NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline scope

Neonatal infection (early onset): antibiotics for prevention and treatment (update)

This guideline will update the NICE guideline on Neonatal infection (early onset): antibiotics for prevention and treatment (CG149). The guideline will be extended to cover for late-onset neonatal infection.

The guideline will be developed using the methods and processes outlined in developing NICE guidelines: the manual.

This guideline will also be used to update the NICE quality standard for Neonatal infection.

1 Why the update is needed

New evidence that could affect recommendations was identified through the surveillance process. Topic experts, including those who helped to develop the existing guideline, advised NICE on whether areas should be updated or new areas added. The surveillance review advised that risk factors for infection and clinical indicator of possible infection, intrapartum antibiotics, and maternal group B streptococcus status to guide the decision on timing of delivery in women with preterm prelabour prolonged rupture of membranes should be updated and the guideline should be extended to cover late-onset neonatal infection. Full details are set out in the surveillance review decision.

As part of the scoping process, NICE has identified 2 areas not included in the surveillance report where the evidence needs to be reviewed:

- prophylactic antifungal treatment when starting antibiotic treatment
- prophylaxis for catheter-associated late-onset neonatal infection.

Why the guideline is needed

Key facts and figures

Neonatal infection is a significant cause of mortality and morbidity in newborn babies. It may be early-onset (within 72 hours of birth) or late-onset (more than 72 hours after birth). Neonatal infection can lead to life-threatening sepsis, which accounts for 10% of all neonatal deaths.

Neonatal infection is present in 8 of every 1000 newborn babies and is responsible for 71 of every 1000 neonatal admissions. Of these infections, 82% occur in premature babies (born before 37 weeks) and 81% in low birthweight babies (below 2500 grams).

Early-onset neonatal infection is less common than late-onset neonatal infection, but it is often more severe. It is present in 0.9 of every 1000 live births and 9 of every 1000 neonatal admissions. Group B Streptococcus (GBS) and *Escherichia coli* are the most common organisms identified. Overall mortality is reported to be about 10%, but is even higher in premature babies. Up to 7% of babies who survive GBS infection have a consequent disability.

Late-onset neonatal infection is present in 7 of every 1000 live births and 61 of every 1000 neonatal admissions. Coagulase-negative staphylococci, Enterobacteriaceae and *Staphylococcus aureus* are the most common organisms identified.

Prompt antibiotic treatment for neonatal infection can save lives. Antibiotic treatment during labour reduces the risk of a baby developing a GBS infection in their first week of life from around 1 in 400 to 1 in 4000.

Current practice

To reduce mortality from early-onset neonatal sepsis, the current NICE guideline recommends risk-based antibiotic prophylaxis during labour and neonatal antibiotic treatment. However, guidance from Royal College of Obstetricians and Gynaecologists recommends only giving antibiotics to

women who are proven GBS carriers. The evidence in this area will be reviewed in light of this difference.

Widespread antibiotic use is associated with a risk of antimicrobial resistance. The risk factors and clinical assessments recommended in the current guideline can help guide antibiotic use, and ensure antibiotics are only given to women and babies who need them. New evidence has emerged that maternal obesity may need to be considered as a risk factor for early-onset neonatal infection and used to guide management.

Pregnant women are not routinely assessed for GBS colonisation status so their status and transmission risk to the baby is not routinely known. In practice there is inconsistency around to whom intrapartum antibiotic prophylaxis should be given. Some centres provide this to all women with preterm prelabour prolonged rupture of membranes, but some only do so for women who also have proven GBS colonisation. New evidence has emerged on the impact of timing of delivery on neonatal infection.

2 Who the guideline is for

This guideline is for:

- healthcare professionals in primary and secondary care
- commissioners and providers of neonatal services
- commissioners and providers of maternity services
- parents and carers of babies with neonatal infections

It may also be relevant for voluntary organisations and patient support groups.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government and Northern Ireland Executive.

Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope.

The guideline will look at inequalities relating to vulnerable women.

3 What the updated guideline will cover

3.1 Who is the focus?

Groups that will be covered

- Unborn babies who may be at risk of early-onset neonatal bacterial infection (within 72 hours of birth).
- Newborn babies (term and preterm) with an increased risk of infection through transmission of bacteria from the mother.
- Newborn babies (term and preterm) with suspected or confirmed early-onset neonatal bacterial infection.
- Babies with suspected or confirmed late-onset neonatal bacterial infection (more than 72 hours after birth). This group is not covered in the existing guideline, but will be covered in the update.
- Pregnant women.

Specific consideration will be given to preterm babies and babies with suspected late-onset neonatal bacterial infection who have been readmitted from home.

Groups that will not be covered

- Babies with suspected or confirmed non-bacterial infections.
- Babies with suspected or confirmed syphilis.
- Babies with localised infections.

3.2 Settings

Settings that will be covered

The guideline will cover all settings where NHS-funded care is provided.

3.3 Activities, services or aspects of care

Key areas that will be covered in this update

We will look at evidence in the areas below when developing this update. We will consider making new recommendations or updating existing recommendations in these areas only.

Note that guideline recommendations for medicines will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

Early-onset neonatal infection

1 Risk factors for infection and clinical indicators of possible infection.
   - Recognising the risk factors and clinical indicators, including 'red flags'.

2 Intrapartum antibiotics to prevent early-onset neonatal infection.

3 Timing of delivery in women with preterm prelabour prolonged rupture of membranes.
   - Timing of delivery in women with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation.

Late-onset neonatal infection

4 Risk factors for infection and clinical indicators of possible infection.

5 Investigations before starting treatment for late-onset neonatal infection in babies.

6 Antibiotics for treating late-onset neonatal infection.
   - Optimal antibiotic regimen for late-onset neonatal infection
   - Prophylactic antifungal treatment when starting antibiotic treatment

7 Prophylaxis for catheter-associated late-onset neonatal infection.

Proposed outline for the guideline

The table below outlines all the areas that will be included in the guideline. It sets out what NICE plans to do for each area in this update.

Area in the guideline	What NICE plans to do
Early-onset neonatal infection	
1.1 Information and support	
Information and support	No evidence review: retain recommendations from existing guideline.
1.2 Risk factors for infection and clinical indicators of possible infection	
Recognising risk factors and clinical indicators	Review evidence: update existing recommendations as needed.
Before the birth	No evidence review: retain recommendations from existing guideline. Remove cross-reference to 'NICE CG55' and replace with cross reference to the NICE guideline on intrapartum care for healthy women and babies (CG190).
After the birth	No evidence review: retain recommendations from existing guideline.
1.3 Intrapartum antibiotics	
Intrapartum antibiotics	Review evidence: update existing recommendations as needed. Cross-refer to the NICE guideline on preterm labour and birth (NG25) as needed.
1.4 Avoiding routine use of antibiotics in the baby	
Avoiding routine use of antibiotics in the baby	No evidence review: retain recommendation from existing guideline.
1.5 Investigations before starting antibiotics in the baby	
Investigations before starting antibiotics in the baby	No evidence review: retain recommendations from existing guideline.
1.6 Antibiotics for suspected infection	
Antibiotics for suspected infection	No evidence review: retain recommendations from existing guideline.
1.7 Duration of antibiotic treatment	
Investigations during antibiotic treatment	No evidence review: retain recommendations from existing guideline.
Decisions 36 hours after starting antibiotic treatment	No evidence review: retain recommendations from existing guideline.
Early-onset infection without meningitis	No evidence review: retain recommendations from existing guideline.
Meningitis (babies in neonatal units)	No evidence review: retain recommendations from existing guideline.
Discharge after antibiotic treatment	No evidence review: retain recommendations from existing guideline.
1.8 Therapeutic drug monitoring for gentamicin	
Trough concentrations	No evidence review: retain recommendations from existing guideline.
Peak concentrations	No evidence review: retain recommendations from existing guideline.

1.9 Care setting	
Care setting	No evidence review: retain recommendations from existing guideline.
Timing of delivery in women with preterm prelabour prolonged rupture of membranes	
Timing of delivery in women with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation	Review evidence: new area in the guideline.
Late-onset neonatal infection	
Risk factors for infection and clinical indicators of possible infection	Review evidence: new area in the guideline.
Investigations before starting treatment for late-onset neonatal infection in babies	Review evidence: new area in the guideline.
Antibiotics for treating late-onset neonatal infection	Review evidence: new area in the guideline.
Prophylaxis for catheter-associated late-onset neonatal infection.	Review evidence: new area in the guideline.

Recommendations in areas that are being retained from the existing guideline may be edited to ensure that they meet current editorial standards, and reflect the current policy and practice context.

Areas that will not be covered by the guideline

1 Non-antibiotic management of suspected or confirmed early-onset or late-onset neonatal infection.

2 Recognising and treating bacterial meningitis and meningococcal septicaemia in neonates who are not receiving care in neonatal units. This is covered by the NICE guideline on Meningitis (bacterial) and meningococcal septicaemia in under 16s.

3 Antenatal screening (including for group B streptococcus). This is covered by the UK National Screening Committee.

4 Antenatal antibiotic prophylaxis for bacterial infections. This is covered by the NICE guideline on antenatal care for uncomplicated pregnancies .

5 Antibiotic prophylaxis and management for term pregnancies with prelabour rupture of membranes. Antibiotic treatment of infections after birth for babies born to women with prelabour rupture of the membranes

is covered in the NICE guideline on intrapartum care for healthy women and babies.

6 Established and diagnosed early-onset neonatal infection due to sexually transmitted infections or congenital or acquired viral infections.

7 Surgical incisions in the skin and incisional infections after the initial procedure, including minimally invasive surgeries. This is covered in the NICE guideline on surgical site infections.

Related NICE guidance

Published

- Biopatch for venous or arterial catheter sites (2017) NICE Medtech innovation briefing 117
- Sepsis: recognition, diagnosis and early management (2016) NICE guideline NG51
- CytoSorb therapy for sepsis (2016) NICE Medtech innovation briefing 87
- Tests for rapidly identifying bloodstream bacteria and fungi (LightCycler SeptiFast Test MGRADE, SepsiTest and IRIDICA BAC BSI assay) (2016) NICE diagnostics guidance 20
- Preterm labour and birth (2015) NICE guideline NG25
- Inducing labour (2008) NICE guideline (CG70)
- Bronchiolitis in children: diagnosis and management (2015) NICE guideline NG9
- Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) (2015) NICE diagnostics guidance 18
- Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (2015) NICE guideline NG15
- Xpert GBS test for the intrapartum detection of group B streptococcus (2015) NICE Medtech innovation briefing 28
- Intrapartum care for healthy women and babies (2014) NICE guideline CG190

- Fever in under 5s: assessment and initial management (2013) NICE guideline CG160
- Healthcare-associated infections: prevention and control in primary and community care (2012) NICE guideline CG139
- Caesarean section (2011) NICE guideline CG132
- Surgical site infections (2008, updated 2017) NICE guideline CG74
- Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (2010) NICE guideline CG102
- Antenatal care for uncomplicated pregnancies (2008) NICE guideline CG62
- Urinary tract infection in under 16s: diagnosis and management (2007, updated 2017) NICE guideline CG54

NICE guidance that will be updated by this guideline

- Neonatal infection (early onset): antibiotics for prevention and treatment (2012) NICE guideline CG149

NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to neonatal infection:

- Medicines optimisation (2015) NICE guideline NG5
- Patient experience in adult NHS services (2012) NICE guideline CG138
- Service user experience in adult mental health (2011) NICE guideline CG136
- Medicines adherence (2009) NICE guideline CG76

3.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic

analyses, using an NHS and personal social services (PSS) perspective, as appropriate.

3.5 Key issues and draft questions

While writing the scope for this updated guideline, we have identified the following key issues and draft questions related to them:

Early-onset neonatal infection

1 Risk factors for infection and clinical indicators of possible infection
   1.1 Which maternal and fetal risk factors for early-onset neonatal infection/sepsis should be used to guide management?
   1.2 What risk factors in the baby (including symptoms and signs) should raise suspicion of infection/sepsis within 72 hours of birth?
2 Intrapartum antibiotics
   2.1 What is the clinical and cost effectiveness of intrapartum antibiotic prophylaxis for preventing early-onset neonatal infection (compared with no treatment)?
3 Timing of delivery in women with preterm prelabour prolonged rupture of membranes
   3.1 What is the clinical and cost effectiveness of immediate delivery versus expectant management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?

Late-onset neonatal infection

4 Risk factors for infection and clinical indicators of possible infection
   4.1 Which maternal risk factors for late-onset neonatal infection/sepsis should be used to guide management?
   4.2 Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection/sepsis?
5 Investigations before starting treatment for late-onset neonatal infection in babies

5.1 What investigations should be performed before starting treatment in babies with symptoms of late-onset neonatal infection?

6 Antibiotics for treating late-onset neonatal infection

6.1 What is the optimal antibiotic treatment regimen for suspected late-onset neonatal infection?

6.2 What is the clinical and cost effectiveness of starting prophylactic antifungal treatment when starting antibiotic treatment for suspected late-onset neonatal infection?

7 Prophylaxis for catheter-associated late-onset neonatal infection

7.1 What is the clinical effectiveness of intravascular catheters impregnated with antibiotics in reducing the risk of the baby developing late-onset neonatal infection?

The key issues and draft questions will be used to develop more detailed review questions, which guide the systematic review of the literature.

3.6 Main outcomes

The main outcomes that may be considered when searching for and assessing the evidence are:

- neonatal mortality
- neonatal morbidity, including infection, bronchopulmonary dysplasia, chronic lung disease, respiratory distress syndrome, intraventricular haemorrhage, necrotising enterocolitis, periventricular leucomalacia, length of hospital stay and complications of therapy
- neurodevelopmental assessment
- health-related quality of life of the baby
- impact on the baby's family, including subsequent pregnancies and psychological distress
- antimicrobial resistance
- maternal morbidity.

4 NICE quality standards and NICE Pathways

4.1 NICE quality standards

NICE quality standards that may need to be revised or updated when this guideline is published

- Neonatal infection (2014) NICE quality standard 75

4.2 NICE Pathways

When this guideline is published, we will update the existing NICE Pathway on Early-onset neonatal infection. NICE Pathways bring together everything NICE has said on a topic in an interactive flow chart.

5 Further information

This is the draft scope for consultation with registered stakeholders. The consultation dates are 14 September to 12 October 2018.

The guideline is expected to be published in January 2020.

You can follow progress of the guideline.

Our website has information about how NICE guidelines are developed.