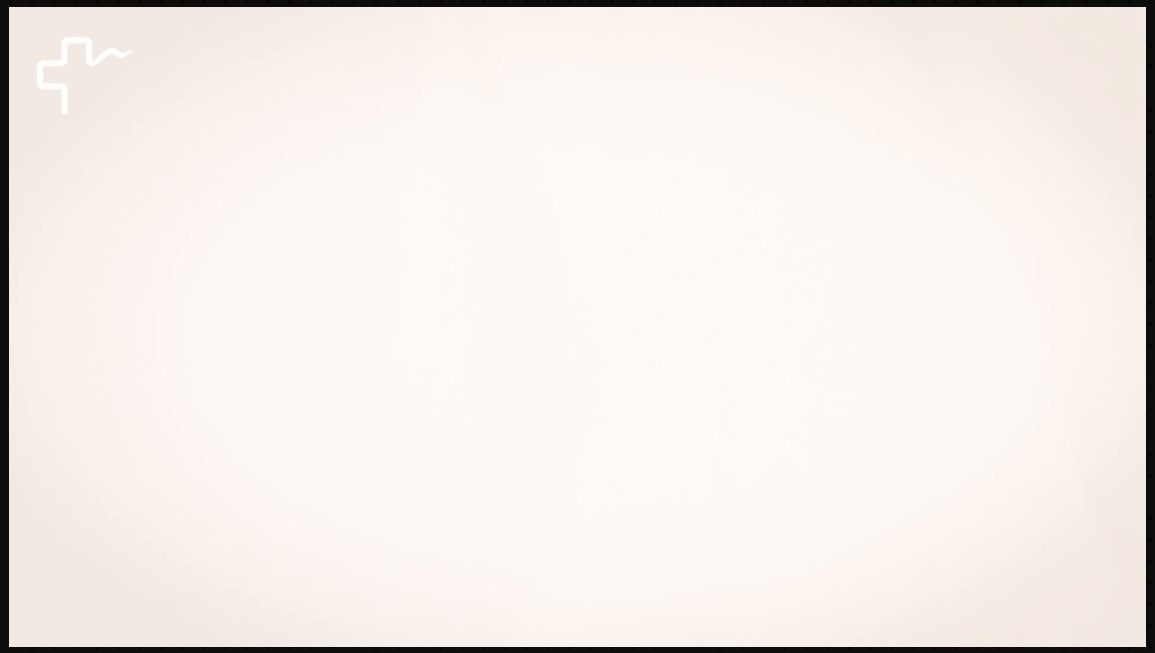
Cervical pessaries for prevention of spontaneous preterm birth: past, present and future

B. ARABIN*† and Z. ALFIREVIC‡

*Centre for Mother and Child of the Philipps University Marburg, Marburg, Germany; †Clara Angela Foundation, Witten, Germany; ‡Centre for Women's Health Research, University of Liverpool, Liverpool Women's Hospital, Liverpool, UK •

UOG Oct. 2013

(Video)



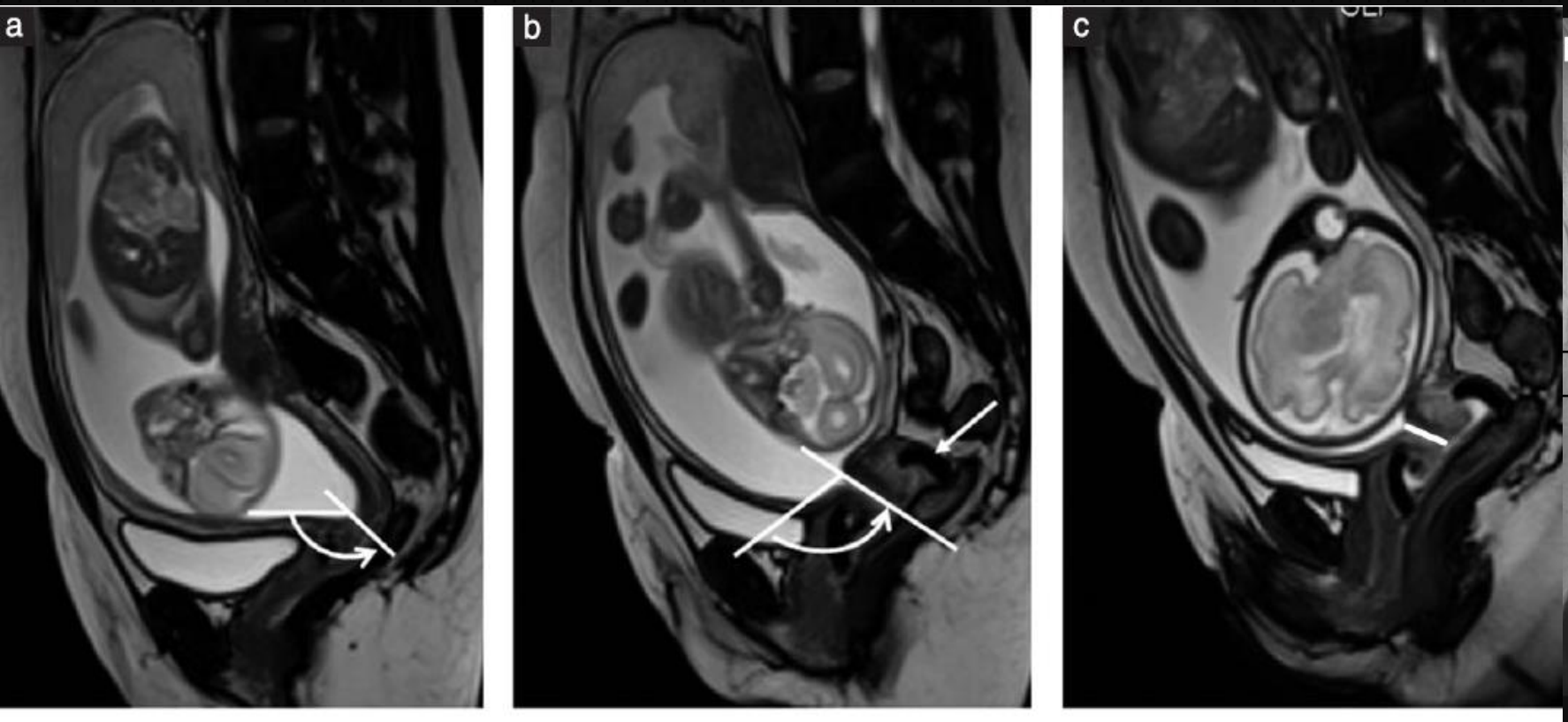
2+

Ultrasound Obstet Gynecol 2013; 42: 426–433
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.12507

Arabin cervical pessary in women at high risk of preterm birth: a magnetic resonance imaging observational follow-up study

M. M. CANNIE*†, O. DOBRESCU‡, L. GUCCIARDO‡, B. STRIZEK‡, S. ZIANE‡, E. SAKKAS‡, F. SCHOONJANS*, L. DIVANO* and J. C. JANI‡

**Department of Radiology, University Hospital Brugmann, Brussels, Belgium; †Department of Radiology, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium; ‡Department of Obstetrics and Gynecology, University Hospital Brugmann, Brussels, Belgium*



3/ C

Pessary in patients with TTTS and Laser

> 50% of Patients with TTTS and a CL<20 mm deliver before 28 weeks !

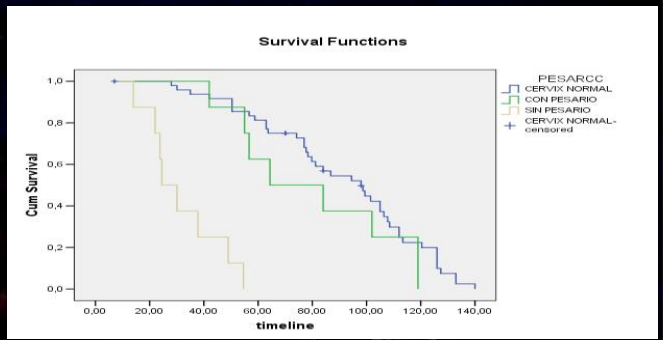
Robyr et al. UOG 2004; 25: 27-41

Carreras et al. Prent. Diagnosis 2012; 32: 1-5

TTTS and CL before fetoscopy laser (n= 79)

CL > 25 mm (n=63)

CL ≤ 25 mm (n=16)



Expectant management (n = 8)

Pessary placement (n=8)

	Expectant	Pessary	P
Median time interval between laser/delivery (days)	32	80	<0,05
Mean GA at delivery (weeks)	28	32	<0,01
Neonatal survival (%)	5 (71)	8 (100)	<0,05
Severe neonatal outcome (%)	4 (50)	2 (25)	<0.01

1-

Pessary in Twin Pregnancies

First RCT / TVS in Twin Pregnancies

(817 twin pregnancies, 143 with a CL< 25 centile, <38mm @ 16-20 weeks)

Thursday, February 14, 2013 • 8:00 am – 10:00 ar

GENERAL

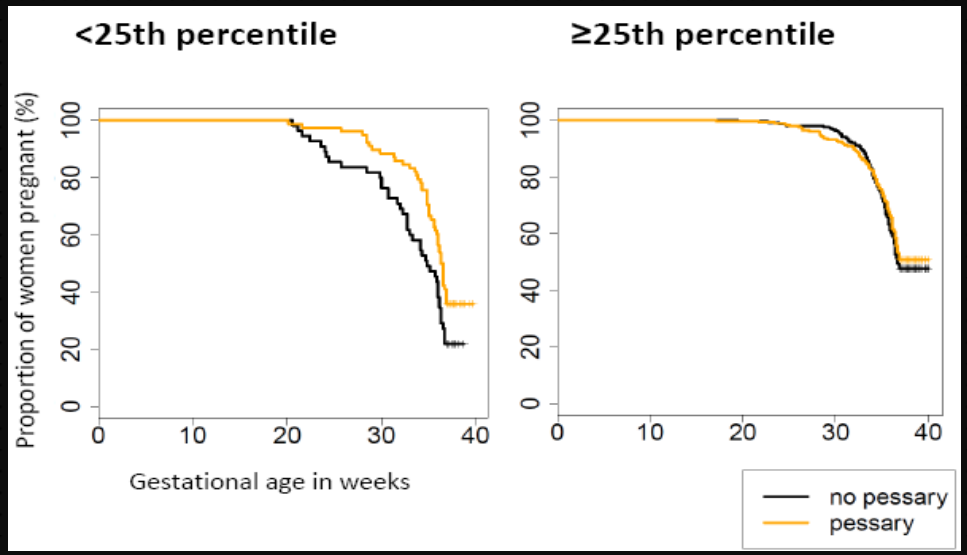
AJOG 213, suppl.

Abstracts 1 – 8

Moderators: Kate Menard, MD, President, SMFM; George Saade, 2013 Honorary Member

1 **Pessaries in multiple pregnancy as a prevention of preterm birth (ProTWIN): a randomized controlled trial**

Sophie Liem[1], Ewoud Schuit[2], Joke Bais[3], Karin de Boer[4], Kitty Bloemenkamp[5], Josien Brons[6], Hans Duvekot[7], Bas Nij Bijvanck[8], Maureen Franssen[9], Ingrid Gaugler[10], Jan Molkenboer[11], Martijn Oudijk[12], Dimitri Papatsonis[13], Paula Pernet[14], Martina Porath[15], Liesbeth Scheepers[16], Marko Sikkema[17], Jan Sporken[18], Harry Visser[19], Wim van Wijngaarden[20], Mallory Woiski[21], Marielle van



	Pessary (N=78)	No pessary (N=55)	Relative Risk (95% CI)
GA at delivery (median (IQR))	36+3 (35+0-37+2)	35+0 (30+5-36+5)	0.49 (0.41-0.77)
< 28 wk	3 (4%)	9 (16%)	0.23 (0.06-0.87)
< 32 wk	11 (14%)	16 (29%)	0.49 (0.24-0.97)
< 37 wk	50 (64%)	43 (78%)	0.82 (0.54-1.2)

	Pessary (N=78)	No pessary (N=55)	Relative Risk (95% CI)
Neonatal outcome			
Composite poor perinatal outcome	9 (12%)	16 (29%)	0.40 (0.19-0.83)
Death before discharge	**2 (3)**	**10 (18)**	**0.14 (0.03-0.65)**

PROTWINTRIAL

1-

Cervical pessaries for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicentre, open-label randomised controlled trial

Sophie Liem, Ewoud Schuit, Maud Hegeman, Joke Bais, Karin de Boer, Kitty Bloemenkamp, Jozien Brons, Hans Duvekot, Bas Nij Bijvank, Maureen Franssen, Ingrid Gaugler, Irene de Graaf, Martijn Oudijk, Dimitri Papatsonis, Paula Pernet, Martina Porath, Liesbeth Scheepers, Marko Sikkema, Jan Sporken, Harry Visser, Wim van Wijngaarden, Mallory Woiski, Mariëlle van Pampus, Ben Willem Mol, Dick Bekedam

"The expected impact of the pessary is likely to be strong.

In the NL, there are 3200 women with a twin pregnancy/year. We estimate among the 6400 children a reduction of 742 (12%) to 563 (8%) children with poor perinatal outcome per year and a mortality reduction from 384 (6%) to 206 (3%) by the pessary in women with a multiple pregnancy.

Important other advantages of the pessary are its low costs and its mechanical working mechanism, thus virtually guaranteeing the absence of side effects on the offspring".

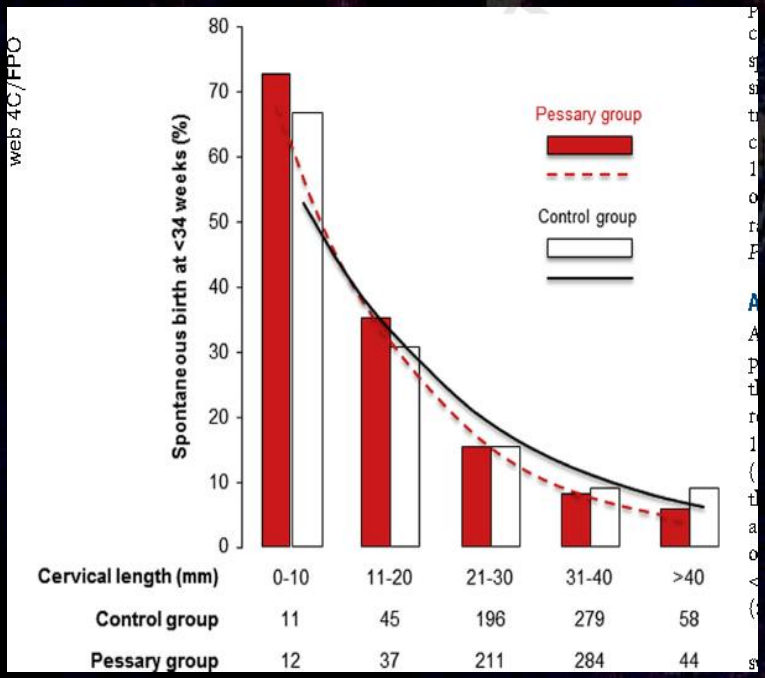
Liem et al., Dutch Consortium, Lancet 2013

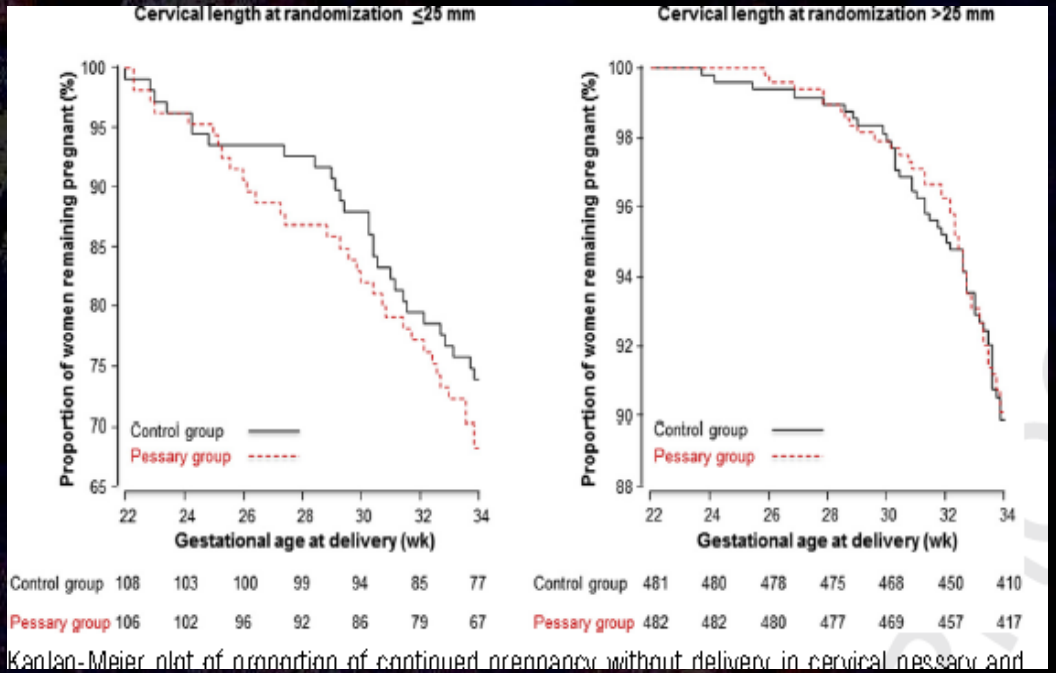
1-

Results of a Multi-Center Study

"Care givers should be trained, and their results should be subjected to external quality assurance"

*Nicolaides KH. Am J Obstet Gynecol 2004; **191**: 45-67*

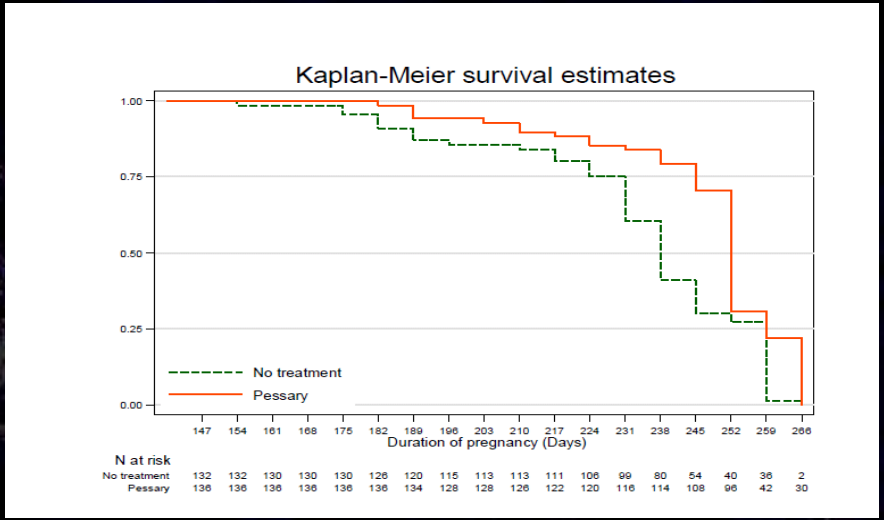




Randomized Trial in Twins with a CL< 25 mm

AJOG 2016, Team Hebron, Barcelona, with local teaching and audit! 1+

2287 screened twins,
154 with Cl< 25 weeks



n=68 no treatment versus n= 65 pessary

SPT < 34 weeks	26 %	versus	11%	p<0.001
PTL	50%	versus	24%	p<0.001

?

Do not trust all cost-effectiveness analysis

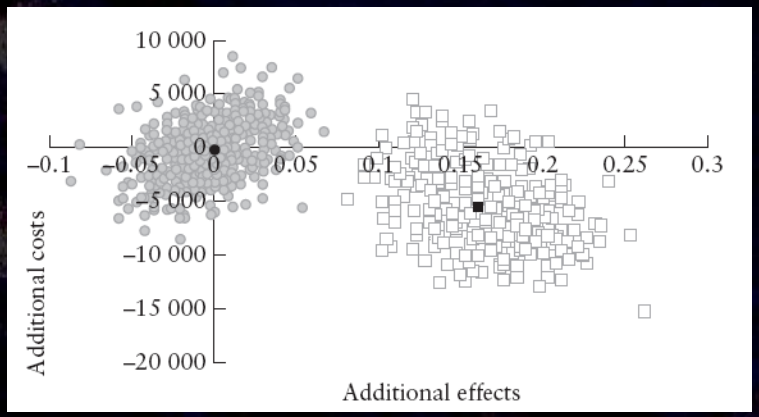
What are the costs of a surviving/ dead child?

In this trial : zero (increased in control group)

Ultrasound Obstet Gynecol 2014
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.13432

Economic analysis of use of pessary to prevent preterm birth in women with multiple pregnancy (ProTWIN trial)

S. M. S. LIEM*, G. J. VAN BAAREN*, F. M. C. DELEMARRE†, I. M. EVERS‡, G. KLEIVERDA§, A. J. VAN LOON¶, J. LANGENVELD**, N. SCHUITEMAKER††, J. M. SIKKEMA‡‡, B. C. OPMEER§§, M. G. VAN PAMPUS¶¶, B. W. J. MOL*** and D. J. BEKEDAM¶¶



In women with a CL <38mm:significant reduction in poor perinatal outcome:12% vs 29%; RR, 0.40; 95% CI 0.19–0.83.

Mean costs in pessary vy. Control group €25 141 vs €30 577 Difference, −€5436 (95% CI, −€11 001 to €1456).

Pessary treatment was more effective and less costly.

2+

Per Protocol Analysis

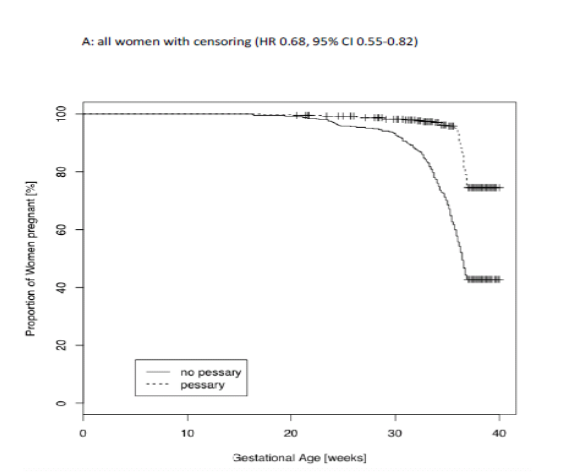
Liem et al. Acta Scand. accepted

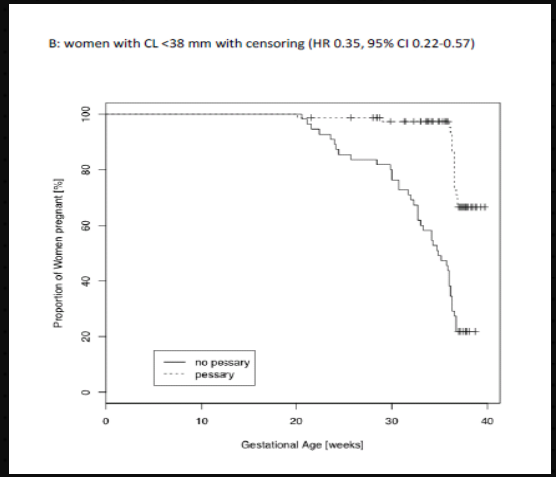
Cervical pessaries to prevent preterm birth in women with a multiple pregnancy: a per-protocol analysis of a randomized clinical trial

Short running title: ProTWIN trial

Sophie LIEM[1], Ewoud SCHUIT[1,2,7], Mariëlle VAN PAMPUS[3], Marjo VAN MELICK[4], Maurice MONFRANCE[5], Josje LANGENVELD[5], Ben Willem MOL[6] & Dick BEKEDAM[3]

Per Protocol Analysis with censoring of cases. Larger reduction of poor perinatal outcome and very preterm birth when consistently applied.



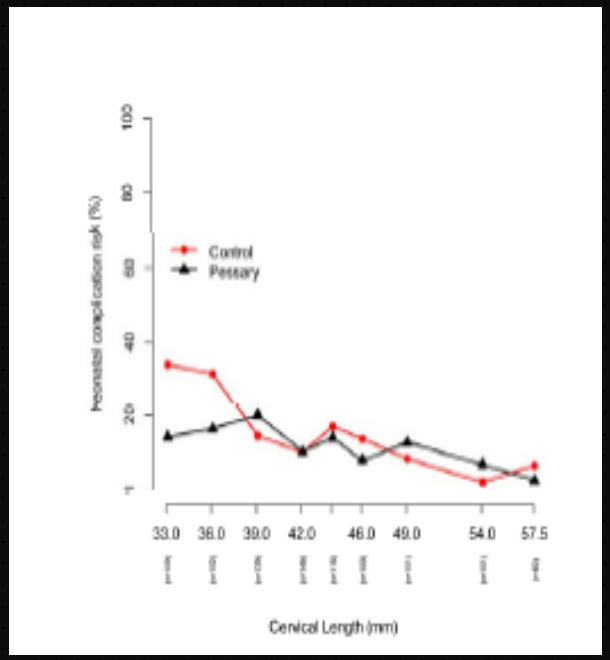


2+

Multivariable models may guide our decisions

When to place a pessary in women with multiple pregnancy?

Accepted article UOG Tajik et al. (from RCT, n=801)



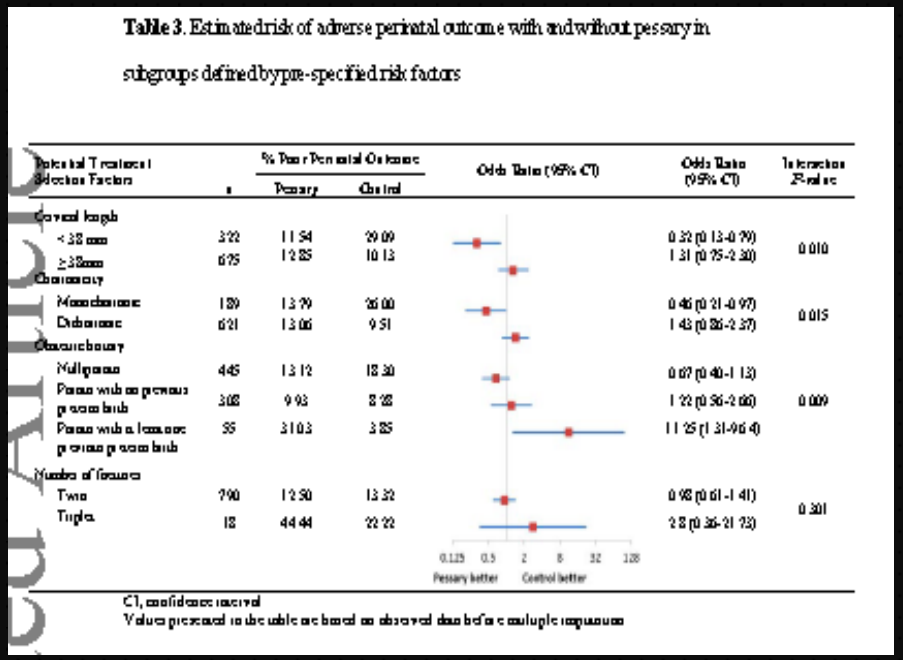


Table 3. Estimated risk of adverse perinatal outcome with and without pessary in subgroups defined by pre-specified risk factors

Potential Treatment Selection Factors	n	% Poor Perinatal Outcome: Pessary	% Poor Perinatal Outcome: Control	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Interaction P-value
Cervical length						
< 38 mm	322	11.54	29.09		0.32 (0.13-0.79)	0.010
≥ 38mm	675	12.85	10.13		1.31 (0.75-2.30)	
Chorionicity						
Monochorionic	139	13.79	26.00		0.46 (0.21-0.97)	0.015
Dichorionic	621	13.06	9.51		1.43 (0.86-2.37)	
Obstetric history						
Nulliparous	445	13.12	18.30		0.67 (0.40-1.13)	
Parous with no previous preterm birth	308	9.93	8.28		1.22 (0.56-2.66)	0.009
Parous with a history of previous preterm birth	55	31.03	3.85		11.25 (1.31-96.4)	
Number of fetuses						
Twin	790	12.50	13.32		0.93 (0.61-1.41)	0.301
Triplet	18	44.44	22.22		2.8 (0.35-21.73)	

0.125 0.5 2 8 32 128
Pessary better | Control better

CI, confidence interval
Values presented in the table are based on observed data before multiple imputation

Short cervix, monochorionicity and nulliparity were predictive factors for a benefit from pessary insertion.

2+

Long-term effects of cervical pessary for PB prevention in twin pregnancy with short CL: 3 years follow-up

van't Hoofd et al 2016 SMFM, AJOG 2016 suppl.1

In total 27 children died (7 in pessary vs 20 control group).
A higher survival without disability in the pessary group when compared to controls (92.4 vs 73.8%, p=0.006).

CONCLUSION: In women with a twin pregnancy & a CL < 38 mm, cervical pessary increases survival without neurodevelopmental disability in children at 3 years corrected age.
Among survivors Bayley-III scores were similar between pessary and non-pessary users, a pessary was without adverse neurodevelopmental effects for children.

The Future in EBM 1++

Network for a Prospective Meta-Analysis

PROMPT: PROspective Meta-Analysis for Pessary Trials

Feb/ 2016 George Saade and his team in Washington DC

Core Outcomes in Women's Health (CROWN)

- **13 Core outcomes: Primary / Secondary / Baseline data collection**
- **Gestational age cut-off values in singleton and twin gestation**
- **No intervention; vaginal progesterone; vaginal placebo; cerclage**
- **Collaboration Guidelines / Eligibility / Roles and responsibilities**
- **Ethics / Data Safety / Monitoring Committees / Authorship / Draft**
- **Communication / Timeline, meeting s schedule**

We all agree that the best answers to clinical problems will come from international collaboration. Whether we can all speak with one voice, only time will tell.
(Arabin & Alfirevic, UOG 10-2013)

The Future: PROMPT May-2016 (Mail Lynda Ugwu)

Currently included: 11 trials from 6 countries
All studies open for recruitment

1++

5 studies in singleton pregnancies (2xGB, NL, 2x US)
5 studies in twin pregnancies (GB,NL,2x US,France)
1 study in both, singleton & twin pregnancies (Brazil)
Further trials starting in Australia, Canada, Haiti, Israel, Vietnam, US

Minimal criteria for inclusion in PROMPT

Protocols and consent forms approved

Willingness to share study protocol and data forms

Registered trial i.e. Clinical trials.gov; ICPTR

The Future: Teach the Teachers: Yearly Certificate of Competence ?

2-

14th World Congress in Fetal Medicine

The importance of learning curve in practice of cervical pessary

Franca MS, Hamamoto TENK, Hatanaka AR, Mattar R, Moron AF

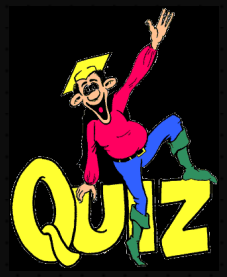
Methods

Patients were included between 16 to 26 weeks and 6 days, at the time of morphological second trimester ultrasound, and if a short cervix (under 25mm) was detected, the patients were treated, after signing an informed consent form. At present, the group has been following up approximately 80 cases and has identified important improvement in the perinatal results, with same technique throughout this 4 years of experience. The comparison of perinatal results between pessary users at the initial phase (first 1. 5 years) (Group 1), against pessary users in the final phase (last 2. 5 years) (Group 2), was procedure. This material was collected by few researches and 50 singleton pregnancies were included between 16 and 26 weeks and 6 days. Statistical analysis and comparison of the groups was submitted to Student t test.

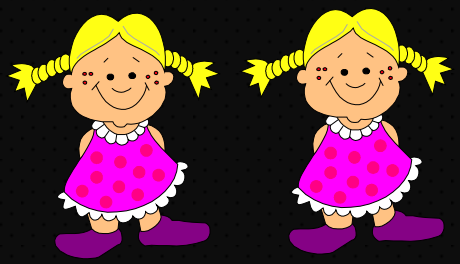
Results

The descriptive results present no difference between the groups regarding age, parity, cervical length or gestational age at diagnosis of short cervix. The results for Group 1 presented 35 w 5d ± 28 days and Group 2 presented 37 w 6d ± 12 days, for the mean gestational age at birth (P = 0, 02*). The mean weight at birth was 2624g ± 885g in Group 1 and was 3091g ± 415g in Group 2 (P=0, 05*).

Although pessary treatment is simple, there is a learning curve. Results improved within 4 years of experience. RCTs frequently imply centers with no experience and decentralize experience due to the many doctors involved.



Delivery



An absolute indication for a planned Cesarean delivery is:

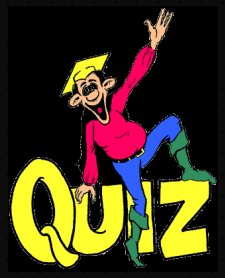
a) DCDA Twins, 36 wks, 1st in vertex & 2nd in transverse presentation,

b) DCDA Twins, 36 wks, 1st in transverse & 2nd in vertex presentation,

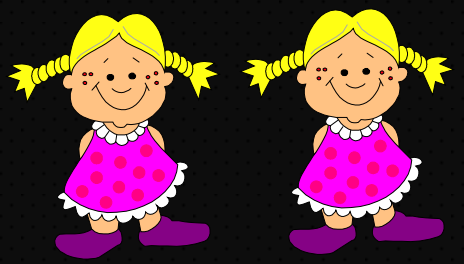
c) MCDA Twins, 34 wks, 1st in vertex, 2nd in transverse presentation,

d) MCDA Twins with s IUGR gr. 3, 28 weeks, both in vertex presentation

e) MCMA Twins, 33 wks, 1st in vertex, 2nd in foot presentation



Delivery



In vaginal delivery in twins – what is right?

a) **Vertex-transverse presentation: After delivery of the first twin increase oxytocin to avoid post partum bleeding.**

b) **Vertex-breech presentation: Try to do an external version of the second twin when FHR is non-reassuring and deliver.**

c) **Vertex-vertex (not engaged): After delivery of the first twin perform amniotomy and push with increasing levels of oxytocin.**

d) **Consider that the interval between the delivery of both twins should be as short as possible and call an experienced obstetrician.**

e) **The longest interval between the delivery of DC twins was 2 days.**

Advances of Obstetrics Today

- Many twins „expected“ by ART
- Early prenatal ultrasound diagnosis
- FHR monitoring, ultrasound during labor
- Emergency and epidural anesthesia
- Asepsis/Antibiotics, Tocolytics, Oxytocin
- Perinatal Centers: Neonatology
- Systematic Audits (?)

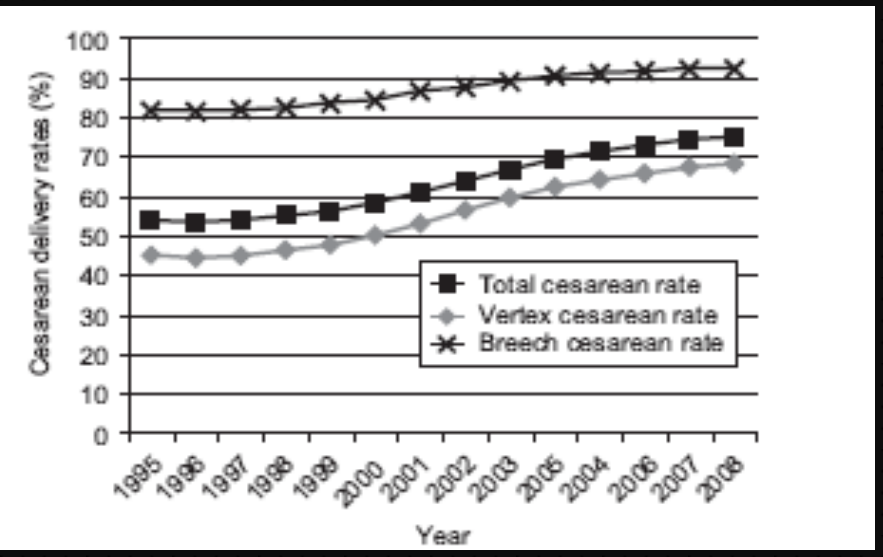
Advances of Obstetrics Today?

Obstet Gynecol 2011, 118, 5

Trends in Cesarean Delivery for Twin Births in the United States

1995–2008

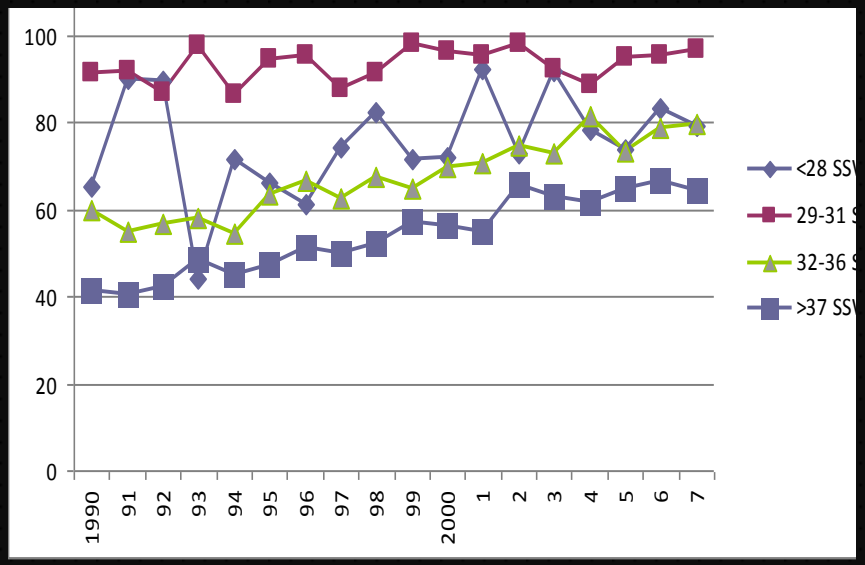
Henry C. Lee, MD, MS, Jeffrey B. Gould, MD, MPH, W. John Boscardin, PhD, Yasser Y. El-Sayed, MD, and Yair J. Blumenfeld, MD



Re: Obstet Gynecol 2012, 119, 3

Trends in Cesarean Delivery for Twin Births in the United States: 1995–2008

To the Editor:



Increase of CD in vertex twins: 45% - 68.2%

Highest rate in low-risk pregnancies

After correction with all risks: 5% increase/yr.

CD Hessen: n= 27565

< 28: 79%, 28-31: 97 %,

32-36:80 % > 37: 65 %,

Guidance by Guidelines?

ACOG:

"The mode of delivery should be determined by position, ease of FHR, maternal & fetal status.

Data are insufficient to determine the best route of delivery".

ACOG Practice Bulletin #56: Obstet Gynecol 2004;104(4):869-83

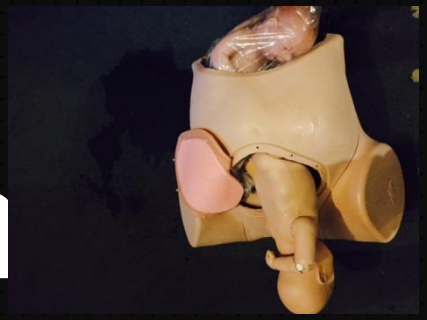
Germany: ???

France:

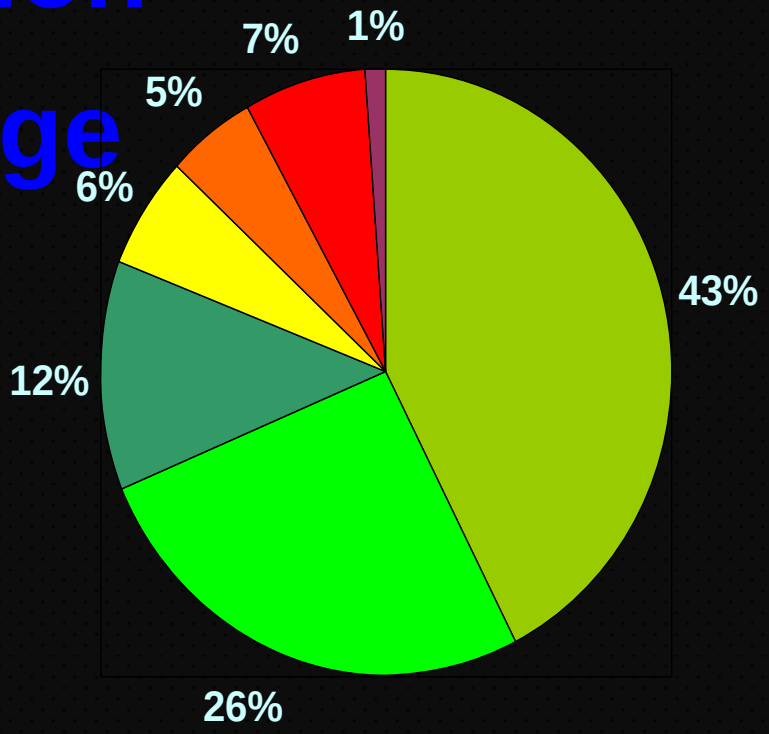
"…availability of an obstetrician with experience is required, epidural anesthesia desirable". "Studies lack of power. Active management of the 2nd twin and if non-vertex, breech extraction, possibly after int. manoeuvres is recommended as opposed to oxytocin, pushing or rupture of membranes."

Vayssiere C et al. CNGOF. Eur J Obstet Gynecol Reprod Biol 2011

•Presentation



- Chorion/Amnion
- Gestational Age



Modified acc. to: Chervenak et al. Obstet Gynecol 1985;65(1):119-24

Criteria?

2	Vx	Br	Tr	1
Vx				
Br				
Tr				

Informed consent & postgraduate teaching?

Learning Curve/Selection/Audit/Evaluation

Breech First

Delivery of Breech First Twins:
Multicenter Retrospective Study

ISAAC BLICKSTEIN et al.

Obstet Gynecol 2000;95:37– 42.

***Conclusion*:**

There was no evidence that vaginal birth is unsafe, in terms of Apgar scores and neonatal mortality, for breech first twins that weighed at least 1500 g.

Video

Vaginal Delivery in Triplets?

2-

Accepted Manuscript

On 29th of April 2016

Maternal and Neonatal Outcomes of Attempted Vaginal Compared With Planned Cesarean Delivery in Triplet Gestations

Justin R. Lappen, MD, David N. Hackney, MD, MS, Jennifer L. Bailit, MD MPH

Maternal and neonatal outcome of 93 consecutive triplet pregnancies with 71% vaginal delivery

Acta Obstet Gynecol Scand 2004; 83: 554–559
Printed in Denmark. All rights reserved

Séverine Alran, Olivier Sibony, Dominique Luton, Séverine Touitou, Virginie Fourchotte, Olivia Feraud, Jean-François Oury and Philippe Blot

From the Department of Obstetrics and Gynecology, Robert Debré Hospital, Paris, France

Neonatal Outcomes	Attempted VD n=72	Planned CD n=168	Unadjusted IRR [95%CI]	Adjusted aIRR [95%CI]
Neonatal asphyxia£	6 (8.3)	2 (1.2)	7.0 [0.76-64.84]	6.37 [0.60-67.35]
Mechanical ventilation€	19 (26.4)	13 (7.7)	**1.17 [1.03-1.33]**	**1.12 [1.01-1.24]**
Composite morbidity£	9 (12.5)	5 (3.0)	**4.20 [1.03-17.19]**	4.23 [0.94-19.12]

Composite neonatal morbidity = birth injury, 5-minute Apgar < 4, arterial pH < 7.0 or base excess < -12.0, neonatal asphyxia, or neonatal death

£ Adjusted for gestational age and birth order
€ Adjusted for gestational age, birth order and antenatal corticosteroid administration

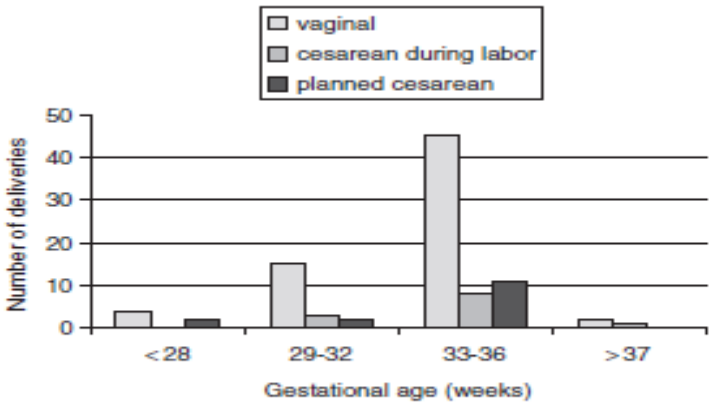


Fig. 1. Distribution of completed gestational weeks and mode of delivery in triplet gestation.

Conclusion(s): In a multi-center US cohort, attempted vaginal delivery of triplets is associated with higher risks of maternal transfusion and neonatal mechanical ventilation. Composite severe neonatal morbidity may be higher with attempted vaginal delivery though studies with greater power are required. The low probability of successful vaginal delivery raises questions regarding the utility of attempted vaginal delivery in triplet gestations. Our data support planned prelabor cesarean delivery as the preferred mode of delivery for triplet gestations.

Results. Sixty-six of 78 women (84%) who underwent a trial of labor had a successful vaginal delivery of all three neonates. The other 12 delivered their infants by cesarean delivery. Perinatal mortality referred to 104 triplet pregnancies was 48/1000.

Conclusions. Our experience suggests that offering vaginal delivery is an acceptable management plan for triplet gestation in a center with a sufficient number of triplet deliveries.

2+

“Prophylactic” Cesarean?

Large Observational Study/ Meta-Analysis

Legendre et al. Gynecol Obstet Fertil 2010;38(4):238-43

“Stress incontinence not increased by vaginal twin delivery“

Vendittelli et al , 2011: France

AOGS
ACTA Obstetricia et Gynecologica Scandinavica

MAIN RESEARCH ARTICLE

Is a planned cesarean necessary in twin pregnancies?

FRANÇOISE VENDITTELLI[1,2,3], OLIVIER RIVIÈRE[1], CATHERINE CRENN-HÉBERT[1,4], DIDIER RIETHMULLER[5], JEAN-PATRICK SCHAAL[6], MICHEL DREYFUS[7] FOR THE PERINATAL SENTINEL NETWORK AUDIPOG

[1]AUDIPOG (Association of Health Workers Using an Electronic File in Paediatrics, Obstetrics and Gynaecology), Medical University RTH Laennec, Lyon, [2]Department of Obstetrics, Gynaecology and Reproductive Health, Academic Hospital of Clermont-Ferrand, Clermont-Ferrand, [3]Auvergne's Perinatal Network, Academic Hospital of Clermont-Ferrand, Clermont-Ferrand, [4]Ward of Obstetrics and Gynaecology, AP-HP, Louis Mourier Hospital, Colombes, [5]Ward of Obstetrics and Gynaecology, Academic Hospital of Besançon, Besancon, [6]Ward of Obstetrics and Gynaecology, Academic Hospital of Grenoble, Grenoble, and [7]Ward of Gynaecology, Obstetrics and Reproductive Health, Academic Hospital of Caen, Caen, France

2597 Vertex-First deliveries >34 wks intention-to-treat analysis (ev II).

Neonatal complicatioons :

26.5 vs. 31.7% , 2nd: 27.6 vs. 32.7%

Rossi et al. 2011: General

Neonatal outcomes of twins according to birth order, presentation and mode of delivery: a systematic review and meta-analysis*

AC Rossi,[a] PM Mullin,[b] RH Chmait[b]

[a] Clinic of Obstetrics and Gynaecology, 'San Giacomo' Hospital, Monopoli, Bari, Italy [b] Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Correspondence: Dr AC Rossi, Via Celentano 42, 70121 Bari, Italy. Email acristinarossi@yahoo.it

39571 Twin pregnancies, Meta-Analysis

Neonatal morbidity: 1.1 vs. 2%

Lower mortality for V & NV 2nd twin

1+

“Prophylactic”Cesarean ?Twin Birth Trial

Characteristic	Planned Cesarean Delivery (N=1393)	Planned Vaginal Delivery (N=1393)
Mode of delivery — no./total no. (%)		
Cesarean for both†	1252/1392 (89.9)	551/1393 (39.6)
Vaginal and cesarean	11/1392 (0.8)	59/1393 (4.2)
Vaginal for both	129/1392 (9.3)	783/1393 (56.2)
Timing of cesarean section — no./total no. (%)		

Severe maternal morbidity

Acute respiratory distress syndrome	1 (0.1)	0
Disseminated intravascular coagulation	2 (0.1)	0
Amniotic-fluid embolism	1 (0.1)	0
Bowel obstruction or paralytic ileus requiring nasogastric suction	3 (0.2)	0

Mean interval 4 vs. 10 min.

MCDA twins: 24,9% vs. 23%

Presence of an “experienced obstetrician“(?)
Possibility to perform a CD within 30 minutes.

Secondary Studies after the Twin Birth Trial

Maternal outcomes at 3 months after planned caesarean section versus planned vaginal birth for twin pregnancies in the Twin Birth Study: a randomised controlled trial

BJOG 2015;122:1653–1662.

EK Hutton,[a] ME Hannah,[b] S Ross,[c] KS Joseph,[d] A Ohlsson,[e] EV Asztalos,[f] AR Willan,[g] AC Allen,[h] BA Armson,[i] A Gafni,[a] K Mangoff,[j] JJ Sanchez,[j] JF Barrett[b] for the Twin Birth Study Collaborative Group*

2+

For women with twins randomised to planned CS vs planned VB, maternal outcomes at 3 months p.p. did not differ in terms of urinary incontinence that affected quality of life. Breastfeeding at 3 months was not increased with planned VB.

24 Twin birth study: 2-year follow-up of the randomized trial comparing planned cesarean vs planned vaginal delivery for twin pregnancy

Elizabeth Asztalos[1], Mary Hannah[1], Eileen Hutton[2], Andrew Willan[1], Alexander Allen[3], Anthony Armson[3], Amiram Gafni[2], K. S. Joseph[4], Arne Ohlsson[1], Susan Ross[5], Jon Barrett[1]

SMFM 2016

2-year Follow-up Outcomes of the Twin Birth Study

Outcomes at 2-years of age	Planned CS N=2320, n (%)	Planned VB N=2283, n (%)	Odds Ratio	95% Conf Limits	P-value
2-year Composite outcome	139 (5.99)	133 (5.83)	1.04	0.77, 1.41	0.79
Death	35 (1.51)	23 (1.01)	1.48	0.84, 2.64	0.18
Surviving children	N=2285, n (%)	N=2260, n (%)			
Neuro-developmental delay	104 (4.55)	110 (4.87)	0.95	0.67, 1.34	0.77
Cerebral palsy	2 (0.09)	1 (0.04)	.	.	.
Motor delay	62 (2.71)	78 (3.45)	0.78	0.51, 1.20	0.26
Cognitive delay	95 (4.16)	105 (4.65)	0.91	0.64, 1.30	0.61

A policy of planned Cesarean does not provide benefit in children @ 2 years of age compared with vaginal delivery (first twin vertex)

“Combined Delivery” 3

The emergency situation…

- could not be expected: abruption, cord prolapse, cervical spasm
- could be predicted, but obstetrician thought vag. delivery too risky:
- was not diagnosed: such as dorsoinferior transverse position

Frequent mistakes... 75% estimated „iatrogenic“ !

risks of a “combined delivery”?

NO or INAAPROPRITE USE OF ULTRASOUND

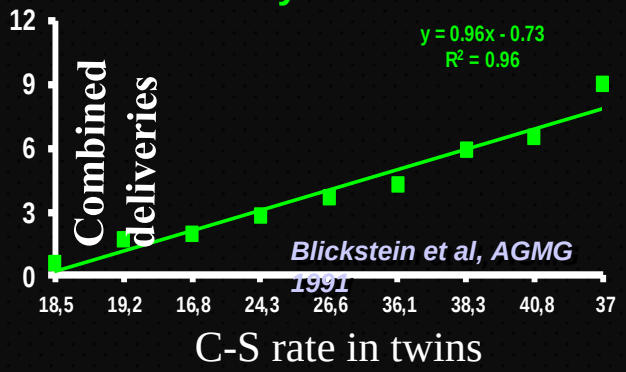
NEONATAL MORBIDITY

19.8% vs. 9.5% (VD) vs. 9.8% (CS)

MATERNAL MORBIDITY: HIGHEST

Rossi et al. BJOG 2011; 1471;528

Combined delivery *vs.* C-S rate in twins



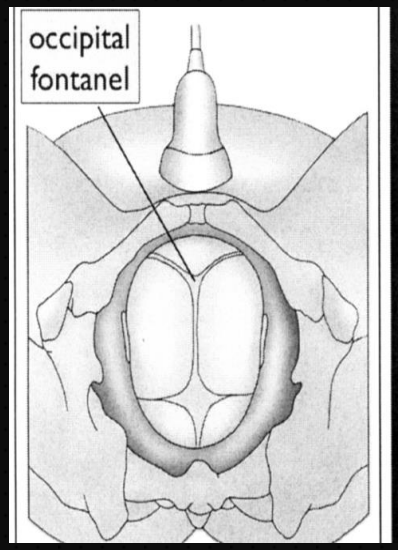
“Physicians trained after the 1970s have no idea how to perform internal manoevers”.

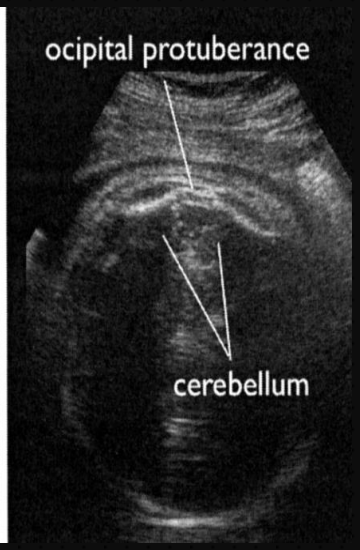
Cruikshank DP. Obstet Gynecol 2007;109(5):1167-76.

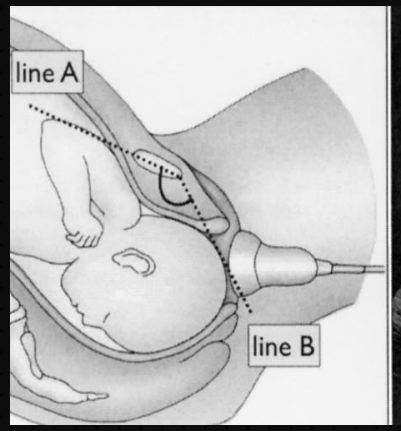
Decision for Vaginal Delivery

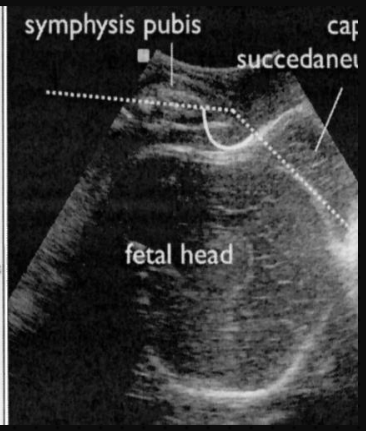
As in singletons US can be used to measure the AOP

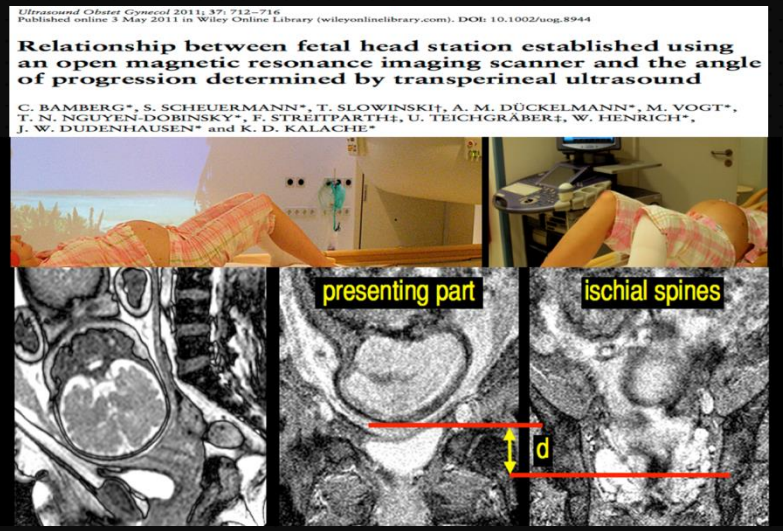
First Twin

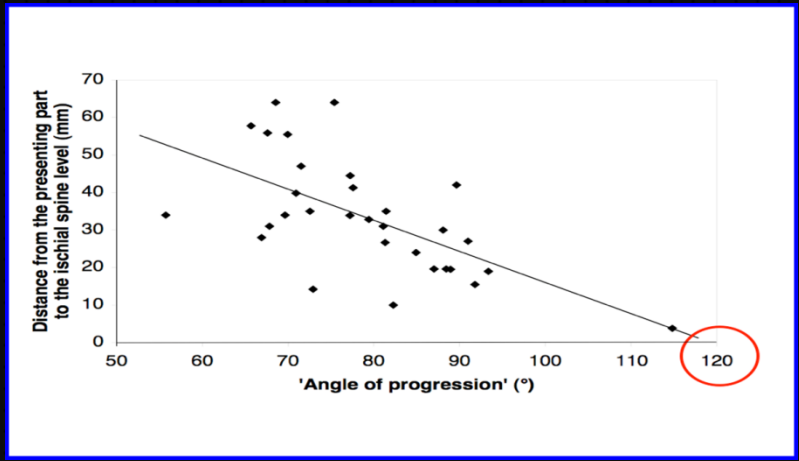










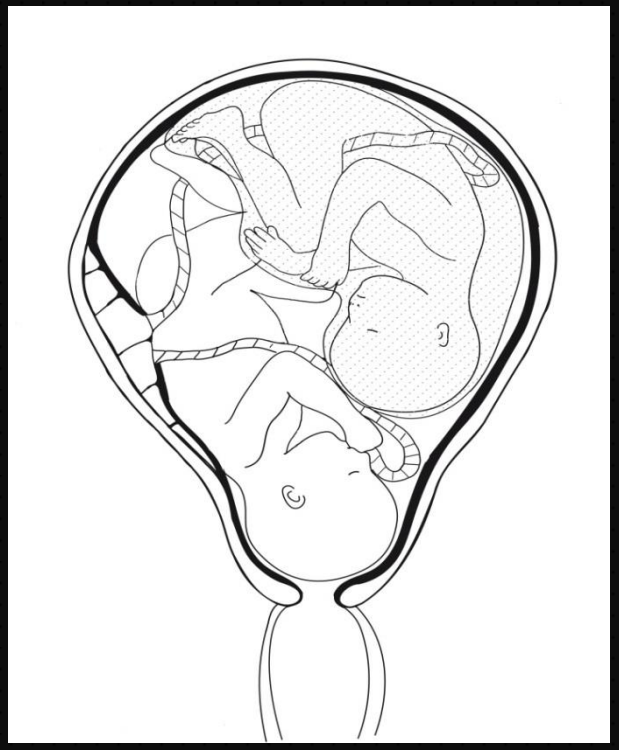


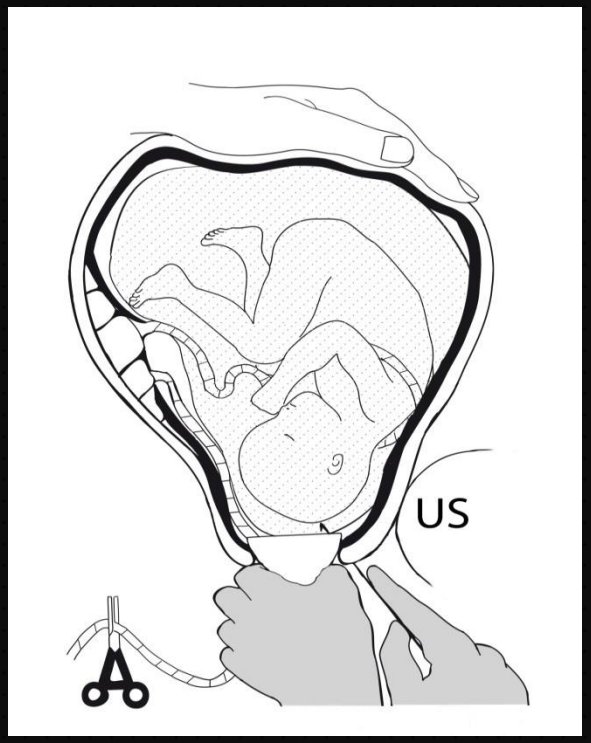
Non-Engagement 2nd Twin?

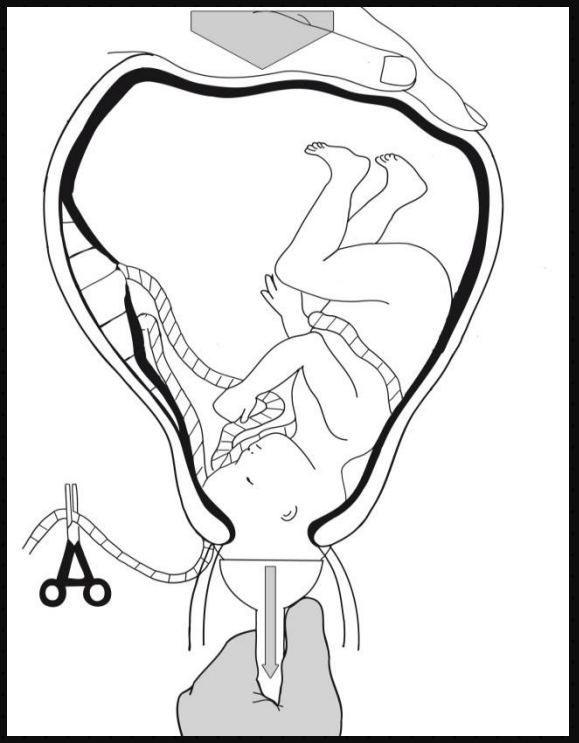
D/
GPP

Ultrasound - No Amniotomy, No Oxytocin!

2 x Vertex (2.head reachable, no forelying parts)





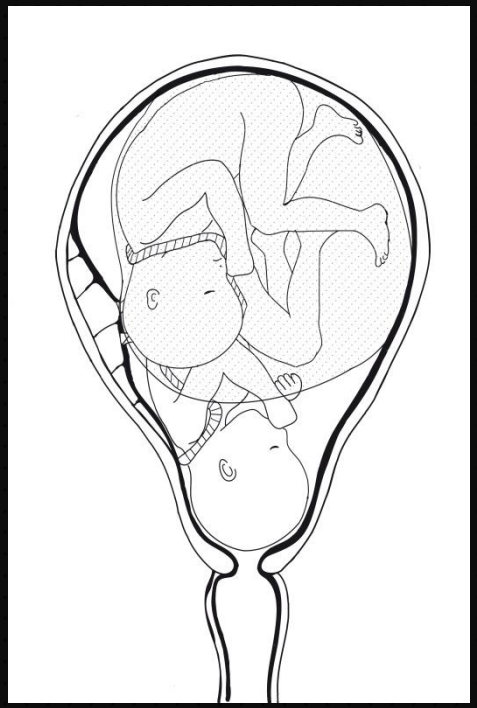


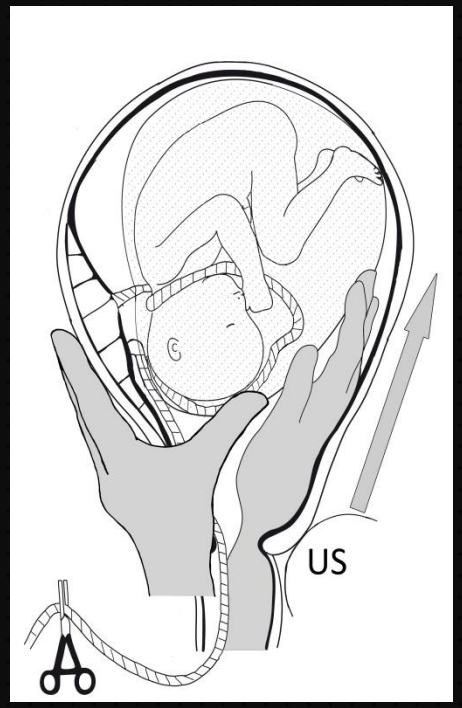
Non-Engagement 2nd Twin?

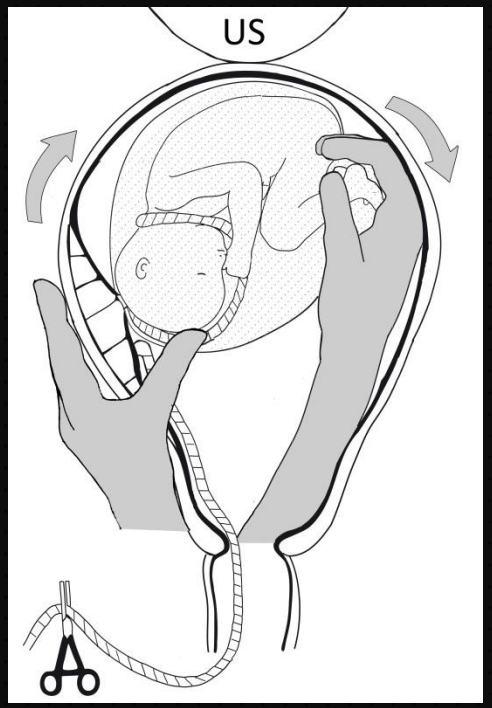
D/ GPP

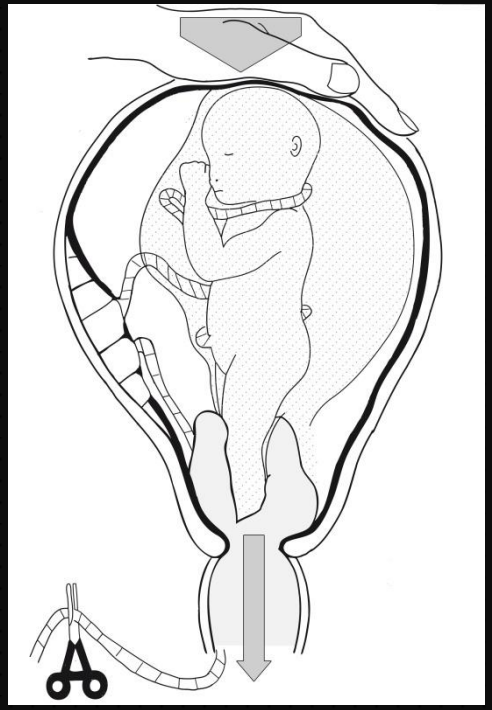
Ultrasound - No Amniotomy, No Oxytocin!

2 x Vertex (2.head not reachable, forelying parts







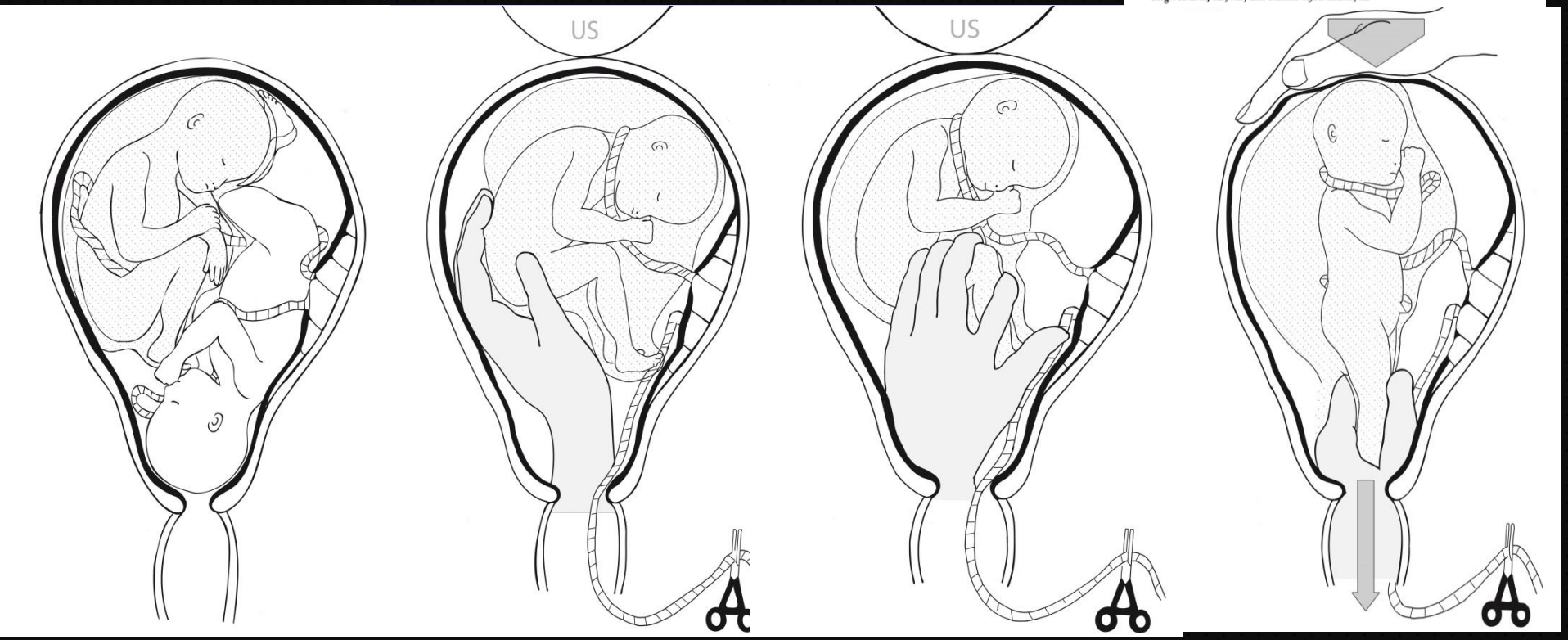


Non-Engagement 2nd Twin?

D/ GPP

Ultrasound - No Amniotomy, No Oxytocin!

Vertex/Breech



Vaginal Delivery of the Second Nonvertex Twin

Avoiding a Poor Outcome When the Presenting Part Is Not Engaged

Birgit Arabin, MD, PhD, and Ioannis Kyvernitakis, MD

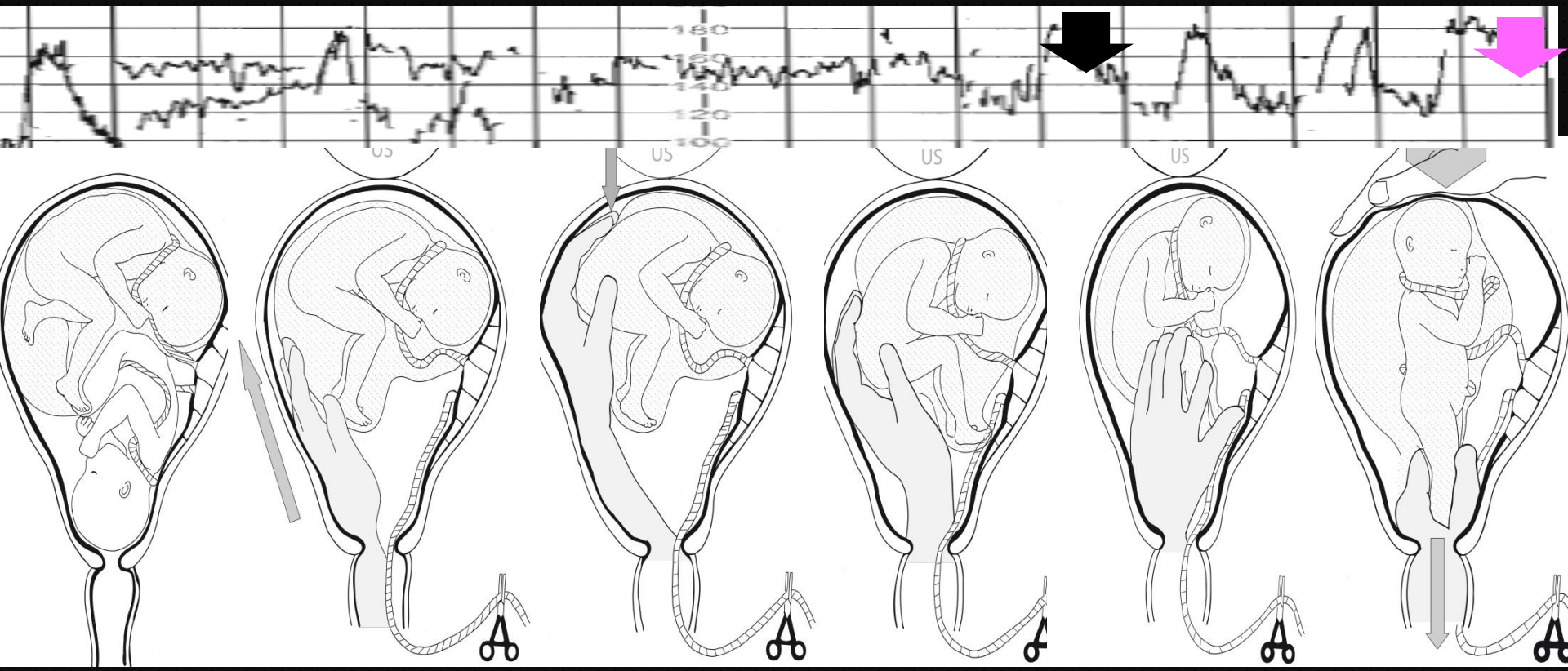
Arabin & Kyvernitakis Obstet Gynecol 2011, 118:950-54

Non-Engagement 2nd Twin?

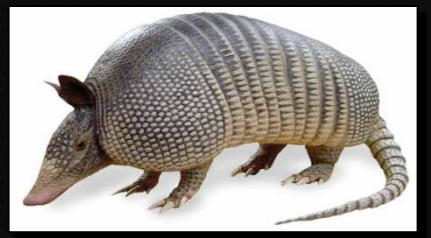
D/ GPP

Ultrasound - No Amniotomy, No Oxytocin!

Vertex / Transverse

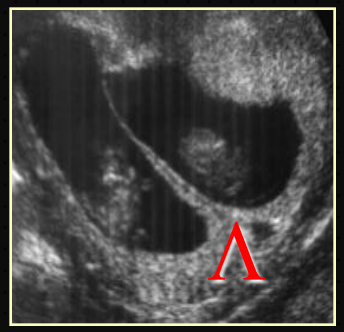


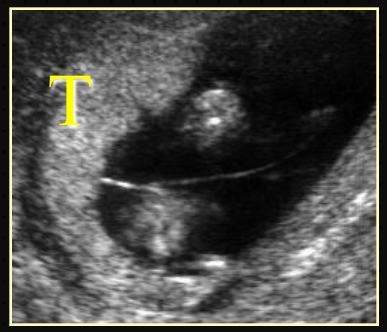
Arabin & Kyvernitakis Obstet Gynecol 2011, 118:950-54



Neun-Band- Armadillo

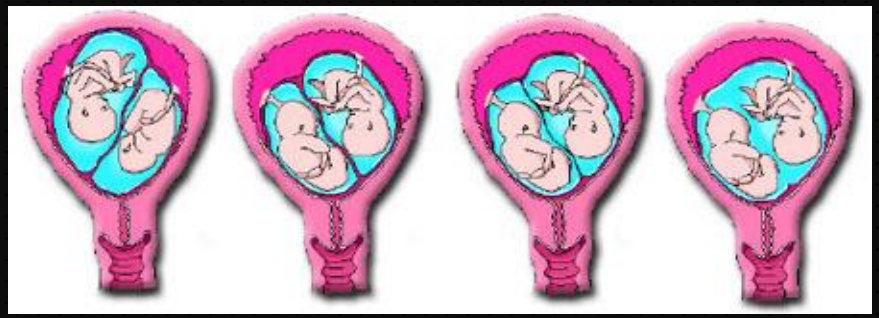
Presentation





Timing: WHEN?

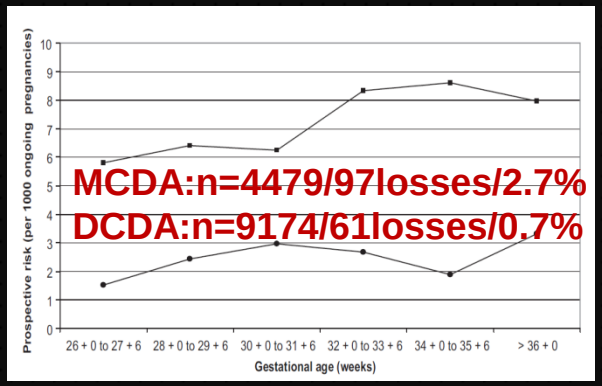
Gestational Age

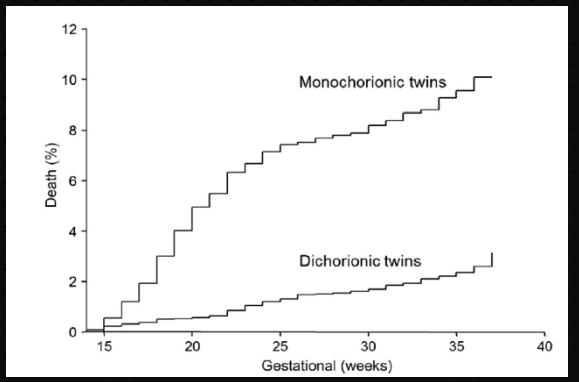


	DC		MC	
	sep	fused	DC	MA
Frequency:	35%	27%	36%	2%
Mortality:	13%	11%	32%	44%

2+

Timing DC and MC Twins





Summary of cohort studies D'Antonio et al.UOG 2013;41:632–6

Risk of stillbirth in DC twins not different from 28-38 wks. Uncomplicated DC twins should be managed expectantly. In discordant fetal wellbeing, timing of delivery balanced .

In uncompl. MC twins 32-37 wks, no significant increase of stillbirth. Pregnancies are monitored until birth@ 37 weeks. The threshold for early delivery may be lower in MC twins.

2+

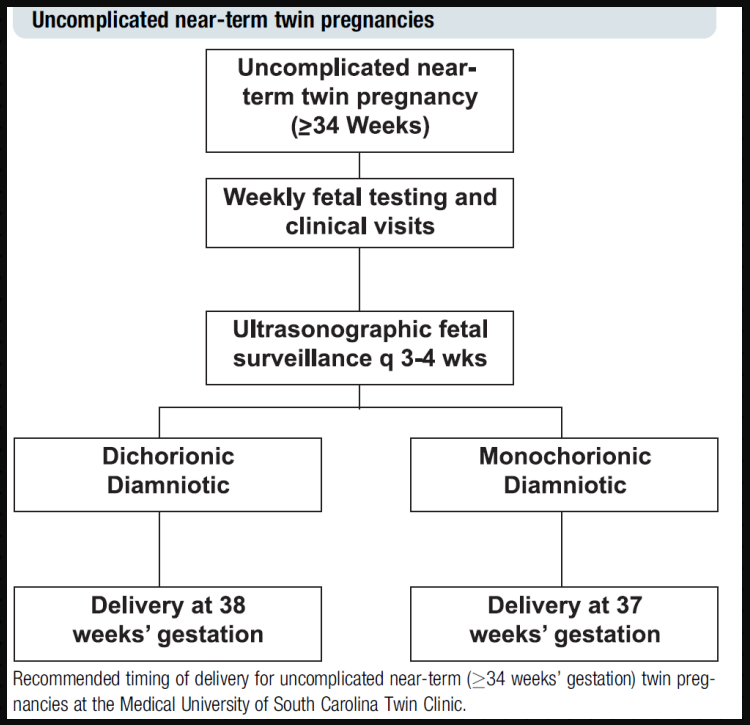
Timing DC and MC Twins

Risk of late-preterm stillbirth and neonatal morbidity for monochorionic and dichorionic twins

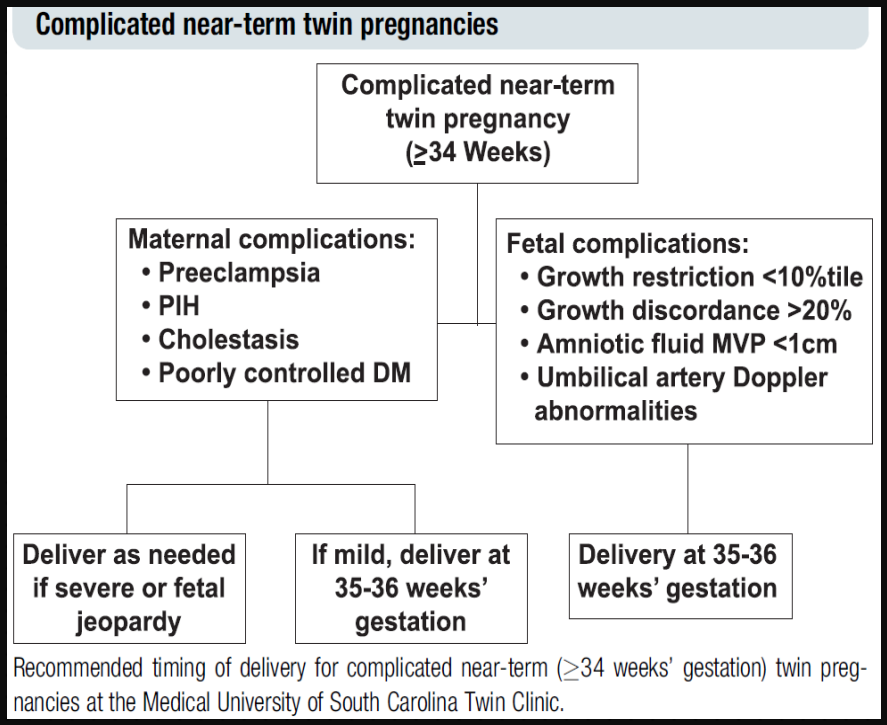
Jennifer L. Burgess, MD; Elizabeth R. Unal, MD, MSCR; Paul J. Nietert, PhD; Roger B. Newman, MD

AJOG 2014

768 twin gestations (601 DC,167 MC), only 1 DC IUFD, risk @ 34 weeks was 0.17% for DC. Comp. neonatal morbidity decreased each week (P<.0001). The nadir of composite neonatal morbidity occurred @ 36/0-36/6 weeks for MC twins and 37/0-37/6 weeks for DC twins.



Recommended timing of delivery for uncomplicated near-term (≥34 weeks' gestation) twin pregnancies at the Medical University of South Carolina Twin Clinic.



Recommended timing of delivery for complicated near-term (≥34 weeks' gestation) twin pregnancies at the Medical University of South Carolina Twin Clinic.

Timing & Monitoring MC Twins (cohort)

Increased perinatal mortality and morbidity in monochorionic versus dichorionic twir pregnancies: clinical implications of a large Dutch cohort study

BJOG 2008;115:58–67.

KEA Hack,[a] JB Derks,[a] SG Elias,[b] A Franx,[c] EJ Roos,[c] SK Voerman,[a] CL Bode,[a] C Koopman-Esseboom,[d] GHA Visser[a]

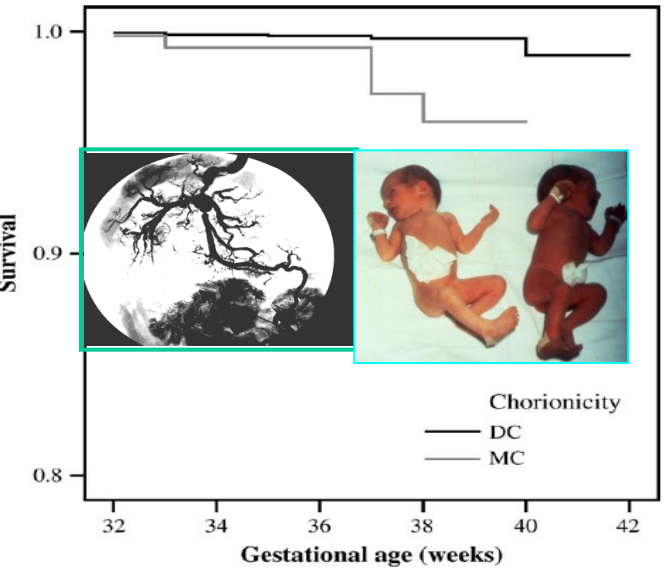
N=1407

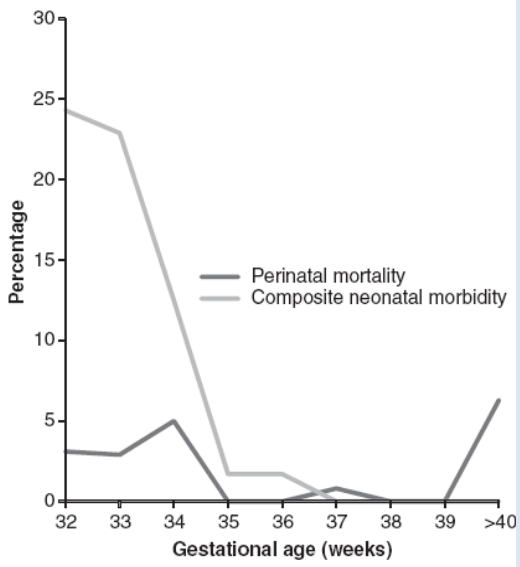
Perinatal mortality 11.6% in MC vs, 5.0% in DC twin pregnancies.

After 32 wks, IUD was significantly higher in MC vs. DC twins.

Trial of labor in 77% successful.

Adverse outcome / mode of delivery in 10 centers





	Trial of labour			Crude OR (95% CI): planned CS vs trial of labour	Adjusted OR (95% CI)*
	Planned CS (no labour) (*n* = 150)	CS during labour (*n* = 158)	Vaginal delivery (*n* = 594)		
5-minute Apgar Score <7	5 (3.3)	4 (2.5)	14 (2.4)	1.5 (0.6–4.0)	1.3 (0.5–3.5)
Umbilical artery pH < 7.05	1 (0.7)	3 (1.9)	9 (1.5)	0.4 (0.0–2.9)	0.4 (0.1–3.4)
Neonatal mortality	3 (2.0)	1 (0.6)	2 (0.3)	7.4 (1.0–53.1)	5.4 (0.7–41.5)
Admission to NICU	37 (24.7)	10 (6.3)	33 (5.6)	5.1 (3.1–8.4)	2.7 (1.5–4.8)
Overall neonatal morbidity	21 (14.0)	5 (3.2)	19 (3.2)	4.8 (2.6–9.2)	2.0 (1.0–4.2)
Respiratory distress syndrome	14 (9.3)	2 (1.3)	13 (2.2)	4.9 (2.3–10.5)	2.2 (1.0–5.3)

CS, caesarean section; NICU, neonatal intensive care unit; OR, odds ratio.
*Adjusted for birth weight (per gram) and gestational age (per day).

1-

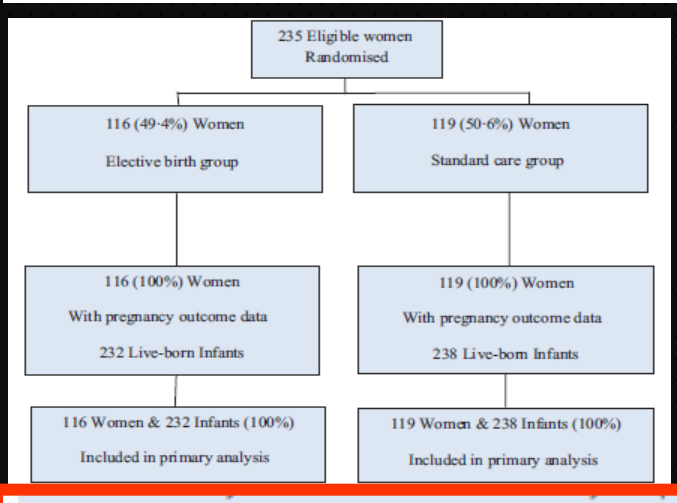
Timing delivery DC Twins? RCT !

Results support Induction/delivery @ 37 weeks

Elective birth at 37 weeks of gestation versus standard care for women with an uncomplicated twin pregnancy at term: the Twins Timing of Birth Randomised Trial

BJOG 2012;119:964

JM Dodd,[a] CA Crowther,[a] RR Haslam,[b] JS Robinson,[a] for the Twins Timing of Birth Trial Group



Smoker* **	31 (26.7)	30 (25.2)
Chorionicity***		
Monochorionic	19 (16.4)	21 (17.6)
Dichorionic	95 (81.9)	98 (82.4)
Conception* **		
Spontaneous	88 (75.9)	93 (78.2)
Assisted Conception	17 (14.7)	19 (16.0)
Planned mode of birth* **		
Vaginal birth	71 (61.2)	78 (65.5)
Caesarean birth	45 (38.8)	41 (34.5)

Outcome	Elective birth group (*n* = 232 infants) *n* (%)	Standard care group (*n* = 238 infants) *n* (%)	Risk ratio (95% CI)	*P* value
Serious adverse infant outcome*	4 (1.7)	12 (5.0)	0.34 (0.11–1.05)	0.06
Morbidity from adverse outcomes at term**	3 (1.3)	9 (3.8)	0.34 (0.09–1.23)	0.10
Birthweight less than third centile**	0 (0.0)	4 (1.7)	Not estimable	

MCDA Twins–always by Cesarean Delivery?

No !

Effect of chorionicity and twin-to-twin delivery time interval on short-term outcome of the second twin.

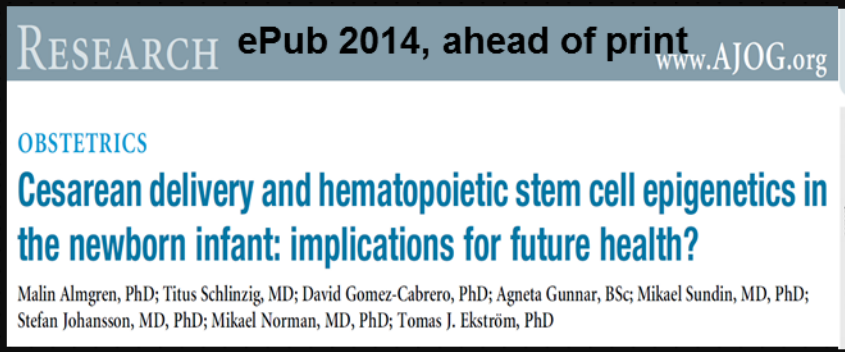
Hjortø et al.: Matern Fetal Neonatal Med. 2013

Delivery interval & outcome: 57 MC/ 485 DC twin pregnancies.

No difference in decrease of pH, Apgar or admission to NICU in relation to time interval between twin 1 + 2.

- **Increasing delivery interval associated with significant decrease in pH and Apgar,**
- **but no difference between MC and DC twins.**

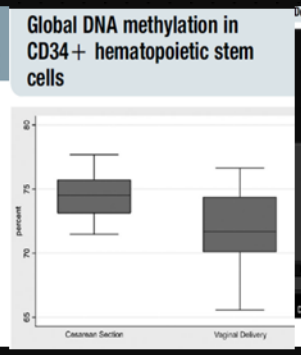
Consecutive risks for offspring/Epigenetics/ Methylation

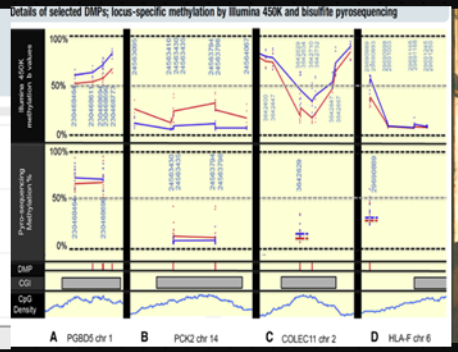

RESEARCH ePub 2014, ahead of print www.AJOG.org

OBSTETRICS

Cesarean delivery and hematopoietic stem cell epigenetics in the newborn infant: implications for future health?

Malin Almgren, PhD; Titus Schlinzig, MD; David Gomez-Cabrero, PhD; Agneta Gunnar, BSc; Mikael Sundin, MD, PhD; Stefan Johansson, MD, PhD; Mikael Norman, MD, PhD; Tomas J. Ekström, PhD





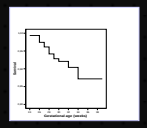
343 loci identified with a difference in DNA methylation of >10% (P < .01). 76% of methylated loci in neonatal CD34þ cells were hypermethylated after vaginal delivery, correlated to the duration of labor. The methylated loci involve processes such as immunoglobulin biosynthesis, regulation of glycolysis and ketone metabolism, and of the response to food.

An important task is to investigate whether any of theDMPs associated with the mode of delivery retain their epigenetic marks in CD34þ hematopoietic stem cells into adolescence/adulthood.

Asthma, Intestinal Disease, Autism, Obesity

2+

Multicenter-study MCMA Twins 10 years



4.3% congenital heart anomalies, 10.4% cerebral injuries.

Cumulative overall perinatal mortality acc. to gest. age

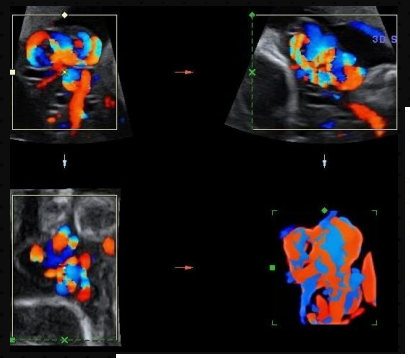
(restricted to pregnancies with two surviving fetuses ≥24 weeks)

GA at delivery or IUD (weeks)	Continuing (n)		IUD rate per period (n/N)		NND rate per period (n/N)		Total mortality rate per period (n/N)	
	Pregnancies	Fetuses	Per pregnancies	Per fetuses	Per pregnancies	Per fetuses	Per pregnancies	Per fetuses
24-25	80	160	0	0	1 (1.3)	2 (1.3)	1 (1.3)	2 (1.3)
26-27	78	156	1 (1.3)	2 (1.3)	1 (1.3)	1 (0.6)	2 (2.6)	3 (1.9)
28-29	75	150	3 (4.0)	3 (4.0)	4 (5.3)	4 (2.7)	5 (6.7)	7 (4.7)
30-31	63	126	0	0	1 (1.6)	1 (1.6)	1 (1.6)	1 (1.6)
32-33	55	110	1 (1.8)	2 (1.8)	0	0	1 (1.8)	2 (1.8)
34-35	28	56	1 (3.6)	1 (1.8)	1 (3.6)	1 (1.8)	1 (3.6)	2 (3.6)
≥36	12	24	0	0	0	0	0	0

Hack KH, Derks JB, Schaap A, Lopriore E, Elias S, Arabin B, Eggink A, Sollie KM, Mol BWJ, Duvekot JJ, Willekes C, Go ATJ, Vandenbussche FPHA, Visser GHA, Obstet Gynecol, 2009; 113:353-60

2-

Does Entanglement Matter in MCMA Twins?

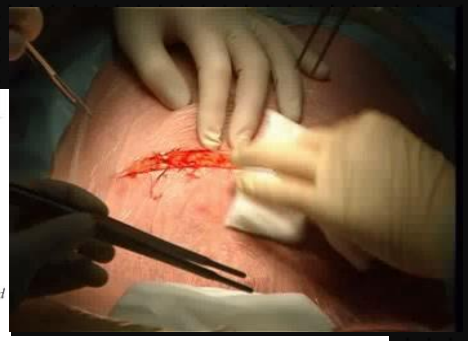


Ultrasound Obstet Gynecol 2013; **41**: 131–135
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.12345

Impact of cord entanglement on perinatal outcome of monoamniotic twins: a systematic review of the literature

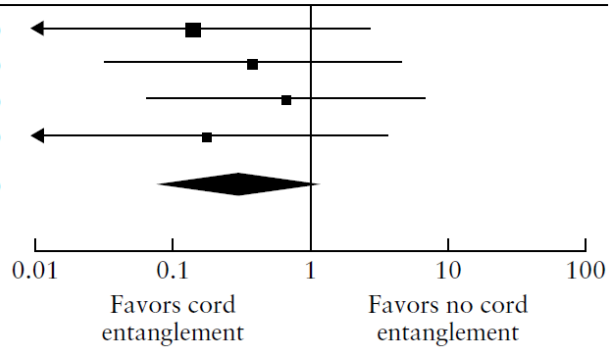
A. C. ROSSI* and F. PREFUMO†

**Department of Obstetrics and Gynaecology, University of Bari, Bari, Italy; †Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynaecology, University of Brescia, Brescia, Italy*



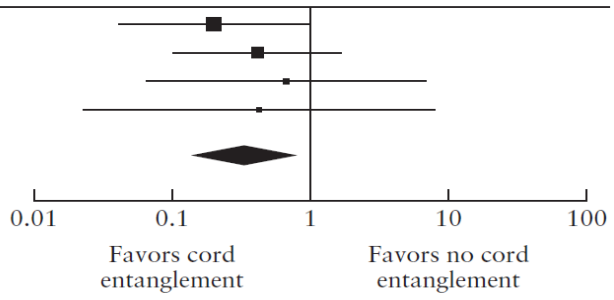
Study or Subgroup	Cord entanglement Events	Total	No cord entanglement Events	Total	Weight	Odds ratio M–H, fixed, 95% CI
Cordero[2]	0	30	4	42	40.9%	0.14 (0.01, 2.71)
DeFalco[11]	1	22	2	18	23.2%	0.38 (0.03, 4.58)
Sau[13]	4	10	2	4	18.9%	0.67 (0.06, 6.87)
Suzuki[14]	3	20	1	2	17.0%	0.18 (0.01, 3.66)
Total (95% CI)		82		66	100.0%	0.30 (0.08, 1.10)
Total events	8		9			

Heterogeneity: $Chi^2 = 0.85$, df = 3 (P = 0.84); $I^2 = 0\%$
Test for overall effect: Z = 1.81, (P = 0.07)



Study or Subgroup	Cord entanglement Events	Total	No cord entanglement Events	Total	Weight	Odds ratio M–H, fixed, 95% CI
Cordero[2]	2	30	11	42	48.0%	0.20 (0.04, 0.99)
DeFalco[11]	13	22	14	18	35.3%	0.41 (0.10, 1.67)
Sau[13]	4	10	2	4	9.6%	0.67 (0.06, 6.87)
Suzuki[14]	6	20	1	2	7.1%	0.43 (0.02, 8.04)
Total (95% CI)		82		66	100.0%	0.34 (0.14, 0.82)
Total events	25		28			

Heterogeneity: $Chi^2 = 0.84$, df = 3 (P = 0.84); $I^2 = 0\%$
Test for overall effect: Z = 2.39, (P = 0.02)



MCMA Twins–always by Cesarean Delivery?

No !

May 16, 2016
ACOG HIGHLIGHTS

15/ 29 women with MoMo twins had a planned CD & 14/29 attempted a vaginal delivery; 10 delivered both neonates vaginally (20/58) within a median interval of 3 minutes. Cesarean delivery was needed for 3 women because of a nonreassuring FHR, 1 woman required a CD of the 2nd twin.
ICH was lower in the vaginal vs CD group: (0 vs 8, *P*=.006),
GA at delivery was 33.3 weeks vs 32.7 weeks, *P*=.5.
Fetal loss: 1/14 vs 2/15, *P*=NS)
Respiratory complications and neonatal stay (18 vs 25, *P*=.09)
In 28/ 29 pregnancies, entangled umbilical cords were present.
***Composite* maternal outcomes were similar.**
Comments "ACOG guidelines are used as 'standard of care' by most practitioners; so it is important that they discourage 'expert opinion' statements in their guidelines and encourage evidence-based medicine."

Khandelwal et al. 2016, abstract winner ACOG meeting 2016

Assisted versus natural conception

Rossi and D´Áddario. J Perinat Med 2011

13 Articles

In non-controlled studies, outcomes equal except for CS rates:
ART: 71.8%; NC: 49.6%; P<0.0001; OR: 2.34; 95% CI: 1.55-3.54.

2-

In controlled studies, different rates of preterm delivery:
ART :55% , NC: 53% P=0.03; OR: 1.30; 95% CI: 1.03-1.65.

1-

Unlike-sex-twins higher preterm & perin. death rate:
ART: 58.6%; NC: 49.5%; P<0.0001; OR: 1.51; 95% CI: 1.25-1.83),
ART: 3.6%; NC: 1.8%; P<0.0001; OR: 1.95; 95% CI: 1.41-2.71.

Problems of Informed Consent

Chance of survival of 3 premature infants (1995 US/GB)

	24 weeks 68%	24 weeks 68%	28 weeks 94%
Parents	White 63%	Black (Surin.) 73%	Spanish 93%
Weight	720 gram 57%	770 gram 86%	740 gram 74%
Gender	Boy 37%	Girl 91%	

Alexander et al : Pediatrics 2003; 111:61-66

Costeloe et al: Pediatrics 2000;106:659-71

„A Policy of elective CS in early preterms?“

- is associated with increased maternal morbidity / mortality
- may lead to „unnecessary early delivery“ in pregnancies in which preterm labor would otherwise have stopped.
- If there are potential benefits it is uncertain and it is not possible to say whether they do outweigh maternal risks.“

3

Multicenter cohort (diff. policies)

OBSTETRICS AJOG 2015; 213: 73

Neonatal outcome of very preterm twins: policy of planned vaginal or cesarean delivery

Loïc Sentilhes, MD, PhD; Anne Oppenheimer, MD; Anne-Charlotte Bouhours, MD; Estelle Normand; Bassam Haddad, MD; Philippe Descamps, MD; Loïc Marpeau, MD; François Goffinet, MD, PhD; Gilles Kayem, MD, PhD

CONCLUSION: A policy of planned vaginal delivery of very preterm twins with the first twin in cephalic presentation does not increase either severe neonatal morbidity or mortality.

Retrospective cohort < 1500g

OBSTETRICS AJOG 2015; 213: 219

Mode of delivery of twin gestation with very low birthweight: is vaginal delivery safe?

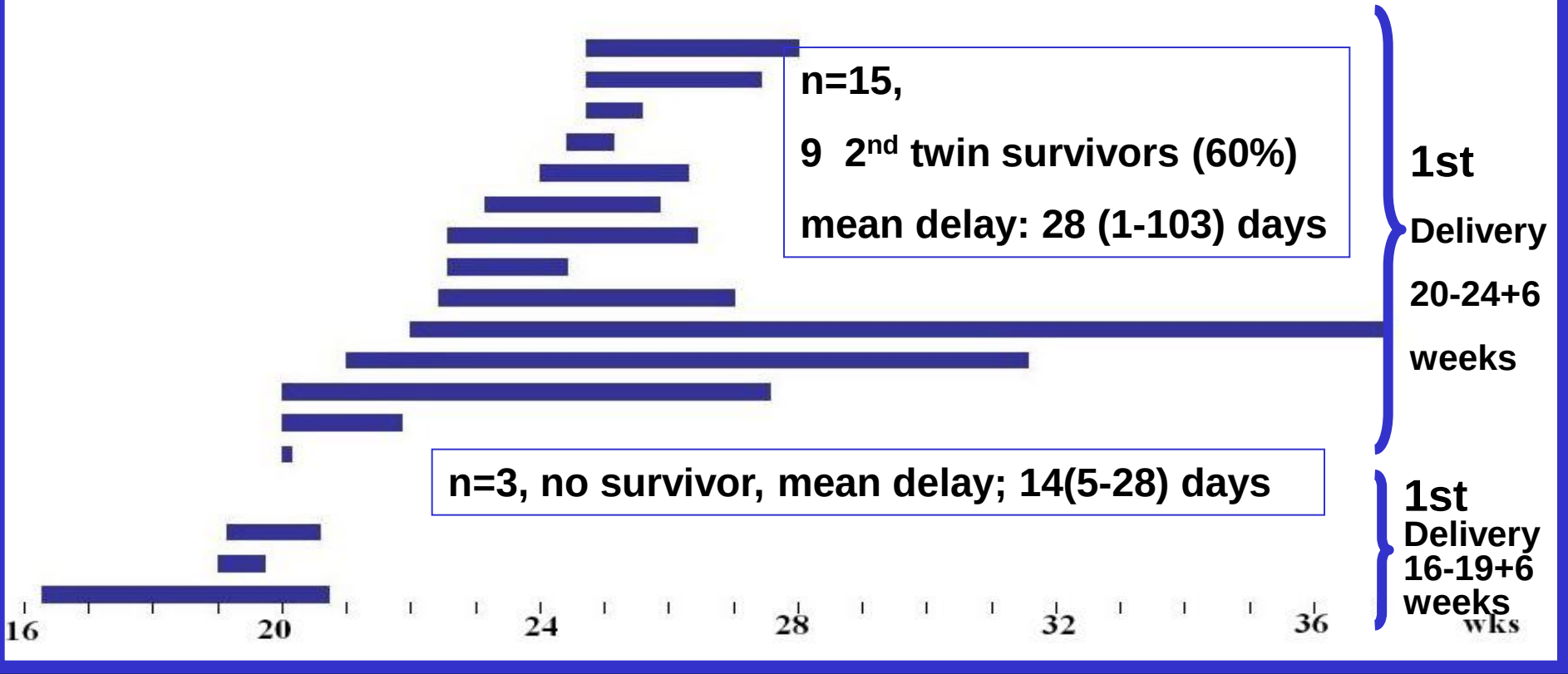
Eran Barzilay, MD, PhD; Shali Mazaki-Tovi, MD; Uri Amikam, BSc; Hila de Castro, MD; Jigal Haas, MD; Ram Mazkereth, MD; Eyal Sivan, MD; Eyal Schiff, MD; Yoav Yinon, MD

CONCLUSION: Vaginal delivery of very low birthweight twins is associated with an increased risk of intraventricular hemorrhage, regardless of presentation. Because of the small sample size and the retrospective cohort design, large prospective randomized studies are needed.

2+

Delayed Interval Delivery I

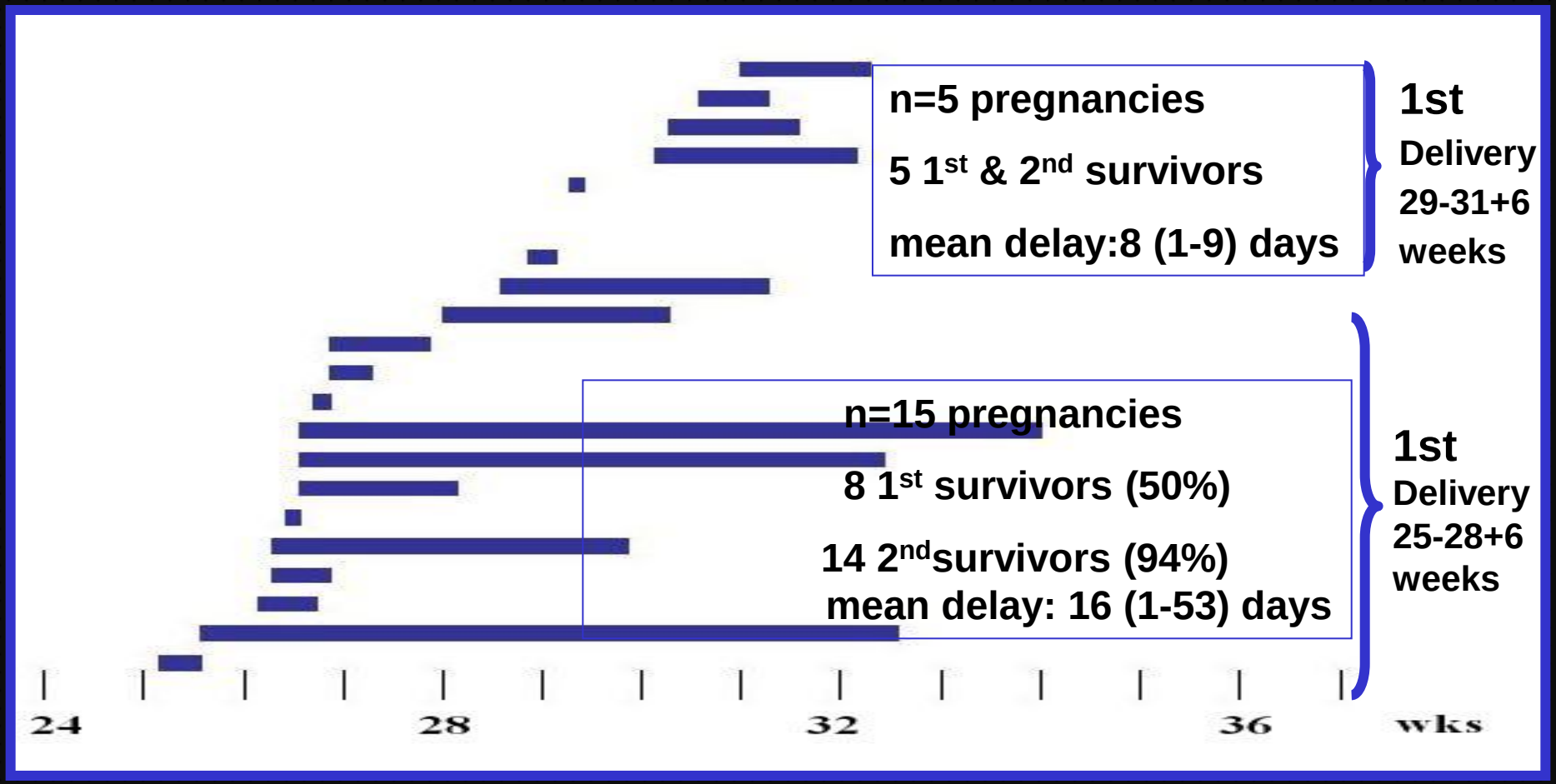
In most cases, the fate of one fetus affects the fate of its co-twin with the exception of successful procedure of delayed interval delivery.



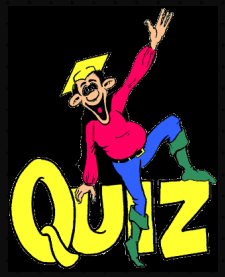
Arabin & van Eyck AJOG 2009; 154: e 1-8

2+

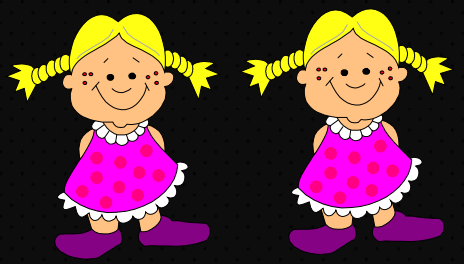
Delayed Interval Delivery II



Arabin & van Eyck AJOG 2009; 154: e 1-8



Postnatal Considerations



a) Mothers of twins have the same morbidity rates than of singletons if they have the same age.

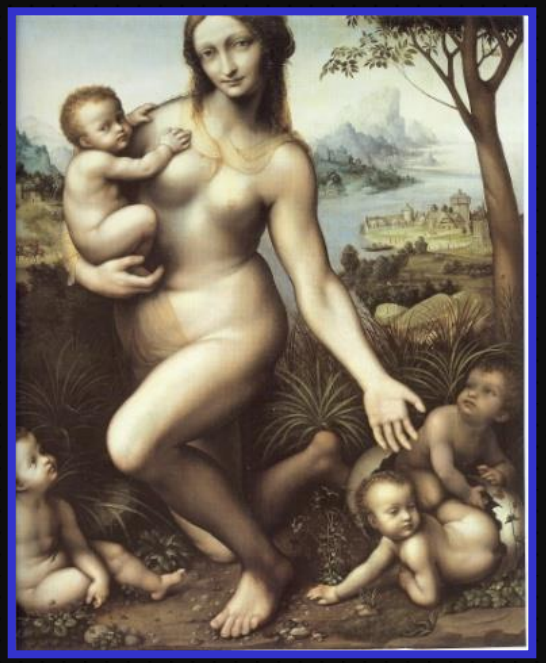
b) If one twin has died it is the best therapy to congratulate for the living one and do not mention the dead one.

c) Breastfeeding of twins should not be prolonged > 3 months because it increases the risk for maternal cardiovascular disease due to tiring.

d) Mothers of twins are less motivated to breastfeed thier children.

Unconventional care may improve outcome

Video



Maternal Morbidity in multiple pregnancies

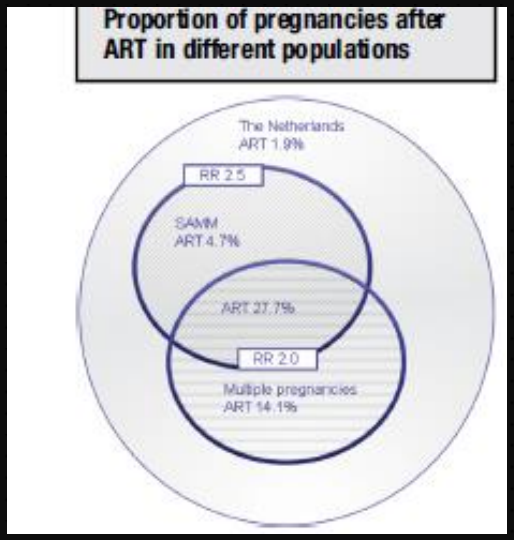
Witteveen et al. AJOG 2016;214: 641

2+

OBSTETRICS

Severe acute maternal morbidity in multiple pregnancies: a nationwide cohort study

Tom Witteveen, MD; Thomas Van Den Akker, MD, PhD; Joost J. Zwart, MD, PhD; Kitty W. Bloemenkamp, MD, PhD; Jos Van Roosmalen, MD, PhD



2552 cases of severe acute maternal morbidity during the 2 years 202 multiple pregnancies (8.0%), 197 twins (7.8%),5 triplets (0.2%). Overall incidence severe acute maternal morbidity 7.0 per 1000; 6.5 vs. 28.0 per 1000 for singletons and multiple pregnancies. RR twins: 4.3 (95% CI 3.7–5.0); RR triplets: 6.2 (95% CI 2.5–15.3). Risk indicators: age of ≥ 40 years, (RR, 2.5 95% CI, 1.4–4.3), nulliparity (RR, 1.8, 95% CI, 1.4–2.4), use of ART (RR, 1.9, 95% CI, 1.4–2.5), and nonspontaneous onset (RR, 1.6, 95% CI, 1.2–2.1). No significant difference was found between MC/DC twins.

Breastfeeding

Twins breastfed for 1 to 3 months are larger than twins breastfed for 4 to 6 months; mean BMI (0.61 kg/m^2; P = .02; 95% CI 0.17-1.05), arm circumference (0.66 cm; P = .006; 95% CI, 0.26-1.06), abdominal circumference (1.16 cm; P = .03; 95% CI, 0.26-2.06). Twins breastfed < 1 month larger than for 4 - 6 months: mean arm circumference (0.72 cm; P = .009; 95% CI, 0.26-1.17).

Temples et al. , J Hum Lact 2016 Mar 23. [Epub ahead of print]

2+

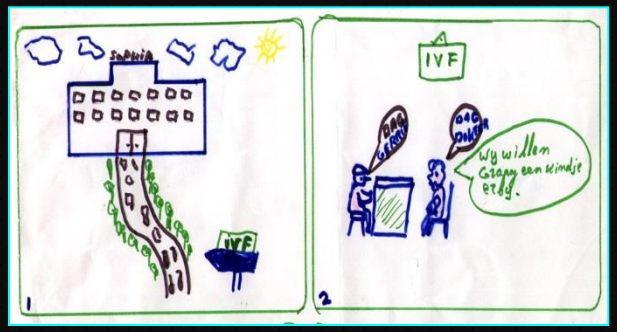
Mothers made intensive efforts to breastfeed their twins. Women who expect and/or have multiple babies need much more support and guidance, which may include advice for nutritional & daily care.

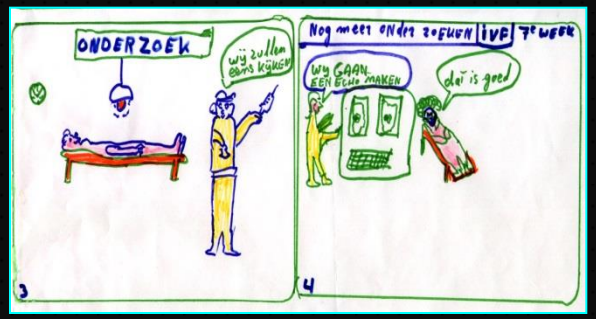
Cinar et al. J Health Nutr 2013;31:504

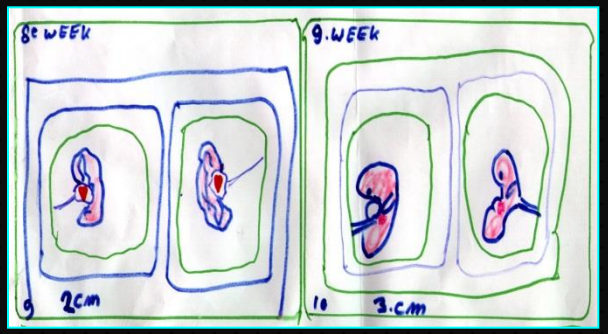
92,364 women, 85.3% intended to breastfeed, which was higher amongst older women with no health problems or only midwive care (a.OR 3.64, 95% CI 3.13-4.23). Pregnant with twins (a.OR 0.73, 95% CI 0.57-0.94), not attending antenatal classes (a. OR 0.58, 95% CI 0.54-0.62), and delivering in a level-1 hospital (a.OR 0.85, 95% CI 0.77-0.93) was associated with a lower intention to breastfeed.

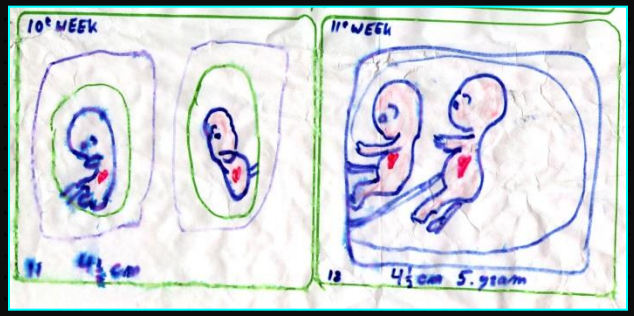
Lutsiv O, BJOG. 2013;120 :1490

Social Aspects









“A double present”

(co-bedded)

Bereavement

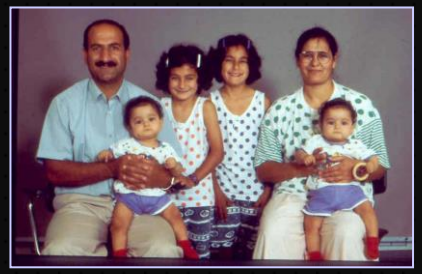
Swanson et al. Twin Res Hum Genet 2009 ;12:392

Do not forget the lost twin!

Mothers experienced significantly more depression and grief than fathers. Fathers believed that they should be able to cope regardless of their grief. The strength of parents' spiritual beliefs had increased significantly since their loss, and there was some evidence that depressed and grieving mothers turned to spiritual support.

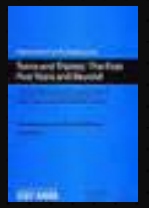
Parents whose children died earlier reported levels of depression similar to those reported by parents whose children died later. To date, this is the largest study of grief in couples who have experienced the death of a twin and who have a surviving twin or higher order multiple.

Information



Inform about Multiple Birth Foundations
Seperate for each country

Care for follow-up & social support.

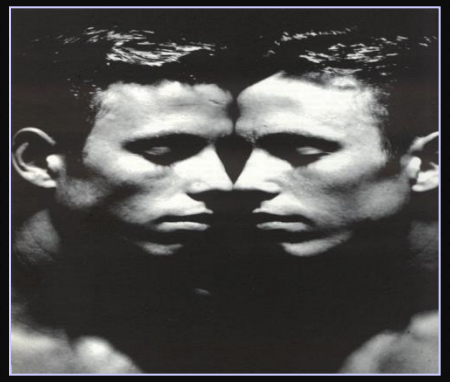


Stay Fascinated by Chrono (epi) genetics

"Heritabie /Epigenetic impact may increase during lifetime"

Retrospective religiousness in MZ/DZ twins: small difference, higher similarity within MZ twins in adulthood.

Koenig & Bouchard J Pers. 2005 73: 471-88



The intellectual experience of children is generated by others

(variation of IQ rises from 20 % in infancy to 80% past middle age)

Adults generate their own intellectual & emotional challenges

Mc Gue & Bouchard : Nature, Nurture and Psychology. Science 1997; 276: 1560-3

Thanks for your cooperation

EBCOG 2018, Paris

~~Liberté, Egalité, Fraternité~~

Communauté , Diversité, Maternité

In case of questions or comments: bine.clara.angela@gmail.com

The presentations will be seen on www.clara-angela.info