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Gestació gemel·lar: quan acabar?

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Introducció

- Augment incidència gestacions gemel·lars: TRA i augment edat mares
- Alta taxa de prematuritat en gestacions gemel·lars (espontània i iatrogènica), però +/- 46% superen 37 set
- Increment de la morbi-mortalitat perinatal (materna, fetal, neonatal) a mesura que avança l'edat gestacional
- Estudis descriuen millors resultats si finalització a partir de setmanes amb "baixa" taxa de complicacions neonatals (32, 34 o 36 setmanes)
- Múltiples estudis descriuen menor morbi-mortalitat perinatal entre les 37-38 setmanes però major mortalitat intrauterina a partir de les 39 setmanes (observacionals, retrospectius...)
- Redefinir el concepte de post-terme en les gestacions gemel·lars?



Introducció

- Última revisió de la Cochrane al 2003, recomana finalitzar gemel·lars no complicats a partir de setmana 37
- Pocs estudis randomitzats sobre edat gestacional òptima per finalitzar gemel·lars no complicats:
 - 2000 estudi japonès amb 39 gestacions gemel·lars
 - 2010 publicació britànica mostra petita
- Al 2011 últimes recomanacions de la NICE (National Institute for Health and Clinical Excellence) al Regne Unit



Gestational age at delivery and perinatal outcomes of twin gestations

Amy E. Doss, MD; Melissa S. Mancuso, MD; Suzanne P. Cliver, BA; Victoria C. Jauk, MPH, BSN; Sheri M. Jenkins, MD

OBJECTIVE: The optimal gestational duration for twin gestations is unknown. Epidemiologic studies show that the lowest perinatal mortality rate for twins is at 37-38 weeks, but these studies lack information on pregnancy complications and neonatal morbidities. This study evaluates pregnancy characteristics and perinatal outcomes of twins in order to assess the optimal gestational age for delivery.

STUDY DESIGN: This is a retrospective study of twins delivered at ≥ 36 weeks at our institution from 1991-2009. The composite rate of perinatal morbidity and mortality (including perinatal death, respiratory distress, suspected sepsis, and need for neonatal inten-

sive care) was determined for weekly intervals from 36-39⁺ weeks.

RESULTS: There were 377 twin gestations included. Of those 83% were dichorionic. Fifty-three percent had spontaneous labor and 48% were delivered by cesarean section. Perinatal outcomes improved as gestational age advanced to 38 weeks.

CONCLUSION: Perinatal morbidity and mortality rates suggest that the optimal time for delivery of twins is at 38 weeks or greater.

Key words: delivery, gestational age, perinatal morbidity, perinatal mortality, twins



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- Inclou només bessons de 36 o més setmanes
- Criteris exclusió: anomalies fetals severes, aneuploidia, mort d'un o els 2 bessons abans de la set 36
- Revisió d'història clínica materna i neonatal
- Divideix per grups setmanals entre 36 i 39+
- Inclouen al mateix grup gestacions entre 39 i 41 set degut a numero reduït (n=6)
- Valora un “composite” de complicacions perinatals: mortalitat fetal/neonatal, distress respiratori, sepsis, ingres UCIN
- Comparen amb cohort comparable de gestacions úniques



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TABLE 2

Maternal and obstetric conditions by gestational week of delivery

Condition	36 wks, % (n = 130)	37 wks, % (n = 118)	38 wks, % (n = 84)	39+ wks, % (n = 45)	P value trend
Diabetes	11.5	5.9	6.0	0	< .01
Chronic HTN	5.4	11.0	4.8	2.2	.43
Gestational HTN	13.1	17.8	15.5	13.3	.85
Preeclampsia	19.2	19.5	10.7	6.7	.02
Steroids received	16.9	10.2	6.0	0	< .01
Spontaneous labor	59.2	53.4	47.6	40.0	.02
Cesarean section	43.9	50.9	50.0	46.7	.54
Growth restriction	15.4	11.9	8.3	4.4	.03
Oligohydramnios	6.2	5.9	13.1	11.1	.08
Polyhydramnios	1.5	0.9	0	0	.18
Meconium	4.6	4.3	9.5	13.3	.02

HTN, hypertension.

Doss. Gestational age and perinatal outcomes of twins. Am J Obstet Gynecol 2012.



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TABLE 3

Perinatal outcomes by gestational week of delivery

Perinatal outcome	36 wks, % (n = 260)	37 wks, % (n = 236)	38 wks, % (n = 168)	39+ wks, % (n = 90)	P value
Composite ^a	30.0	15.7	7.1	7.8	< .01
NICU admission	28.9	15.3	6.6	7.8	< .01
Suspected sepsis	18.5	9.3	5.4	4.4	< .01
Any respiratory distress	16.2	9.8	3.6	5.6	< .01
Respiratory support	5.4	4.2	2.4	2.2	.41
Transient tachypnea	1.9	2.1	3.0	3.3	.76
Hyperbilirubinemia	5.8	1.3	0.6	0.0	< .01
SGA	31.9	19.0	25.5	32.6	.71
Perinatal death	1.2	0.4	0.6	1.1	.79

NICU, neonatal intensive care unit; SGA, small for gestational age.

^a Composite includes perinatal death, NICU admission, suspected sepsis, or any respiratory distress.

Doss. Gestational age and perinatal outcomes of twins. *Am J Obstet Gynecol* 2012.



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CONCLUSION: Perinatal morbidity and mortality rates suggest that the optimal time for delivery of twins is at 38 weeks or greater



Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

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OBJECTIVE: To determine the optimum timing for planned delivery of uncomplicated monochorionic and dichorionic twin pregnancies.

METHODS: Unselected twin pregnancies were recruited for this prospective cohort study (N=1,028), which was conducted in eight tertiary referral perinatal centers in Ireland. Perinatal mortality and a composite measure of perinatal morbidity (respiratory distress, necrotizing enterocolitis, hypoxic ischemic encephalopathy, periventricular leukomalacia, or sepsis) were compared between uncomplicated twins that underwent planned preterm delivery compared with monochorionic twins that continued in utero beyond 34 weeks of gestation, and dichorionic twins who continued beyond 36 weeks.

RESULTS: Perinatal outcome data were recorded for 100% of the 1,001 twin pairs that completed the study (n=200 monochorionic and n=801 dichorionic). Overall perinatal mortality was 30 per 1,000 in monochorionic twins and 3.8 per 1,000 among dichorionic twins. The prospective risk of in utero death was 1.5% after 34 weeks of gestation for uncomplicated monochorionic pregnancies, with no deaths among dichorionic twins after 33 weeks. The risk of a composite measure of perinatal morbidity for uncomplicated monochorionic twins fell from 41% (13/32 neonates, 3/6 among elective deliveries) at 34 weeks to 5% (4/84) at 37 weeks ($P<.001$). Among dichorionic twins, the risk of morbidity fell from 4% (2/52) among elective deliveries at 36 weeks to 1% (5/344) in pregnancies continuing to 38 weeks ($P=.231$).



Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

- Gestacions gemel·lars “no complicades” entre 11 i 22 set: no RPM, no defectes estructurals severos, no aneuploidia (comprovada o altament sospitada)
- Vigilància fetal exhaustiva amb eco cada 2 setmanes a partir de 16 set MC i a partir de 24 set BC
- Avaluació complicacions obstètriques: EHE, preeclàmpsia, RPM, DG, hemorràgia, APP, TFFS, ingrés hospitalari i administració corticosteroides
- Definint la gestació gemel·lar no complicada quan els MC passades les 34w i els DC passades les 36w tenien PFE > percentil 10, LAN i doppler AU normal, i en absència d'indicació materna o fetal de finalitzar la gestació.
- Analitza esdeveniments relacionats amb la morbi-mortalitat fetal i neonatal: mort, distress respiratori, enterocolitis, encefalopatia, leucomalàcia i sèpsis
- Compara aquests esdeveniments als MC abans i després 34w i als BC abans i després 36w



Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

Table 3. Prospective Risk of Perinatal Mortality and Perinatal Morbidity Among Apparently Uncomplicated Monochorionic Twin Gestations From 34 Weeks of Gestation (n=131 Twin Pregnancies)

Gestational Age (wk)	Prospective Risk of Mortality (per Pregnancy)*	Perinatal Morbidity [†] Rate (per Neonate) Among Elective [‡] Deliveries	Elective Deliveries: Morbidity [†] Details (per Neonate)	Perinatal Morbidity [†] Rate (per Neonate) Among Indicated [§] Deliveries	Indicated Deliveries: Morbidity [†] and Mortality Details (per Neonate)	Overall Morbidity Risk [†] (per Neonate) Among Elective and Indicated Deliveries	NICU Admission Rate (n=256 Neonates)
34–34 6/7	2/131 (1.5) (95% CI upper limit 6.0)	3/6 (50)	RDS (3/6)	10/26 (39)	RDS (6/26) Sepsis (5/26)	13/32 (41) 95% CI upper limit 59)	28/32 (88)
35–35 6/7	2/118 (1.7)	2/14 (14)	Sepsis (2/14)	2/30 (7)	Dual mortality (fetomaternal hemorrhage) (2/30)	2/44 (5)	23/44 (52)
36–36 6/7	1/96 (1.0)	3/26 (12)	RDS (2/26) HIE and sepsis (1/26)	4/56 (7)	RDS (4/56) death (“recipient TTTS”) (1/56)	7/82 (9)	27/82 (33)
37–37 6/7	0/49 (0)	3/46 (7)	RDS (3/46) NEC and sepsis (1/46)	1/38 (3)	RDS (1/38)	4/84 (5) (95% CI upper limit 12)	22/84 (26)
38 or more	0/11 (0)	0/16	NA	0/6 (0)	NA	0/22 (0)	2/22 (9)



Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

Table 4. Prospective Risk of Perinatal Mortality and Perinatal Morbidity Among Apparently Uncomplicated Dichorionic Twin Gestations From 36 Weeks of Gestation (n=565 Twin Pregnancies)

Gestational Age (wk)	Prospective Risk of Mortality (per Pregnancy)	Perinatal Morbidity Rate (per Neonate) Among Elective* Deliveries	Elective Deliveries: Morbidity [†] Details (per Neonate)	Perinatal Morbidity Rate (per Neonate) Among Indicated [‡] Deliveries	Indicated Deliveries: Morbidity [†] Details (per Neonate)	Overall Perinatal Morbidity Risk (per Neonate) Among Elective and Indicated Deliveries	NICU Admission Rate (n=1,130 Neonates)
36–36 6/7	0	2/52 (4) (95% CI upper limit 14)	RDS (2/52)	16/202 (8)	RDS (14/202) Sepsis (6/202)	18/254 (7) (95% CI upper limit 11)	92/254 (36)
37–37 6/7	0	7/222 (3)	RDS (7/222)	10/280 (4)	RDS (9/280) Sepsis (3/280) NEC (1/280)	17/502 (3)	114/502 (23)
38–38 6/7	0	3/222 (1)	RDS (2/222) Sepsis (3/222)	2/122 (2)	RDS (2/122) Sepsis (2/122)	5/344 (1) (95% CI upper limit 3.6)	49/344 (14)
39 or more	0	0/20 (0)	NA	0/8 (0)	NA	0/28 (0)	0/20 (0)



Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

CONCLUSION: Applying a strategy of close fetal surveillance, perinatal morbidity can be minimized by allowing uncomplicated monochorionic pregnancies continue to 37 weeks of gestation and dichorionic twins to 38 weeks. Among monochorionic twins, this approach must be balanced against a 1.5% risk of late in utero death.



Effectiveness of timing strategies for delivery of monochorionic diamniotic twins

Barrett K. Robinson, MD, MPH; Russell S. Miller, MD; Mary E. D'Alton, MD; William A. Grobman, MD, MBA

OBJECTIVE: The purpose of this study was to compare strategies for delivery timing of uncomplicated monochorionic diamniotic twin pregnancies.

STUDY DESIGN: A decision tree compared 9 strategies that included scheduled delivery between 32 and 38 weeks' gestation, with or without confirmation of fetal lung maturity. Outcomes in the model included fetal death, infant death, respiratory distress syndrome, mental retardation, and cerebral palsy.

RESULTS: A scheduled delivery at 38 weeks' gestation was the preferred strategy, which resulted in the highest quality adjusted life years

under base-case assumptions. Decreased, but comparable, quality adjusted life years estimates resulted from scheduled deliveries at 36 and 37 weeks' gestation, with or without amniocentesis. Sensitivity analyses demonstrated that the optimal gestational age for delivery was always ≥ 36 weeks' gestation.

CONCLUSION: This decision analysis suggests that, for women with uncomplicated monochorionic twins, delivery between 36 and 38 weeks' gestation is the preferred strategy for timing of delivery.

Key words: decision analysis, monochorionic twins, timing of delivery



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Strategy	Gestational age at scheduled delivery
1	32 wks after steroid administration
2	33 wks after steroid administration
3	34 wks after steroid administration
4	35 wks after steroid administration
5	36 wks
6	36 wks pending amniocentesis
7	37 wks
8	37 wks pending amniocentesis
9	38 wks



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Outcome	<i>P</i> value or RR ^a
Respiratory distress syndrome rate	
At 32 wk (with steroids) ^{21,23,24,29,30}	.30 ^b (.30, .41)
At 33 wk (with steroids) ^{21,23,24,29,30}	RR, 1.0
At 34 wk (with steroids) ^{21,23,24}	RR, 0.43
At 35 wk (with steroids) ^{21,23,24}	RR, 0.21
At 36 wk without steroids ^{21,23,24}	RR, 0.22
At 37 wk without steroids ^{21,23,24}	RR, 0.07
At 38 wk without steroids ^{21,23,24}	RR, 0.0055



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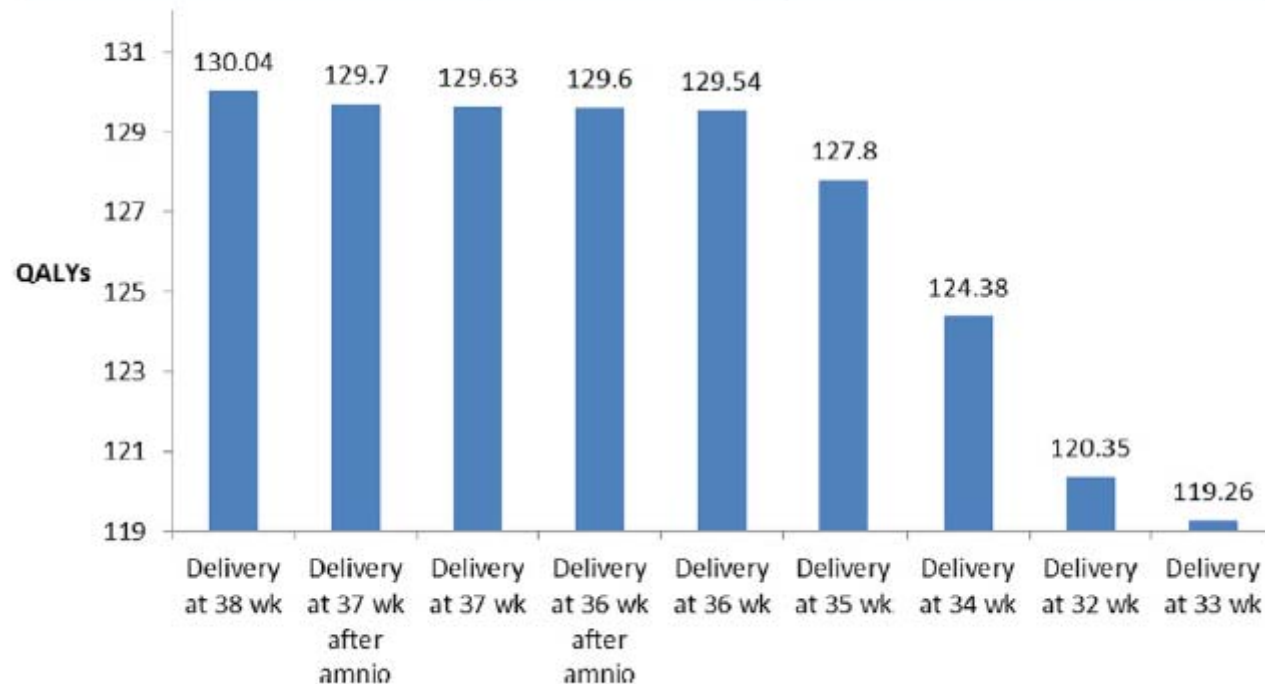
Outcome	<i>P</i> value or RR ^a
Rate of infant mortality after birth ^{20,21,38}	
At 34 wk	RR, 0.704
At 35 wk	RR, 0.488
At 36 wk	RR, 0.344
At 37 wk	RR, 0.312
At 38 wk	RR, 0.224



Effectiveness of timing strategies for delivery of monochorionic diamniotic twins

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FIGURE
Ranked QALY outcomes by different strategy



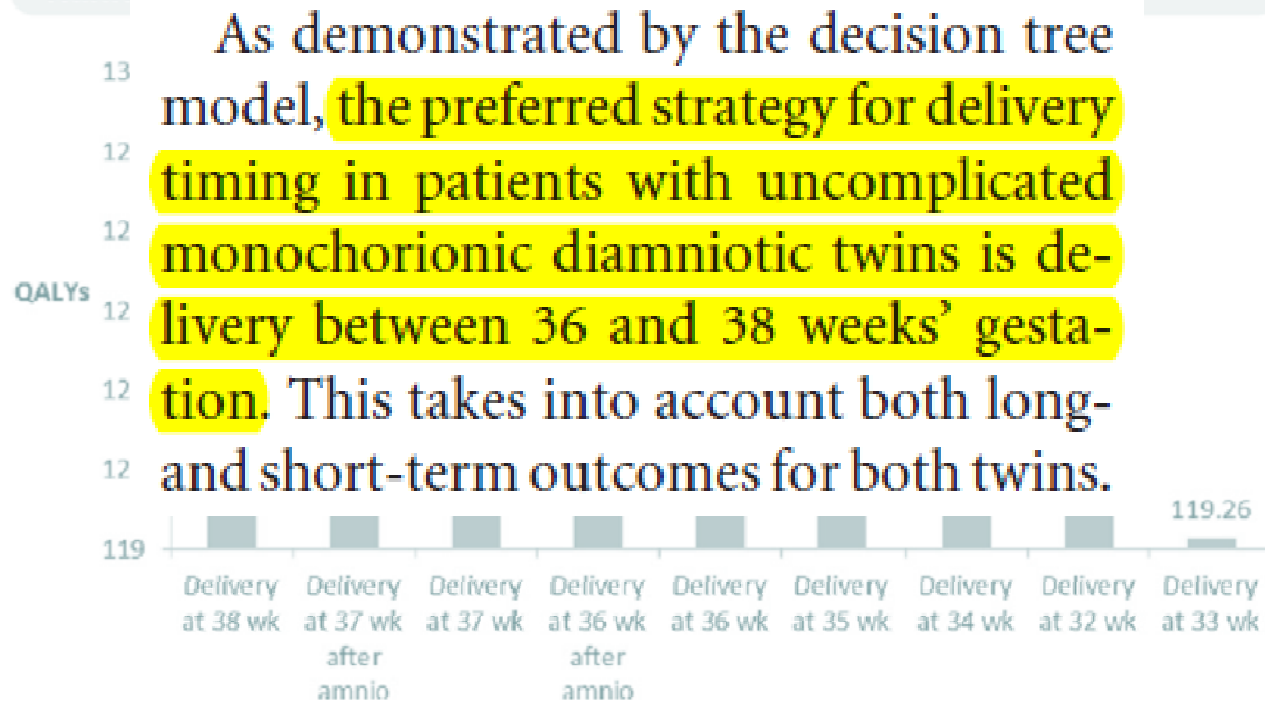
Amnio, amniocentesis; *QALY*, quality-adjusted life year; *wk*, weeks' gestation.



Effectiveness of timing strategies for delivery of monochorionic diamniotic twins

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FIGURE
Ranked QALY outcomes by different strategy



Amnio, amniocentesis; QALY, quality-adjusted life year; wk, weeks' gestation.



— 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 —

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Objective To evaluate whether for women with an uncomplicated twin pregnancy, elective birth at 37 weeks of gestation was associated with reduced risk of death or serious outcomes for babies, without increasing harm.

Design Randomised controlled trial.

Setting Maternity hospitals across Australia, New Zealand and Italy.

Population A total of 235 women with an uncomplicated twin pregnancy at 36⁺⁶ weeks of gestation, with no contraindication to continuing their pregnancy.

Methods Using a computer-generated, central telephone randomisation service, 235 women were randomised to Elective Birth (birth at 37 weeks; $n = 116$) or Standard Care (continued expectant management, with birth planned from 38 weeks; $n = 119$). Outcome assessors were masked to treatment allocation.

Main outcome measure A composite of serious adverse outcome for the infant.

Results For women with an uncomplicated twin pregnancy, elective birth at 37 weeks of gestation was associated with a significant reduction in risk of serious adverse outcome for the infant (Elective Birth 11/232 [4.7%] versus Standard Care 29/238 [12.2%]; risk ratio [RR] 0.39; 95% CI 0.20–0.75; $P = 0.005$), reflecting a reduction in birthweight less than the third centile using singleton gestational age-specific charts (Elective Birth 7/232 [3.0%] versus Standard Care 24/238 [10.1%]; RR 0.30; 95% CI 0.13–0.67; $P = 0.004$). In a *post hoc* analysis using twin gestational age-specific charts, there was evidence of a trend towards a reduction in the primary composite of serious adverse infant outcome (Elective Birth Group 4/232 [1.7%] versus Standard Care Group 12/238 [5.0%]; RR 0.34; 95% CI 0.11 to 1.05; $P = 0.06$).

Conclusion The findings of our study support recommendations for women with an uncomplicated twin pregnancy to birth at 37 weeks of gestation.

Keywords Infant morbidity, low birthweight, randomised trial, timing of birth, twin pregnancy.



— 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

- Dones amb gestació gemel·lar sense complicacions de 36+6 o més setmanes, sense contraindicació per prosseguir amb la gestació
- Exclusió:
 - Mort fetal d'un o ambdós bessons
 - Trabajo de paro activo
 - NST “no tranquil·litzador”
 - Compromís matern o fetal que necessités controls exhaustius prenatals
- Mida de la mostra
 - Estimat de 460 pacients
 - 235 pacients va finalitzar el reclutament per falta de fons



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

Table 1. Baseline characteristics at the time of trial entry

	Elective birth group (n = 116)	Standard care group (n = 119)
Age* (years)	28.6 (5.6)	29.2 (5.3)
Gestational age at randomisation** (weeks)	36.9 (36.9–36.9)	36.9 (36.9–36.9)
Body Mass Index** (kg/m ²)	26.6 (23.8–31.0)	25.9 (23.3–30.3)
Public patient***	114 (98.3)	118 (99.2)
Race***		
Caucasian	99 (85.3)	105 (88.2)
Asian	5 (4.3)	2 (1.7)
Other	12 (10.3)	12 (10.1)
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)



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

Table 2. Primary infant outcome and morbidity components by treatment group

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*	11 (4.7)	29 (12.2)	0.39 (0.20–0.75)	0.005
Perinatal death	0 (0.0)	1 (0.4)	Not estimable	
Stillbirth	0 (0.0)	0 (0.0)	Not estimable	
Neonatal death	0 (0.0)	1 (0.4)	Not estimable	
Morbidity from adverse outcomes at term**	10 (4.3)	28 (11.8)	0.37 (0.18–0.73)	0.004
Morbidity from immaturity**	2 (0.9)	2 (0.8)	1.03 (0.15–7.16)	0.98
Birth trauma**	0 (0.0)	1 (0.4)	Not estimable	
Seizures**	1 (0.4)	0 (0.0)	Not estimable	
Apgar <4 at 5 minutes**	0 (0.0)	0 (0.0)	Not estimable	
Cord pH <7.0**	2 (0.9)	4 (1.7)	0.51 (0.10–2.75)	0.43
Birthweight <3rd centile**	7 (3.0)	24 (10.1)	0.30 (0.13–0.67)	0.004
Stage 3 encephalopathy**	1 (0.4)	0 (0.0)	Not estimable	
NICU admission >4 days***	2 (0.9)	2 (0.8)	1.03 (0.15–7.16)	0.98
Severe lung disease***	0 (0.0)	0 (0.0)	Not estimable	
Ventilation ≥24 hours***	2 (0.9)	1 (0.4)	2.05 (0.19–22.32)	0.56
Chronic lung disease***	0 (0.0)	0 (0.0)	Not estimable	
Necrotising enterocolitis***	0 (0.0)	0 (0.0)	Not estimable	
Systemic infection***	0 (0.0)	0 (0.0)	Not estimable	



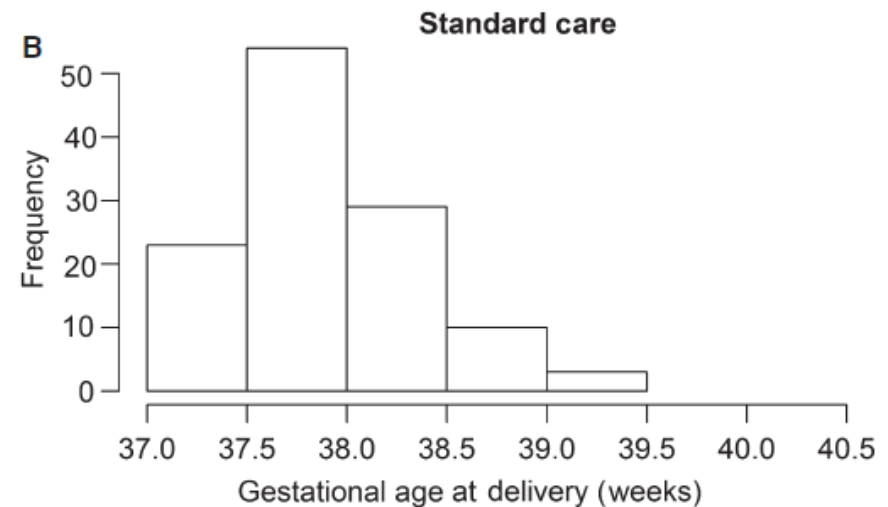
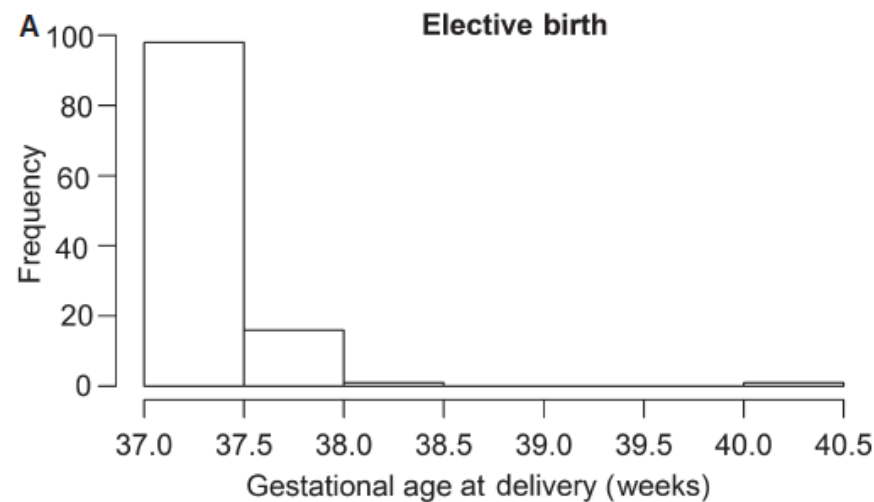
Elective birth at 37 weeks of gestation versus standard care for women with an uncomplicated twin pregnancy at term: the Twins Timing of Birth Randomised Trial

Table 3. Antenatal, labour and birth outcomes by treatment group

Outcome	Elective birth group (<i>n</i> = 116 women; <i>n</i> = 232 infants) <i>n</i> (%)	Standard care group (<i>n</i> = 119 women; <i>n</i> = 238 infants) <i>n</i> (%)	Risk ratio (95% CI)	<i>P</i> value
Antenatal medical and obstetric complications				
Pre-eclampsia/Eclampsia	6 (5.2)	2 (1.7)	3.08 (0.63–14.94)	0.16
Antepartum haemorrhage	0 (0.0)	0 (0.0)	Not estimable	
Abnormal umbilical artery Doppler study	0 (0.0)	0 (0.0)	Not estimable	
Mean gestational age at birth*	37.3 (0.4)	37.9 (0.5)	−0.67 (−0.79 to −0.56)	<0.0001
Labour and birth complications				
Induction of labour	59 (50.9)	45 (37.8)	1.35 (1.00–1.80)	0.046
Mode of birth				
Vaginal birth	50 (43.1)	57 (47.9)	0.90 (0.68–1.19)	0.56
Elective caesarean section	44 (37.9)	40 (33.6)	1.13 (0.80–1.59)	0.49
Emergency caesarean section	22 (19.0)	22 (18.5)	1.03 (0.60–1.75)	0.93
Birthweight (kg)*	2.74 ± 0.312	2.83 ± 0.364	−0.10 (−0.17 to −0.02)	0.01
Serious maternal outcome**	2 (1.7)	7 (5.9)	0.29 (0.06–1.38)	0.12



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



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

The findings of our study support recommendations for women with an uncomplicated twin pregnancy to birth at 37 weeks of gestation



Discussió

- Coneguts els avantatges de la inducció al part a les 41 set en gestacions úniques
- Corba similar de les gestacions gemel·lars a partir de les 37w
- Possible paper beneficiós la inducció al part en període “a terme precoç” (“early at term”)
- Redefinir el concepte de post-terme per les gestacions gemel·lars posant el límit a la setmana 38
- Finalització gestació gemel·lar a les 37w associa una menor taxa de mortalitat fetal i esdeveniments perinatal adversos
- No s’ha descrit que la finalització a les 37w s’associï a esdeveniments adversos relacionats amb immaduresa fetal
- Nivell d’evidència II-III



Evidencia científica

- Majoria d'estudis són observacionals
 - No control dels factors de confusió
 - Alguns no tenen en compte la corionicitat
- Un sol estudi ranzomitizat. Certes limitacions
 - N estimada de 460, reclutament finalitza a les 235
 - 45% de pacients en el grup Standard care es finalitzen <38w
- L'escàs n^o d'events adversos perinatal obligava a incrementar la mida mostral per trobar diferències estadísticament significatives entre dues intervencions.



