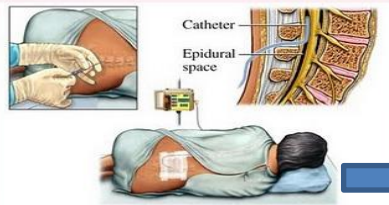


# The PIL Study - Pyrexia in Labour or within four hours of delivery: Risk Factors, diagnostic criteria and infection outcomes

David Fitzgerald, Antimicrobial Pharmacist  
National Maternity Hospital, Holles Street, Dublin

## Epidural Pain Relief (硬膜外麻醉)



## Are 2 or more of the following SIRS criteria present?

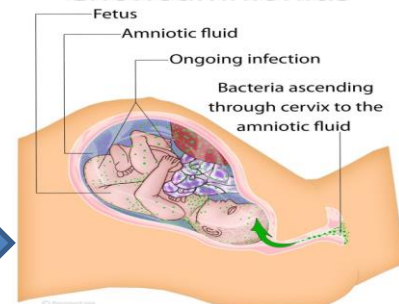
- Temperature  $\geq 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$
- Respiratory rate  $\geq 20$  breaths per min
- Heart rate  $\geq 100$  beats per min
- White cell count  $> 16.9$  or  $< 4.0 \times 10^9/\text{L}$
- Bedside glucose  $> 7.7$  mmol/L (in the absence of diabetes)
- Acutely altered mental status

AND

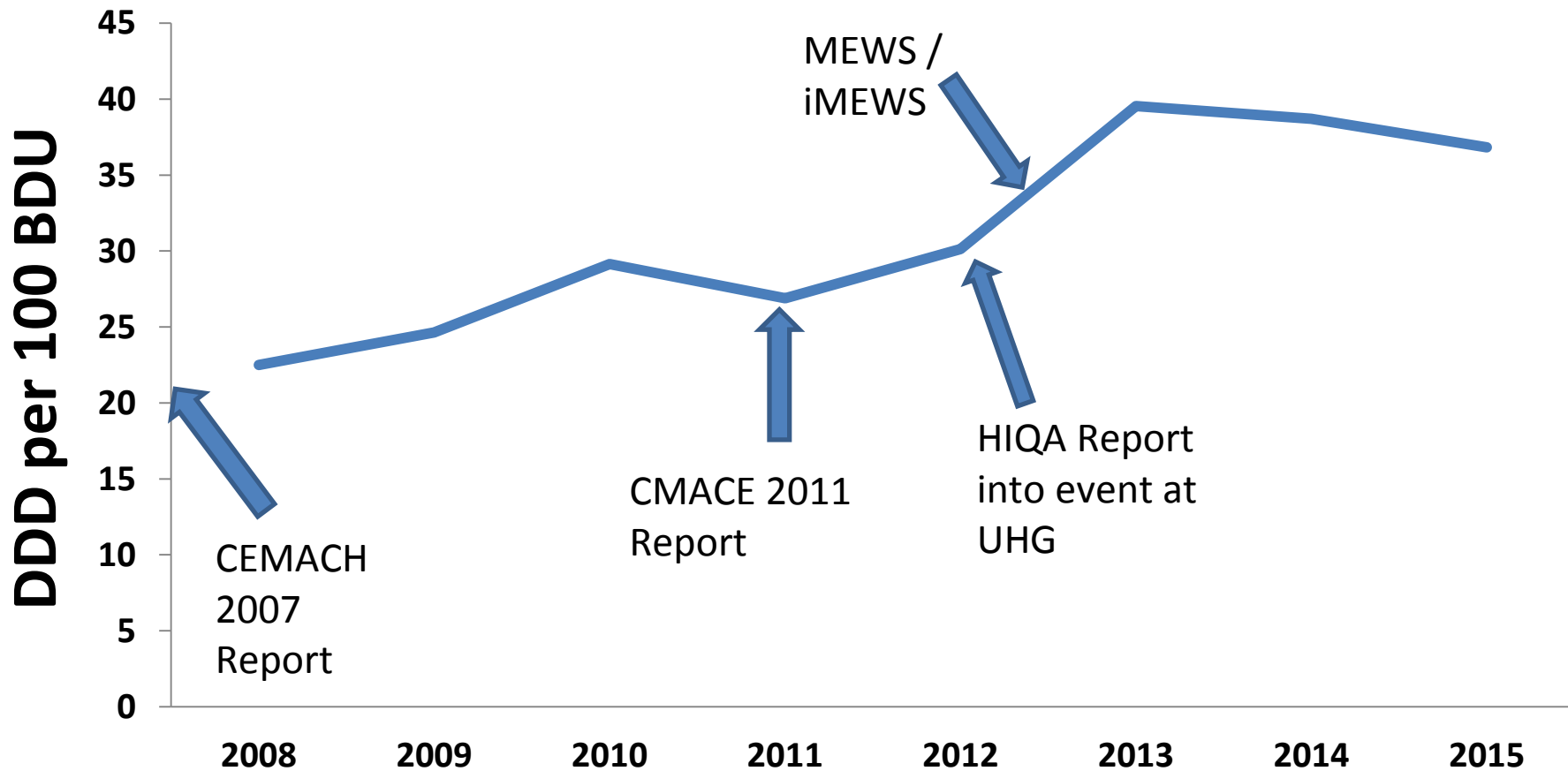
If infection  
is suspected  
after medical  
review



## Chorioamnionitis

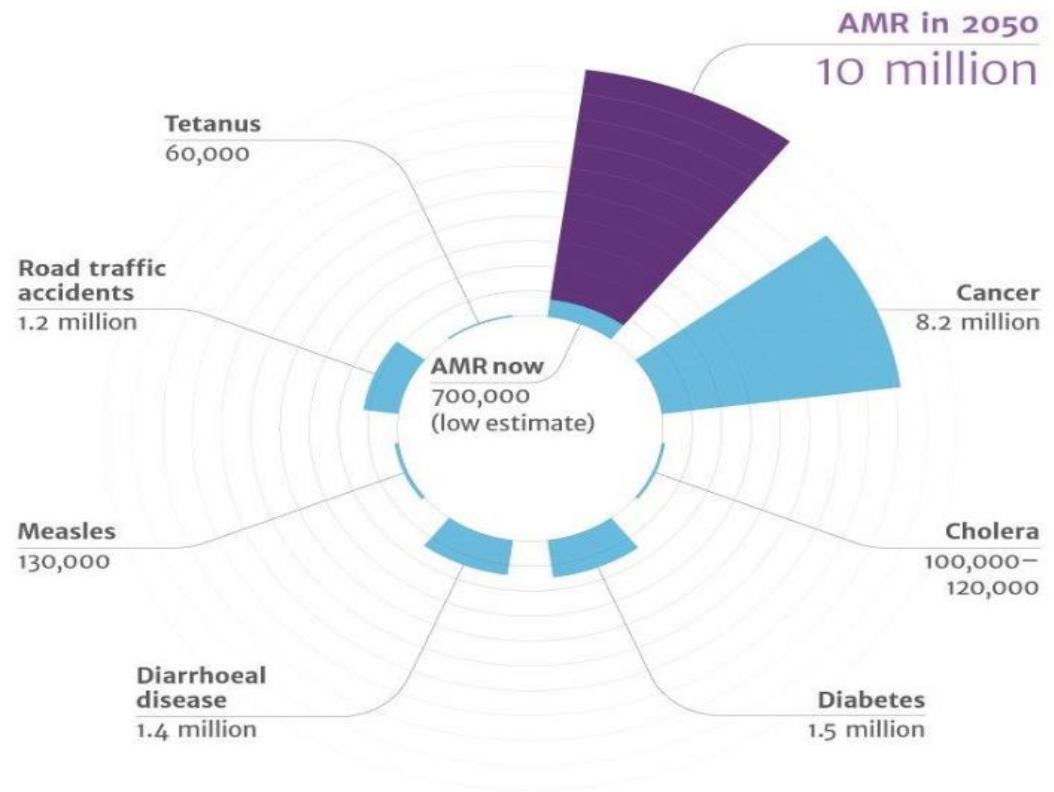


# 3 Dublin Maternities Antimicrobial Consumption



## Consequences

- Disruption of newborn microbiota – obesity<sup>1</sup>, asthma, allergic disease<sup>2</sup>
- Antimicrobial Resistance



<sup>1</sup>Ajslev, T. A., Andersen, C. S., Gamborg, M., Sørensen, T. I. A., & Jess, T. (2011). Childhood overweight after establishment of the gut microbiota: the role of delivery mode, pre-pregnancy weight and early administration of antibiotics. *International Journal of Obesity* (2005), 35(4), 522–9.

<sup>2</sup>Kozyrskyj, A. L., Bahreinian, S., & Azad, M. B. (2011). Early life exposures: impact on asthma and allergic disease. *Current Opinion in Allergy and Clinical Immunology*, 11(5), 400–6.

# Pyrexia in Labour

- PIL accounts for approx 40% of antibiotic indications in NMH

- Hallmark of Clinical Chorioamnionitis

But.....

- Non-infectious causes of PIL
  1. Physiological – Uterine Contractions, Overheating, Nulliparity
  2. Iatrogenic – Prostaglandins, Epidural (RR 3.34)<sup>3</sup>



3. Anim-Somuah, M., Smith, R., & Jones, L. (2005). Epidural versus non-epidural or no analgesia in labour ( Review ). *Library*, Oct 19(4)

# Sepsis Screening Form

(ALWAYS USE CLINICAL JUDGEMENT)

ADULT PATIENTS

There is separate sepsis criteria for women in pregnancy

Complete this form and apply if the National Early Warning Score (NEWS) is  $\geq 4$  (5 on supplementary O<sub>2</sub>), or if infection is suspected

CLINICIAN TO COMPLETE THIS SECTION

Date:  Time:

NEWS:

Clinician's Name:

Name of Doctor contacted:

Clinician's Signature:

MCRN/NMBI PIN:

Patient label here

Doctor must review *within 30 mins* (use ISBAR). DOCTOR TO COMPLETE REMAINDER OF THIS DOCUMENT AS APPROPRIATE

Are any **2 or more modified Systemic Inflammatory Response Syndrome (SIRS) criteria present**

Respiratory rate  $> 20$  (bpm)

WCC  $< 4$  or  $> 12 \times 10^9/L$

Acutely altered mental status

Heart rate  $> 90$  (bpm)

Temperature  $< 36^\circ C$  or  $> 38.3^\circ C$

Bedside glucose  $> 7.7$  mmol/L  
(in the absence of diabetes mellitus)

**+ INFECTION SUSPECTED**

Note: Some groups of patients, such as older people, may not meet the modified SIRS criteria, even though infection is suspected. Where this occurs check for signs of organ dysfunction and raised biomarkers such as C-reactive protein (CRP)

# Vs

## CONSIDER MATERNAL SEPSIS

Are 2 or more of the following SIRS criteria present?

- Temperature  $\geq 38^\circ C$  or  $< 36^\circ C$
- Respiratory rate  $\geq 20$  breaths per min
- Heart rate  $\geq 100$  beats per min
- White cell count  $> 16.9$  or  $< 4.0 \times 10^9/L$
- Bedside glucose  $> 7.7$  mmol/L (in the absence of diabetes)
- Acutely altered mental status

AND

If infection is suspected after medical review



Intervention: within one hour COMPLETE SEPSIS SIX

TAKE 3

1. Appropriate cultures\*
2. FBC +/- lactate
3. Start urine output chart

GIVE 3

4. Maintain O<sub>2</sub> (94-98%)
5. Consider IV fluid bolus\*\*
6. IV antibiotics

\*e.g. blood, wound, vaginal swab, urine etc

\*\*exercise caution in presence of pre-eclampsia

# The PIL Study

## AIM

Provide info. on aetiology and clinical characteristics of Peripartum Maternal Pyrexia (pyrexia in labour / within 4 hours of delivery) to assist decisions to initiate and de-escalate antibiotic therapy for mothers and infants

## OBJECTIVES

1. Determine the rate of infection following peripartum pyrexia
2. Evaluate diagnostic accuracy of obstetric SIRS criteria and CTG for identification of infection related to peripartum maternal pyrexia.
3. Investigate associations between epidural analgesia and peripartum pyrexia, along with other potential risk factors, using matching pairs of cases and controls.

# Methodology

**Setting:** Tertiary Referral Maternity Hospital

**Participants:** 175 women with peripartum pyrexia and 175 time-matched controls prospectively recruited over a 5 month period

**Inclusion Criteria:** Women who presented with peripartum temperature  $\geq 38^{\circ}\text{C}$  on at least 1 occasion, and the infants born to them, who underwent Septic Work Ups

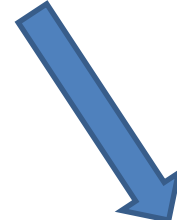
**Exclusion Criteria:** Patients who had antenatal pyrexia or other evidence of infection at the time of onset of labour, patients who did not go into labour and those who were immunocompromised.

**Design:** Case-control study. Information recorded on:

- Patient and Labour demographics
- Clinical observations
- Risk factors for Pyrexia
- Maternal and Neonatal Microbiological Data
- Placental Histology

**175 Pyrexia Cases with Septic Work-Up:**

FBC, Maternal and Neonatal Blood Cultures, MSU, Vaginal Swab (+/- Rectal or Placental Swab)



***Confirmed Infection:***

1. Sterile Site Infection e.g. BSI
2. Confirmed UTI
3. Significant pathogen isolated in placental swab
4. Micro-organism at other non-sterile site plus histological chorioamnionitis

***No Evidence of Infection:***

1. No microbiological evidence of infection at any site
2. Colonisation at non-sterile site e.g. Vaginal / Rectal / Urine, and no evidence of chorioamnionitis upon histological examination of placenta



# Maternal Demographics

## Similarities between cases and controls

- Age, IVF Pregnancy, Diabetes Status, Multiple Pregnancy, MROP
- No Severe Sepsis

## Differences between cases and controls

	Cases	Controls
Nulliparous	79.4%	41.1%
Induction of Labour	47.4%	32%
Term Labour	99.4%	92.5%

# Delivery Outcomes

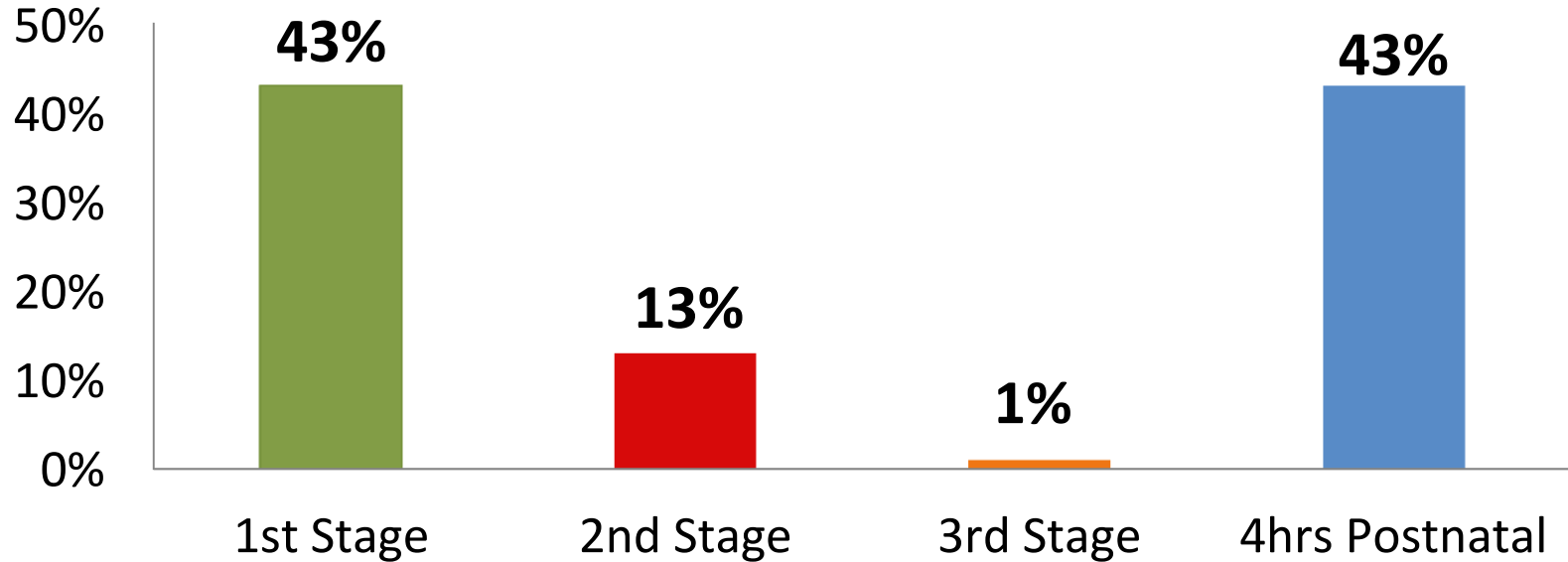
## Maternal Outcomes

	Cases (n =175)	Controls (n = 175)
Labour Duration	7.9 hours	4.5 hours
Instrumental Delivery	33.7%	17.7%
EM-LSCS	28%	6.9%
PPH $\geq$ 500ml	34.5%	11.1%
Episiotomy	64.3%	27%
3 <sup>rd</sup> / 4 <sup>th</sup> Degree Tear	2.4%	0.6%

## Neonatal Outcomes

	Case (n = 176)	Control (n = 179)
Live Births	176 (100%)	179 (100%)
Immediate Admission to NICU / SCBU from Delivery Ward or Theatre	25 (14.2%)	11 (6.1%)
Apgar Score < 7 at 1 minute	16 (9.1%)	5 (2.8%)
Apgar Score < 7 at 5 minutes	1 (0.6%)	0 (0%)

# Proportion of Pyrexia Cases by Labour Stage



Pyrexia within 4 hours of delivery (n = 75)			
Mean Time to Pyrexia (hours : mins)	Standard Deviation (mins)	Minimum Time to Pyrexia (mins)	Maximum Time to Pyrexia (hours:mins)
1:42	45	14	3:29

**No Infection or Colonisation**

68.6%

**Colonisation**

14.3%

**Confirmed Infection**

**17.1% (30 / 175)**

Microbiologically Confirmed

Histologically Confirmed

2.3%

1.7%

2.3%

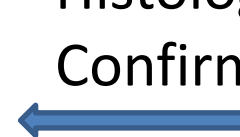
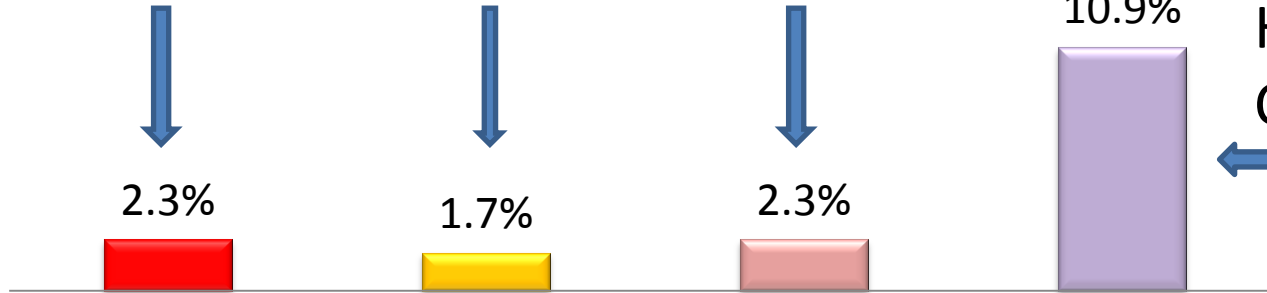
10.9%

BSI

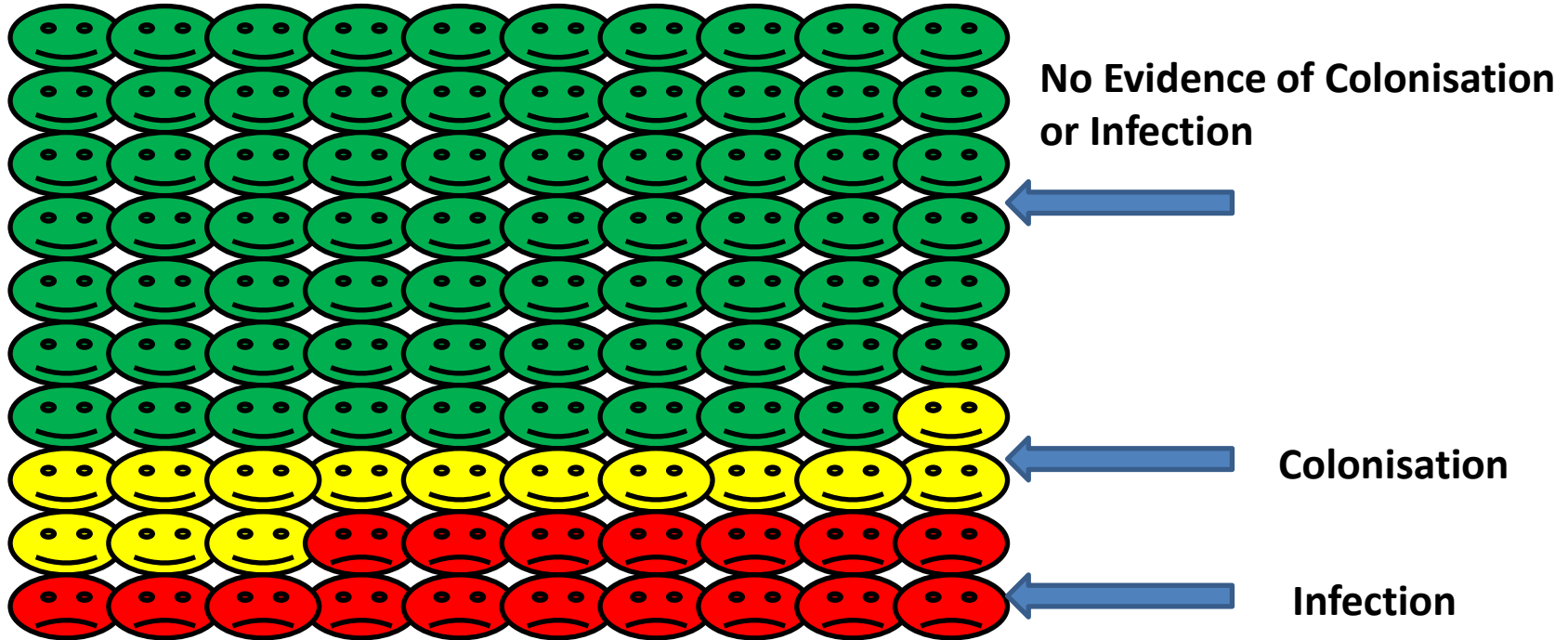
UTI

Chorio

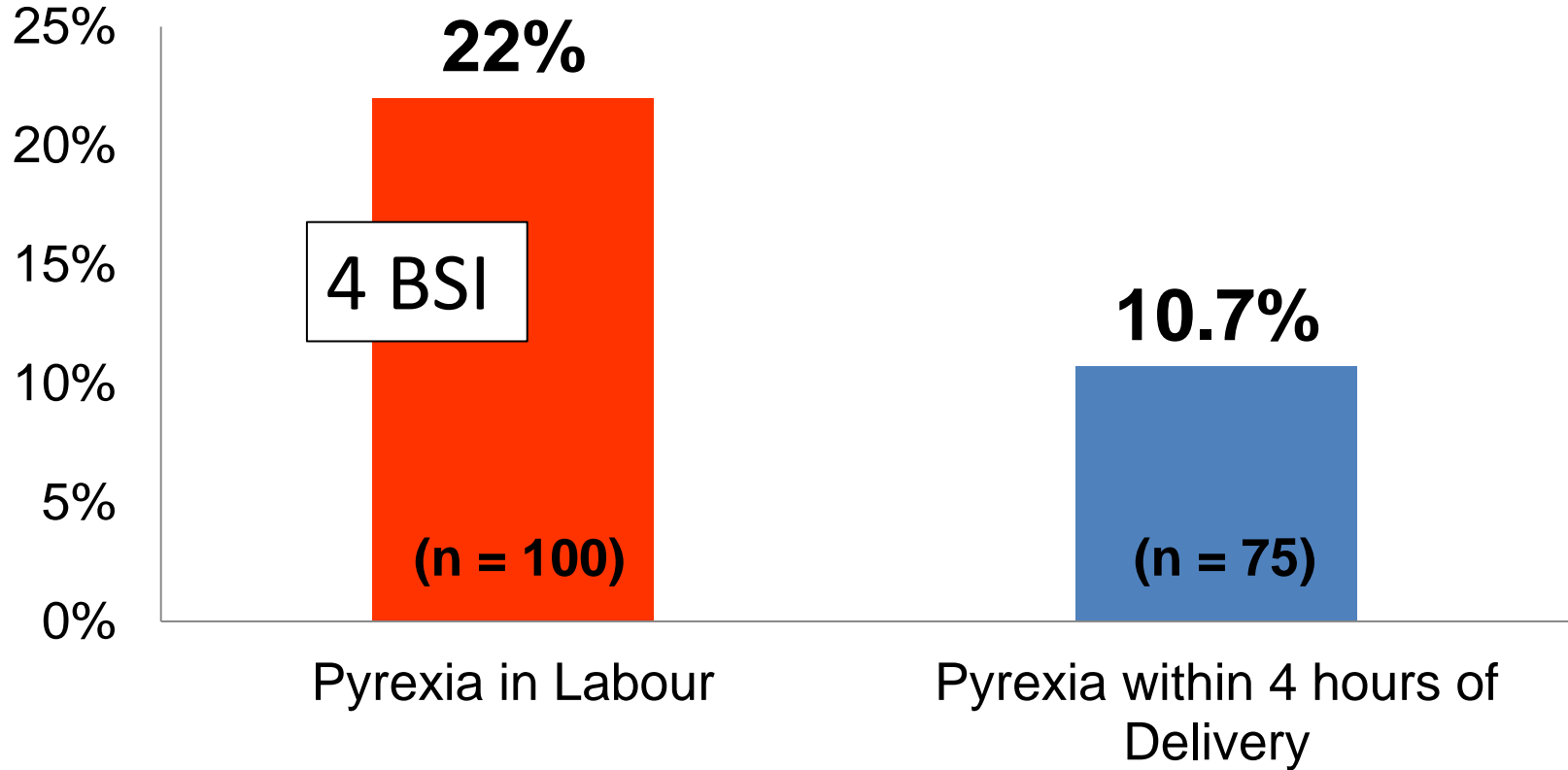
Chorio



# Infection Outcomes for 100 women with Peripartum Pyrexia



# Confirmed Infection Rate

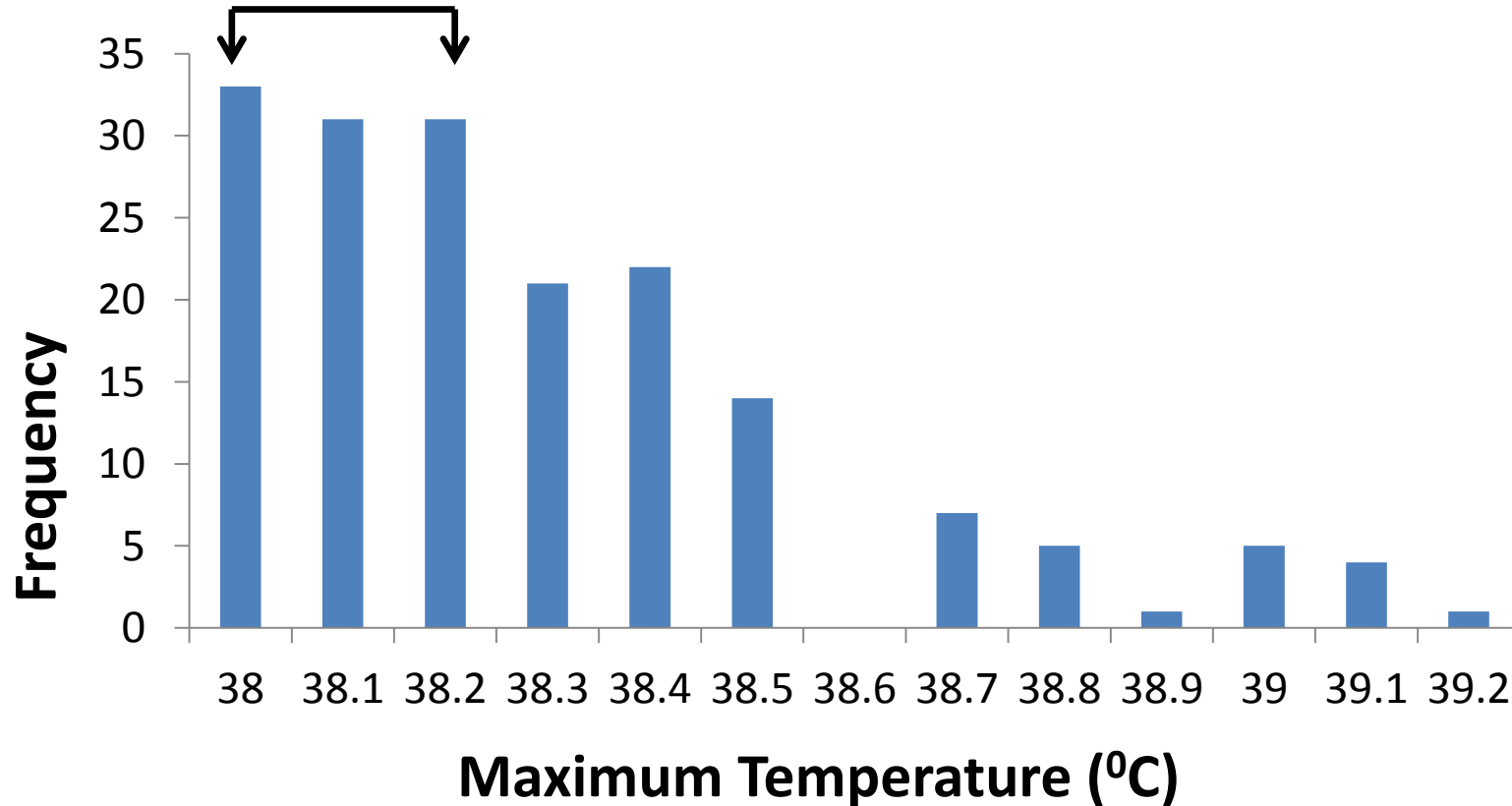


# Baseline Maternal Vital Signs

Maternal Vital Sign	Number of Matching Pairs	Case	Control	p-value
Temperature (°C)	167	36.7	36.6	.52
Heart Rate (bpm)	168	83.2	81.6	.124
Respiratory Rate (breaths per min)	164	16.6	16.5	.12
Systolic Blood Pressure (mmHg)	168	117.7	119.6	.107
Diastolic Blood Pressure (mmHg)	168	69.8	70.6	.449

# Max Recorded Temperatures in Case Group

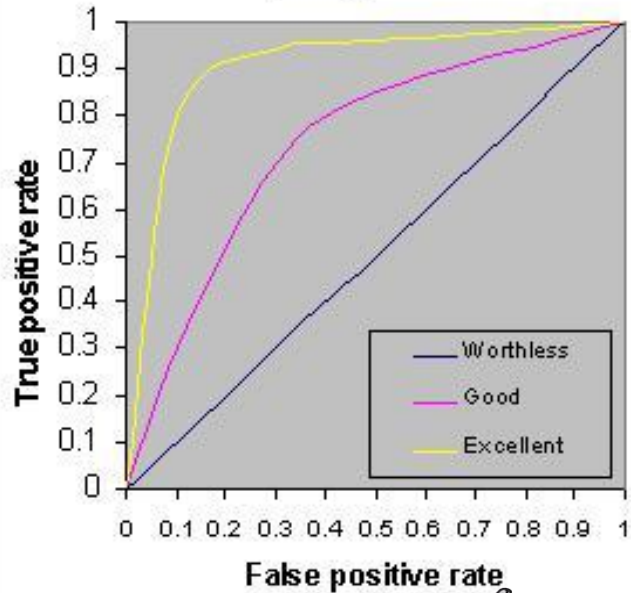
60% of Confirmed Infections





# Diagnostic Accuracy of SIRS Criteria

Comparing ROC Curves



True Positive Rate

True Negative Rate

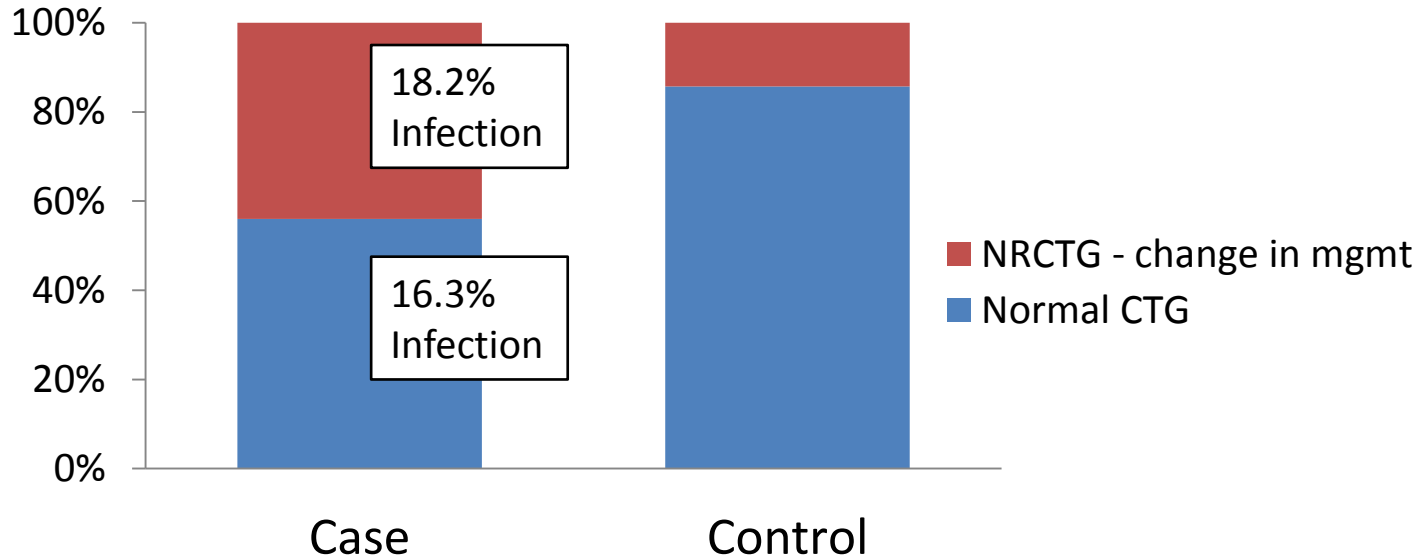


2 SIRS Criteria (Temp $\geq 38^{\circ}\text{C}$ <i>plus</i> )	Sensitivity	Specificity
Heart Rate $\geq 90$ bpm	55.2%	41.8%
Heart Rate $\geq 100$ bpm ( <i>obstetric</i> )	41.4%	60.7%
White Cell Count $> 12 \times 10^9/\text{L}$	93.3%	0.7%
White Cell Count $> 16.9 \times 10^9/\text{L}$ ( <i>obstetric</i> )	53.3%	40.6%
Respiratory Rate $\geq 20$ breaths per min	3.6%	97.4%
Systolic Blood Pressure $< 90$ mmHg	3.3%	99.2%
Systolic Blood Pressure $< 100$ mmHg ( <i>obstetric</i> )	10%	99.2%

# CTG changes and Pyrexia / Infection

Non-reassuring CTG (NRCTG) resulting in a change of obstetric mgmt:

- associated with peripartum pyrexia
- Odds Ratio 5.73 (95% CI 3.02 – 10.87);  $p < 0.001$

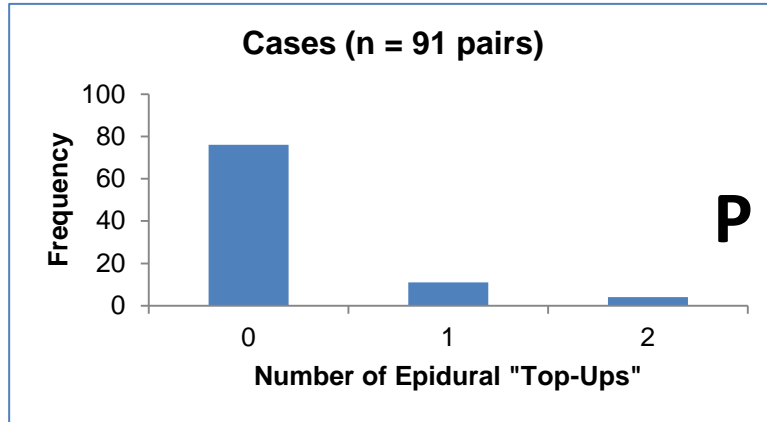


Risk Factor	Odds Ratio	95% Confidence Interval and P-value
<b>Significantly Increased OR</b>		
Epidural	25.33	7.99 – 80.31; p < .001
In-Out Urinary Catheter	13.5	5.89 – 30.94; p < .001
Nulliparity	5.79	3.28 – 10.2; p < .001
Indwelling Urinary Catheter	5.77	3.2 – 10.4; p < .001
Propress to Induce	5.2	2.0 – 13.54; p < .001
Oxytocin to Augment	4.43	2.48 – 7.91; p < .001
Prolonged Labour (> 12 hours)	2.57	1.07 – 6.16; p = .043
Oxytocin to Induce	2.2	1.2 – 4.05; p = .013
ROM > 18 hours	2.04	1.25 – 3.33; p = .005
Induction	1.82	1.19 – 2.78; p = .007
Amniotomy to Induce	1.71	1.1 – 2.66; p = .021
<b>Significantly Decreased OR</b>		
PPROM	0.18	0.04 – 0.82; p = .022
Preterm Delivery	0.08	0.01 – 0.59; p = .002
<b>Not Significantly Increased OR</b>		
Amniotomy to Augment	0.82	0.53 – 1.27; p = .434
Carboprost	1	0.06 – 15.99; p = 1
Entonox	0.91	0.6 – 1.39; p = .747
Misoprostol	6.0	0.72 – 49.84; p = .125
Obesity (BMI ≥ 30)	1.15	0.63 – 2.09; p = .761
Pethidine	1.87	1.0 – 3.5; p = .066
Prostin to Induce	1.9	0.88 – 4.09; p = .136
Spinal Analgesia	1	0.29 – 3.45; p = 1

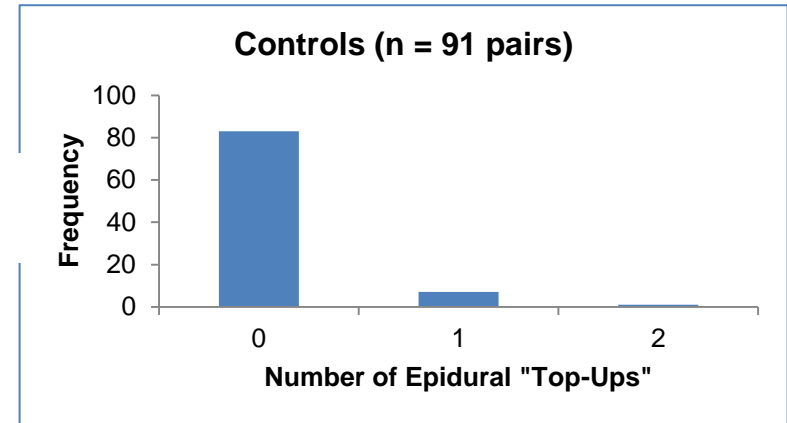
# Adjusted Odds Ratios

Risk Factor for Pyrexia	Adjusted Odds Ratio and 95% CI	p-value
Epidural	10.7 (1.5 – 73.8)	.016
Nulliparity	6.5 (2.1 – 20.1)	.001

	Case (mean)	Control (mean)	Significance of difference
Total Duration of labour (hours)	7.9 hrs	4.5 hrs	p < .001
Duration of Epidural (hours)	6.5 hrs	4.6 hrs	p < .001
Volume of PCEA (mls)	72.7ml	67.3ml	p = 0.372



**P = .23**

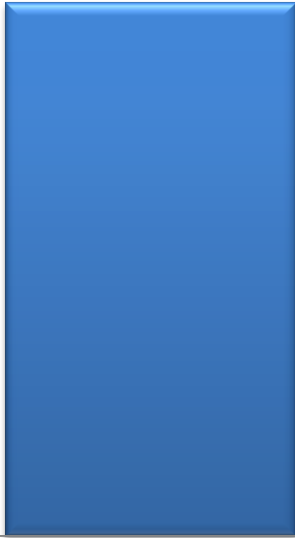


- No difference in Choice of Initial Block Combination

Time to Pyrexia Post-Epidural (n = 164)				
	Mean	SD	Minimum	Maximum
Hours	6.1	2.3	1.1	13.5

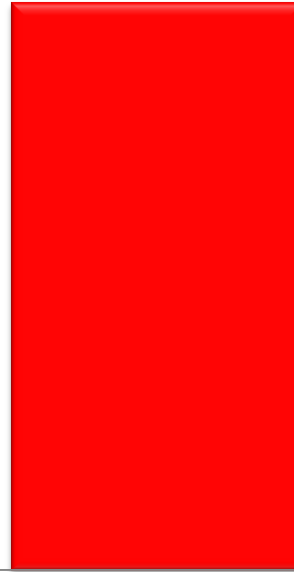
## Confirmed Infection Rate

**17.1%**



Pyrexia Post-Epidural (n = 164)

**18.2%**



Pyrexia without epidural (n = 11)

# Conclusions



## 1. 17.1% rate of infection with peripartum pyrexia

- Pyrexia in Labour 22% infection rate
- Pyrexia within 4 hours of delivery 10.7% infection rate

## 2. Novel criteria needed to identify patients at risk of sepsis around the time of labour

- Low rate of infection among peripartum pyrexia cases + poor diagnostic accuracy of the obstetric SIRS criteria and CTG as markers of peripartum infection
- Validation of 38°C temperature threshold for diagnosis of maternal infection around the time of labour

## 3. Epidural Analgesia strongly associated with peripartum pyrexia (adjusted OR 10.7)

- Effect is not dose-related
- Possibly patient specific
- It would be unsafe to withhold antibiotic therapy in situations of suspected “Epidural Fever”

# Recommendations

## PYREXIA IN LABOUR

- 57% of Peripartum Pyrexias
- 22% have infections
- For patients who had no signs of infection **prior** to labour, delivered at **Term** and no evidence of **Severe Sepsis**
- Perform septic workup on mother & infant
- **STOP** antibiotics at 48 hours if blood culture negative and clinically well



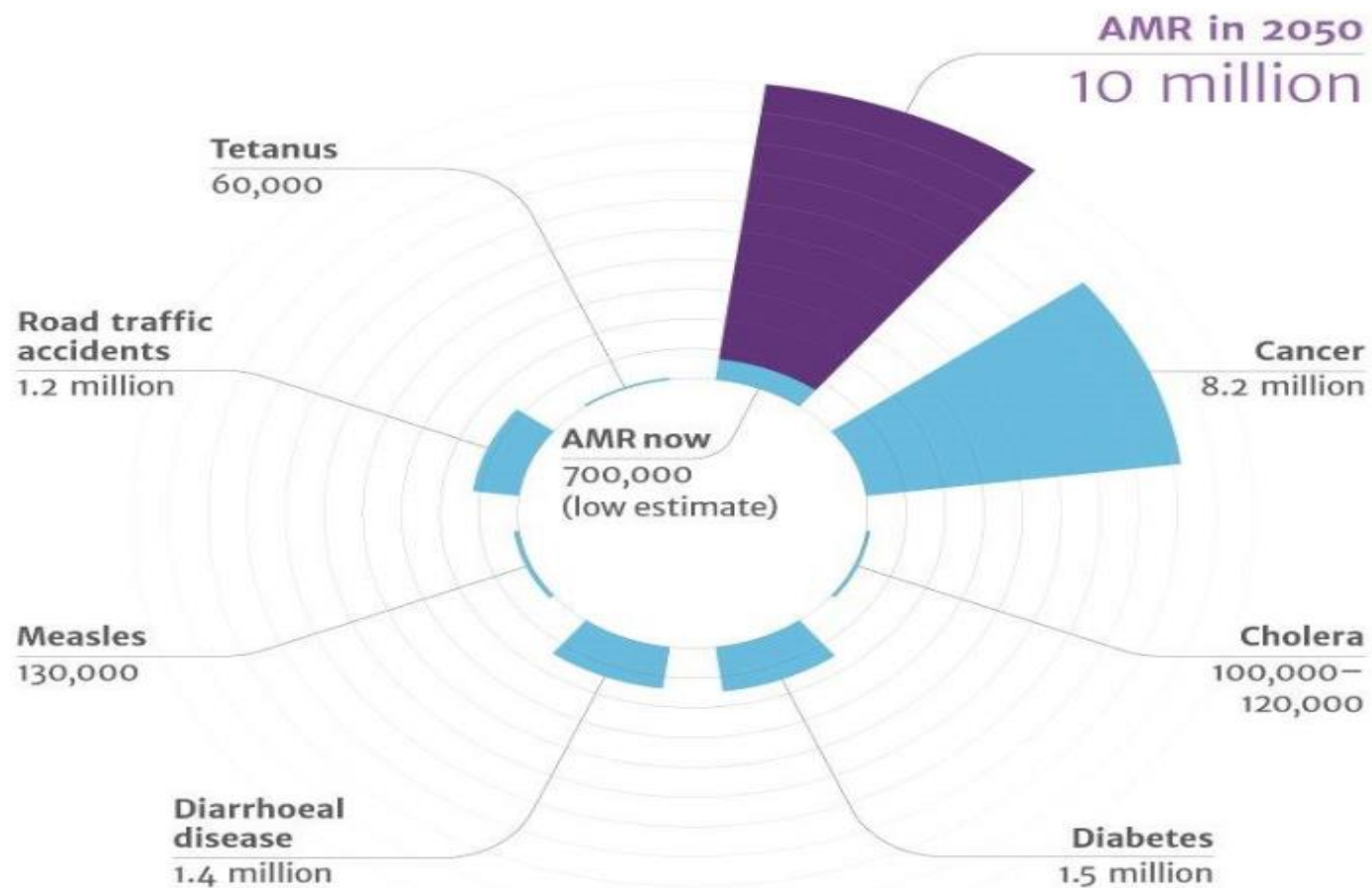
**48 hr Blood  
Culture Negative**

## PYREXIA WITHIN 4 HOURS OF DELIVERY

- 43% of Peripartum Pyrexias
- 10.7% have infections
- For patients who had no signs of infection **prior** to or **during** labour, delivered at **Term** and no evidence of **Severe Sepsis**
- **Monitor** – cooling methods, iMEWS once cooled
- Perform septic workup if SIRS criteria persists after 60 minutes, or clinical deterioration
- **STOP** antibiotics at 48 hours if blood culture negative and clinically well

**MONITOR**







# Acknowledgements



- Infection Control Team - Dr Susan Knowles, Shideh Kiafar, David Fitzgerald
- Histology - Dr Paul Downey and Histology Lab Staff
- Statistics - Ricardo Segurado
- Midwifery - Martina Cronin and Delivery Ward Staff
- Anaesthetics - Dr Ingrid Browne
- Obstetrics - Dr Mike Robson, Dr Fionnuala Mone