Αιτιολογημένη χορήγηση κορτικοστεροειδών στην κύηση.

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Δεν υπάρχει καμία σύγκρουση οικονομικών συμφερόντων!

Κορτικοστεροειδή στην κύηση

- **Ιστορία κι οδηγίες χορήγησης**
- **Όψιμα πρόωρα**
- **Εξαιρετικά πρόωρα**
- **Εκλεκτική Καισαρική Τομή**
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- **Επανάληψη δόσεων**
- **Σύγκριση κατευθυντηρίων οδηγιών**

History of Steroid Used in Preterm Birth

Graham Liggins

Liggins & Howie

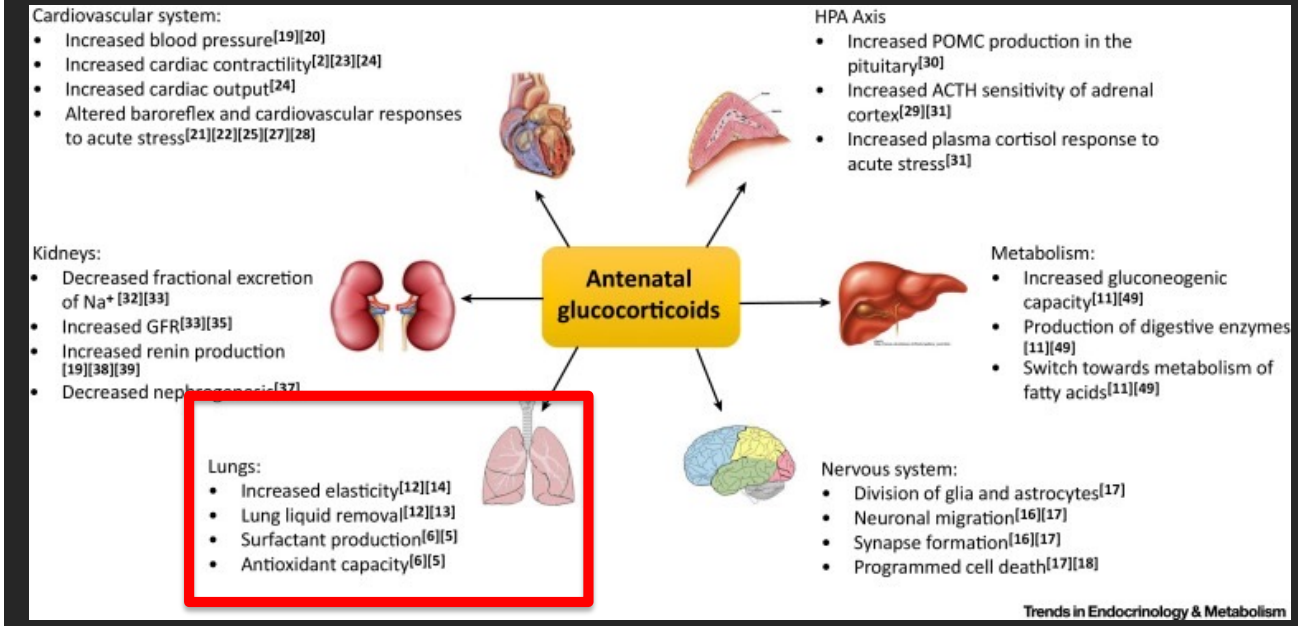
1960

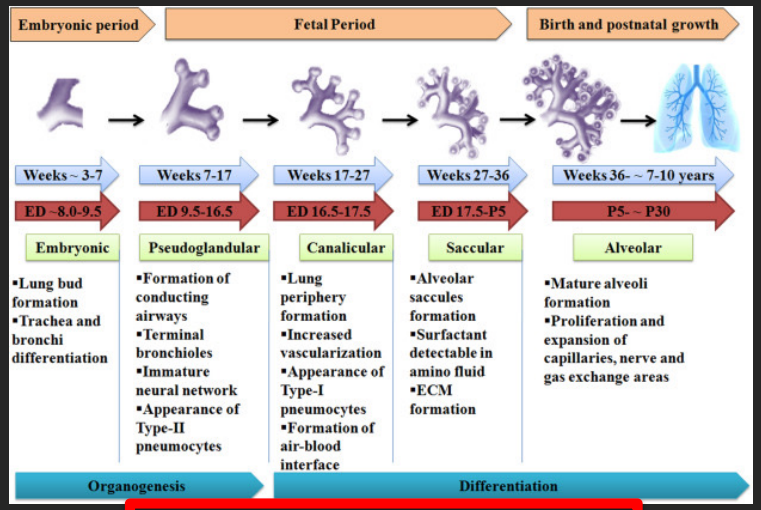
Graham Liggins was investigating factors involved in the initiation of labor in a sheep model. His hypothesis was that the fetus produces substances that trigger labor, possibly steroid hormones. In postmortem analyses, Liggins incidentally found that preterm lambs exposed to corticosteroids had structurally more mature lungs than expected, and were also viable at an earlier gestational age and had less severe respiratory distress at birth.

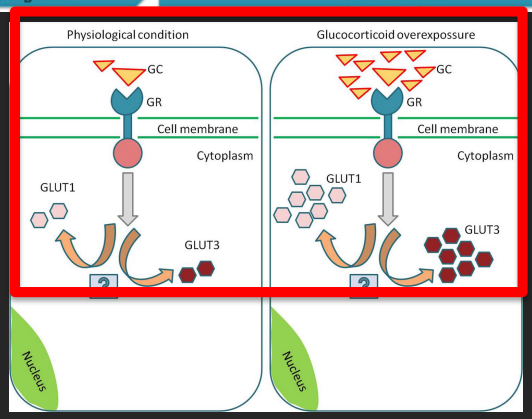
1972

Landmark study
A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics 1970;50:515-25.

Pathways for corticosteroids in lung maturity







Κορτικοστεροειδή

- Σύνδρομο αναπνευστικής δυσχέρειας (RDS)
- Εγκεφαλική αιμορραγία (intracranial hemorrhage)
- Νεκρωτική εντεροκολίτιδα (NE)
- Περιγεννητικής θνησιμότητας

Βηταμεθαζόνη: 12mg IM σε 2 δόσεις με 24 ώρες διαφορά η κάθε δόση
Δεξαμεθαζόνη: 6mg IM σε 4 δόσεις με 12 ώρες διαφορά η κάθε δόση

48ωρο σχήμα

Meta-analysis: corticosteroids and neurodevelopment

Neurodevelopmental Outcome After a Single Course of Antenatal Steroids in Children Born Preterm

A Systematic Review and Meta-analysis

Alexandros Sotiriadis, MD, PhD, Alexandra Tsiami, MD, Stefania Papatheodorou, MD, PhD, Ahmet A. Baschat, MD, PhD, Kosmas Sarafidis, MD, PhD, and George Makrydimas, MD, PhD

Mainly non-randomized trials

Cerebral palsy	RR 0.68
PDI <70	RR 0.83
Severe disability	RR 0.79
Healthy survival	RR 1.18

Neonates born <34 weeks

Courtesy of A. Sotiriadis

RCOG guidelines: Corticosteroid Use in Pregnancy 2010

- 24^{+0} - 34^{+6} wks
- Elective Cesarean Section until 38^{+6} wks
- IUGR: 24^{+0} - 35^{+6} wks
- Repeat dose: only if the first dose <26wks
- Attention: Tuberculosis or inflammatory conditions
- Gestational diabetes: Increased insulin doses

Οδηγίες ACOG για χορήγηση κορτικοστεροειδών 2017

- 24^{+0} έως 33^{+6} wks: αν επίκειται τοκετός στις επόμενες 7 ημέρες
- 34^{+0}-36^{+6}wks (όψιμα πρόωρα): Αν επίκειται τοκετός στις επόμενες 7 ημέρες και δεν έχουν χορηγηθεί κορτικοστεροειδή μέχρι τότε
- ΟΧΙ σε χοριοαμνιονίτιδα, σοβαρή προεκλαμψία & επείγοντα
- Επανάληψη δόσης <34wks: ναι αν επίκειται τοκετός στις επόμενες 7 ημέρες και το προηγούμενο σχήμα κορτικοστεροειδών είχε δοθεί >14 μέρες
- Επανάληψη δόσης σε πΡΕΥ: Ανεπαρκή δεδομένα

SOGC: Antenatal Corticosteroid Therapy for Improving Neonatal Outcomes 2018

- Administer if medically indicated delivery planned within 7 days
- Do **NOT** administer in absence of cervical dilation/change or in the absence of regular contractions
- Administer at the time of diagnosis of pPROM
- Administer in cases of significant antepartum hemorrhage with a high risk of delivery within **7 days**
- Administer in cases of asymptomatic vasa previa or placenta previa with a high risk of delivery within **7 days**
- Do **NOT** administer rescue dose or course routinely

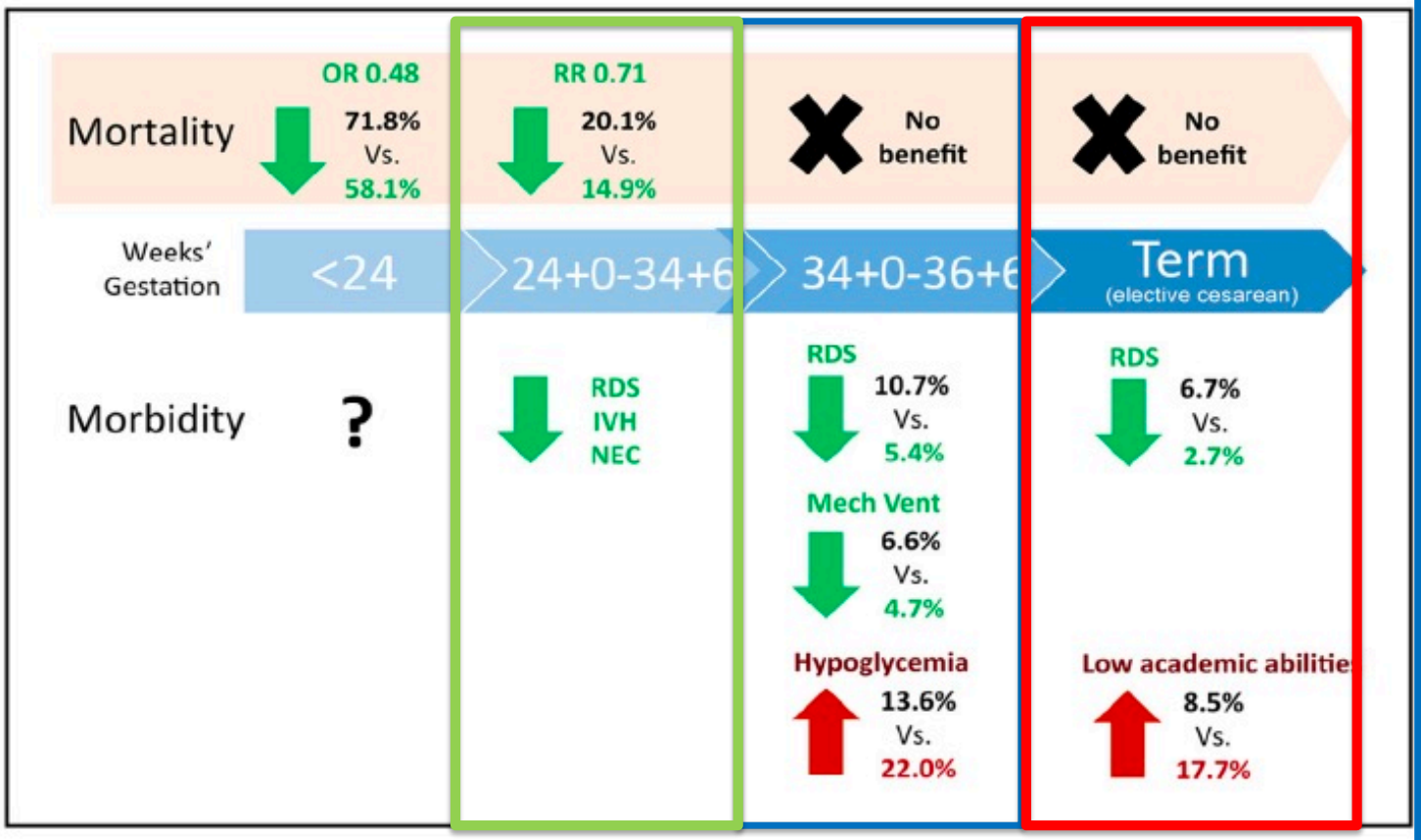
Table 7. Summary table of recommendations for agents, dosage and regimens

Agents, dosage, and regimens	Recommendation when gestational age criteria for antenatal corticosteroid therapy are met	Level of evidence	Strength of recommendation
Agents and dosage	2 × 12 mg doses of betamethasone IM, 24 hours apart **or** 4 × 6 mg doses of dexamethasone IM, 12 hours apart	Moderate	Strong
Timing of antenatal corticosteroid initiation	Administer if medically indicated delivery planned within 7 days	Low	Strong
	Administer if woman is in spontaneous preterm labour (ie, regular uterine contractions associated with significant cervical dilation or significant cervical change on repeated examination)	Low	Strong
	Do not administer in absence of cervical dilation/change or in the absence of regular contractions	Low	Strong
	Administer at the time of diagnosis of preterm premature rupture of membranes	Low	Strong
	Administer in cases of significant antepartum hemorrhage with a high risk of delivery within 7 days	Low	Strong
	Administer in cases of asymptomatic vasa previa or placenta previa with a high risk of delivery within 7 days	Low	Strong
	Do not administer prior to transfer unless a diagnosis of preterm labour has been firmly established	Low	Strong
Repeated dose or course	Consider cancellation of a second dose if the risk of preterm delivery decreases significantly following administration of the first dose After cancellation, consider administration of 1 dose or 1 course if a high risk of preterm birth arises, taking into account gestational age and time interval since the first course	Low	Strong
	Do not administer rescue dose or course routinely Gestational age and time interval since the first course of antenatal corticosteroid therapy (at least 14 days) should be taken into account A single rescue course may be administered after risks and benefits are discussed with the woman	Moderate	Conditional

IM: intramuscularly.

SOGC: Antenatal Corticosteroid Therapy for Improving Neonatal Outcomes 2018

Figure 1. Summary of the evidence.

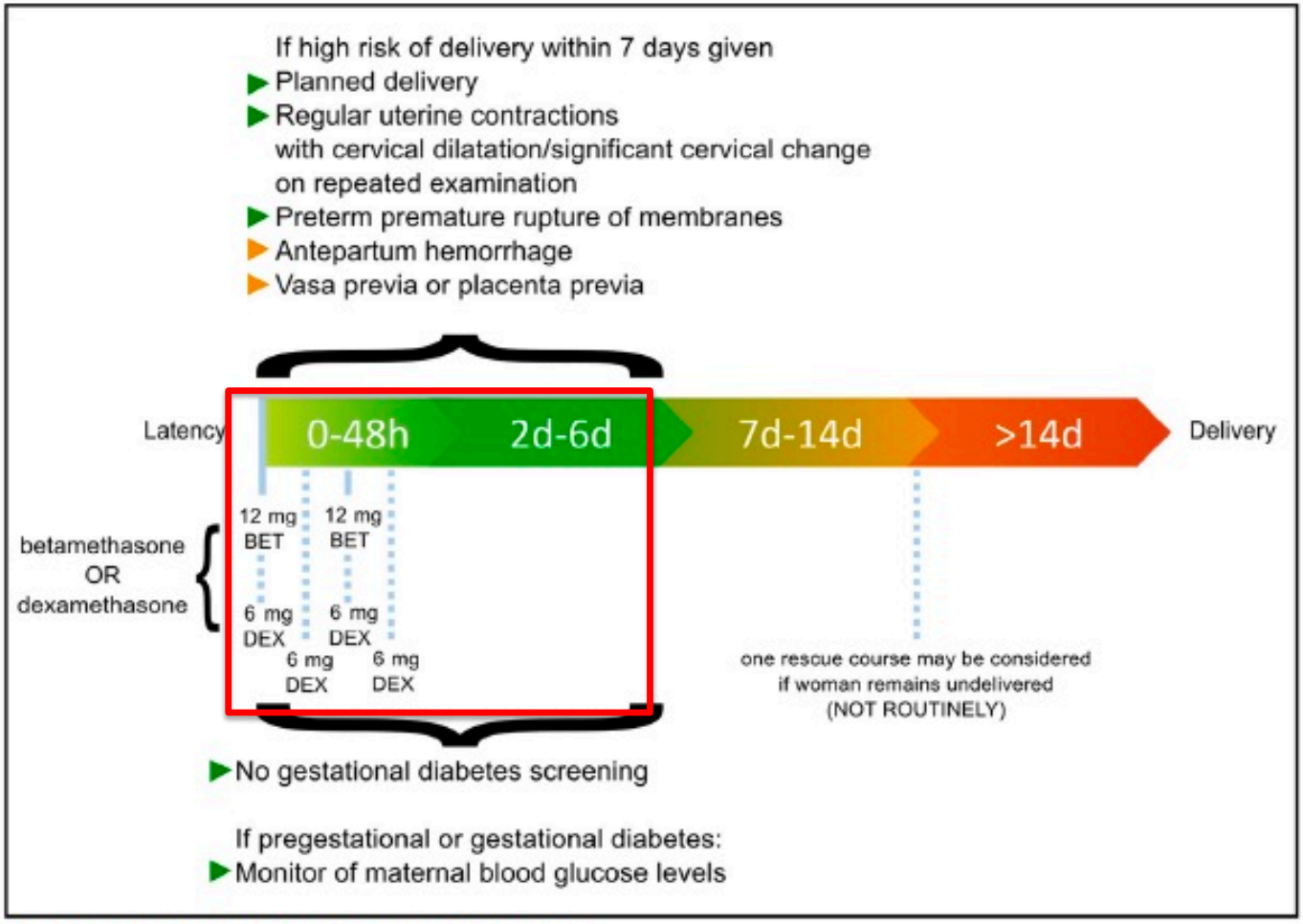


IVH: intraventricular hemorrhage; Mech Vent: mechanical ventilation; NEC: necrotizing enterocolitis; OR: odds ratio; RR: risk ratio; RDS: respiratory distress syndrome; green arrow: benefit; red arrow: harm. (From S. Mc-

SOGC: Antenatal Corticosteroid Use in Pregnancy

2018

Figure 2. Summary of the evidence (agents, dosage, and target timing). Note: the same recommendation applies to women with multifetal pregnancies, pre-gestational or gestational diabetes, obesity, or growth-restricted fetuses. See the text for further details.



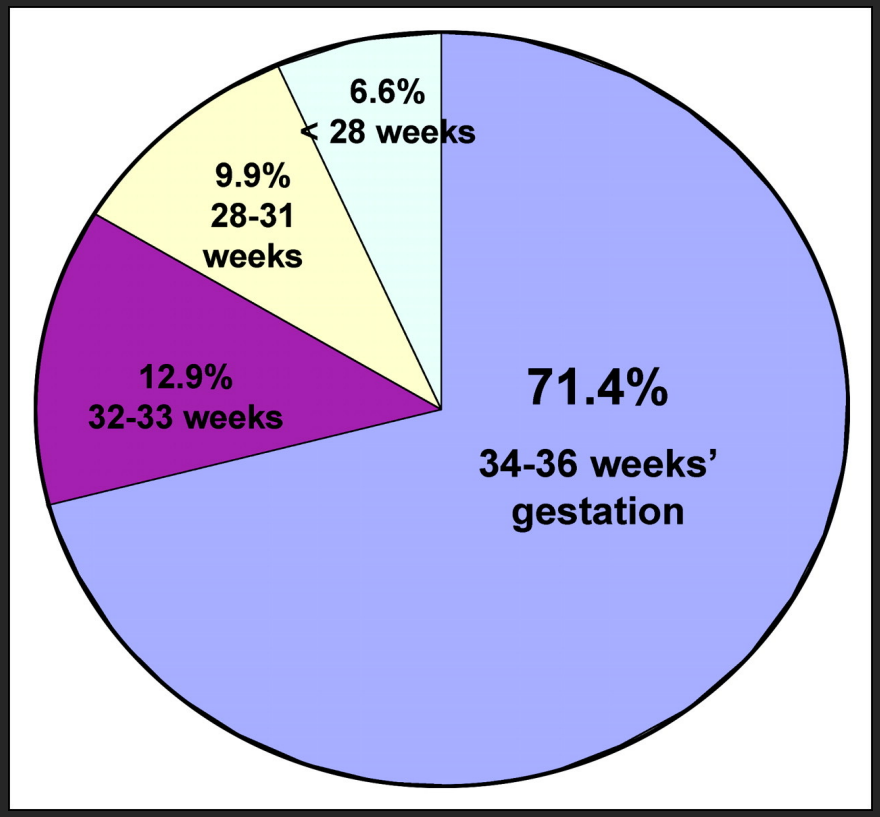
BET: betamethasone: DEX: dexamethasone.

SOGC: Antenatal Corticosteroid Use in Pregnancy

2018

- **Δε συνιστώνται συνεχείς, προγραμματισμένες δόσεις >2**
- **Δίνεται η 1η δόση του σχήματος, ακόμα κι αν δεν προλαβαίνει να ολοκληρωθεί**
- **Μεγαλύτερο όφελος υπάρχει 2-7 ημέρες μετά από την 1η δόση**

Όλες οι κατευθυντήριες οδηγίες συμφωνούν στην χορήγηση κορτικοειδών μέχρι ηλικία κύησης ≈34εβδομάδων



Κορτικοστεροειδή στην κύηση

- **Ιστορία κι οδηγίες χορήγησης**
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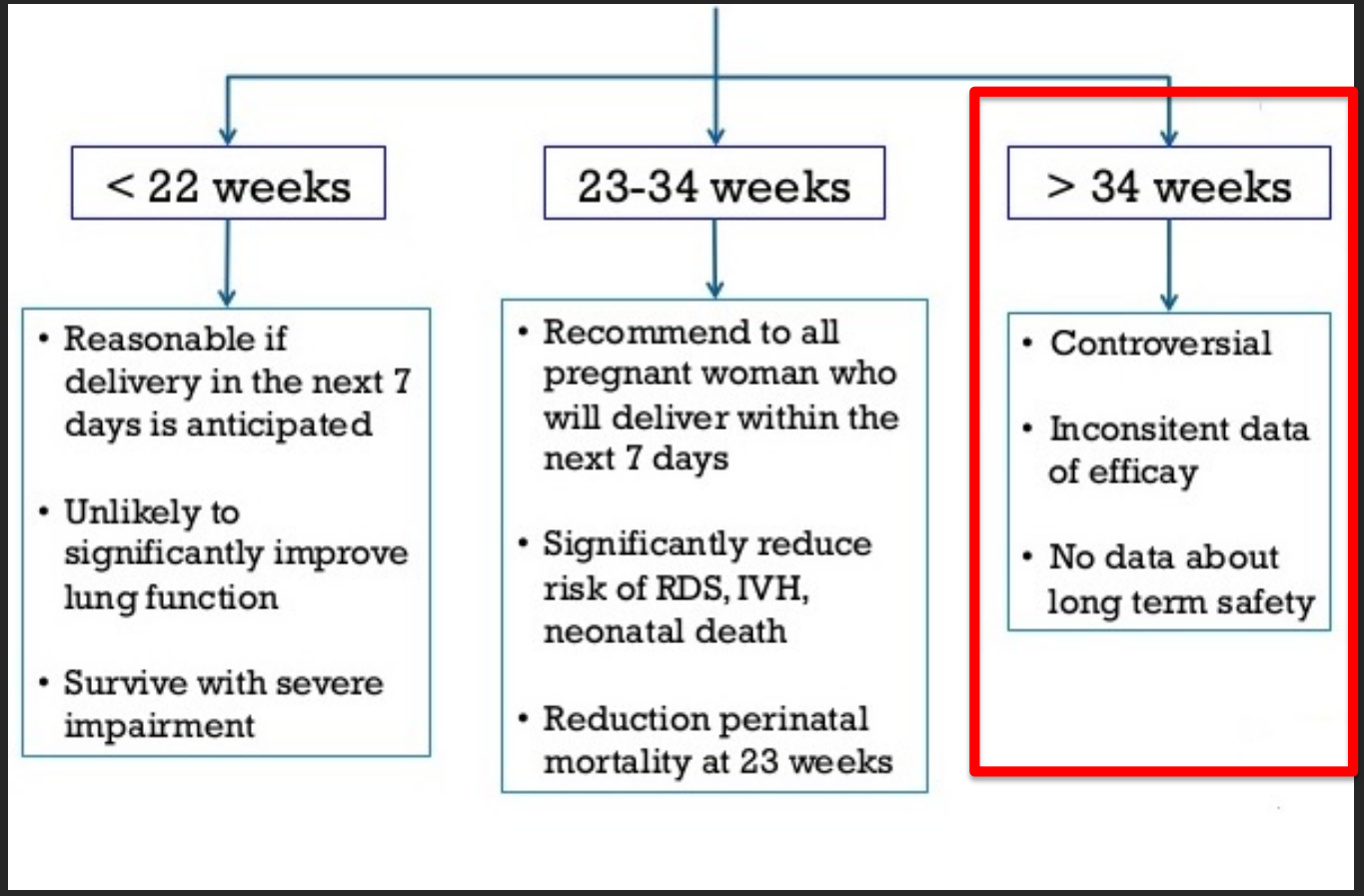
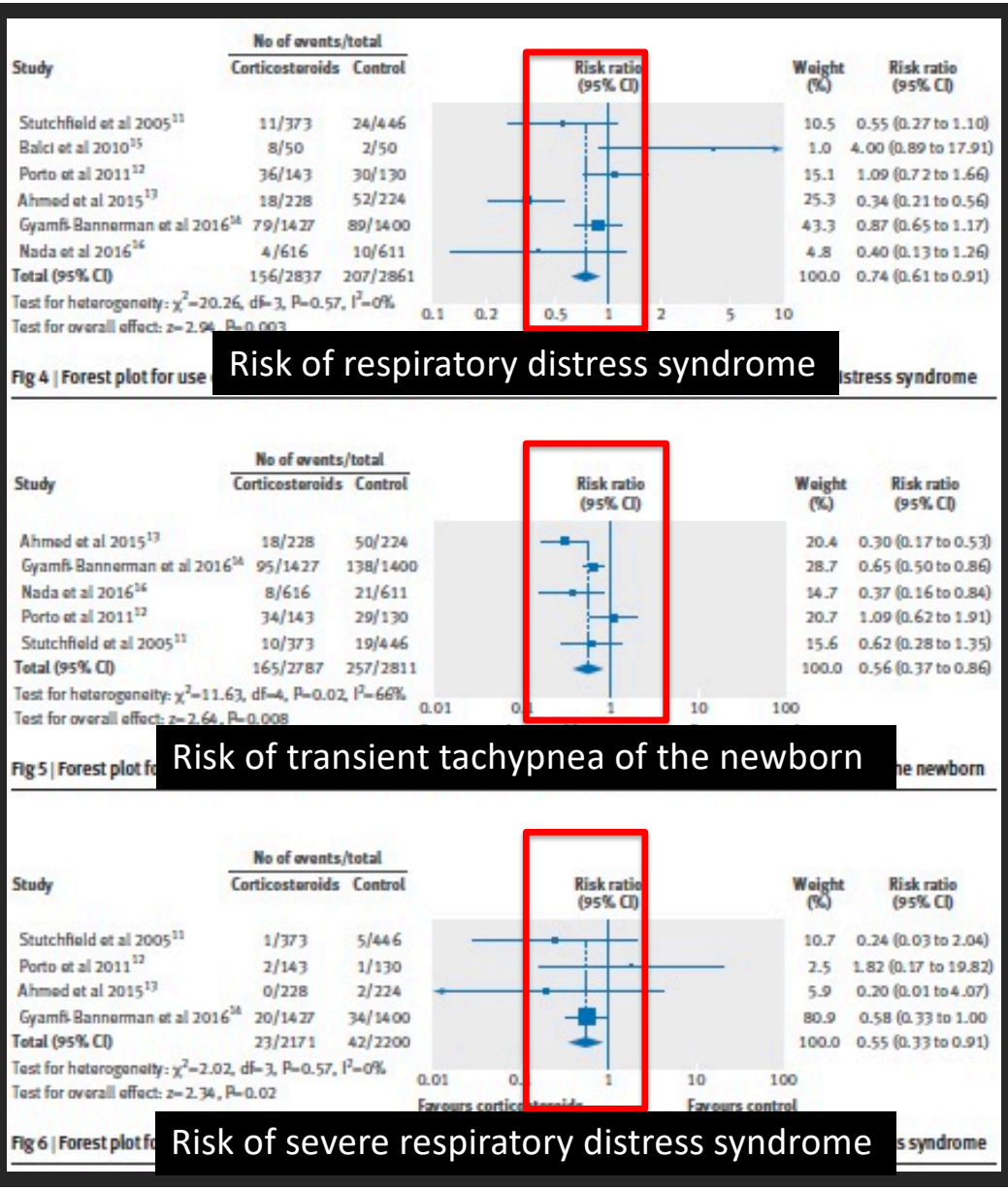
When to administer corticosteroids?



ACOG, 2017



Antenatal corticosteroids for maturity of term or near term fetuses: systematic review and meta-analysis of randomized controlled trials

Gabriele Saccone,[1] Vincenzo Berghella[2]

Antenatal steroids at ≥34 weeks' gestation reduce neonatal respiratory morbidity

A single course of corticosteroids can be considered for women at risk of imminent late premature delivery **34⁰-36⁶ weeks' gestation**, as well as for women undergoing **planned cesarean delivery at ≥37 weeks' gestation**.

BMJ, 2016

Newborn complications by gestational week on delivery by eligibility and reason for ineligibility for antenatal steroids among late preterm deliveries

Gestational week on delivery	34 wk			35 wk			36 wk		
	Eligible N = 315	Ineligible, steroids[a] N = 187	Ineligible, c/d[b] N = 20	Eligible N = 637	Ineligible, steroids[a] N = 149	Ineligible, c/d[b] N = 26	Eligible N = 1411	Ineligible, steroids[a] N = 144	Ineligible, c/d[b] N = 53
	%	%	%	%	%	%	%	%	%
Newborn respiratory complications	24.1	13.9	35.0	14.9	7.4	15.4	5.5	4.9	17.0
Resuscitation at delivery	16.5	11.8	20.0	11.6	8.7	7.7	7.3	6.3	22.6
Glucose instability	7.9	4.8	20.0	5.2	6.0	23.1	3.7	0.7	17.0
NICU admission	87.0	96.3	85.0	45.1	61.7	65.4	20.1	27.8	47.2

NICU, neonatal intensive care unit.

[a] Ineligible for late preterm steroids due to prior receipt of antenatal steroids in this pregnancy; [b] Ineligible due to prepregnancy chorioamnionitis or diabetes.

Souter et al. Potential impact of late preterm antenatal steroid guidelines. Am J Obstet Gynecol 2017.

Souter et al, AJOG, 2017

- Careful consideration of which pregnancies should receive late preterm antenatal steroids
- How to identify these pregnancies is important to optimize benefits and mitigate potential risks of this intervention.

Antenatal corticosteroids beyond 34 weeks gestation: What do we do now?

TABLE 2

Studies comparing the use of antenatal corticosteroids for late preterm infants at risk of preterm delivery

Authors	Treatment, n	Control, n	Antenatal corticosteroid used	Deaths, %	Neonatal intensive care admission, %	Respiratory distress syndrome, %	Transient tachypnea of newborn infant, %	Respiratory morbidity, %	Hypoglycemia, %
Balci, et al (2010)[16]	50	50	Betamethasone: 12 mg × 1 dose 24 hr before delivery	None reported	Only reported as respiratory distress syndrome with admission	4% vs 16% (*P*=.046)	Did not report	Did not report	Did not report
Porto et al (2011)[17]	143	130	Betamethasone: 12 mg × 2 doses, 24 hr apart	0 vs 2[a]	33 vs 33[a]	1 vs 1 (*P*=.54)	24 vs 22 (*P*=.77)	25 vs 23 (*P*=.69)	11 vs 7[a]
Ramadan et al (2016)[18]	74	221	Betamethasone: 12 mg × 2 doses, 24 hr apart	0 vs 1[a]	27 vs 19 (*P*=.14)	8.1 vs 6.8 (*P*=.70)	8.1 vs 6.8 (*P*=.70)	17.6 vs 15.4 (*P*=.66)	20.3 vs 10.9 (*P*=.04)
Gyamfi-Bannerman (2016)[19]	1427	1400	Betamethasone: 12 mg × 2 doses, 24 hr apart	0.1 vs 0 (*P*=.50)	41.8 vs 44.9 (*P*=.09)	5.5 vs 6.4 (*P*=.36)	6.7 vs 9.9 (*P*<.01)	11.6 vs 14.4 (*P*=.02)[b]	24.0 vs 15.0 (*P*<.01)

Yes / No / No / Yes

[a] Not significant; no probability value reported; [b] Primary outcome for this study was defined by any of the following occurrences within 72 hours after birth: continuous positive airway pressure or high-flow nasal cannula for at least 2 continuous hours, supplemental oxygen with a fraction of inspired oxygen of ≥0.30 for at least 4 continuous hours, mechanical ventilation, stillbirth or neonatal death, or the need for extracorporeal membrane oxygenation.

Kamath-Rayne. Antenatal corticosteroids beyond 34 weeks. Am J Obstet Gynecol 2016.

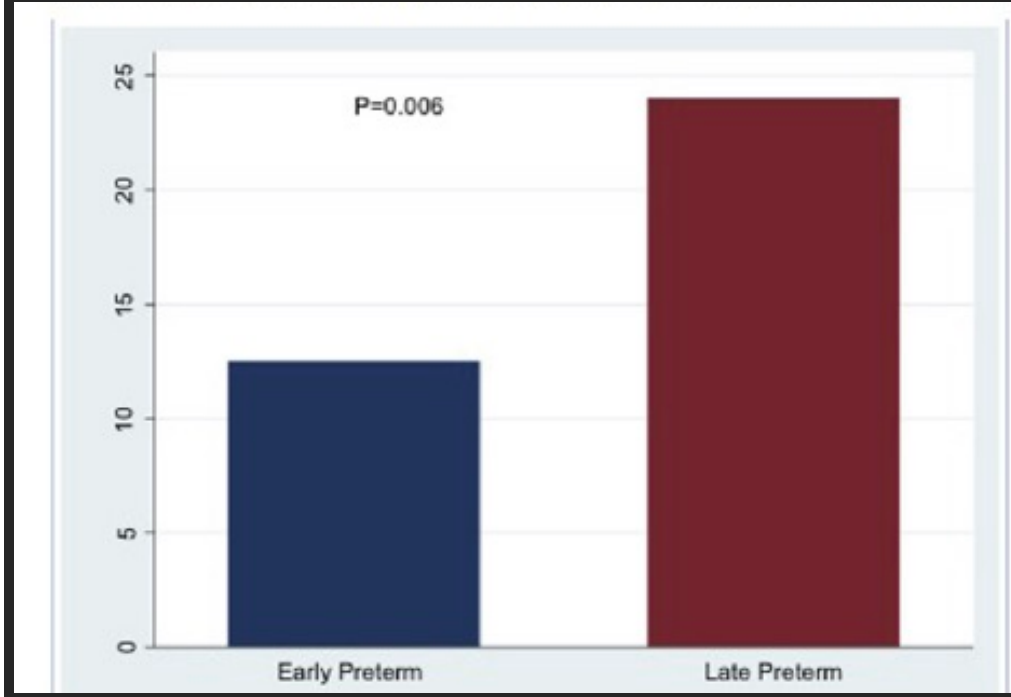
Beena D. Kamath-Rayne, AJOG, 2016

The association of antenatal corticosteroids with neonatal hypoglycemia and hyperbilirubinemia

- Of 6675 preterm deliveries, in neonates exposed to antenatal betamethasone were observed significantly higher rates of:
  - neonatal hypoglycemia (5.7% versus 4.2%, $p<0.05$)
  - hyperbilirubinemia (45.9% versus 24.1%, $p<0.05$)
- Controlling for potential confounders including gestational age, these findings persisted with betamethasone-exposed neonates 1.6 times more likely to have hypoglycemia and 3.2 times more likely to have hyperbilirubinemia

Pettit KE , JMFNM, 2014

Antenatal steroids and neonatal hypoglycemia



- Early preterm (23-33 6/7 wks): 264
- Late preterm (34-36 6/7 wks): 104
- Steroid administration to delivery, (7.9 vs 9.5 days, p.0.12)

Table: Maternal glucose and neonatal hypoglycemia

Maternal Blood Glucose	Neonatal hypoglycemia	No neonatal hypoglycemia	P
24h after steroids (n=137) Mean±SD Median (IQR)	 145.8 ± 50.8 135.5 (123.0, 160.5)	 133.8 ± 40.1 121.0 (111.0, 144.0)	0.19
48h after steroids(n=90) Mean±SD Median (IQR)	 119.9 ± 34.1 108.5 (99.0, 134.0)	 124.3 ± 33.0 114.5 (104, 142.0)	0.64
At Delivery (n=100) Mean±SD Median (IQR)	 105.3 ± 36.0 100.0 (88.0, 114.0)	 106.9 ± 37.2 103.0 (90.0, 118.0)	0.76

SD=standard deviation; IQR=interquartile range

Sondgeroth KE, AJOG, 2018

Neonatal corticosteroid therapy affects growth patterns in early infancy

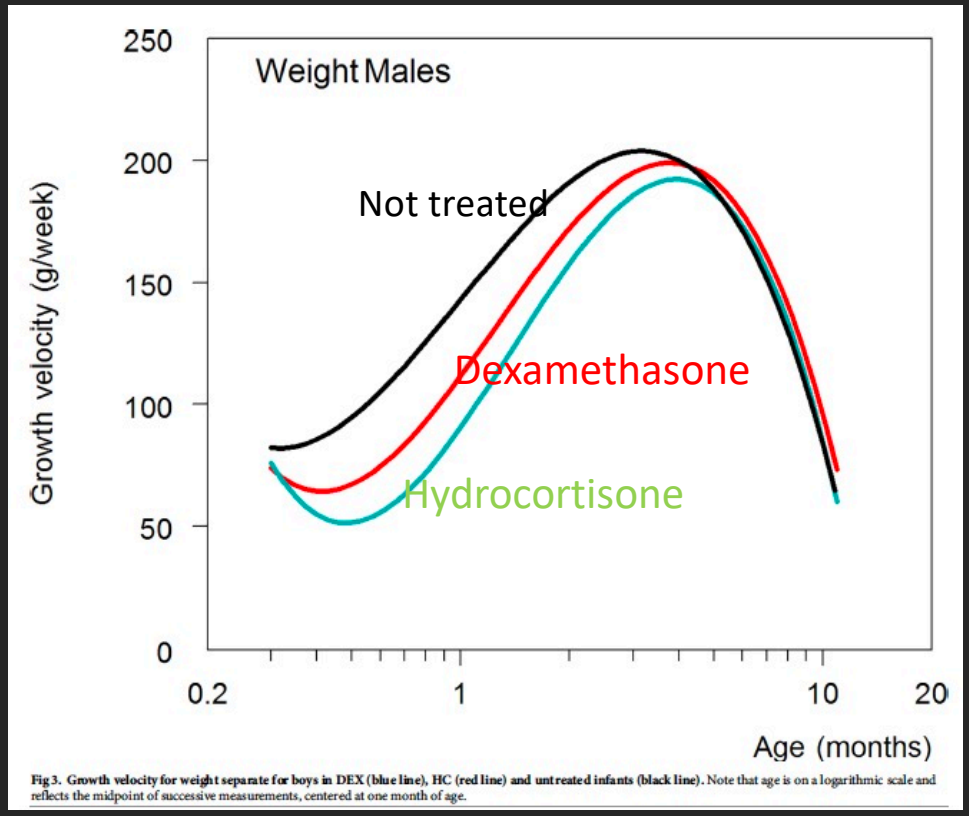


Fig 3. Growth velocity for weight separate for boys in DEX (blue line), HC (red line) and untreated infants (black line). Note that age is on a logarithmic scale and reflects the midpoint of successive measurements, centered at one month of age.

- Growth velocity curves of corticosteroids treated neonates showed a delay in time
- They had decreased absolute growth velocities during and shortly after treatment and the first two months, followed by an increase in growth velocity in the following months.

Deodata Tijsseling, PLOS, 2018

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 7, 2016 VOL. 374 NO. 14

Antenatal Betamethasone for Women at Risk for Late Preterm Delivery

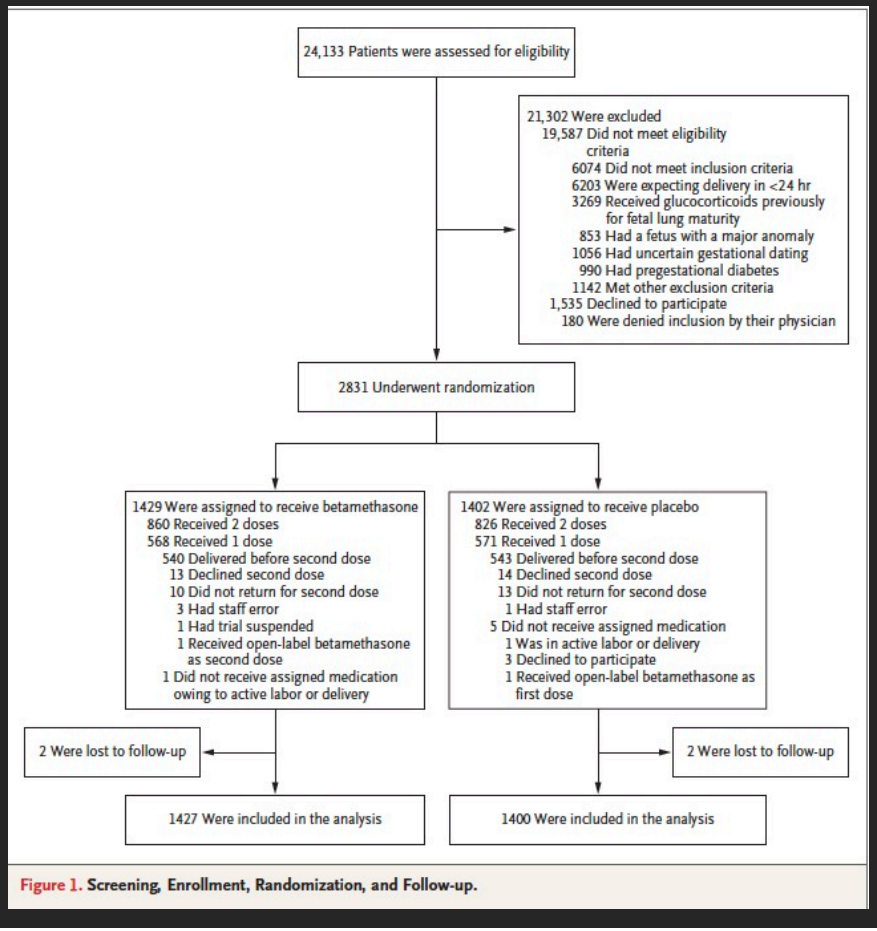


Figure 1. Screening, Enrollment, Randomization, and Follow-up.

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 7, 2016 VOL. 374 NO. 14

Antenatal Betamethasone for Women at Risk for Late Preterm Delivery

Table 2. Neonatal Respiratory Outcomes.*

Outcome	Betamethasone (N=1427)	Placebo (N=1400)	Relative Risk (95% CI)	P Value
	no. (%)			
Severe respiratory complication‡	115 (8.1)	169 (12.1)	0.67 (0.53–0.84)	<0.001
CPAP or high-flow nasal cannula for ≥12 continuous hr	93 (6.5)	147 (10.5)	0.62 (0.48–0.80)	<0.001
Need for resuscitation at birth§	206 (14.5)	260 (18.7)	0.78 (0.66–0.92)	0.003
Transient tachypnea of the newborn	95 (6.7)	138 (9.9)	0.68 (0.53–0.87)	0.002
Apnea	33 (2.3)	37 (2.6)	0.88 (0.55–1.39)	0.57
Mechanical ventilation	34 (2.4)	43 (3.1)	0.78 (0.50–1.21)	0.26
Respiratory distress syndrome	79 (5.5)	89 (6.4)	0.87 (0.65–1.17)	0.36

Hypoglycemia — no. (%)†	343 (24.0)	210 (15.0)	1.60 (1.37–1.87)	<0.001

Summary of studies regarding antenatal corticosteroid therapy between 34^{+0} - 36^{+6} weeks of gestation

Studies		No. of patients		Effect			
No. of studies	Study design	ACS	No treatment (or placebo)	RR (95% CI)	Absolute (95% CI)	Certainty	Importance
Perinatal death							
3	RCT	6/1658 (0.4%)	6/1638 (0.4%)	RR 1.03 (0.29–3.67)	0 fewer per 1000 (from 3 fewer to 10 more)	⨁◯◯◯ Very low	Critical
Respiratory distress syndrome							
6	RCT	102/1901 (5.4%)	202/1882 (10.7%)	RR 0.71 (0.56–0.91)	31 fewer per 1000 (from 10 fewer to 47 fewer)	⨁⨁⨁◯ Moderate	Important
Chorioamnionitis							
3	RCT	20/1604 (1.2%)	35/1598 (2.2%)	RR 0.57 (0.33–0.99)	9 fewer per 1000 (from 0 fewer to 15 fewer)	⨁⨁◯◯ Low	Important
Hypoglycemia							
3	RCT	367/1666 (22.0%)	222/1628 (13.6%)	RR 1.62 (1.39–1.88)	85 more per 1000 (from 53 more to 120 more)	⨁⨁⨁◯ Moderate	Important

RCT: randomized controlled trial.

Based on data from Roberts et al.[27] and additional information from original studies.

Skoll, A, SOGC, 2018

- Σημαντική μείωση σοβαρών αναπνευστικών επιπλοκών, χορήγησης ΕΔΠ, ΒΠΔ
- ΣΑΔ, άπνοια και μηχανικός αερισμός δεν παρουσίαζαν διαφορά
- Όχι διαφορά στη χοριοαμνιονίτιδα και νεογνική σήψη
- Συχνότερη η υπογλυκαιμία στην ομάδα βηταμεθαζόνης

- The balance of benefits and risks supports routine antenatal corticosteroid at 34^{+0} - 34^{+6} weeks
- Does not support routine antenatal corticosteroid therapy at 35^{+0} - 35^{+6} and especially at 36^{+0} - 36^{+6} weeks

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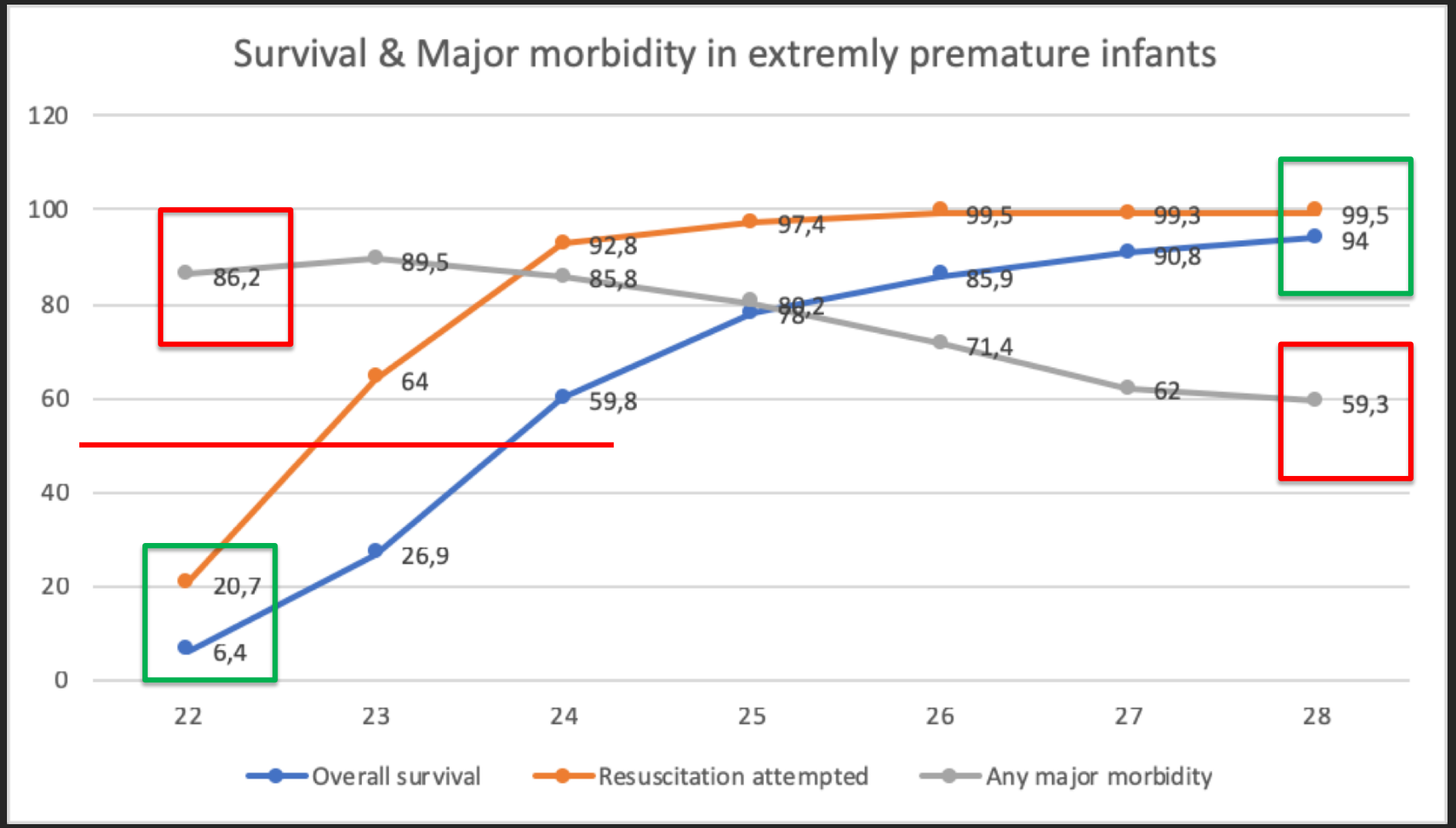
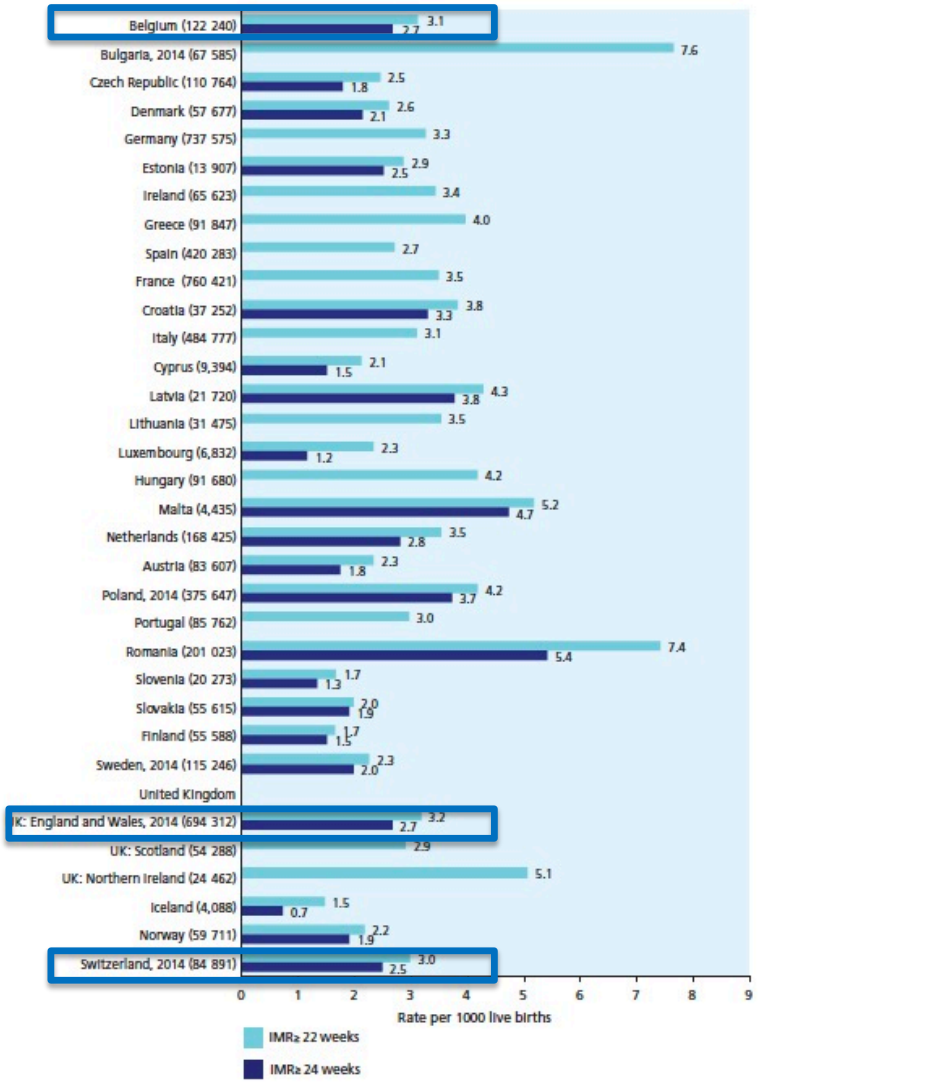


Anderson GA, Pediatrics, 2016

Figure C3.2 Infant mortality at and after 22 and 24 weeks in 2015



NOTE: Data are cohort data when available (Belgium, Denmark, Estonia, Croatia, Cyprus, Latvia, Malta, Austria, Slovenia, Finland, Northern Ireland, Iceland, Norway, England and Wales, and Switzerland) or annual rates when cohort data were not available (Bulgaria, Czech Republic, Germany, Ireland, Greece, Spain, France, Italy, Lithuania, Luxembourg, Hungary, Netherlands, Poland, Portugal, Romania, Scotland, Slovakia, and Sweden).

Europe Peristat, 2015

Κατευθυντήριες οδηγίες αναζωογόνησης των εξαιρετικά προώρων νεογνών, διαφόρων κρατών

TABLE 1 Recommendations According to Week of Gestation

Country	Year	Weeks of Gestation				Potential Biases		
		22	23	24	25	Assessment	Definition	Denominator
Argentina[14]	2012	CC	NR	NR	NR	Yes	No	No
Australia[15]	2006	CC	CC	AC	AC	No	No	No
Australia[16]	2013	CC	PW	PW	AC	No	No	No
Belgium[17]	2014	CC	CC	PW	PW	Yes	No	Yes
Canada[18]	2012	CC	IND	IND	AC	Yes	Yes	Yes
Finland[19]	2014	IND	IND	AC	AC	No	No	No
France[20]	2010	CC	CC	PW	AC	Yes	Yes	No
Germany[21]	2008	IND	IND	AC	AC	Yes	No	No
FIGO, international association[22]	2006	NR	NR	NR	NR	No	No	No
ILCOR, international association[23]	2006	CC	NR	NR	NR	No	No	No
WAPM, international association[24]	2010	CC	IND	AC	AC	Yes	No	No
European Resuscitation Counsel, international association[25]	2010	CC	PW					
Ireland[26]	2006	CC	CC					
Italy[27]	2008	IND	IND					
Japan[28]	2012	NR	NR					
Dutch Pediatric Society, the Netherlands[29]	2006	CC	CC					
Dutch Ministry of Health, the Netherlands[30]	2010	NR	NR					
New Zealand[31]	2011	NR	NR					
Poland[32]	2011	CC	CC					
Portugal[33]	2012	CC	CC	AC	AC	Yes	No	Yes
Singapore[34]	1998	IND	IND	IND	AC	No	No	No
Spain[35]	2004	CC	NR	NR	NR	No	No	No
Sweden[36]	2004	CC	IND	IND	AC	Yes	No	Yes
Switzerland[1]	2011	CC	CC	AC	AC	Yes	No	No
Nuffield Council, United Kingdom[37]	2006	CC	PW	AC	AC	Yes	Yes	Yes
BAPM, United Kingdom[38]	2009	CC	CC	AC	AC	Yes	No	No
Royal College of Obstetricians and Gynaecologists, United Kingdom[39]	2014	CC	IND	IND	AC	Yes	No	No
AAP, United States[40]	2009	IND	IND	IND	IND	Yes	No	No
ACOG, United States[41]	2012	IND	IND	IND	IND	Yes	No	Yes
AHA, United States[42]	2010	CC	PW	PW	AC	No	No	No
Joint Workshop, United States[43]	2014	CC	IND	AC	AC	Yes	No	Yes

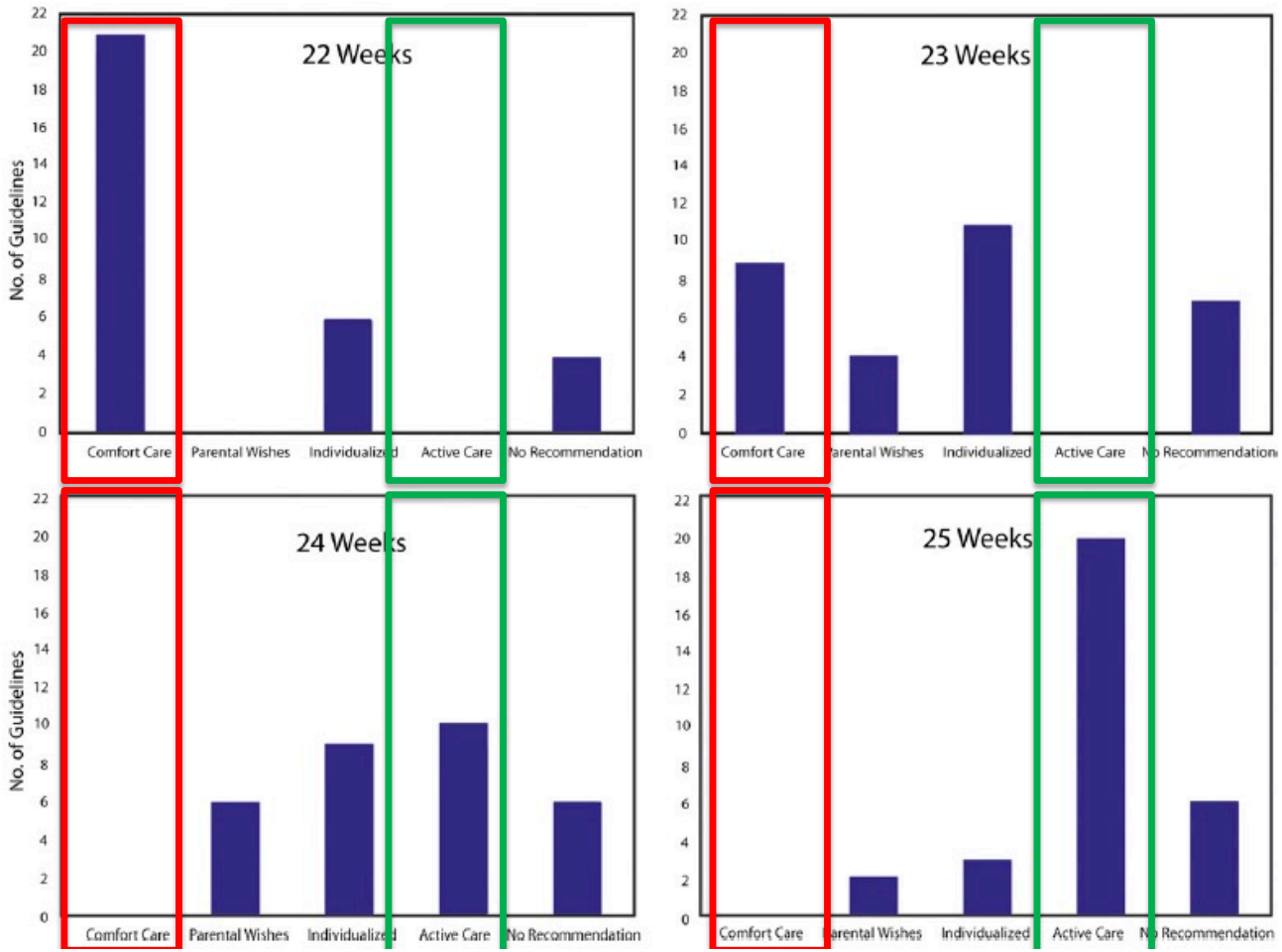
AAP, American Academy of Pediatrics; AC, active care; ACOG, American College of Obstetricians and Gynecologists; AHA, American Heart Association; BAPM, British Association of Perinatal Medicine; FIGO, International Federation of Gynecology and Obstetrics; ILCOR, International Liaison Committee on Resuscitation; IND, individualized care; CC, comfort care; NR, no recommendation; PW, parental wishes; WAPM, World Association of Perinatal Medicine.

Belgium	CC
Switzerland	CC
England & Wales	CC
European Res Coun	CC

AC	Active Care
CC	Comfort Care
IND	Individualized Care
NR	No Recommendation
PW	Parental Wishes

Ú. Guillén, et al: Pediatrics, 2015

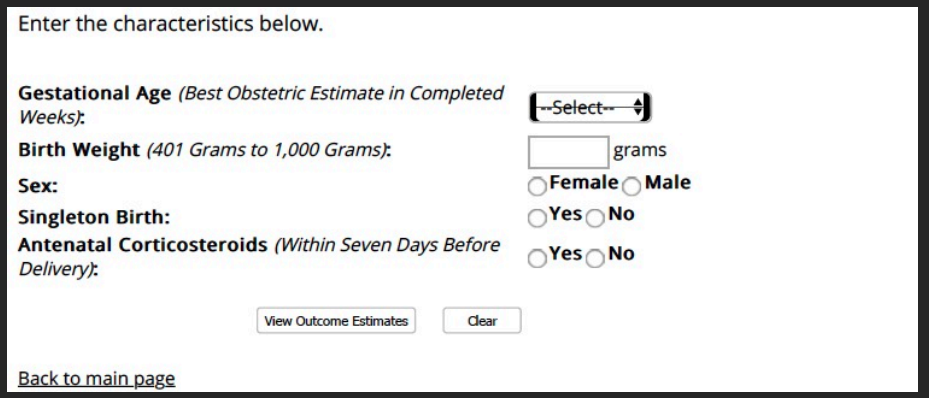
Guidelines for neonatal care in extreme preterm deliveries of different countries



AC	Active Care
CC	Comfort Care
IND	Individualized Care
NR	No Recommendation
PW	Parental Wishes

Ú. Guillén, et al: Pediatrics, 2015

NICHD
Extremely Preterm Birth Outcome Data


Enter the characteristics below.

Gestational Age *(Best Obstetric Estimate in Completed Weeks)*: --Select--

Birth Weight *(401 Grams to 1,000 Grams)*: grams

Sex: Female Male

Singleton Birth: Yes No

Antenatal Corticosteroids *(Within Seven Days Before Delivery)*: Yes No

View Outcome Estimates Clear

Back to main page

Based on the following characteristics:

Gestational Age *(Best Obstetric Estimate in Completed Weeks)*:22 weeks
Birth Weight:550 grams
Sex:Female
Singleton Birth:Yes
Antenatal Corticosteroids:Yes

Estimated outcomes* for infants in the NRN sample are as follows:

Outcomes	Outcomes for All Infants	Outcomes for Mechanically Ventilated Infants
Survival	11%	30%
Survival Without Profound Neurodevelopmental Impairment	6%	18%
Survival Without Moderate to Severe Neurodevelopmental Impairment	3%	11%
Death	89%	70%
Death or Profound Neurodevelopmental Impairment	94%	82%
Death or Moderate to Severe Neurodevelopmental Impairment	97%	89%

TABLE 3

General guidance regarding obstetric interventions for threatened and imminent periviable birth by best estimate of gestational age[a]

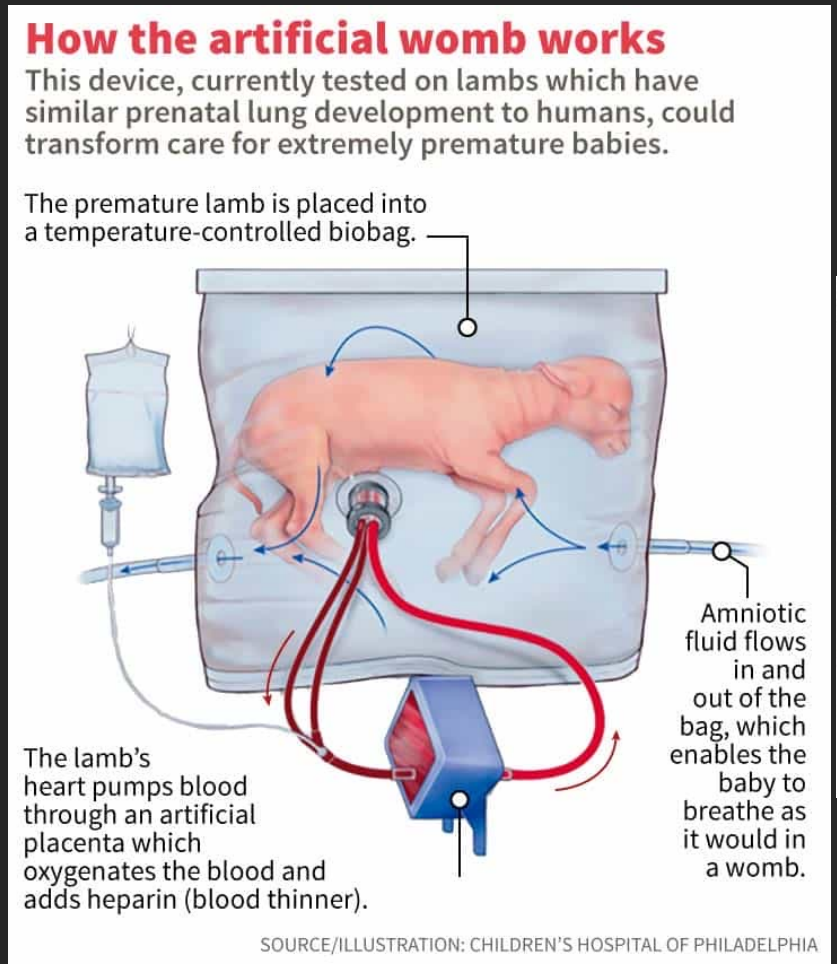
	20 0/7 weeks to 21 6/7 weeks	22 0/7 weeks to 22 6/7 weeks	23 0/7 weeks to 23 6/7 weeks	24 0/7 weeks to 24 6/7 weeks	25 0/7 weeks to 25 6/7 weeks
Neonatal assessment for resuscitation[a]	Not recommended 1A	Consider 2B	Consider 2B	Recommended 1B	Recommended 1B
Antenatal corticosteroids	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Tocolysis for preterm labor to allow for antenatal corticosteroid administration	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Magnesium sulfate for neuroprotection	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Antibiotics to prolong latency during expectant management of preterm PROM if delivery is not considered imminent	Consider 2C	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Intrapartum antibiotics for group B streptococci prophylaxis[b]	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Cesarean delivery for fetal indication[c]	Not recommended 1A	Not recommended 1A	Consider 2B	Consider 1B	Recommended 1B

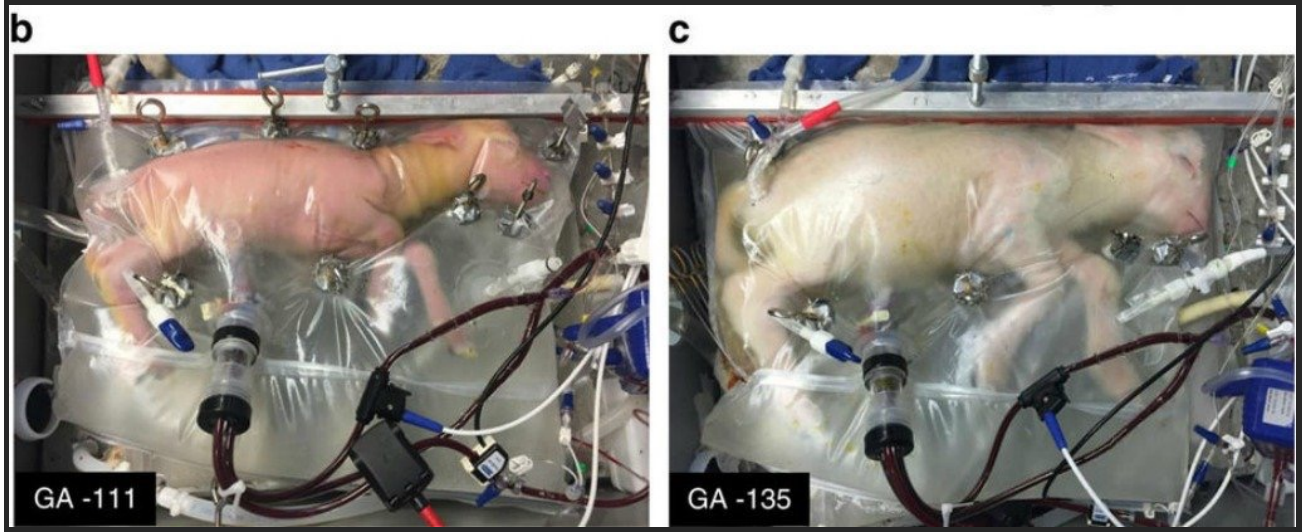
PROM, premature rupture of membranes.

[a] Survival of infants born in the periviable period is dependent on resuscitation and support. Between 22 weeks and 25 weeks of gestation, there may be factors in addition to gestational age that will affect the potential for survival and the determination of viability. Importantly, some families, concordant with their values and preferences, may choose to forgo such resuscitation and support. Many of the other decisions on this table will be linked to decisions regarding resuscitation and support and should be considered in that context; [b] Group B streptococci carrier, or carrier status unknown; [c] For example, persistently abnormal fetal heart rate patterns or biophysical testing, malpresentation.

ACOG. Periviable birth. Am J Obstet Gynecol 2016.

Artificial womb





Κορτικοστεροειδή στην κύηση

- **Ιστορία κι οδηγίες χορήγησης**
- **Όψιμα πρόωρα**
- **Εξαιρετικά πρόωρα**
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- **πΡΕΥ – Πολύδυμα**
- **Επανάληψη δόσεων**
- **Σύγκριση κατευθυντηρίων οδηγιών**

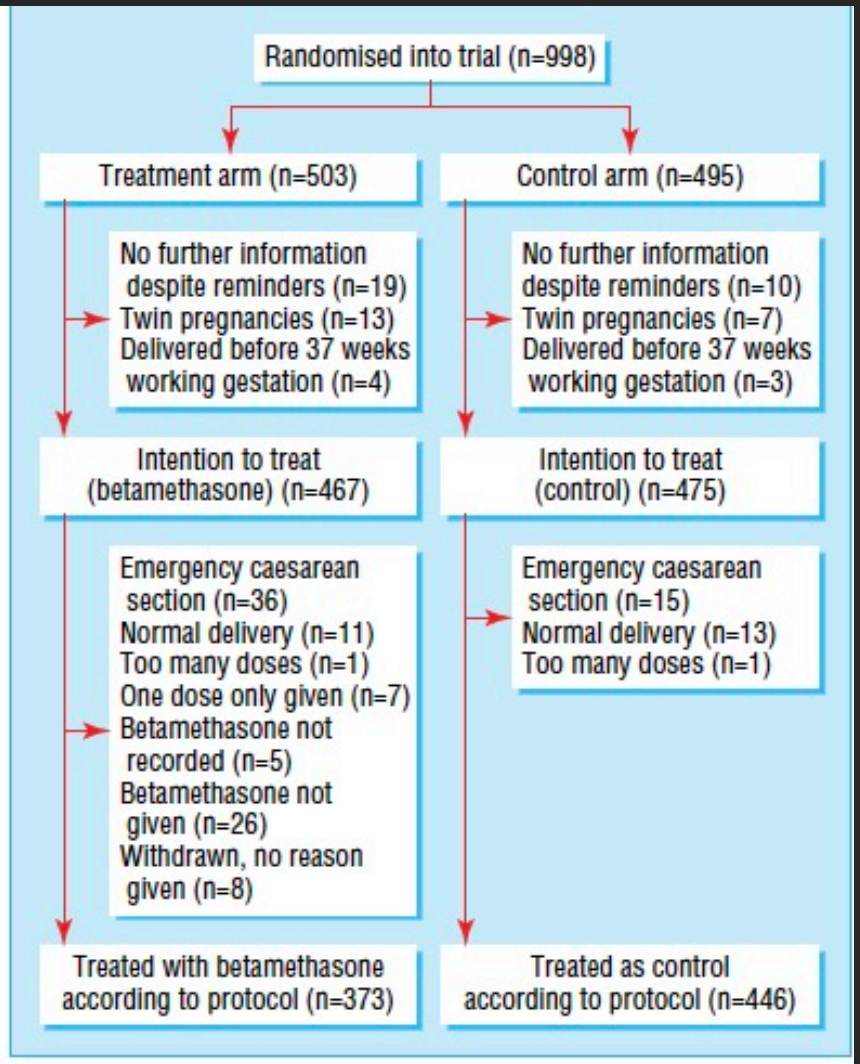


Fig 1 Flow of participants through the trial

Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomised trial

Peter Stutchfield, Rhiannon Whitaker, Ian Russell, on behalf of the Antenatal Steroids for Term Elective Caesarean Section (ASTECS) Research Team

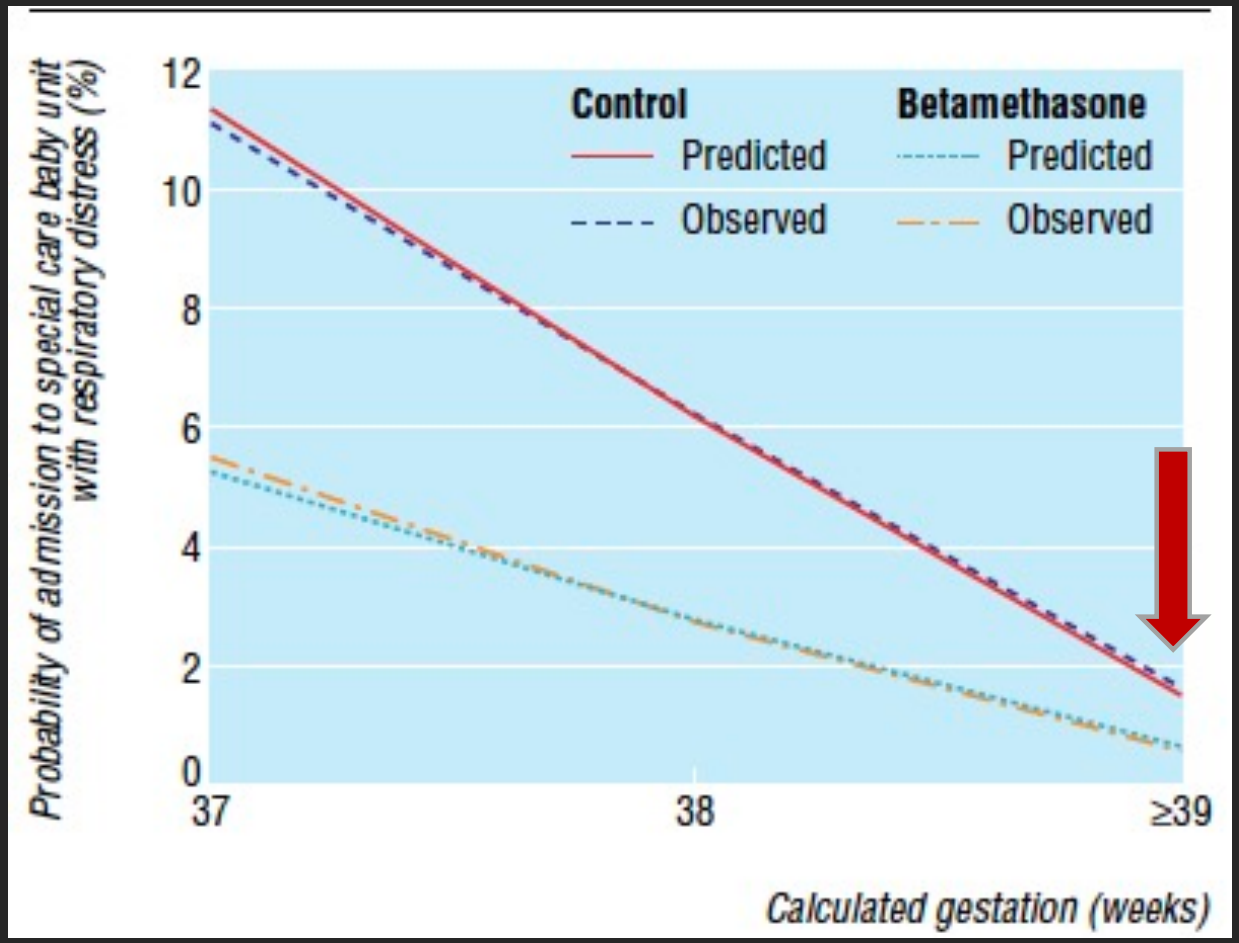
BMJ, 2005

Probability for admission to NICU due to respiratory problems

Table 3 Reason for admission to special care baby unit by group

Reason for admission	Betamethasone group	Control group
Respiratory distress by severity:		
Mild	4	9
Moderate	6	10
Severe	1	5
Respiratory distress by type:		
Transient tachypnoea of the newborn	10	19
Respiratory distress syndrome	1	5
Total No of babies admitted	**26**	**32**
With respiratory distress (subtotal)	11	24
Other (without respiratory distress)	15	8

Stutchfield ,BMJ, 2005


Probability of admission to special care baby unit with respiratory distress (%)
12
10
8
6
4
2
0
Control
Predicted
Observed
Betamethasone
Predicted
Observed
37
38
≥39
Calculated gestation (weeks)

Risk of respiratory morbidity in term infants delivered by elective caesarean section

Gestational age† and type of delivery	No of deliveries	No (%) of infants	No (%) of infants
37 weeks:			
Elective caesarean section	261	26 (10.0)	5 (1.9)
38 weeks:			
Elective caesarean section	1173	60 (5.1)	10 (0.9)
39 weeks:			
Elective caesarean section	1074	23 (2.1)	2 (0.2)
40 weeks:			
Elective caesarean section	132	2 (1.5)	0 (0.0)
Intended vaginal delivery (Reference)	**11 177**	**180 (1.6)**	**16 (0.1)**

Anne Kirkeby Hansen, BMJ, 2013

Behavioural, educational and respiratory outcomes of antenatal betamethasone for term caesarean section (ASTECS trial)

Peter Roy Stutchfield,[1] Rhiannon Whitaker,[2] Angela E Gliddon,[2] Lucie Hobson,[3] Sailesh Kotecha,[4] Iolo J M Doull[5]

Table 2 Summary of scores for the strengths and difficulties subscales for the participants by treatment group and school assessment of additional help and quartile of ability

Outcome measure: mean (SD)	Control N=190	Betamethasone N=217	Difference (95% CI)	Significance
Hyperactivity scale	3.06 (2.74)	3.32 (2.85)	0.26 (−0.29 to 0.81)	0.19
Emotional symptoms scale	1.98 (2.28)	2.05 (2.33)	0.07 (−0.38 to 0.52)	0.40
Conduct problems scale	1.34 (1.59)	1.31 (1.72)	−0.03 (−0.36 to 0.29)	0.80
Peer problems scale	1.47 (1.88)	1.36 (1.91)	−0.11 (−0.48 to 0.26)	0.87
Total difficulties score	7.85 (6.49)	8.03 (6.83)	0.18 (−1.12 to 1.48)	0.19
Prosocial scale	8.58 (1.66)	8.72 (1.76)	0.14 (−0.19 to 0.48)	0.90
Additional help required n (%)	N=166	N=189		
	22 (13.3)	34 (18.0)	$\chi^2(1)=1.492$	0.22
School assessment of child's quartile of ability	N=164	N=186		
Top quarter of academic ability	74 (45.1)	70 (37.6)		
Middle half of academic ability	76 (46.3)	83 (44.6)	$\chi^2(2)=6.74$	0.03
Lower quarter of academic ability	14 (8.5)	33 (17.7%)		

Arch Dis Child Fetal Neonatal Ed 2013

Antenatal betamethasone

- **did not result in any adverse outcomes or reduction in asthma or atopy**
- **had lower academic ability**
- **It should be considered for elective CS at 37–38 weeks of gestation**

Κορτικοστεροειδή στην κύηση

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Prelabor Rupture of membranes

>37^{+0}	34^{+0}-36^{+6}	24^{+0}-33^{+6}	<23^{+6}
Deliver (induced with OXT (12-18h) (*prostaglandins equally effective, but more chorioamnionitis*)	Recommend Delivery (*option of expectant management until 37wks -discuss risks/benefits*)	Expectant management if no maternal/fetal contraindication	counselling
Corticosteroids NO	*Corticosteroids ONLY if they were NOT given till then*	*Corticosteroids YES*	Expectant/induction
	Treat intraamniotic infection if present	Antibiotics (for latency)	Antibiotics YES >20wks
~ GBS prophylaxis YES	~ GBS prophylaxis YES	~ GBS prophylaxis YES MgSO4 if birth anticipated <32wks (cerebral palsy)	GBS prophylaxis No <23+6 MAYBE >24^{+0} ,

ACOG Committee Opinion, 2020

SOGC: Antenatal Corticosteroid Therapy for Improving Neonatal Outcomes 2018

Table 8. Summary table of recommendations according to subpopulation

Subpopulation	Recommendation given high risk of delivery within 7 days and if gestational age criteria are met	Level of evidence	Strength of recommendation
Multifetal gestation	Administer according to the same indications and in the same gestational age range as for singleton pregnancies		
	days		
Pre-gestational or gestational diabetes	Administer at the same dosage, according to the same indications and in the same gestational age range as that recommended for non-diabetic women	Low	Conditional
	Pay close attention to control of maternal blood glucose in the days following	Low	Strong
Obesity	Administer at the same dosage as that recommended for women without obesity	Low	Conditional
Intrauterine growth restriction	Administer according to the same indications and in the same gestational age range as in normal pregnancies after risks and benefits are discussed with the woman		
	diagnosis unless there is a high risk of preterm birth within the next 7 days		

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Repeated antenatal corticosteroids: effects on cerebral palsy and childhood behavior

- Nonrandomized regional cohort of 541 very preterm infants born in Western Australia from singleton pregnancies and alive at 3& 6 years
- Increasing numbers of antenatal corticosteroid courses were associated with a reduction in the rate of cerebral palsy
- Three or more courses were also associated with increased rates of aggressive/destructive, distractible, and hyperkinetic behavior and these effects were present at both ages 3 and 6 years

French NP, AJOG, 2004

Cesarean Section, corticosteroids and neurodevelopment

Multiple doses of corticosteroids

Laboratory animals

Low birth weight
Reduced brain weight
Reduced number of neurons
Delayed myelination

Ikegami 1997, Moss 2006, Huang 1999, Uno 1990, Huang 2001, Sloboda 2002

Human

Reduced head circumference

French 1999, Kumar 2005

Courtesy of A. Sotiriadis

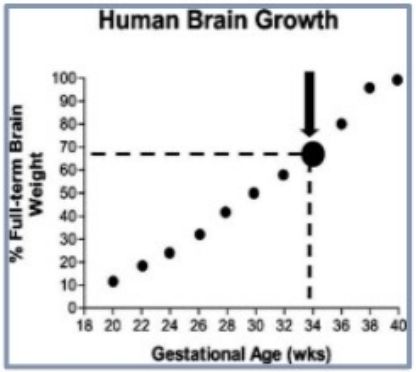
Outcome	Term (≥37 weeks) N = 462	
	Multiple ACS N = 213[a]	Single ACS N = 249
Death or severe disability (neuromotor, neurosensory, neurocognitive)§	48/213 (22.5%)	38/249 (15.3%)
Death up to 5 years	1/213 (0.5%)	2/249 (0.8%)
Neuromotor disability †† (non-ambulatory cerebral palsy)	0/212 (0%)	1/247 (0.4%)
Neurosensory disability	19/212 (9.0%)	7/247 (2.8%)
Needing visual aids	17/212 (8.0%)	7/247 (2.8%)
Deafness	3/212 (1.4%)	1/247 (0.4%)
Pre-existing (diagnosed at 2 years or earlier)	0	0
New (diagnosed after 2 years of age)	3	1
Neurocognitive/neurobehavioural disability	31/212 (14.6%)	30/246 (12.2%)

Outcomes of children at 5 years by gestational age at birth and ACS groupings

Asztalos, BMC Pregnancy and Childbirth 2014

Fetal brain

Fetal Brain Growth at 34 Weeks Gestation is 65% of Full-Term Weight



- Brain weight at different ages from 20 to 40 gestational weeks is illustrated at each gestational age as a percent of term brain weight.
- At 34 gestational weeks, the overall brain weight is 65% of term weight. Arrow highlights brain weight at 34 weeks' gestation.

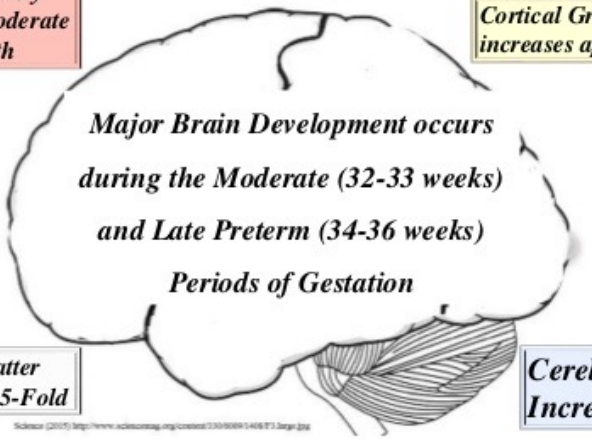
The percent brain weights were based on the data of Guihard-Costa and Larroche (1990).

(Jain, 2008; Kinney,2006 in 2008)

4

Brain tissue are uniquely vulnerable during moderate and late Preterm Birth

Cortical Gray Matter weight increases approximately 50%.



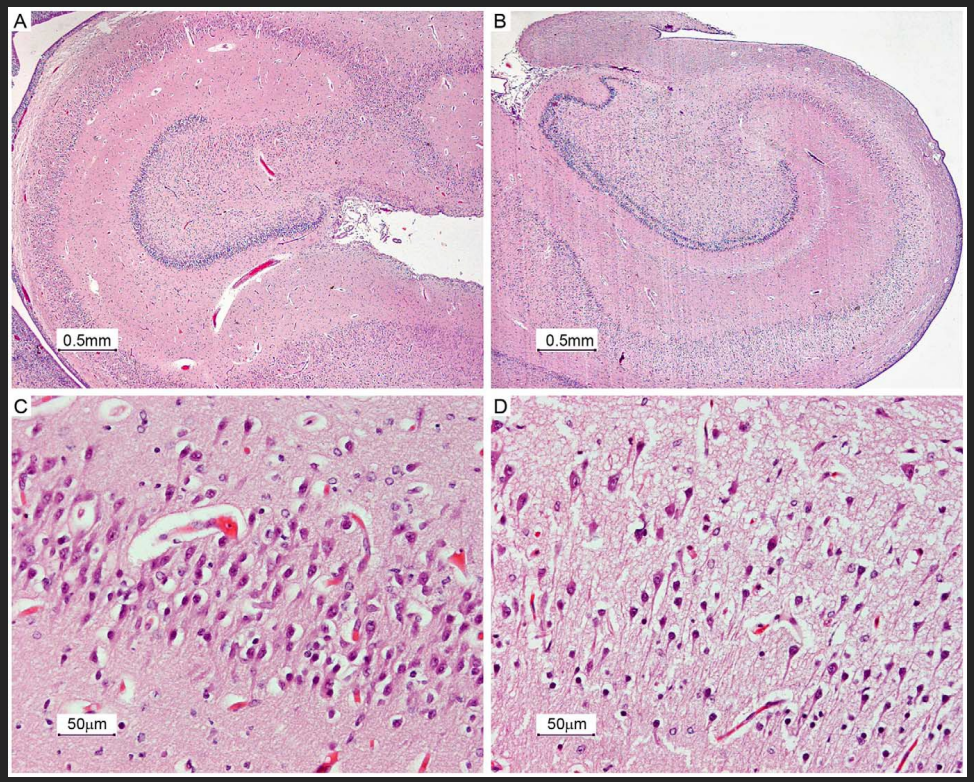
Myelinated White Matter Volumes increase by 5-Fold

Cerebellar Volume Increase by 25%

(Cheong, et al., 2016; Huppi, et al., 1998 in 2016; Limperopoulos, et al., 2005 in 2016; Sciencemag.org, 2015)

ozella.brundidge@gmail.com 4/9/2017

Effects of Antenatal Glucocorticoid Therapy on Hippocampal Histology of Preterm Infants



- The hippocampi of ten neonates who had been treated with antenatal glucocorticoids showed a lower density of large neurons ($p = 0.01$) and
- Neurons irrespective of size ($p = 0.02$) as compared to eleven neonates who had not been treated with glucocorticoids

Deodata Tijsseling, PLOS, 2012

Κορτικοστεροειδή στην κύηση

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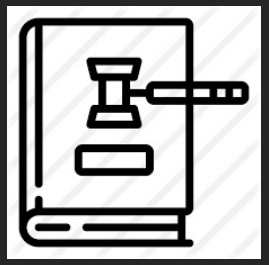


Comparison of guidelines for administration of corticosteroids in pregnancy

	NICE Clinical Guideline	ACOG Committee Opinion	SOGC Guideline	New Zealand and Australian Guidelines	WHO recommendations	FIGO Committee report
Country	United Kingdom	United States	Canada	New Zealand and Australia	International	International
Issued	2019	2017	2018	2015	2015	2019
Corticosteroid regimens	Not mentioned	IM dexamethasone or betamethasone	IM dexamethasone or betamethasone	IM dexamethasone or betamethasone	IM dexamethasone or betamethasone	IM dexamethasone or betamethasone
Timing	24^{+0} - 33^{+6}	24^{+0} - 34^{+0}	24^{+0} - 34^{+6}	24^{+0} - 34^{+6}	24^{+0} - 34^{+0}	24^{+0} - 34^{+0}
Periviable period	23^{+0}-23^{+6} discuss with the woman	23^{+0} and 23^{+6} may be considered. Periviable period should be considered	22^{+0}-23^{+6} should be considered	Not mentioned	Not mentioned	linked to family's decision regarding resuscitation. Based on local limits of viability
Late preterm period	34^{+0} and 35^{+6}	34^{+0}-36^{+6}	35^{+0}-36^{+6}			34^{+0}-36^{+6}
	Consider	Recommended if no previous course	Maybe after risks and benefits are discussed	Not mentioned	Not mentioned	Recommended if no previous course

Tsakiridis et al, Ob Gyn Surv, 2020

Comparison of guidelines for administration of corticosteroids in pregnancy

	NICE Clinical Guideline	ACOG Committee Opinion	SOGC Guideline	New Zealand and Australian Guidelines	WHO recommendations	FIGO Committee report
Country	United Kingdom	United States	Canada	New Zealand and Australia	International	International
Issued	2019	2017	2018	2015	2015	2019
Repeated doses and rescue course of corticosteroids	**No repeat** courses of corticosteroids. Take into account the interval from the last course, gestational age and the likelihood of birth within 48 hours	**No repeat** courses of corticosteroids. Should be considered if prior course more than 14 days before. Rescue course could be provided as early as 7 days from the prior dose	**No repeat** courses of corticosteroids. Rescue course should be considered after a time interval of at least 14 days	**A single repeat** course of corticosteroids, if preterm labor does not occur within 7 days is recommended or **up to 3 single repeat doses before 32+6w**	**A single repeat** course of antenatal corticosteroids if preterm labor does not occur within 7 days after the initial dose is recommended	**No repeat** courses of corticosteroids, (more than two). Refers to ACOG and WHO
CS	Not mentioned	Not mentioned	Not recommended at term	48 h prior to planned CS > 34+6w, only if known fetal lung immaturity.	Not recommended in late preterm	Consider for planned CS at 37–38+6 w.

Tsakiridis et al, Ob Gyn Surv, 2020

Κατηγορίες & ηλικία κύησης	Διαχείριση	Παρατηρήσεις
Κολπικός τοκετός / Καισαρική τομή 23^{+0}-23^{+6} εβδ	Συζήτηση	Σύμφωνα με το πρωτόκολλο και τις οδηγίες του περιγεννητικού
Κολπικός τοκετός / Καισαρική τομή 24^{+0}-33^{+6} εβδ	**Προτείνεται**	**Μόνο σε περιπτώσεις αναμενόμενου τοκετού εντός των επόμενων 7 ημερών**
Κολπικός τοκετός / Καισαρική τομή 34^{+0}-36^{+6} εβδ	Συζήτηση	πρωτόκολλο της νεογνολογικής μονάδας υποδοχής, μόνο σε περιπτώσεις αναμενόμενου τοκετού εντός των επόμενων 7 ημερών
Τελειόμηνη καισαρική τομή (≥37 εβδ.)	Δεν συστήνεται ως ρουτίνα	Συζητείται στις 37^{+0}-37^{+6} ανάλογα με το πρωτόκολλο της νεογνολογικής μονάδας υποδοχής
Πολύδυμη κύηση	**Ίδιες συστάσεις με τις μονήρεις κυήσεις**	**Δεν συστήνεται προφυλακτική χορήγηση, εφόσον δεν προβλέπεται τοκετός εντός των επόμενων 7 ημερών**
εμβρυικών υμένων <34 εβδ.		
Σακχαρώδης διαβήτης	Ίδιες συστάσεις με τις μη διαβητικές εγκύους	

Πίνακας χορήγησης κορτιζόνης των κατευθυντηρίων οδηγιών ΕΜΕΕ 2021

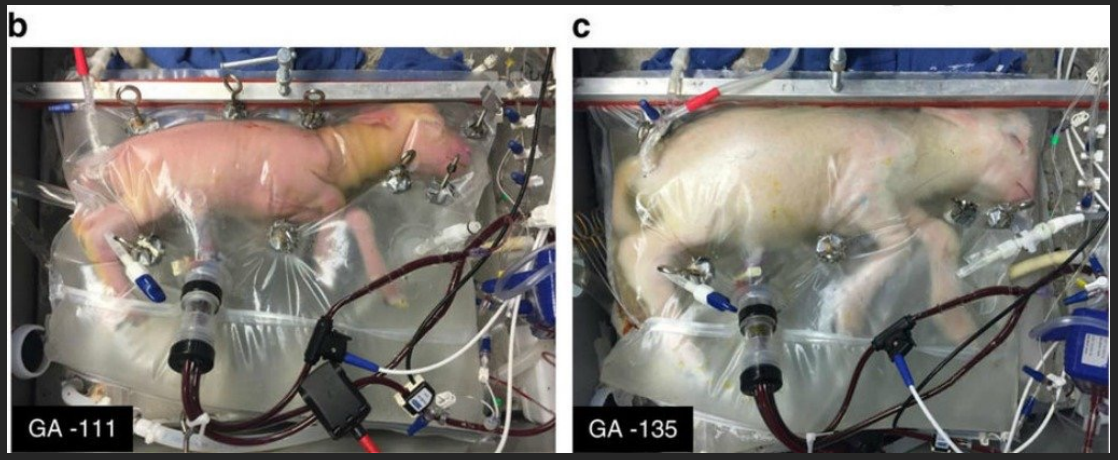
Σακχαρώδης διαβήτης — **Ίδιες συστάσεις με τις μη διαβητικές εγκύους**

Κολπικός τοκετός / Καισαρική τομή 23^{+0}-23^{+6} εβδομάδες	Συζήτηση	Σύμφωνα με το πρωτόκολλο και τις οδηγίες του περιγεννητικού κέντρου και μετά από συζήτηση
		Στην απόφαση συνεκτιμώνται η
Κολπικός τοκετός / Καισαρική τομή 34^{+0}-36^{+6} εβδομάδες	Συζήτηση	Στην απόφαση συνεκτιμώνται η εβδομάδα κύησης και το πρωτόκολλο της νεογνολογικής μονάδας υποδοχής, μόνο σε περιπτώσεις αναμενόμενου τοκετού εντός των επόμενων 7 ημερών
Πολύδυμη κύηση	Ίδιες συστάσεις με τις μονήρεις κυήσεις	χορήγηση, εφόσον δεν προβλέπεται τοκετός εντός των επόμενων 7 ημερών
Πρώιμη πρόωρη ρήξη εμβρυικών υμένων <34 εβδ.	Προτείνεται	
Σακχαρώδης διαβήτης	Ίδιες συστάσεις με τις μη διαβητικές εγκύους	

κατευθυντηρίων οδηγιών ΕΜΓΕ 2021 (υπό συζήτηση)

Κατηγορίες και ηλικία κύησης	Διαχείριση	Παρατηρήσεις
Κολπικός τοκετός / Καισαρική τομή 23^{+0}-23^{+6} εβδομάδες	Συζήτηση	Σύμφωνα με το πρωτόκολλο και τις οδηγίες του περιγεννητικού κέντρου και μετά από συζήτηση
Τελειόμηνη καισαρική τομή (≥37 εβδ.)	Δεν συστήνεται ως ρουτίνα	Συζητείται στις 37^{+0}-37^{+6} ανάλογα με το πρωτόκολλο της νεογνολογικής μονάδας υποδοχής
Επαναλαμβανόμενο σχήμα	Όχι περισσότερα των δύο σχημάτων σε όλη τη διάρκεια της κύησης	1. Το πρώτο σχήμα κορτικοστεροειδών χορηγήθηκε τουλάχιστον 14 μέρες πριν 2. Η κύηση είναι <34 εβδομάδων
Πολύδυμη κύηση	Ίδιες συστάσεις με τις μονήρεις κυήσεις	Δεν συστήνεται προφυλακτική χορήγηση, εφόσον δεν προβλέπεται τοκετός εντός των επόμενων 7 ημερών
Πρώιμη πρόωρη ρήξη εμβρυικών υμένων <34 εβδ.	Προτείνεται	
Σακχαρώδης διαβήτης	Ίδιες συστάσεις με τις μη διαβητικές εγκύους	

κορτιζόνης των κατευθυντηρίων οδηγιών ΕΜΓΕ 2021 (υπό συζήτηση)



Ευχαριστώ πολύ!

Περιστατικό 1

- Έγκυος 49 χρονών
- IVF, Δωρεά ωαρίων
- Δίδυμος κύηση 31 εβδ
  - Α – 1380 (14η εκ.θ)
  - Β – 850 (0,1η εκ.θ), (Αυξημένες αντιστάσεις στο φλεβώδη πόρο)
- Προεκλαμψία
  - Υπέρταση
  - Λευκωματουρία
- Κορτιζόνη προ 6 ημερών

- Αναμονή μέχρι 34 εβδομάδες
- Γέννηση άμεσα

Περιστατικό 2

- Έγκυος 39 χρονών
- IVF
- Δίδυμος κύηση 31 εβδ
  - Α – 1380 ($14^{η}$ εκ.θ)
  - Β – 850 ($0,1^{η}$ εκ.θ), (Αναστροφή κύματος α στο φλεβώδη πόρο)
- Προεκλαμψία
  - Υπέρταση
  - Λευκωματουρία
- Κορτιζόνη προ 6 εβδομάδων

- Χορήγηση νέου σχήματος κορτιζόνης;