Corticothérapie anténatale après 34 SA

Département de périnatalogie, Hôpital Mére Enfant, CHU de Nantes

Balance
Bénéfice - Risque

- Le bénéfice attendu
- Le risque éventuel lié à la thérapeutique
- Le nombre nécessaire de patients à traiter pour observer un effet

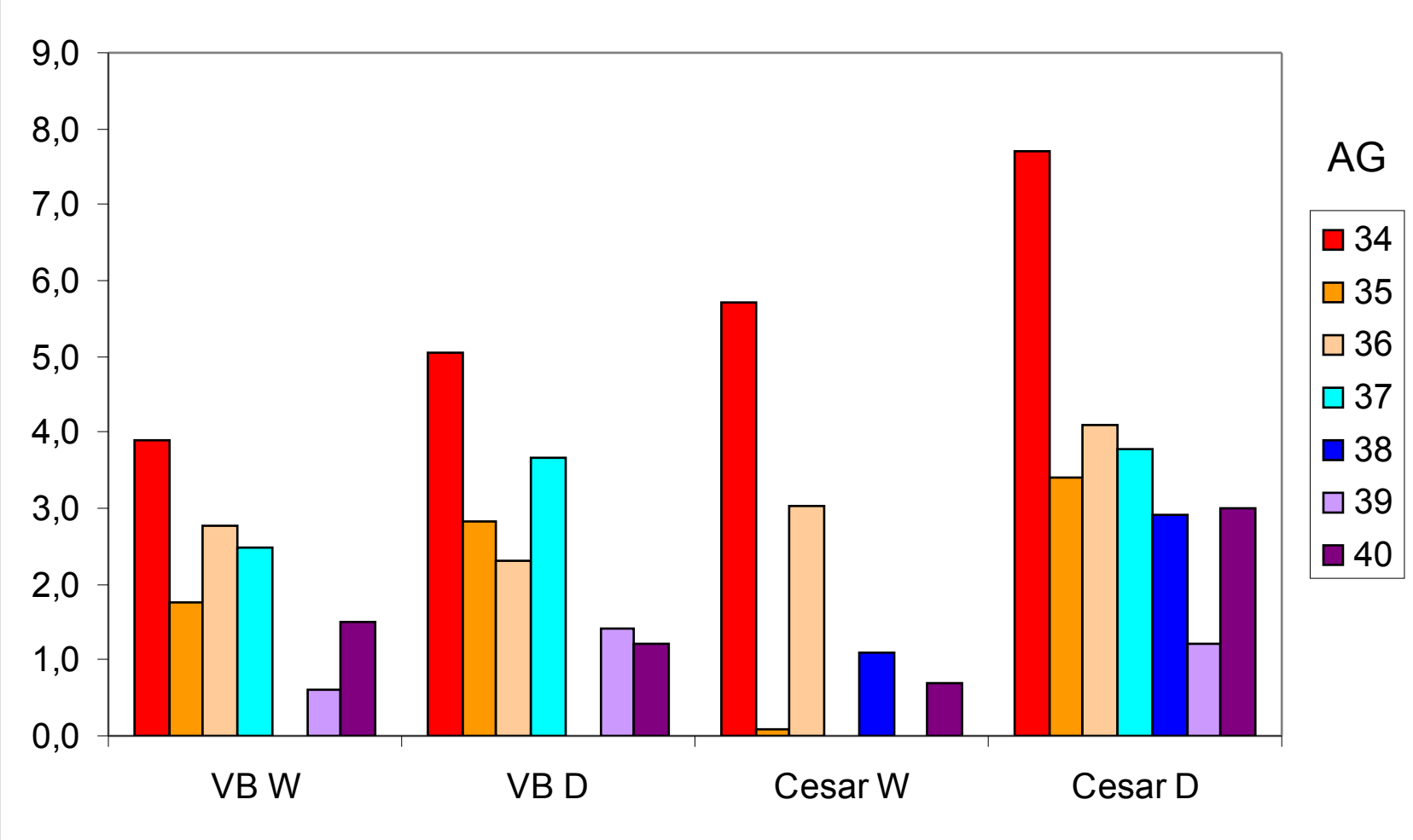
Le Bénéfice attendu ?

- Diminuer la détresse respiratoire transitoire du nouveau-né

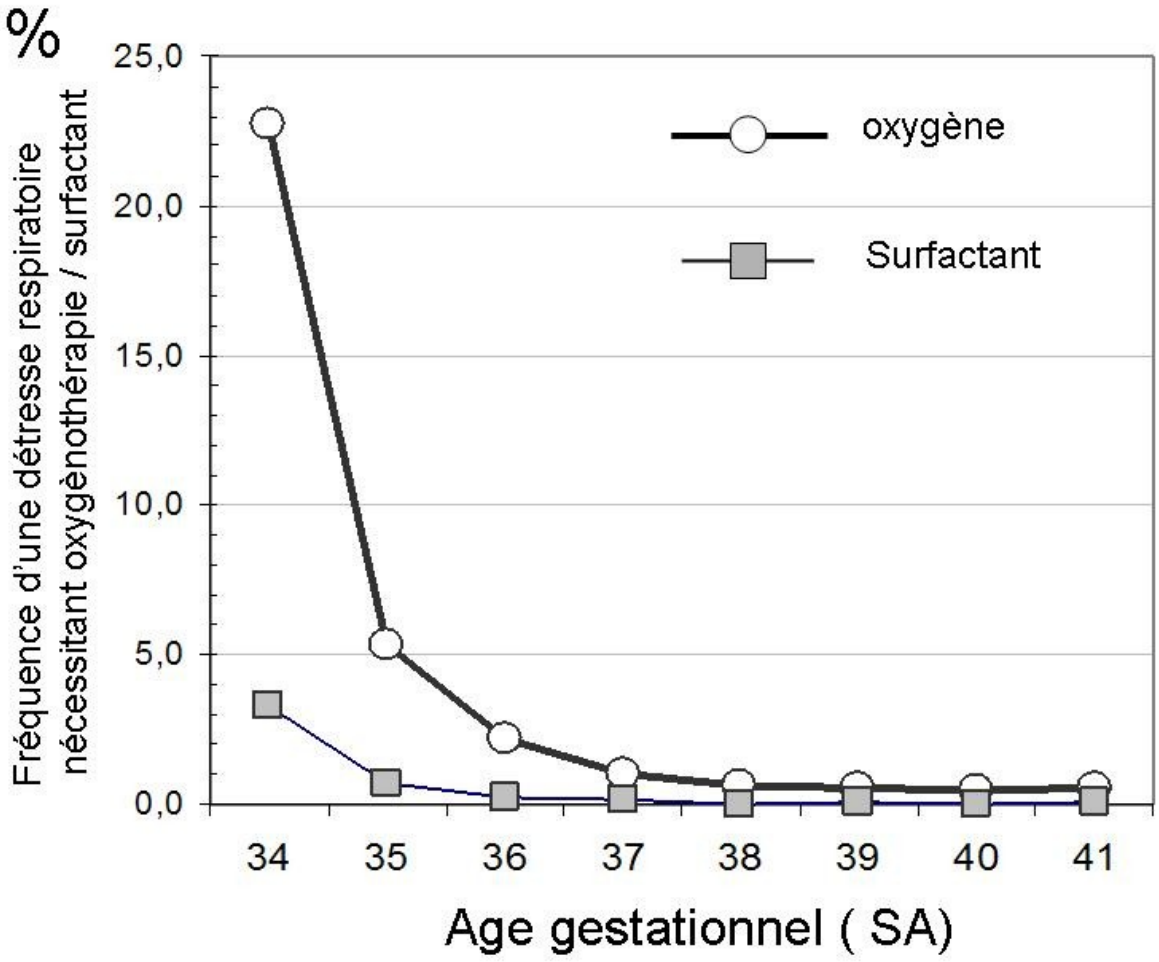
« Stutchfield and coworkers recently reported a randomized pragmatic trial evaluating the efficacy of betamethasone in preventing respiratory distress in infants delivered by ECS. Their results show that two doses of betamethasone given in the 48 hours before delivery significantly decreased admissions due to respiratory distress **(RR 0.46, 95% CI 0.23- 0.93) ».**

BMJ 2005

Fréquence des détresses respiratoires nécessitant plus de 48 heures de ventilation assistée parmi les nouveau-nés hospitalisés en néonatalogie au CHU de Nantes



Fréquence des détresses respiratoires nécessitant de l'O2 ou du surfactant parmi les enfants nés au CHU de Nantes



Ces résultats sont retrouvés dans d'autres bases de données

Table 2. Neonatal and Maternal Costs and Outcomes by 250-g Birth Weight Intervals fo

Birth weight (g)	*n*	Neonatal LOS (d)		Neonatal cost		RDS (%)	Ventilation (%)	C/D rate (%)	Nonnormal DRG (%)
		Mean	Median	$1000/ case	$ million				
500–749	266	103.0	98	224.4	59.7	78.6	91.7	52.3	98.9
750–999	581	78.2	74	144.0	83.7	75.9	79.5	59.9	99.3
1000–1249	872	55.2	51	92.7	80.9	58.1	61.9	58.1	98.5
1250–1499	1058	36.5	35	51.9	54.9	42.2	42.0	56.4	96.2
1500–1749	1565	25.5	23	33.4	52.3	31.8	29.9	48.8	97.9
1750–1999	2423	14.6	13	18.9	45.9	19.1	16.3	38.1	96.9
2000–2249	4597	7.9	5	9.9	45.3	11.0	9.4	30.7	89.1
2250–2499	10,188	3.9	2	4.3	43.9	4.6	3.9	23.3	67.8
2500–2749	21,215	2.4	1	2.1	44.0	2.0	1.8	18.9	36.2
2750–3000	48,610	1.9	1	1.3	60.8	0.9	0.9	16.8	25.1
≥3000 or more	366,968	1.7	1	1.0	372.2	0.4	0.5	19.5	22.3

Abbreviations as in Table 1.

Obstet Gynecol 2003;102:488 –92. © 2003

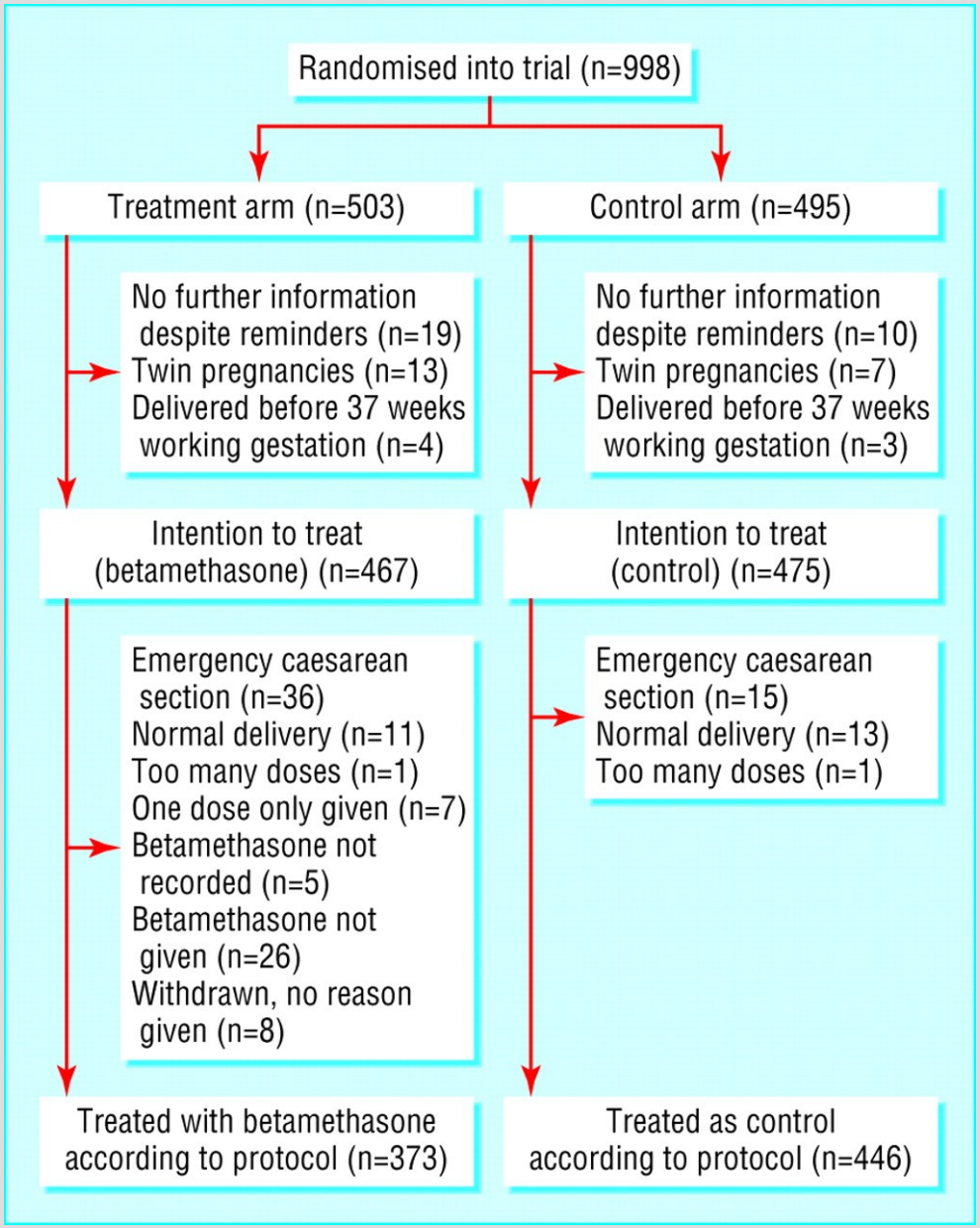
Le Bénéfice attendu ?

- Diminuer la détresse respiratoire transitoire du nouveau-né

« Stutchfield and coworkers recently reported a randomized pragmatic trial evaluating the efficacy of betamethasone in preventing respiratory distress in infants delivered by ECS. Their results show that two doses of betamethasone given in the 48 hours before delivery **significantly decreased admissions due to respiratory distress (RR 0.46, 95% CI 0.23- 0.93) ».**

BMJ 2005

Fig 1 Flow of participants through the trial



Stutchfield, P. et al. BMJ 2005;331:662

Outcomes*	Betamethasone group	Control group	Net benefit from steroid (95% confidence interval)
Binary*			
Resuscitated	44/467 (9.4)	54/475 (11.4)	2.0 (–2.0 to 6.0)
Resuscitation:			
Mask ventilation	22/467 (4.7)	20/475 (4.2)	–0.5 (–3.3 to 2.2)
Intubation	4/467 (0.9)	1/475 (0.2)	–0.6 (–2.0 to 0.4)
Admitted to special care baby unit with respiratory distress	11/467 (2.4)	24/475 (5.1)	2.7 (0.3 to 5.3)
Quantitative†			
Apgar score at 1 minute	8.48 (0.07)	8.57 (0.05)	–0.09 (–0.26 to 0.08)
Apgar score at 5 minutes	9.27 (0.06)	9.29 (0.05)	–0.02 (–0.18 to 0.14)
Time in special care baby unit in days	0.18 (0.05)	0.35 (0.09)	0.18 (–0.02 to 0.37)
Time on oxygen in hours	0.64 (0.35)	3.44 (1.20)	2.80 (0.34 to 5.25)
Maximum inspired oxygen concentration in %	21.29 (0.13)	21.99 (0.31)	0.68 (0.12 to 1.42)

11(2.4%) 24 (5.1%) gain de 13 hospitalisations

BMJ

Stutchfield, P. et al. BMJ 2005;331:662

Outcomes*	Betamethasone group	Control group	Net benefit from steroid (95% confidence interval)
Binary*			
Resuscitated	31/373 (8.3)	46/446 (10.3)	2.0 (–2.1 to 6.0)
Resuscitation:			
Mask ventilation	15/373 (4.0)	17/446 (3.8)	0.2 (–2.5 to 3.1)
Intubation	2/373 (0.5)	1/446 (0.2)	0.3 (–0.7 to 1.7)
Admitted to special care baby unit with respiratory distress	7/373 (1.9)	22/446 (4.9)	3.1 (0.6 to 5.7)
Quantitative†			
Apgar score at 1 minute	8.53 (0.07)	8.59 (0.05)	-0.06 (-0.23 to 0.10)
Apgar score at 5 minutes	9.36 (0.05)	9.30 (0.05)	0.05 (-0.09 to 0.20)
Time in special care baby unit in days	0.14 (0.05)	0.32 (0.09)	0.18 (-0.02 to 0.37)
Time on oxygen in hours	0.74 (0.43)	2.80 (1.12)	2.06 (-0.31 to 4.43)
Maximum inspired oxygen concentration in %	21.27 (0.16)	21.93 (0.33)	0.65 (0.19 to 1.42)

BMJ

Stutchfield, P. et al. BMJ 2005;331:662

Ceci est l’illustration de :

Une différence
statistiquement significative
n’est pas toujours
cliniquement signifiante

Conclusions de l'article

What this study adds

Babies born after 37 weeks by elective caesarean section also benefit from antenatal betamethasone

---

This reduces the incidence of respiratory distress by more than 50%, mainly by reducing transient tachypnoea of the newborn

---

These findings imply that antenatal steroids can aid the clearing of lung fluid after delivery

---

When counselling a mother before elective caesarean section at term, the increased risk of admission with respiratory distress should be considered

---

The likely benefits of antenatal betamethasone should be compared with those of delaying caesarean section until 39 weeks when possible

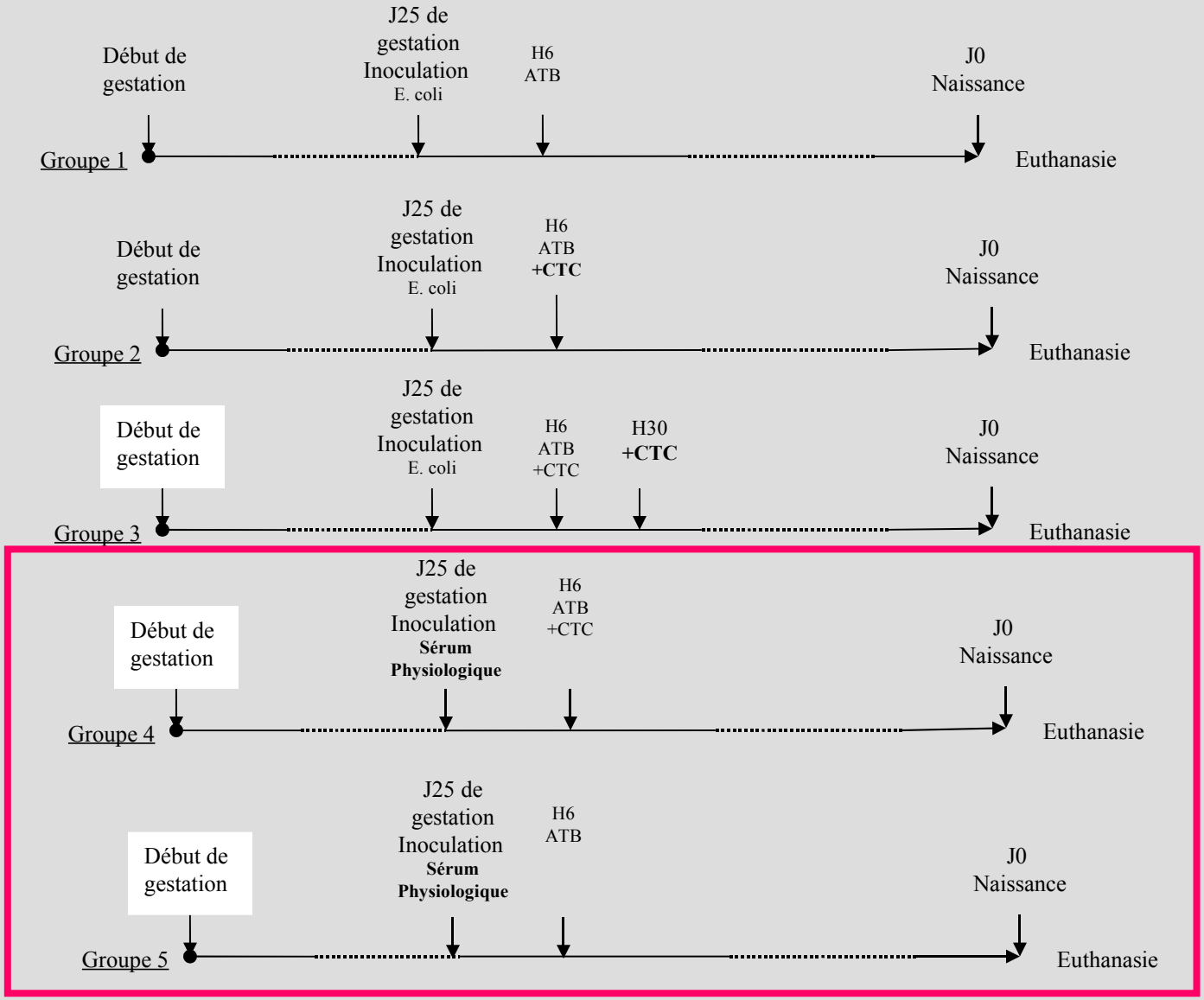
Le bénéfice est léger

Balance
Bénéfice - Risque

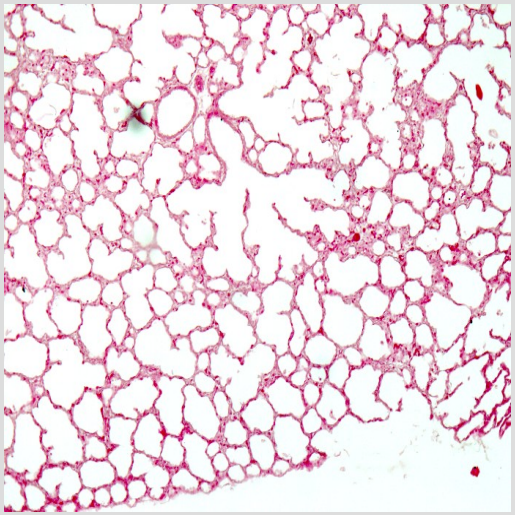
- Le bénéfice attendu
- Le risque éventuel lié à la thérapeutique
- Le nombre nécessaire de patients à traiter pour observer un effet

MODELE CHEZ LE LAPIN
Schéma de l'étude

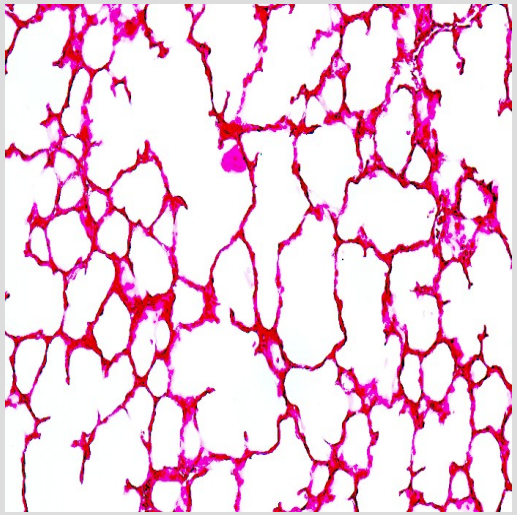
Nicolas Joram,
Christele Gras-Le Guen
Data non publiés



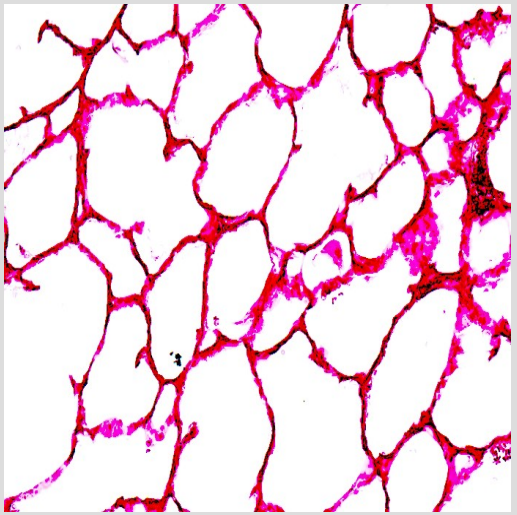
Morphométrie



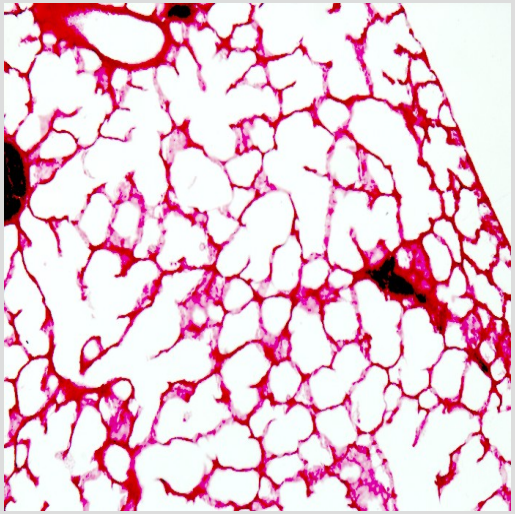
Groupe1: E.coli seul



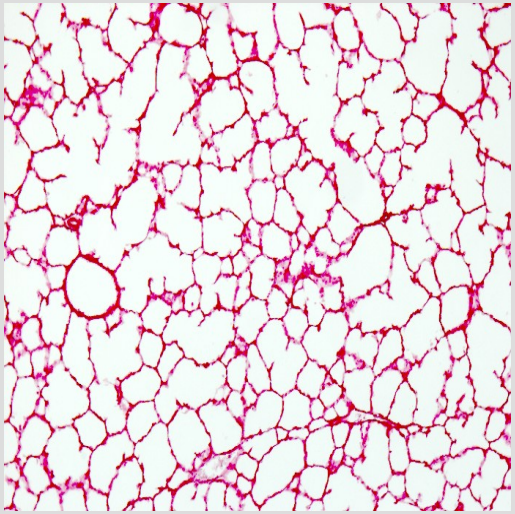
Groupe 2 : E. coli
+ 1 dose bétaméthasone



Groupe 3 : E coli
+ 2 doses bétaméthasone



Groupe 4 : 1 dose bétaméthasone seule



Groupe 5 : témoin

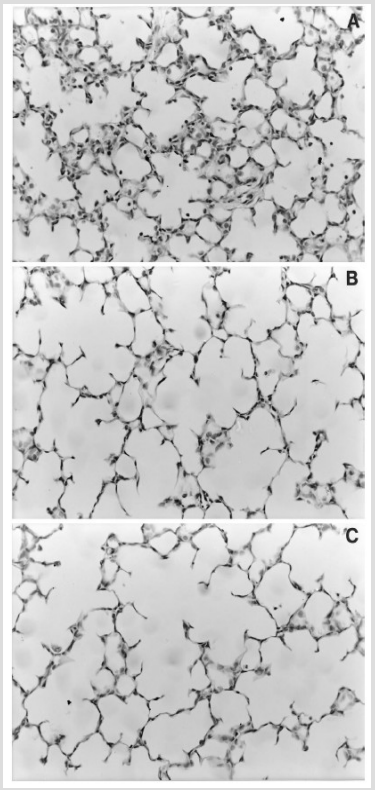
La corticothérapie

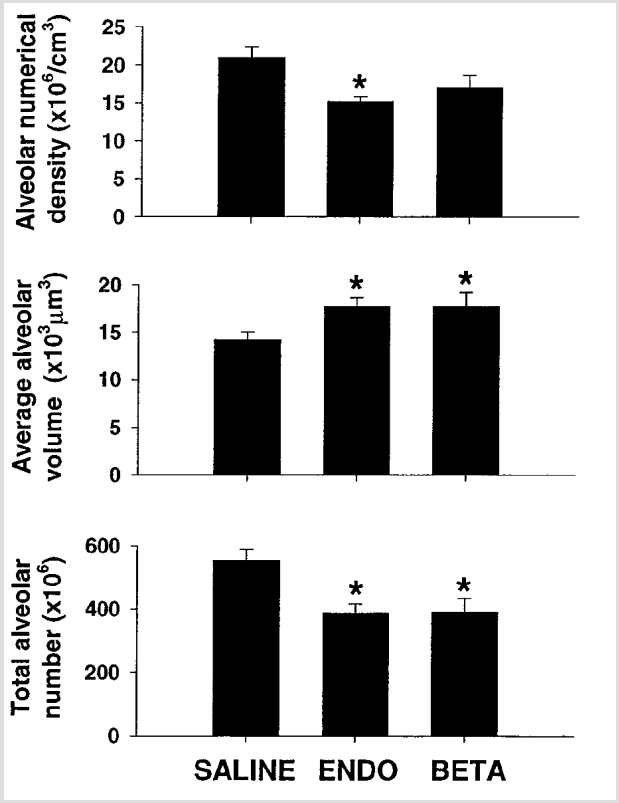
- Rôle délétère possible

Témoin

Endotoxine

Betamethasone





Willet KE. Pediatric Research

EFFET SUE LE DEVELOPPEMENT PULMONAIRE

- These data suggest that prenatal hormone treatment may cause significant "dysmaturational" changes in the lung parenchyma, the most profound effects resulting from exposure early in gestation. Although the present study did not examine longterm effects, similar studies in rats suggest that precocious attenuation of alveolar septa may permanently impair the lungs' ability to septate.

Le cerveau

ELSEVIER

Neuroscience Letters 297 (2001) 147–150

Neuroscience Letters

www.elsevier.com/locate/neulet

Antenatal betamethasone treatment reduces synaptophysin immunoreactivity in presynaptic terminals in the fetal sheep brain

Iwa Antonow-Schlorke[a], Birgit Kühn[a], Thomas Müller[b], Harald Schubert[b], Ulrich Sliwka[a], Peter W. Nathanielsz[c], Matthias Schwab[a,*]

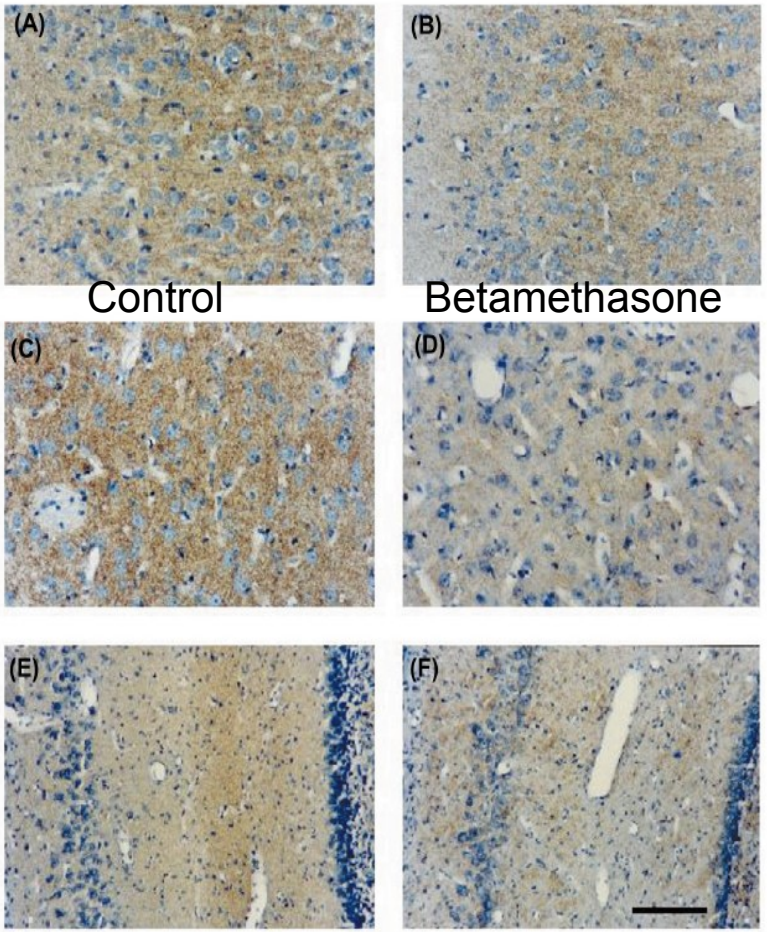


Fig. 1. Immunohistochemical distribution of synaptophysin (brown precipitate) in the frontal neocortex, caudate putamen and CA1 region of the hippocampus of a vehicle (A,C,E) and a betamethasone treated fetus (B,D,F) at 0.87 of gestation. Loss of synaptophysin-LI in the frontal neocortex (B), the caudate putamen (D) and the CA1 region of the hippocampus (F) of the betamethasone treated fetuses is clearly visible. Counterstaining with hematoxylin did not demonstrate irreversible neuronal damage. Scale bar = 100 μm.

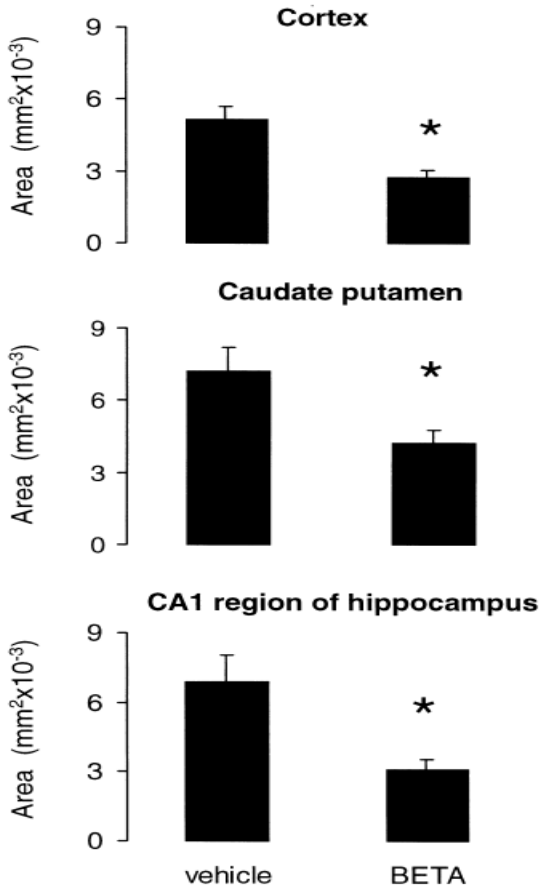


Fig. 2. Acute effects of antenatal betamethasone (BETA) treatment on synaptophysin-LI (area of positive immunostaining) in fetal sheep brain at 0.87 of gestation. Vehicle treated fetuses $n = 7$, betamethasone treated fetuses $n = 7$, mean ± SEM, $^{*}P < 0.05$.

Cardiovascular risk factors after antenatal exposure to betamethasone: 30-year follow-up of a randomised controlled trial.

Stuart R Dalziel, NatalieK Walker, VarshaParag, ColinMantell, HaroldH Rea, AnthonyRodgers, JaneEHarding

***Lancet* 2005; 365: 1856–62**

Correspondence to:
Prof Jane Harding, **Liggins Institute**,
University of Auckland,
Private Bag 92019, Auckland,
New Zealand

Pas de différence à l'âge de 30 ans

	Betamethasone		Placebo		Difference (95% CI)	p
	Mean value*	n	Mean value*	n		
Body size						
Height, cm†	171·7	224	169·8	234	1·9 (0·1 to 3·7)	0·04
Height Z score	0·19	224	0·05	234	0·15 (−0·05 to 0·34)	0·13
Weight, kg	79·3	224	76·7	234	2·6 (−0·7 to 5·9)	0·13
Weight Z score	0·87	224	0·77	234	0·10 (−0·09 to 0·29)	0·29
Body-mass index, kg/m²	26·8	224	26·5	234	0·3 (−0·7 to 1·2)	0·60
Head circumference, cm	56·3	224	56·2	234	0·1 (−0·3 to 0·5)	0·76
Waist/hip ratio	0·83	223	0·82	233	0·01 (0 to 0·02)	0·16
Geometric mean triceps skinfold, mm	14	223	14	233	0·98 (0·90 to 1·07)‡	0·68
Geometric mean biceps skinfold, mm	7	223	7	233	0·99 (0·89 to 1·09)‡	0·80
Geometric mean subscapular skinfold, mm	17	215	17	226	1·01 (0·93 to 1·11)‡	0·78
Geometric mean suprailiac skinfold, mm	13	220	13	232	0·99 (0·89 to 1·11)‡	0·87
Blood pressure						
Systolic, mm Hg	119	221	118	234	1 (−2 to 3)	0·66
Diastolic, mm Hg	74	221	74	234	0 (−2 to 1)	0·87
Lipids (fasting sample)						
Total cholesterol, mmol/L	4·9	218	5·0	227	−0·1 (−0·3 to 0·1)	0·23
HDL cholesterol, mmol/L	1·4	218	1·4	227	0 (−0·1 to 0)	0·57
LDL cholesterol, mmol/L	3·0	218	3·1	227	−0·1 (−0·2 to 0·1)	0·28
Cholesterol ratio (total/HDL)	3·8	218	3·9	227	−0·1 (−0·3 to 0·2)	0·52
Geometric mean triglyceride, mmol/L	1·1	218	1·0	227	0·93 (0·73 to 1·17)‡	0·63

*Or geometric mean where indicated. †After adjustment for sex, difference=0·9 (−0·3 to 2·3), p=0·14. Differences are difference between means (95% CI) or ‡ratio of geometric means (95% CI). A 95% CI for a ratio of geometric means is non-significant if it includes 1.[16]

Table 4: Outcome at 30 years in betamethasone-exposed and placebo-exposed groups

Sauf pour le test de tolérance au glucose ….

Findings There were no differences between those exposed to betamethasone and to placebo in body size, blood lipids, blood pressure, plasma cortisol, prevalence of diabetes, or history of cardiovascular disease. After a 75 g oral glucose tolerance test, participants exposed to betamethasone had higher plasma insulin concentrations at 30 min (60·5 *vs* 52·0 mIU/L; ratio of geometric means 1·16 [95% CI 1·03 to 1·31], p=0·02) and lower glucose concentrations at 120 min (4·8 *vs* 5·1 mmol/L; difference –0·26 mmol/L [–0·53 to 0·00], p=0·05) than did those exposed to placebo.

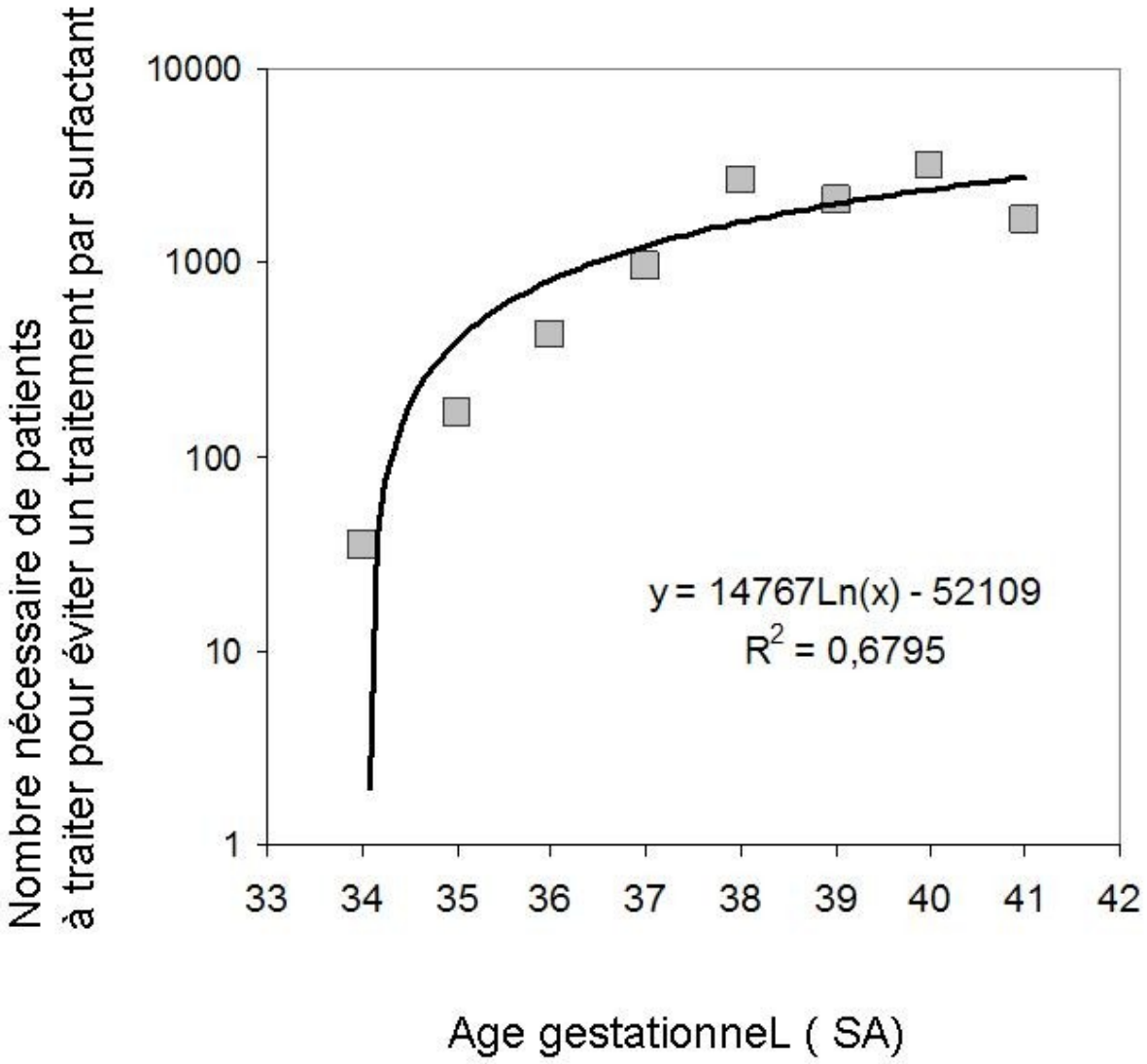
Interpretation Antenatal exposure to betamethasone might result in insulin resistance in adult offspring, but has no clinical effect on cardiovascular risk factors at 30 years of age. Thus, obstetricians should continue to use a single course of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome.

Lancet 2005; 365: 1856–62

Le risque à long terme est à préciser ….

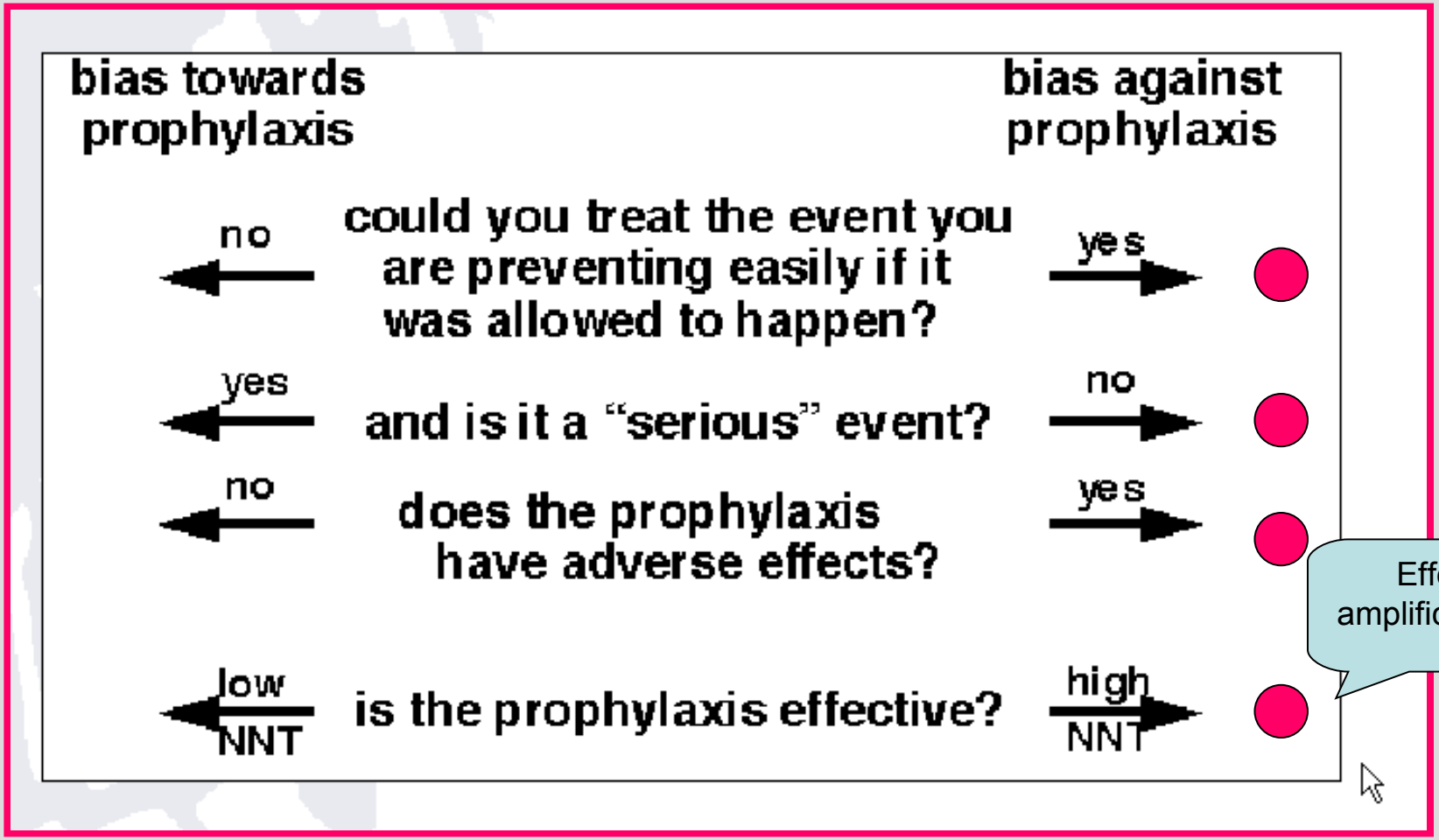
Balance
Bénéfice - Risque

- Le bénéfice attendu
- Le risque éventuel lié à la thérapeutique
- Le nombre nécessaire de patients à traiter pour observer un effet


Nombre nécessaire de patients
à traiter pour éviter un traitement par surfactant
10000
1000
100
10
1
33
34
35
36
37
38
39
40
41
42
y = 14767Ln(x) - 52109
R2 = 0,6795
Age gestationneL (SA)


Nombre nécessaire de patients
à traiter pour éviter 1 oxygénothérapie
500
450
400
350
300
250
200
150
100
50
0
y = 2411,3Ln(x) - 8498,4
R2 = 0,9101
33
35
37
39
41
Age gestationneL (SA)

NNTs for Preventative Interventions



Bénéfice

Risque

Chez
le nouveau-né
de plus de 34 SA

Risque

Bénéfice

- Chez le grand prématuré
- À 33-34 par césarienne
- La hernie diaphragmatique
- L’omphalocèle

Bénéfice

Risque

Chez
le nouveau-né
de plus de 34 SA

BMJ 2005;331:645-646 (24 September),

Editorial

Giving steroids before elective caesarean section ??

single course of steroids reduces neonatal mortality in babies born before 34 weeks and this perhaps justifies the small risk of long term side effects.

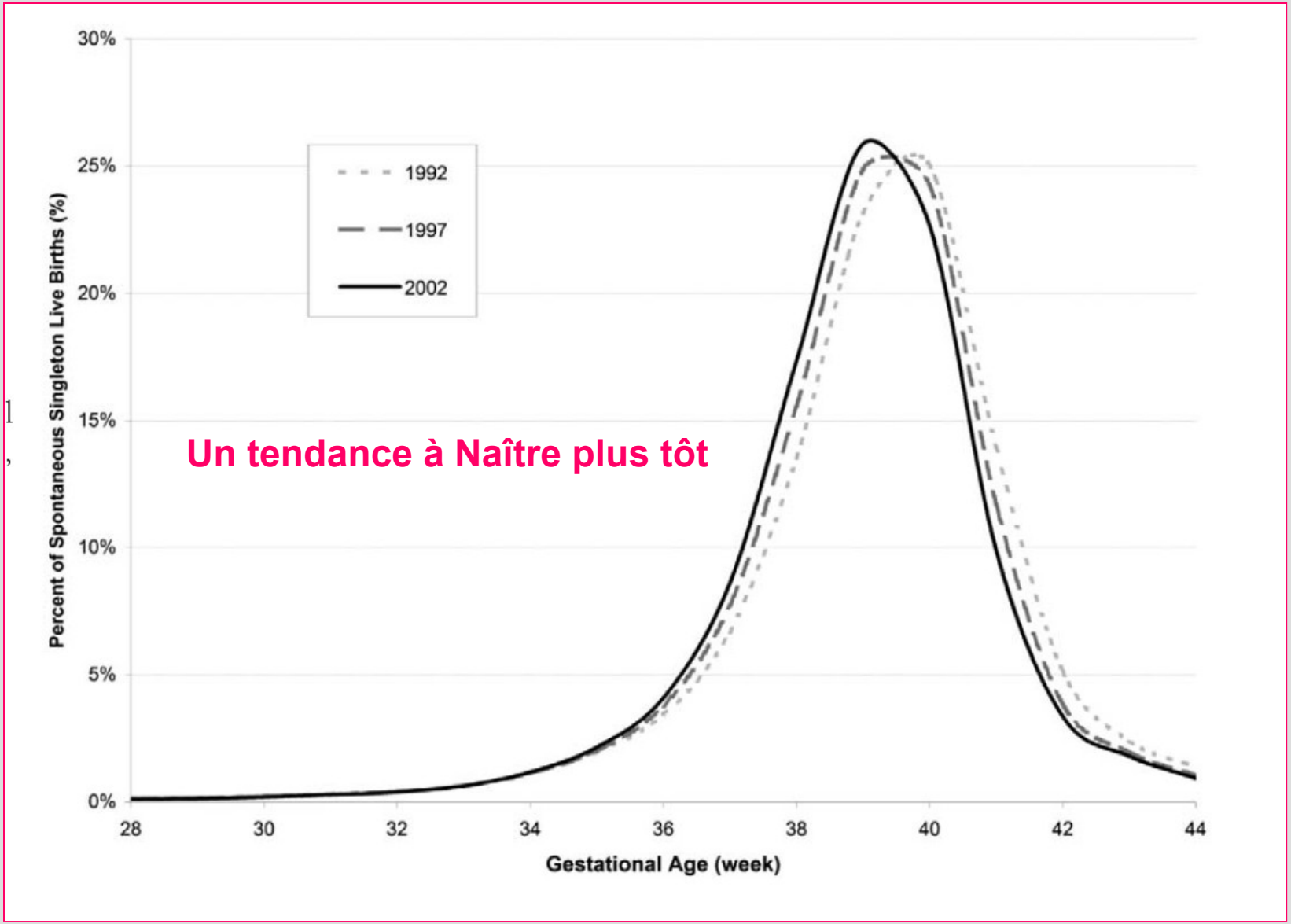
However, no such substantial benefit has been shown after this gestation. Delaying delivery until 39 weeks, unless necessary, would seem a more prudent option than giving steroids whose long term safety,

even as a single course, remains questionable.

Philip J Steer, *professor of obstetrics*

En commentaire de l'article de **Stutchfield, P**

Plutôt changer le contexte



EN CONCLUSION

- Cette option ne semble pas raisonnable en l'absence de données sur le long terme chez des enfants de plus de 34SA