

# OB anaesthesia and neonatal outcomes



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***“Half the world are women,  
the other half are their children.”***

# Fair Inclusion of Pregnant Women in Clinical Research

## Research Paradox

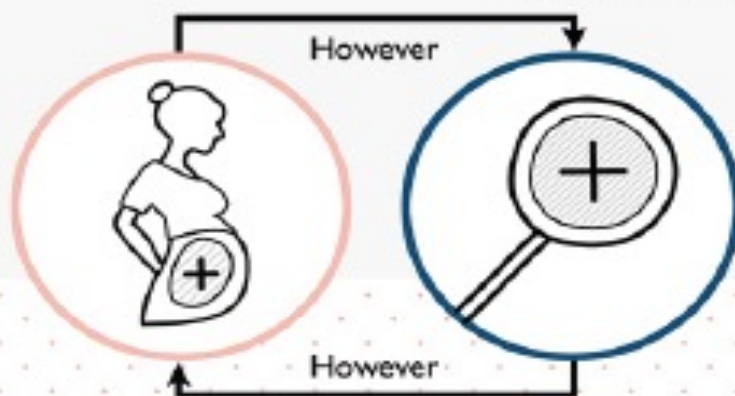
WHY

We intuitively prefer to exclude pregnant women from clinical research.

Exclusion leads to harm: 9/10 pregnant women take medications while > 90% of approved medications has an undetermined risk for use in pregnancy.

We want to protect pregnant women and fetuses from harm.

Sound evidence can only be gathered through fair inclusion of pregnant women in research.





**Not all questions can be  
answered with an RCT**



**To improve maternal and childhood outcomes  
using population level data**

# A unique cohort linking mums, babies and all healthcare interactions



Maternal Health Data



Community Health Index



Offspring Health Data

**~2.5 million mother-infant pairs  
over 40 years with annual updates**

## ANAESTHESIA & THE NEONATE



## ANAESTHESIA & THE FETUS



## NEURODEVELOPMENT



## EPIDURAL RELATED FEVER



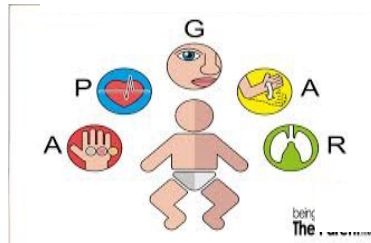
Is mode of anaesthesia for  
caesarean associated with  
adverse neonatal &  
childhood outcomes?





# All Scottish singleton livebirths 2007-2016

# Outcomes



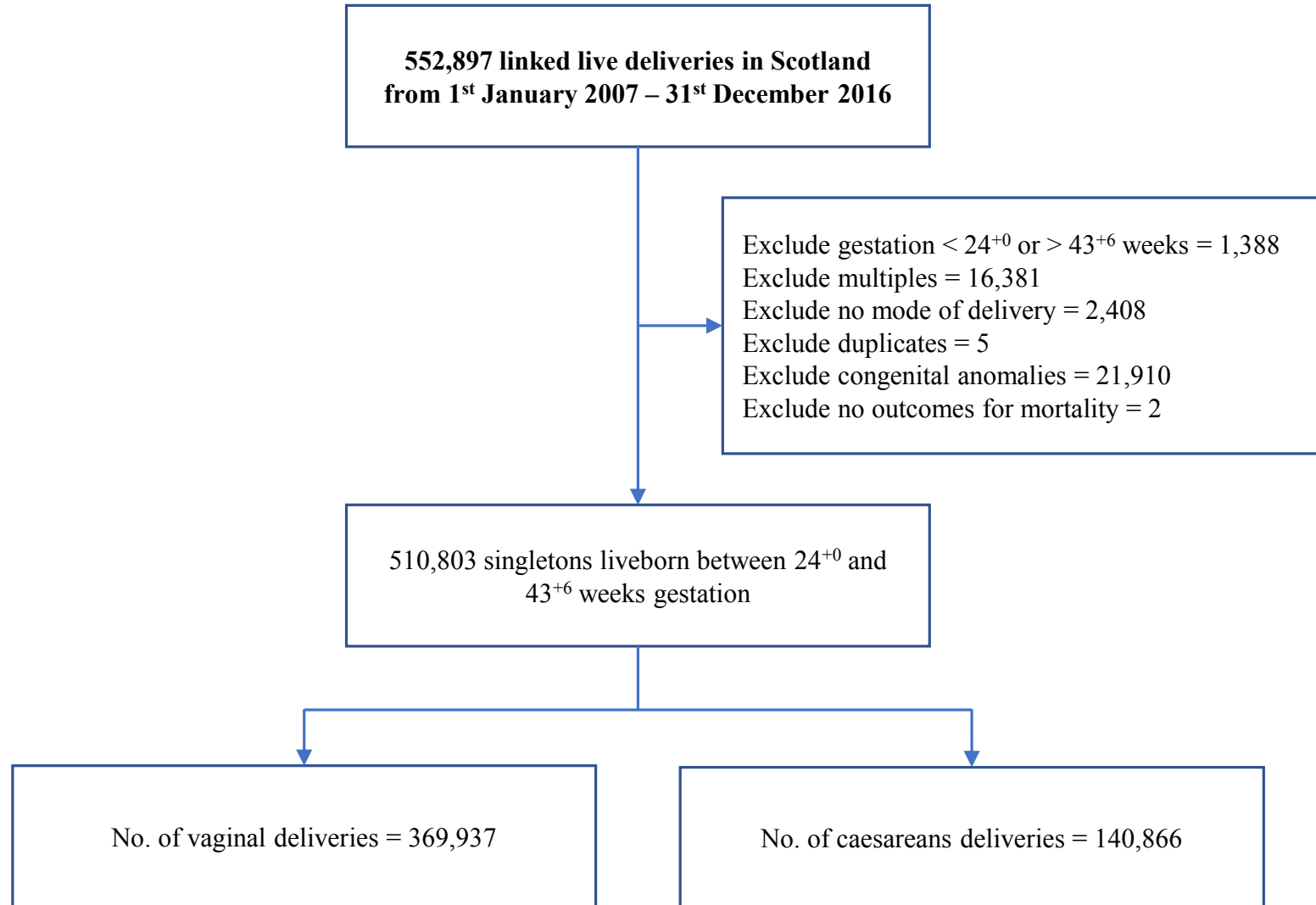
# Statistics

- Missing data – imputation
- Cluster robust Poisson regression modelling
- Adjustment for confounders using DAGs
- Separate analyses for elective & emergency cases
- R Foundation for Statistical Computing



# 40% elective, 60% emergency

## GA more common in emergency (9.8 v 3.2%)



# Greatest difference in elective cases

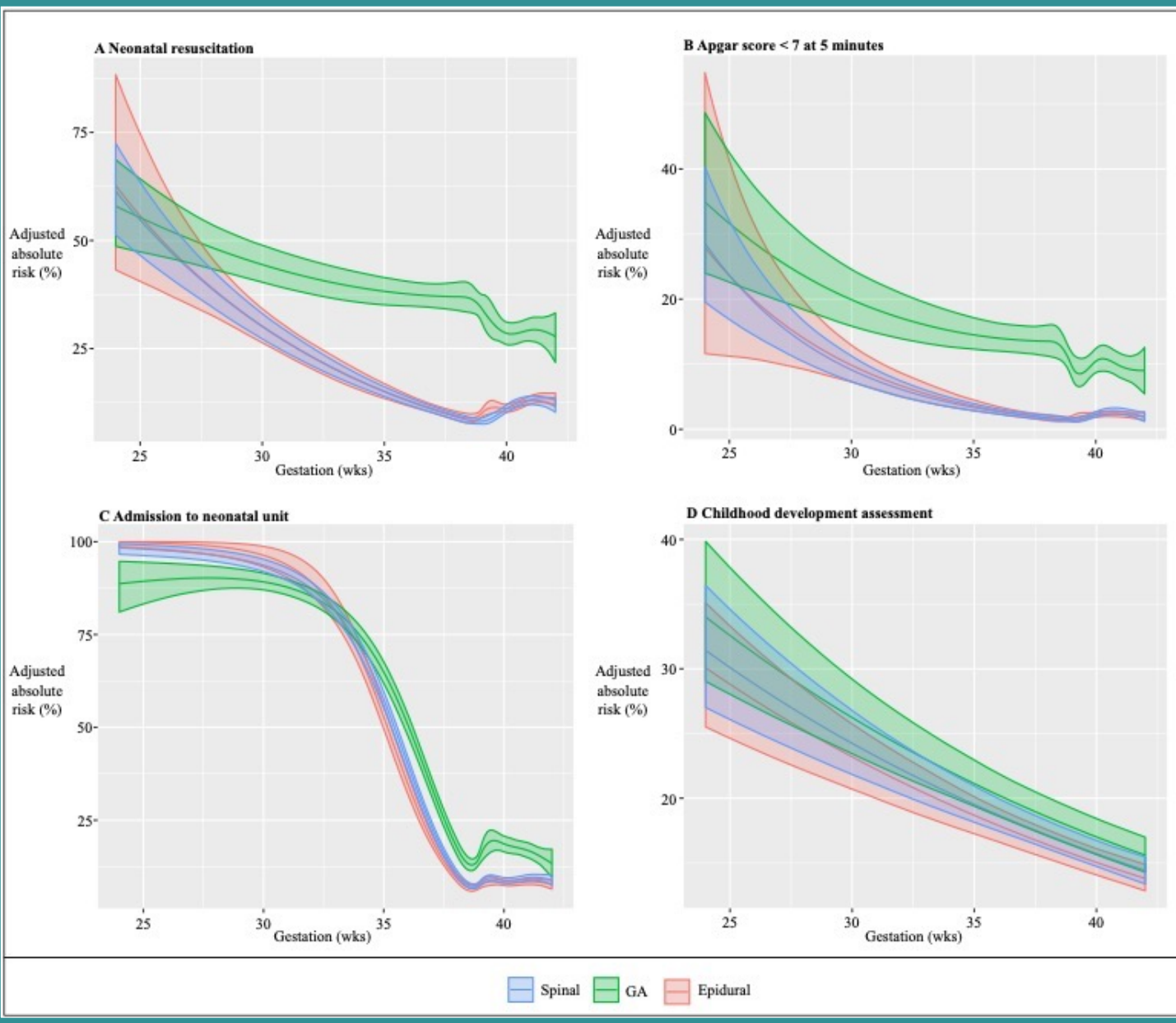
Kearns et al 2021

UK population-based study  
140,866 CB  
2007-2016

Elective  
(n=57,971)

Emergency  
(n=82,895)

Neonatal resus, Apgar <7 @ 5m, NICU admission, development @ 2y



# Anaesthesia type made *least* difference in *most* urgent deliveries

**Sub-group analysis of 14,808 emergency cases**

## **Neonatal resuscitation**

- category-1 (adjRR 2.36, 95% CI 1.31, 4.26)
- category-2 (adjRR 3.26, 95% CI 1.26, 8.48)
- category-3 (adjRR 7.75, 95% CI 2.21, 27.18)

## **Neonatal admission**

- category-1 (adjRR 1.39, 95% CI 0.79, 2.43)
- category-2 (adjRR 1.60, 95% CI 0.63, 4.09)
- category-3 (adjRR 2.43, 95% CI 0.77, 7.70)

# Findings

GA (irrespective of urgency) associated with adverse neonatal outcomes

Associations strongest in elective cases and at term

Associations with longer-term outcomes weak

# What does this mean?

Avoid GA in cases with no clear clinical indication

Necessary GA should *not* be avoided

Where GA is used, a neonatologist must be present at delivery



Is anaesthesia in pregnancy safe for the fetus?

# Do not deny a pregnant woman necessary surgery regardless of trimester

Bleeser et al 2022

Ambi-directional cohort study  
Pre-natal anaesthesia  
Propensity matched

129 Cases

453  
Controls

Neurodevelopment  
Mental health / learning disorders

64% response rate

**NO difference:**

- Neurodevelopment
- Mental Health outcomes
- Learning disorders

Exploratory analysis - ↑ risk with

- Intra-abdominal
- Laparoscopic
- Surgery > 1 hr



# Minimise known risks

## Anaesthesia

- 15° left lateral tilt to avoid aortocaval compression
- Regional anaesthesia preferable. Smaller volumes required for neuraxial techniques
- Higher risk of difficult intubation
- General anaesthesia, rapid sequence induction, ramped position, videolaryngoscope, down-sized tracheal tube.

## Postoperative

- Fetal monitoring as directed by obstetric team, with specific focus on preterm labour
- Thromboprophylaxis
- Breastfeeding should be encouraged as normal following surgery
- There is no need to express and discard breast milk after anaesthesia

- Reversal with neostigmine and atropine (glycopyrrate does not cross the placenta).
- No clinical data on sugammadex use on pregnancy. Recommended only if strongly clinically indicated (e.g. 'can't intubate, can't ventilate' scenario) due to concerns about progesterone binding
- Analgesia: paracetamol (weight appropriate dose), opioids and regional techniques can be used, avoid NSAIDs after 32-weeks' gestation



Does having an epidural in labour  
harm the baby...?

# Association between epidural & autism / adverse neurodevelopment????

JAMA Pediatrics | [Original Investigation](#)

## Association Between Epidural Analgesia During Labor and Risk of Autism Spectrum Disorders in Offspring

Chunyuan Qiu, MD, MS; Jane C. Lin, MS; Jiaxiao M. Shi, PhD; Ting Chow, MPH; Vimal N. Desai, MD; Vu T. Nguyen, MD; Robert J. Riewerts, MD; R. Klara Feldman, MD; Scott Segal, MD, MHCM; Anny H. Xiang, PhD



## No evidence that labour epidurals cause autism

Published: 13/10/2020

BJA

*British Journal of Anaesthesia*, 133 (2): 247–254 (2024)



doi: [10.1016/j.bja.2024.05.009](https://doi.org/10.1016/j.bja.2024.05.009)

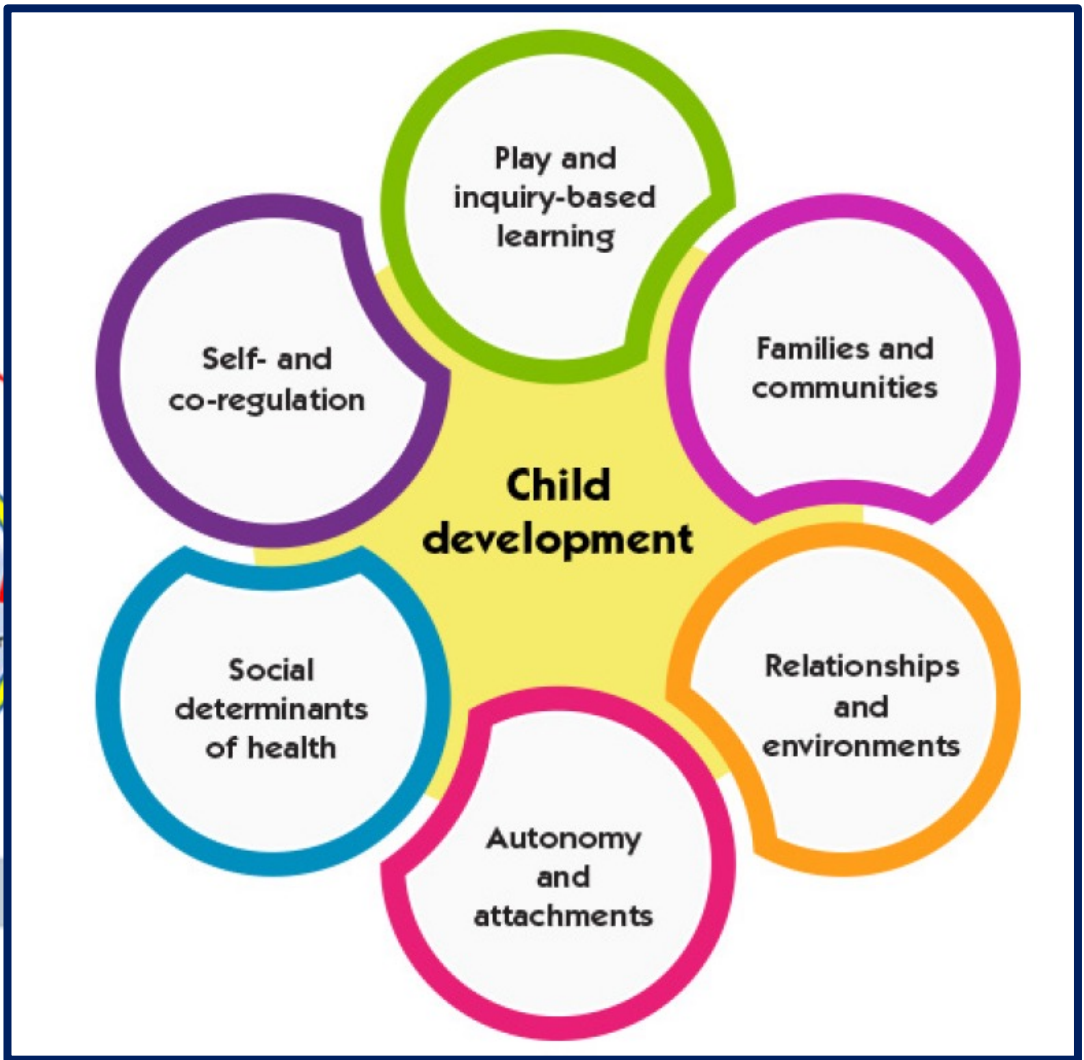
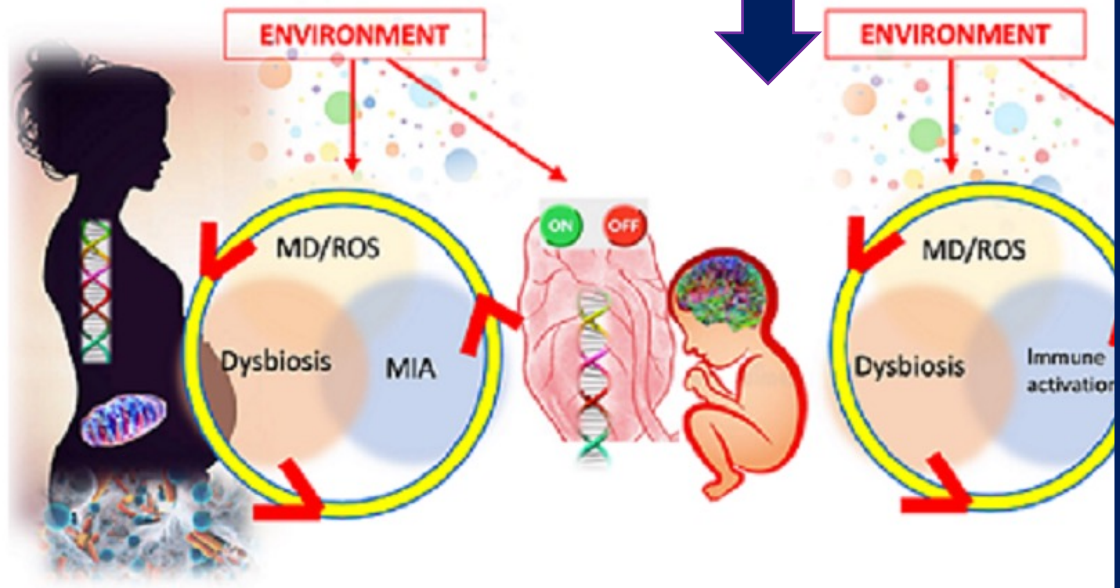
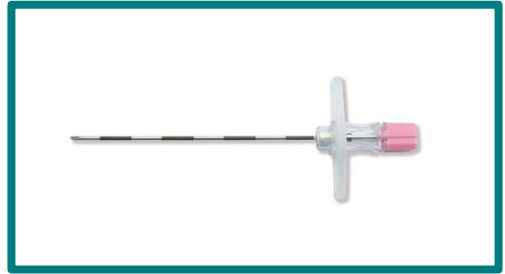
Advance Access Publication Date: 13 June 2024

Editorial

EDITORIAL

## Epidural analgesia in labour: separating fact from fiction for autism and neurodevelopment

Rachel J. Kearns<sup>1,\*</sup> , Scott M. Nelson<sup>2</sup> and Steffen Rex<sup>3,4</sup> 



# Epidural analgesia in labour not associated with adverse neonatal outcomes

Kearns *et al* 2021

UK Population-based study  
435,281 livebirths  
2007-2016

Epidural  
N=94,323  
(22%)

No epidural  
N=340,958

Resus, low Apgar, NICU  
Childhood development at age 2-3y

Neonatal resus



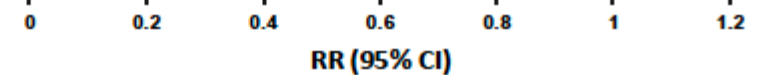
Apgar <7 at 5m



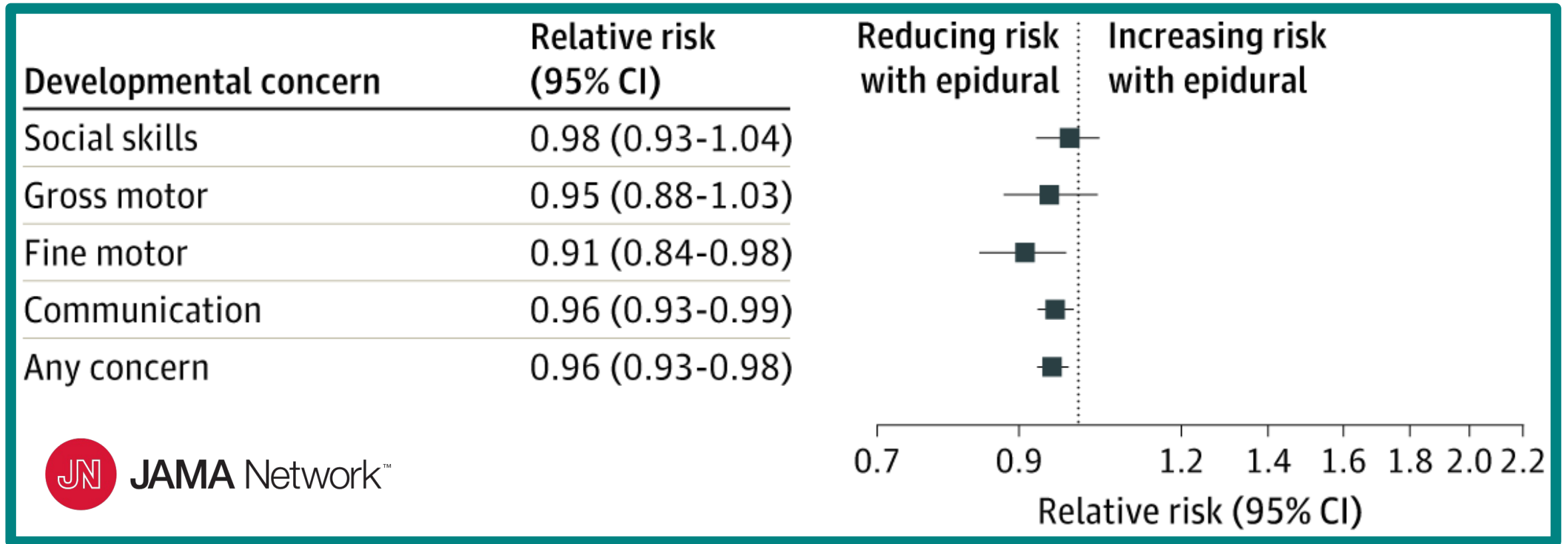
NICU admission



RR (95% CI)

A horizontal axis representing Relative Risk (RR) with 95% Confidence Intervals (CI). The axis ranges from 0 to 1.2 with major tick marks at 0, 0.2, 0.4, 0.6, 0.8, 1, and 1.2. A vertical line is drawn at RR = 1.0.

# Epidural associated with small ↓ in adverse development outcomes at 2-years



## Epidural during childbirth does not harm baby and has no impact on brain development, study suggests

- Third of women who give birth in UK opt for epidural to make labour less painful
- Some experts suggested it may have an effect on the developing brain of a baby
- But a new study found epidural in childbirth does not harm baby's development



© Alamy Stock Photo

Almost a third of women who give birth in the UK opt for an epidural, which makes labour less painful, but some experts suggested it may have an effect on the developing brain of a baby (stock image)

# NO association with adverse neurodevelopment in offspring

Li et al 2026

Systematic review &  
meta-analysis  
19 studies

Epidural

No epidural

ASD, ADHD, intellectual  
impairment

ASD – 14 studies (N=7.9M): aHR 1.10; 1.08–1.13;  
non-significant when sibling matched studies used

ADHD – 2 studies (N=5.1M): aHR 1.09; 0.89–1.33

Communication – 4 studies (N=2.6K): aHR 1.01; 0.81-1.26

Motor – 4 studies (N=2.6K): aHR 1.03; 95% CI 0.86-1.23

Intellectual – 5 studies (N=6.7K; aHR 1.09; 95% CI 0.93-1.28

Behaviour – 1 study (N=2K); HR 1.11; 95% CI 0.75-1.64

# Does maternal immune response to epidural matter??

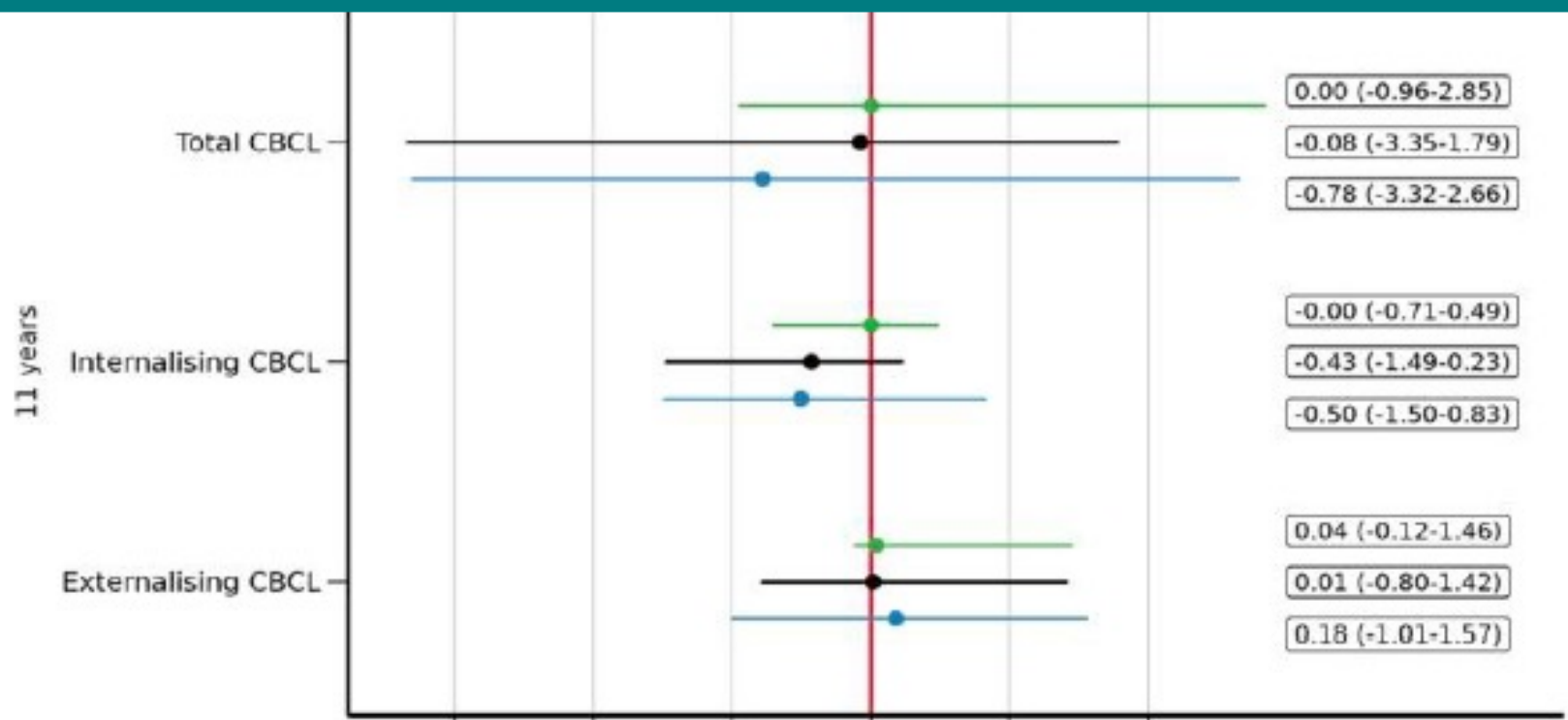
Asif et al 2026

Longitudinal population study  
2010-2019  
1962 mother-infant pairs

Epidural  
(37%)

No epidural

Swedish CBCL score  
@ 18 mths, 6 yrs, 11 yrs



**EXPLORATORY**

Low levels of TNFSF14 and CXCL6  
cytokines assoc with higher scores



What about epidural-related maternal fever?

# Fever in labour



**INFECTION**

**NON-INFECTIOUS**

*Excess ambient heat, drug reaction, VTE, hyperthyroid*

**EPIDURAL**

- Temp  $\geq 38^{\circ}\text{C}$  on one occasion
- Temp  $\geq 37.5^{\circ}\text{C}$  on two occasions two hours apart

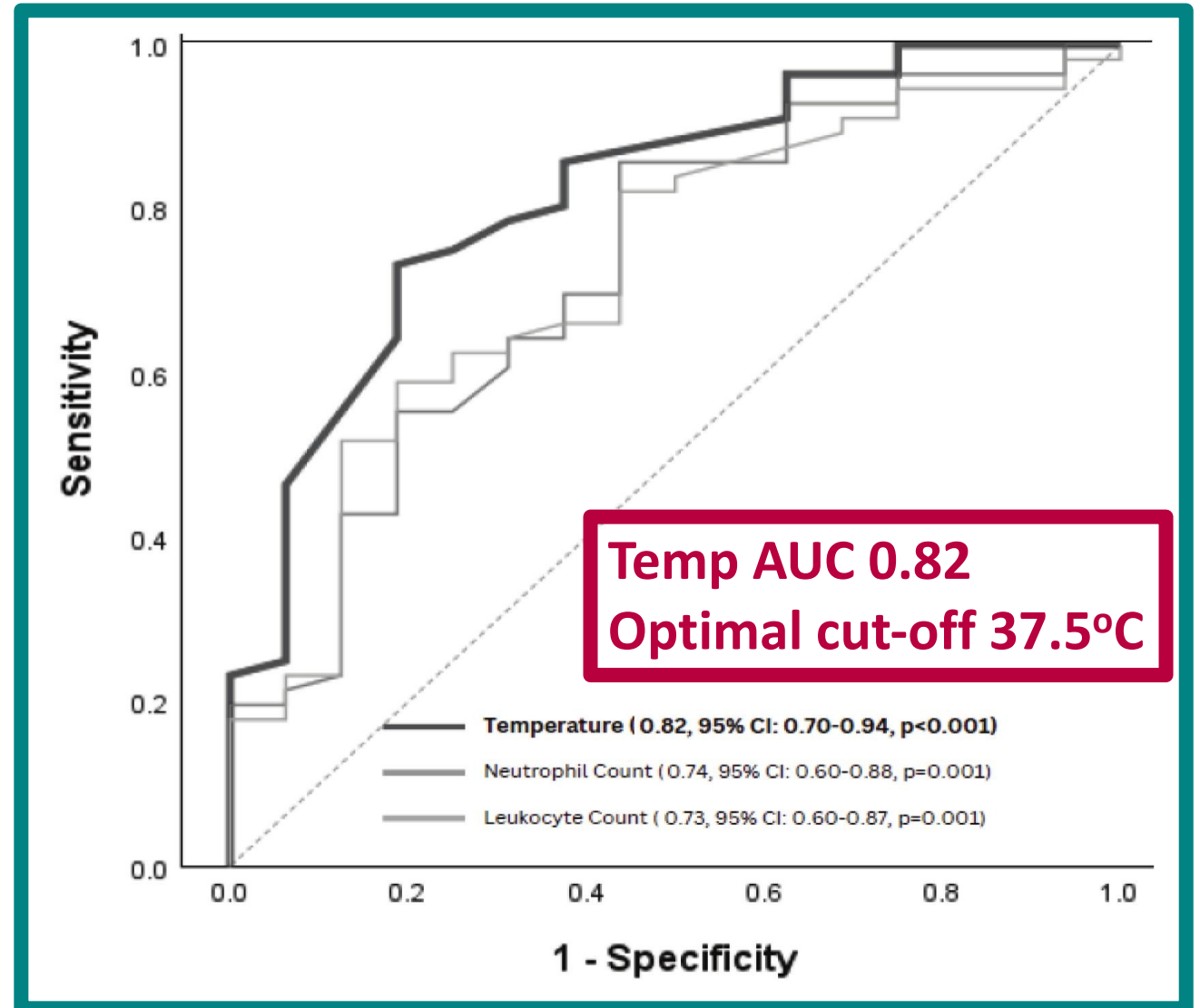
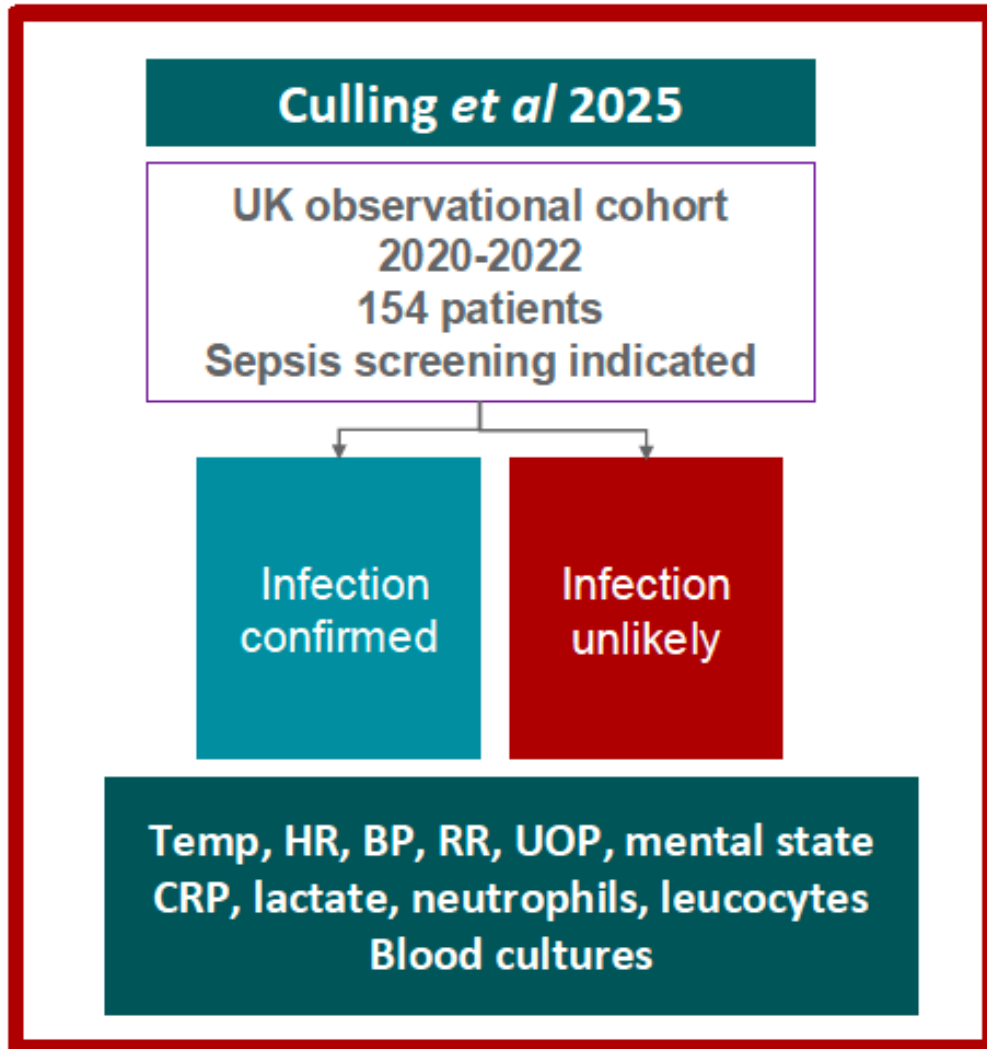


# Sepsis – leading cause of maternal and fetal morbidity and mortality

- Hypoxia
- Acidosis
- Cytokine changes
- FHR abnormalities
- Obstetric interventions

- Low Apgar
- NICU admission
- **Seizures**
- **HIE**
- **Cerebral palsy**

# Temp most predictive for infection (37.5°C)





Where do epidurals fit in??



# Epidural related hyperthermia

## CHARACTERISTICS OF THE STUDY GROUP

	Pethidine (n = 15)	Epidural (n = 18)	P value
Mean (SD) age (yr)	26 (5)	27 (6)	NS
Parity			
Primipara	7	13	<0.02
Multipara	8	5	
Mean (SD) length of labour* (h)	9.3 (7.1)	12.1 (5.5)	NS
Mean (SD) length of labour† (h)	10.2 (6.4)	11.5 (5.2)	NS
Mean (SD) time from rupture of membranes to analgesia (h)	4.2 (3.1)	3.1 (2.2)	NS
Mean (SD) room temperature (°C)			
Beginning	24.8 (2.0)	25.5 (1.1)	NS
End of study	25.1 (1.7)	25.6 (1.5)	NS

\*From rupture of membranes.

†From a frequency of three uterine contractions in 10 min.

NS, not significant.



# Epidural assoc with fever in labour

Neonatology

Systematic Review and Meta-Analysis

Neonatology 2020;117:259–270  
DOI: 10.1159/000504805

Received: September 19, 2019  
Accepted after revision: November 15, 2019  
Published online: January 28, 2020

## Epidural-Related Fever and Maternal and Neonatal Morbidity: A Systematic Review and Meta-Analysis

Sophie Jansen<sup>a</sup> Enrico Lopriore<sup>a</sup> Christiana Naaktgeboren<sup>b</sup> Marieke Sueters<sup>c</sup>  
Jacqueline Limpens<sup>d</sup> Elisabeth van Leeuwen<sup>e</sup> Vincent Bekker<sup>a,f</sup>

- 38 studies, 12 RCTs
- N = 579,157
- All: RR 5.60 (95% CI 4.50-6.97)
- RCTs: RR 3.54 (95% CI 2.61-4.81)

BJA

British Journal of Anaesthesia, 126 (2): 500–515 (2021)

doi: 10.1016/j.bja.2020.09.046

Advance Access Publication Date: 18 November 2020

Review Article

OBSTETRIC ANAESTHESIA

## Epidural analgesia, intrapartum hyperthermia, and neonatal brain injury: a systematic review and meta-analysis

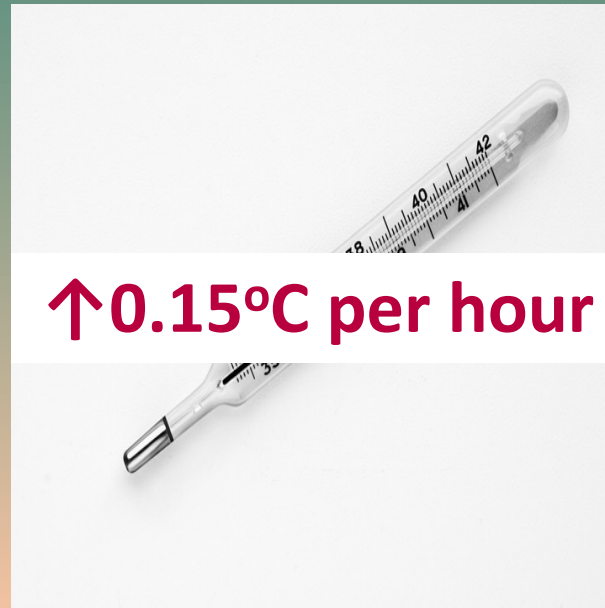
Sarah Morton<sup>1</sup>, Justin Kua<sup>2,3</sup> and Christopher J. Mullington<sup>4,5,\*</sup>

<sup>1</sup>Anaesthetic Department, Chelsea and Westminster NHS Trust, London, UK, <sup>2</sup>Surgical Outcomes Research Centre, Centre for Perioperative Medicine, Research Department for Targeted Intervention, Division of Surgery and Interventional Science, University College London, London, UK, <sup>3</sup>Health Services Research Centre, National Institute of Academic Anaesthesia, Royal College of Anaesthetists, London, UK, <sup>4</sup>Anaesthetic Department, Imperial College Healthcare NHS Trust, London, UK and <sup>5</sup>MSk Lab, Imperial College London, London, UK

\*Corresponding author. E-mail: c.mullington@imperial.ac.uk

- 41 studies, 13 RCTs
- N = 646,296
- All: OR 5.26 (95% CI 4.98-5.56)
- RCTs: OR 4.21 (95% CI 3.49-5.09)

# Incidence ~ 15-25% of labouring women with epidural analgesia

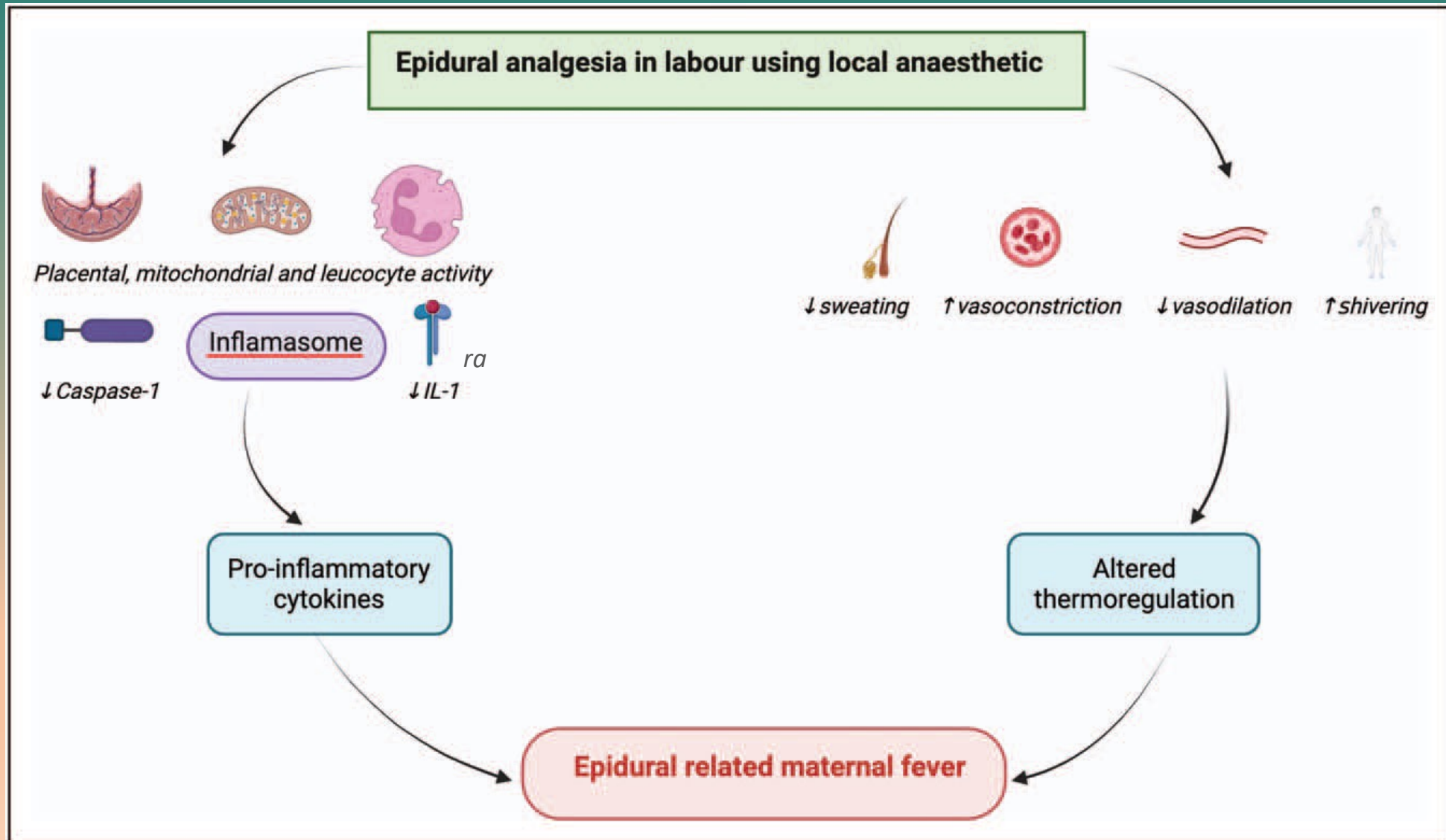




- **Ix / Rx of infection**
- **Unnecessary antibiotics**
- **Allergy / drug reaction risk**
- **Healthcare costs**
- **Anxiety**

Why?

# Likely multifactorial



# Other inflammatory mediators likely...

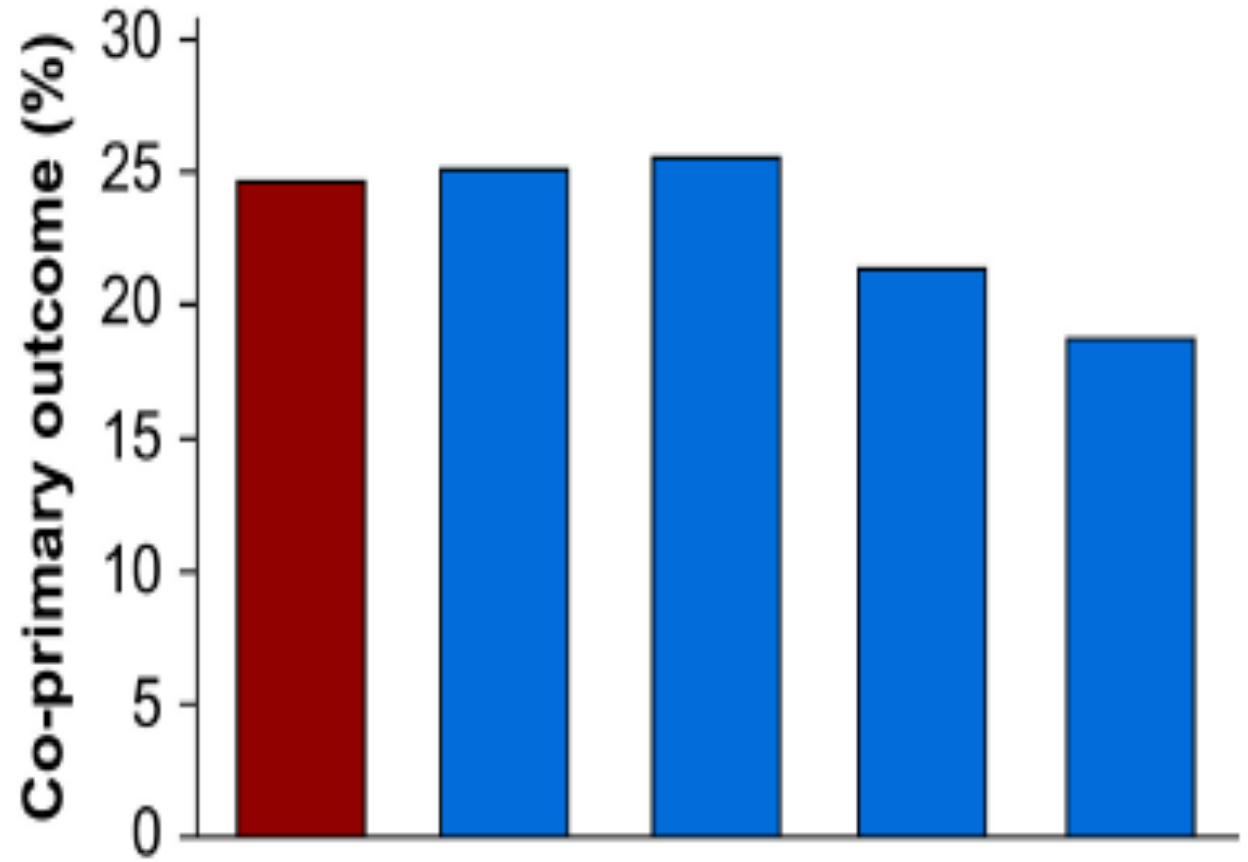
Ackland et al 2025

UK Biobank  
Mendelian Randomisation  
634 women  
IL1-ra genotype

Epidural

Intrapartum hyperthermia  
Antibiotic treatment

a



IL1-Ra allele score

A top-down view of various hammers and mallets arranged on a wooden surface. The tools include a claw hammer with a light wood handle, a black rubber mallet, a red-handled claw hammer, a black-handled claw hammer, a yellow-handled mallet, a black-handled mallet, a red-handled claw hammer, a black-handled claw hammer, a white mallet, a black-handled claw hammer, and a black-handled claw hammer. The text "Can we prevent it??" is overlaid in the center.

Can we prevent it??

# Common sense approach: Treat as for sepsis

Cartledge et al 2022

Meta-analysis  
34 RCTs (n=10,221)  
Preventative strategies  
Women with ERMF in labour

Epidural

Other

Incidence of fever  
Neonatal sepsis / admission

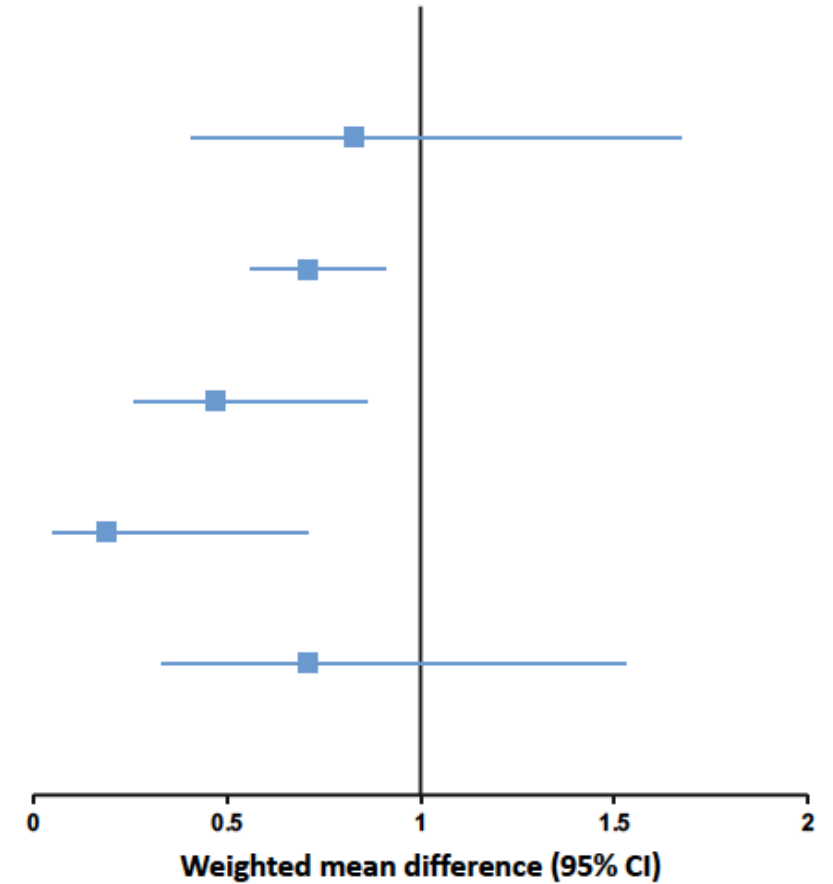
↓ epidural dose

Int vs continuous

Remi vs epidural

High dose steroids

Paracetamol



**SO**

**WHAT !!!**



Does epidural related fever harm the baby??

*To have an epidural or  
not to have an epidural?*

*That is the question...*



**Epidural-Related Fever and Maternal and Neonatal Morbidity: A Systematic Review and Meta-Analysis**

Gophie Jansen<sup>a</sup>, Erico Lencioni<sup>a</sup>, Christiana Neelkeboer<sup>b</sup>, Marijke Susters<sup>c</sup>

- 12 RCTs and 16 cohort studies (579,157 women)
- Epidurals ↑ fever risk
- RCTs RR 3.54 (95% CI 2.61-4.81)
- ***BUT not neonatal sepsis evaluations, bacteremia, or antibiotic treatment***

**Fever of any aetiology associated with adverse neonatal outcomes**

**No evidence of harm assoc with epidural related fever *specifically***

**BUT studies lacking...**

- ***Evidence on neonatal outcomes inconclusive***

# Epidural assoc with low Apgar but NOT encephalopathy

## Tornell et al 2015

Population based study  
1999-2008  
Nulliparae  
294,329 mother-infant pairs

Epidural

No epidural

Apgar <7 at 5min  
Neonatal encephalopathy

	Apgar < 7 at 5 min (adj OR)	Encephalopathy (adj OR)
<b>Maternal fever</b>	2.27 (1.71-3.02)	1.97 (1.19-3.26)
<b>Epidural analgesia</b>	1.27 (1.16-1.39)	1.11 (0.96-1.29)

# BUT NO association between epidural analgesia and HIE

## Cornet et al 2024

Retrospective cohort study  
15 centres, 2012-2019  
233,056 singleton births

Epidural

No epidural

Fever

Hypoxic Ischaemic Encephalopathy

HIE

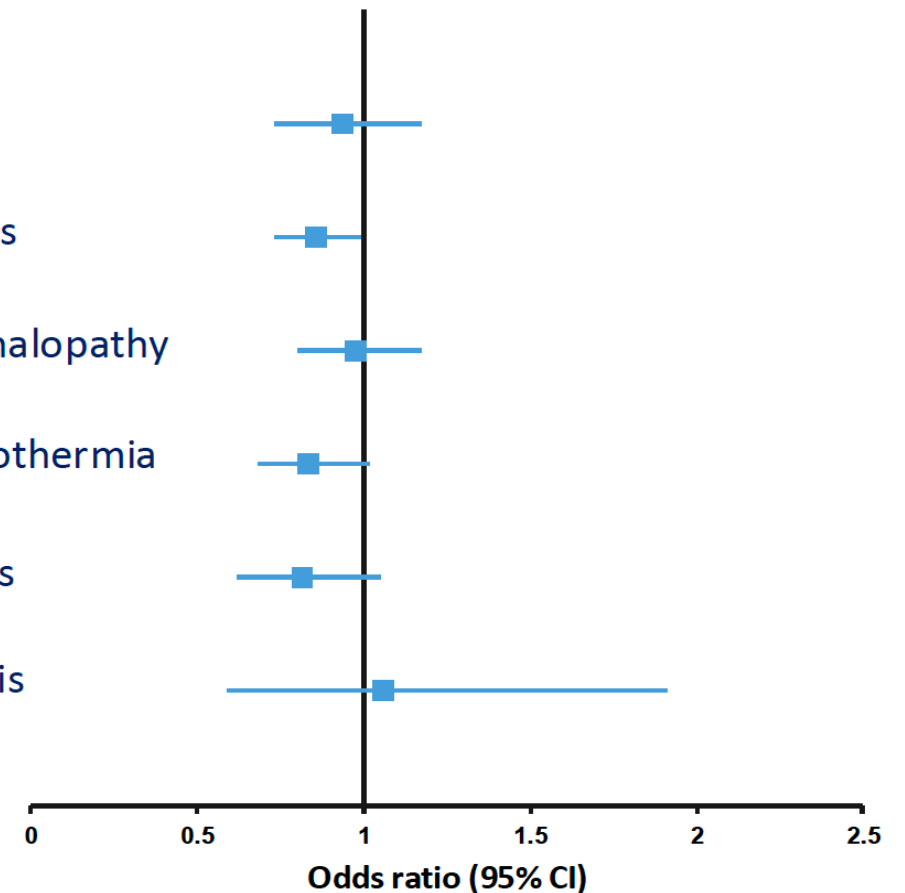
Neonatal acidosis

Neonatal encephalopathy

Therapeutic hypothermia

Neonatal seizures

Culture +ve sepsis



WATCH

THIS

SPACE

No signal of neonatal harm

Reduced morbidity

Anaesthesia

Improved satisfaction

Pain relief

Fever is one such risk

Risks of procedure

Optimise epidural regime

Actively Rx  $T \geq 37.5^{\circ}\text{C}$

# Conclusions



- AVOID UNNECESSARY GA
- GREATER DIFFERENCE IN OUTCOME IN ELECTIVE CASES AT TERM
- NO SIGNAL OF LONGTERM HARM



- ANAESTHESIA FOR INCIDENTAL SURGERY IN PREGNANCY DOES NOT ADVERSELY IMPACT FETAL NEURODEVELOPMENT
- OPTIMISE CARE USING GUIDELINES - COMMUNICATION IS KEY



- NO CAUSAL ASSOCIATION BETWEEN EPIDURAL AND ADVERSE NEURODEVELOPMENT



- FEVER IN LABOUR ASSOC WITH ADVERSE NEONATAL OC
- EPIDURAL ANALGESIA ASSOC WITH FEVER
- NO ASSOC BETWEEN EPIDURAL ANALGESIA AND ADVERSE NEONATAL / CHILDHOOD OC
- ? IMMUNE RESPONSE



TACK!



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