

# remifentanil

## for labour analgesia

# Outline

Overview of remifentanyl for labour

Pros vs cons

Controversies

RESPITE study

Real-world lessons

Recommendations for its use

# Outline

## Overview of remifentanyl for labour

Pros vs cons

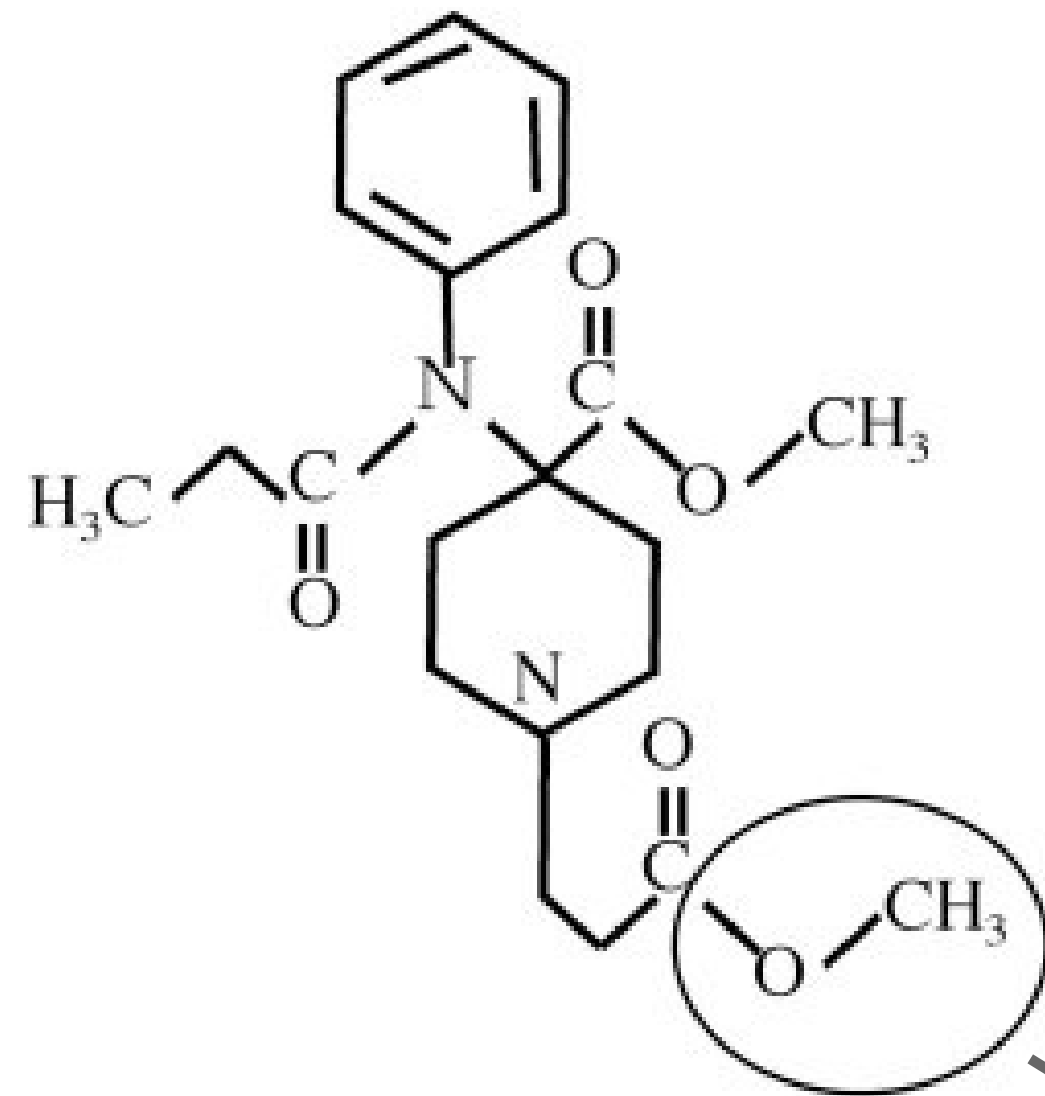
Controversies

RESPITE study

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Recommendations for its use

# Remifentanyl overview



Rapid onset

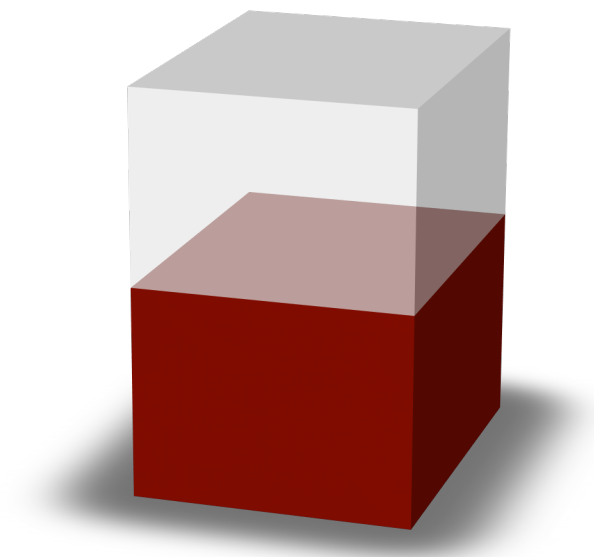
$t_{1/2}$  3–6 minutes

Analgesic  $t_{1/2}$  6 minutes

Non-specific esterases

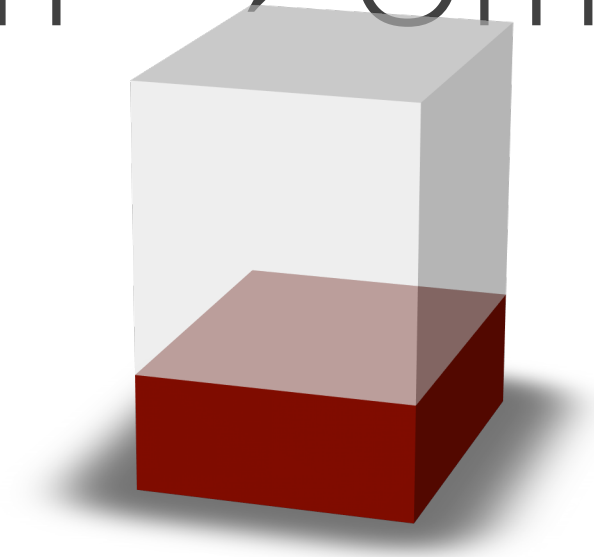
# Placental transfer

Maternal artery → Umbilical vein



= 88%

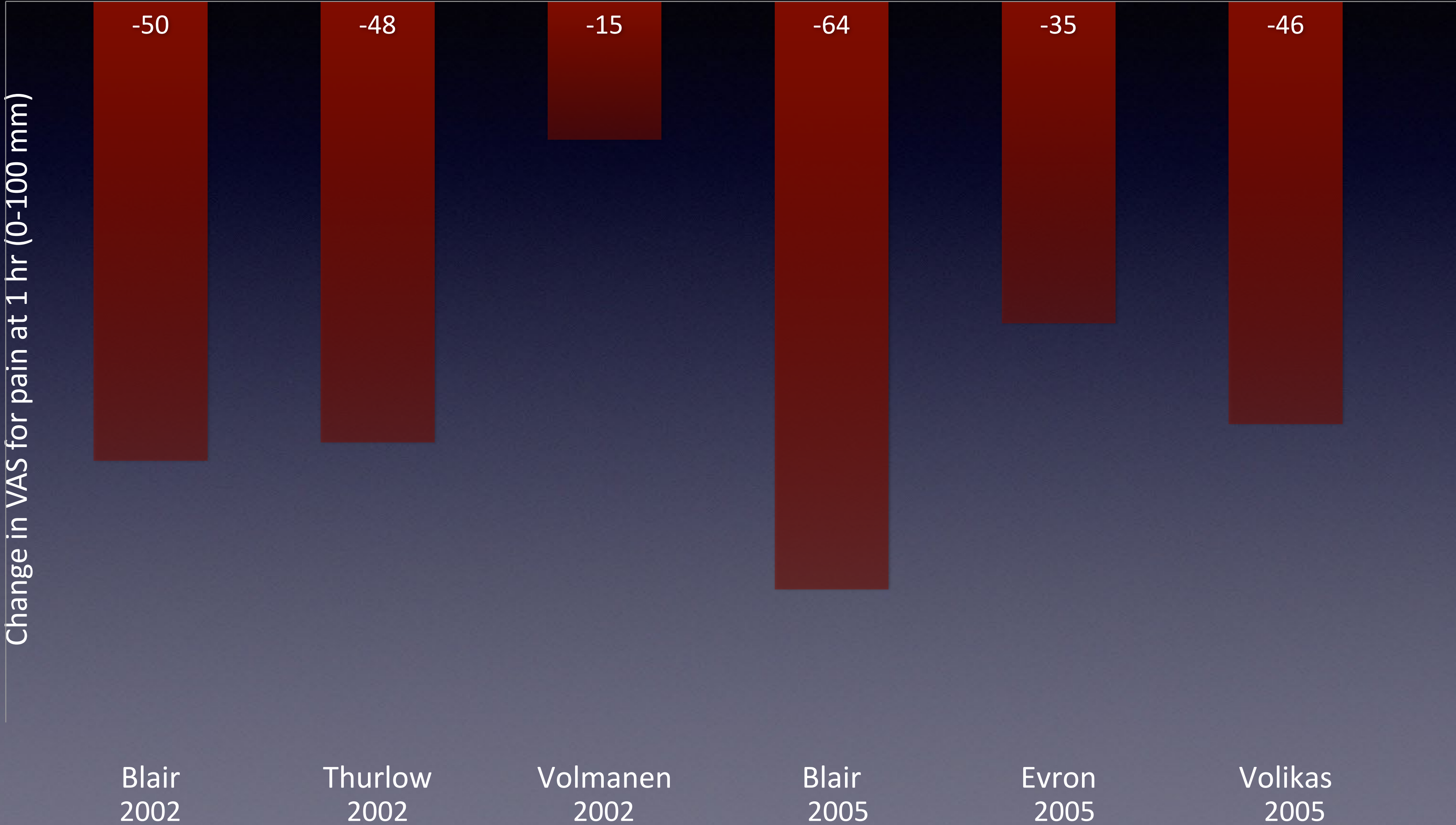
Umbilical vein → Umbilical artery



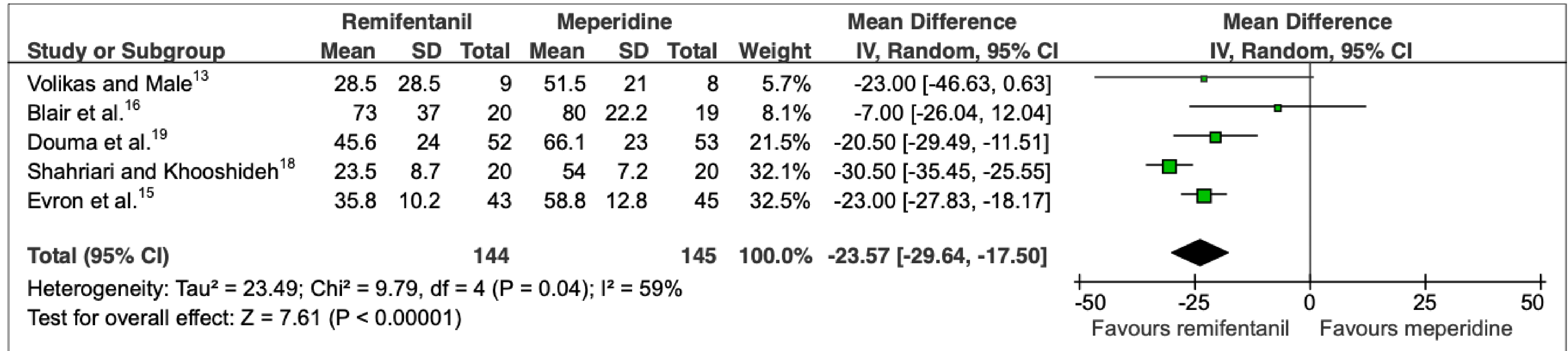
= 29%

Is remifentanyl a useful labour analgesic?

# Analgesic efficacy



# Remifentanil vs pethidine





# Remifentanil vs Epidural

Equally excellent satisfaction scores

Volmanen 2008

Douma 2011

Tveit 2012

Stocki 2014

# Fetal & neonatal effects

Blair 2002

Thurlow 2002

Volmanen 2002

Blair 2005

Volmanen 2008

Evron 2005

Volikas 2004

Baker 2007

**NO ADVERSE EFFECTS**

Volmanen 2011

Shen 2013

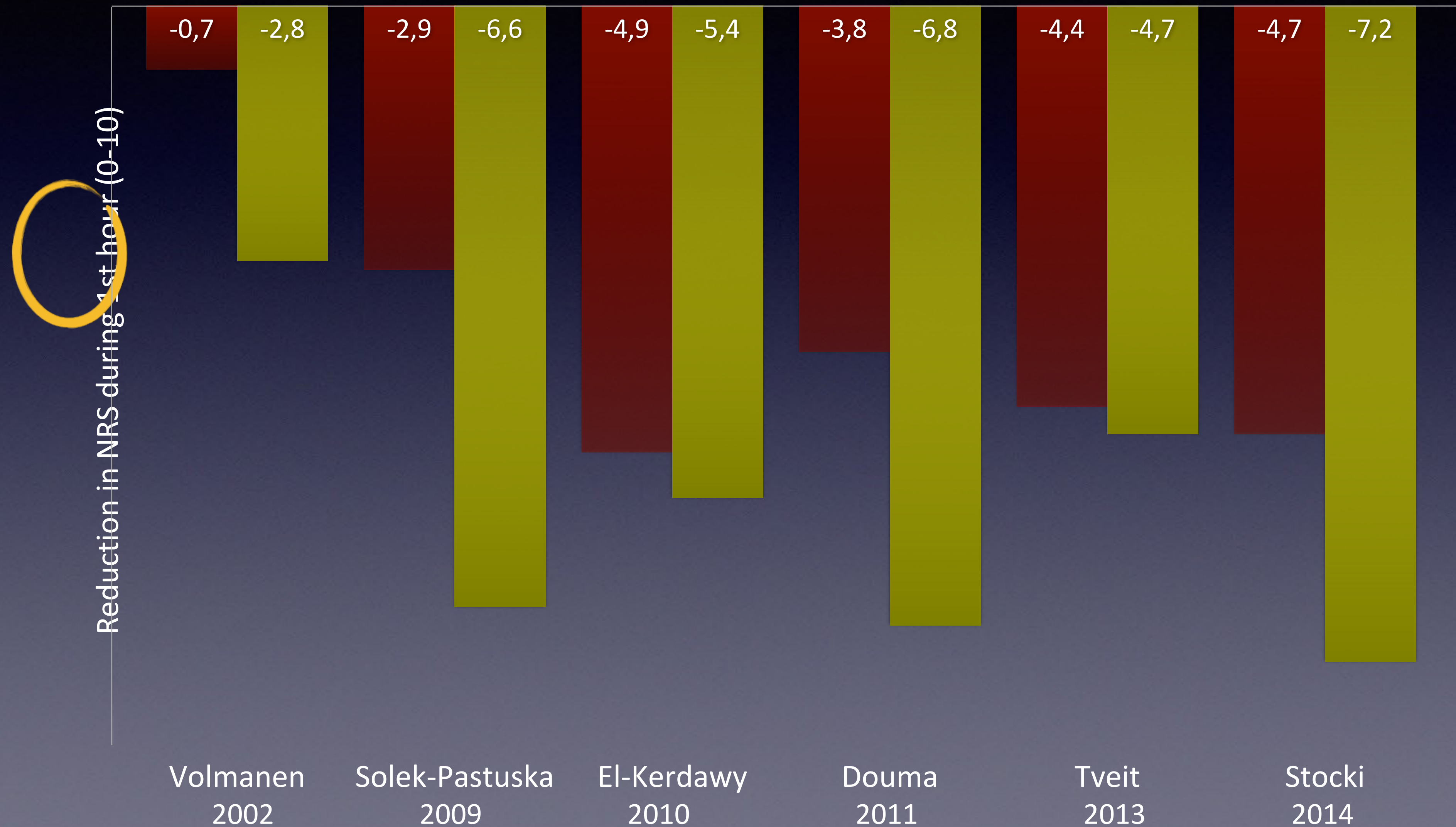
Konefał 2013

As effective as an epidural?

# Remifentanil vs Epidural

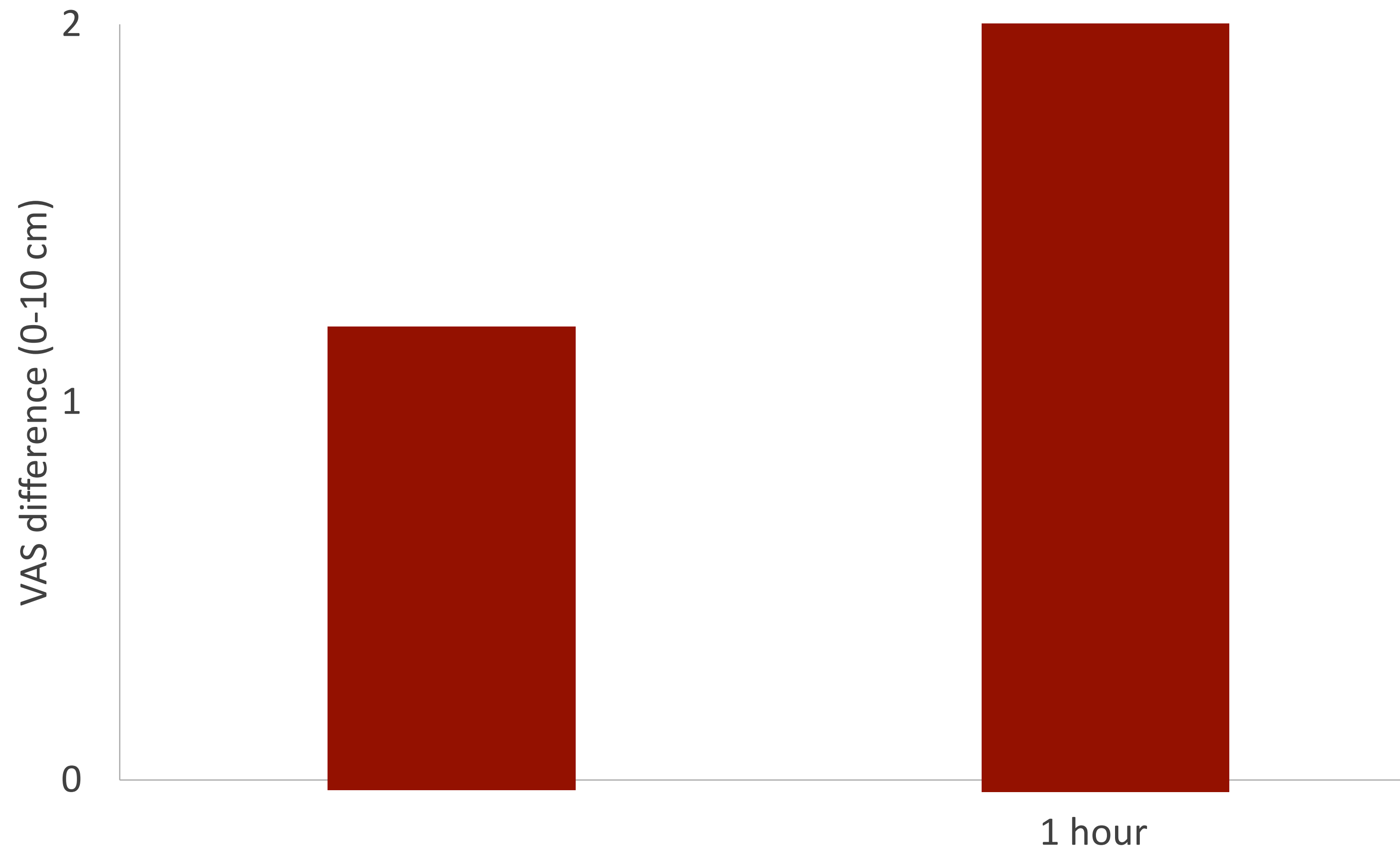
■ Remifentanil

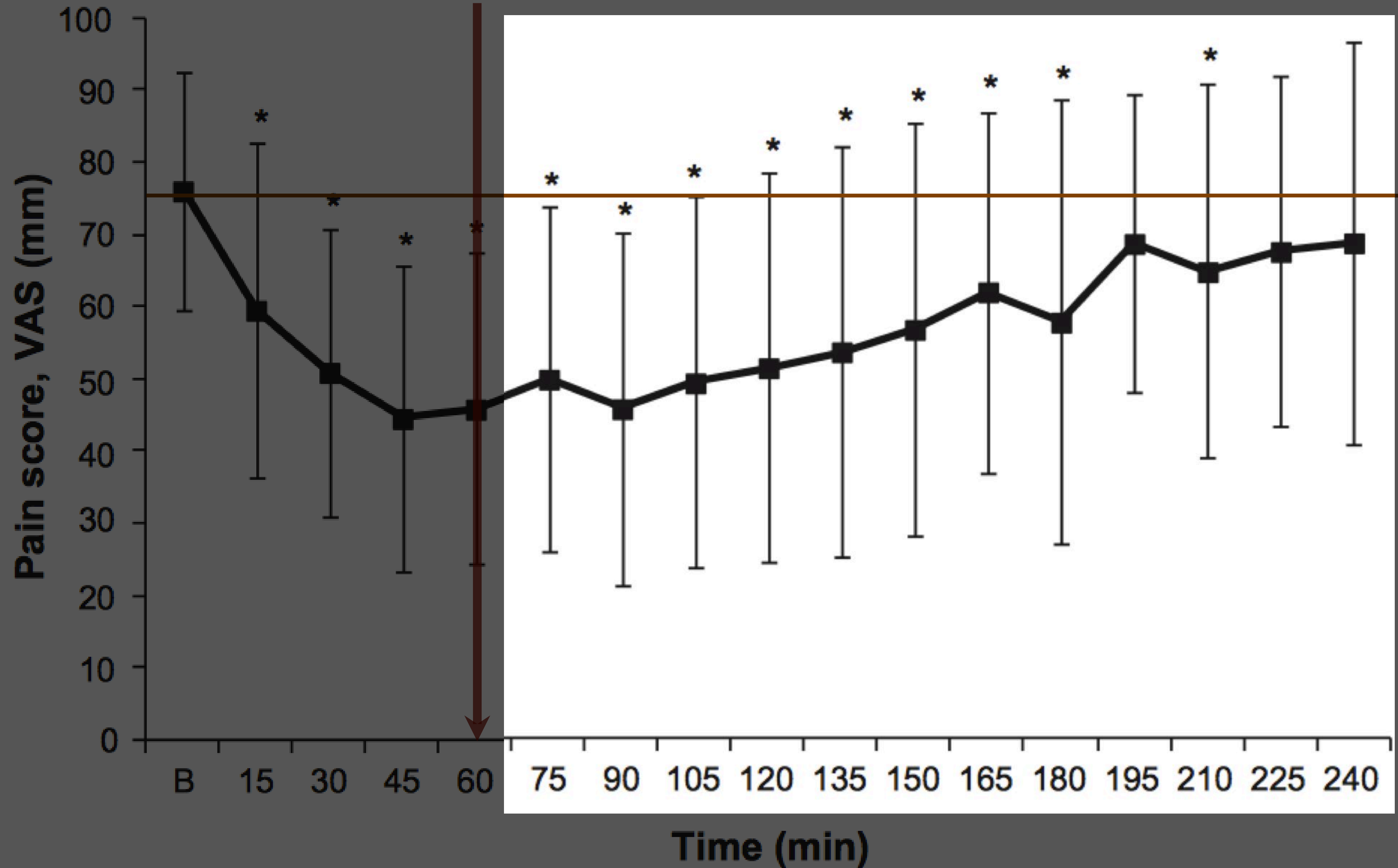
■ Epidural



# A Comparison of Remifentanyl Parturient-Controlled Intravenous Analgesia with Epidural Analgesia: A Meta-Analysis of Randomized Controlled Trials

Zhi-Qiang Liu, MD, PhD,\* Xiu-Bin Chen, MD,\* Hai-Bing Li, MD,\* Man-Tang Qiu, MD, PhD,† and Tao Duan, MD, PhD‡





# Controversies

# Dosing

40 mcg bolus  
2 minute lockout



# Doses used in clinical trials

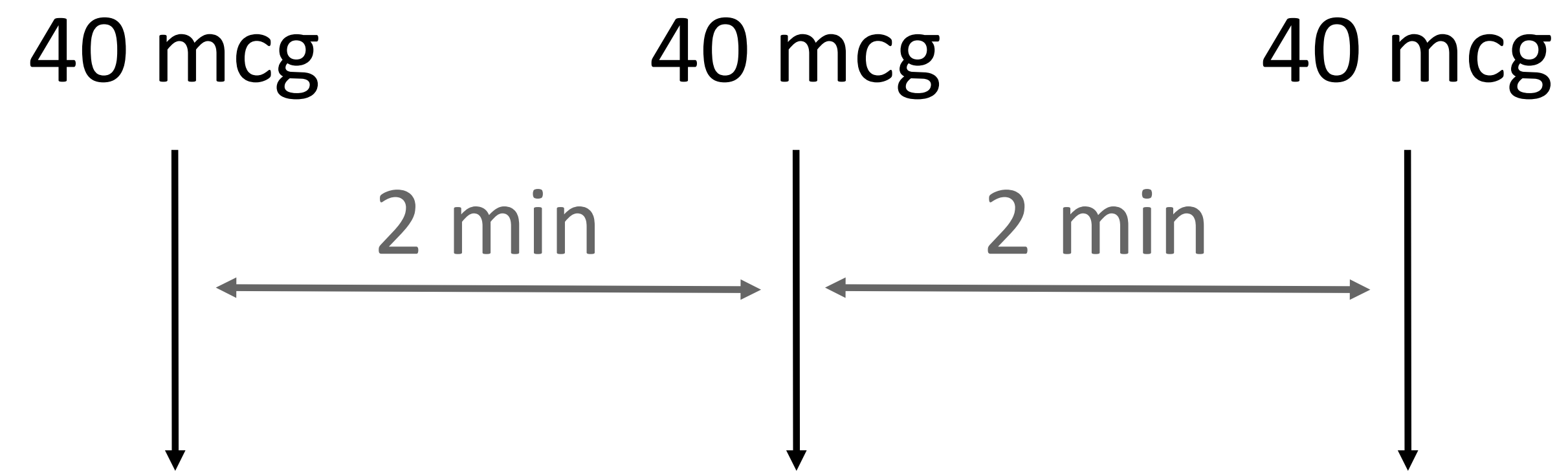
	Bolus dose
Blair 2002	0.25–0.5 mcg/kg
Thurlow 2002	0.2 mcg/kg
Volmanen 2005	0.4 mcg/kg
Blair 2005	40 mcg
Evron 2005	0.27–0.93 mcg/kg
Volikas 2005	0.5 mcg/kg
Balki 2007	0.25 mcg/kg (plus infusion)

# Doses used in clinical trials



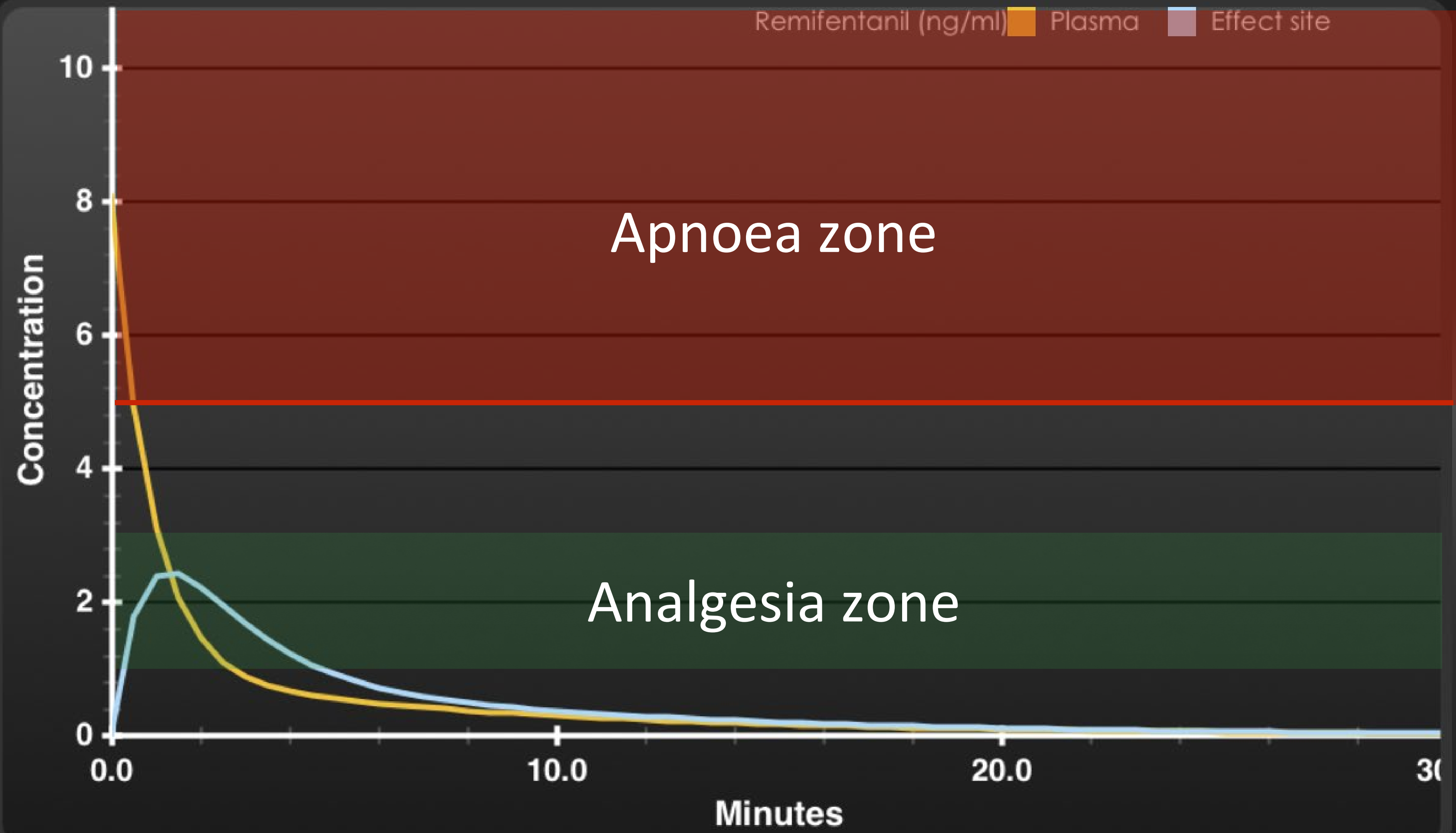
VS

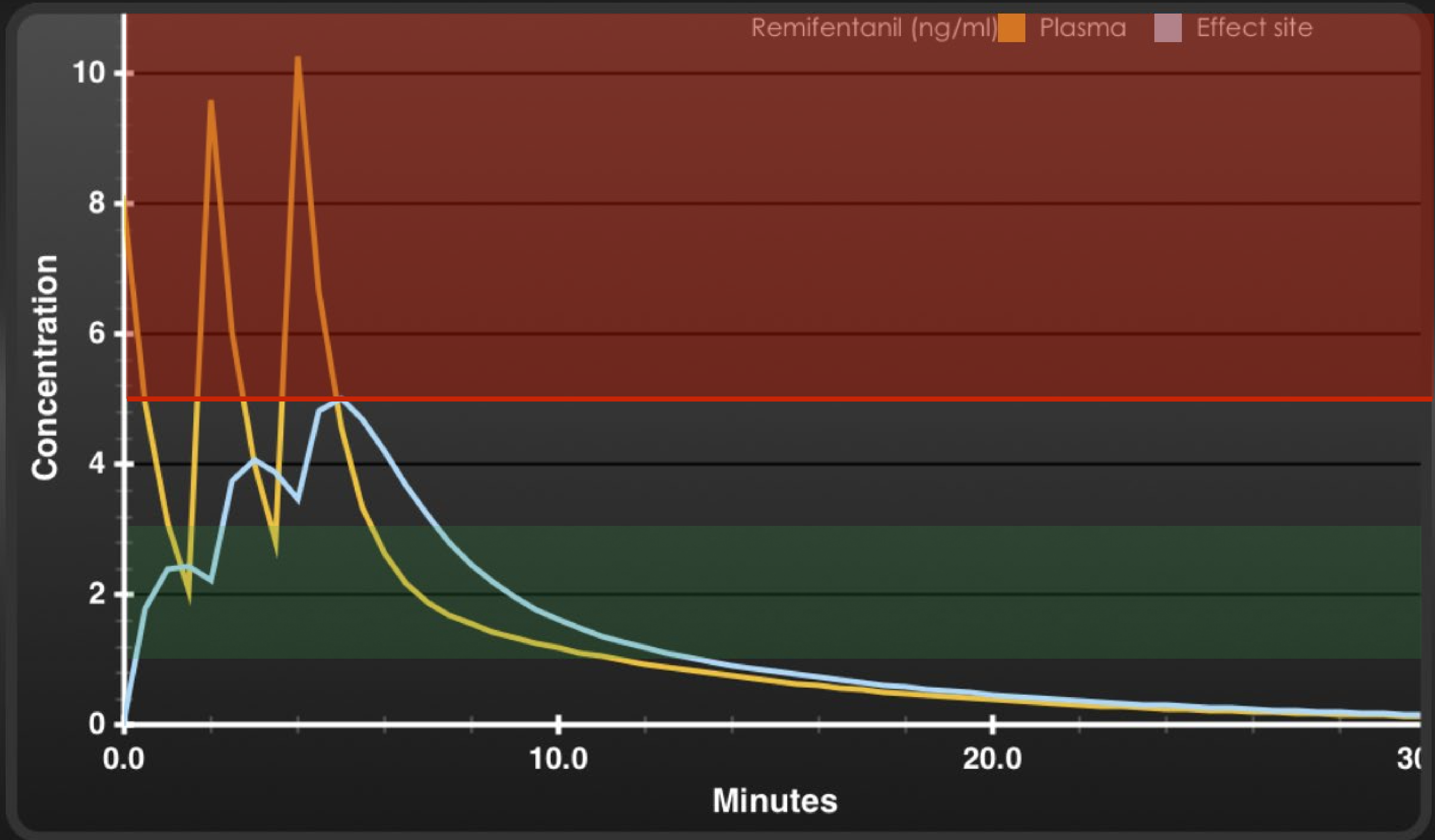




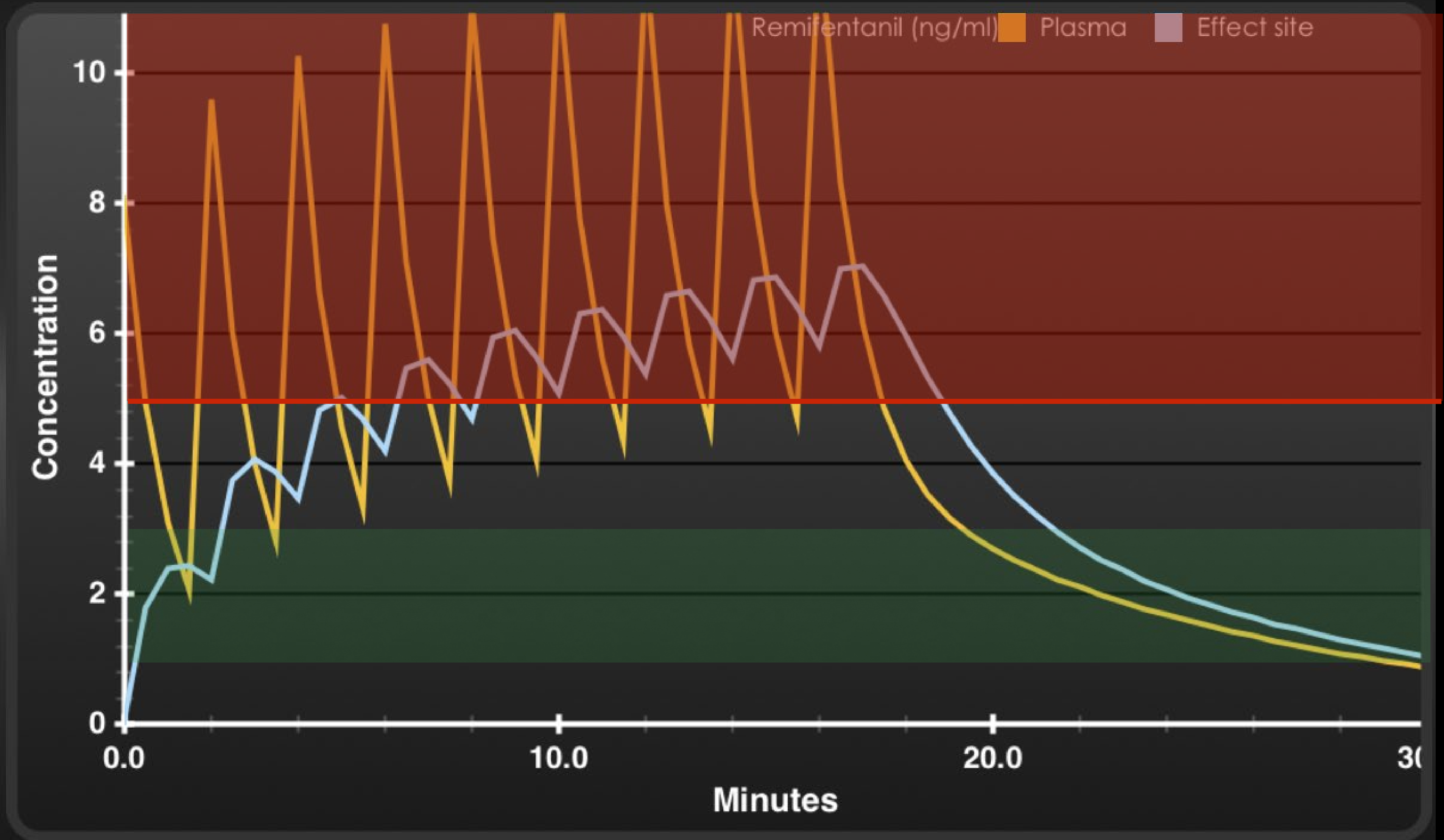
$$= 0.38-0.5 \text{ mcg/kg/min}$$

60-80 kg





40 mcg bolus, 2 min lockout



40 mcg bolus, 2 min lockout

2012–13

Anaesthesia 2012, 67, 538–540

doi:10.1111/j.1365-2044.2011.06997.x

## Case Report

Respiratory arrest in an obstetric patient using remifentanil patient-controlled analgesia\*

J. C. Bonner<sup>1</sup> and W. McClymont<sup>2</sup>

*1 Specialist Registrar, 2 Consultant Anaesthetist, Ninewells Hospital, Dundee, UK*

Kinney et al. *BMC Research Notes* 2012, 5:412  
<http://www.biomedcentral.com/1756-0500/5/412>



**CASE REPORT**

**Open Access**

### Emergency bedside cesarean delivery: lessons learned in teamwork and patient safety

Michelle A O Kinney<sup>1,3\*</sup>, Carl H Rose<sup>2</sup>, Kyle D Traynor<sup>2</sup>, Eric Deutsch<sup>1</sup>, Hafsa U Memon<sup>2</sup>, Staci Tanouye<sup>2</sup>, Katherine W Arendt<sup>1</sup> and James R Hebl<sup>1</sup>

### Respiratory arrest with remifentanil patient-controlled analgesia – another case

We would like to describe a case very similar to that of Bonner and McClymont involving a respiratory arrest within five minutes of commencing remifentanil patient-controlled analgesia (PCA) for labour analgesia [1].

Anaesthesia 2013, 68, 283–287

doi:10.1111/anae.12099

## Case Report

Cardiac arrest in an obstetric patient using remifentanil patient-controlled analgesia

R. Marr,<sup>1</sup> J. Hyams<sup>2</sup> and V. Bythell<sup>1</sup>

*1 Consultant Anaesthetist, 2 Specialty Trainee, The Royal Victoria Infirmary, Newcastle upon Tyne, UK*

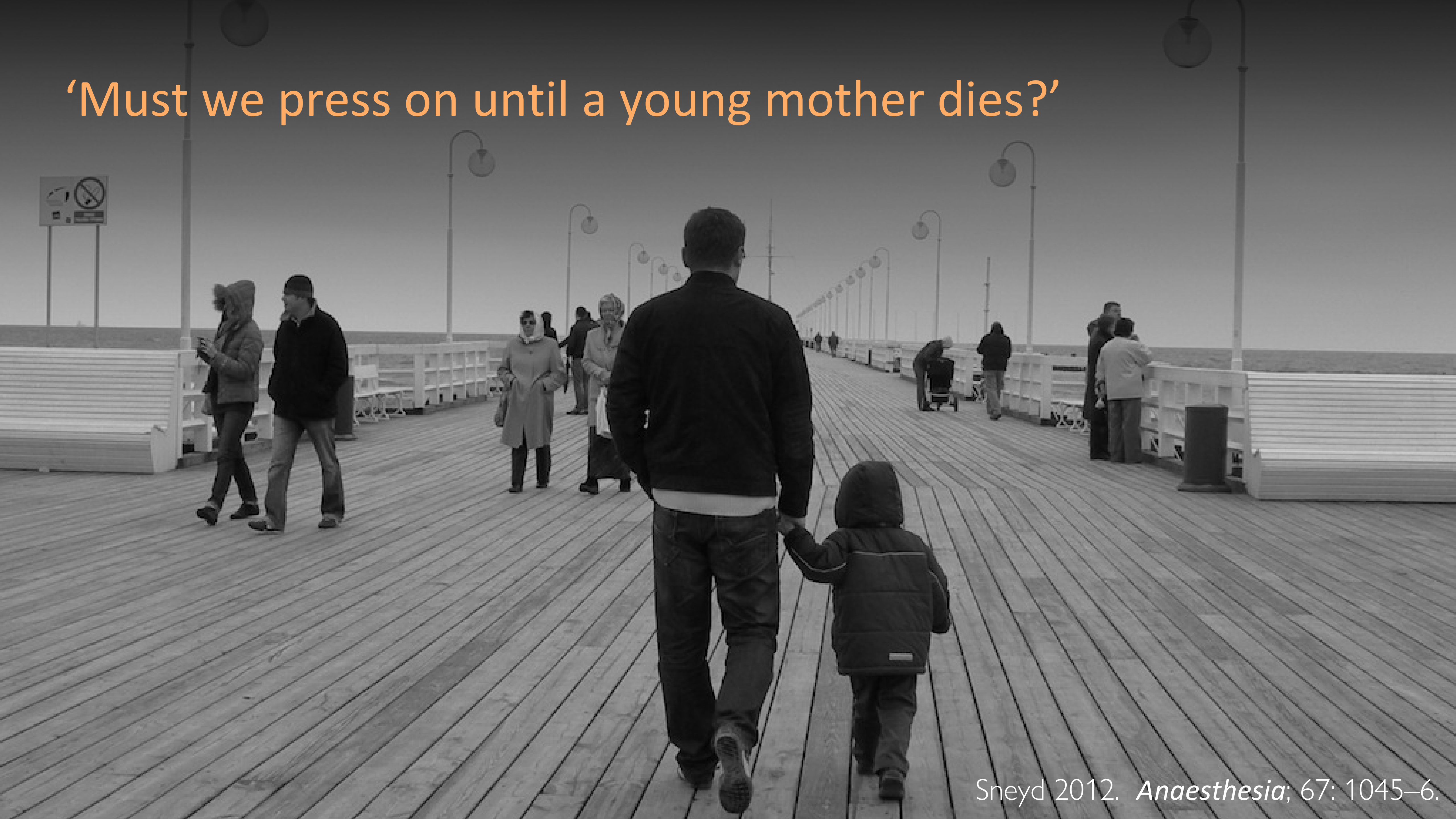
Bonner 2012  
Kinney 2012  
Pruefer 2012  
Marr 2013

**32%** of

women in studies had  
some degree of  
**respiratory depression**



‘Must we press on until a young mother dies?’



# Editorial

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Remifentanyl for labour analgesia: time to draw breath?

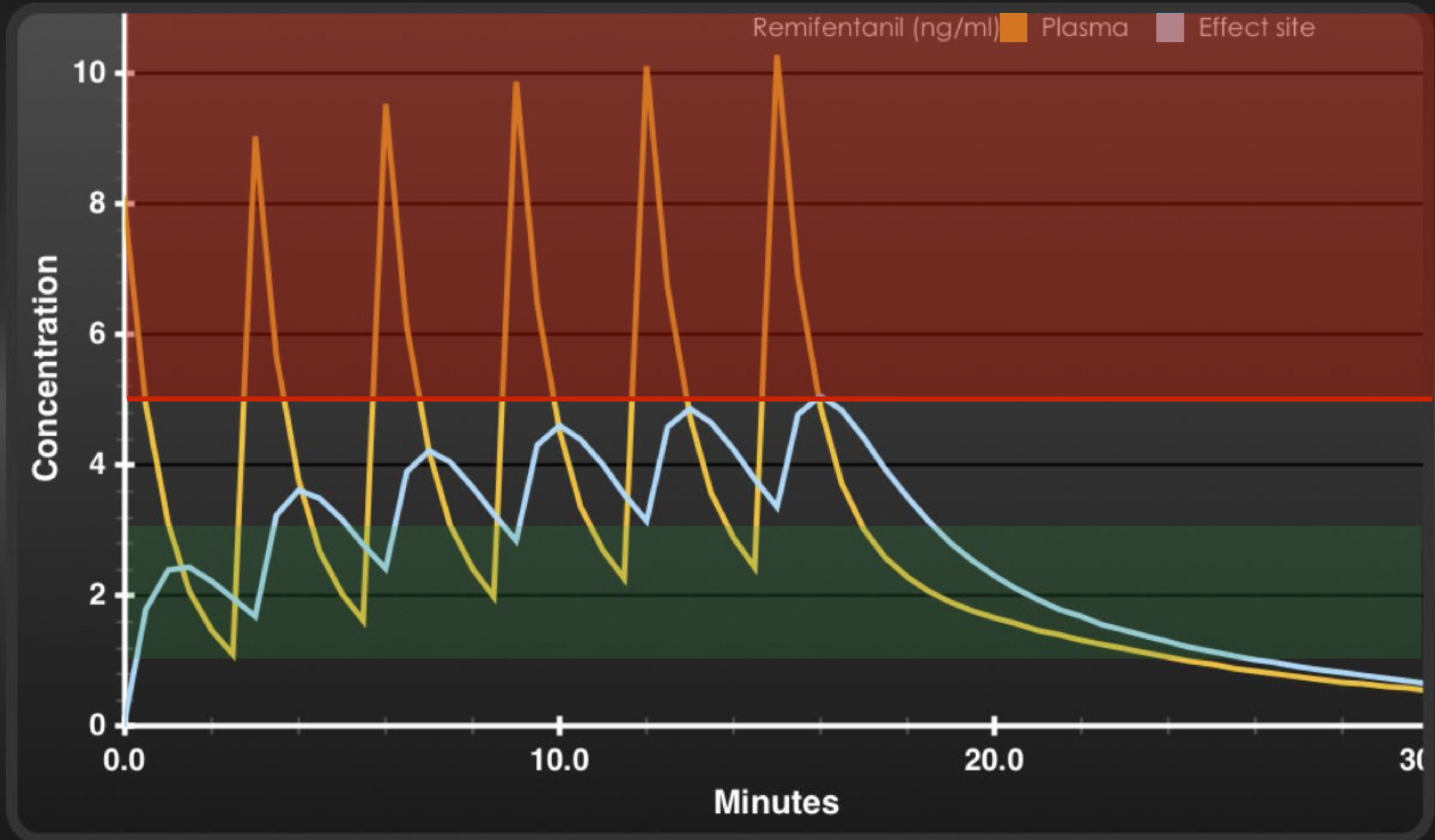
Limit bolus dose to 20–30 mcg

Increase lock-out to 3 mins

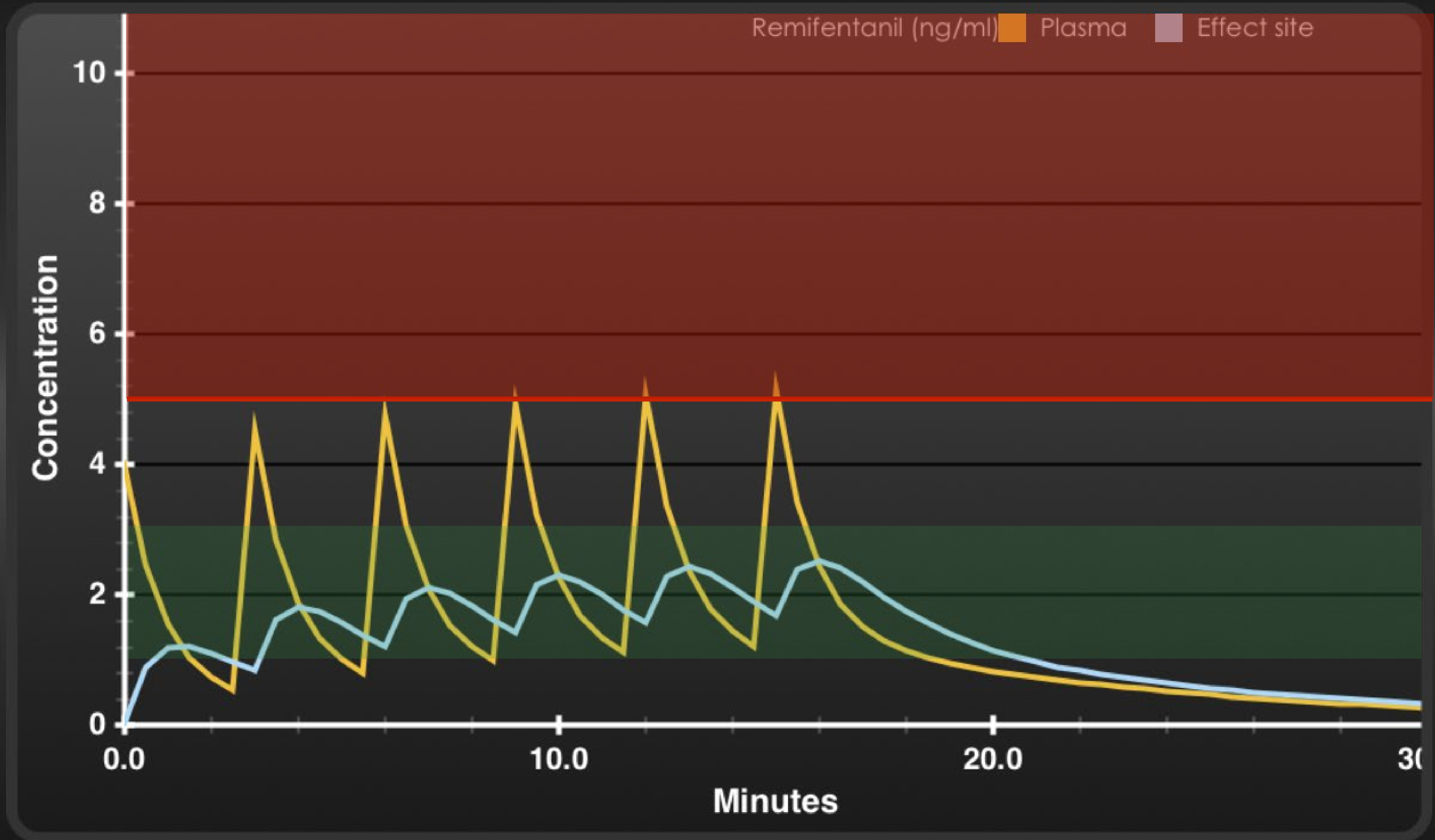
Avoid if opioids given in last 4 hours

Avoid in intrauterine death

Continuous presence of a midwife/equivalent



40 mcg bolus, 3 min lockout



20 mcg bolus, 3 min lockout

# Outline

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**RESPITE study**

Real-world lessons

Recommendations for its use

# Pain relief drug could halve number of women needing epidurals during labour, study finds

Remifentanil is more effective than commonly used medicine, scientists say

**Ellie Cullen** | Tuesday 14 August 2018 19:27 |



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**Boris Johnson will 'test the law to the**

**Leave voters back a Brexit alliance to**

**Britain's SAS and SBS advertise for**

**John McDonnell says any caretaker**

## Pregnant women could be spared epidurals if doctors switched to a more effective painkiller barely used by the NHS

- Experts say remifentanil is more effective than injection pethidine during labour
- Forty per cent of women end up needing an epidural after the pain relief
- If remifentanil was used, it could halve the number of women who have one

By [BEN SPENCER](#) MEDICAL CORRESPONDENT FOR THE DAILY MAIL

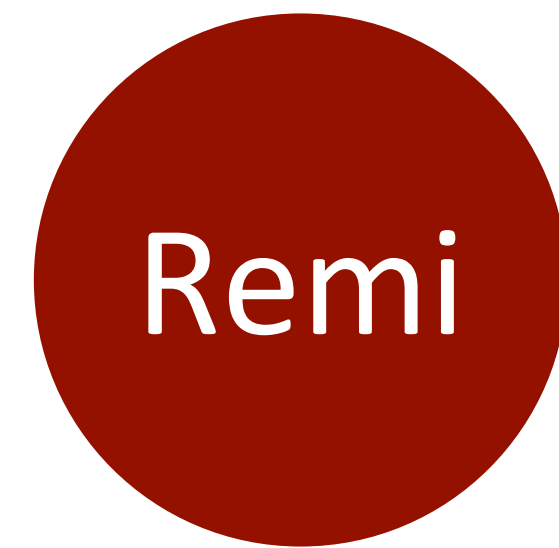
**PUBLISHED:** 00:10, 14 August 2018 | **UPDATED:** 01:08, 14 August 2018



# Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE): an open-label, multicentre, randomised controlled trial

Matthew J A Wilson, Christine MacArthur, Catherine A Hewitt, Kelly Handley, Fang Gao, Leanne Beeson, Jane Daniels, on behalf of the RESPITE Trial Collaborative Group\*

## Remifentanil vs Pethidine



40 mcg, 2 min



100 mg IM, 4 hr

$n = 401$

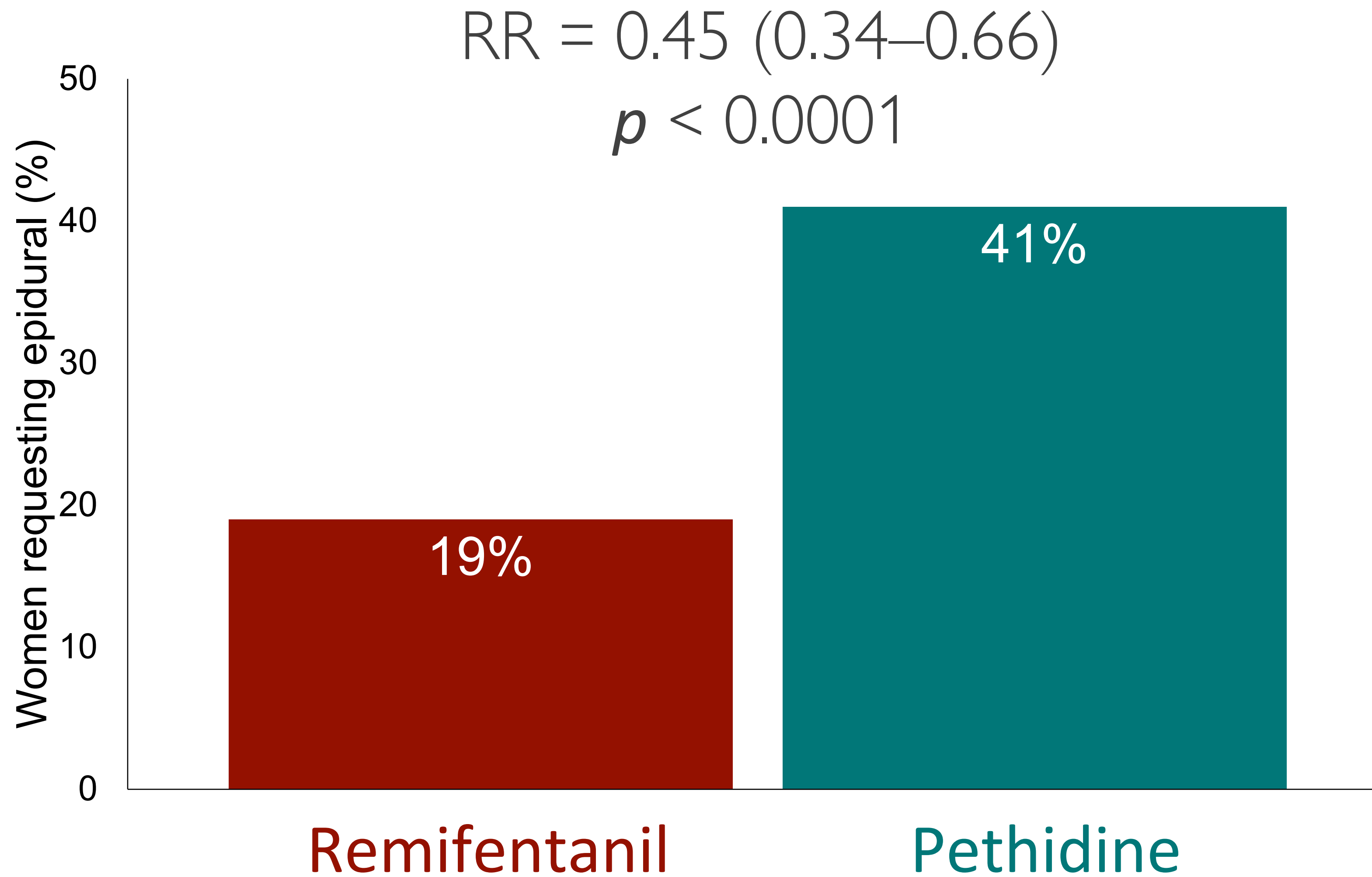
primary outcome: number of women receiving epidural afterwards



# RESPITE study – background

pethidine given to 250,000/yr in UK  
midwives prescription exemption  
maternal and fetal side-effects  
1 in 3 end up with epidural analgesia

# RESPITE study – primary outcome



# RESPITE study – maternal results



# RESPITE study – fetal results



Remi



Peth



## Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE): an open-label, multicentre, randomised controlled trial

Matthew J A Wilson, Christine MacArthur, Catherine A Hewitt, Kelly Handley, Fang Gao, Leanne Beeson, Jane Daniels, on behalf of the RESPITE Trial Collaborative Group\*

Remifentanil  
PCA

epidural requests halved  
better analgesia  
more satisfaction with analgesia  
fewer fetal side effects



## Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE): an open-label, multicentre, randomised controlled trial

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Remifentanil  
PCA

is remifentanil vs pethidine fair comparison?  
not a study of safety of remifentanil  
more maternal side effects  
1:1 midwifery care & 'RCT' care

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Controversies

RESPITE study

**Real-world lessons**

Recommendations for its use

# Belfast experience





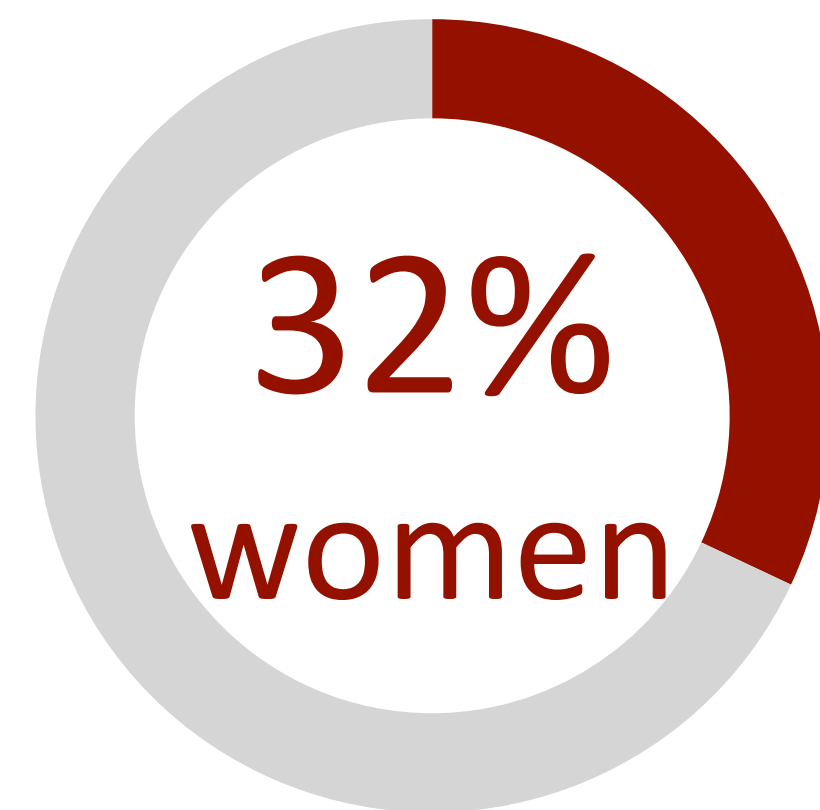
# Remifentanil patient-controlled intravenous analgesia during labour: a retrospective observational study of 10 years' experience

H. Murray,<sup>a</sup> P. Hodgkinson,<sup>b</sup> D. Hughes<sup>b</sup>

<sup>a</sup>*Belfast City Hospital, Belfast, N. Ireland, UK*

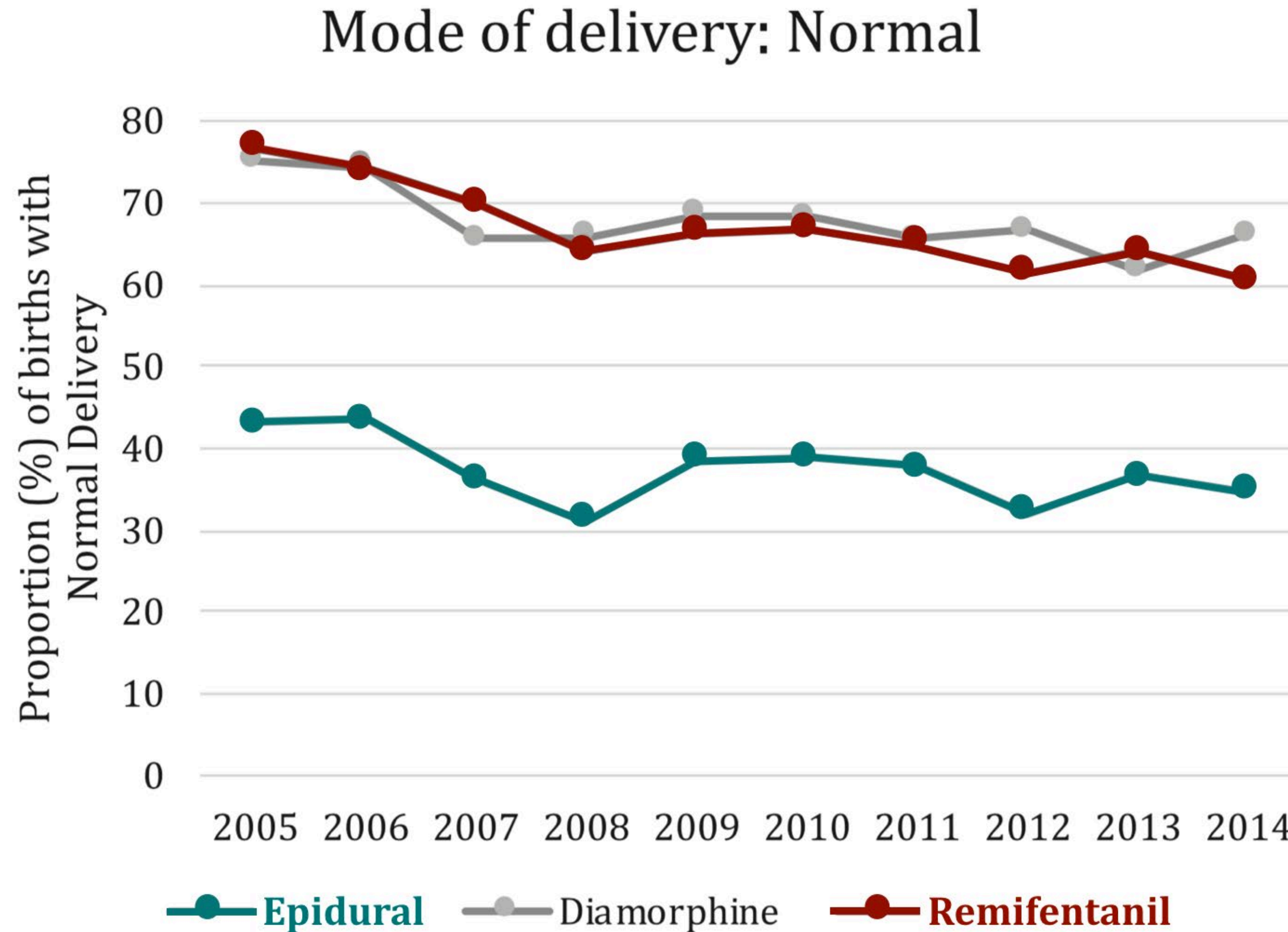
<sup>b</sup>*Ulster Hospital, Dundonald, N. Ireland, UK*

> 8,100 deliveries using remifentanil PCA  
4 mcg, 2 min

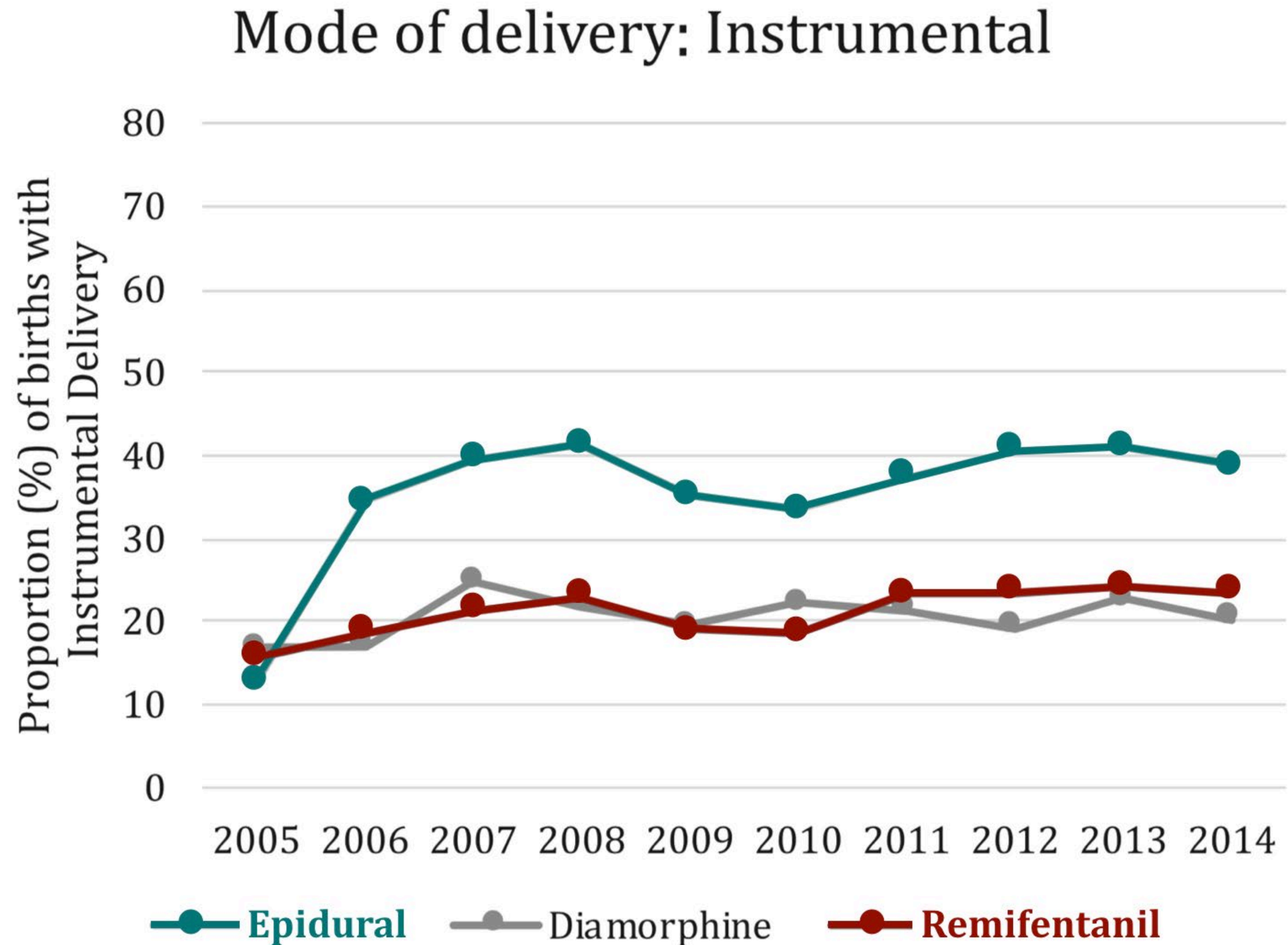
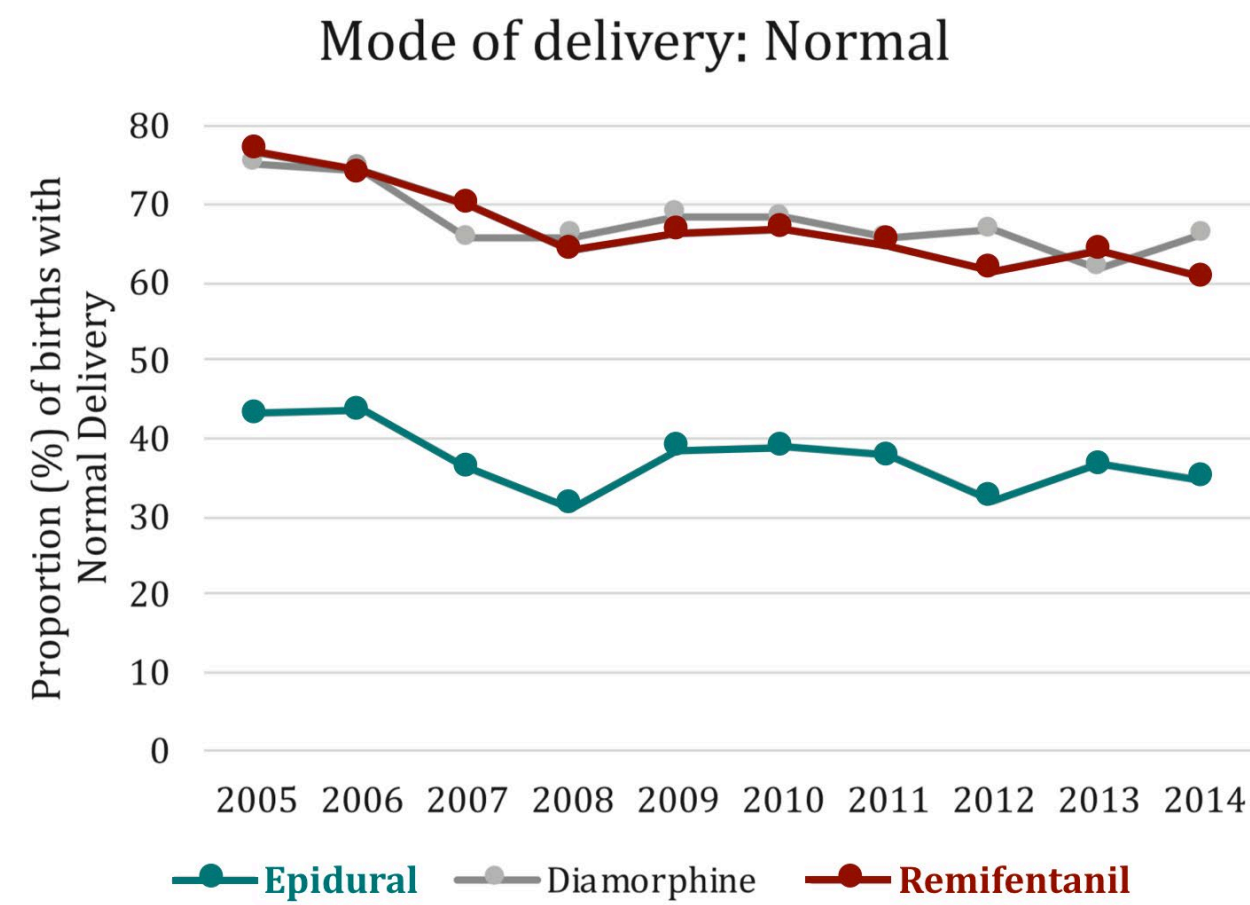


receive remifentanil (vs 25% epidural)

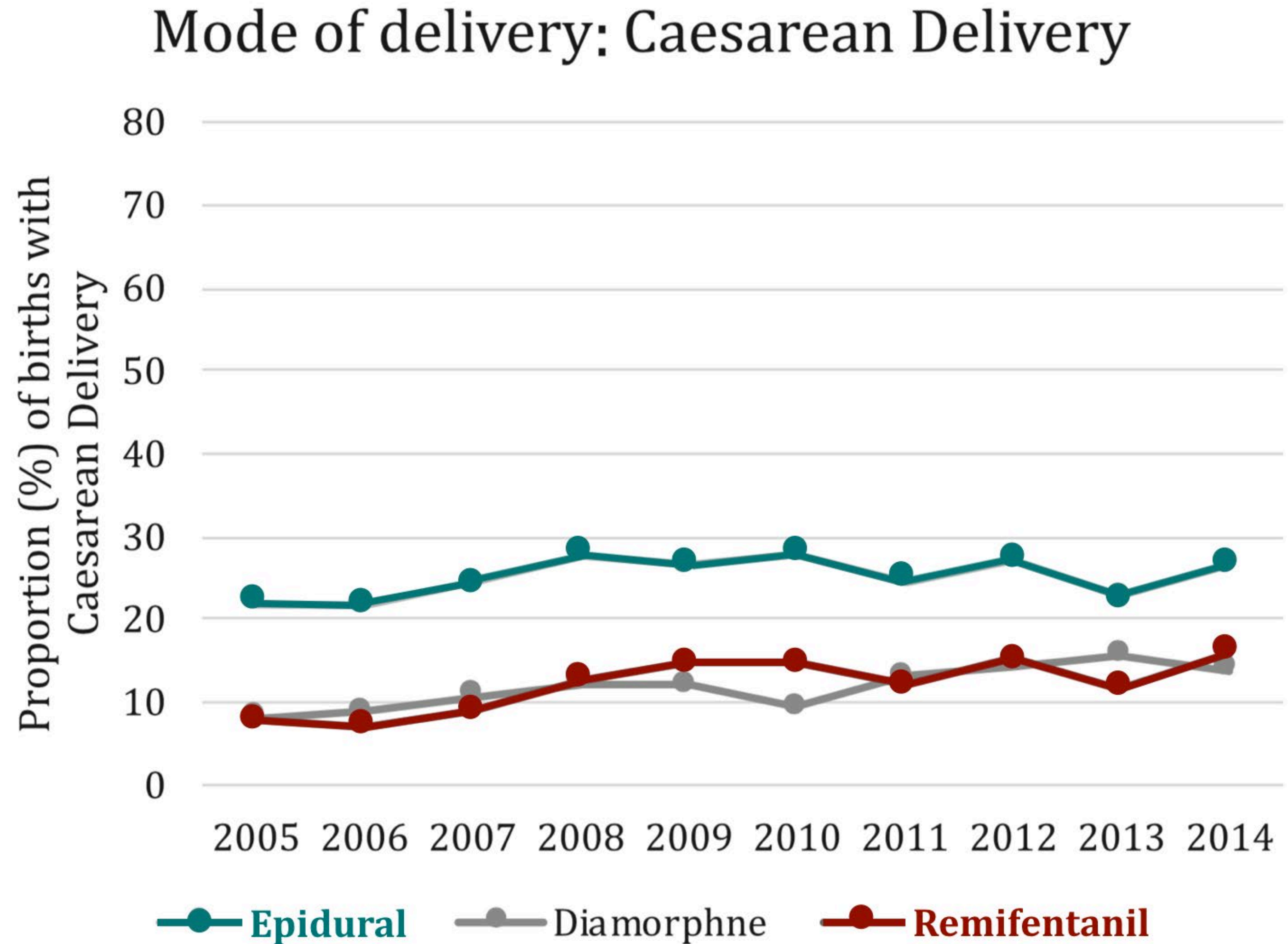
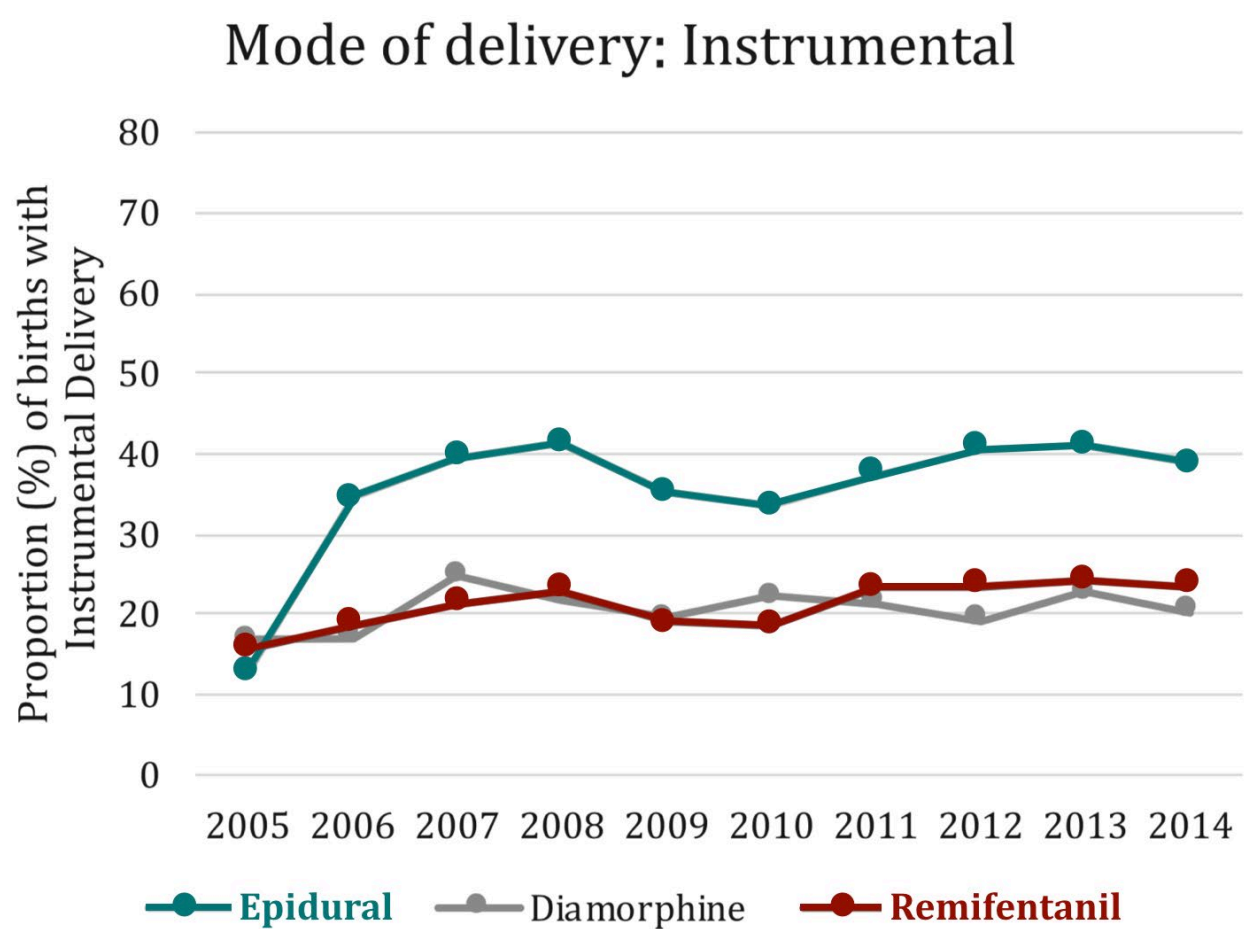
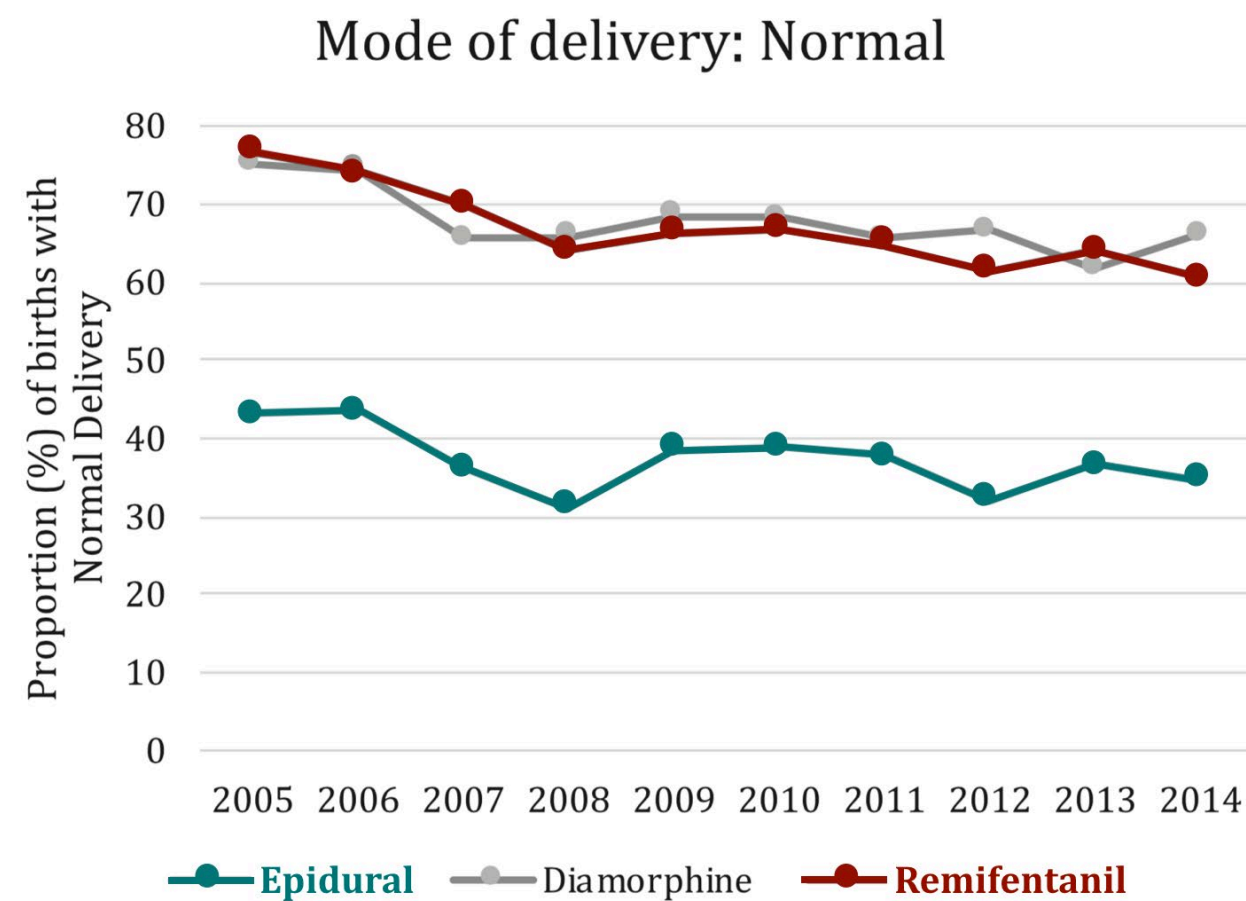
# Belfast – mode of delivery



# Belfast – mode of delivery



# Belfast – mode of delivery



# Belfast experience

 **56%** oxygen supplementation ( $\text{SpO}_2 < 95\%$ )

# Serious adverse events attributed to remifentanil patient-controlled analgesia during labour in The Netherlands

S.L.M. Logtenberg,<sup>a,b</sup> M.L. Vink,<sup>c</sup> M.B. Godfried,<sup>d</sup> I.C.M. Beenackers,<sup>e</sup>  
F.G. Schellevis,<sup>f,g</sup> B.W. Mol,<sup>h</sup> C.J. Verhoeven<sup>i,j</sup>

61 Dutch units use remifentanil PCA

100% responded

up to 10 years experience

27 maternal adverse events:

1 mask ventilation  
1 intubation  
1 CPR (3 compressions)  
1 CPR (3 minutes)

2 fetal adverse events:

1 stiff chest (intubated)  
1 mask inflation breaths

**21,000 IN 1 YEAR**

# Serious adverse events attributed to remifentanyl patient-controlled analgesia during labour in The Netherlands

S.L.M. Logtenberg,<sup>a,b</sup> M.L. Vink,<sup>c</sup> M.B. Godfried,<sup>d</sup> I.C.M. Beenackers,<sup>e</sup>  
F.G. Schellevis,<sup>f,g</sup> B.W. Mol,<sup>h</sup> C.J. Verhoeven<sup>i,j</sup>

National standard operating procedure (SOP)

1:1 midwife presence for 1st hour

# A Randomized Controlled Trial of the Efficacy and Respiratory Effects of Patient-Controlled Intravenous Remifentanyl Analgesia and Patient-Controlled Epidural Analgesia in Laboring Women

Daniel Stocki, MD,\*† Idit Matot, MD,† Sharon Einav, MD,‡ Smadar Eventov-Friedman, MD,§  
Yehuda Ginosar, MBBS,\* and Carolyn F. Weiniger, MB ChB\* ||

**23%** had apnoea events  
**½ after 2 hours**



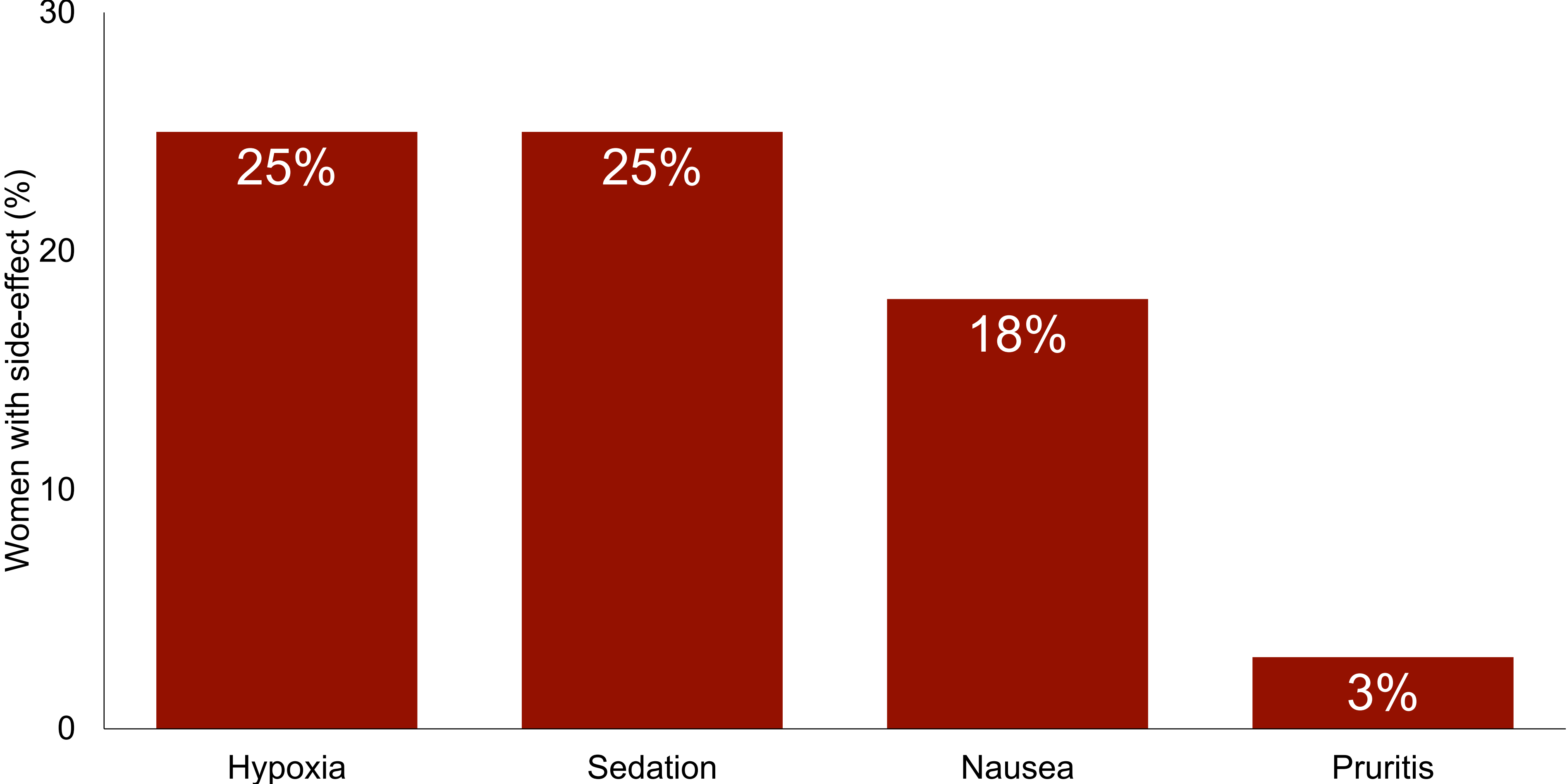
# Remifentanil patient-controlled analgesia in labour: six-year audit of outcome data of the RemiPCA SAFE Network (2010–2015)

A.A. Melber,<sup>a</sup> Y. Jelting,<sup>b</sup> M. Huber,<sup>c</sup> D. Keller,<sup>d</sup> A. Dullenkopf,<sup>e</sup> T. Girard,<sup>f</sup>  
P. Kranke<sup>b</sup>

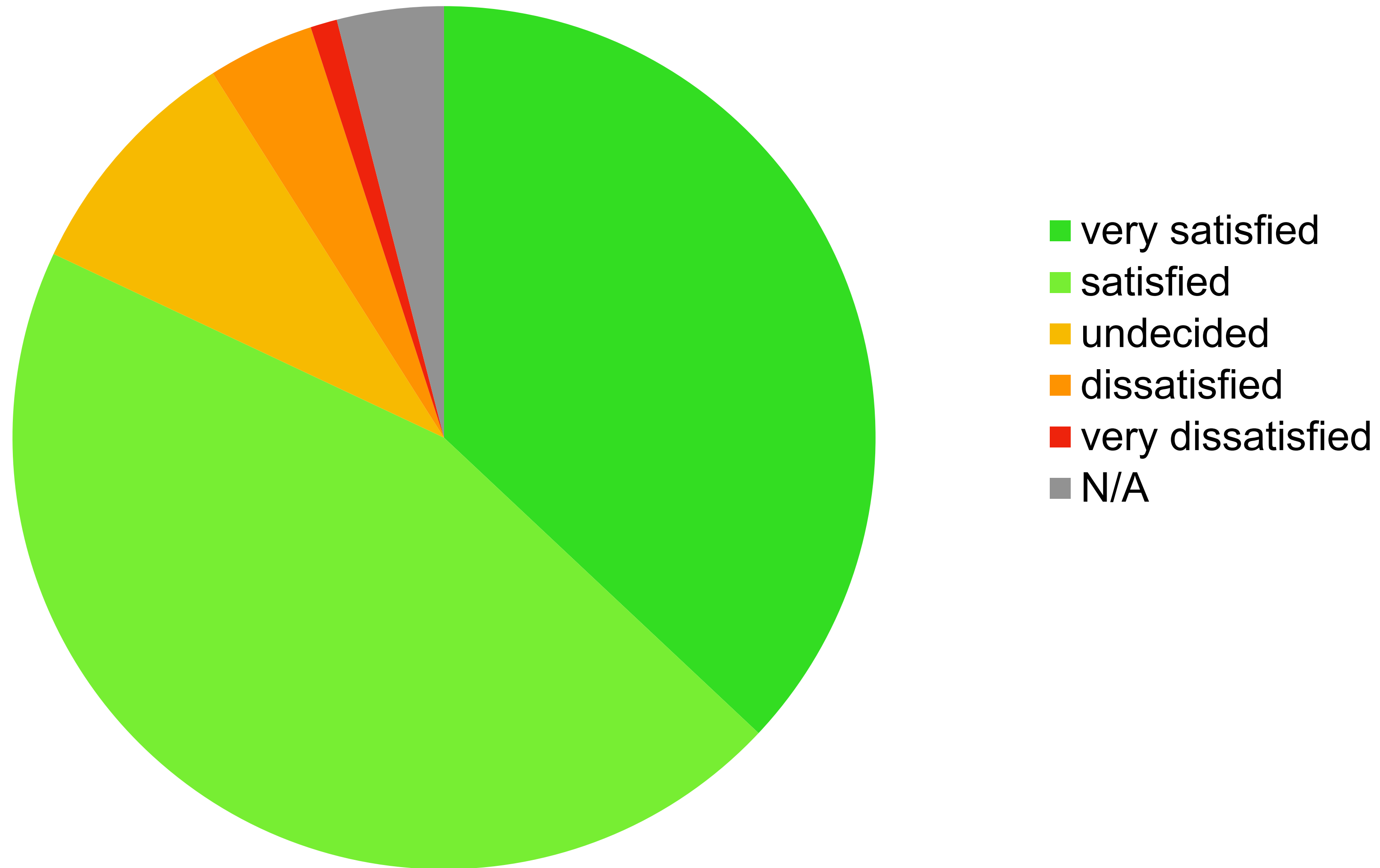
registry of remifentanil PCA users  
based in Switzerland  
experience of > 5,700 uses



# Side effects



# Maternal satisfaction



# RemiPCA – standard operating procedure

	original	updated
<b>bolus</b>	20–40 mcg	10–30 mcg

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Real-world lessons

**Recommendations for its use**

A man in a blue short-sleeved shirt and a pregnant woman in a red dress are standing together outdoors. The man is on the left, and the woman is on the right, holding her belly. The background is a bright, hazy outdoor setting, possibly a beach or a park. The text "One to One" is overlaid in the center of the image.

One to One

# Protocols & Training



## REMIFENTANIL PCA RECORD Anaesthetic Assessment

Date:..... Assessing Anaesthetist:.....

Time:..... GMC No:.....

Medical history: ..... ASA: .....

Indication: .....

**Absolute contraindications:**  
1. Fetal demise  
2. Continuous presence of a midwife not guaranteed

**Relative contraindication:**  
Opioids administered in the last 4 hours: increased risk of respiratory depression.

**Quick set-up:**

- 1 mg of remifentanil made up to 50 mL with 0.9% saline to make 20 mcg/mL
- Fluids to run concurrently to keep vein open via volumetric pump with an occlusion alarm
- Dedicated cannula with anti-syphon valve (i.e. PCA giving set)
- Ensure no remifentanil in dead-space of giving set

**Safety:**

If SpO<sub>2</sub> < 93%  
If RR < 10  
If sedation score = 4  
If conscious level is P or U

then:

1. Remove PCA button
2. Encourage breathing
3. Give high-flow oxygen
4. Call anaesthetist (3037)

**If the midwife wishes to leave the room:**

Call for a replacement  
or  
Remove PCA button, wait 5 minutes, then leave

Surname:	Unit No:
Forename:	
Address:	
Date of Birth:	Consultant:
<b>Risks Discussed</b>	
Information card read	Y / N.....
Drowsiness	Y / N.....
Incomplete pain relief	Y / N.....
Nausea	Y / N.....
Itching	Y / N.....
Reduced breathing	Y / N.....
Questions answered?	Y / N.....
Other .....	
Signature .....	
Witnessed .....	

**Pump settings:**

- Only use dedicated remifentanil PCA pump
- Concentration: **20 micrograms/mL**
- Bolus: **20 micrograms (= 1 mL)**
- Lockout: **3 minutes**
- Bolus dose given: **STAT**
- **No background infusion**

**Midwife:** Apply continuous CTG monitoring. Check observations every 30 minutes for the first 2 hours, then hourly.

Date																			
Time																			
O <sub>2</sub> Saturations																			
Respiratory rate																			
Sedation score 1–4 (see overleaf)																			
Consciousness level: AVPU (see overleaf)																			
Total demands																			
Total successful demands																			
Total amount (micrograms) received																			
Initials																			

Each shift handover or change of syringe: patient, prescription and pump settings must be checked and signed by 2 trained staff (date/time/initials)


**PCA discontinuation:**

Date: ..... Time:..... Total amount of opioid infused: ..... Total amount discarded: .....

Cannula flushed. Discarded opioid destroyed/witnessed and signed in CD book. RGN/OPD/MW initials ..... / .....





**REMIFENTANIL PCA RECORD**  
**Anaesthetic Assessment**

Date:..... Assessing Anaesthetist:.....

Time:..... GMC No:.....

Medical history: ..... ASA: .....

Indication: .....

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Surname: ..... Unit No: .....

Forename: .....

Address: .....

Date of Birth: ..... Consultant: .....

**Risks Discussed**

Information card read Y / N.....  
Drowsiness Y / N.....  
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Reduced breathing Y / N.....

Questions answered? Y / N.....

Other .....

Signature .....

Witnessed .....

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Date	Time	O <sub>2</sub> Saturations	Respiratory rate	Sedation score 1-4 (see overleaf)	Consciousness level: AVPU (see overleaf)	Total demands	Total successful demands	Total amount (micrograms) received	Initials

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**PCA discontinuation:**

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**Safety:**

If SpO<sub>2</sub> < 93%

If RR < 10

If sedation score = 4

If conscious level is P or U

then:

1. Remove PCA button
2. Encourage breathing
3. Give high-flow oxygen
4. Call anaesthetist (3037)



# Continuous



4 hrs



# Intra-uterine death

patient. She also had the recommended 'one to one' care, although her attendant had briefly left the room. In discussion with the midwives, it is clear that where there is no live fetus, there is felt not to be the need for the same level of monitoring. Indeed, many midwives feel intrusive and try to minimise their involvement.



Lowest effective dose  
(e.g. 20–30 mcg)

Longest effective lock-out time  
(e.g. 3 minutes)

## **A Survey of Intravenous Remifentanil Use for Labor Analgesia at Academic Medical Centers in the United States**

Jaime Aaronson, MD,\* Sharon Abramovitz, MD,\* Richard Smiley, MD, PhD,† Virginia Tangel, MA,\* and Ruth Landau, MD†

“ No complications occurred in the four centres that reported using remifentanil more than 10 times in the previous year ”

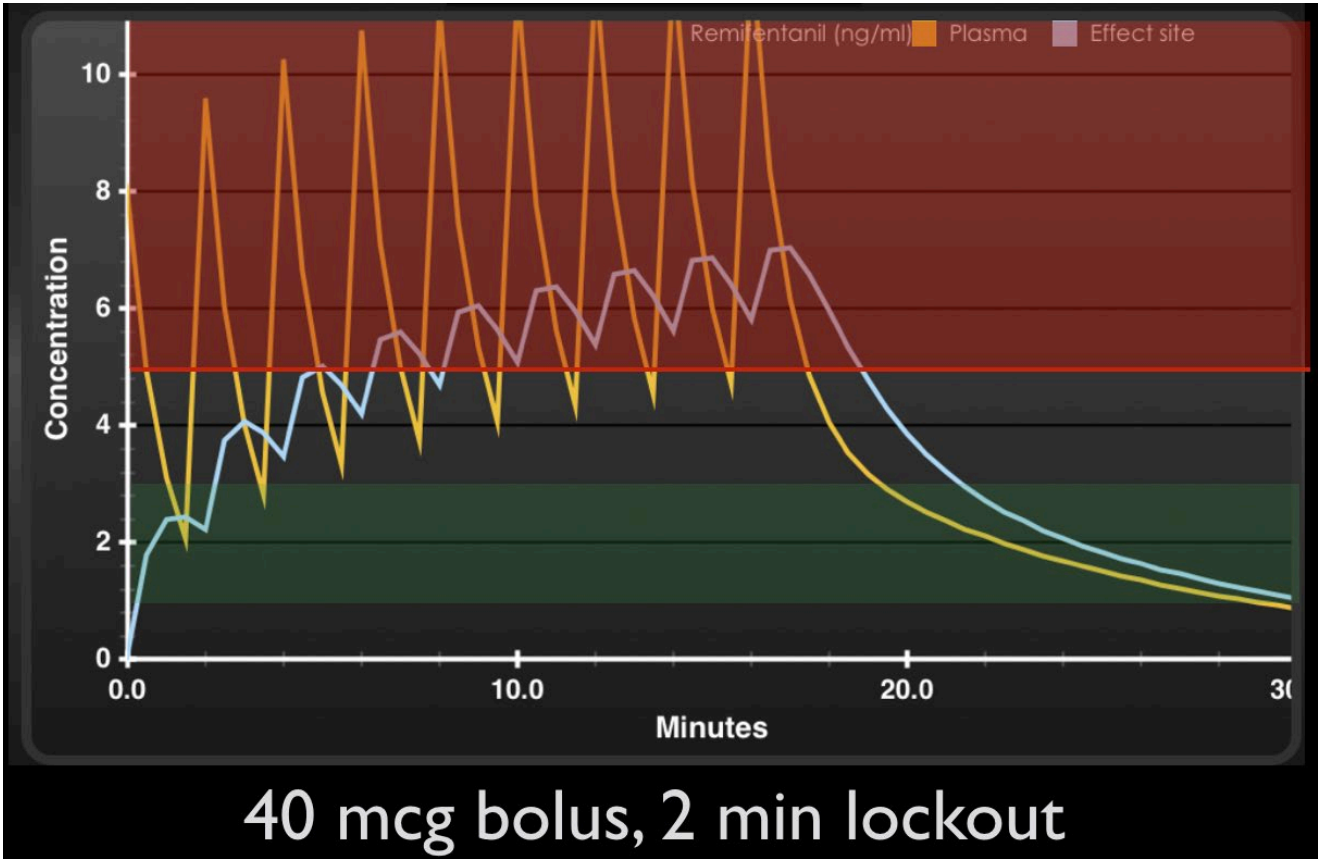


# Summary

## Fetal & neonatal effects

Blair 2002  
Thurlow 2002  
Volmanen 2002  
Blair 2005  
Volmanen 2008  
Evron 2005  
Volikas 2005  
Raj 2007  
Volmanen 2011  
Shen 2013  
Konefat 2013

**NO ADVERSE EFFECTS**



“No complications occurred in the four centres that reported using remifentanyl more than 10 times in the previous year”

## Intra-uterine death



**23%** had apnoea events  
1/2 after 2 hours

