Faut-il déclencher toutes les femmes enceintes à 39SA?

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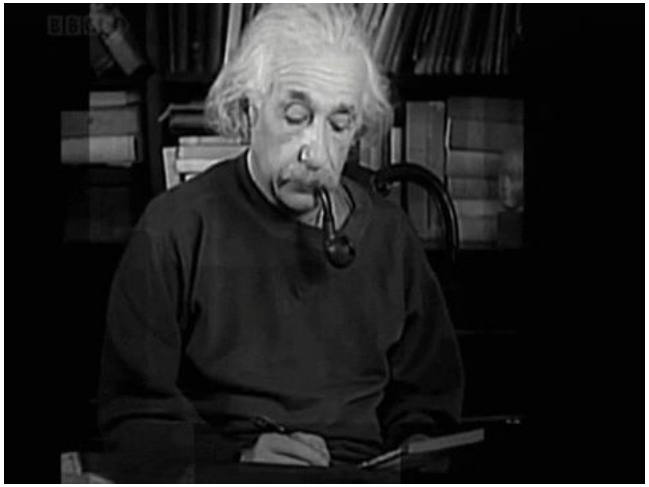
Liège, Avril 2023

*Pas de lien d'intérêt à déclarer



Il est plus facile de désintégrer un atome qu'un préjugé.

Position médicale du problème

- **Objectif du déclenchement artificiel du travail:**

Parvenir à un accouchement par voie basse lorsque les avantages de l'accouchement imminent l'emportent sur le risque potentiel de poursuivre la grossesse

ACOG practice bulletin no. 107, Obstet Gynecol 2009

- **Evaluation cruciale:**

Balance des risques/bénéfices liés au déclenchement ou à l'expectative (poursuite de la grossesse)

Risques liés à l'expectative

Risques liés à l'expectative

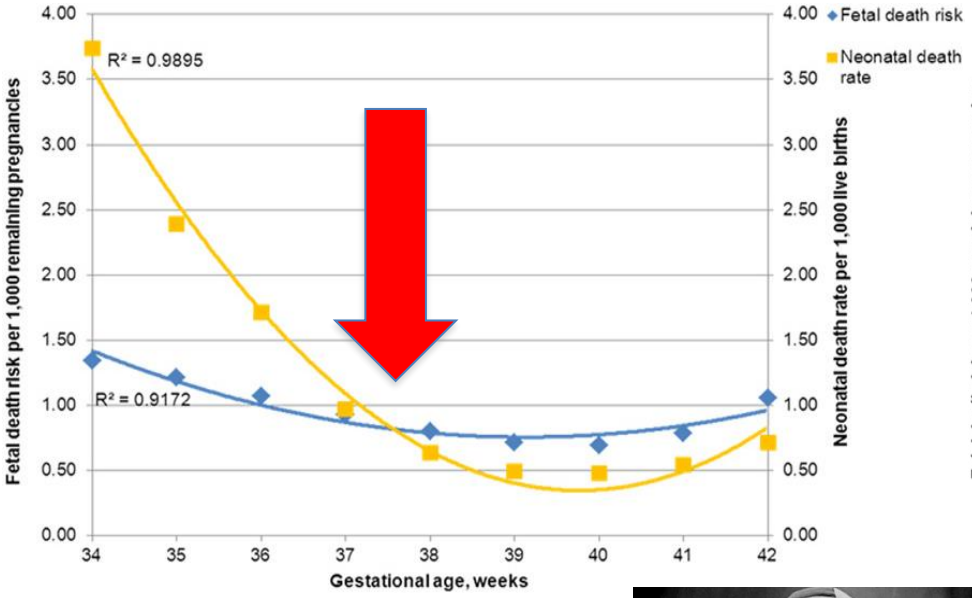
Mortalité périnatale

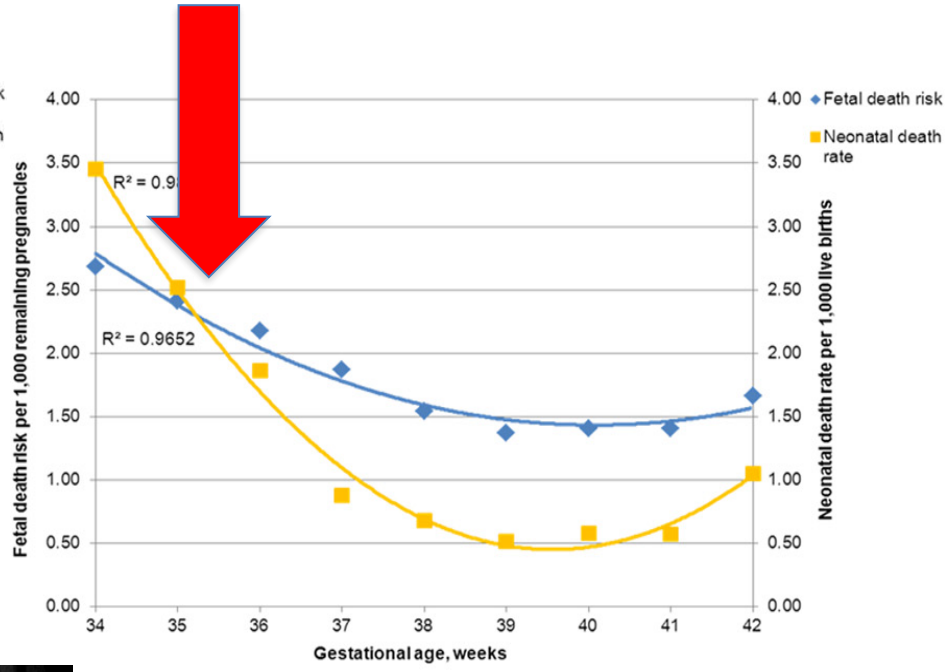
- **Comparaison de la mortalité fœtale et de la mortalité néonatale entre 34 et 42 SA**
- ***National Center for Health Statistics* (USA)**
- **Grossesses uniques sans malformation**
- **8 785 132 naissances vivantes et 12 777 morts fœtales**

Mandujano A, Am J Obstet Gynecol 2013

Risques liés à l'expectative

Mortalité fœtale évitable par l'accouchement > mortalité néonatale
-entre 37 et 38 SA dans les grossesses à bas risque
-entre 35 et 36 SA dans les grossesses à haut risque





Bas risque

Haut risque

Mandujano A, Am J Obstet Gynecol 2013

Risques liés à l'expectative

Etude de la mortalité fœtale/infantile par âge gestationnel à terme stratifiée sur l'âge maternel

TABLE 3

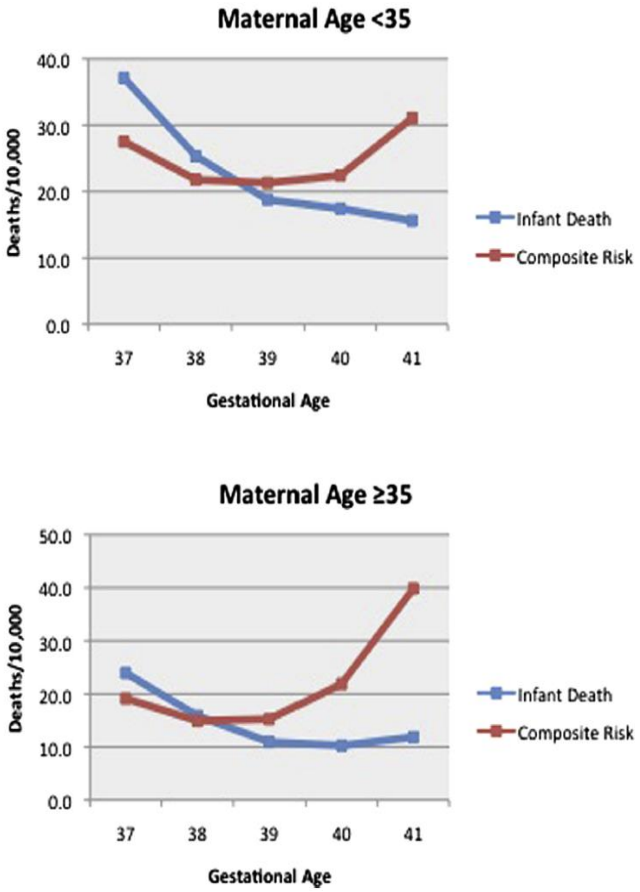
Risk of infant death and expectant management stratified by maternal age 35 years and GA

GA	Maternal age <35 years (95% CI)		Maternal age ≥35 years (95% CI)	
	Infant death per 10,000 live births	Risk of expectant management for 1 week per 10,000	Infant death per 10,000 live births	Risk of expectant management for 1 week per 10,000
37	37.1 (34.6–39.6)	27.5 (25.4–29.7)	23.9 (18.9–29.0)	19.1 (14.6–23.7)
38	25.4 (24.0–26.7)	21.8 (20.6–23.0)	15.9 (13.3–18.4)	14.9 (12.5–17.4)
39	18.8 (17.8–19.7)	21.3 (20.3–22.3)	10.9 (9.2–12.7)	15.2 (13.1–17.4)
40	17.4 (16.4–18.4)	22.4 (21.3–23.5)	10.3 (8.2–12.3)	21.9 (18.9–24.8)
41	15.6 (13.9–17.3)	31.1 (28.7–33.5)	11.9 (7.7–16.0)	39.8 (32.2–47.5)

Infant death was a death occurring within the first year of life. Expectant management risk includes risk of stillbirth and infant death.

CI, confidence interval; *GA*, gestational age.

Page. Term fetal/infant mortality risk stratified by maternal age. Am J Obstet Gynecol 2013.



Page JM, Am J Obstet Gynecol 2013

Risques liés à l'expectative

Comparaison du risque de mort fœtale à terme vs. le risque de mortalité néonatale

- **Etude de cohorte rétrospective (N=3 820 826)**
- **Tous les accouchement à terme (sans malformation) en Californie (1997-2006)**

38 SA: risque de mort similaire entre expectative et accouchement

A chaque âge gestationnel plus tardif:
risque de mortalité de l'expectative plus élevé que le risque d'accouchement
39 SA: 12.9 vs 8.8/10 000
40 SA : 14.9 vs 9.5/10 000
41 SA : 17.6 vs 10.8/10 000

Rosenstein MG, Obstet Gynecol 2011

Risques liés au déclenchement

Risques liés au déclenchement

Déclenchement artificiel du travail:

Augmentation du risque de césarienne, en particulier parmi les nullipares avec un col défavorable

Yeast JD, Am J Obstet Gynecol 1999
Johnson DP, Am J Obstet Gynecol 2003
van Gemund N, Gynecol Obstet Invest 2003
Vrouenraets FP, Obstet Gynecol 2005
Vahratian A, Obstet Gynecol 2005
Hoffman MK, Obstet Gynecol 2006

Risques liés au déclenchement

- **Défaut méthodologique majeur de ces études =**

Erreur dans la sélection du groupe contrôle (validité interne)

- **à savoir, <u>les femmes en travail spontané</u>**

scénario clinique irréel (les cliniciens ne peuvent pas choisir le travail spontané)

- **Groupe de comparaison approprié: <u>femmes gérées par expectative</u>**

➢ **travail spontané**

➢ **ou finalement déclenchement pour indication médicale accouchant ensuite à un âge gestationnel plus tardif**

Caughey AB, Am J Obstet Gynecol 2006

Risques liés au déclenchement

- **Etude de cohorte rétrospective**

Base de données : *Vital Statistics Natality birth certificate registry* en 2005 *(Centers for Disease Control and Prevention)*

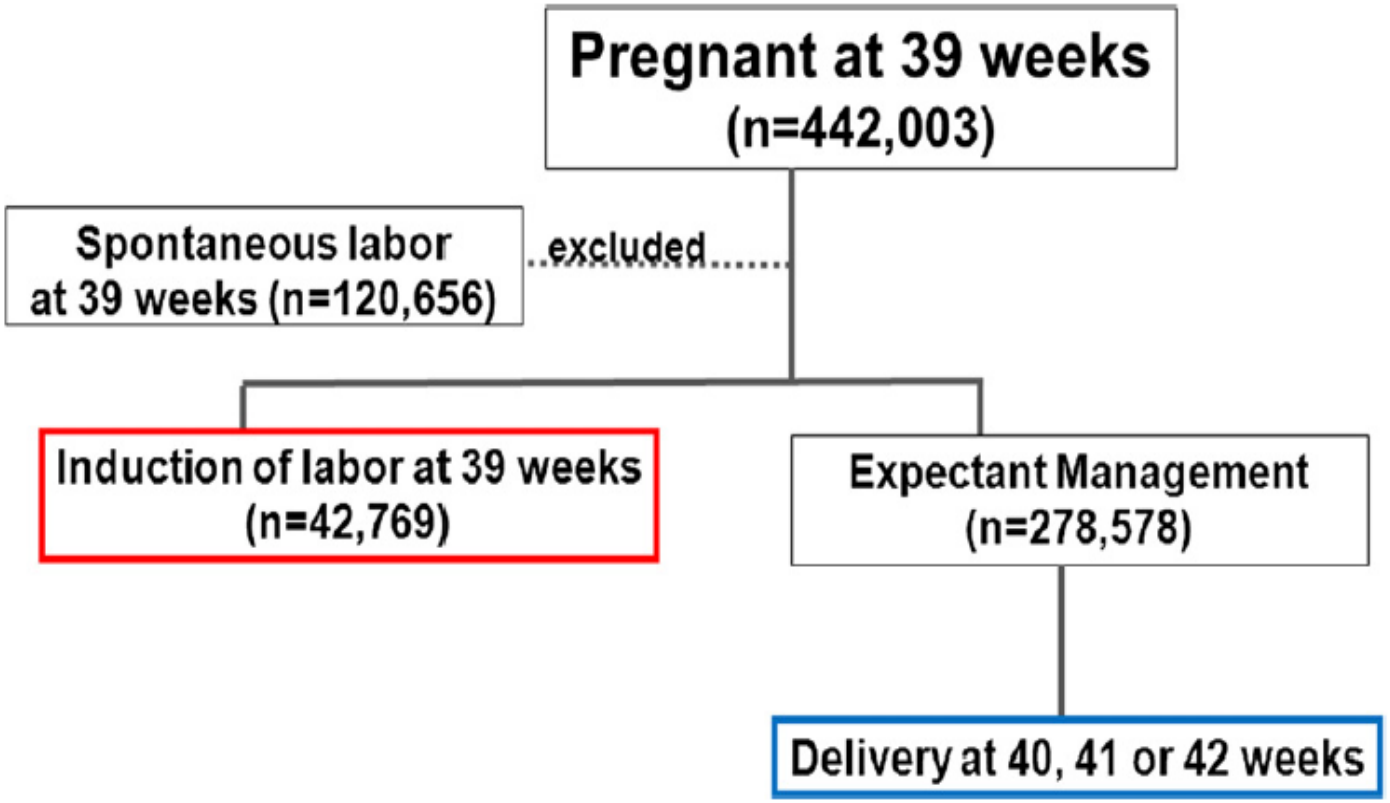
- **Nullipares à terme à bas risque avec grossesse unique, en présentation céphalique de 39 à 42 SA**

- **Comparaison déclenchement artificiel à un âge gestationnel donné (*i.e.* 39 SA) vs. poursuite de la grossesse avec accouchement (travail spontané ou déclenché) à un âge gestationnel plus tardif (*i.e*. 40, 41, ou 42 SA)**

Cheng YW, Am J Obstet Gynecol 2012

Risques liés au déclenchement

FIGURE
Flow diagram of study groups comparing induction of labor at a given GA to delivery at a later GA



Cheng YW, Am J Obstet Gynecol 2012

Risques liés au déclenchement

TABLE 2
Frequency and adjusted ORs of mode of delivery and birthweight at time of induction compared to delivery at later GA

Variable		aOR[a]	95% CI
Cesarean delivery			
39 wk' GA			
Induction (n = 42,769)	26.2%	0.90	0.88–0.91
Expectant (n = 278,578)	28.4%	Referent	
40 wk' GA			
Induction (n = 52,383)	31.0%	0.88	0.86–0.92
Expectant (n = 74,860)	33.7%	Referent	
41 wk' GA			
Induction (n = 28,325)	36.0%	0.89	0.83–0.95
Expectant (n = 4744)	39.0%	Referent	

TABLE 4
Frequency and adjusted ORs of neonatal outcomes at time of induction compared to delivery at later GA

Variable		aOR[a]	95% CI
5 min Apgar <7			
39 wk' GA			
Induction (n = 42,793)	0.89%	0.81	0.72–0.92
Expectant (n = 278,612)	1.09%	Referent	
40 wk' GA			
Induction (n = 52,469)	1.00%	0.80	0.71–0.90
Expectant (n = 74,952)	1.27%	Referent	
41 wk' GA			
Induction (n = 28,381)	1.19%	0.66	0.51–0.86
Expectant (n = 4729)	1.78%	Referent	
NICU admission			
39 wk' GA			
Induction (n = 18,890	2.57%	0.87	0.78–0.97
Expectant (n = 100,892)	3.05%	Referent	
40 wk' GA			
Induction (n = 22,194)	2.70%	0.74	0.66–0.83
Expectant (n = 26,364)	3.60%	Referent	
41 wk' GA			
Induction (n = 10,980)	3.48%	0.97	0.72–1.30
Expectant (n = 2003)	4.04%	Referent	

Cheng YW, Am J Obstet Gynecol 2012

Risques liés au déclenchement

- **Etude de cohorte rétrospective de tous les accouchements sans césarienne programmée en Californie en 2006**

- **Grossesses uniques, en présentation céphalique, sans malformation (n=362 154, 46.5% nullipares)**

- **Comparaison à chaque âge gestationnel (37-40 SA): déclenchement électif vs prise en charge expectative**

Darney BG, Obstet Gynecol 2013

Risques liés au déclenchement

- **Proportion de césariennes dans les groupes expectative significativement plus élevée à chaque âge gestationnel:**

- 37 SA: 15.4% vs 7.6%
- 38 SA: 15.9% vs 8.0%
- 39 SA: 17.3% vs 9.3%
- 40 SA: 19.0% vs 12.4%

Gestational Age Group (wk)	Model	Cesarean Delivery
All deliveries		
37	305,099	0.44 (0.34–0.57)
38	245,006	0.43 (0.38–0.50
39	150,730	0.46 (0.41–0.52)
40	58,845	0.57 (0.50–0.65)
Nulliparous		
37	143,982	0.66 (0.49–0.89)
38	118,283	0.74 (0.63–0.87)
39	75,828	0.75 (0.67–0.83)
40	30,837	0.77 (0.67–0.88)
Prior vaginal only		
37	161,117	0.44 (0.30–0.63)
38	126,723	0.41 (0.33–0.52)
39	74,902	0.44 (0.37–0.53)
40	28,008	0.51 (0.40–0.65)

- **Déclenchement électif :**

pas d'augmentation du risque de décès périnatal, transfert en USIN, détresse respiratoire à chaque âge gestationnel

Darney BG, Obstet Gynecol 2013

Risques liés au déclenchement

- **Etude transversale rétrospective**
- **Base de données issue du *Consortium on Safe Labor Consortium* (19 hôpitaux, 2002-2008)**

- **Inclusion des grossesses uniques à bas risque, en présentation céphalique entre 37 et 41 SA**

- **Comparaison par semaine: déclenchement électif (sans indication médicale) vs expectative**

Gibson KS, Am J Obstet Gynecol 2014

Risques liés au déclenchement

Cesarean delivery

	Nulliparous and unfavorable						Nulliparous and favorable					
	eIOL		Exp				eIOL		Exp			
Wk	No.	%	No.	%	aOR	95% CI	Wk	No.	%	No.	%	aOR	95% CI
37	8/43	18.6	7353/21,520	34.2	0.402	0.183–0.884	37	1/28	3.6	4943/33,486	14.8	0.164	0.022–1.228
38	81/285	28.4	6053/17,099	35.4	0.647	0.494–0.847	38	9/110	8.2	4142/26,352	15.7	0.430	0.213–0.864
39	142/602	23.6	4004/10,404	38.5	0.466	0.381–0.569	39	78/955	8.2	2615/14,201	18.4	0.497	0.389–0.633
40	353/1094	32.3	1482/3509	42.3	0.689	0.588–0.807	40	116/917	12.7	695/3292	21.1	0.694	0.551–0.874

	Multiparous and unfavorable						Multiparous and favorable					
	eIOL		Exp				eIOL		Exp			
Wk	No.	%	No.	%	aOR	95% CI	Wk	No.	%	No.	%	aOR	95% CI
37	2/85	2.4	1715/19,782	8.7	0.265	0.064–1.088	37	0/64	0.0	941/35,572	2.7	—	—
38	23/474	4.9	1293/14,815	8.7	0.553	0.360–0.850	38	4/429	0.9	752/26,400	2.9	0.421	0.156–1.137
39	66/2197	3.0	751/7033	10.7	0.346	0.262–0.456	39	27/3677	0.7	386/10,830	3.6	0.352	0.231–0.534
40	46/912	5.0	250/2033	12.3	0.437	0.307–0.622	40	16/959	1.7	91/2121+A48	4.3	0.536	0.297–0.968

Gibson KS, Am J Obstet Gynecol 2014

Risques liés au déclenchement

Morbidité néonatale composite plus faible avec le déclenchement électif à partir de 38 SA parmi les nullipares:

38 SA: ORa, 0.43; IC 95%, 0.26-0.72
39 SA : ORa, 0.75; IC 95%, 0.61-0.92
40 SA : ORa, 0.65; IC 95%, 0.54-0.80

Gibson KS, Am J Obstet Gynecol 2014

Risques liés au déclenchement

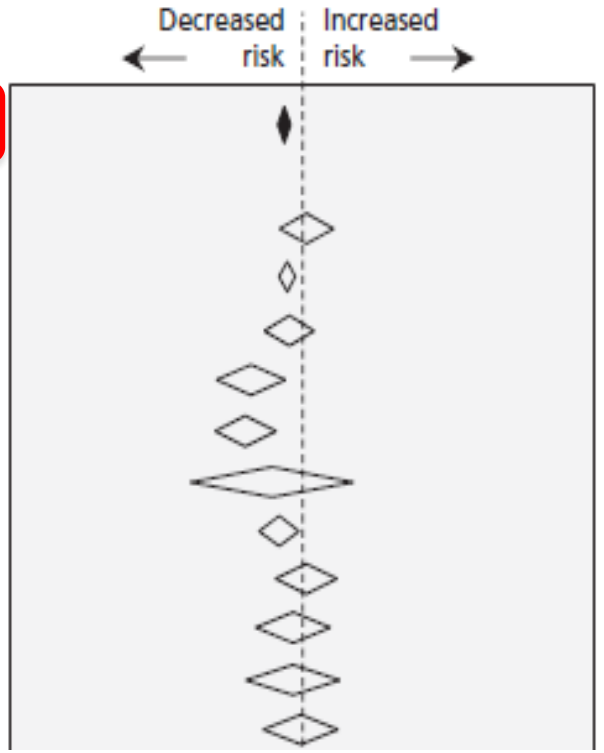
- **Revue systématique et méta-analyse évaluant le risque de césarienne après déclenchement artificiel du travail par rapport à l'expectative**

- **157 essais contrôlés randomisés éligibles (n = 31 085)**

Mishanina, CMAJ. 2014

Risques liés au déclenchement

Variable	No. of trials	Relative risk (95% CI)	I^2 value, %
Overall	157	0.88 (0.84–0.93)	0.0
Method of induction			
Oxytocin	15	1.03 (0.83–1.28)	0.0
Prostaglandin E2	67	0.90 (0.84–0.96)	0.0
Membrane sweep	17	0.90 (0.74–1.10)	0.0
Alternative method*	8	0.66 (0.50–0.86)	60.7
Misoprostol	11	0.62 (0.48–0.81)	0.0
Relaxin	4	0.79 (0.42–1.50)	0.0
Mixed	17	0.81 (0.70–0.95)	0.0
Isosorbide mononitrate	3	1.03 (0.81–1.31)	0.0
Amniotomy and oxytocin	6	0.96 (0.72–1.29)	10.7
Mifepristone	4	0.93 (0.64–1.34)	0.0
Mechanical	4	1.01 (0.75–1.35)	0.0

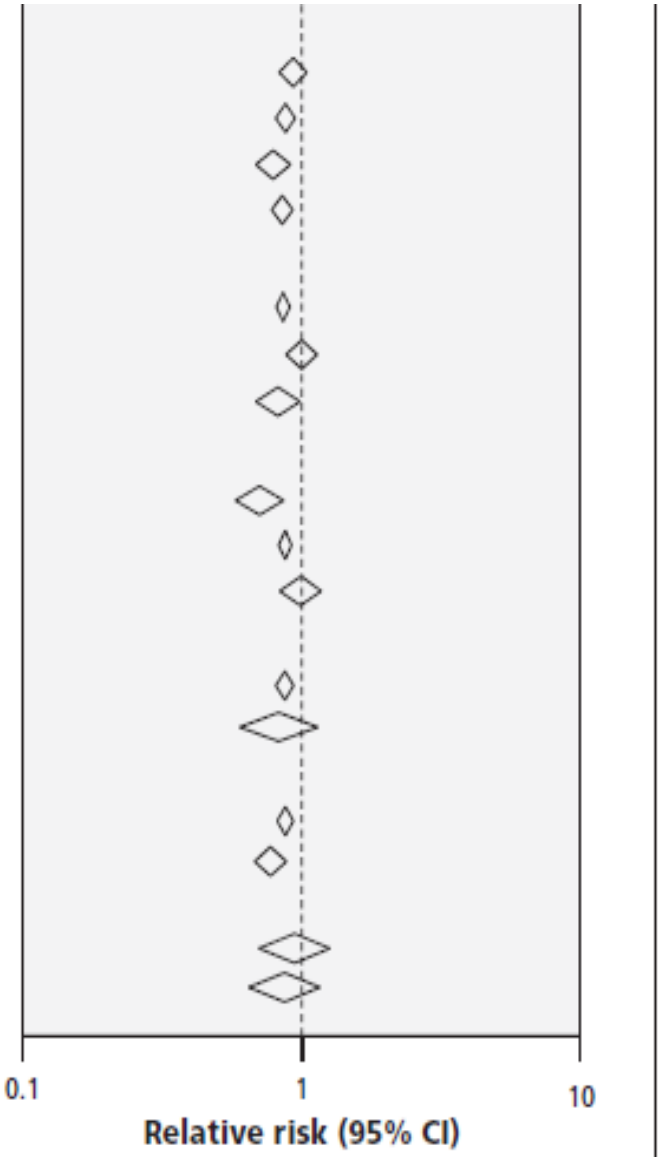


Globalement, réduction de 12% du risque de césarienne avec le déclenchement vs l'expectative (RR 0.88, IC 95% 0.84-0.93)

Mishanina E, CMAJ. 2014

Risques liés au déclenchement

Indication for induction			
Rupture of membranes before labour	30	0.95 (0.84–1.07)	0.0
Mixed (fetal, maternal, obstetric)	60	0.87 (0.81–0.95)	0.0
No medical indication	33	0.81 (0.70–0.93)	13.5
Post-dates pregnancy†	34	0.88 (0.80–0.96)	0.0
Gestational age			
Term (37–< 42 wk)	113	0.87 (0.82–0.92)	0.0
Preterm (< 37 wk)	26	1.00 (0.88–1.14)	0.7
Post-term (≥ 42 wk)	14	0.82 (0.69–0.99)	0.0
Definition of induction			
Cervical ripening	17	0.71 (0.58–0.86)	2.3
Induction of uterine contractions	22	1.01 (0.85–1.19)	0.0
Both	118	0.88 (0.84–0.93)	0.0
Cervical status			
Unfavourable	98	0.87 (0.81–0.94)	1.4
Favourable	7	0.83 (0.60–1.14)	0.0
Pregnancy risk			
High	103	0.89 (0.84–0.94)	0.0
Low	54	0.84 (0.75–0.94)	6.9
Parity			
Nulliparous	16	0.97 (0.81–1.17)	0.0
Parous	7	0.94 (0.77–1.13)	9.2



Mishanina E, CMAJ. 2014

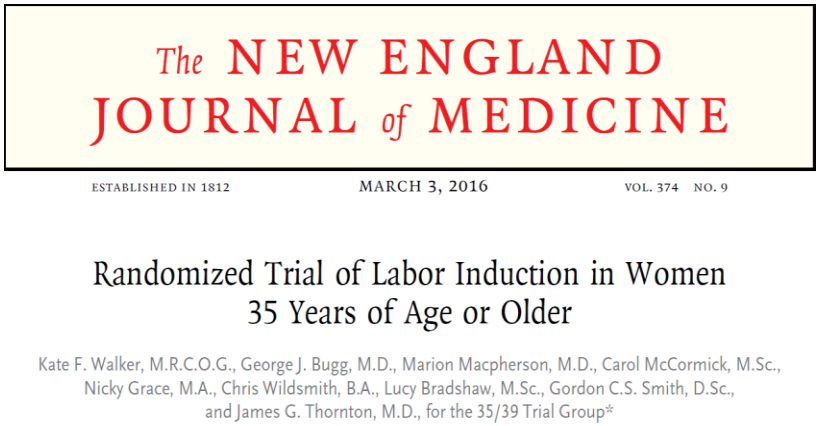
Risques liés au déclenchement

Table 1: Risk of adverse outcomes associated with labour induction versus expectant management

Outcome	Relative risk (95% CI)	I^2 value, %	No. of trials
Fetal death	0.50 (0.25–0.99)	0	60
Admission to NICU	0.86 (0.79–0.94)	0	55
Maternal death	1.00 (0.10–9.57)	0	20

Mishanina E, CMAJ. 2014

Risques liés au déclenchement



- **Risque de mort fœtale antepartum à terme plus élevé ≥ 35 ans**
- **Déclenchement : réduction du risque de MFIU, mais augmentation du risque de césarienne?**

- **Essai randomisé contrôlé avec analyse en ITT**
- **Nullipares ≥ 35 ans**
- **Randomisation**

- déclenchement artificiel du travail entre 39^{+0} et 39^{+6} SA

- vs expectative (travail spontanée ou déclenchement d'indication médicale)

- **Critère de jugement principal: césarienne**

Essai non conçu pour évaluer les effets du déclenchement sur la MFIU

Walker KF, N Engl J Med 2016

Risques liés au déclenchement

- **619 femmes randomisées**

Taux de césariennes similaires (RR, 0.99; IC 95% 0.87-1.14)

Fréquence similaires d'issues maternelles ou néonatales indésirables

Table 3. Maternal Outcomes.*

Outcome	Induction Group (N=304)	Expectant-Management Group (N=314)	Relative Risk (95% CI)†	P Value
Method of delivery				
Cesarean section — no. (%)	98 (32)	103 (33)	0.99 (0.87–1.14)	0.92
Age 35–37 yr‡	44 (26)	52 (29)	0.89 (0.67–1.19)	0.45
Age 38–39 yr ‡	29 (39)	27 (39)	1.00 (0.70–1.41)	0.99
Age ≥40 yr‡	25 (42)	24 (38)	1.13 (0.75–1.70)	0.56
Assisted vaginal delivery — no. (%)	115 (38)	104 (33)	1.30 (0.96–1.77)	0.08
Complications — no.				
Placental abruption	0	0		
Cord prolapse	1	0		
Postpartum hemorrhage¶	95	90	1.09 (0.85–1.40)	0.47
Shoulder dystocia	6	9	0.68 (0.25–1.83)	0.45
Blood transfusion required	10	17	0.61 (0.30–1.21)	0.16
Systemic infection	12	10	1.24 (0.45–3.37)	0.68

Walker KF, N Engl J Med 2016

Risques liés au déclenchement

The NEW ENGLAND JOURNAL of MEDICINE

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Labor Induction versus Expectant Management in Low-Risk Nulliparous Women

William A. Grobman, M.D., Madeline M. Rice, Ph.D., Uma M. Reddy, M.D., M.P.H., Alan T.N. Tita, M.D., Ph.D.,

- **Essai randomisé multicentrique**
- **Nullipare, bas-risque**
- **Déclenchement à 39SA-39SA+4 ou expectative**
- **CJP: *composite neonatal outcome* et CJS: césarienne**

Risques liés au déclenchement

Outcome	Induction Group (N=3059)	Expectant-Management Group (N=3037)	Relative Risk (95% CI)†	P Value‡
	no. (%)			
Primary composite outcome	132 (4.3)	164 (5.4)	0.80 (0.64–1.00)	0.049
Perinatal death	2 (0.1)	3 (0.1)	0.66 (0.12–3.33)	
Respiratory support	91 (3.0)	127 (4.2)	0.71 (0.55–0.93)	
Apgar score ≤3 at 5 min	12 (0.4)	18 (0.6)	0.66 (0.32–1.37)	
Hypoxic–ischemic encephalopathy	14 (0.5)	20 (0.7)	0.70 (0.35–1.37)	
Seizure	11 (0.4)	4 (0.1)	2.74 (0.91–8.12)	
Infection	9 (0.3)	12 (0.4)	0.74 (0.31–1.76)	
Meconium aspiration syndrome	17 (0.6)	26 (0.9)	0.65 (0.35–1.19)	
Birth trauma	14 (0.5)	18 (0.6)	0.77 (0.38–1.55)	
Intracranial or subgaleal hemorrhage	9 (0.3)	7 (0.2)	1.28 (0.48–3.42)	
Hypotension requiring vasopressor	2 (0.1)	5 (0.2)	0.40 (0.06–1.79)	
Maternal				
Cesarean delivery — no. (%)	569 (18.6)	674 (22.2)	0.84 (0.76–0.93)	<0.001‡
Operative vaginal delivery — no. (%)	222 (7.3)	258 (8.5)	0.85 (0.72–1.01)	0.07
Hypertensive disorder of pregnancy — no. (%)	277 (9.1)	427 (14.1)	0.64 (0.56–0.74)	<0.001‡
Chorioamnionitis — no. (%)	407 (13.3)	429 (14.1)	0.94 (0.83–1.07)	0.35
Third-degree or fourth-degree perineal laceration — no. (%)	103 (3.4)	89 (2.9)	1.15 (0.87–1.52)	0.33
Postpartum hemorrhage — no. (%)	142 (4.6)	137 (4.5)	1.03 (0.82–1.29)	0.81
Postpartum infection — no. (%)	50 (1.6)	65 (2.1)	0.76 (0.53–1.10)	0.15
Admission to ICU — no. (%)	4 (0.1)	8 (0.3)	0.50 (0.13–1.55)	0.26

Pour finir

SMFM Statement

smfm.org

SMFM Statement on Elective Induction of Labor in Low-Risk Nulliparous Women at Term: the ARRIVE Trial

Check for updates

Society of Maternal-Fetal (SMFM) Publications Committee

Despite these remaining questions, this large trial demonstrates that IOL in low-risk nulliparous women at 39 weeks of gestation does not have adverse neonatal effects and provides maternal benefit, with a decrease in rates of cesarean delivery and gestational hypertension/preeclampsia.

SMFM Statement, July 2019

Take home message

Fin probable d'un dogme…

Déclenchement vs. poursuite de la grossesse à partir de 39 SA

- **Diminution du risque de césarienne probable et semblant constant**
- **Diminution de la mortalité périnatale probable**
- **Pas d'augmentation de la morbidité néonatale**

- **Augmentation de l'utilisation des ressources en SdN+++**
- **Vécu des patientes à mettre en balance+++**
- **Attendre l'étude FRENCH-ARRIVE?**

Aucun argument scientifique pour refuser un déclenchement sur demande maternelle à 39SA
Importance de l'information délivrée++

Position du problème

- **Sujet très chaud….. Explosif**
- **Femme est au centre de sa prise en charge**
- **Problème de la médicalisation de la grossesse *sine materia?***
- **Problème de l'information donnée**
- **Attaques/ réponses dans le Lancet**

Merci de votre attention

Position du problème

Offline: FRENCH-ARRIVE—elles accusent

The accusation is direct and unflinching. The FRENCH-ARRIVE trial "obeys a pseudo-scientific rational logic" that is "a denial of what childbirth and motherhood mean to women". Claudine Schalck and Raymonde Gagnon are both registered midwives. Their book, *When Inducing Labor Compromises a Woman's Motherhood* (L'Harmattan, 2022), is one of the most remarkable denunciations of an ongoing research study ever published. It is also a sustained critique of the contemporary approach to obstetric care in many western nations today. Their analysis raises important questions about scientists' ethical responsibilities to research participants, and more especially medicine's attitudes to women.

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The original ARRIVE trial (A Randomised Trial of Induction Versus Expectant Management) was published in the *NEJM* in 2018 by William Grobman and colleagues. Over 6000 low-risk nulliparous women at 38 weeks to 38 weeks and 6 days gestation were randomised to labour induction or expectant management. The primary outcome was combined perinatal death or severe neonatal complications: the relative risk reduction in the induction group was 0·8 (95% CI 0·64–1·00). Caesarean delivery, the main secondary endpoint, was significantly lower among women undergoing induction (relative risk 0·84; 95% CI 0·76–0·93). Grobman et al comment that their results contradict observational reports of adverse maternal and perinatal outcomes after labour induction. They wrote that "the trial provides information that can be incorporated into discussions that rely on principles of shared decision making". According to its record on ClinicalTrials.gov, the FRENCH-ARRIVE trial began in April, 2021, and is expected to complete by the end of 2023. The main sponsor is the University Hospital in Bordeaux, in collaboration with France's Ministry of Health. The French investigators argue that "the expected benefits of elective labor induction at 39 weeks have to be confirmed in other settings outside [the] US before considering routine induction of labor for all low-risk nulliparous women at 39 weeks of gestation worldwide". The primary outcome of FRENCH-ARRIVE is incidence of caesarean section. About 4200 women are anticipated to take part. Schalck and Gagnon begin their indictment with a quote from François Rabelais: "Science without conscience is but the ruin of the soul." They acknowledge that "Limiting the C-section rate has become an international public health issue." But they point out that inducing labour without any medically justified reason can be considered nothing less than "obstetric violence". In FRENCH-ARRIVE, the calculation is one of measured risks and benefits: "The experiences, emotions, and subjectivity of the pregnant women are not taken into account." Induction of birth is not a benign intervention: Schalck and Gagnon argue that induction interferes with physiological birthing processes and breastfeeding. FRENCH-ARRIVE seems to reduce birth to a purely medical event. One might argue that women give their consent to take part in the study. But that consent may not be based on the fullest possible information. Schalck and Gagnon claim that the effects of the trial are minimised in the brochure describing the study. And what freedom do first-time mothers really have in the consent process when faced by a medical expert in the setting of a hospital? What this trial seems to do, they suggest, is to tell women where, when, and how they should give birth. In FRENCH-ARRIVE, "The uterus is seen as a machine used to produce and expel a baby within a certain period of time, under the supervision of medical personnel." This situation of "control" and "abuse" is a "form of domination over women". The woman "has neither body, nor power, nor place, nor role in childbirth".

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There are unique French dimensions to these arguments. France has a chronic shortage of midwives, whose working conditions are increasingly unacceptable. Compared with Sweden, France has twice the maternal mortality rate and fewer than half the number of midwives per 100 000 livebirths. But there are also general questions posed by this critique of FRENCH-ARRIVE. Does the simultaneous activity of scientist and doctor create a dangerous conflict of interest? Is medical research an enterprise dedicated more to its idealised progress than to meeting the specific needs of a person at a particular place and time in the health system? Schalck and Gagnon have written a visceral condemnation of a single research study. But their "j'accuse" is far broader. It deserves serious scrutiny and discussion.

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Horton Lancet 2023

Wellcome Trust, Medical Research Council, The Chief Scientist Office of Scotland, and Tommy's Charity, all paid to her institution; consulting fees on pre-term birth treatments to Natera; honoraria for educational speaking from Hologic, all paid to her institution; participation in the National Institute of Healthcare Research Health Technology and Assessment data monitoring committee and trial steering committee in the past 36 months; and a leadership role in the Trustee of Sands charity. All other authors declare no competing interests.

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1 Cinelli H, Lelong N, Le Ray C. Enquête nationale périnatale. Rapport 2021. 2022. https://enp.inserm.fr/wp-content/uploads/2022/10/rapport-2022-v5.pdf (accessed March 3, 2023).
2 Olié V, Moutengou E, Grave C, et al. Prevalence of hypertensive disorders during pregnancy in France (2010–2018): the Nationwide CONCEPTION Study. *J Clin Hypertens* 2021; **23:** 1344–53.
3 Horton R. Offline: FRENCH-ARRIVE—elles accusent. *Lancet* 2022; **400:** 1911.
4 Grobman WA, Rice MM, Reddy UM, et al. Labor induction versus expectant management in low-risk nulliparous women. *N Engl J Med* 2018; **379:** 513–23.
5 Schalck C, Gagnon R. When inducing labor compromises a woman's motherhood: a psycho-sociological analysis of maternity as labor. France: Editions L'Harmattan, 2022.
6 Alkmark M, Keulen JKJ, Kortekaas JC, et al. Induction of labour at 41 weeks or expectant management until 42 weeks: a systematic meta-analysis of randomised trials. *PLoS Med* 2020; **17:** e1003436.
7 Chan SW. Tulloch, Cooper ES, Smith A, Wojcik W, Norman JE. Montgomery and informed consent: where are we now? *BMJ* 2017; **12:** 357.
8 Schmitz T, Fuchs F, Closset E, et al. Outpatient cervical ripening by nitric oxide donors for prolonged pregnancy: a randomized controlled trial. *Obstet Gynecol* 2014; **124:** 1089–97.
9 Senat MV, Affres H, Letourneau A, et al. Effect of glyburide vs subcutaneous insulin on perinatal complications among women with gestational diabetes: a randomized clinical trial. *JAMA* 2018; **319:** 1773–80.

FRENCH-ARRIVE: a serious, evidence-free, and false accusation of unethical research

We—the investigators and Trial Steering Committee of the FRENCH-ARRIVE trial, members of the Groupe de Recherche en Obstétrique Gynécologie, representatives of the French College of Obstetrics and Gynecology, and Bordeaux University Hospital (appendix)—were stunned to read Richard Horton's[1] Comment spreading the erroneous accusations of Claudine Schalck and Raymonde Gagnon[2] claiming that the FRENCH-ARRIVE trial (NCT04799912) is scientific misconduct and unethical research that "obeys a pseudo-scientific rational logic" and is "a denial of what childbirth and motherhood mean to women". Schalck and Gagnon, who, like Horton, have never contacted us for accurate information about this trial, falsely suggest that the study provides the eligible women with incomplete information and that their "experiences, emotions, and subjectivity…are not taken into account".[1] As Horton pointed out, the rationale of the FRENCH-ARRIVE trial is based on the results of the ARRIVE trial.[8] That trial, done in the USA, showed a reduction of the composite adverse perinatal outcome (primary outcome) at the limit of significance, but a significantly lower frequency of caesarean births (secondary outcome). Based on this trial, the Society of Maternal-Fetal Medicine[2] stated that "[i]t is reasonable to offer elective induction of labor to low-risk nulliparous women ≥39 weeks 0 days of gestation".

The generalisability of this US study to populations with different characteristics or different contexts of care has been questioned in France and elsewhere.[3] The FRENCH-ARRIVE trial is being done precisely because we believe that additional evidence is required before elective induction of labour can be considered "a reasonable option"[3] for low-risk nulliparous women at 39 weeks or more of gestation and that one single multicentre trial, robust as it might be, is far from enough to implement such a medical intervention, especially when it is based on a positive result for a secondary outcome.[3] The FRENCH-ARRIVE trial is urgently necessary because practices have already changed, with labour induction rates increasing in many countries since the 2018 publication of the ARRIVE trial.

Contrary to the fact-free accusations made against us, we are particularly concerned about the implementation of a policy proposing routine labour induction for low-risk nulliparous women at 39 weeks or more of gestation, particularly because we have shown that induction of labour for medical reasons is an independent risk factor for post-traumatic stress disorders 2 months after vaginal childbirth.[4]

We therefore decided to test the hypothesis raised by the ARRIVE trial that elective induction of labour in low-risk nulliparous women at 39 weeks or more of gestation might reduce the

See Online for appendix

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Risques liés à l'expectative

Evaluation de l'effet d'une politique institutionnelle limitant l'accouchement électif < 39 SA sur les issues néonatales dans un centre universitaire

- **Etude de cohorte rétrospective**

12 015 naissances vivantes uniques 2 ans avant
12 013 naissances 2 ans après l'application de la politique

- **Taux global d'accouchements avant 39 SA:**

réduction de 33.1% à 26.4% (P <0.001)

- **admission en USIN : 9.29% vs 8.55%, P = 0.044**
- **augmentation des morts fœtales entre 37 et 38 SA:**

2.5 vs 9.1 pour 10.000 grossesses (RR 3.67, IC 95% 1.02 -13.15, P=0.032)

Ehrenthal DB, Obstet Gynecol 2011

Risques liés au déclenchement

BMJ 2012;344:e2838 doi: 10.1136/bmj.e2838 (Published 10 May 2012)

RESEARCH

Outcomes of elective induction of labour compared with expectant management: population based study

OPEN ACCESS

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Risques liés au déclenchement

- **Étude de cohorte rétrospective (1981-2007)**
- **Base de données de population non sélectionnée (registres écossais)**

1 271 549 femmes ayant une grossesse unique ≥ 37 SA

938 364 femmes sans déclenchement du travail

333 185 femmes avec déclenchement du travail

- 157 049 femmes avec indication médicale

- 176 136 femmes sans indication médicale

- **<u>Comparaison des issues</u>**

- déclenchement électif du travail (sans indication médicale) à 37, 38, 39, 40, et 41 SA

- prise en charge expectative (poursuite de la grossesse avec travail spontané, déclenchement du travail ou césarienne à un âge gestationnel plus tardif)

Stock. BMJ. 2012

Risques liés au déclenchement

Table 3| **Mode of delivery after elective induction of labour (IOL) compared with expectant management**

Mode of delivery: gestation week of IOL	No with outcome/Total No in group (%)		Univariate analysis, IOL *v* expectant		Multivariable analysis, IOL *v* expectant	
	Expectant management	Elective IOL	Odds ratio (99% CI)	P value	Adjusted odds ratio* (99% CI)	P value
Caesarean delivery:						
37	100 854/1 214 245 (8.3)	439/4432 (9.9)	1.21 (1.07 to 1.38)	<0.001	1.02 (0.89 to 1.17)	0.662
38	86 948/1 073 649 (8.0)	998/11 390 (8.8)	1.09 (1.00 to 1.19)	0.010	1.03 (0.94 to 1.13)	0.352
39	67 828/811 057 (8.4)	1524/16 347 (9.3)	1.13 (1.05 to 1.21)	<0.001	1.08 (1.00 to 1.16)	0.007
40	37 892/350 791 (10.8)	3740/44 778 (8.4)	0.75 (0.72 to 0.79)	<0.001	0.83 (0.79 to 0.88)	<0.001
41	8161/58 052 (14.1)	8154/76 054 (10.7)	0.73 (0.70 to 0.77)	<0.001	0.66 (0.63 to 0.69)	<0.001

Table 2| **Extended perinatal mortality after elective induction of labour (IOL) compared with expectant management**

Gestation week of IOL	No with outcome/Total No in group (%)		Univariate analysis, IOL *v* expectant		Multivariable analysis, IOL *v* expectant	
	Expectant management	Elective IOL	Odds ratio (99% CI)	P value	Adjusted odds ratio* (99% CI)	P value
37	2829/1 213 639 (0.23)	4/4429 (0.90)	0.39 (0.11 to 1.40)	0.0578	0.15 (0.03 to 0.68)	0.001
38	2190/1 073 170 (0.20)	9/11 384 (0.08)	0.39 (0.16 to 0.92)	0.0045	0.23 (0.09 to 0.58)	<0.001
39	1 521/810 720 (0.19)	9/16 344 (0.06)	0.29 (0.12 to 0.69)	0.0002	0.26 (0.11 to 0.62)	<0.001
40	627/350 643 (0.18)	37/44 764 (0.08)	0.46 (0.30 to 0.71)	<0.001	0.39 (0.24 to 0.63)	<0.001
41	127/58 028 (0.22)	50/76 028 (0.07)	0.30 (0.20 to 0.46)	<0.001	0.31 (0.19 to 0.49)	<0.001

Risques liés au déclenchement

Table 6| Neonatal admission to neonatal unit or special care baby unit after elective induction of labour (IOL) compared with expectant management

Gestation week of IOL	No with outcome/Total No in group (%)		Univariate analysis, IOL *v* expectant		Multivariable analysis, IOL *v* expectant	
	Expectant management	Elective IOL	Odds ratio (99% CI)	P value	Adjusted odds ratio* (99% CI)	P value
37	95 309/1 214 245 (7.8)	782/4432 (17.6)	2.52 (2.27 to 2.79)	<0.001	2.01 (1.80 to 2.25)	<0.001
38	79 204/1 073 649 (7.4)	1283/11 390 (11.3)	1.59 (1.48 to 1.72)	<0.001	1.53 (1.41 to 1.67)	<0.001
39	59 285/811 057 (7.3)	1310/16 347 (9.3)	1.10 (1.02 to 1.19)	0.001	1.17 (1.07 to 1.26)	<0.001
40	25 572/350 791 (7.3)	3605/44 778 (8.0)	1.11 (1.06 to 1.17)	<0.001	1.14 (1.09 to 1.20)	<0.001
41	4859/58 052 (8.4)	5051/76 054 (6.6)	0.78 (0.74 to 0.82)	<0.001	0.99 (0.93 to 1.05)	0.618

NNT pour prévenir un décès périnatal : 1040 (IC 95% 792-1513)
NNH (admission en USI) : 131 (IC 95% 97-202)

Pour chaque 1040 femmes avec déclenchement électif du travail à 40 SA
- 1 mort périnatale évitée
- mais 7 admissions supplémentaires en USI