

CELEBRATING THE 33RD ANNIVERSARY OF THE SAOA

*“OBSTETRIC ANAESTHESIA IN SWITZERLAND:
WHERE WE COME FROM, WHERE WE ARE, WHERE WE GO”*

MAINTENANCE OF LABOR EPIDURAL: OLD, NEW AND FUTURE?

Prof Georges Savoldelli
Service d'anesthésiologie, HUG

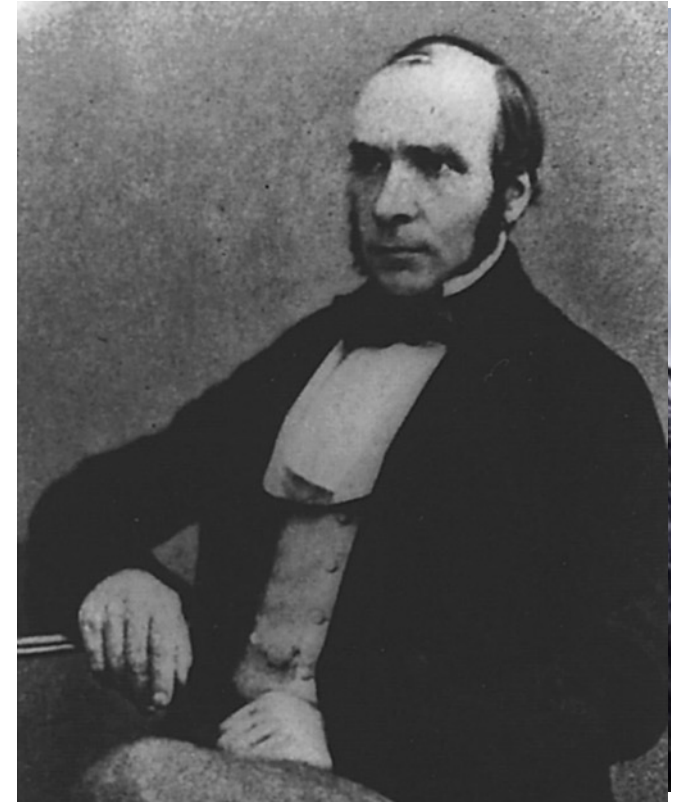
Plan

- **Impact of neuraxial analgesia on labor**
- **Local anesthetic mixture**
- **Maintenance technique**
- **The future...**

John Snow

*“The object being to **relieve the patient without diminishing the strength of uterine contractions** and the auxiliary action of the respiratory muscles, or with diminishing it as little as possible...”*

J Snow. On Chloroform and Other Anesthetics 1858



1813-1858

Epidural versus non-epidural or no analgesia for pain management in labour (Review)

Anim-Somuah M, Smyth RMD, Cyna AM, Cuthbert A

40 studies (1974-2017) involving 11'000 women

2018



The good !

Outcome efficacy vs opioids	N	RR or MD
Efficacy (Pain relief)	N = 1166	Epidural better (MD = -3.36)
Satisfaction (excellent or very good)	N = 1911	RR = 1.47 [1.03, 2.08]

Anim-Somuah M, Smyth RMD, Cyna AM, Cuthbert A

40 studies (1974-2017) involving 11'000 women

The good !

Outcome efficacy vs opioids	N	RR or MD
Efficacy (Pain relief)	N = 1166	Epidural better (MD = -3.36)
Satisfaction (excellent or very good)	N = 1911	RR = 1.47 [1.03, 2.08]
Outcome safety vs opioids	N	RR
Cesarean for dystocia	N = 5938	NS
Cesarean for fetal distress	N = 5735	NS
Oxytocin augmentation	N= 8351	RR = 1.12 [1.00, 1.26]
Malposition	N = 673	NS
Nausea and vomiting	N = 4440	RR = 0.62 [0.45, 0.87]
Long-term backache	N = 814	NS
Fetal acidosis (pH<7.2)	N = 4783	RR = 0.81 [0.69, 0.94]
NICU ; Apgar < 7@5'	N = 4488 ; N = 8752	Both NS

Anim-Somuah M, Smyth RMD, Cyna AM, Cuthbert A

40 studies (1974-2017) involving 11'000 women

The bad !

Outcome vs opioids	N	RR or MD
Motor blockade	N = 322	RR = 31.67
Instrumental delivery (Forceps/Vacuum)	N= 9948	RR = 1.44 [1.29, 1.60] → NNH = 25
Hypotension	N= 4212	RR = 11.34 [1.89, 67.95]
Duration of 1 st stage	N= 2259	MD = + 32.28 min [18.34, 46.22]
Duration of 2 nd stage	N= 4979	MD = + 15.38 min [8.97, 21.79]
Urinary retention	N = 343	RR = 14.18 [4.52, 44.45]
Maternal fever > 38 ° C.	N = 4276	RR = 2.51 [1.67, 3.77]

Anim-Somuah M, Smyth RMD, Cyna AM, Cuthbert A

40 studies (1974-2017) involving 11'000 women

The bad !

Outcome vs opioids	N	RR or MD
Motor blockade	N = 322	RR = 31.67
Instrumental delivery (Forceps/Vacuum)	N= 9948	RR = 1.44 [1.29, 1.60] → NNH = 25
Hyp	<p style="text-align: center;">IMPORTANT WARNING: These conclusions include the results of old trials and clinical practices that should no longer be used</p>	
Duration of 1 st stage	N= 2259	MD = + 32.28 min [18.34, 46.22]
Duration of 2 nd stage	N= 4979	MD = + 15.38 min [8.97, 21.79]
Urinary retention	N = 343	RR = 14.18 [4.52, 44.45]
Maternal fever > 38 ° C.	N = 4276	RR = 2.51 [1.67, 3.77]

Plan

- Impact of neuraxial analgesia on labor
- **Local anesthetic mixture**
- Maintenance technique
- The future...

slido



What is your standard solution (LA type; concentration; adjuvant) to maintain labor epidural analgesia?

① Start presenting to display the poll results on this slide.

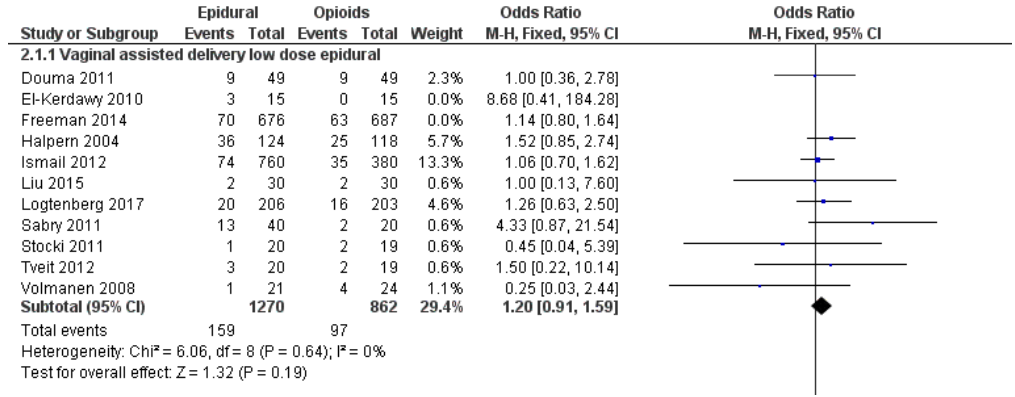
Low concentrations LA + lipophilic opioids is the standard ! (bupi \leq 0.1% or Ropi \leq 0.17%)

- **Reduced LA dose** (WMD -27.00; 95% CI -35.22 to -18.78)
- **Reduced motor blockade** (OR 3.90; 95% CI 1.59 to 9.55)
- **Shorter 2nd stage** (WMD -14.03; 95% CI -27.52 to -0.55)
- **Improved ambulation** (OR 2.80; 95% CI 1.10 to 7.14)
- **Reduced incidence of Instrumental delivery** (OR 0.7 ; 95 % CI 0.56 to 0.86)
- **Increased incidence of pruritus** (OR 3.36; 95% CI 1.00 to 11.31)

Let's redo the Cochrane review meta-analysis for instrumental delivery !

Studies using low dose LA

Opioids n/N : 97/862 = 11,3 %
 Epidural n/N: 159/1270 = 12.5 %
 RR = 1.20 [0.91, 1.59]
 NNH = 79 !



Let's redo the Cochrane review meta-analysis for instrumental delivery !

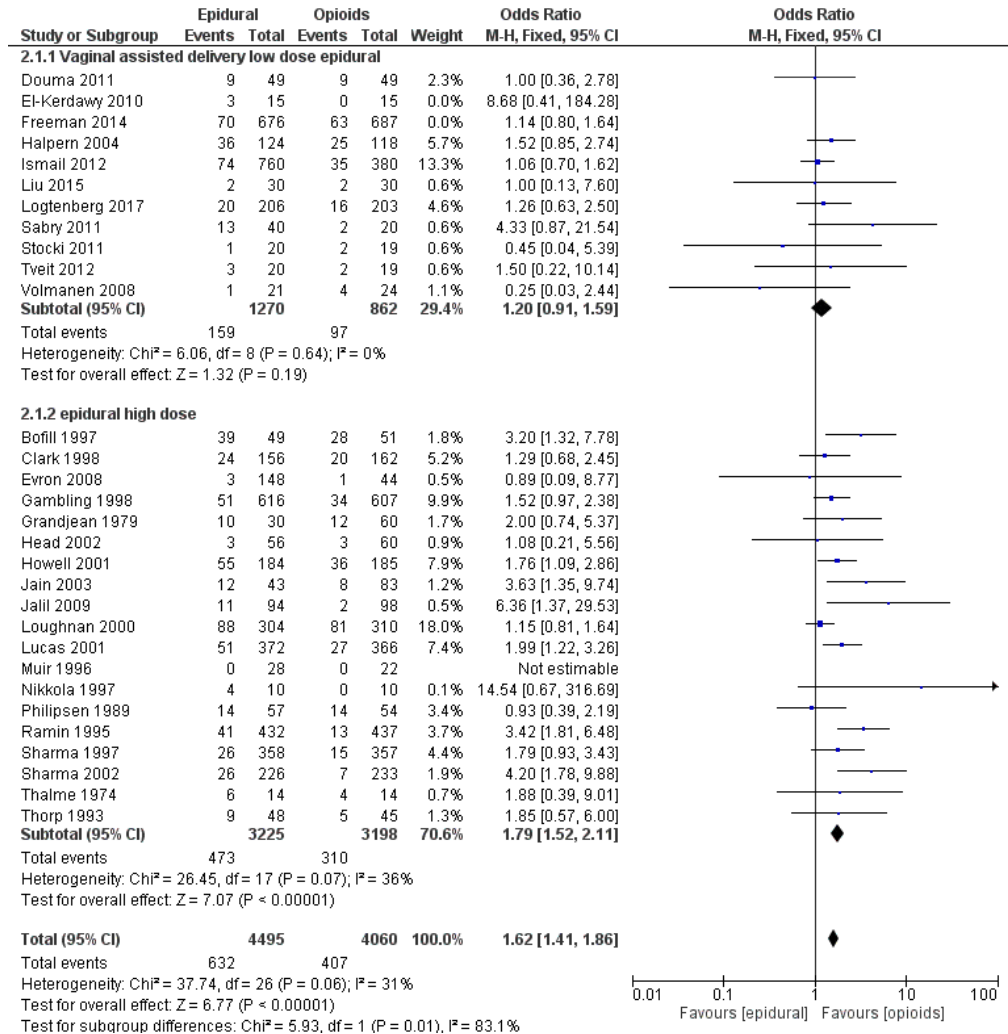
Studies using low dose LA

Opioids n/N : 97/862 = 11,3 %
 Epidural n/N: 159/1270 = 12.5 %
 RR = 1.20 [0.91, 1.59]
 NNH = 79 !

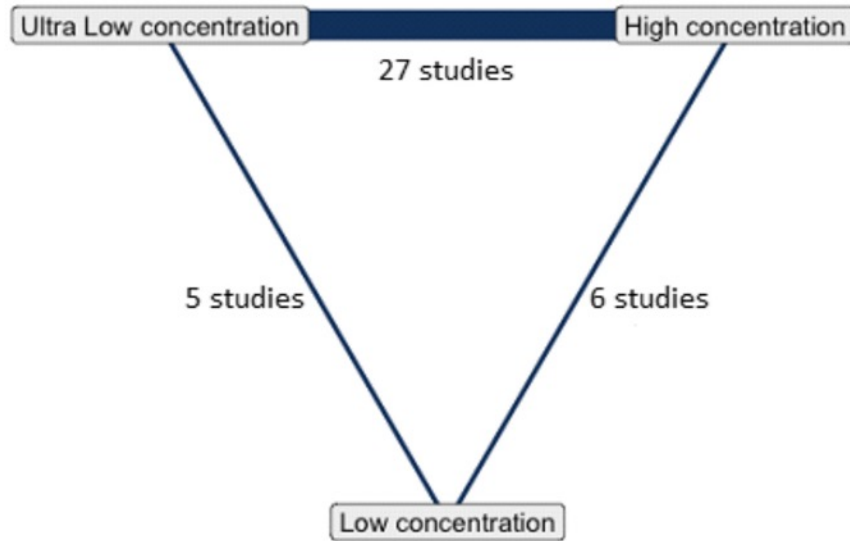
Studies using high doses LA

Opioids n/N : 310/3198 = 10.0 %
 Epidural n/N: 473/3225 = 14 %
 RR = 1.79 [1.52, 2.11]
 NNH = 16 !

Savoldelli GL & Haller G, unpublished data



Should we go for “ultra-low” concentration ? ≤0.08% bupivacaine or equivalent



“ Ultra-low concentration local anaesthetic for labour epidural achieves similar or better maternal and neonatal outcomes as low and high concentration, but with reduced local anaesthetic consumption.”

Ok then :

Concentration matters but what about the type of LA ?

Choice of LA : Less motor blockade using Ropivacaine (+FNT) ?

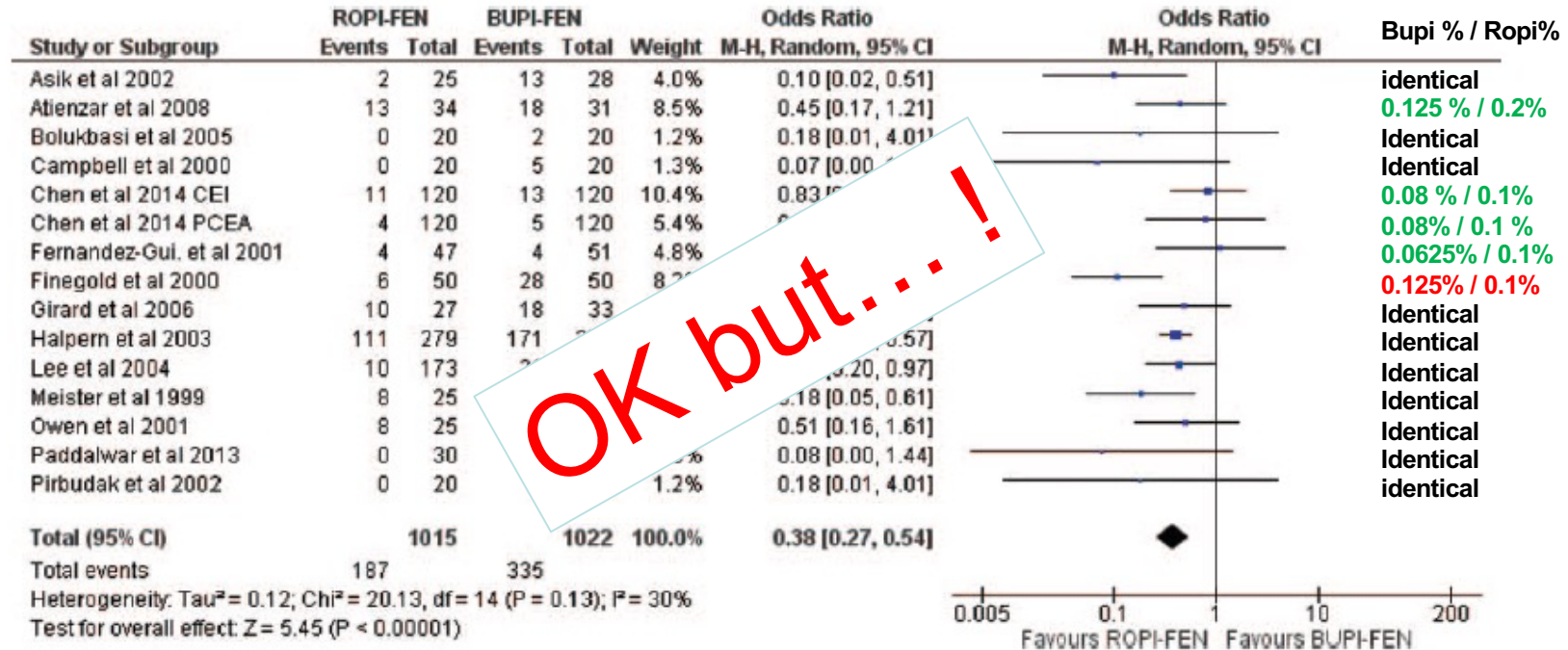


FIGURE 3. Forest plot showing significantly lower incidence of motor blockade in epidural ROPI-FEN administered women in the meta-analysis under random effects model. In Chen et al, 2014, PCEA = patient control epidural analgesia, CEI = continuous epidural infusion.

Potency ratio matters !

Ropi is less potent than Bupi

- Analgesic potency ratio of Ropi/Bupi \cong 60% (Poley 1999)
- Motor blockade potency ratio of Ropi/Bupi \cong 65-75%

Less motor blockade with Ropi compared to Bupi ?

- Yes, if used at identical concentrations !
- No, if used at equipotent concentrations: Ropi 0.1 % \cong Bupi 0.0625 %

Ropivacaine or Levobupivacaine or bupivacaine are equivalent choices for labor analgesia when used at equipotent doses with a lipophilic opioid

Plan

- Impact of neuraxial analgesia on labor
- Local anesthetic mixture
- **Maintenance technique**
- The future...

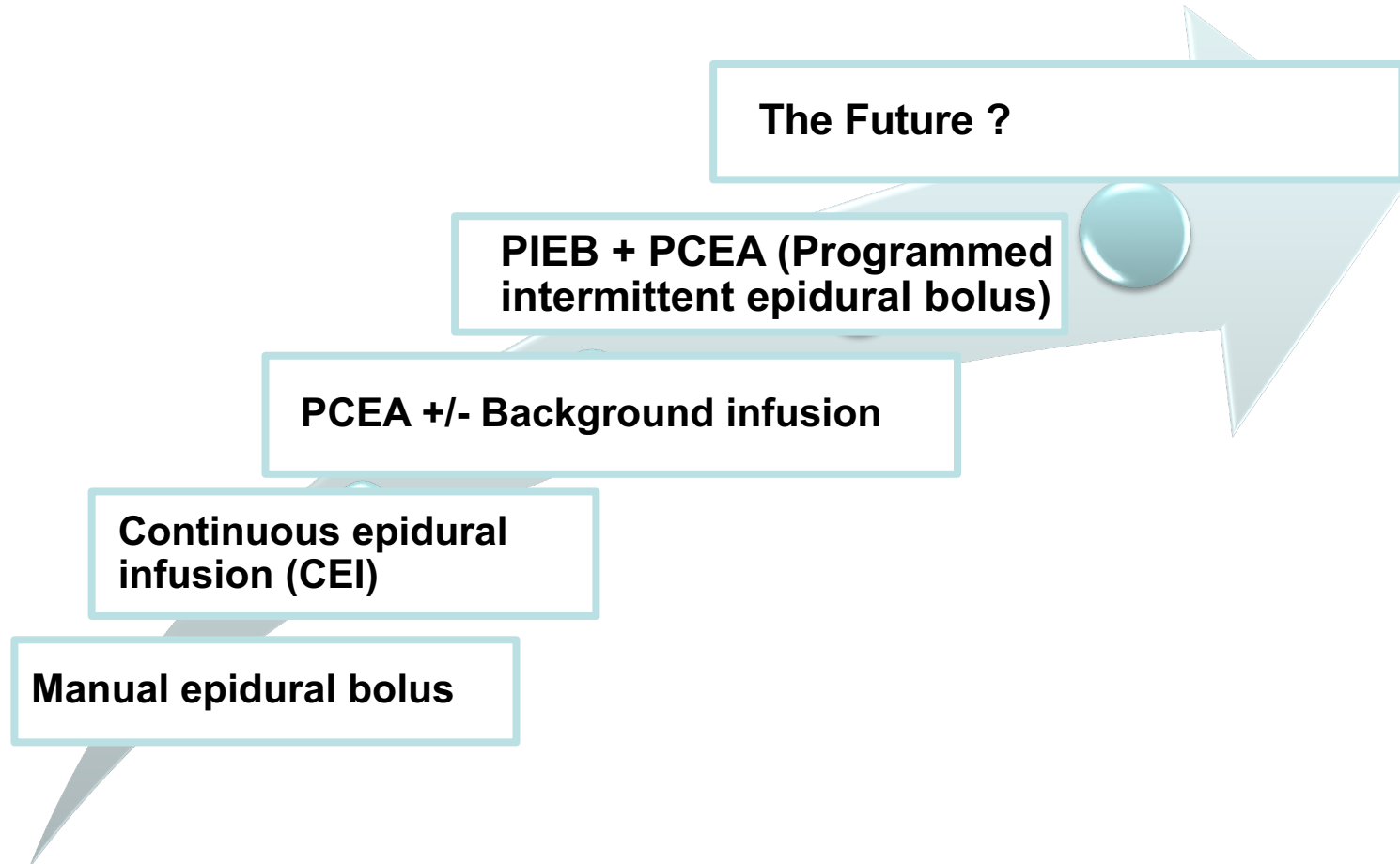
slido



How do you maintain labor epidural analgesia ?

① Start presenting to display the poll results on this slide.

Maintenance of labor epidural : What is the best option ?



PCEA an old story but still a benchmark !

- Women can tailor their analgesia as labor progresses

PCEA versus CEI (continuous epidural infusion)

- ↑ mother's autonomy
- ↑ mother's satisfaction
- ↑ motor function
- ↓ consumption of LA
- ↓ physician workload



*van der Vyver BJA 2002. 89(3); 459–465
Halpern & Carvalho. A&A 2009. 108(3); 921–928*

PCEA + background infusion: a double-edged sword !

The use of a background infusion rate ≥ 6 ml/h appears to:

↓ breakthrough pain

↓ workload (physician manual boluses)

Loubert et al. Anaesthesia, 2011; 66: 191–212

Meta-analysis of 7 high quality studies, background infusion :

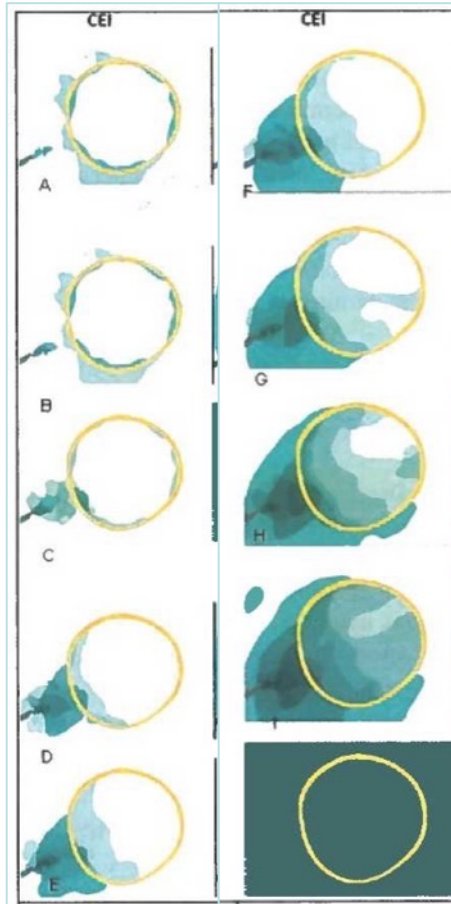
↑ risk of instrumental delivery (RR 1.66; 95% CI 1.08–2.56)

↑ duration of 2nd stage of labor (WMD 12.3 min; 95% CI 5.1–19.5)

↓ workload (physician manual boluses) (RR 0.35; 95% CI 0.25–0.47)

Heesen et al. A&A 2015;121: 149e58

Continuous infusion



Continuous infusion:

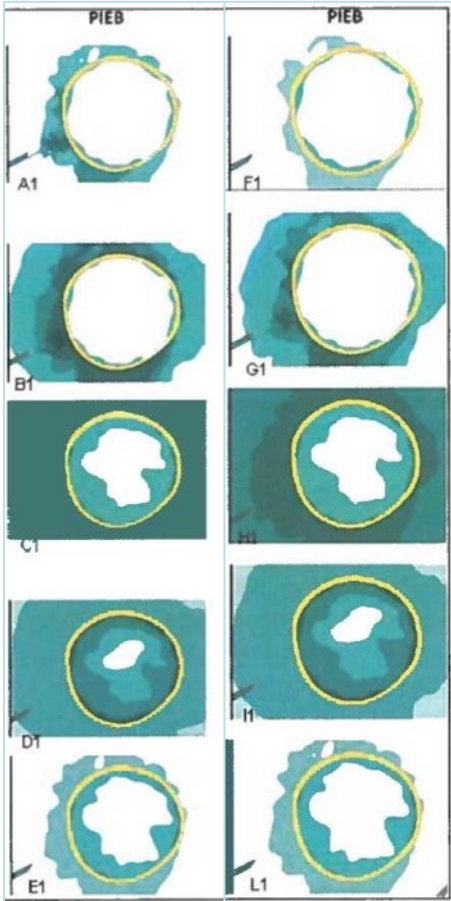
Longer time to reach steady state

Spread of LA less uniform

Concentration of LA inside the nerve increases over time

Threshold for motor block may be reached

Intermittent bolus



Intermittent bolus

Better spread of LA

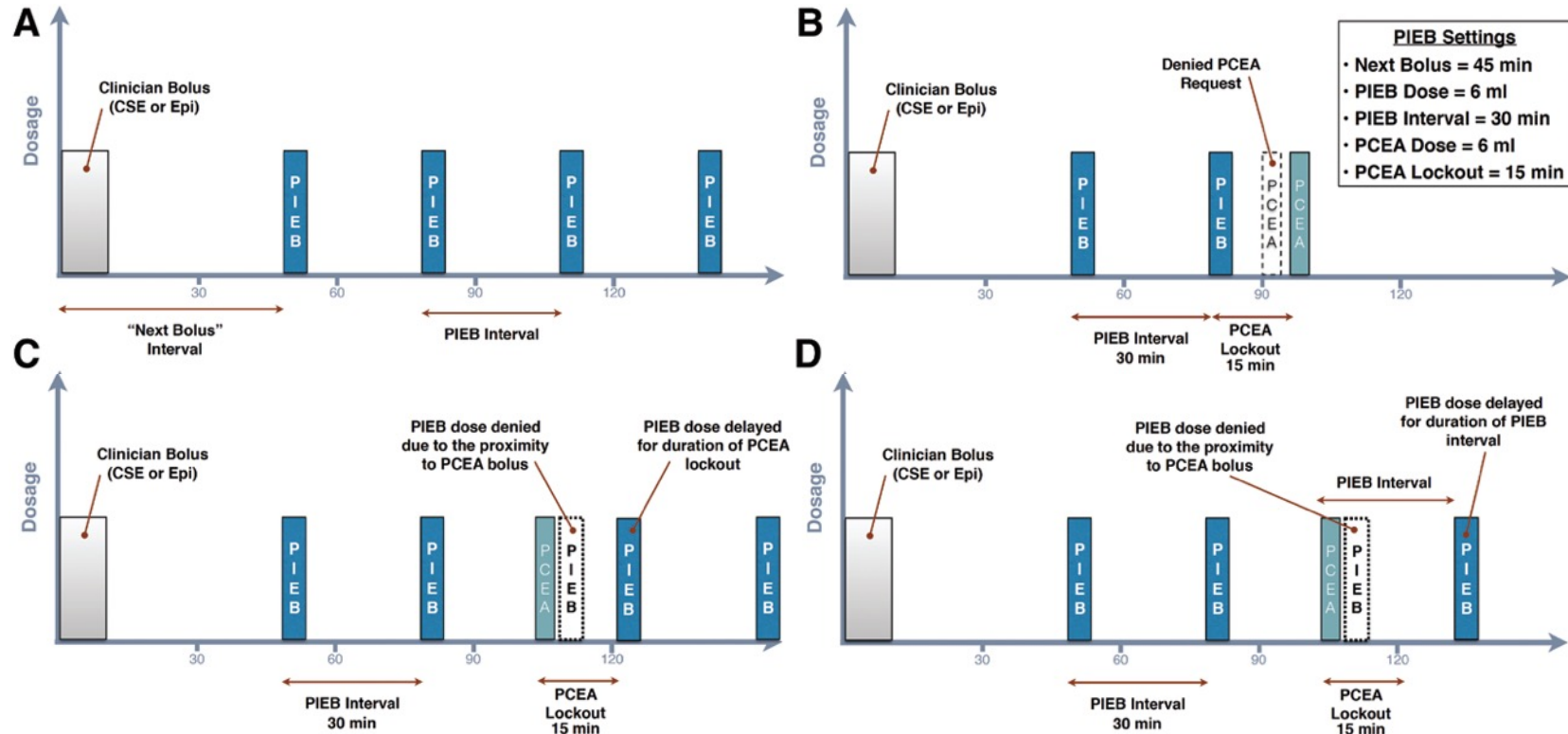
Extraneural-intraneural gradient concentration of LA has time to reverse its cycle between two boluses

Concentration of LA inside the nerve does not reach motor block threshold

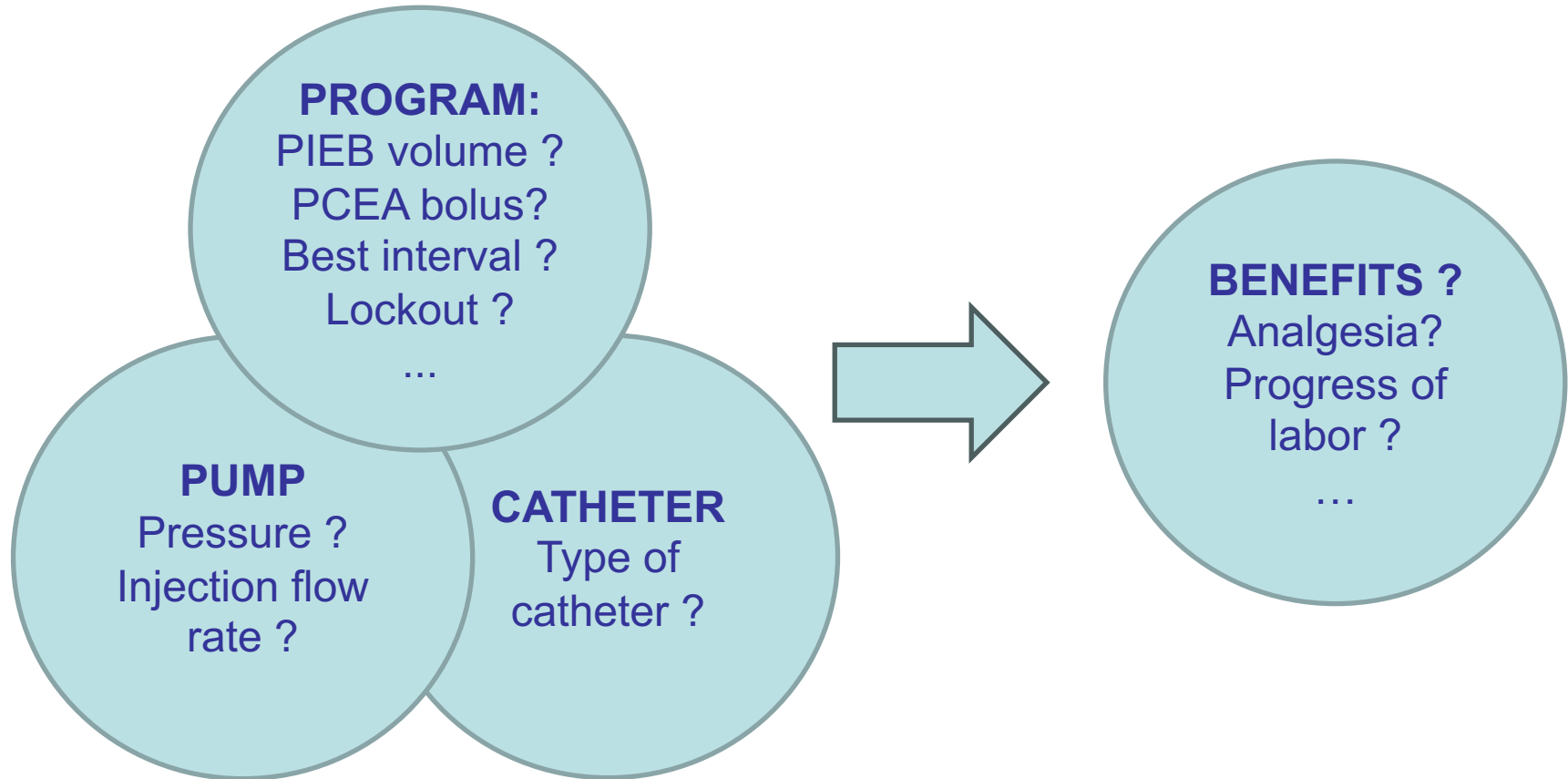
What is PIEB + PCEA ?

“The concept of PIEB is to combine the improved LA spread inherent in manual or PCEA bolus techniques with automated ongoing analgesia inherent in CEI”

Carvalho et al. A&A 2016;123(4):965-71



Factors influencing PIEB for labor analgesia



Determining the interval using a fixed bolus

n = 40

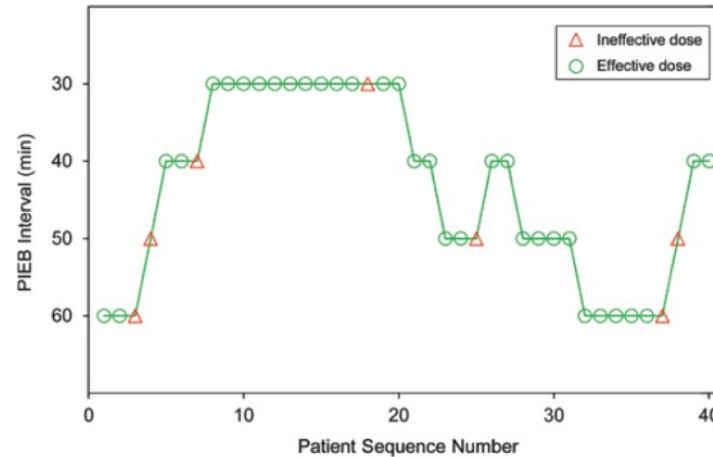
Programmed Intermittent Epidural Bolus for Labor Analgesia During First Stage of Labor: A Biased-Coin Up-and-Down Sequential Allocation Trial to Determine the Optimum Interval Time Between Boluses of a Fixed Volume of 10 mL of Bupivacaine 0.0625% With Fentanyl 2 µg/mL

Anesth Analg 2017

Marcelo Epsztein Kanczuk, MD,* Nicholas Martin Barrett, MB BCh,* Cristian Arzola, MD, MSc,* Kristi Downey, MSc,* Xiang Y. Ye, MSc,† and Jose C. A. Carvalho, MD, PhD*

Primary outcome :

“No requirement for a PCEA or a manual bolus for 6h after initiation of the epidural”



Determining the interval using a fixed bolus

n = 40

Programmed Intermittent Epidural Bolus for Labor Analgesia During First Stage of Labor: A Biased-Coin Up-and-Down Sequential Allocation Trial to Determine the Optimum Interval Time Between Boluses of a Fixed Volume of 10 mL of Bupivacaine 0.0625% With Fentanyl 2 µg/mL

*Anesth Analg*2017

Marcelo Epsztein Kanczuk, MD,* Nicholas Martin Barrett, MB BCh,* Cristian Arzola, MD, MSc,*
Kristi Downey, MSc,* Xiang Y. Ye, MSc,† and Jose C. A. Carvalho, MD, PhD*

Is this what we want ??

Primary outcome :

“No requirement for a PCEA or a manual bolus for 6h after initiation of the epidural”

Authors' conclusions:

- Optimal interval between PIEB of 10 mL of bupi 0.0625% + FNT 2 µg/mL is ≈ 40 min
- With this regimen 34% of women had a sensory block to ice > T6

Other studies used the EI90 approach

Fixed bolus 5 ml

Bupi/FNT 0.125%/2 μ g → EI90 \approx 35 min

Bittencourt et al. Can J Anaesth 2019)

Fixed bolus 2.5 ml

Bupi/FNT 0.25%/8 μ g → EI90 \approx 20 min

Shatalin et al. Can J Anaesth 2021)

Consumption of LA with this regimen was higher than in their previous studies

Fixed bolus 10 ml

Ropi/Suf 0.08%/0.3 μ g → EI90 \approx 42 min

Zhou et al. Chin Med J. 2020

Fixed bolus 8 ml (initiation DPE)

Ropi/Suf 0.1%/0.3 μ g → EI90 \approx 41 min

Song et al. J Clin Anesth. 2022

Determining bolus volume (EV90) using a fixed interval

Fixed interval 40 min

Bupi/FNT 0.0625%/2 µg → EV90 ≈ 11 ml

A high proportion of women developed a sensory block > T6

Zakus et al. Anaesthesia 2017

Ropi/Suf 0.075%/0.5 µg → EV90 ≈ 10 ml

Ropi/Suf 0.1%/0.5 µg → EV90 ≈ 9 ml

Ran et al. BMC Pregnancy and Childbirth 2022

Primary outcome :

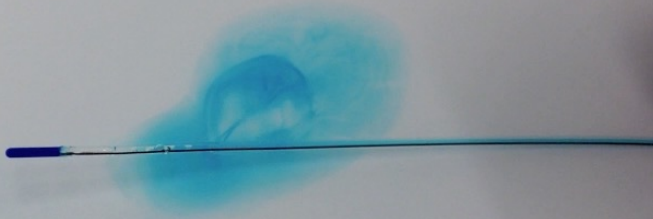
“No requirement for a PCEA or a manual bolus after initiation of the epidural”

**Is this what
we want ??**

Bolus distribution is influenced by: delivery rate/pressure + epidural catheter type (size/orifices/wire)

2 in-vitro studies: Krawczyk et al A&A 2019 / Klumpner et al. J Clin Anesth 2016

bolus with 100 ml/h



bolus with 250 ml/h



Videos: courtesy of Prof T. Girard, USB

Effect of Epidural Infusion Bolus Delivery Rate on the Duration of Labor Analgesia

A Randomized Clinical Trial

Elizabeth M. S. Lange, M.D., Cynthia A. Wong, M.D., Paul C. Fitzgerald, R.N., M.S.,
Wilmer F. Davila, M.D., Suman Rao, M.D., Robert J. McCarthy, Pharm.D.,
Paloma Toledo, M.D., M.P.H.

Anesthesiology 2018

100 ml/h

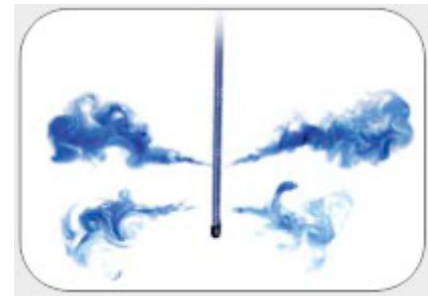
Bupi / FNT 0.0625/2

PIEB = 10ml/60'

PCEA = 5ml/10'

Flex Tip Plus, Arrow

300ml/h



Effect of Epidural Infusion Bolus Delivery Rate on the Duration of Labor Analgesia

A Randomized Clinical Trial

Elizabeth M. S. Lange, M.D., Cynthia A. Wong, M.D., Paul C. Fitzgerald, R.N., M.S.,
Wilmer F. Davila, M.D., Suman Rao, M.D., Robert J. McCarthy, Pharm.D.,
Paloma Toledo, M.D., M.P.H.

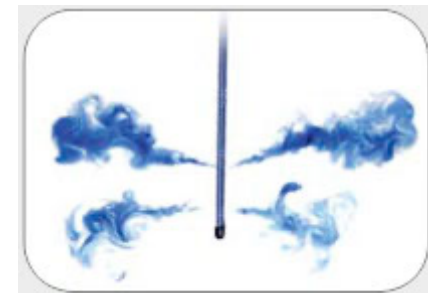
Anesthesiology 2018

Bupi / FNT 0.0625/2

PIEB = 10ml/60'

PCEA = 5ml/10'

Flex Tip Plus, Arrow




	100 ml/h Low Delivery Rate (n = 108)	300ml/h High Delivery Rate (n = 102)	Difference (95% CI of the Difference)	P Value
Primary outcome				
Requests for provider-administered supplemental bolus	43 (40)	37 (36)	4 (-10 to 18)	0.67
Secondary outcomes				
Bupivacaine consumption (mg/h)	10.8 [8.6 to 11.4]	9.9 [8.1 to 11.4]	0.9 (-0.1 to 1.8)	0.08
PCEA doses				
Requests	17 [10 to 31]	14 [6 to 27]	3 (-3 to 8)	0.21
Delivered	10 [7 to 17]	9 [5 to 18]	1 (-2 to 4)	0.14
Request/delivery ratio			(-0.2 to 0.3)	0.66
Exploratory outcomes				
Time to provider-administered bolus			(-162 to 142)	0.92
Weighted mean pain score			(-5.3 to 3.0)	0.58
Stage of labor at redose request				0.67
First	40 (93)	34 (92)	1 (-7 to 9)	
Second	3 (7)	3 (8)	-1 (-9 to 6)	
Number of redoses				0.99
1	31 (72)	27 (73)	-1 (-14 to 12)	
2	6 (14)	5 (13.5)	0.5 (-10 to 11)	
≥ 3	6 (14)	5 (13.5)	0.5 (-10 to 11)	
Satisfaction with labor analgesia	98 [88-100]	98 [86-100]	0 (-2 to 4)	0.37

PIEB fast injection speed do not appear superior to PIEB slow injection speed

Data presented as N (%) or median [25th to 75th percentiles].

**Programmed intermittent epidural bolus for labour analgesia:
a randomized controlled trial comparing bolus delivery speeds
of 125 mL·hr⁻¹ versus 250 mL·hr⁻¹**

Yusuke Mazda, MD, PhD  · Cristian Arzola, MD, MSc · Kristi Downey, MSc ·
Xiang Y. Ye, MSc · Jose C. A. Carvalho, MD, PhD

Can J Anesth/J Can Anesth (2022) 69:86–96

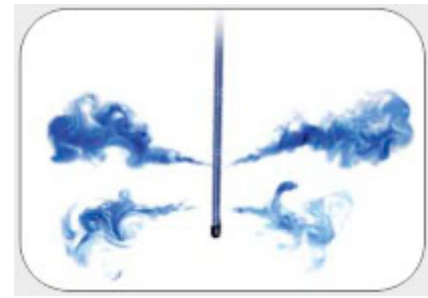
250 ml/h 125 ml/h

Bupi / FNT 0.0625/2

PIEB = 10ml/40'

PCEA = 5ml/10'

Flex Tip Plus, Arrow



Programmed intermittent epidural bolus for labour analgesia: a randomized controlled trial comparing bolus delivery speeds of 125 mL·hr⁻¹ versus 250 mL·hr⁻¹

Yusuke Mazda, MD, PhD · Cristian Arzola, MD, MSc · Kristi Downey, MSc · Xiang Y. Ye, MSc · Jose C. A. Carvalho, MD, PhD

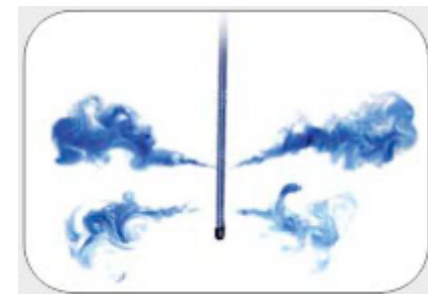
Can J Anesth/J Can Anesth (2022) 69:86–96

Bupi / FNT 0.0625/2

PIEB = 10ml/40'

PCEA = 5ml/10'

Flex Tip Plus, Arrow



250 ml/h 125 ml/h

	Control group (250 mL·hr ⁻¹) N = 45	Intervention group (125 mL·hr ⁻¹) N = 45	P value	Difference in rate (%) / median (95% CI)
Highest VNRS, n (%)			0.67*	
0 to 1	32 (71%)	29 (64%)		
2 to 3				
4 to 6				
7 to 10				
Patients requiring PCEA, n (%)				
Number of PCEA boluses				
Manual top-up administered, n (%)				
Manual top-up administered, median [IQR] ^b				
Hourly bupivacaine consumption (mg·hr ⁻¹), median [IQR] ^b	8.6 [8.3-9.4]	9.4 [8.3-10.4]	0.07	0.8 (-0.2 to 1.4)
Patient satisfaction, median [IQR] ^b	10 [10-10]	10 [9, 10]	0.08	0 (-0.5 to 0.5)
Fully dilated at the study completion, n (%) ^a	16 (36%)	20 (44%)	0.39	9% (-11 to 29)
Cervical dilatation at the study completion, median [IQR] ^b	8 [5-10]	8 [5-10]	0.87	0 (-2 to 2)
Duration of study in hours, median [IQR] ^b	6 [4-6]	6 [5, 6]	0.80	0 (-1 to 1)

**PIEB fast injection speed do not appear superior to PIEB slow injection speed
less hypotension with slow injection**

Optimal regime of PIEB + PCEA is still discussed

	Old regimen	Current regimen in HUG
Epidural initiation	Test dose 2-3 ml Lido 2% Bupi 0.125% 10 ml + FNT 50 mcg	Test dose 2-3 ml Lido 2% Ropi 0.2% 8-10 ml + FNT 50 mcg
Maintenance solution	Bupi 0.0625 % + FNT 2 mcg/ml	Ropi 0.1 % + SUF 0.25 mcg/ml
PEIB settings	10 ml every 60 min	8 ml every 50 min
PCEA settings	5 ml, 15 min lockout	same
Max dose	120 ml / 4h	same

What is the evidence supporting use of PIEB versus CEI ?

Recent systematic reviews in the field:

Tan et al. Cochrane Database of Systematic Reviews 2023

Wydall et al. Can J Anesth 2023

Hussain et al. BJA 2020

Xu et al. Sci Rep 2019

What is the evidence supporting use of PIEB versus CEI ?

Studies are in accordance that PIEB is associated with :

- 1) Improved labor pain control
- 2) Decrease breakthrough pain (RR 0.71 [0.55 , 0.91])
- 3) Decrease hourly LA consumption (MD -0.84 [-1.29 , -0.38])
- 4) Increased maternal satisfaction
- 5) Equal rate of CD (RR 0.85 [0.69 , 1.06])

Remaining areas of discord :

- 1) Motor block
- 2) Duration of labor
- 3) Rates of instrumental delivery

Recent systematic reviews in the field:

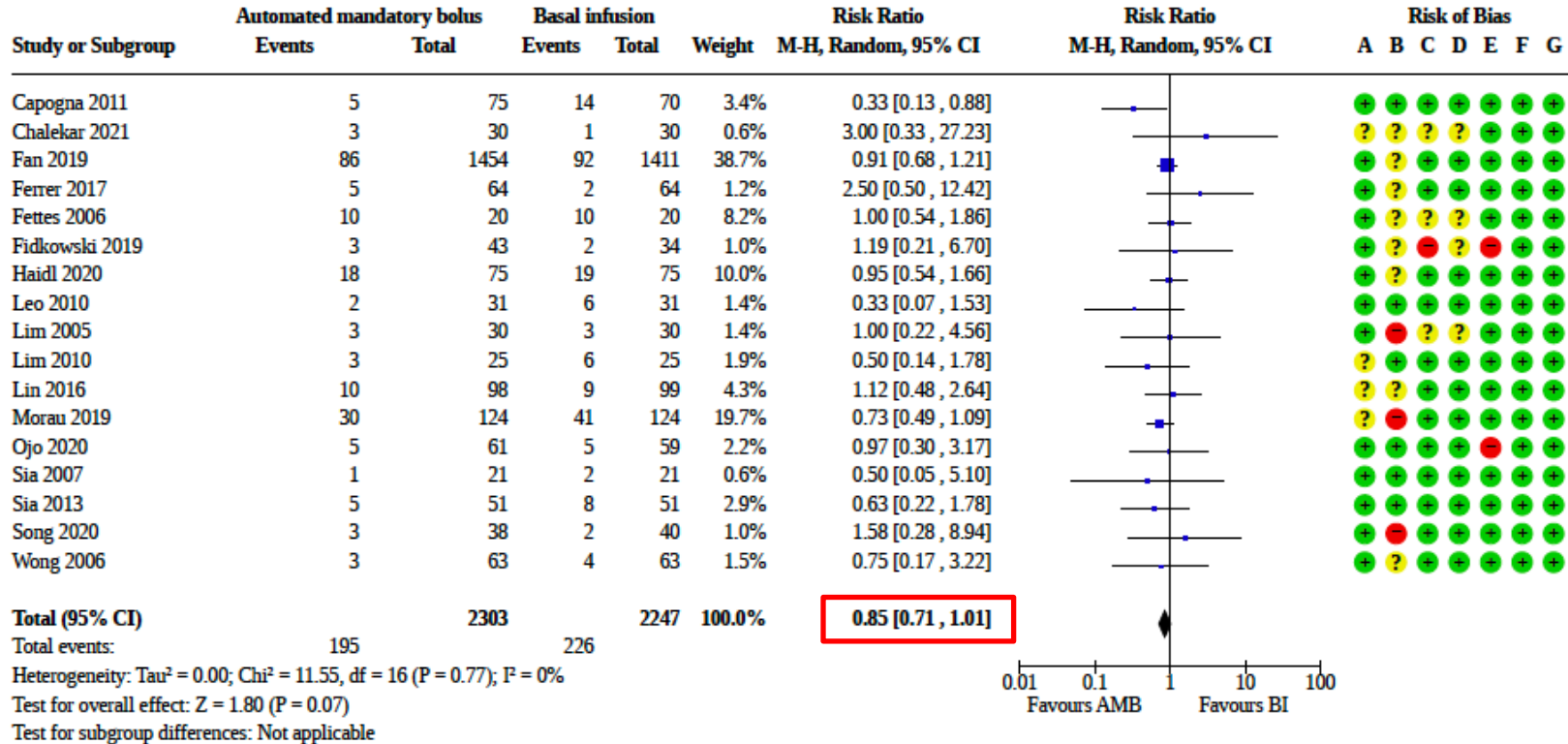
Tan et al. Cochrane Database of Systematic Reviews 2023

Wydall et al. Can J Anesth 2023

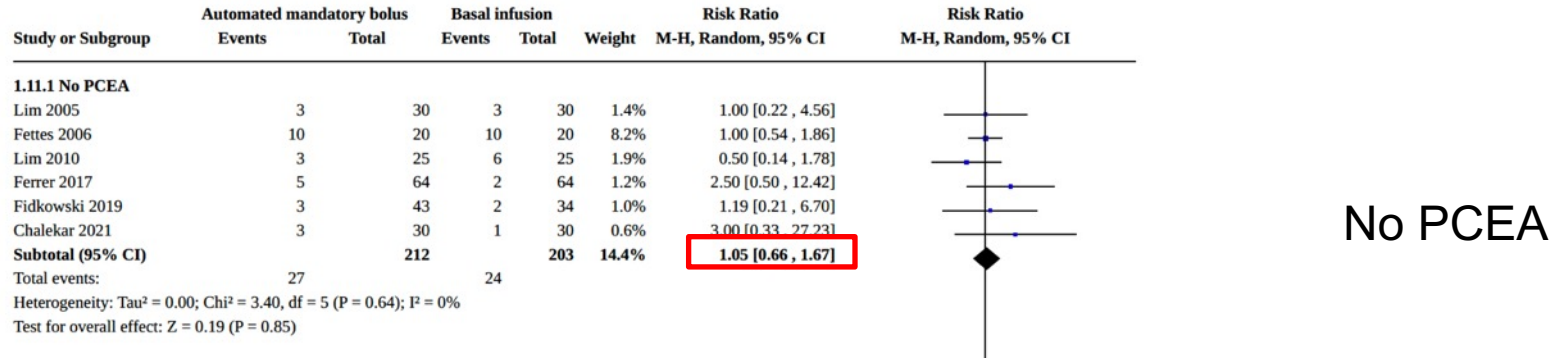
Hussain et al. BJA 2020

Xu et al. Sci Rep 2019

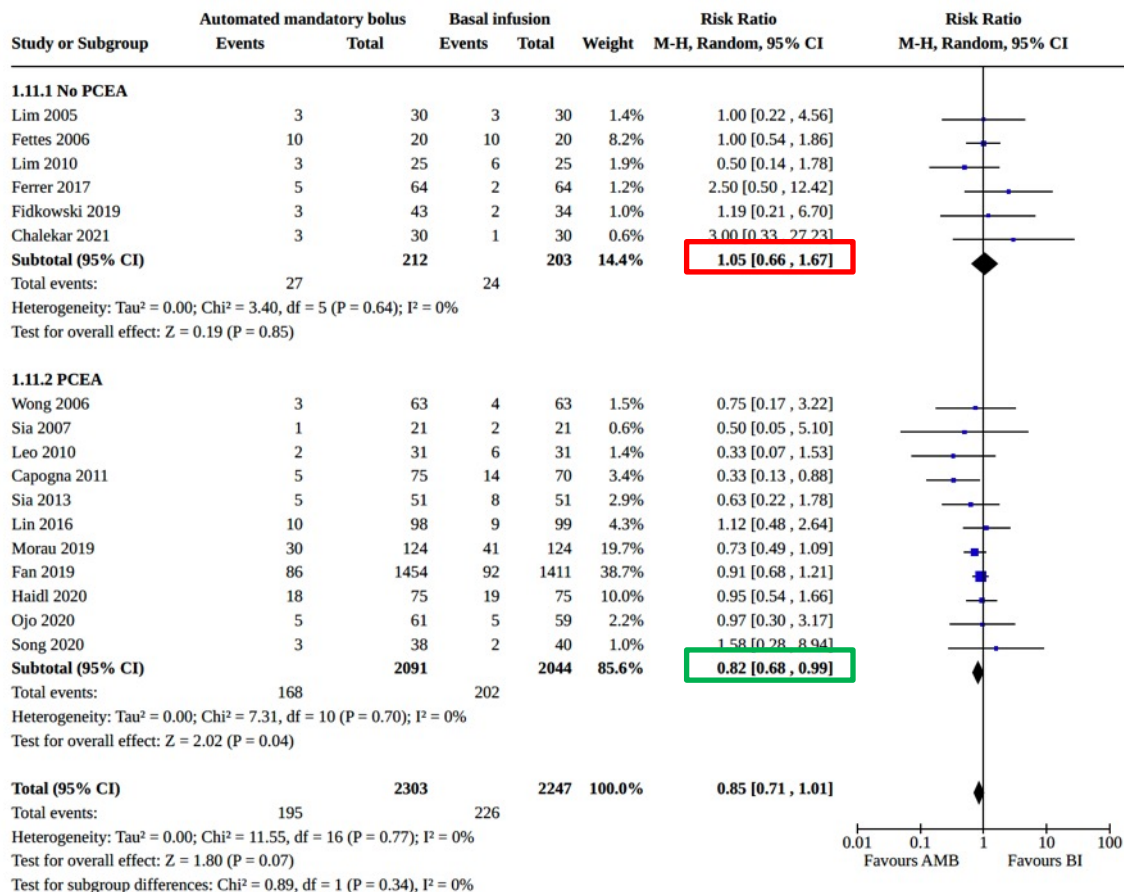
Instrumental delivery: PIEB versus CEI



PIEB and instrumental delivery: use of PCEA



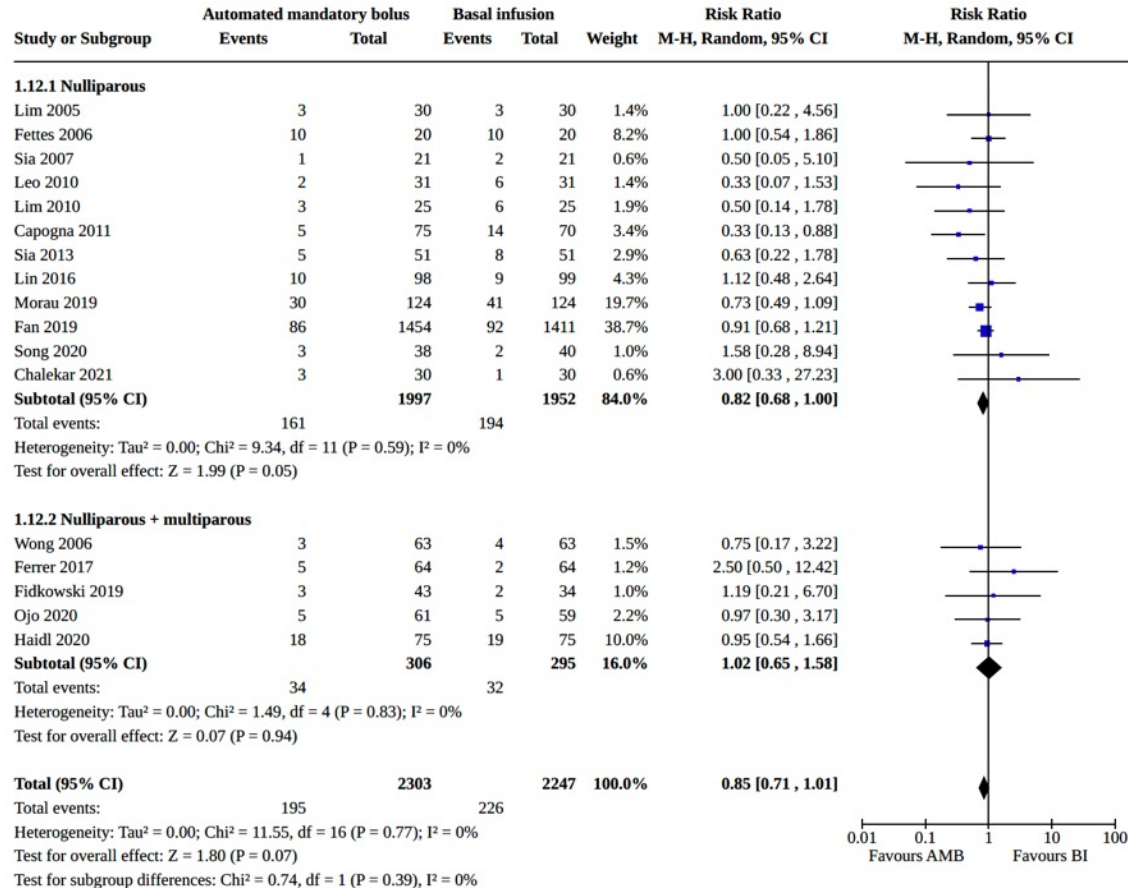
PIEB and instrumental delivery: use of PCEA



No PCEA

The use of a PCEA combined with PIEB appears beneficial

PIEB and instrumental delivery: nulliparous may benefit !



Nulliparous

Nulliparous + multiparous

Plan

- Impact of neuraxial analgesia on labor
- Local anesthetic mixture
- Maintenance technique and regimen
- **The future...**

How can we possibly improve maintenance techniques ?



Prediction of breakthrough pain

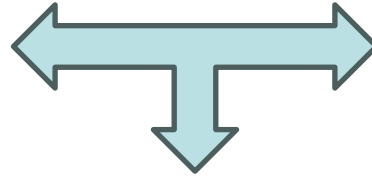


Adaptative / variable PIEB + PCEA

How can we possibly improve maintenance techniques ?



Prediction of breakthrough pain



Adaptative / variable PIEB + PCEA

**Personalized
regimen and
pre-emptive
management**



CORRESPONDENCE

Developing the BreakThrough Pain Risk Score: an interpretable machine-learning-based risk score to predict breakthrough pain with labour epidural analgesia

Hon Sen Tan, MMed (Anaes) · Nan Liu, PhD · Chin Wen Tan, PhD ·
Alex Tiong Heng Sia, MMed (Anaes) · Ban Leong Sng, MMed (Anaes), FANZCA



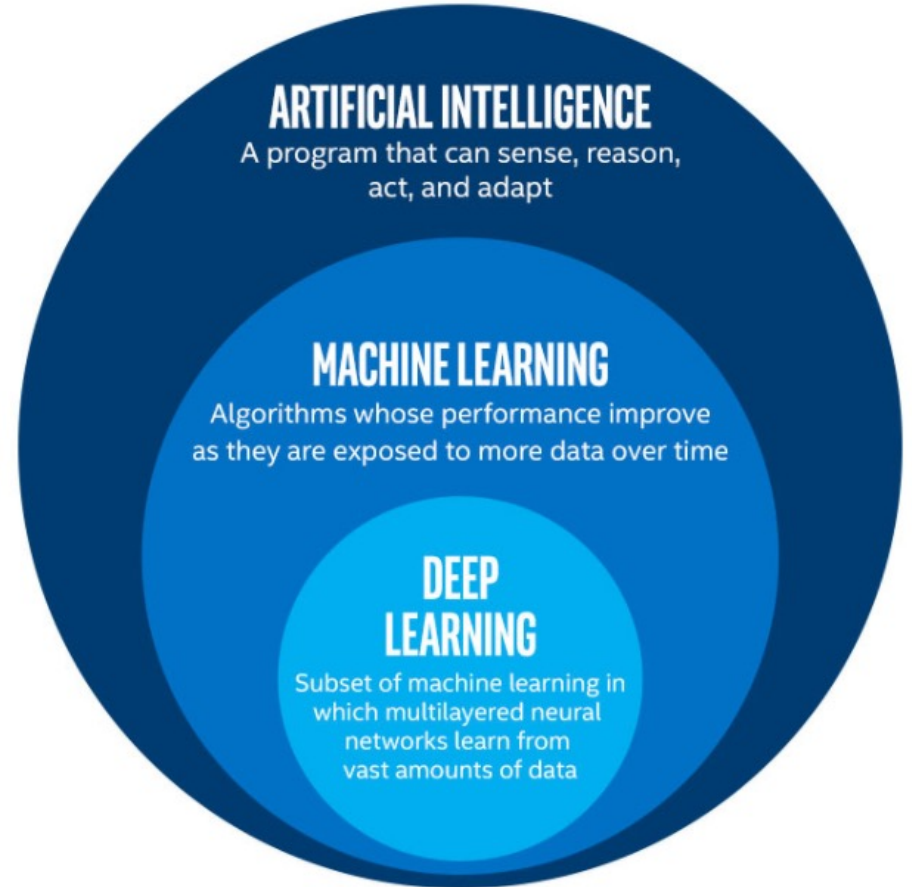
ELSEVIER

www.obstetanaesthesia.com

ORIGINAL ARTICLE

Prediction of breakthrough pain during labour neuraxial analgesia: comparison of machine learning and multivariable regression approaches

H.S. Tan,^{a,1} N. Liu,^{b,c,1} R. Sultana,^b N-L.R. Han,^d C.W. Tan,^a J. Zhang,^b
A.T.H. Sia,^{a,b} B.L. Sng^{a,b}



Conclusions

- Maintenance techniques have evolved considerably
- Modern neuraxial techniques have minimal impact on labor
- Use “ultra low” concentrations LA (Bupi \leq 0.08 % or Ropi \leq 0.12 %) + opioid
- PCEA has become the standard
- Avoid continuous background infusion and prefer PIEB
- PIEB + PCEA using “ultra low” concentration LA + opioid is the best technique !

CELEBRATING THE 33RD ANNIVERSARY OF THE SAOA

*“OBSTETRIC ANAESTHESIA IN SWITZERLAND:
WHERE WE COME FROM, WHERE WE ARE, WHERE WE GO”*

Thank you for your attention !

Questions ?

PIEB vs physician regular manual bolus

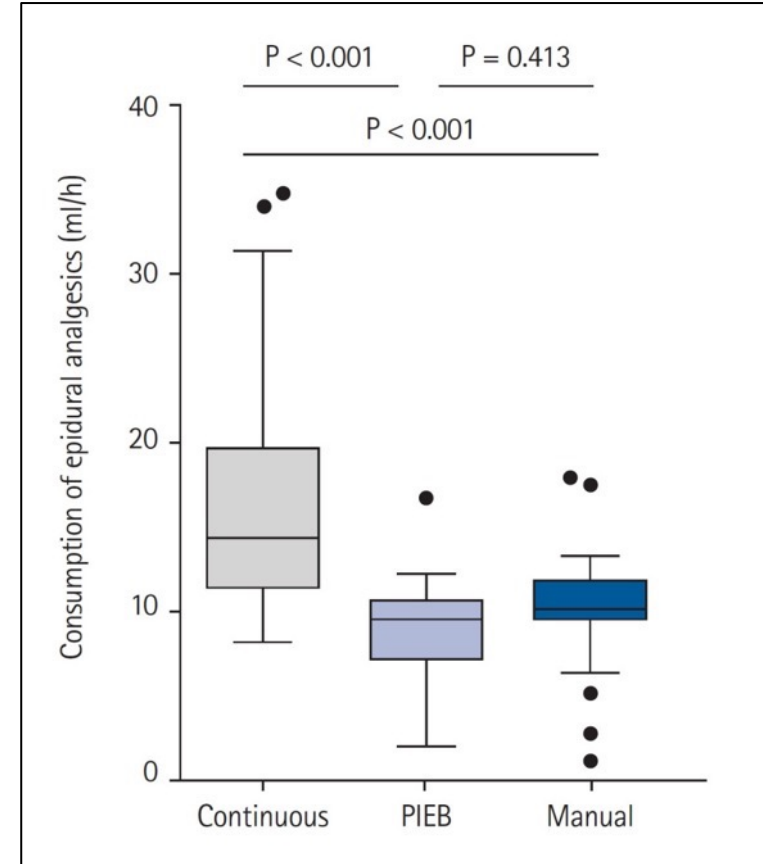
LA consumption is higher with CEI compared to PIEB and manual bolus

Time to breakthrough pain is longer with PIEB

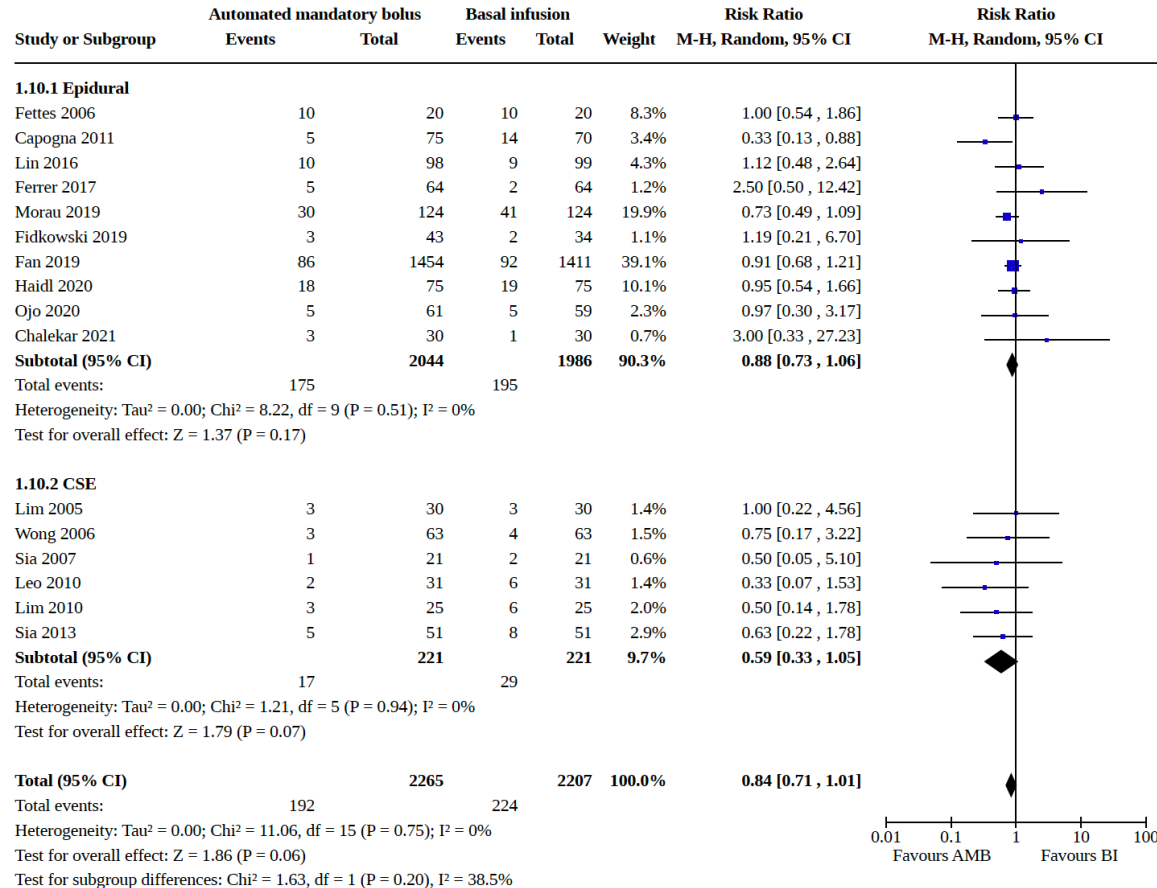
“High pressure” physician’s boluses confers no benefit compared to PIEB

Physician’s workload is greatly reduced by PIEB

Kim et al. Korean J Anesthesiol 2024



PIEB and instrumental delivery: epidural vs CSE initiation



The initiation technique seems to have little influence

Are the S-enantiomers really less toxic or just less potent ?

“It has become clear from errors in the development of enantiomers for clinical application that the determination of the relative potencies is of prime importance in evaluating claims for perceived advantages in toxicity and blocking characteristics”

M.O. Columb (Oxford Textbook of Anaesthesia, 2017)

At concentrations 0.0625% to 0.1% cardiac toxicity is highly unlikely !

Ropivacaine, Levobupivacaine and bupivacaine potency ratios

Epidural administration : 0.7 / 0.9 / 1.0 (Ropi / Levo / Bupi)

Intrathecal administration: 0.65 / 0.81 / 1.0 (Ropi / Levo / Bupi)

Ropivacaine or Levobupivacaine or bupivacaine are equivalent choices for labor analgesia when used at equipotent doses with a lipophilic opioid

Determining bolus volume using a fixed interval of 40'

n = 40

Anaesthesia 2017 doi:10.1111/anae.14159

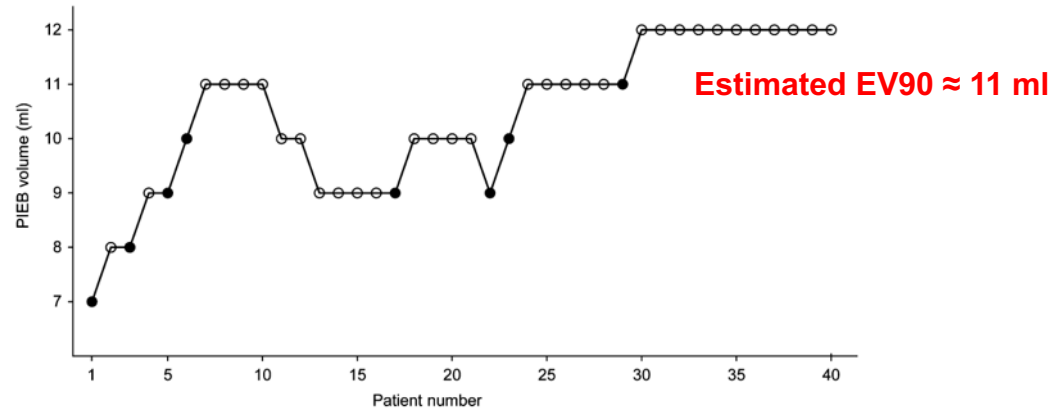
Original Article

Determination of the optimal programmed intermittent epidural bolus volume of bupivacaine 0.0625% with fentanyl $2 \mu\text{g}\cdot\text{ml}^{-1}$ at a fixed interval of forty minutes: a biased coin up-and-down sequential allocation trial*

P. Zakus,¹ C. Arzola,² R. Bittencourt,¹ K. Downey,³ X. Y. Ye⁴ and J. C. Carvalho⁵

Primary outcome :

“No requirement for a PCEA or a manual bolus after initiation of the epidural”



Determining bolus volume using a fixed interval of 40'

n = 40



Is this what we want ??

Primary outcome :

“No requirement for a PCEA or a manual bolus after initiation of the epidural”

Authors' conclusions:

- Reducing the bolus volume below 10 ml compromised the quality of analgesia
- With this regimen, a high proportion of women developed a sensory block > T6
- However, no women required ttt for hypotension