



Impact of discontinuing oxytocin in active labour on neonatal morbidity: an open-label, multicentre, randomised trial

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Grant: National ministry of health 2018



Oxytocine – produit synthétique

- 82% des femmes déclenchées et 30 % des femmes en travail spontané en reçoivent
- Effets indésirables maternels et foetaux
 - Hyperstimulation utérine
 - Anomalie du RCF
 - **Acidose néonatale**
 - HPP
 - Césarienne ?
- Balance bénéfice/risque en faveur de son utilisation → non systématique
- Plusieurs études sur dose et durée maximale de perfusion pour diminuer effets indésirables



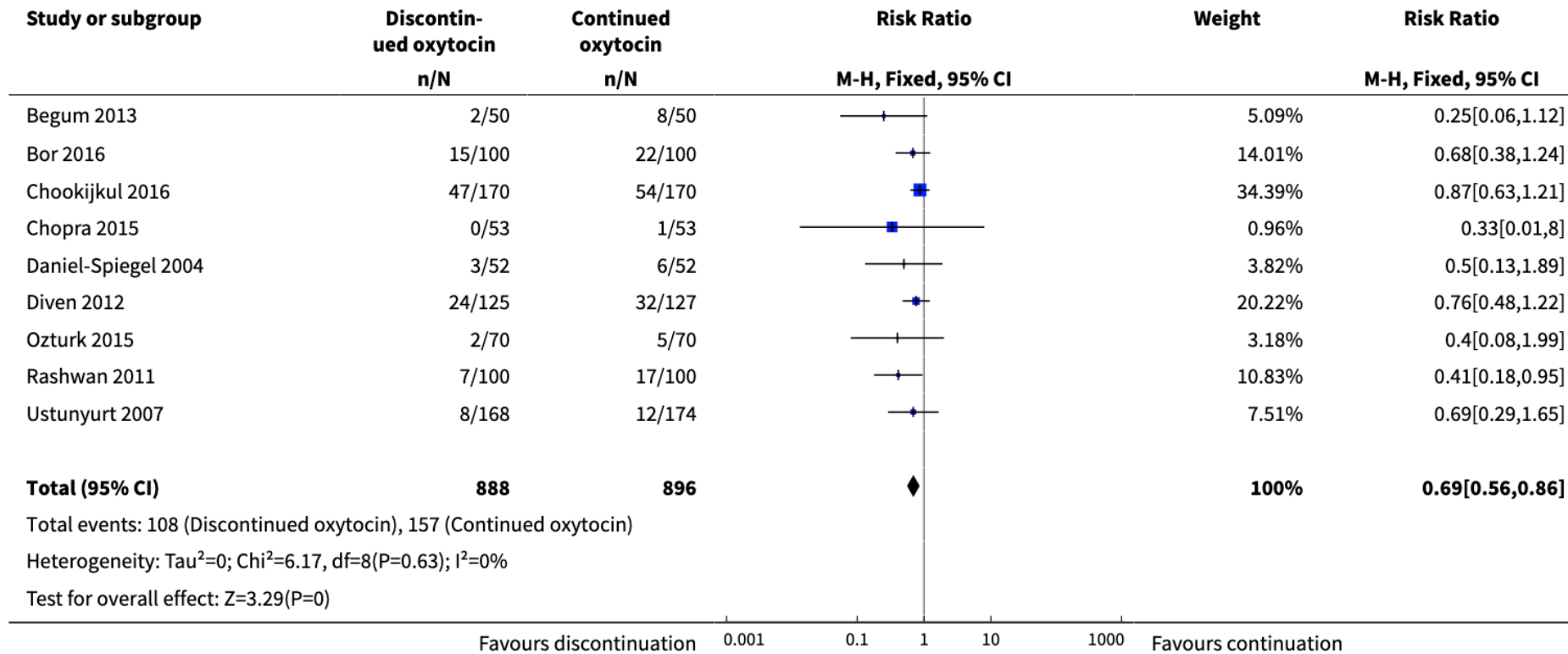
Hypothèse sous-jacente

- Lorsque le col est dilaté (5-6 cm) et que la tête foetale est appliquée,
 - sécrétion naturelle d'ocytocine prend relais
 - permettant d'arrêter perfusion d'oxytocine
-
- Ceci permettrait de réduire les risques liés à ce traitement
-
- Cochrane 2018 : 10 études, N=1888, plus large essai 342 femmes
CJP des essais : durée phase active



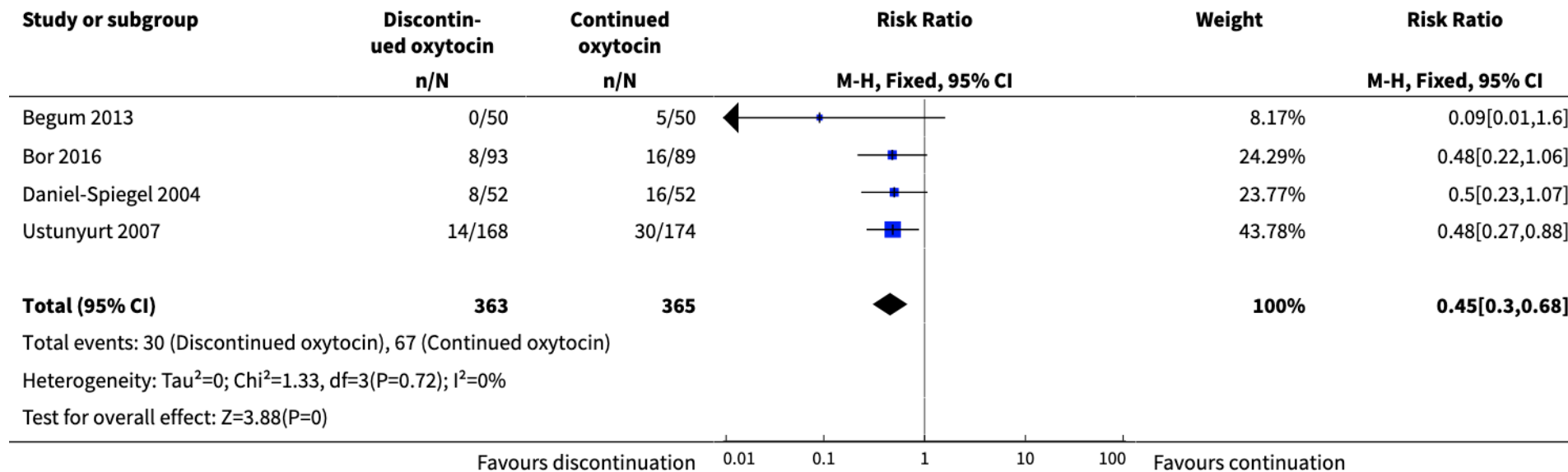
Rationnel – Césariennes

Analysis 1.1. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 1 Caesarean delivery.



Rationnel – Hypercinésie

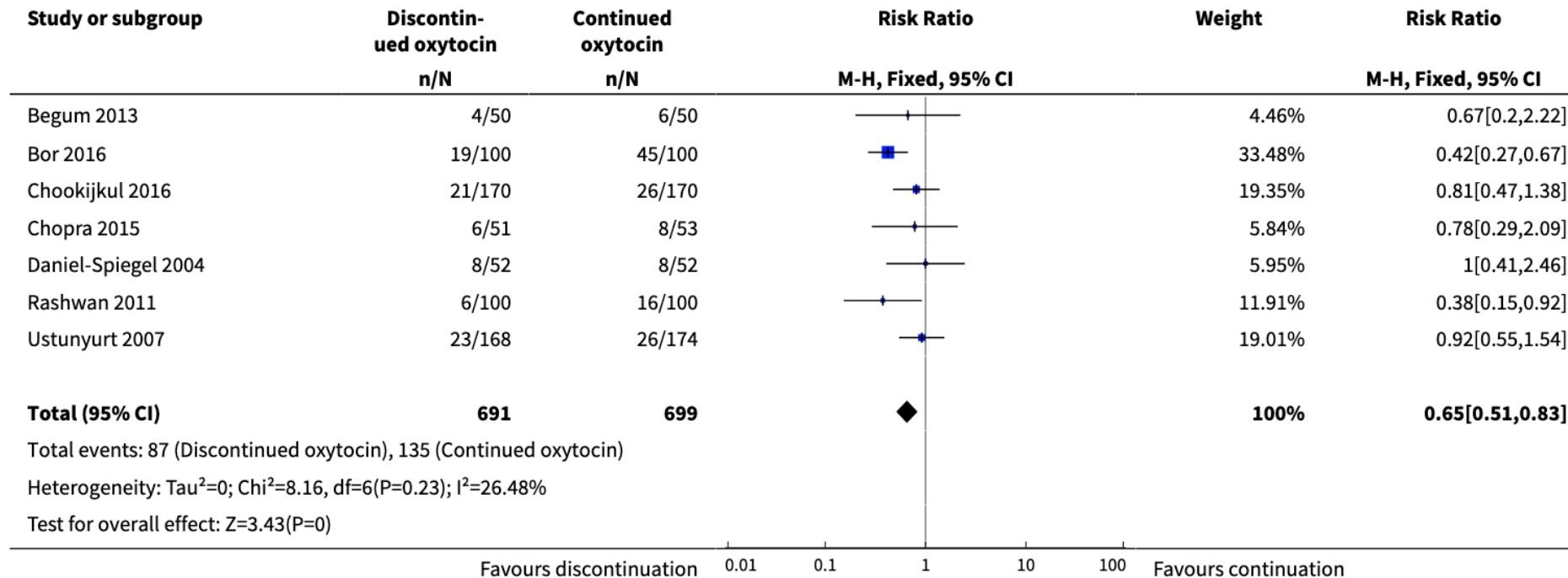
Analysis 1.5. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 5 Uterine tachysystole.





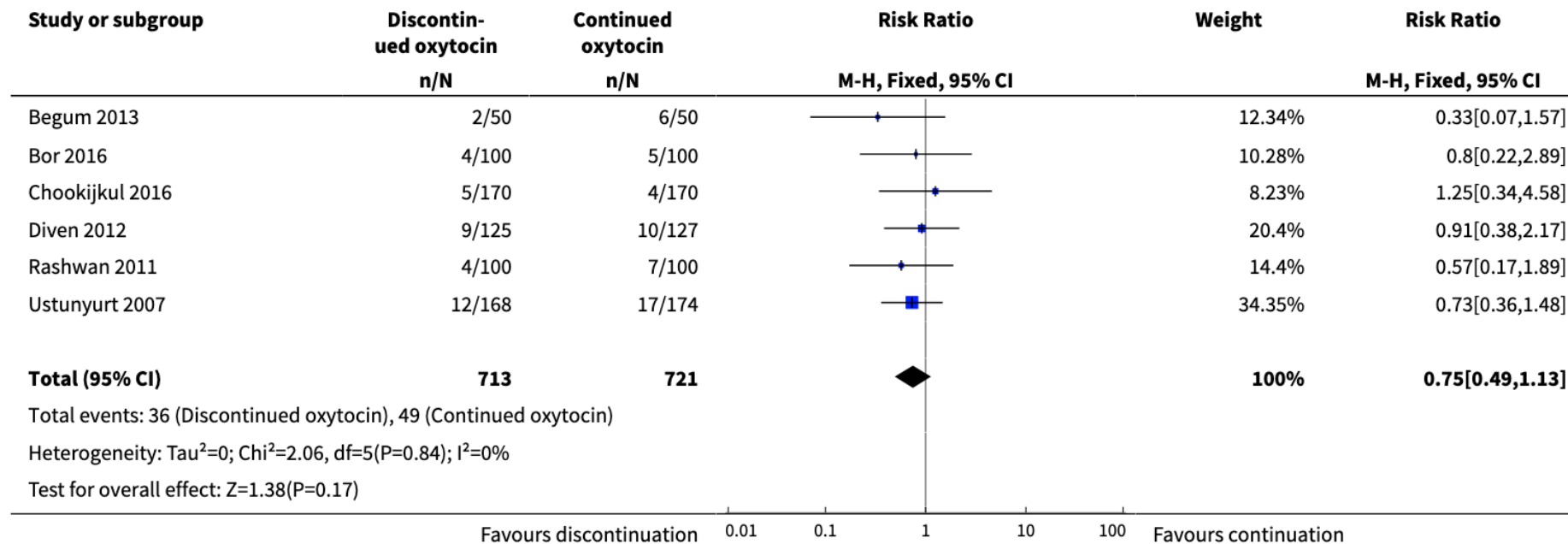
Rationnel – ARCF

Analysis 1.12. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 12 Intrapartum cardiotocography (CTG) abnormalities (suspicious/pathological CTGs).



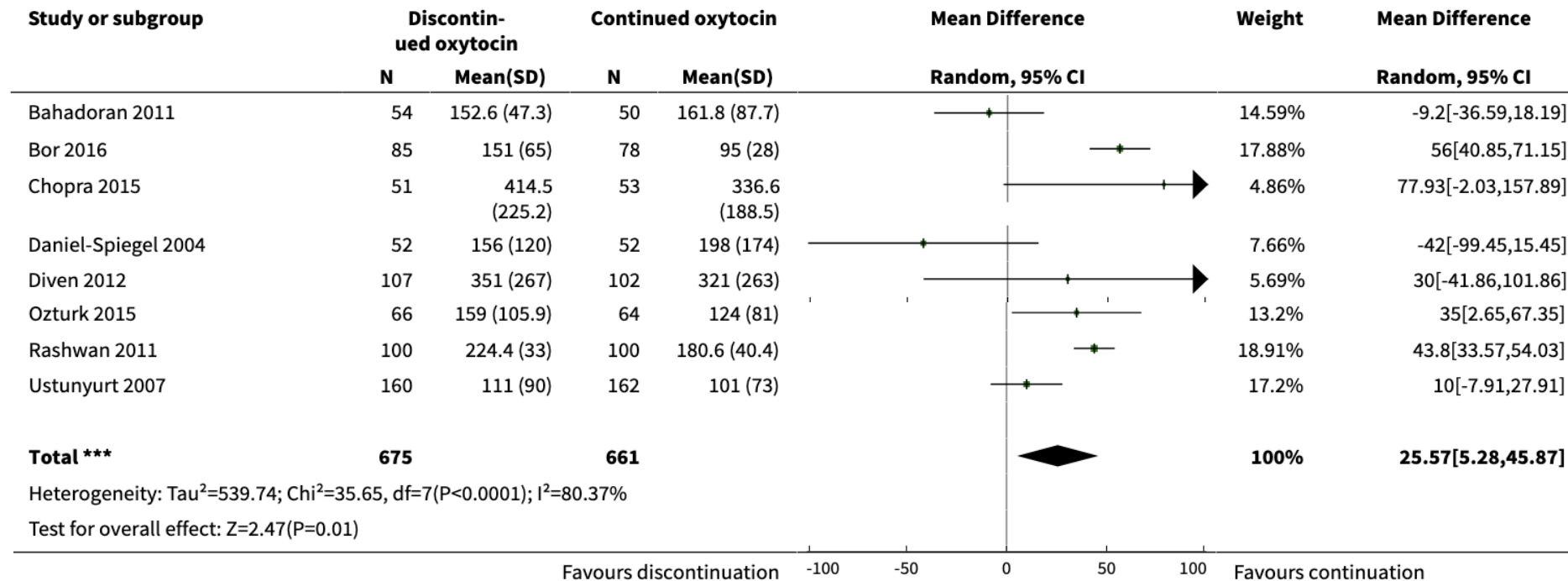
Rationnel – Admission NICU

Analysis 1.15. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 15 Neonatal admission to the neonatal intensive care unit.



Rationnel – Durée du travail

Analysis 1.2. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 2 Duration of the active phase of labour.





Rationnel- Oxytocine Discontinue

- Diminution du risque de césarienne
 - Diminution de risque d'hypercinésie et d'ARCF
 - Durée 1^{er} stade actif plus longue

 - Pas de modification du taux de transfert en réa néonat
- Morbidité néonatale ?



Objectif et critère principal

Evaluer l'impact de **l'arrêt de l'administration d'oxytocine en phase active** du premier stade du travail sur le **taux de morbidité néonatale**,

Critère de jugement principal **composite** :

- **pH artériel <7,10**
- **et/ou excès de base >10mmol/L**
- **et/ou lactates artériels >7mmol/L**
- **et/ou Apgar à 5 min <7**
- **et/ou admission en néonatalogie**



Objectifs Secondaires

Objectifs Secondaires :

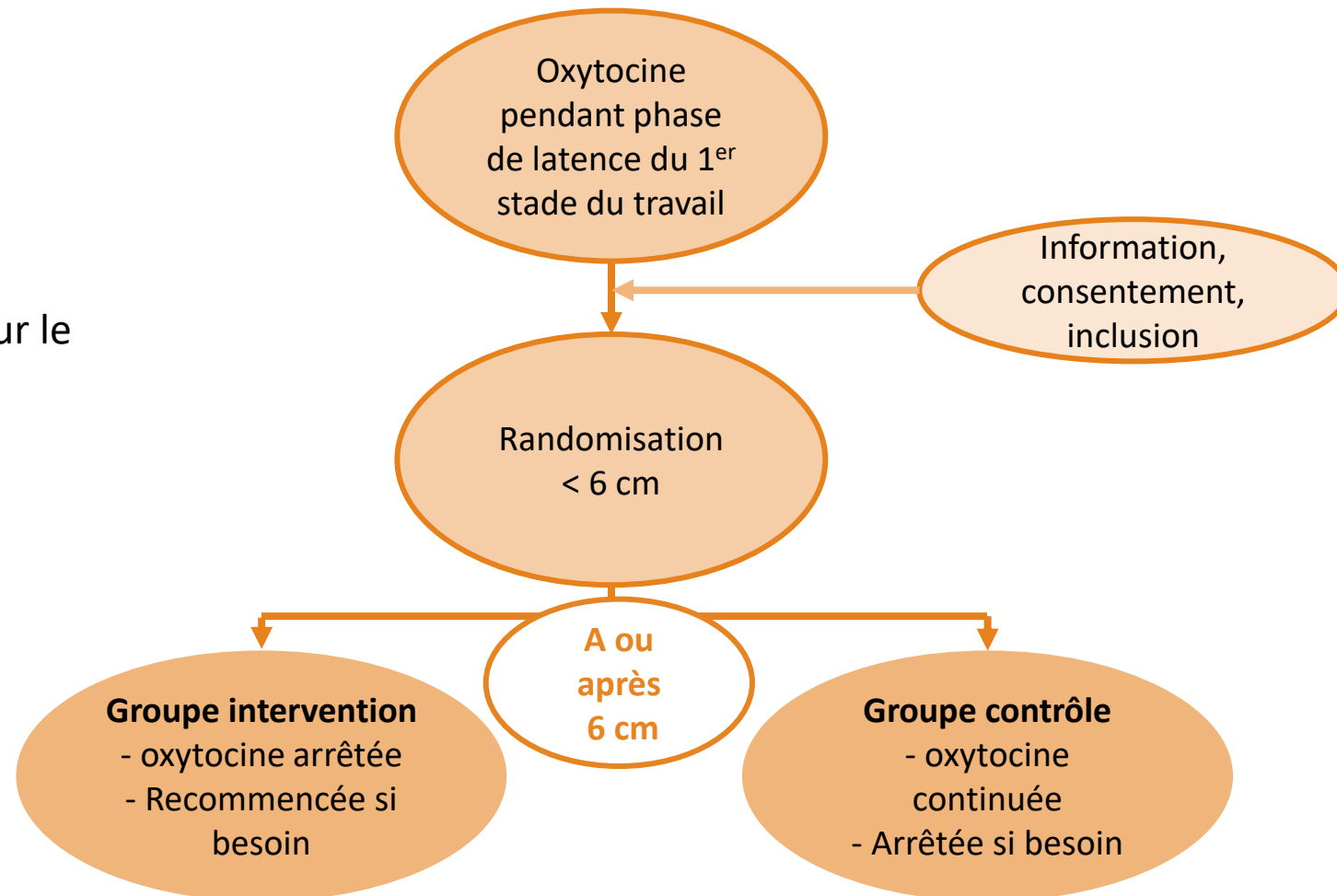
- autres critères de morbidité néonatale
- mode d'accouchement
- complications materno-foetales pdt travail et accouchement
- Le vécu maternel

Critères de jugement secondaires

- pH artériel <7,20, <7,10, <7,00
- réanimation à la naissance et hypothermie
- transfert en néonatalogie, durée d'hospit
- taux de césarienne et césarienne pour ARCF
- taux d'accouchement instrumental et pour ARCF
- durée travail
- hyperstimulation utérine
- présentation postérieure
- hyperthermie maternelle > 38°C
- HPP >500mL
- Labor Agency Scale avt sortie
- Edinburgh Postnatal Depression Scale à 2 mois PP

Design de l'étude

- RCT
- En ouvert
- Multicentrique
- Randomisation stratifiée sur le centre et parité



Critères d'inclusion



- Oxytocine pendant la phase de latence du premier stade du travail, <4cm
- Terme \geq 37 SA
- Grossesse unique
- Fœtus en présentation céphalique
- Parlant et lisant le Français
- Affiliée à la sécurité sociale (hors AME)

- Utérus cicatriciel
- RCIU ou PAG <3^{ème} percentile
- Fœtus avec anomalie congénitale
- ARCF à la randomisation
- Age maternel < 18 ans
- Participation à un autre essai impliquant des médicaments





Nombre de sujets à inclure

MEDIP : 8% morbidité néonatale parmi les femmes recevant de l'oxytocine (*Blanc-Petitjean et al, JGOBR 2017*)

Hypothèse : **diminution de 8% à 5%** du CJP

- 1125 femmes ds chaque gpe, puissance 80% et alpha 5%
- + 10% femmes incluses et/ou randomisées mais ayant césarienne avant début intervention (< 6 cm)

➔ **2475 femmes à inclure**

- Seul un essai (Bor et al,) diminution de 6% à 3% taux de pH <7,10 ds gpe oxytocine discontinuée
 - ➔ puissance de 91% avec notre échantillon

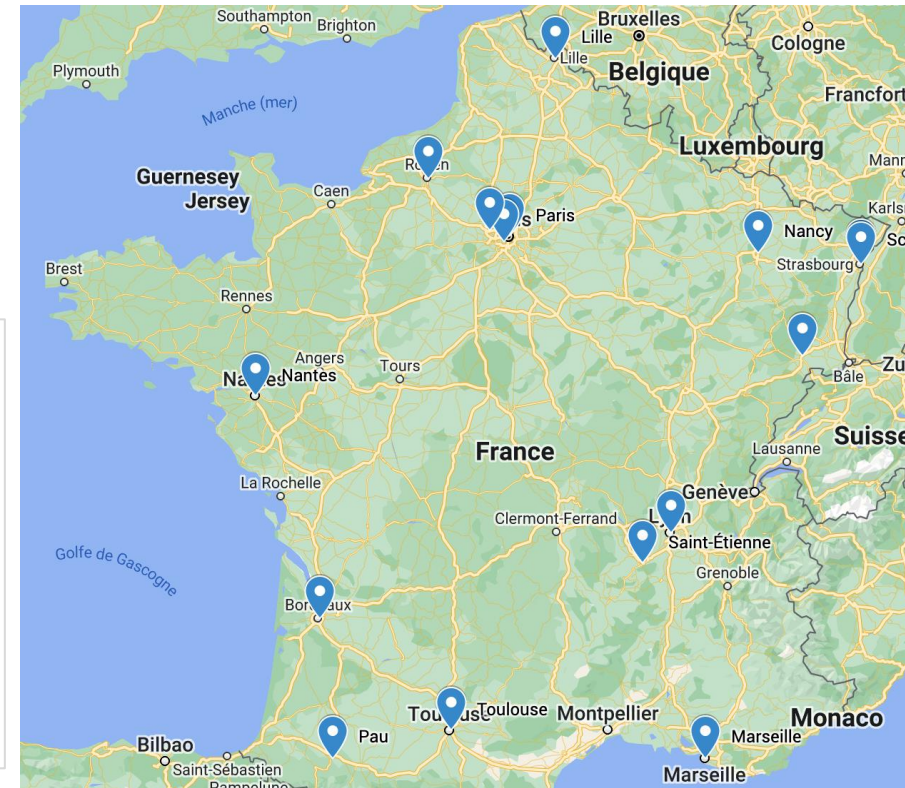
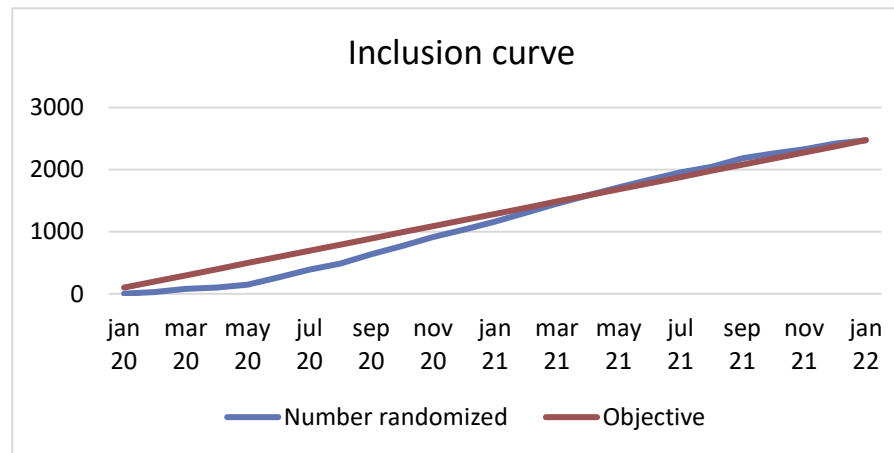


Stratégie d'analyse

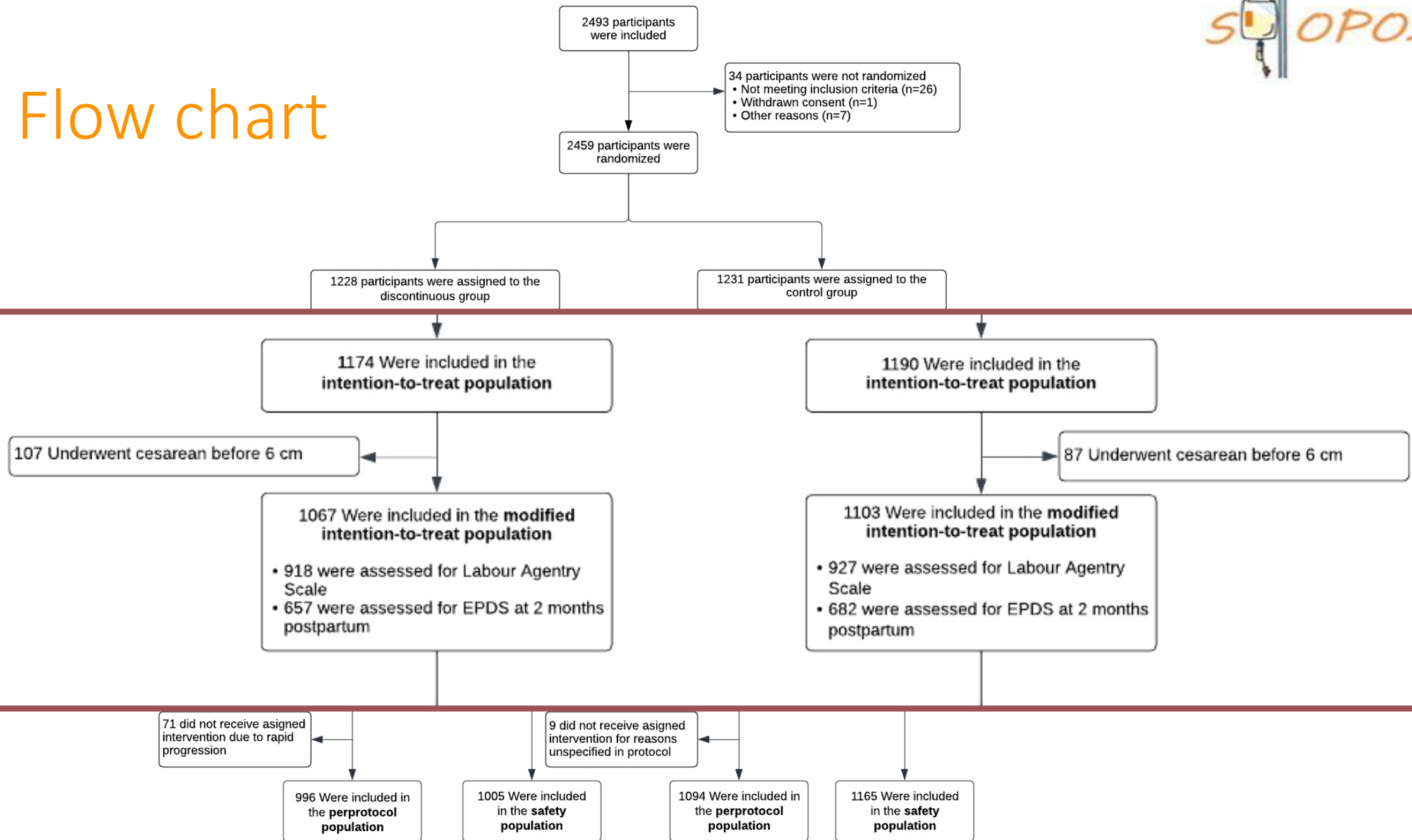
- Analyse descriptive des caractéristiques cliniques à l'inclusion:
 - moyenne \pm écarts-type ou médiane et intervalle interquartile
 - effectifs et pourcentages
- Analyse des critères de jugement principal et secondaires en intention de traiter modifiée (exclusion césarienne avant 6 cm): test du Chi-2, Mann Withney
- Deux analyses en sous-groupes : mode de début du travail, parité
- Analyse vécu de l'accouchement (Labor agency score, EPDS)

Inclusions

- Pendant 2 ans
- Janvier 2020-2022
- 2493 inclusions
- 2459 randomisations



Flow chart



Comparabilité groupes

- Age médian 32 ans
- IMC 24 kg/m²
- Nullipares 48%
- Déclenchement 81%
 - Rupture des membranes
 - Terme atteint
 - Pathologie maternelle
- Péridurale 98%

	Discontinuous oxytocin group (n=1067)	Continuous oxytocin group (n=1103)
Individual characteristics		
Maternal age, years	31 (28–35)	32 (28–35)
Pre-pregnancy BMI, kg/m ²	24.0 (21.0–28.0)*	24.0 (21.2–28.2)*
Smoking during pregnancy	99/1050 (9.4%)	96/1089 (8.8%)
Nulliparous	521/1067 (48.8%)	521/1103 (47.2%)
Preexisting pathology		
Chronic hypertension	18/1065 (1.7%)	20/1101 (1.8%)
Diabetes	11/1065 (1.0%)	18/1101 (1.6%)
Pathology during pregnancy		
Hypertensive disorder (gestational hypertension or pre-eclampsia)	53/1066 (5.0%)	47/1100 (4.3%)
Gestational diabetes	226/1066 (21.2%)	231/1101 (21.0%)
Labour onset		
Induction of labour	864/1067 (81.0%)	917/1103 (83.1%)
Indication for labour induction		
Ruptured membranes	183/864 (21.2%)	156/916 (17.0%)
Postdate pregnancy	180/864 (20.8%)	188/916 (20.5%)
Suspected macrosomia	97/864 (11.2%)	114/916 (12.4%)
Maternal pathology	179/864 (20.7%)	170/916 (18.6%)
Maternal request	103/864 (11.9%)	128/916 (14.0%)
Other indications†	122/864 (14.1%)	160/916 (17.5%)
First method of induction		
Amniotomy	68/864 (7.9%)	100/913 (11.0%)
Oxytocin	386/864 (44.7%)	375/913 (41.1%)
Dinoprostone vaginal slow-release system	126/864 (14.6%)	143/913 (15.7%)
Misoprostol	130/864 (15.0%)	98/913 (10.7%)
Balloon catheter	124/864 (14.3%)	162/913 (17.7%)
Prepidil or prostin gel	30/864 (3.5%)	35/913 (3.8%)
Epidural analgesia	1044/1067 (97.8%)	1081/1103 (98.0%)

Data are n/N (%) or median (IQR). *Data on pre-pregnancy BMI were missing for 21 participants in the discontinuous oxytocin group and 12 in the continuous oxytocin group. †Oligohydramnios, reduced fetal movements, SGA above the third percentile, late-pregnancy bleeding, or maternal anxiety.

Table 1: Baseline participant and pregnancy characteristics in the modified intention-to-treat population



Contraste entre les deux groupes

	Discontinuous oxytocin group (n=1067)	Continuous oxytocin group (n=1103)
Cervical dilation at oxytocin onset, cm	2 (2-3)*	2 (2-3)*
Cervical dilation at inclusion, cm	2 (2-3)	2 (2-3)†
Total duration of oxytocin infusion, min	345 (221-541)	424 (290-630)‡
Total dose of oxytocin received during labour, mUI	1921 (990-3965)	2599 (1405-4814)§
Oxytocin restarted after 6 cm dilation	432/1067 (40.5%)	NA
Oxytocin stopped after 6 cm dilation for abnormal fetal heart rate or hypertonus	NA	58/1102 (5.3%)
Duration from oxytocin onset to active labour, min	260 (170-396)¶	262 (168-395)¶

Data are n/N (%) or median (IQR). *Data on cervical dilation at oxytocin onset were missing for two participants of the discontinuous oxytocin group and four participants of the continuous oxytocin group. †Data on cervical dilation at inclusion were missing for one participant of the discontinuous oxytocin group. ‡Data on total duration of oxytocin infusion were missing for one participant of the continuous oxytocin group. §Data on total dose of oxytocin received during labour was missing for one participant of the continuous oxytocin group. ¶Data on duration from oxytocin onset to active labour were missing for 44 participants of the discontinuous oxytocin group and one participant of the continuous oxytocin group.

Table 2: Characteristics of oxytocin infusion in the modified intention-to-treat population

Oxytocine repris dans 40,5% groupe arrêt

Oxytocine arrêté dans 5,3% groupe contrôle



Morbidité néonatale et voie d'accouchement

	Discontinuous oxytocin group (n=1067)	Continuous oxytocin group (n=1103)	Relative risk or median difference (95% CI)
Primary outcome, neonatal morbidity at birth*	102/1067 (9.6%)	101/1103 (9.2%)	1.0 (0.8 to 1.4)
Secondary outcomes			
Severity of neonatal acidosis			
Umbilical arterial pH <7.20	178/1002 (17.8%)	192/1013 (18.9%)	0.9 (0.8 to 1.1)
Umbilical arterial pH <7.10	31/1002 (3.1%)	32/1013 (3.2%)	1.0 (0.6 to 1.6)
Umbilical arterial pH <7.00	0/1002 (0.0%)	5/1013 (0.5%)	..
Need for hypothermia	2/1067 (0.2%)	0/1103 (0.0%)	..
Mode of delivery			
Spontaneous	734/1067 (68.8%)	782/1103 (70.9%)	1.0 (0.9 to 1.0)
Instrumental vaginal delivery	219/1067 (20.5%)	212/1103 (19.2%)	1.1 (0.9 to 1.2)
Caesarean delivery	114/1067 (10.7%)	109/1103 (9.9%)	1.1 (0.8 to 1.3)
Caesarean for abnormal fetal heart rate	26/1067 (2.4%)	39/1103 (3.5%)	0.7 (0.4 to 1.1)
Instrumental delivery for abnormal fetal heart rate	80/1067 (7.5%)	97/1103 (8.8%)	0.8 (0.6 to 1.1)

fetal heart rate



Travail et complications

- 10 min, stade actif
- 37 min, 2^{ème} stade
- 47 min, intervention-accouchement
- Moins d'hyperstimulation utérine
- Pas différence échelles postpartum

	Discontinuous oxytocin group (n=1067)	Continuous oxytocin group (n=1103)	Relative risk or median difference (95% CI)
Course of labour			
Active first stage of labour duration†, min	100 (50 to 208)‡	90 (45 to 150)‡	10.0 (0.0 to 16.0)
Second stage duration, min	120 (33 to 184)§	83 (23 to 166)§	37.0 (21.0 to 51.0)
Active first stage to delivery duration ¶, min	244 (122 to 386)	197 (93 to 317)	47.0 (24.0 to 65.5)
Occiput-posterior presentation at delivery	37/1016 (3.6%)	41/1038 (3.9%)	0.9 (0.6 to 1.4)
Uterine tachysystole	62/978 (6.3%)	106/1019 (10.4%)	0.6 (0.4 to 0.8)
Maternal fever during labour	112/993 (11.3%)	117/1027 (11.4%)	1.0 (0.8 to 1.3)
Post-partum haemorrhage	111/960 (11.6%)	119/993 (12.0%)	1.0 (0.8 to 1.2)
Labour Agency Scale, score	163 (143 to 177)**	164 (145 to 177)**	-1.0 (-5.2 to 1.0)
Edinburgh Postnatal Depression Scale score >12	139/655 (21.2%)	141/680 (20.7%)	1.0 (0.8 to 1.3)



Analyse selon mode début travail

Primary outcome	Induced labor			Spontaneous labor		
	Discontinuous group (n = 864)	Control group (n = 917)	RR (95%CI)	Discontinuous group (n = 203)	Control group (n = 186)	RR (95%CI)
Neonatal morbidity, n (%)	82 (9.5)	78 (8.5)	1.1 (0.8 ; 1.5)	20 (9.8)	23 (12.4)	0.8 (0.4 ; 1.4)
Umbilical arterial pH <7.10	24 (3.0)	27 (3.2)		7 (3.7)	5 (2.9)	
Base excess >10mmol/L	26 (3.2)	31 (3.8)		6 (3.2)	5 (3.0)	
Umbilical arterial lactates >7 mmol/L	44 (5.6)	54 (6.6)		13 (7.1)	14 (8.3)	
5-minute Apgar score <7	10 (1.2)	9 (1.0)		1 (0.5)	1 (0.5)	
NICU admission	22 (2.5)	18 (2.0)		6 (3.0)	6 (3.2)	



Analyse selon parité

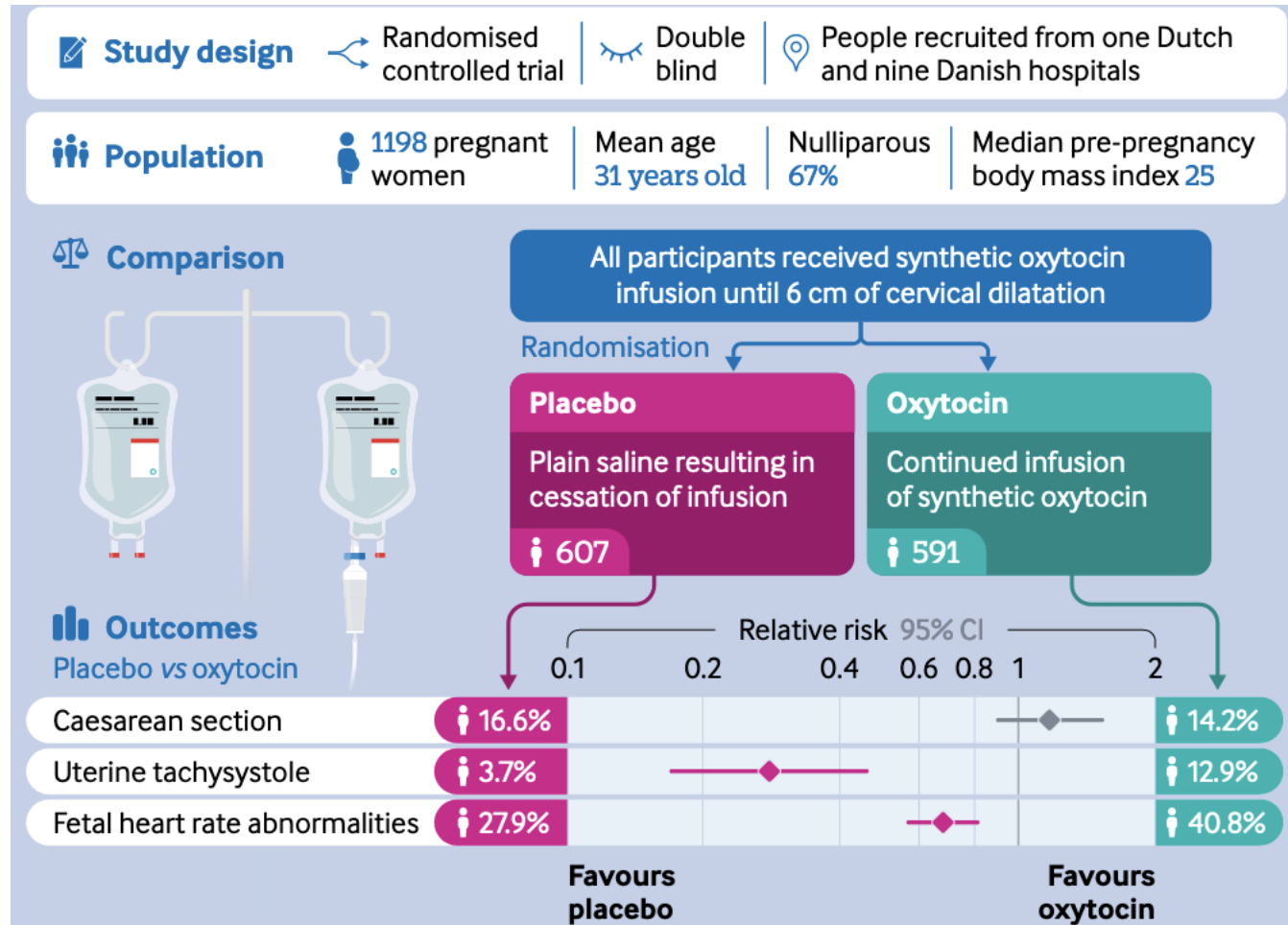
Primary outcome	Nulliparous			Multiparous		
	Discontinuous group	Control group	RR (95%CI)	Discontinuous group	Control group	RR (95%CI)
	(n = 546)	(n = 582)		(n = 521)	(n = 521)	
Neonatal morbidity, n (%)	75 (13.7)	88 (15.1)	0.9 (0.7 ; 1.2)	27 (5.2)	13 (2.5)	2.1 (1.1 ; 4.0)
Umbilical arterial pH <7.10	23 (4.5)	28 (5.2)		8 (1.6)	4 (0.8)	
Base excess >10mmol/L	25 (5.0)	30 (5.7)		7 (1.4)	6 (1.3)	
Umbilical arterial lactates >7 mmol/L	47 (9.4)	62 (11.8)		10 (2.1)	6 (1.3)	
5-minute Apgar score <7	7 (1.3)	8 (1.4)		4 (0.8)	2 (0.4)	
NICU admission	19 (3.5)	20 (3.4)		9 (1.7)	4 (0.8)	

Résumé des résultats

- Pas de différence sur critère de morbidité composite 9,6% dans le groupe d'oxytocine discontinue vs 9,2% dans groupe continue
- Pas de différence sur voie d'accouchement et HPP
- Différence modérée sur durée du travail
- Pas de différence sur vécu accouchement ni score dépression du postpartum

Condisox - Continued versus discontinued oxytocin stimulation in the active phase of labour

(CONDISOX): double blind randomised controlled trial, Sidsel Boie, et al.



Danemark et
Hollande,
4 ans
Femmes
déclenchées

42% de levée
d'aveugle



Stopoxy vs Condisox

	Discontinuous oxytocin		Continuous oxytocin	
	(n = 1175) n (%)	(n = 607) n (%)	(n = 1192) n (%)	(n = 591) n (%)
Neonatal morbidity	102 (9.6)	–	101 (9.2)	–
Arterial pH < 7.10	31 (3.1)	42 (6.9)	32 (3.2)	40 (6.8)
Base excess > 10 mmol/L	32 (3.2)	–	36 (3.6)	–
Lactates > 7 mmol/L	57 (5.8)	–	68 (6.9)	–
5-minute Apgar score <7	11 (1.0)	6 (1.0)	10 (0.9)	4 (0.7)
Transfer to NICU	28 (2.6)	52 (8.7)	24 (2.2)	52 (8.8)
Cesarean delivery rate	114 (10.7)	101 (16.6)	109 (9.9)	84 (14.2)
Uterine tachysystole	62 (6.3)	20 (3.7)	106 (10.4)	70 (12.9)
Severe PPH (>1000mL)	43 (4.0)	84 (13.8)	33 (3.1)	102 (17.3)
Oxytocin onset to delivery duration, minutes	516 [350-763]	535 [314-797]	477 [329-708]	477 [272-727]

Conclusions

- Pas de réduction (ni d'augmentation) de :
 - Morbidité néonatale
 - Taux de césarienne
 - Taux HPPlors de l'arrêt de l'oxytocine en phase active du premier stade du travail
- Augmentation de la durée du travail modérée (stade actif 10 min, stade actif-accouchement 47 min) mais sans effet sur le vécu maternel, ni score de dépression à 2mois PP.
- Dans 60% des cas l'oxytocine peut être arrêtée sans nécessité de reprise, il faut maintenant évaluer s'il existe des caractéristiques associées à la nécessité de reprise.



Rationale

Induction of labor

Subgroup description

Breastfeeding

Merci,
des questions?

Group comparability

Oxytocin protocol

EPDS

Open label design

Choice of open-label design

- After long discussions within the GROG
- Need for un-blinding would have been too frequent
- 30 to 40% in previous studies
 - Re-start in case of labor arrest
 - Stop in case of non-reassuring fetal heart rate





Regulatory framework

- Version du Protocole V1,1 du 11/07/2019
- Autorisation ANSM du 25/07/2019
- Avis Favorable CPP le 5/12/2019
- CNIL : MR001
- Financement: PHRCN 2018
- Clinical Trial : NCT03991091

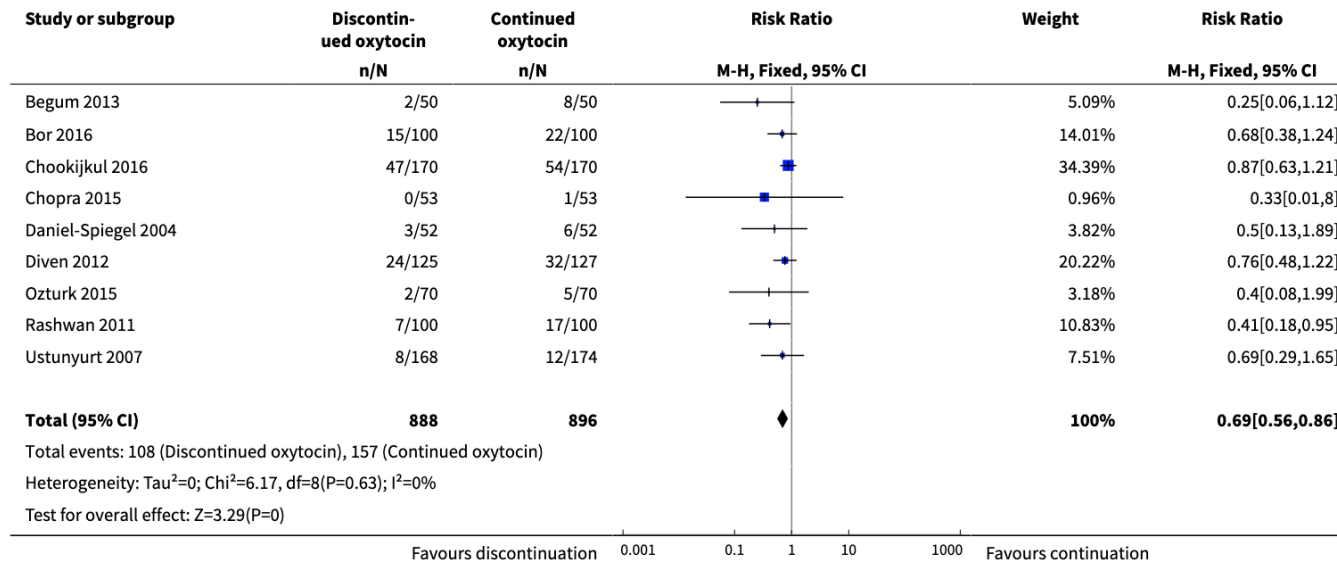


Stopoxy_mep_vn°1_201908
22



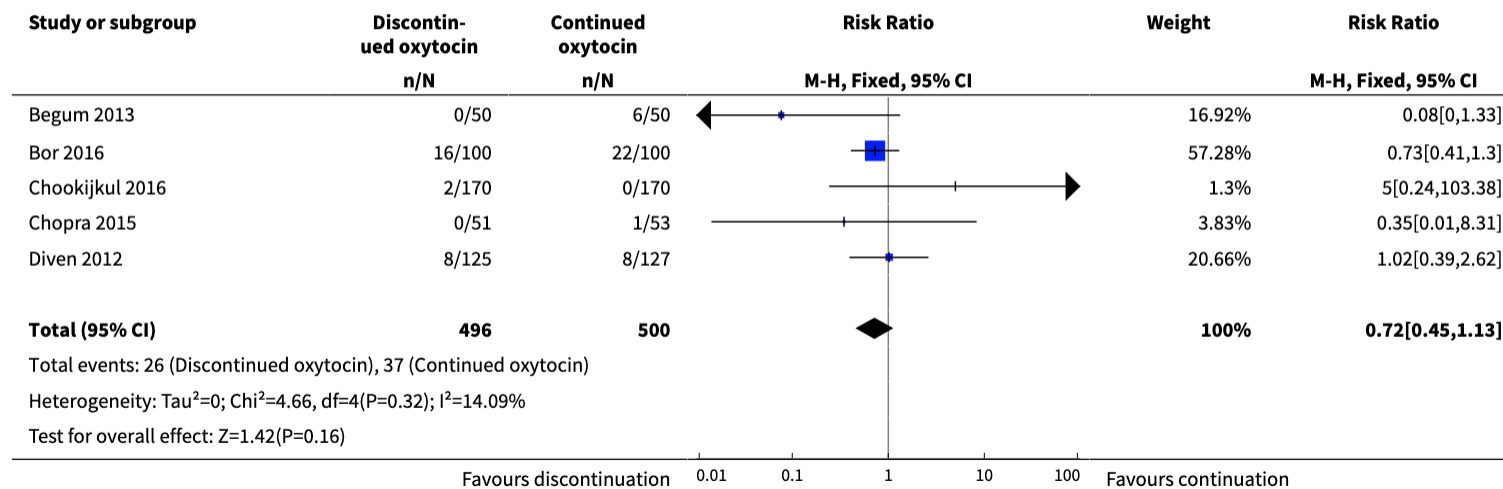
Rationale – Cesarean delivery

Analysis 1.1. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 1 Caesarean delivery.



Rationale – Postpartum hemorrhage

Analysis 1.3. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 3 Postpartum haemorrhage of 500 mL or more.

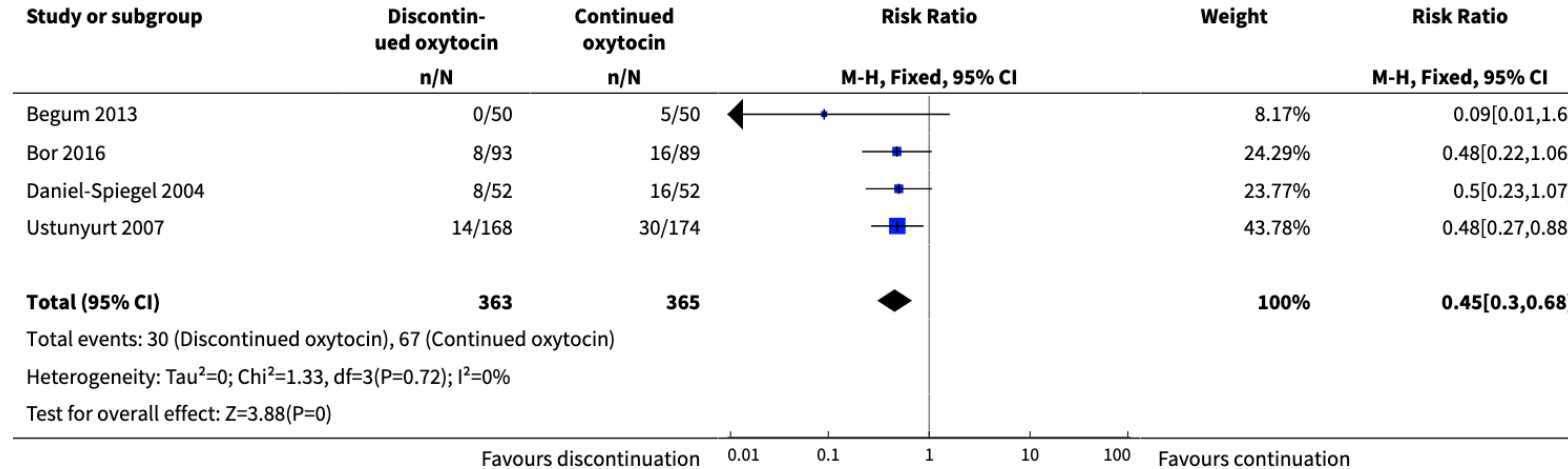


Boie S, et al. Cochrane Database Syst Rev 2018



Rationale – Uterine tachysystole

Analysis 1.5. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 5 Uterine tachysystole.

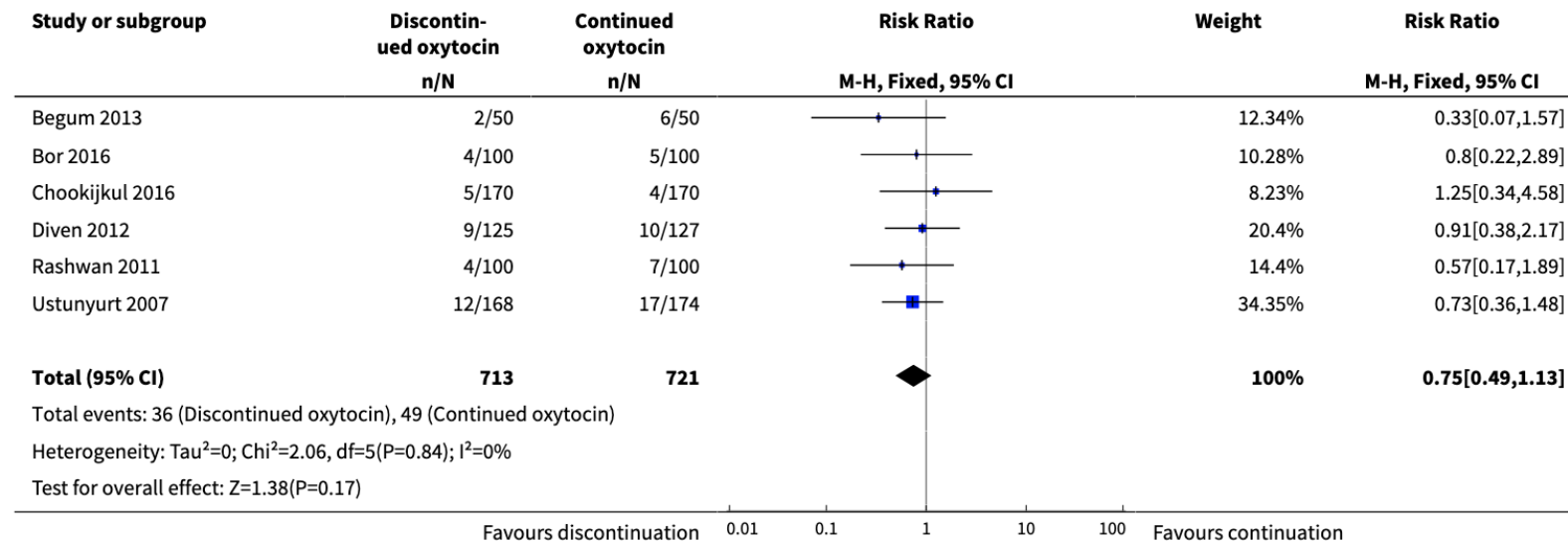


Boie S, et al. Cochrane Database Syst Rev 2018



Rationale – Admission to NICU

Analysis 1.15. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 15 Neonatal admission to the neonatal intensive care unit.

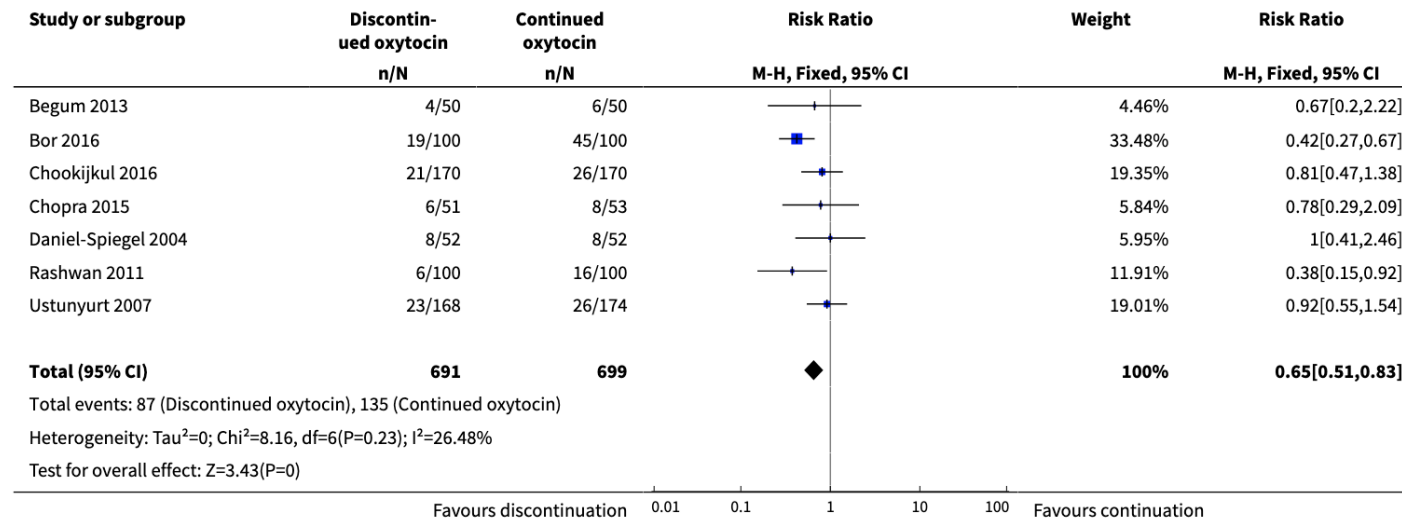


Boie S, et al. Cochrane Database Syst Rev 2018



Rationale – Abnormal fetal heart rate

Analysis 1.12. Comparison 1 Continued versus discontinued oxytocin stimulation in the active phase, Outcome 12 Intrapartum cardiotocography (CTG) abnormalities (suspicious/pathological CTGs).



Boie S, et al. Cochrane Database Syst Rev 2018



Oxytocin protocol

- Low dose oxytocin infusion
- Less than 4 mUI/min
(usually 2 to 2.5 mUI/min)
- Increments every 30 min
- Without exceeding a 20 mUI/min flow rate

Dupont C, et al. J Gynecol Obstet Hum
Reprod. 2017

5UI/50cc rate mL/h	5UI/500cc rate mL/h	Correspondance rate mUI/min
1,2	12	2
1,5	15	2,5
2,4	24	4
3	30	5
3,6	36	6
4,5	45	7,5
4,8	48	8
6	60	10
7,2	72	12
7,5	75	12,5
8,4	84	14
9	90	15
9,6	96	16
10,5	105	17,5
12	120	20
13,5	135	22,5
15	150	25



Group comparability – preexisting characteristics

	Discontinuous oxytocin (n = 1175) n (%)	Continuous oxytocin (n = 1192) n (%)
Age (years, median [IQR])	31 [28-35]	32 [28-35]
< 30	430 (34.6)	400 (33.6)
30-34	413 (35.1)	446 (37.4)
35-39	246 (20.9)	260 (21.8)
≥ 40	86 (7.3)	86 (7.2)
BMI (kg/m ² , median [IQR])	24.1 [21.1-28.3]	24,0 [21.3-28.1]
BMI ≥ 30 kg/m ²	225 (19.6)	207 (17.6)
Country of Birth		
France	844 (75.4)	847 (74.0)
Oversea French territories	19 (1.7)	19 (1.7)
Other	257 (22.9)	279 (24.4)
Universitary level of education	480 (81.6)	481 (83.6)
Smoking during pregnancy	112 (9.7)	105 (8.9)



Group comparability

	Discontinuous oxytocin (n = 1175) n (%)	Continuous oxytocin (n = 1192) n (%)
Parity (including ongoing pregnancy, median [IQR])	1 [1-2]	1 [1-2]
Nullipara	651 (55.4)	667 (56.1)
History of PPH	42 (4.2)	45 (4.5)
History of hypertensive disorder	19 (5.1)	20 (5.2)
Chronic diabetes	13 (3.5)	21 (5.4)
Cervical dilation at inclusion (cm, median [IQR])	2 [2-3]	2 [2-3]
Cervical dilation at oxytocin onset (cm, median [IQR])	2 [2-3]	2 [2-3]
Oxytocin flow rate at inclusion (mUI/min, median [IQR])	4 [2-6]	4 [2-6]
Artificial membrane rupture	738 (63.6)	781 (66.2)



Induction of labor methods

	Discontinuous oxytocin (n = 955) n (%)	Continuous oxytocin (n = 993) n (%)
Amniotomy	71 (7.4)	101 (10.2)
Oxytocin	400 (41.9)	382 (38.6)
Dinoprostone slow-release vaginal insert	149 (15.6)	162 (16.4)
Prostin gel	6 (0.6)	11 (1.1)
Dinoprostone gel	21 (2.2)	23 (2.3)
Oral misoprostol	148 (15.5)	125 (12.6)
Trancervical balloon	157 (16.4)	183 (18.5)
Other	3 (0.3)	2 (0.2)



Breastfeeding questionnaire at 2 months PP

	Discontinuous oxytocin (n= 717) n (%)	Continuous oxytocin (n= 745) n (%)	p
Breastfeeding wish before delivery			0.73
No	130 (18.4)	127 (17.2)	
Yes	517 (73.0)	554 (74.9)	
I didn't know	61 (8.6)	59 (8.0)	
Did you breastfeed?			0.43
No	199 (28.1)	194 (26.2)	
Yes	509 (71.9)	545 (73.7)	
If yes *			0.72
Still breastfeed exclusively	242 (47.5)	268 (49.2)	
Mixed feeding	128 (25.1)	140 (25.7)	
Stopped	139 (27.3)	137 (25.1)	

* On the 509 and 545 patients who breastfed

EPDS



In the past 7 days:

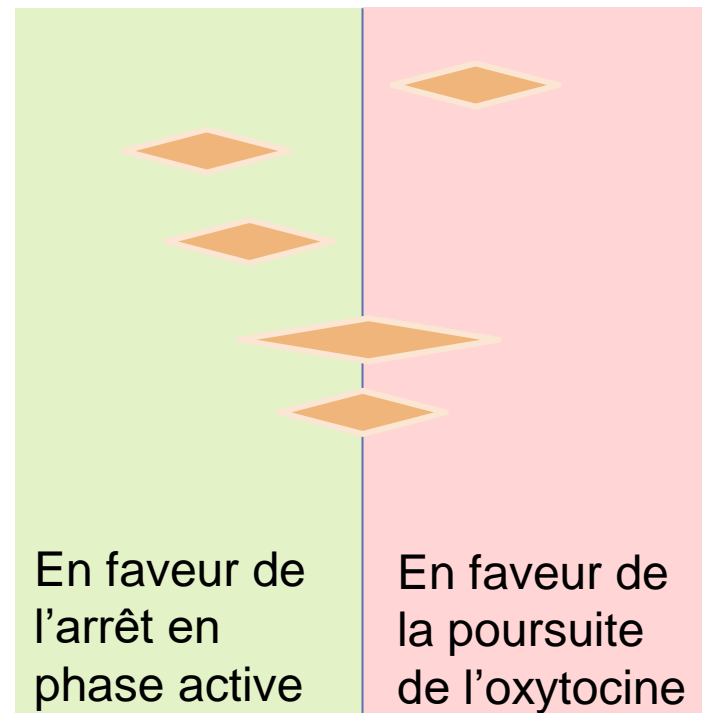
1. I have been able to laugh and see the funny side of things
 - As much as I always could
 - Not quite so much now
 - Definitely not so much now
 - Not at all
2. I have looked forward with enjoyment to things
 - As much as I ever did
 - Rather less than I used to
 - Definitely less than I used to
 - Hardly at all
- *3. I have blamed myself unnecessarily when things went wrong
 - Yes, most of the time
 - Yes, some of the time
 - Not very often
 - No, never
4. I have been anxious or worried for no good reason
 - No, not at all
 - Hardly ever
 - Yes, sometimes
 - Yes, very often
- *5. I have felt scared or panicky for no very good reason
 - Yes, quite a lot
 - Yes, sometimes
 - No, not much
 - No, not at all
- *6. Things have been getting on top of me
 - Yes, most of the time I haven't been able to cope at all
 - Yes, sometimes I haven't been coping as well as usual
 - No, most of the time I have coped quite well
 - No, I have been coping as well as ever
- *7. I have been so unhappy that I have had difficulty sleeping
 - Yes, most of the time
 - Yes, sometimes
 - Not very often
 - No, not at all
- *8. I have felt sad or miserable
 - Yes, most of the time
 - Yes, quite often
 - Not very often
 - No, not at all
- *9. I have been so unhappy that I have been crying
 - Yes, most of the time
 - Yes, quite often
 - Only occasionally
 - No, never
- *10. The thought of harming myself has occurred to me
 - Yes, quite often
 - Sometimes
 - Hardly ever
 - Never

Rationnel de l'étude

Review, 10 études, N=1888, plus large essai 342 femmes

- CJP des essais : durée phase active
- CJS des essais : césarienne, hypercinésie, HPP, pH<7,10
- Résultats :

- durée du travail
- césarienne
- hypercinésie utérine
- HPP
- pH<7,10





Questionnaires

Après l'accouchement, **deux questionnaires**:

- **En suite de couche**
 - Auto questionnaire (Labor Agency Scale Questionnaire), format papier
- **A 2 mois du post-partum**
 - Questionnaire (Experience of childbirth questionnaire, EPDS), e-version
 - par Email (ou courrier, et relance téléphone)

Table S2. Baseline, pregnancy and oxytocin characteristics of induced and spontaneous labor subgroups in the modified intention-to-treat population

Baseline characteristics	Induced labor		Spontaneous labor	
	Discontinuous group (n = 864)	Control group (n = 917)	Discontinuous group (n = 203)	Control group (n = 186)
Individual characteristics				
Maternal age, years	32 [28; 35]	32 [29; 35]	30 [26; 34]	31 [27; 34]
Pre-pregnancy BMI, kg/m ²	24.2 [21.1; 28.1]*	24.1 [21.3; 28.4]*	23.5 [20.7; 27.6]*	23.1 [20.8; 26.7]*
Smoking during pregnancy	86/848 (10.1%)	80/906 (8.8%)	13/202 (6.4%)	16/183 (8.7%)
Nulliparous	410/864 (47.4%)	443/917 (48.3%)	136/203 (67.0%)	139/186 (74.7%)
Preexisting pathology				
Chronic hypertension	16/863 (1.8%)	19/915 (2.1%)	2/202 (1.0%)	1/186 (0.5%)
Diabetes	10/863 (1.2%)	17/915 (1.9%)	1/202 (0.5%)	1/186 (0.5%)
Pathology during pregnancy				
Hypertensive disorder (gestational hypertension or preeclampsia)	53/863 (6.1%)	45/915 (4.9%)	0/203 (0.0%)	2/185 (1.1%)
Gestational diabetes	199/863 (23.1%)	198/915 (21.6%)	27/203 (13.3%)	33/186 (17.7%)
Labor onset				
Epidural analgesia	843/864 (97.6%)	895/917 (97.6%)	201/203 (99.0%)	186/186 (100.0%)
Oxytocin				
Cervical dilation at oxytocin onset, cm	2 [2; 2]§	2 [2; 3]§	3 [2; 3]§	3 [2; 3]§
Cervical dilation at inclusion, cm	2 [2; 3]	2 [2; 3]	3 [3; 3]	3 [3; 4]
Total duration of oxytocin infusion, min	357 [228; 553]	434 [303; 654]¶	295 [196; 457]	355 [254; 556]
Total dose of oxytocin received during labor, mUI	2065 [1077; 4106]	2817 [1481; 5164]**	1394 [783; 2928]	1938 [1160; 3587]
Oxytocin restarted after 6cm	337/864 (39.0%)	NA	95/203 (46.8%)	NA
Oxytocin stopped after 6cm for abnormal fetal heart rate or hypertonus	NA	40/916 (4.4%)	NA	18/186 (9.7%)
Duration from oxytocin onset to active labor, min	274 [180; 420] ⁺	278 [182; 420] ⁺	201 [130; 312] ⁺	200 [131; 276] ⁺

Table S3. Baseline, pregnancy and oxytocin characteristics of nulliparous and multiparous subgroups in the modified intention-to-treat population

OXY

	Nulliparous		Multiparous	
	Discontinuous group (n = 546)	Control group (n = 582)	Discontinuous group (n = 521)	Control group (n = 521)
Individual characteristics				
Maternal age, years	30 [26; 33]	30 [27; 33]	33 [30; 37]	33 [30; 36]
Pre-pregnancy BMI, kg/m ²	23.6 [20.8; 27.2]*	23.4 [20.8; 27.5]*	24.5 [21.2; 28.8]*	24.4 [21.5; 28.6]*
Smoking during pregnancy	42/536 (7.8%)	48/573 (8.4%)	57/514 (11.1%)	48/516 (9.3%)
Preexisting pathology				
Chronic hypertension	4/544 (0.7%)	10/581 (1.7%)	14/521 (2.7%)	10/520 (1.9%)
Diabetes	5/544 (0.9%)	5/580 (0.9%)	6/521 (1.1%)	13/521 (2.5%)
Pathology during pregnancy				
Hypertensive disorder (gestational hypertension or preeclampsia)	28/546 (5.1%)	27/580 (4.7%)	25/520 (4.8%)	20/520 (3.8%)
Gestational diabetes	98/545 (18.0%)	108/580 (18.6%)	128/521 (24.6%)	123/521 (23.6%)
Labor onset				
Induction of labor	410/546 (75.1%)	443/582 (76.1%)	454/521 (87.1%)	474/521 (91.0%)
Indication for labor induction				
Ruptured membranes	110/410 (26.8%)	98/443 (22.1%)	73/454 (16.1%)	58/473 (12.3%)
Postdate pregnancy	98/410 (23.9%)	109/443 (24.6%)	82/454 (18.1%)	79/473 (16.7%)
Suspected macrosomia	28/410 (6.8%)	37/443 (8.3%)	69/454 (15.2%)	77/473 (16.3%)
Maternal pathology	85/410 (20.7%)	80/443 (18.1%)	94/454 (20.7%)	90/473 (19.0%)
Maternal request	25/410 (6.1%)	35/443 (7.9%)	78/454 (17.2%)	93/473 (19.7%)
Other indications [†]	64/410 (15.6%)	84/443 (19.0%)	58/454 (12.8%)	76/473 (16.1%)
First method of induction				
Amniotomy	24/410 (5.8%)	38/442 (8.6%)	44/454 (9.7%)	62/471 (13.2%)
Oxytocin	123/410 (30.0%)	128/442 (29.0%)	263/454 (57.9%)	247/471 (52.4%)
Dinoprostone vaginal slow-release system	79/410 (19.3%)	89/442 (20.1%)	47/454 (10.4%)	54/471 (11.5%)
Misoprostol	82/410 (20.0%)	67/442 (15.2%)	48/454 (10.6%)	31/471 (6.6%)
Balloon catheter	82/410 (20.0%)	96/442 (21.7%)	42/454 (9.2%)	66/471 (14.0%)

Table S3. Baseline, pregnancy and oxytocin characteristics of nulliparous and multiparous subgroups in the modified intention-to-treat population

2XY

	Nulliparous		Multiparous	
	Discontinuous group (n = 546)	Control group (n = 582)	Discontinuous group (n = 521)	Control group (n = 521)
Prepidil or prostin gel	20/410 (4.9%)	24/442 (5.4%)	10/454 (2.2%)	11/471 (2.3%)
Epidural analgesia	542/546 (99.3%)	579/582 (99.5%)	502/521 (96.3%)	502/521 (96.3%)
Oxytocin				
Cervical dilation at oxytocin onset, cm	2 [2; 3] [§]	2 [2; 3] [§]	2 [2; 2]	2 [2; 3]
Cervical dilation at inclusion, cm	3 [2; 3]	3 [2; 3]	2 [2; 3]	2 [2; 3]
Total duration of oxytocin infusion, min	437 [295; 687]	541 [385; 745]	275 [195; 395]	330 [242; 448] [¶]
Total dose of oxytocin received during labor, mUI	2528 [1304; 5103]	3708 [1835; 6539]	1483 [828; 2870]	1910 [1076; 3479] ^{**}
Oxytocin restarted after 6cm	312/546 (57.1%)	NA	120/521 (23.0%)	NA
Oxytocin stopped after 6cm for abnormal fetal heart rate or hypertonus	NA	41/582 (7.0%)	NA	17/520 (3.3%)
Duration from oxytocin onset to active labor, min	290 [195 ; 457] ⁺	300 [190 ; 451] ⁺	225 [155 ; 334] ⁺	232 [155 ; 320] ⁺

Data are n/N (%) or median [IQR].