All Wales Neonatal Network Guideline
Early Onset Sepsis Risk Assessment for Infants ≥34 Weeks Gestation

Purpose:
To provide guidance on risk assessment and management of early onset sepsis (EOS) in neonates of ≥ 34 weeks gestation, including the use of the Kaiser Permanente Sepsis Risk Calculator (SRC). In Wales, SRC is in clinical use for management of EOS since March 2019. This paper provides additional updates based on published data from our clinical experience and incorporates recent changes to NICE guideline. It also includes an addendum offering guidance for midwives assessing risk of EOS in low-risk babies delivered in a midwifery led setting (Appendix 4)

Background:
Culture proven EOS in UK in term and near-term infants is infrequent (about 0.5/1000 live births) but can be associated with high morbidity & mortality. Group B streptococcus (GBS) is the commonest organism for EOS in the UK followed by Gram negative organisms. Nearly 15-20% of infants on postnatal wards are screened by traditional univariate risk-based algorithms (e.g., NICE and RCOG guidelines) and offered prophylactic antibiotics, until investigations rule out infection. These risk-based strategies can identify only 50-60% of all EOS cases. In addition, a significant proportion of EOS cases are symptomatic at birth and do not require any algorithm for identification. Thus, the number of infants needing treatment to identify a case of culture proven sepsis in the early asymptomatic phase is estimated to be 1 in 600-800 near-term live births.
Developed in the USA, The Kaiser Permanente Sepsis Risk Calculator (SRC) is a multivariate model of assessing the risk of EOS using maternal risk factors and the infant's clinical state after birth (https://neonatalsepsiscalculator.kaiserpermanente.org). The use of SRC in Wales has safely reduced antibiotic use by 46%, replicating reports in the USA and other parts of the developed world. For more information, please review references at the end of this document.

No sepsis algorithm can function without excellent clinical care and professional judgment. **The following generic principles apply in all situations and supercede any sepsis algorithm -**

1. All infants symptomatic of sepsis must be investigated and treated promptly with antibiotics within 1 hour of the decision to treat. This is irrespective of their sepsis risk score. See appendix 1 for common signs of clinical sepsis. If you are unsure seek senior help.

2. Investigations for sepsis should include a blood culture **(a minimum of 1ml of blood must be inoculated into the blood culture bottle)**, FBC and a CRP. The latter should be repeated in 18-24 hours.

3. Where there is a history of confirmed Group B Streptococcal sepsis or death of a neonate in previous pregnancy, **AND** the mother **has not** received adequate intrapartum prophylaxis in this pregnancy, the newborn infant should be screened and presumptively treated irrespective of the sepsis risk score.

Guidance:
The following parameters should be collected as routine during labour or at elective caesarean section by attending midwives in **all infants**:

- **Gestational age – Weeks + days**
- **Highest maternal intrapartum temperature in ^{0}C (i.e., from onset of established labour to first hour after delivery)**
- **Duration of rupture of membranes in hours – membrane rupture to time of birth**
- **GBS status – positive / negative / unknown**
- **Type of intrapartum antibiotics and time of first dose**

The midwife should **contact the neonatal team if any ONE criterion of the following** in the two boxes applies either at birth or during routine observations for any reason for infants ≥34 weeks gestation:

- **Rupture of membranes: > 18 hours in preterm OR >24 hours in term**
- **Preterm < 37 weeks Gestation**
- **Highest maternal pyrexia in labour > 38 ^{0}C**
- **Maternal GBS in current pregnancy**
- **Maternal antibiotics (other than prophylaxis for LSCS)**

OR

- **HR >160/min**
- **Baby temp <36 ^{0}C or ≥ 38 ^{0}C (not environmental)**
- **RR >60/min or apnoea**
- **Grunting, nasal flaring or recession**
- **Oxygen saturations <95%**
- **Altered responsiveness, persistent hypotonia, seizures, signs of shock**
- **Early jaundice within 24 hours of birth**
- **Suspected/confirmed infection in another baby with multiple pregnancy**

Neonatal team should then thoroughly examine the baby and follow the steps as below:

Step 1:

Apply the NICE criteria (see Appendix 1) for treatment

a) If NICE **does not** recommend treatment or observations –> ROUTINE CARE

b) If NICE recommends antibiotic treatment or observations, then proceed to **Steps 2 & 3**

Step 2:

Assign the infant to one of the following three clinical status using the guide in this table:

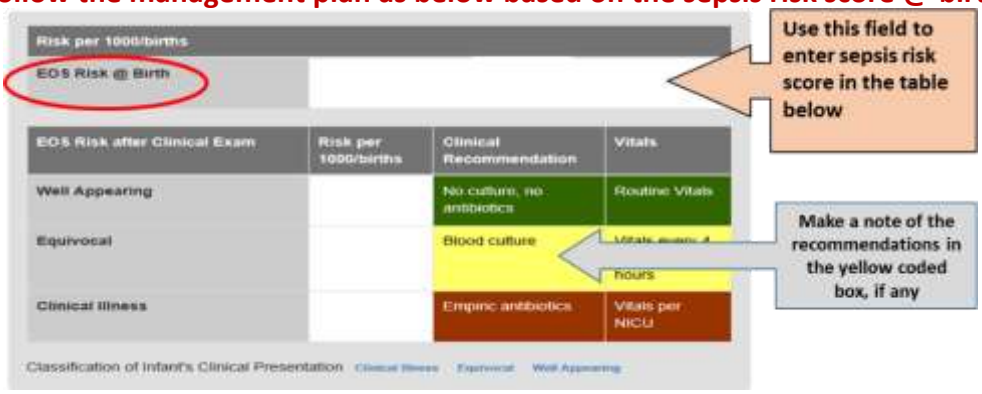
Clinical Exam	Description
Well appearing	No persistent physiologic abnormalities
Equivocal	Any one persistent physiologic abnormality ≥ 4 hrs ** • Tachycardia (HR ≥ 160) • Tachypnoea (RR ≥ 60) • Temperature instability (<36.4 OR ≥ 38^0 C) • Respiratory distress (grunting, nasal flaring or chest recessions) not requiring supplemental oxygen Two or more physiologic abnormalities lasting ≥2 hours ** • Tachycardia (HR ≥ 160) • Tachypnoea (RR ≥ 60) • Temperature instability (<36.4 OR ≥ 38^0 C) • Respiratory distress (grunting, nasal flaring or chest recessions) not requiring supplemental oxygen ***Abnormalities can be intermittent*** ***Equivocal state persisting beyond 6 hours should be classed as 'clinical illness'. Late onset symptoms beyond the first few hours and in particular after an asymptomatic period should also be classed as 'clinical illness'***
Clinical Illness	1. Need for mechanical ventilation (outside delivery room) 2. Haemodynamic instability requiring fluid bolus or inotropes 3. Persistent need for CPAP/HFNC (must be designated by 4 hours of age) 4. Need for supplemental oxygen ≥ 2 hours to maintain oxygen saturation >90% 5. Neonatal encephalopathy / Perinatal depression • Neonatal seizure • Apgar score < 5 @ 5 minutes 6. Any other symptoms of serious illness – clinician determined

Step 3: Calculate Sepsis Risk Score to determine individual infant's risk for EOS.

The Sepsis Risk Score can be accessed at the following websites

- https://kp.org/eoscalc
- https://neonatalsepsiscalculator.kaiserpermanente.org
- Guidance on how to enter the risk factors used in to determine the Sepsis Risk Score can be found in Appendix 2.
- In the unlikely scenario that the SRC tool is not available, follow NICE guideline

<u>Step 4:</u> Please follow the management plan as below based on the sepsis risk score @ birth and clinical status:



- Apply the **EOS Risk score @ birth** and baby's '**Clinical Status**' in the table below to make action plan.

  <u>Please note:</u> If following calculation, there is a <u>yellow coded clinical recommendation</u> on the SRC website, make a note of the two possibilities No culture, no antibiotics OR Blood culture

  If blood culture is recommended for the clinical status, treat the baby with antibiotics until culture results are available (Wales's modification of SRC)

Clinical status in first 12 hours	Sepsis Risk Score @ birth		
	< 0.65	**0.65 - 1.54**	**> 1.54**
Well-Appearing	**Observe for minimum of 24 hours on postnatal ward; Follow observation guidance using NEWTTS chart**	**If SRC recommends 'no culture', observe for a minimum of 24 hours on postnatal ward; Follow observation guidance using NEWTTS chart**	**Sepsis screen and treat empirically**
		If SRC recommends 'blood culture', then start antibiotics, continue observations	
Equivocal	**If SRC recommends 'no culture', observe for minimum of 24 hours in postnatal ward; Follow observation guidance using NEWTTS charts**	**Sepsis screen and treat empirically**	
	If SRC recommends 'blood culture', then start antibiotics, continue observations		
Clinical Illness	**Sepsis screen and treat empirically**		
If at any point during observations, there is clinical worsening then perform sepsis screen and treat with antibiotics and further management as per your current practice			

Observations:

Clinical Status	Well Appearing	Equivocal	Unwell
Observation schedule	Routine observations at 1 hour, 2 hours and then every 2-hourly until 12 hours of age. Thereafter continue observations every 4 hourly until the end of observation period (24 hours).	Hourly until all observations within normal range X 2 Thereafter, follow guidance for well appearing child	Admit to NICU and observation as directed by clinician

Use guidance for NEWTTS chart. The SRC can be re-applied based on infant's clinical status at any time up to 12 hours of age.

Discharge: All infants on observation pathway should be re-examined by the neonatal team or newborn examination midwives before discharge to confirm well-being. Parents should be given the ***'Screening for infection in newborn babies -information for parents'*** leaflet.

Appendix 1: NICE guidance:

Indications for EONS screening and treatment of infants

Maternal risk factors – 2 Non-red flags OR 1 red flag
Infant clinical indicators – 2 Non-red flags OR 1 red flag
If only one non-red flag present, then observe and keep low threshold for screening

Maternal risk factors are:

Maternal Risk Factors for Early-Onset Neonatal Infection - 'red flags'
Suspected or confirmed infection in another baby in the case of a multiple pregnancy

Maternal Risk Factors for Early-Onset Neonatal Infection - 'non-red flags'
Invasive group B streptococcal infection in a previous baby or Maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy
Preterm birth following spontaneous labour (before 37 weeks' gestation)
Confirmed rupture of membranes for more than 18 hours before a pre-term birth
Confirmed prelabour rupture of membranes at term for > 24 hours before the onset of labour
Intrapartum fever higher than 38°C, if there is suspected or confirmed bacterial infection
Clinical diagnosis of chorioamnionitis

Infant risk factors are:

Clinical Indicators of possible Early-Onset Neonatal Infection (observations and events in the baby)	
'Red Flags'	
Apnoea (temporary stopping of breathing)	
Seizures	
Need for cardiopulmonary resuscitation	
Need for mechanical ventilation	
Signs of shock	
'Non-Red Flags'	
Altered behaviour or responsiveness	Persistent pulmonary hypertension of newborns
Altered muscle tone (for example, floppiness)	Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors
Feeding difficulties (for example, feed refusal)	Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation
Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension	Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)
Abnormal heart rate (bradycardia or tachycardia)	Metabolic acidosis (base deficit of ≥ 10 mmol/litre)
Signs of respiratory distress (including grunting, recession, tachypnoea)	
Hypoxia (for example, central cyanosis or reduced oxygen saturation level)	
Jaundice within 24 hours of birth	
Signs of neonatal encephalopathy	

Appendix 2:

Calculator Input	Value to be entered	Notes
Incidence of Early-Onset Sepsis	0.5/1000 live births	Based on UK national incidence – NeoNIN data
Gestational Age (GA)	GA at birth, in weeks and days	"Weeks" value range 34-43 "Days" value range 0-6
Highest Maternal Intrapartum Temperature (^{0}C)	Enter the value and remember to choose "**Celsius**" for the temperature unit. ***Note***: Highest intrapartum maternal temperature including up to 1 hour following delivery	Value may be whole number or number with single decimal place ***Examples***: 37, 37.1, 37.0 are all acceptable entry values ***Note*: Midwives to document and flag up to the neonatal team, if postpartum temperature taken within 1 hour of birth is at least 0.5^{0}C higher than intrapartum temperature so that the correct figure is used in calculation**.
ROM (hours)	Duration of time between rupture of membrane and birth, in hours ***Please enter for SRC the actual duration of rupture of membranes till birth and not just pre-labour duration**	Value may be whole number rounded up to the nearest 0.5 hours (single decimal place) ***Example***: ROM time 4 hours and 30 minutes should be entered as 4.5 hours. ***Example***: ROM time 4 hours and 55 minutes can be entered as 5.0 hours
GBS	Enter maternal GBS screening result if available. If not known enter 'unknown'	
Type of Intrapartum Antibiotics And Interval from first dose to birth	***GBS-specific antibiotics*** are defined ONLY as Penicillin G. This should apply only to mothers who are GBS positive or GBS unknown. **If erythromycin, clindamycin or vancomycin ALONE are given for GBS prophylaxis, choose the option "No antibiotics or any antibiotics given < 2 hours prior to delivery."** ***Broad-spectrum antibiotics (BSAB)*** are defined as two or more antibiotics given in combination when there is concern for the mother developing chorioamnionitis. ***Timing*** of administration of **GBS-specific antibiotics** or ***BSAB administration*** = interval between the first dose of Penicillin G or the second antibiotic in the combination to the time of birth. **Example**: Cefuroxime is given at 2:00 PM; Metronidazole is given at 3:30 PM. Birth is at 4:30 PM. Because the second antibiotic of the combination was given 1 hour prior to delivery, choose option **"No antibiotics or any antibiotics given < 2 hours prior to delivery."** ***If a mother has been given BOTH GBS-specific antibiotics and BSAB – of the 4 possible options, select the category with the longest duration of treatment.*** **Example**: Mother is given Penicillin G at 8:00 AM and 12:00 PM for GBS +ve. She develops a fever to 38.3^0 C at 2:00 PM, and Cefuroxime is given at 3:00 PM. Penicillin G is given at 4:00 PM. Birth is at 4:30 PM. In this case, GBS-specific antibiotics were given > 4 hours prior to delivery, but BSAB were given only 1 ½ hours prior to delivery. For calculating the SRS, in this case choose **"GBS specific antibiotics given > 2 hours prior to birth."**	

Appendix 3:
Possible systemic signs and symptoms of sepsis:

System	Signs and Symptoms
Respiratory	Grunting, flaring, retracting, cyanosis, oxygen requirement, apnoea, tachypnoea
Neurological	Hypotonia, hypertonia, lethargy, irritability, bulging/full/tense fontanels, seizures (associated with meningitis)
Cardiovascular	Bradycardia, tachycardia, hypotension, hypertension, decreased perfusion
Gastrointestinal	Feeding intolerance, abdominal distention, visible loops of bowel, gastric aspirates, emesis, diarrhoea, bloody stools
Other	Temperature instability, unexplained blood glucose instability, metabolic acidosis, rash, petechiae, purpura, unexplained jaundice

References:

1. Puopolo KM, Benitz WE, Zaoutis TE. Committee On Fetus And Newborn, Committee On Infectious Diseases. Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Paediatrics. Volume 142, number 6, December 2018:e20182894

2. Centers for Disease Control & Prevention (2010). Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines from CDC, 2010. Morbidity & Mortality Weekly Report, Nov, 19, 2010; 59(RR10); 1-32. http://www.cdc.gov/groupbstrep/guidelines/guidelines.html accessed 8/11/2015

3. Neonatal infection: antibiotics for prevention and treatment (NG195). Published April 2021. www.nice.org.uk/guidance/ng195

4. Newman T, Puopolo KM, Wi S, Draper D, Escobar GJ. Interpreting Complete Blood Counts Soon After Birth in Infants at Risk for Sepsis. Pediatrics 2010; 126:903-909.

5. Puopolo KM, Draper D, Wi S, Newman TB, Zupancic J, Lieberman E, Smith M, Escobar GJ. Estimating the Probability of Neonatal Early-Onset Infection Based on Maternal Risk Factors. Pediatrics. 2011; 128:e1155-1163.

6. Escobar GJ, Puopolo KM, Wi S, Turk BJ, Kuzniewicz MW, Walsh EM, Newman TB, Zupancic J, Lieberman E, Draper D. Stratification of risk of early-onset sepsis in newborns >=34 weeks' gestation. Pediatrics. 2014 Jan;133(1):30-6.

7. Dudhasia MB, Mukhopadhyay S, Puopolo KM. Implementation of the Sepsis Risk Calculator at an Academic Birth Hospital. Hospital Pediatrics 2018;8(5): 243-250. DOI:https://doi.org/10.1542/hpeds.2017-0180

8. Goel N, Shrestha S, Smith R …… Banerjee S. Screening for early onset neonatal sepsis: NICE guidance-based practice versus projected application of the Kaiser Permanente sepsis risk calculator in the UK population. Arch Dis Child Fetal Neonatal Ed. 2020;105:118-22

9. Morris R, Jones S, Banerjee S et al. Comparison of the management recommendations of the Kaiser Permanente Sepsis Risk Calculator with NICE guideline CG149 in infants ≥ 34 weeks gestation who developed early onset sepsis. Arch Dis Child Fetal Neonatal Ed 2020;105:F581-F586

10. Goel N, Cannell S, Davies G et al. Implementation of an adapted Sepsis Risk Calculator algorithm to reduce antibiotic usage in the management of early onset neonatal sepsis: a multicenter initiative in Wales, UK. Arch Dis Child Fetal Neonatal Ed 2021;0: F1–F8. doi:10.1136/archdischild-2020-321489

Appendix 4: Midwifery led Addendum

All Wales Neonatal Network Guideline

Early Onset Sepsis Risk Assessment for Infants >37 Weeks Gestation Born in Midwifery led settings with total duration rupture of membranes >24 hours.

Where a woman is in established labour within 24 hours of rupture of membranes (ROM) and is otherwise suitable for midwifery led intrapartum care, a midwifery led setting is a safe birthing environment and no additional monitoring is recommended during labour or in the postnatal period. The chance of early onset neonatal sepsis (EOS) is very low[1,2].

Where a woman is not in established within 24 hours of ROM (pre-labour rupture of membranes) obstetric led care is appropriate with birth recommended in a unit where there is access to neonatal services[1]. This is standard care and women should be informed of this recommendation in the antenatal period.

When birth occurs in a midwifery led setting and total duration rupture of membranes is more than 24 hours, the EOS risk assessment will not be applied to these infants. Current routine postnatal care will be provided in line with national guidance[1,2,3,4], this will include routine neonatal observation and early discharge at 2-3 hours of age where appropriate. Parents will need to be informed of the different EOS risk assessment that would be applied when compared to birth in obstetric led secondary care environment, and provided with the opportunity to make an informed choice about the sepsis risk assessment and newborn observations.

Midwifery actions in the case of total duration of rupture membranes of more than 24 hours at birth, with no co-existing complication:

- Babies with this history will be identified at birth.
- Parents of identified babies will be provided with the Parent Information leaflet, and should be informed that; in a healthy term baby the risk of EOS in this instance is low < 1/1000. In healthy babies where no red flag/non red flag events are identified as per NICE (2021) 'enhanced' neonatal observation, screening or antibiotic therapy would not be required, the guideline would recommend routine postnatal care (NICE 2021b). Within the EOS risk assessment guideline initial review by the neonatal team would be recommended and observation for 24 hours would be offered.
- If parents wish to be referred to the neonatal team for initial assessment as per EOS risk assessment guideline,
- Transfer to nearest obstetric / neonatal hospital unit should be arranged in after discussion with the neonatal /midwifery team.
- Observation of the baby will be completed, in the midwifery setting, and documented on a NEWTTS chart at 1 and 2 hours of age.
- Where all observations are within normal parameters, transportation will be via parents own car or hospital taxi, a midwife will not need to accompany the baby during transfer from the FMU or home birth.

Reference list

1.National Institute for Health and Care Excellence (2014).*Intrapartum care: care of healthy women and their babies during childbirth*. Retrieved from: https://www.nice.org.uk/guidance/cg190/resources/guidance-intrapartum-care- care-of-healthy-women-and-their-babies-during-childbirth-

2.National Institute for Health and Care Excellence (2021) Neonatal infection : antibiotics for prevention and treatment. Retrieved From: https://www.nice.org.uk/guidance/ng195.

3.National Institute for Health and Care Excellence (2021b). Postnatal Care. Retrieved from: https://www.nice.org.uk/guidance/ng194

4.Welsh Government (WG) (2020) The All Wales Clinical Pathway for Normal Labour. Cardiff: Welsh Government

Appendix 4 Flowchart: Identification of a baby born in midwifery led setting with RoM > 24 hours