Frequently Asked Questions from The Royal Devon University Healthcare NHS Foundation Trust NOAH implementation process

Does the evidence suggest that sending babies with suspected early onset infection home with oral antibiotics is safe?

The evidence supports the use of oral antibiotics for neonates with suspected early-onset infection under certain conditions, particularly when the neonate is clinically stable and feeding well. Studies, including the RAIN trial and Carlsen et al., demonstrate that an early switch from intravenous (IV) to oral antibiotics can effectively reduce hospital stays without increasing adverse events. The available evidence suggests that these babies are not at increased risk of treatment failure or partially treated infections, provided they are clinically stable, feeding well, and appropriately monitored. All of these criteria are included in the NOAH eligibility criteria. Studies show that oral antibiotics can achieve therapeutic serum concentrations similar to IV therapy, with no significant increase in adverse outcomes or reinfections. Studies suggest that outpatient follow-up is essential to ensure safety and early detection of any issues and for this reason, a robust process for outpatient review is included in the NOAH pathway.

How did the implementation of the Royal Devon pilot differ from the research studies?

The NOAH pathway as detailed in these resources aligns closely with the protocol described in the RAIN study, with the following differences:

The NOAH pathway limits eligible babies to term only (>37 weeks) whereas the RAIN protocol concluded babies >35 weeks. NOAH was limited to term babies at present as an additional safety precaution.
The RAIN study had no peak CRP limit. Babies on the NOAH pathway must have a peak CRP of not more than 50. Again, this is an additional safety precaution.

Can oral antibiotics be effective in neonates with suspected early-onset infection?

Studies show that antibiotics generally, and amoxicillin specifically, achieve sufficient serum concentrations when administered orally. Autret et al. reported that oral amoxicillin peaks within 2–6 hours post-dose and remains above the minimum inhibitory concentration for most neonatal pathogens. Gras-le-Guen et al. demonstrated that oral antibiotics maintain effective serum levels after IV-to-oral transition. Evidence suggests that the primary concern around giving oral antibiotics to neonates is that there may be a delay in achieving bactericidal serum levels in neonates when compared with adults or older children. This may be due to altered

intestinal absorption in the newborn. Initial antibiotic doses should be given parenterally in order to achieve bactericidal serum concentrations rapidly. The evidence suggests that thereafter, oral routes can deliver therapeutically adequate levels, provided neonates are clinically stable. (9,10,11) These findings support the use of oral antibiotics in the cohort of babies eligible for NOAH. These babies have, by definition, already commenced on IV antibiotics for suspected early onset infection.

What benefits of NOAH does the evidence suggest?

The published evidence suggests several benefits of the Neonatal Oral Antibiotics at Home (NOAH) strategy:

- **Reduced Hospitalisation**: Multiple studies conclude that switching to oral antibiotics in clinically stable neonates significantly shortens hospital stays, with no increase in adverse events or treatment failure (Keij, Carlsen, Gyllensvärd).
- **Non-Inferiority**: The evidence indicates that, in this context, oral antibiotics are non-inferior to intravenous antibiotics. Both groups had similar reinfection rates and adverse events, suggesting that oral antibiotics provide an equally effective alternative to IV therapy (Keij et al., 2019; Carlsen et al., 2023).
- **Cost-Effective**: By reducing hospital stays, the NOAH approach lowers healthcare costs while ensuring that neonates continue their treatment effectively (Gyllensvärd et al., 2020).
- **Improved Family Bonding**: Discharging neonates on oral antibiotics avoids separating families and allows parents to care for their baby in their own home, which can improve the neonatal experience and support family health and well-being (Carlsen et al., 2023).

Can NOAH be used to treat late onset neonatal infection (infection after the first 72 hours of life)?

NOAH relates specifically to a switch to oral antibiotics for the management of suspected early-onset neonatal infection in term babies. **The evidence and resources provided here do not relate to the management of neonatal infection outside of this.**

Will NOAH project increase overall antibiotic usage?

There may be concerns about potential overprescribing, particularly for stable neonates with suspected bacterial infection who might more appropriately stop antibiotics completely at 36-48 hours. Reassuringly, an increase in antibiotic

consumption following IV-to-oral switch was not observed in the literature (Carlsen). Furthermore, the Royal Devon pilot demonstrated that all babies on the NOAH pathway were eligible and the proportion of babies taking up the pathway was similar to expected, based on previous years' predictions. Following a review of the patient records, all babies were on the appropriate pathway. This suggests that when implemented well, the NOAH pathway will only pick up those babies where there is a clinical need for continued antibiotics.

Is there a risk of late-onset Group B Streptococcus (GBS) infection among babies treated with NOAH?

Late onset GBS cannot be prevented with intrapartum or early neonatal antibiotic therapy. Therefore, it may be assumed that NOAH will be no more effective in preventing late onset GBS than a course of IV antibiotics. This highlights the necessity to provide parents with verbal and written information about the signs of infection in their baby and when and how to seek help.

How soon can the first in-hospital oral dose of Amoxicillin be given after the last dose of IV Benzylpenicillin?

With the support of the paediatric pharmacist, at RDUH we agreed the oral Amoxicillin should be given no sooner than 8 hours after the last dose of IV Benzylpenicillin.

What is the impact of oral antibiotics on neonatal gut flora?

This is an important question for further research as currently the impact of oral antibiotics on neonatal gut flora is unknown.

Are syringes single use?

Most syringes can be re-used. This will be stated on the packaging. If the syringe can be re-used, wash your syringe in warm soapy water after each use so it is ready for the next time you need it. Leave to dry. Use a new syringe each week. Bungs can stay in the bottle until it is finished or the course is complete.

See medicines for children website for further info.

How do we ensure parents are confident and capable of administering oral antibiotics?

All NOAH babies should have their first dose of oral Amoxicillin prior to discharge. This is an opportunity for staff to show parents how to administer the oral antibiotic and answer any questions.

How do we educate parents on recognising signs of sepsis or complications?

Parents should be verbally counselled prior to discharge and also be given written information in the form of the NOAH patient information leaflet.

What do we do if parents don't feel confident to look for signs of deterioration?

If parents are not confident to go home the baby can remain an inpatient on either oral or IV antibiotics. If parents are unclear about concerning features during the telephone follow-up these should be re-iterated to them.

Is the recommended telephone follow-up supported by the evidence?

The evidence supports various follow-up approaches after the intravenous to oral antibiotic switch. Gyllensvärd et al. conducted clinical reviews and CRP measurements on day 7 post-discharge. Keij et al. (RAIN) monitored patients with telephone interviews on days 4 and 14, without repeating inflammatory markers. Malchau Carlsen et al. recommended a more conservative follow-up with clinical reviews and repeat CRP measurements two days after the oral switch, followed by another review two to four days after completing antibiotics. Therefore, for NOAH, it was decided that a telephone consultation on day 4-5 of antibiotics would provide an appropriate safety net whilst allowing flexibility to allow for staff capacity and timing of discharge home.

What do we do if there is no response to parent follow-up calls?

Plans to manage this situation should be discussed and agreed as part of the NOAH planning process. Our local plan at the Royal Devon to manage this, is to make 3 attempts at calling and then inform the named consultant who will write a letter to the family.

What if the family don't have a phone?

Care must be tailored to the individual family's needs. If safety after discharge is a concern, the baby should remain in hospital.

What happens if parent/s miss a dose or are unable to administer the antibiotics?

Direct parents to the Amoxicillin leaflet on the Medicines for Children website.

- If you remember up to 1 hour after you should have given a dose, give the missed dose.
- If you remember after this time, do not give the missed dose. Wait until the next normal dose.

Are there opportunities for future research?

Although the RAIN study suggests non-inferiority, it was not powered to detect a small increase in an extremely rare outcome; late reinfection/treatment failure among babies on oral antibiotics vs IV antibiotics.

The unknowns surrounding the use of oral antibiotics in neonates include long-term outcomes, particularly regarding antimicrobial resistance and the impact on the neonatal gut microbiome. Additionally, while current studies suggest safety in stable neonates, the full impact of outpatient follow-up protocols and monitoring remains uncertain. The approach's generalizability across various healthcare settings, especially those with different resource levels, also requires further exploration. More research is needed to establish optimal criteria for oral antibiotic use in this population. For NOAH at the Royal Devon, we set a CRP threshold of 50. Babies with a CRP above this value are not eligible. This threshold was chosen as it was felt to add an extra layer of safety, but we do not have evidence to guide this decision making at present.