ARHAI Scotland
Antimicrobial Resistance and Healthcare Associated Infection

NHS National Services Scotland

Literature Review and Practice Recommendations: Management of Incidents and Outbreaks in Neonatal Units (NNUs)

Publication date: 8 June 2022

Key Information

Document title:	Literature Review and Practice Recommendations: Management of Incidents and Outbreaks in Neonatal Units (NNUs).
Date published/issued:	8 June 2022
Date effective from:	8 June 2022
Version/issue number:	Version 2.0
Document type:	Literature review
Document status:	Final

Document information

Description: Management of outbreaks in neonatal units (NNUs).

Purpose: To inform the Addendum for Infection Prevention and Control within Neonatal Settings (NNU). The Addendum includes setting-specific recommendations that are supplementary to the key recommendations in Chapter 3 of the National Infection Prevention and Control Manual (NIPCM).

Target Audience: All NHS staff involved in the prevention and control of infection in NHSScotland.

Update/review schedule: Updated as new evidence emerges with changes made to recommendations as required.

Cross reference: National Infection Prevention and Control Manual

NIPCM Literature Review: Healthcare Incidents and Outbreaks in Scotland (2017)

NIPCM Literature Review: Safe Management of the Care Environment (2020)

Update level: **Practice** – The implications for practice are updated based on a review of the extant scientific literature and available international guidance on incidents and outbreaks in the neonatal unit setting.

Research - The implications for practice are updated based on a review of the extant scientific literature and available international guidance on incidents and outbreaks in the neonatal unit setting.

Contact

ARHAI Scotland Infection Control team:

Telephone: 0141 300 1175

Email: NSS.ARHAIinfectioncontrol@nhs.scot

Version History

This literature review will be updated in real time if any significant changes are found in the professional literature or from national guidance/policy.

Version	Date	Summary of changes
2.0	June 2022	Review of the extant scientific evidence on incidents and outbreaks in the neonatal setting using the National Infection Prevention and Control Manual (NIPCM) methodology. New recommendations added.
1.2	November 2018	Reference to Group B streptococci removed.
1.1	June 2018	Risk assessment reworded for clarity.
1.0	May 2018	New

Approvals

This document requires the following approvals

Version	Date Approved	Name
2.0	May 2022	National Policies, Guidance and Evidence Working Group

Contents

1. Objectives

The aim of this review is to examine the extant scientific literature regarding incidents and outbreaks in the neonatal unit setting (NNU) to form evidence-based setting-specific recommendations for practice that are supplementary to the key recommendations in the National Infection Prevention and Control Manual.

The specific objectives of the review are to determine:

- What are the definitions of a healthcare infection incident/outbreak in a neonatal unit (NNU)?
- What are the key measures to prevent incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?
- How should NNU incidents/outbreaks be investigated and managed?
- What are the key measures to control incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?
- How should NNU incidents/outbreaks be reported?
- How should a healthcare infection incident be 'closed', with lessons learned recorded and disseminated nationally?

2. Methodology

This systematic literature review was produced using a defined methodology as described in the National Infection Prevention and Control Manual: Development Process.

Supplementary sections to the applied methodology for this specific literature review can be found in Appendix 1.

The adapted PRISMA diagram for systematic search results can be found in Appendix 2.

3. Discussion

3.1 Implications for practice

What are the definitions of a healthcare infection incident/outbreak in a neonatal unit (NNU)?

There were no guidelines identified in this review which provided information regarding a general definition or 'trigger' of a healthcare infection incident or outbreak in neonatal unit (NNU) settings specifically. However, pathogen-specific guidance was identified which related to *Pseudomonas aeruginosa* infections in NNUs - including a British Standard, a UK National Institute for Health and Care Excellence (NICE) guideline, an independent review and a UK-led expert guidance document concerning Gram-negative bacteria.[1-4] The British Standard (BS 8580-2:2022) published in 2022, specified that a single case of hospital-acquired *P. aeruginosa* in a neonatal unit should prompt an incident meeting.[1] The UK NICE guideline by Wilson et al. on the control of Gram-negative bacteria also indicated that traditional epidemiological linking of cases would be insufficient in a *P. aeruginosa* incident, due to the unique profile and epidemiology of *P. aeruginosa* hospital outbreaks.[2] The guidelines stated that where a single or sporadic series of cases can be seemingly unlinked, this is largely related to in-house plumbing contamination[2] (see section: water management). The independent review into *P. aeruginosa* outbreaks in NNUs in Northern Ireland concluded that for *P. aeruginosa* in neonatal intensive care and high dependency units, a single sporadic case should be investigated and recommended surveillance as an 'alert organism' across UK care settings.[3] Finally, an expert guidance document concerning Gram-negative bacteria in UK NNUs produced in 2012 by the UK Department of Health outlined a definition of an outbreak trigger for initiating a response, stating that the following scenarios would warrant an outbreak response: a single MDRO; rare or novel Gram-negative bacteria or *P. aeruginosa* infection; two or more sterile site isolates within 2 weeks which share the same species and antibiogram, or alternatively three or more colonisations with the same organism.[4] The development of this guidance was led by neonatology and infectious disease experts.

There were also numerous outbreak reports from neonatal units, including neonatal intensive care units (NICUs), where the initial trigger/definition of an outbreak was reported. In five international outbreak investigations it was reported that a single case (colonisation or infection) in the unit led to an immediate outbreak response.[5-9] The organisms involved in these outbreaks included methicillin-resistant *Staphylococcus aureus* (MRSA), *Salmonella*, Extended-Spectrum

Beta-Lactamase (ESBL) producing *Escherichia coli* and extensively drug-resistant *Acinetobacter baumannii*. This led to prompt implementation of control measures such as patient screening, enhanced cleaning and decontamination[5-8] and in one outbreak, allowed investigators an early opportunity to close the unit to further admissions.[5]

Conversely, in six outbreak investigations identified in this review, it was reported that at least two episodes of infection or colonisation with the same organism triggered an outbreak response;[10-15] including two units where the hospital IPC team were only notified after two linked episodes of infection were detected.[11, 12] In four of these outbreaks, waiting for a second case to trigger an investigation directly led to a delay in implementing response measures and subsequently, a rise in incident cases was observed. For example, in three separate MRSA/MSSA (methicillin-sensitive *Staphylococcus aureus*) skin infection outbreaks that occurred (two in NICUs in England and one at a joint maternity and neonatal unit in Italy) there was a delay of 2-3 weeks where a response was not initiated until a second case was found.[10, 11, 15] In another report from the Netherlands, an outbreak response was not initiated until a second *E. cloacae* sepsis case occurred within 3 months, whereupon the organism was found to be a multidrug resistant ESBL-producer, identical to the index strain.[14] In total there were 15 patients, and the outbreak lasted 6 months.

In other studies, the lack of a formal procedure in place resulted in healthcare staff working on the unit reactively reporting a suspected outbreak, due to a rise in cases which were considered unusual.[16-19] In two of these studies, it was clearly reported that a lack of a formal trigger led to a delay in the outbreak response from several days, to months after the index case was identified.[16, 19] For example, a lengthy multiclonal MRSA outbreak investigation in a hospital NICU in the USA was first declared after 6 neonates were infected over the course of 3 months. As a result of the increase, the outbreak management team was formed several months after the index case and the response continued for one year, with a total of 68 infant cases affected.[19]

There was widespread heterogeneity in how outbreaks were defined, investigated and reported in the international outbreaks literature. Other outbreak reports which recorded information on the initial onset of outbreaks in NNUs, provided insufficient information on how the outbreaks were defined or triggered and were therefore excluded from this review. Generally, such reports are also subject to widespread publication bias, and therefore due to limitations, they were broadly not generalisable to NNUs in NHSScotland. However, from this literature, it is clear that early communication and surveillance of episodes of infection or colonisation in NNUs through

notification to the IPCT can allow for a prompt response to a potential outbreak and the use of a formal definition of an outbreak is essential in alerting staff to a suspected outbreak.

In NHSScotland, Chapter 3 of the National Infection Prevention and Control Manual (NIPCM) currently defines a healthcare associated infection outbreak as two or more linked cases with the same infectious agent in the same healthcare setting over a specified time period; or a higher than expected number of cases of HAI in a given healthcare area over a specified time period.[20] The scientific evidence for the general definition of healthcare infection incidents, outbreaks or data exceedance has been appraised in the NIPCM Healthcare Incidents and Outbreaks in Scotland literature review. Additionally, Healthcare Improvement Scotland's (HIS) Infection Prevention and Control (IPC) Standards 2022 describe how the Infection Prevention & Control Team (IPCT) should be aware of the national minimum list of alert organisms and refer to this during local surveillance of infections and alert organisms.[21] The National minimum list of alert organisms can be found in the NIPCM Appendix 13.[20]

In the Scottish Government's Neonatal Care Quality Framework, it is recognised that neonates, as highly vulnerable patients, require timely provision of clinical care, with minimised delays in access to care, and with an emphasis on patient safety.[22] In support of this, a more sensitive trigger/definition of a healthcare incident/outbreak has been developed through Scottish expert consensus, for NNU settings: a single case of infection with an alert organism or two or more colonisations with the same organism, linked in time and place. This should trigger an incident/outbreak investigation, where action should be taken by the local IPCT to investigate and report. Similarly, where a single case of colonisation with an alert organism is identified in a NNU, this should warrant local IPCT consideration for any potential onward transmission which may result in an outbreak/incident. It is noted that this represents a more sensitive trigger/definition compared to the mandatory definition in Chapter 3, in a setting where typically patients have only ever been in the healthcare environment, recognising the acquisition of any colonisation/infection is likely healthcare acquired.

What are the key measures to prevent incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?

Infection risk assessments at the point of entry and during stay on the unit

Clinical risk-based screening

In acute care settings in NHSScotland, current national guidance is in place for screening patients for both MRSA and carbapenemase-producing Enterobacterales (CPE) upon entry to the unit, using a designated clinical risk assessment (CRA) – this applies to patients for the duration of their care within an acute hospital and extends to all admissions, readmissions and transfers from another healthcare facility.[23, 24] The CRA represents the national minimum mandatory screening policy in Scotland, required for both organisms; local IPCTs may choose to extend the scope of their own local policy based on local risk assessment.[23, 24] The Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guideline for prevention and control of MRSA in healthcare settings, accredited by NICE, provided an appraisal of the evidence for the clinical and cost-effectiveness of targeted admission screening. Authors found weak evidence from three studies (which specifically excluded neonates), reporting no difference between targeted versus universal admission screening.[25] The guideline also stated that careful consideration should be given to establish which patients are at risk, and local risk factors should be taken into consideration.

Universal microbiological screening

The Framework of Actions to Contain CPE published by the UK Health Security Agency (previously Public Health England) in 2020 specifies that for NICUs, as a high-risk speciality unit, universal CPE admission screening should be considered.[26] The NICE guidelines by Coia et al. stated in 2021 that while universal MRSA screening is not currently recommended in acute settings, it is often conducted for high-risk patients such as those entering ICUs (including NICUs).[25] While no guidelines specific to NICUs or NNUs were identified, there were seven observational outbreak reports from large NNUs in NHS Trusts in England which provide intensive care, as well as NICUs in Japan and Switzerland which described having a permanent policy of microbiological testing all neonates for MRSA upon admission.[9, 10, 15, 16, 27-29] None of the studies provided a clear rationale for this screening policy however in two studies, it was stated that MRSA was known to be circulating in other wards in the hospital,[9, 27] while in one NICU, admission screening was successfully used to identify incoming transfer patients who were MRSA positive, when three triplets were screened after admission from another hospital.[29]

Meanwhile, two NNUs, both of which included facilities providing intensive care therapy, also included Gram-negative MDROs[15] and ESBL-producing Enterobacterales in their admission screening.[30] A national survey conducted in 2009 reported that in UK NNUs, 21% of units reported screening for Gram-negative MDROs on admission.[31] However, more robust, controlled studies or trials investigating admission screening policies in neonatal settings are needed.

Ongoing microbiological screening (e.g., weekly)

There were eight outbreak reports from NNUs which reported a permanent policy of weekly testing of admitted patients in the unit as routine practice, including MRSA,[9, 16, 27, 29] and ESBL-producing Enterobacterales.[5, 30, 32, 33] All of these reports took place in NICU settings, or in units where there was an adjoining/included NICU or high dependency unit. In three MRSA outbreaks, it was not clear whether weekly microbiological screening expedited the discovery of the organism on the unit, since admission screening and clinical sampling were also in place.[9, 27, 29] However in one MRSA outbreak in England, weekly testing led to the discovery of three colonised neonates, two of which went on to develop bacteraemia. The authors reported a history of low numbers of MRSA cases in the unit in previous years.[16] In one outbreak report from a NICU in the Republic of Ireland, screening for ESBL-producers was targeted to high-risk neonates only (premature or long-stay infants).[5] In two further outbreak reports which took place in neonatal units with adjoining NICUs, routine weekly screening for ESBL-producing *E. coli* had been in place to monitor nosocomial cases and was successful in identifying the onset of an outbreak.[30, 33] In one of these outbreaks in Italy, a low number of colonisations had been detected in the years prior to the outbreak.[33] Finally, in the 2009 survey by Francis et al., 40% of UK NNUs surveyed reported that weekly microbiological screening was permanent policy.[31] This dated survey did not delineate between different levels of neonatal care / acuity level. More evidence is required on practices across the UK (especially in NICUs). Universal microbiological screening of neonates receiving intensive care is not routinely carried out in Scotland, however some units currently choose to undertake this based on their assessment of risk:benefit for their patient group.

There was very little evidence regarding the selection of specific body sites when screening neonatal patients routinely for MDRO colonisation; however the US Centers for Disease Control and Prevention (CDC) published in their 2021 *Staphylococcus aureus* guidelines for NICU settings, that at least the anterior nares should be sampled in NICU patients, based on moderate evidence from two diagnostic studies.[34] The NHSScotland neonatal CRA states that a nasal swab should be collected for MRSA, and a stool sample obtained for CPE screening,

however no patient-specific data on body sites is provided in either MRSA or CPE national guidance by NHSScotland.[23, 24] Meanwhile, as part of its latest update, the NICE guidelines on the management of MRSA recently removed a recommendation specifically listing umbilicus and throat as site preference in neonates, citing a lack of evidence.[25] In several outbreak reports which have taken place in NNUs, (mainly NICUs), the authors have listed body site preferences used to assess colonisation status routinely among patients, however none of the reports provide a rationale or any assessment of effectiveness.[5, 7, 9, 10, 12, 15, 16, 27, 29, 30, 33, 35]

Based on one US guideline document, as well as thirteen observational outbreak reports and one UK survey, the evidence shows that there is widespread variation in approach to universal microbiological screening for infectious organisms in NNU settings.[5, 7, 9, 10, 12, 15, 16, 27, 29-35] Many of the publications were dated; there was also no robust data supporting any single approach due to a lack of controlled, well-designed studies (for example a comparison of universal screening versus a clinical risk-based approach, or a pre- and post-intervention studies). There was very little evidence related to variation of screening practices across different care levels, unit size and acuity of patients. However, evidence shows that ongoing microbiological screening for MDROs is commonly cited in neonatal units providing intensive care. More evidence is needed to assess the effectiveness of admission and weekly screening practices across neonatal settings.

All patients being admitted to neonatal units in NHSScotland must be promptly assessed for infection risk using the Clinical Risk Assessment for Microbiological Screening of Neonates on Admission or Transfer (CRA),[36] which has been developed based on Scottish mandatory MRSA and CPE guidance,[23, 24] as well as Scottish expert consensus,. This should ideally be arranged prior to arrival where possible (e.g. for planned admissions) or on arrival at the care area before placement is decided. In addition to MRSA and CPE screening, the CRA includes a risk assessment for any other infectious pathogen, and applies to all admissions, readmissions and transfers, including patients from another care area.[23, 24, 36] Furthermore, infection risk should be continuously reviewed throughout the patient's stay; the clinical presentation of the neonate should determine if additional testing is required and the local IPCT, including microbiology, should advise on where additional microbiological screening is required (including the frequency of testing).[36] Neonates who present a cross-infection risk include patients who have:

- been transferred from another unit in Scotland with an ongoing incident/outbreak
- been born outside of Scotland
- been previously positive with an MDRO or other infectious pathogen

or whose mothers have

- been hospitalised outside Scotland in the previous 12 months
- had no antenatal care
- been previously positive with an MDRO

Neonates identified with any single risk factor should be prioritised for placement in an incubator/cot pending investigation i.e. placed in a single room or cohort area/room with a wash hand basin. Information and advice should be provided to parents/carers of all neonates. Any suspected cases that are identified during their stay should be screened and isolated immediately as a precaution, as outlined in the NIPCM.[20]

Ensure staffing levels meet the minimum requirements for the level of care being provided

The staffing requirements for safe care in NNUs in NHSScotland are set out in 'Neonatal care in Scotland: A Quality Framework'; in special care baby units a minimum of 1:4 staff* to baby ratio is required at all times; in high dependency units this increases to a minimum of a 1:2 staff* to baby ratio; in neonatal intensive care a minimum of a 1:1 staff* to baby ratio should be maintained at all times.[22] These staffing levels are also recommended within the Department of Health, health building note 09-03 (2013).[37] Understaffing or excessive staff workloads have been reported as contributing factors in several outbreaks in NNUs[4, 27, 38-43] where low nurse to baby ratios may promote errors and lapses in infection control practices.[4, 43]

*The requirements for staff training, registration status and supervision for each level of care are also set out in 'Neonatal care in Scotland: A Quality Framework'.

Incubator/cot spacing and minimisation of clutter and overcrowding.

Overcrowding was a commonly reported contributory factor to outbreaks occurring in neonatal units.[27, 40-42, 44]

Overcrowding and cluttering of space/equipment may increase the risk of cross-contamination between equipment, the environment, and the patient and should be avoided by adhering to recommended cot space requirements.[4, 42, 44]

The UK Government Department of Health 'Health Building note 09-03' recommends that in intensive care each cot space should be able to accommodate:

- all-round access to the incubator/cot;

- space to enable staff to manoeuvre the incubator/cot, themselves and equipment safely;
- clinical equipment permanently located around the incubator/cot;
- any mobile equipment that may be required;
- a minimum of five members of staff (to attend the baby in an emergency situation);
- space for the mother to express discreetly at the cot-side;
- at least two chairs to accommodate visitors.[37]

In the schedule of accommodation the recommended space allowance for multi-cot/incubator areas in intensive care and high dependency units is 13.5 square metres (sqm) for the 'clinical space envelope', or clinical area, rising to 20 sqm when access space and shared space for core support (pharmacy, storage etc.) is included and in single rooms; in special care units the recommended space allowance is 9 sqm rising to 11.5 sqm when access space and shared space for core support (pharmacy, storage etc.) is included and in single rooms.[37]

Water Management and Usage

A 2017 systematic review included studies examining nosocomial waterborne infections in neonates and mothers.[45] Across 25 observational studies included in the review, the most common source of infectious agents was tap water (15 studies).[45] Additional sources included water baths for warming milk or formula (n=5), water reservoirs from mechanical ventilation equipment or incubator humidifiers (n=3) or water used to bathe neonates (n=2). Other reported water sources included rinse bottles, distilled water, bottled mineral water, a saline solution, and aqueous chlorhexidine. These sources were considered to either be the primary source of transmission or an environmental reservoir.

Water is a known environmental source associated with *P. aeruginosa* outbreaks. Contaminated hospital water systems were implicated in two lengthy *P. aeruginosa* outbreaks in NICUs in the USA between 2013 and 2016 which led to the disruption of day-to-day care, while investigation, renovation and remediation work was undertaken.[46, 47] Another observational study reported an outbreak in a NICU in Italy, where *P. aeruginosa* colonisations lead to the emergence of a multi-drug resistant strain.[48]

In NHSScotland, NNUs should follow the Health Protection Scotland 'Guidance for neonatal units (NNUs) (levels 1, 2 and 3), adult and paediatric intensive care units in Scotland to

minimise the risk of *Pseudomonas aeruginosa* infection from water'; this includes guidance on the specific roles and responsibilities of hospital staff, estates and IPCTs in safe water management and usage. These responsibilities include the estate management of the hospital water delivery system, the daily flushing of all outlets (taps) and reduction of transmission risks from water splashes. The guidance also sets out when and where the use of tap water or sterile water is indicated for neonatal care procedures, as well as instructions for investigation and control following an infection incident.[49] For prevention of colonisation/infection related to direct water usage, ice should not be used in NNUs routinely; ice may be directly used for rare but important clinical conditions. This would remain under senior medical instruction/supervision and sterile water should be used in a closed system. The selection of tap or sterile water for neonatal care procedures requires an assessment of the neonate's condition.[49] Incubators/cots or any other patient equipment should not be placed near any water source where there is any risk of spraying or splashing of water.[49] There should be adequate space allowance in the clinical area to provide sufficient distance between incubators or cots and water outlets (such as handwashing basins), as laid out in the UK Government's Health Building Note 09-03 (see section Incubator/cot spacing).[37]

All neonatal units should also undergo routine water testing for *P. aeruginosa* in NHSScotland, conducted every three months.[50] Where positive samples are detected, the local Water Safety Group must conduct a risk assessment for continued use of tap water. UK NICE guidelines for multi-drug resistant Gram-negative bacteria in healthcare settings also stated in 2016 that in the event *of P. aeruginosa* contamination of the water supply, sterile water should be used for neonates, with additional hand hygiene using alcohol gel after washing.[2] An independent review into *P. aeruginosa* deaths in NNUs in Northern Ireland in 2012 resulted in a change of guidance to routine use of sterile water for neonatal personal care across all NNUs in the country.[3]

Aseptic preparation of medications, ultrasound gels, antiseptics and solutions

Neonatal outbreaks have been traced to multi-use consumable items such as saline, baby shampoo, and topical emollients.[8, 51-53] As far as possible, items being used in patient care should be sterile and prepared and administered using aseptic technique. Single-use patient items should never be re-used for other patients. Aseptic procedures such as drug preparation should not be performed in areas where there is a risk of splashes which could contaminate the aseptic field (e.g. near sink splash zones) and equipment should be stored away from areas or procedures that generate splashes.[49] Ultrasound gel should be single use and sterile for use in NICUs, and other neonatal settings where possible.[54]

Total parenteral nutrition

In this review, there were two observational reports identified where contaminated parenteral nutrition solutions caused serious outbreaks in NICUs, marked by a very rapid rise in bacteraemias in the hours after its administration.[55, 56] In both outbreaks, inappropriate 'stock solutions' of TPN medication were in use, which is not generalisable to UK healthcare settings, where standardised bags are prescribed.[57] Each NHS board should ensure the safe and effective delivery of parenteral nutrition and staff should have the knowledge, skills and experience to deliver complex nutritional care safely and effectively, in line with Healthcare Improvement Scotland (HIS) Standards for complex nutrition care (not specific to neonatal populations).[58] A UK NICE guideline was published in 2020, on the topic of neonatal parenteral nutrition.[57] ARHAI Scotland's literature review includes practice recommendations for preventing central-catheter-associated blood stream infections when accessing, inserting or maintaining a neonatal central vascular catheter, including for administering total parenteral nutrition (TPN).[59]

Hygienic preparation (including expression) and storage of breast milk and infant formula

There were two outbreak reports identified which found contamination of communal milk-expressing equipment with *Enterobacter cloacae*, and *Salmonella Tennessee,* respectively.[32, 40] In both reports, environmental sampling was conducted in response to an ongoing outbreak in the unit, but it was unclear whether sampling was performed post-cleaning or for randomly selected items. In another outbreak, positive isolates were recovered from breast milk samples obtained from a single shared breast pump, which led to the removal of shared breast pumps on the unit.[30] Meanwhile in a *P. aeruginosa* outbreak, it was discovered during a review of practices, that sanitation of communal breast pump equipment was performed too infrequently to comply with the manufacturer's instructions.[47] In 2016 a joint working group between the Healthcare Infection Society (HIS) and the Infection Prevention Society (IPS) published guidelines on the decontamination of breast pump milk collection kits and related items.[60] The guideline development group reported that scientific evidence was limited and inconsistent, and recommendations were formed by expert consensus; the implementation of these guidelines is recommended as best practice. The recommendations state that single-use items should be supplied where possible and breast pump milk collection kits should not be reused by different mothers without sterilization. The authors emphasised the importance of thorough drying after routine cleaning. The NIPCM also outlines how re-usable equipment should be decontaminated including where transmission-based precautions apply; more information can be found in the NIPCM literature review: Management of Care Equipment.[61] Where Transmission-Based

Precautions are in place, disinfection agents should be approved by the manufacturer. Risk assessments by the local IPCT should advise on the correct methods to decontaminate milk-expression equipment when there are concerns regarding *Pseudomonas aeruginosa* risks in NNU settings.

In two outbreaks, environmental sampling revealed environmental contamination of the dedicated expressing room or milk storage fridge in the unit – while both studies lacked sufficient details on the timing and procedure used for sampling, or cleaning regimen or frequency in place, they highlight the importance of shared areas for breast milk expression and storage as a cross-contamination risk.[28, 62] Additionally, in one healthcare infection exposure incident, inadvertent swapping of breast milk with another neonate's milk stored in the same fridge, led to transmission of MRSA.[29] These outbreaks highlight the importance of adequate training of staff and parents/carers on the correct handling and storage of breast milk or infant formula. Parents should be educated on the hygienic expression and storage of breast milk and posters on hand hygiene should be made available in the expressing room.[12, 28]

In an independent review into *P. aeruginosa* outbreaks in NNUs in Northern Ireland, it was reported that use of tap water to defrost breast milk in one NNU may have contributed to onward transmission.[3] Guidance in NHSScotland states that tap water must not be used for warming or defrosting milk; breast milk may be warmed using a warming device designed to ensure no direct contact with non-sterile water, (e.g. waterless devices), or alternatively, sterile water which has been warmed in a warming cabinet may be used.[49]

In light of concerns regarding the infection risk from intrinsically contaminated infant formula, which has been reported as the source of an outbreak of *Enterobacter sakazaki,*[63] the World Health Organization (WHO) produced expert consensus on the safe preparation, storage and handling of powdered infant formula.[64] This guidance emphasises that powdered feed products are typically not sterile; they can be intrinsically contaminated with pathogens. Sterile liquid infant formula is recommended for neonates at high risk of infection and powdered formula milk should be prepared in a designated area, using aseptic technique and following the manufacturer's instructions.[63, 64] Reconstituted milk should be prepared for either immediate use or refrigerated immediately and discarded if not used within 24hrs.[63, 64] Full traceability of powdered infant formula should be in place in care settings; staff should be properly trained in preparation and food hygiene.[64]

How should NNU incidents/outbreaks be investigated and managed?

As outlined in Chapter 3 of the NIPCM, the local IPCT team will establish if an IMT is required during investigation of a healthcare infection/outbreak.[20] Membership of IMTs / outbreak management teams in NNU outbreaks based on observational reports have included neonatologists, NNU/NICU directors and representatives from NICU medical and nursing staff. Ten outbreak reports, and one expert guidance document highlighted importance of multidisciplinary team members at IMTs.[5, 8, 10-12, 15, 44, 65-67] Additional multidisciplinary members have included administration support, bed management, estates, press officers/ communication teams, domestic services, respiratory therapists, occupational health, microbiologists, laboratory staff and paediatric infectious diseases experts as well as IPC experts/ epidemiologists.[5, 8, 10, 12, 44, 65] Representatives from maternity units should also be considered; neonatal services are usually co-located with maternity units, especially those providing highly specialised care.[8, 11] If applicable representatives from labour, midwifery or obstetrics or patient transport services may be considered.[15, 66, 67]

Retrospective review of potential cases

There were two outbreak reports which specifically highlighted that an initial retrospective analysis or case review was successfully used to identify further cases. This was performed using a retrospective review of medical or laboratory records in the hospital.[11, 32] In some outbreaks, tools such as genotyping or whole genome sequencing have been used to distinguish an outbreak strain from historical cases in the unit.[9, 68] A retrospective analysis has also proven helpful for investigators to establish a baseline infection rate or trend during the course of an outbreak investigation.[17, 39, 51]

Microbiological screening of neonates

The primary objective of microbiological screening of patients is to identify unknown colonised cases for isolation or cohorting appropriately, and to support the epidemiological investigation. This review identified thirty-one outbreak reports in NNUs where the screening of all admitted neonates in the unit has been used as a control measure. This includes outbreaks of Gram-negative bacteria, (13 studies: *Serratia marcescens;* ESBL-producing Gram-negative bacteria, a novel Yersinia-producing *Klebsiella pneumoniae*, as well as a multi-drug resistant strain of *A. baumannii)*;[5, 7, 12, 14, 30, 32, 33, 38, 39, 42, 44, 56, 62] outbreaks of *Staphylococcus aureus* including MRSA (n=14),[6, 9-11, 16, 19, 27-29, 41, 66, 69 70] as well as outbreaks of vancomycin-resistant enterococci (VRE) (n=2),[35, 68] *Salmonella* spp. (n=2),[8, 40] and adenovirus (n=1).[71] In the majority of these outbreaks, surveillance was conducted at least weekly;[6, 7, 9, 10, 12, 14, 19, 27, 29, 30, 32, 33, 35, 38-

[40, 42, 62, 66, 68-71] although in four outbreaks, twice-weekly frequency was used, [8, 16, 44, 70] and in another four units, a single cross-sectional screen was employed.[11, 28, 41, 56] In several outbreaks, epidemiological investigations have led to surveillance being extended to neonates in other NNUs or maternity wards in the same healthcare facility, in order to account for patient movement.[11, 42]

A number of guidelines describe neonatal screening in NNUs during outbreaks. The US Centers for Disease Control and Prevention (CDC) published updated guidelines in 2021 for the prevention and control of *Staphylococcus aureus* infections in NICUs.[34] The guidelines stated there was low quality evidence from ten observational studies that active surveillance testing for *S. aureus* colonisation in NICU patients during periods of 'increased incidence of *S. aureus* infection or in an outbreak setting' was effective in reducing colonisation, infection and transmission. Testing patients at regular intervals (e.g. weekly) was also recommended, should screening be implemented. In 2006, Gerber et al. also produced a US-based consensus statement for the management of MRSA outbreaks in NICUs and recommended weekly surveillance among neonates during ongoing clusters.[72] Meanwhile Anthony et al. produced the UK-based expert guidance on Gram-negative infection outbreaks in UK neonatal units.[4] The authors stated that there is some evidence supporting the clinical effectiveness of patient screening during a Gram-negative outbreak and recommended screening at least weekly, for a defined period e.g. 1-2 weeks or until the outbreak is over.

Guidelines that are not specific to neonatal populations, including for both MRSA and multi-drug resistant Gram-negative outbreaks, also support screening of patients as part of a multi-faceted strategy to control and prevent transmission. These include current UK NICE guidance,[2, 25] and the European Society of Clinical Microbiology and Infectious Disease.[73] During CPE outbreaks, Scottish guidance state that in addition to weekly surveillance, local IPC teams may request that the whole ward is screened *plus* discharged patients who occupied the bay at the same time as cases (i.e. discharged contacts).[23] The NIPCM literature review on Healthcare Incidents and Outbreaks in Scotland produced recommendations on the use of microbiological testing during outbreaks in wider care settings.[74]

Where screening is implemented, parents/carers should be provided with timely information regarding screening, and positive results should be communicated to parents/carers immediately. There should be an agreed plan to direct screening and predefined actions dependent on screening results e.g. isolation and treatment, (see sections on Patient isolation/cohorting and Decolonisation of neonates).

A plan should be in place for stepping down reactive patient screening e.g. 2 weeks without any new positive screening results.[20] Anthony et al suggested that screening during an outbreak should be for the specific outbreak strain and should take place weekly for a defined period e.g. 1-2 weeks or until the outbreak is over.[4] There was insufficient evidence from four observational outbreak reports that described stepping down of reactive screening in NNU outbreaks; these were very heterogeneous and there no clear pathogen-specific methods were observed.[10, 13, 46, 71] However, screening was usually stepped down gradually, beginning from at least one week after the last case was discharged, or using the pathogen incubation period as a guide.[10, 13, 46, 71] In one outbreak of VRE, screening was kept as a long-term measure for several years.[35]

Microbiological screening of staff

Chapter 3 of the NIPCM states that during an outbreak, the IMT may determine if staff screening is necessary to identify carriage/ infection among staff groups.[20] US expert guidance relating to the control of *S. aureus* in NICUs, as well as wider MRSA guidance in acute settings both state that staff screening should be reserved for outbreaks with established epidemiological links to staff or where outbreaks have persisted despite implementation of control measures.[25, 72, 75]

While NNU-specific guidance for other pathogens were not identified, UK NICE guidelines have stated that there is no indication for screening healthcare workers during multi-drug-resistant Gram-negative bacteria outbreaks.[2] Meanwhile, Irish expert-led guidance for MDROs excluding MRSA stated in 2012 that the value of staff screening remains unproven.[76] English CPE guidance does not recommend staff screening, and Scottish CPE guidance has stated that there is no compelling evidence that staff screening is beneficial for containing spread.[23, 26]

There were fifteen observational studies included which described microbiological screening of staff during neonatal outbreaks as a means of identifying colonised staff, the majority related to MRSA,[10, 11, 16, 19, 27, 41, 66, 69] or methicillin-sensitive *S. aureus* (MSSA) with particular virulence factors such as Panton-Valentine Leukocidin (PVL)[15] or exfoliative toxins.[17, 77] In some cases, staff screening was widened to other departments such as obstetrics or maternity units to account for patient/staff movement.[15, 27, 51, 67, 77] In 8 out of 11 *S. aureus* outbreaks [10, 11, 15-17, 19, 27, 41, 66, 69, 77] where staff screening took place, staff were colonised with the outbreak strain; however, in only two of these outbreaks were colonised staff thought to be the primary source.[10, 16] Five staff in an NICU in the USA were found to be positive for *Salmonella* during an outbreak however the epidemiological investigation indicated they were not the primary source

of infection.[40] In one VRE outbreak, gastrointestinal screening among staff was negative.[35] Finally, two Gram-negative outbreaks were identified which used staff screening (*K. pneumoniae* via rectal/vaginal swabs, and *S. marcescens* via nares); in both cases these were negative.[51, 67]

In other outbreak reports, staff interviews have been conducted to review for symptoms or recent medical histories related to possible infection.[41, 47, 62, 71] For example, skin breakdown/dermatitis for *S. marcescens,* and *P. aeruginosa*, and MRSA infections; external ear infections (*P. aeruginosa),* and conjunctivitis (adenovirus). In one outbreak, staff members were identified with skin infections positive for *S. marcescens*, and staff were thought to be responsible for colonisation of several neonates.[62] In guidance produced by Anthony et al. hand checks for skin lesions or minor dermatitis as part of an NNU outbreak investigation was recommended as good practice for Gram-negative bacteria.[4] In all outbreaks, screening or interviews were usually carried out by Occupational Health.[41, 47, 48, 62, 71]

In certain circumstances, household contacts of positive staff have also been screened; in two observational studies of PVL-MRSA outbreaks, staff household contacts were linked to the outbreaks in the NICUs.[10, 66]

In summary, there was expert consensus from *S. aureus* guidance that staff screening in NNU outbreaks should be considered where there are established epidemiological links to staff, or an outbreak has persisted despite implementation of control measures. For other pathogens, there was limited evidence from observational outbreak reports that identification of infectious staff may be achieved through screening, as well as other methods such as medical interviews related to symptoms or recent medical histories, achieved through Occupational Health. Staff screening should be linked to specific actions (see section *management of positive staff/decolonisation of staff*). Where this evidence is based on non-controlled observational studies, it is subject to many limitations including publication bias and therefore pathogen-specific guidance should be consulted, where it is available.

Screening of mothers and family contacts

There was no guidance related to screening of mothers or family contacts of neonates during outbreaks in NNUs. There have been several outbreaks in neonatal settings where screening of mothers of cases has been conducted.[35, 42] In only one community-associated MRSA outbreak did screening of mothers help identify new cases and control the outbreak.[66] Additionally, family contacts colonised with MRSA have been identified but were not considered the source of the outbreak.[10, 77] Meanwhile in one ESBL-producing *K. pneumonia* outbreak in a NICU, the father

of the index case was identified as colonised.[44] In these outbreaks, where positive family members are identified, the temporality of the infection/colonisation cannot be established and results should therefore be viewed in the context of wider epidemiological factors. Two *Salmonella* outbreaks in NICUs were identified which were associated with recent gastrointestinal illnesses in family members, and symptomatic interviews of family visitors were employed in addition to screening.[8, 40]

Currently NICE guidelines for control of Gram-negative bacteria outbreaks in acute settings do not recommend screening family contacts.[2] Whilst evidence is very limited, microbiological screening of family contacts in NNUs, particularly NICUs, may be considered as part of a wider epidemiological investigation, in the context of pathogen-based transmission modes; advice from IPCTs should be sought.

Microbiological sampling of care equipment and the environment

There was a paucity of guidance specific to NNUs relating to environmental sampling during outbreaks. Twenty outbreak reports,[6, 11, 14, 17, 18, 28, 30, 32, 35, 38, 39, 41, 48, 51, 62, 65, 67-69, 78] a systematic review of outbreak reports,[45] and two expert opinion based guidance documents[4, 72] reported on environmental sampling during outbreaks in NNUs. One piece of US-based MRSA guidance formed on expert consensus stated that environmental cultures should be performed only to corroborate or refute epidemiological data linking transmission to an environmental source.[72] The guidance also stated that molecular testing should be performed to assess relatedness to case isolates. One expert guidance document for Gram-negative bacteria outbreaks in NNUs stated that environmental sampling is recommended where any *P. aeruginosa* isolates on the unit are found, but also stated that the clinical effectiveness of screening for other Gram-negative bacteria was unproven; however the guidance states that environmental sampling should be considered for Gram-negative outbreaks on a case-by-case basis, as part of a wider program of interventions.[4] Broader guidelines for health and care settings, not specific to NNUs, strongly recommended using environmental sampling in acute settings during unexplained transmission of Gram-negative bacteria,[2] as a common source is possible, and should be considered as part of targeted investigation of MRSA outbreaks.[25] Irish expert-led guidance related to control of MDROs in health and care settings stated that environmental sampling should be considered when organisms associated with environmental reservoirs are involved.[76]

Five outbreak reports discuss the use of microbiological sampling of the environment as a useful tool during outbreaks in NNUs - either for identifying specific reservoirs,[11, 32, 51, 67, 78]

highlighting potential failures in hand hygiene, cleaning or decontamination;[14, 28, 62] and in some cases, it has been used to monitor improvements after an outbreak has been identified.[6, 32, 69] Most investigations performed single cross-sectional sampling, however some chose to implement serial interval (e.g. weekly) or multiple successive rounds.[6, 32, 48] While the subtyping of isolates is usually required to confirm association of environmental isolates with neonatal cases, multi-species and multi-clonal organisms are common with *P. aeruginosa* outbreaks.[48] There have also been cases where unrelated but widespread contamination has alerted the outbreak teams to major lapses in SICPs, or highlighted faulty equipment or problems with facilities.[18, 35, 38, 39, 62, 65] There were few outbreak investigations where air sampling was performed with insufficient detail from studies.[55, 62, 65] In one outbreak report, ventilation problems during a NICU outbreak were confirmed using air samples that were subsequently found positive for the outbreak strain.[18]

Overall, the evidence was limited by heterogeneous reporting, lack of methodological detail in how environmental sampling was conducted, particularly with relation to timing of cleaning, and frequency and location of sites sampled. It is likely there is also significant publication bias present. Furthermore, negative environmental sampling results may reflect the lack of sensitivity from random sampling, and may be misleading to investigators, or provide a false sense of security among staff. In some cases, the negative results have reflected the enhanced cleaning in response to the outbreak itself.[41] In some outbreaks, suspected items for testing had already been discarded as part of outbreak control measures.[8, 56] In two outbreak reports, environmental screening was brought in later in the investigation, when an unknown source has contributed to ongoing cases.[17, 67] Based on the limited evidence from outbreak reports in NNUs, environmental sampling appears to be most effective when focused on areas at high risk for cross-contamination including: designated locations for shared caring duties, such as for bathing/changing/weighing of babies; designated milk expression areas, or shared equipment such as breast pumps, or stethoscopes.[11, 30, 62, 68, 69]. Incubators have also been identified as a reservoir through microbiological testing.[32, 35, 38] The systematic review by Moffa et al. highlighted that during waterborne outbreaks, infectious isolates have been isolated from incubators, as well as handwashing basins or taps.[45]

In summary, the evidence for environmental sampling during outbreaks in NNUs is heavily reliant on biased, observational outbreak reporting, where robust investigations (including environmental sampling) are rarely described with sufficient detail. There is limited evidence that environmental sampling may be useful as an epidemiological tool during NNU outbreaks, especially during unexplained transmission, or where an environmental reservoir is suspected.

What are the key measures to control incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?

Compliance reviews

A review of the international outbreak literature identified twenty-five observational studies and one expert guidance document that reported on a review of compliance with SICPs/TBPs and other procedures in the event of an outbreak.[5, 8, 9, 14, 16, 17, 19, 32, 38, 40-42, 44, 47, 48, 55, 56, 65, 67, 71, 77-79] These included cleaning, equipment processing, hand hygiene and aseptic technique, (including during respiratory therapy, CVC care), feeding and changing practices, and appropriate uses of water in NNUs. Poor compliance with hand hygiene,[9, 41, 47, 48] cleaning and reprocessing incubators,[32, 42] management of equipment[5, 9, 41, 47] and the environment and use of PPE[16] as well as the poor availability of alcohol-based hand rub,[5, 16, 38] and substandard nappy-changing procedures,[9] were frequently associated with outbreaks. Meanwhile, in three outbreaks on NNUs related to *S. marcescens,*[79] *P. aeruginosa,* [47] and *K. pneumoniae*,[32] a compliance review into water management led investigators to either: discover the source (contaminated tap water,[47] and faulty equipment[79]) or identify and correct errors in IPC practices from staff.[32]

Transmission via healthcare worker hands is often assumed to be a mode of transmission in neonatal outbreaks, possibly because poor compliance with hand hygiene is often found when assessed.[9, 16, 41, 47, 48] As such, hand hygiene audit and improvement is one of the most frequently reported outbreak control measures.[5, 6, 8, 9, 16, 17, 19, 27, 28, 30, 38, 41, 42, 44, 47, 48, 55, 56, 79] In several outbreak responses, parent/carer hand hygiene has been targeted for improvement.[12, 14, 28, 32, 40, 68] At least one outbreak has been traced back to contamination of a non-medicated soap dispenser which led to transmission via contaminated hands.[78] In other outbreaks, the lack of timely replenishment of alcohol-based hand rub in dispensers was identified as a risk factor for poor compliance.[5, 16, 38] One expert-led guidance document on Gram-negative bacteria outbreaks stated that hand hygiene audits should be performed early in an outbreak investigation. The guidance also stated that staff and parent/carer re-education and enforcement of hand hygiene should be implemented if compliance is found to be low.[4]

As an investigative technique, microbiological testing of staff members' hands for transient contamination may be indicative of staff-mediated transmission in the unit, via a lack of adequate hand hygiene. Microbiological testing of staff hands has been reported in six Gram-negative outbreaks in NICUs, using various methodologies, such as the use of agar touch plates or rinsing/submersion of staff hands in liquid media.[7, 38, 39, 48, 51, 62] Most studies do not

report timing before/after hand hygiene or have performed sampling impromptu, including immediately after direct patient care, reducing the utility of the results.

In the event of a suspected or confirmed incident/outbreak, a review of compliance with standard infection control precautions (SICPs) and transmission based precautions (TBPs) should be included as part of the incident/outbreak investigation as per Chapter 3 of the NIPCM; this does not replace monitoring of compliance with SICPs and TBPs, which should be performed routinely.[80] Assessment of compliance should also include a review of handwashing stations and water systems and processes against 'Guidance for neonatal units (NNUs) (levels 1, 2 and 3), adult and paediatric intensive care units in Scotland to minimise the risk of *Pseudomonas aeruginosa* infection from water'.[49]

The NIPCM general outbreak checklist, as well as several pathogen-specific checklists (CPE; *P. aeruginosa*) are available for aiding in gathering epidemiological evidence during outbreaks.[23, 49, 80]

Review management of equipment and the environment

Failure to adhere to SICPs for the safe management of equipment has been identified in the outbreak literature including the contamination of baby weighing scales;[6, 35, 62, 68] baby baths;[68] which should be cleaned between patients; shared glucometers;[62] as well as incorrect disinfection of rectal thermometers,[14] and milk expressing equipment.[30, 32, 47] Additionally, two adenovirus conjunctivitis outbreaks were caused by a failure to properly disinfect equipment used for routine eye exams.[71, 81] A review of practice should ensure re-usable equipment is decontaminated (including sterilisation where appropriate) as per appendix 7 of the NIPCM.[20] More specifically, a review into incubator decontamination is commonly reported in Gram-negative bacteria outbreaks: incubator infection control methods have included improvements to cleaning protocols, reprocessing/ sterilisation of all incubators in the unit, as well as inspections of internal parts (either visually or through microbiological sampling) or re-education of staff on incubator decontamination.[7, 14, 32, 38, 42, 67, 79] In particular, during an extensive outbreak of ESBL-producing *K. pneumoniae*, infant incubators were found to be an environmental reservoir, after it was discovered that mattresses had been damaged and damp from steam cleaning.[32] Overall, there is a paucity of literature regarding incubator decontamination methods; in 2012, the Chief Medical Officer in Northern Ireland issued guiding principles on decontamination procedures for infant incubators and specialist equipment for neonatal care.[82] These stated that as a medical device, the manufacturer's instructions should be followed for decontaminating and reprocessing infant incubators and any protocols agreed

with local IPCTs. Health Protection Scotland's *P. aeruginosa* guidance outlines that thorough drying is critical when reprocessing incubators.[49] When following transmission-based precautions, disinfection agents should comply with manufacturer's instructions.[49]

Traceability of equipment such as incubators and consumables assigned to each neonate has been reported as good practice during outbreak investigations.[16, 29, 67] In a *Salmonella* outbreak in a NNU in Glasgow, improvements were also made to equipment sterilisation procedures on the labour ward as part of the outbreak response.[8]

Contamination in the environment has been identified in several outbreaks;[9, 11, 28, 62, 65, 69] Contaminated areas identified in the outbreak literature included changing tables/areas for changing nappies[9, 11] in areas dedicated for breastmilk expression,[28, 62] as well as handwashing basins and taps,[45] and hard to clean places such as air vents[18] and light fittings,[70] and other areas that should be included in routine daily cleans such as computer monitors,[7] or medication fridges.[68]

Enhanced cleaning is described as a control measure in outbreak reports even when environmental contamination has not been found and is recommended as outlined in Chapter 2 of the NIPCM.[7, 8, 14, 20, 30, 35, 38, 40, 62, 66, 68, 69, 77] If substandard cleaning in or around the unit is identified, training and auditing of staff may be considered to ensure methods and frequency of cleaning are sufficient, and/or additional staffing should be put in place;[5, 17, 38, 44, 65] Multiple guidelines have highlighted the importance of avoiding phenolic-based cleaning solutions in neonatal settings due to potential harm of these chemicals to neonates.[83, 84] The NIPCM suggests that hydrogen peroxide vapour (HPV) may be considered for specific organisms (e.g. MDROs), but only as an adjunct to routine cleaning procedures.[85] The periodic use of HPV in NNUs by some NHSScotland boards has been reported as an additional measure for environmental infection control. Furthermore, several outbreaks have also employed HPV as part of a deep-clean;[15, 70] while in one NICU, it was found to be incompatible with the ventilation.[16] However in these outbreaks, use of alternative technologies were reported alongside other multifactorial interventions, therefore their effectiveness cannot be assessed or reported. Additionally, ARHAI Scotland have produced practice recommendations for the use of HPV in care settings, which has important practical and safety considerations.[85]

Use of personal protective equipment (PPE)

Incorrect or insufficient use of personal protective equipment such as gloves has been associated with outbreaks in neonatal units.[8, 16] In two outbreak reports, compliance with the correct use of PPE has been assessed as part of a practice review, in order to ensure staff are

donning and doffing PPE correctly to avoid contamination.[32, 56] Staff reminders or re-education in PPE use has been detailed in a number of NNU outbreak reports, and should be conducted as part of an outbreak response.[8, 12, 19, 56] One expert guidance document stipulated that during an outbreak, plastic aprons and gloves should be worn for all staff contact with patients.[4] Additionally, during three outbreak reports, gowns and gloves were implemented as additional precautions.[14, 35, 38, 62] One report noted this was extended to all contact with the environment around the patient.[69] However, with regard to NHSScotland settings, the NIPCM currently states that gloves should be worn when exposure to blood and body fluids is anticipated, with good maintenance of hand hygiene in between such occasions.[20] The NIPCM also outlines that aprons should be worn to prevent contamination with blood and body fluids and for direct contact with a patient with a suspected/confirmed transmissible pathogen including contact with their direct environment. Staff should therefore refer to the NIPCM, since the overuse of PPE has risks. In one MRSA outbreak in a NICU in Germany, family members were also asked to wear gloves/gowns and a surgical face mask as a precaution during patient care.[69] The Society for Healthcare Epidemiology of America (SHEA) also discussed family/visitor PPE use in their expert consensus white paper, on practical approaches to *S. aureus* disease prevention in NICUs, which was published in 2020.[86] The authors recommended that staff may choose not to make it a requirement for family members or visitors to don PPE when visiting colonised neonates, in order to maximise care and bonding with their child, and cited a lack of evidence on PPE use for family members.

Patient isolation/cohorting and staff cohorting

As per Chapter 3 of the NIPCM, cohort areas may be established as appropriate.[20] Expert guidance by Anthony et al. stated that NNUs should provide sufficient facilities for segregation of infected babies.[4] Additionally, in twenty-six reported outbreaks in NNUs, the isolation and cohorting of infected or colonised neonates was frequently implemented as a control measure.[5, 7-9, 11, 12, 14-16, 19, 27, 30, 35, 38, 40, 42, 44, 45, 56, 62, 68-71, 78, 79] In many outbreak reports, there were insufficient single rooms - a dedicated bay or sectioned off area of the NNU ward has been used,[15, 30, 38, 68, 79] or additional space has been converted into an appropriate clinical area for infected neonates.[44] In some outbreak reports, units have also separately cohorted new admissions into a different ward or area while an outbreak is ongoing.[42, 44, 71] Additionally, dedicated or single-use equipment and consumables should be assigned to each cohort where possible.[4, 5, 12, 30, 35, 40, 56, 68, 70] In one outbreak, new equipment was purchased so that equipment cohorting was possible.[6] Cohorting/isolation of patients and/or essential medical equipment is especially challenging for neonates requiring critical or intensive care;[12, 35, 39] and

in some cases cohorting has been prevented due to the complex medical needs of infants on the unit.[35, 39] A lack of physical space for large complex medical equipment in use in NICUs or lack of staffing have also prevented patient cohorting during some outbreaks.[33, 38, 39]

Where complex medical needs of neonates prohibit cohorting or isolation, staff cohorting may be attempted.[6] Additionally, some practitioners have considered care within an incubator as a form of isolation.[5, 67] However, given the reports of incubator contamination during outbreaks and spread between babies cared for in incubators; there is currently insufficient evidence to support this. Assigning staff to cohorted or infected infants has also been recommended.[4, 72] While many NNU outbreaks have successfully implemented staff cohorting,[5-7, 12, 35, 38] there may not be adequate staffing resources to maintain the minimum staff-to-patient ratio [39, 71] and it may not be suitable for specialist roles.[44] The US expert-led guidance on management of MRSA in NICUs in 2006 stated that staff cohorting should be implemented to the maximum extent possible, and where resource was limited, staff should care for non-cohorted neonates before cohorted patients.[72] There have been outbreaks reported where the direction of care provision from unexposed to exposed has been attempted.[39, 44] In some outbreaks, staff entry restrictions to rooms were implemented.[8, 39, 68]

Decolonisation of neonates

Decolonisation refers to the administration of treatments to patients colonised with a specific MDRO to eradicate carriage of the organism. There are no decolonisation regimens currently recommended for patients harbouring MDROs other than MRSA/ *S. aureus*.[76] The CDC guidelines for the management of *S. aureus* in NICUs has conditionally recommended, based on low quality evidence from observational studies that where nosocomial transmission is ongoing or incidence is increasing, targeted decolonisation of colonised neonates in NICUs should be considered, as part of a comprehensive outbreak response.[34] The potential reduction in infection was balanced by concerns for safety of decolonisation agents in this population, as well as antiseptic tolerance or cross-resistance. The guidelines stated that the optimal decolonisation agent remains an unresolved issue; stating that mupirocin safety and effectiveness data has not been established in patients younger than 12 years, while the US Food and Drug Administration (FDA) have recommended caution using chlorhexidine in premature neonates or infants younger than 2 months.[34] Based on expert consensus, the CDC have suggested that intranasal mupirocin twice daily for 5- 7 days may be acceptable for decolonisation of neonates.[86] However they have highlighted safety concerns regarding intranasal application of mupirocin in very low birth weight infants, where the product could occlude nares or accumulate in nasal cannula prongs.[34]

The UK NICE guidelines for control of MRSA in healthcare settings (not specific for neonates) stated that practitioners should consider using mupirocin for nasal decolonisation, either as a targeted or universal approach (i.e., for all high-risk patients).[25] The guidelines stated that where cohorting/isolation is difficult, decolonisation may help to temporarily suppress and prevent transmission to other patients. The guidelines also stated that chlorhexidine should only be used in neonates if there are no alternatives and no broken skin is present. In support of this, the guideline development team conducted a limited literature review regarding the safety of chlorhexidine in neonates. They concluded, based on thirty-one studies, that chlorhexidine was not safe for premature neonates, and should not be used in this population due to their immature skin. Adverse events have included contact dermatitis, chemical burns and skin irritation, from application via bathing, wipes or local antiseptic use; this included water-based chlorhexidine, at a range of concentrations (0.25-4%). However, the guidelines recommended that there were no concerns about its safe use in babies over 4 weeks old, excluding babies born very small and/or prematurely. Scottish PVL-*S. aureus* guidance stated that octenidine has been used as a safe alternative to chlorhexidine in neonates, but requires individual risk assessment.[87] The guidance states that contact time of 1 minute is required but this may cause a temperature drop in neonates. Concerns about systemic absorption of products were also discussed in both NICE and CDC guidelines, but there remains insufficient evidence for this.

Several MRSA outbreak reports and one PVL-*S. aureus* outbreak report identified in this review used decolonisation agents for colonised neonates in combination with daily linen change.[9-11, 15, 19, 27, 69] Products included mupirocin, octenidine, chlorhexidine as well as other agents, but effectiveness was not discussed in the majority of studies. No adverse events were reported, although use was restricted in some settings and safety concerns were cited in one outbreak as a reason to forgo decolonisation.[16] Several outbreak reports included data on post-decolonisation screening and reported that decolonisation was not successful across all neonates, however these reports lacked sufficient detail.[9, 10, 27, 69] There was insufficient data on the use or effectiveness of universal patient decolonisation.

Due to the complex nature of this issue, decolonisation should be considered on a case-by-case basis. The decision by the practitioner should also be cognisant of the issue that re-colonisation is often possible. Information should be provided to parents, highlighting that results may not be permanent.[25] There was no available guidance specific to neonatal settings that discussed step-down of isolation/cohorting of decolonised infants; however according to NICE guidelines for all patients, repeat screening 2-3 days after therapy should determine if decolonisation was successful.

Management of positive staff/staff decolonisation

Management of staff members colonised with MRSA or outbreak strains of *S. aureus* is discussed in the UK NICE guidelines published in 2021: Coia et al. stated that while the hospital is required to comply with appropriate governance to ensure risk of acquisition is minimised among the patients, staff with nasal carriage only may not require exclusion from interaction with patients; however this may differ for those staff working with patients at high risk for infection such as in neonatal units and a risk assessment should be conducted.[25] The guidelines stated that, based on clinical experience of the guidance development team, positive staff should be offered decolonisation therapy as deemed appropriate. For staff colonised with a skin condition, risk assessment is required to consider re-deployment.[25] In one *S. marcescens* NICU outbreak, a staff member was required to undergo permanent re-deployment after treatment failure for a skin infection on their hands.[62] Staff should be made aware that decolonisation therapy does not necessarily result in complete eradication. Decolonisation of staff was conducted in several MRSA or *S. aureus* outbreaks in NNUs.[6, 10, 11, 16, 17, 19, 66, 69, 77] In some cases, positive staff were excluded between 2-5 days during treatment,[16, 17, 66] while in three studies, positive staff were re-screened following decolonisation to ensure success.[6, 10, 16] Two studies implemented monthly surveillance of previously positive staff following decolonisation, even after resolution of the outbreak.[16] [10] The issue of re-colonisation in staff during or after NNU outbreaks was also reported; in two outbreak reports, multiple cycles of treatment were required before staff were decolonised,[10, 69] while in another outbreak, one staff member later became re-colonised, leading to permanent reassignment.[62] The staff member was potentially re-colonised via their household contacts / in the home setting. Colonised household contacts of staff have been identified in two *S. aureus* NNU outbreaks.[10, 66] There was insufficient evidence regarding the recolonisation of staff via the home environment; this is currently an under-researched topic but may be relevant in cases where decolonisation has proven difficult.

The NIPCM 'Responsibilities' statement stipulates that staff must not provide care while at risk of potentially transmitting infectious agents to others.[88] If in any doubt they must consult with their line manager, Occupational Health Department, local IPC team or Health Protection Team (HPT); and contact the IPC team if there is a suspected or actual HAI incident/outbreak.[88] NHS boards should have a local procedure in place for the management of staff testing positive during healthcare associated incidents/outbreaks. The Scottish Government produced mandatory guidance in 2020 setting out an NHSScotland wide approach to ensuring staff screening processes are effective.[89] This sets out the responsibilities of occupational health,

and the Incident Management Team (IMT), in undertaking appropriate consultation and treatment with positive staff, and managing the event of treatment failure and potential redeployment.[89]

While mandatory Scottish guidance on staff screening should be followed, there was insufficient evidence related to optimal protocols for positive staff or decolonisation of staff in NNUs.

Unit closures to admissions

There were nineteen outbreak reports, and two expert-led guidance documents which discussed the closure of the unit in response to an ongoing outbreak.[5, 7, 8, 12, 13, 15, 16, 19, 30, 33, 35, 38-40, 42, 44, 47, 56, 79] Two guidance documents discussed how closure/partial closure of the unit may increase staff-to-patient ratios during outbreaks.[4, 43] However, guidance related to Gram-negative outbreaks in NNUs by Anthony et al. stated that careful risk assessment should be performed regarding the needs of the wider Neonatal Network when closure is considered as a control measure during outbreaks. Another expert opinion document by Laing et al. outlined that when closure or significant restriction of service in the NNU is considered, other referral units should be involved in this process, and specifically highlighted that over-burdening of other units should be taken into consideration during decision making.[43] In two outbreak reports, including one in Scotland, a risk assessment was conducted, taking account of the wider regional needs of the Neonatal Network,[8, 16] while in five outbreaks, closure of the unit was deemed inappropriate due to either a lack of capacity at neighbouring units to receive re-directed patients,[8, 16, 38] or no alternative NICUs available to the regional population. [12, 38] Temporary closure has often been implemented in the initial stages of outbreak management;[35, 40, 42, 56] or in order to allow for remediation work or deep cleaning.[40, 47] In eight outbreak reports, closure was considered in situations where outbreak measures failed to control incidence i.e. in response to continuing cases.[5, 7, 13, 19, 30, 47, 62, 79] Partial closure of the unit was also implemented [19, 39] including reduction of bed capacity to allow for adequate staffing levels required for staff cohorting.[39] Some units have chosen to restrict new admissions to 'lower risk' neonates of older gestational age (>34 weeks)[15] emergency patients,[5] or inborn neonates only.[30] In one NICU outbreak, it was arranged that high-risk antenatal pregnant patients were transferred to other hospitals in the area in order that high-risk births took place near alterative NICUs.[5] In several reports, closure of the unit has led to reduced overcrowding,[33, 39] increased staff-to-patient ratios[5, 39] and should allow staff to direct greater attention to improvements.[5]

It has also been recommended by two UK expert guidance documents that infected or colonised babies are not transferred to other units during outbreaks, however, this decision

should be made jointly between IPCTs and clinical staff to ensure the decision is appropriate for their clinical needs.[4, 43] Restriction of visitors to only parents or essential visits have also been considered during four outbreaks.[5, 12, 15, 30]

Evidence was limited and heterogeneous regarding temporary closure of both NNUs and NICUs during outbreaks. Expert guidance and outbreak reports highlight the importance of consultation and risk assessment with other regional units for appraising any decision to temporarily divert new admissions elsewhere. Other strategies for closing units included closure of bays/portions of the unit, closure to high-risk patients or planned admissions or transfers.

How should NNU incidents/outbreaks be reported?

As per Healthcare Improvement Scotland's (HIS) IPC Standards 2022, it is the responsibility of staff to communicate with IPC teams for advice and information regarding specialist infection control risks including where an incident/outbreak is suspected, and throughout the outbreak management process.[21] Mandatory guidance for reporting of a healthcare associated incident/outbreak can be found in Chapter 3 of the NIPCM which also applies to neonatal settings. It is the responsibility of the IPC team within the NHS Board, on recognition of a potential healthcare infection incident, to conduct an initial assessment using the Healthcare Infection Incident Assessment Tool (HIIAT), and convene Problem Assessment Group (PAG)/Incident Management Team (IMT) meetings, depending on the status of the HIIAT. The NICPM includes a draft agenda for IMTs.[80] NHS Boards are required to communicate HIIAT assessments to ARHAI Scotland (and through ARHAI Scotland, to the Scottish Government Health and Social Care Department (SGHSCD)), by completing the electronic Outbreak Reporting Tool (ORT), as outlined in Chapter 3 of the NIPCM.[20]

As detailed in the NIPCM, the Chief Nursing Officer (CNO) National Support Framework may be invoked by the SGHSCD or by an NHS Board to optimise patient safety during or following any HAI incident/s.[20]

Staff should be provided with clear, timely and responsive information and guidance on IPC to enable them to provide safe and effective care.[21] Parents must be fully informed of all changes to their child's care, particularly where their baby is unwell, or where there are ongoing incidents in the unit.[4, 12, 17, 43] Support and information should be provided on any specific infection-related care issues. They should also receive education on any IPC measures in place and be provided with frequent situational updates.[44, 68] All information should be fully accessible. The Scottish Neonatal Quality Improvement Framework outlines how communication with parents should be

conducted and evidenced - including provision of support contacts and contact details for a named key worker, so that families can be involved as far as possible in decision-making and planning of care, and ensuring that access to professional support is available.[22]

Additionally, organisations have a legal duty to inform parents openly and transparently regarding any unintended or unexpected adverse incidents as per The Duty of Candour Procedure (Scotland) Regulations 2018.[90, 91] Duty of Candour is included in ARHAI Scotland's draft IMT agenda, which is included in the NIPCM Resources page. Due to the nature of healthcare incidents and outbreaks which are likely to cause anxiety and stress to families, communication should be a priority of IMTs. There should be in-person discussion with families regarding the care and treatment of their baby. Prompt, unambiguous, written information should also be provided.[43, 92] Boards must ensure that suitable communication systems are in place before any public statements are made.[92, 93]

During any patient transfers, step-down of neonatal care to lower dependency units, Local Neonatal Units (LNUs), or postnatal wards; all units should be aware of any ongoing healthcare associated infection during hand over, and continuation of microbiological screening at the receiving unit may be advised.[12, 20] This includes neonatal transport services or ambulances. Information on incidents/outbreaks may be shared through the Neonatal Network. This may be particularly important during closures to units, where regional or national coordination may be required.

In some instances, cases already discharged may have been part of the outbreak.[66, 77] Written communication to parents, involvement of community nursing teams, local hospitals, as well as outpatient clinics, and family GPs have been used to notify relatives or relevant healthcare teams of confirmed/potential cases.[66, 77] Additionally, in some circumstances press and national media have played a role in dissemination or case finding.[77] An Expert guidance document by Anthony et al. also recommended that during NNU or NICU closures due to outbreaks, a press release may be helpful to relatives and pregnant women.[4]

Healthcare Improvement Scotland (HIS) oversees the Maternity and neonatal (perinatal) adverse event review process.[94] This includes the Perinatal Mortality Review Tool (PMRT) in Scotland, where standardised perinatal mortality reviews are undertaken across NHS maternity and neonatal units on the deaths of babies from 22+ week's gestation to 28 days after delivery. These are reviewed using the Mothers and Babies Reducing Risk through Audits and Confidential Enquiries (MBRRACE) and PMRT.[94]

As outlined in the NIPCM literature review for Healthcare Infection Incidents and Outbreaks in Scotland, deaths associated with HAI should be recorded on the Medical Certificate of the Cause of Death (MCCD) and reported to the Infection Control Manager (ICM).[74] A death which is considered to pose an acute and serious public health risk should be reported to the Procurator Fiscal when it has occurred as a result of an infection acquired while under medical/dental care, while on NHS premises.[74]

How should a healthcare infection incident be 'closed, with lessons learned recorded and disseminated nationally?

Stepdown of isolation/cohorting and contact precautions in neonates

There is a paucity of guidelines relating to neonatal populations for the stepdown of contact precautions, or isolation/cohorting during NNU outbreaks, and no guidance related to closure of NNU outbreaks. Looking to pathogen-specific guidance, guidelines for the management of *S. aureus* in NICUs produced by the CDC in 2020 highlighted that discontinuation of contact precautions /cohorting remained an unresolved issue, and due to no available evidence, the authors made no recommendation.[34] Meanwhile, the Society for Hospital Epidemiology of America (SHEA) produced an expert-led white paper for the management of *S. aureus* outbreaks in NICUs.[86] The paper stated that strong consideration should be given to continuing contact precautions for the duration of hospitalisation in high-risk groups, or those who were likely to remain colonised (for example neonates receiving invasive/non-invasive ventilation, patients with tracheostomies or draining/open wounds). Similarly, Gerber et al. stated that MRSA colonised neonates should be cohorted until the last colonised neonate is discharged.[72]

In guidelines for norovirus outbreaks in acute care settings, CDC stated in 2011 that there was evidence infants under 2 years may undergo prolonged viral shedding, and contact precautions should be extended up to 5 days after symptom resolution.[95]

In eight observational studies, where duration of isolation/cohorting was discussed; neonates were kept in isolation/cohorting up until their discharge from hospital, including for outbreaks of ESBL-producing *K. pneumoniae, E. coli,* VRE, PVL-*S. aureus*, MRSA and carbapenem-producing *A. baumannii*.[5, 10, 33, 35, 42, 44, 68] In two Gram-negative outbreaks (caused by *Klebsiella oxytoca,* and *S. marcescens*), isolation was ended after multiple negative consecutive tests.[56, 67]

Due to the heterogeneous limited quality of the evidence, local IPC teams should advise on decisions regarding discontinuation of isolation.[20]

Closure of outbreak; and capturing lessons learned.

According to Healthcare Improvement Scotland's IPC Standards 2022, healthcare organisations should ensure learning from incidents and outbreaks is shared throughout the organisation and across all sectors to support continuous quality improvement in IPC.[21] In the NIPCM literature review for Incidents and Outbreaks in Scotland, it is outlined that following the incident/outbreak, the PAG/IMT should decide on the most appropriate format for a report to communicate incident management/lessons learned.[74] The Outbreak Reporting Tool (ORT) includes a section to capture lessons learned which should therefore be reported for each incident. The final report should be submitted by the NHS Board to ARHAI Scotland. In Chapter 3 of the NICPM, it is recommended that once the incident is over, the PAG/IMT and NHS Board should evaluate and report on the effectiveness and efficiency of the IMT using the Hot Debrief Tool. This is not a mandatory requirement but for the purpose of sharing lessons learned across Scotland. Additionally, the IMT chair should determine if a full IMT report or Situation, Background, Assessment, Recommendations (SBAR) format of the incident should be submitted by the NHS Board to ARHAI Scotland.[20] Debrief sessions have been shown to be effective for capturing areas for improvements in other UK NNU outbreaks[16] however, capturing of lessons learned/ service improvements following outbreaks is a significantly under-published area. Debrief sessions are also likely to be resource dependent. Information should be shared among the Neonatal Network, and potentially through other clinical networks, in order for NNUs to learn from the experience of other units. The Scottish Neonatal Quality Framework outlines the need for regional collaboration to maximise the use of available clinical expertise.[22] An independent review into *P. aeruginosa* deaths in Northern Ireland in 2012 concluded that lack of a formal network among NNUs, led to a lack of sharing of information to inform critical decisions and different approaches to outbreaks.[3]

3.2 Implications for research

It is recognised that there is a lack of specific infection prevention and control guidelines for neonatal care settings. Very little high quality evidence was available to inform this review; the majority of the literature assessed consists of observational studies reporting bundled interventions during outbreaks (outbreak reports), or guidance produced via expert consensus. Reliance on outbreak reports can mean that publication bias is likely to exist.

In particular, there was very little evidence relating to stepping down of outbreak response measures in NNUs, particularly related to microbiological screening of patients. Additionally, the SICPs and TBPs defined in the NICPM are largely based on indirect evidence related to the wider or adult population. For example, there was insufficient evidence pertaining to individual items of PPE (e.g. glove use), specifically for care of neonatal populations including during outbreaks.

In addition, it is clear that there is paucity of guidance on the infection prevention and control requirements during milk preparation, handling and storage.

Future work should include:

1. A gap analysis of local infection control guidelines/procedures in NNUs against the NIPCM in consultation with stakeholders;

This may lead to standardisation of policies, and alterations to SICPs/TBPs based on expert consensus for application in NNU specific settings (and expansion of NNU addendum).

2. A gap analysis of pathogen-specific guidance in relation to NNUs.

This will inform the NIPCM A-Z pathogen list and highlight where any additional pathogen-specific guidance is required.

Consideration of pathogen specific guidance will also inform evidence regarding environmental and patient screening in neonatal units and safe and effective decolonisation strategies where applicable;

3. An outbreak checklist specific to neonatal units.
4. A targeted literature review to inform guidance for milk preparation, handling and storage.

4. Recommendations

This review makes the following recommendations based on an assessment of the extant scientific literature:

What are the definitions of a healthcare infection incident/outbreak in a neonatal unit (NNU)?

A healthcare infection incident/outbreak may be defined as:

- a single case of *Pseudomonas aeruginosa* identified in a neonatal unit; or

(Mandatory)

- a single case of infection with an alert organism or alert condition identified in a neonatal setting; or

(Category C recommendation)

- two or more linked cases with the same infectious agent are associated with the same healthcare setting over a specified time period (applicable to all care settings).

(Mandatory)

The local IPC team should consider the possibility of any onward transmission and potential for an incident/outbreak where there is:

- a single case of colonisation with an alert organism identified in a neonatal setting.

(Category C recommendation)

What are the key measures to prevent incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?

Ensure an assessment for infection risk is undertaken at the point of entry into the unit and continuously throughout the baby's stay.

The Clinical Risk Assessment for Microbiological Screening of Neonates on Admission or Transfer should be used. Neonates who present a cross-infection risk include patients who:

- have been transferred from another unit in Scotland with an ongoing incident/outbreak
- were born outside of Scotland
- have been previously positive with an MDRO e.g. Meticillin Resistant *Staphylococcus Aureus* (MRSA) or Carbapenemase Producing Enterobacterales, or any alert organism or alert condition as found in Appendix 13 of the NIPCM.

or whose mothers have

- been hospitalised outside Scotland in the previous 12 months
- had no antenatal care
- have been previously positive with an MDRO

Neonates that meet any single risk factor of the above criteria should be prioritised for placement in a suitable area to minimise the risk of potential cross infection pending investigation e.g.:

- incubator/cot placed in a single room with a clinical wash hand basin; or
- a cohort area/room with a clinical wash hand basin.

(Mandatory)

Ensure staffing levels meet the minimum requirement for the level of care being provided, this is:

- 1:4 in special care baby units (SCBU);
- 1:2 in high dependency units (HDU);
- 1:1 in neonatal intensive care units (NICU).

(Category B recommendation)

Ensure that there is adequate cot spacing as recommended in Health Building Note 09-03 and that there is no clutter around, or overcrowding of, incubators/cots in the unit.

The recommended space allowance in HBN 09-03 for intensive care and high dependency units is:

- 13.5 square metres (sqm) for the clinical area in multi-cot/incubator areas;
- 20 sqm in single rooms and when access space and shared space for core support (pharmacy, storage etc.) is included in multi-cot/incubator areas space allowance.

The recommended space allowance in special care units is:

- 9 sqm for the clinical area in multi-cot/incubator areas;
- 11.5 sqm in single rooms and when access space and shared space for core support (pharmacy, storage etc.) is included in multi-cot/incubator areas space allowance.

(Category B recommendation)

Ensure the management of water supply and use of water for patient care complies with national guidelines, particularly:

- flushing of all outlets (taps) for 1 minute daily (or for 3 minutes if water pressure has been reduced);
- that there is no risk of splash or spray from water sources in the neonatal care area or into areas where medications such as IV drugs are prepared;
- consider the use of sterile water for routine personal care for those neonates considered at 'high-risk' of infection.
- Neonatal units should undergo routine water testing for *Pseudomonas aeruginosa*

For further guidance refer to 'Guidance for neonatal units (NNUs) (levels 1, 2 and 3), adult and paediatric intensive care units in Scotland to minimise the risk of *Pseudomonas aeruginosa infection* from water'.

(Category C recommendation)

Avoid the use of multi-use containers or consumables e.g. of saline or antiseptics or ultrasound gels. These should be single-use disposable wherever possible. Ensure that medications, antiseptics and solutions such as saline etc. are handled and prepared using aseptic technique

(Category B recommendation)

Documentation should be in place to support the traceability of incubators assigned to neonates during their stay.

(Category C Recommendation)

Ensure staff are adequately trained in correct procedures for safe and effective delivery of total parenteral nutrition.

(Mandatory)

Ensure staff and parents understand and follow the correct procedures for the hygienic preparation (including expression) and storage of breast milk/infant formula.

(Category B recommendation)

Sterile liquid infant formula is recommended, however where powdered formula milk is required, this should be prepared in a designated area, using aseptic technique and following the manufacturer's instructions

(Category C recommendation)

Reconstituted milk should be prepared for either immediate use or refrigerated immediately and discarded if not used within 24hrs.

(Category C recommendation)

Full traceability of powdered infant formula or expressed milk should be in place in care settings; staff should be properly trained in preparation and food hygiene.

(Category C recommendation)

Tap water must not be used for warming or defrosting milk.

(Category C recommendation)

For further guidance refer to 'Guidance for neonatal units (NNUs) (levels 1, 2 and 3), adult and paediatric intensive care units in Scotland to minimise the risk of *Pseudomonas aeruginosa* infection from water'.

How should NNU incidents/outbreaks be investigated and managed?

As part of the epidemiological investigation, the IMT should conduct a retrospective review in order to identify further cases.

(Category B recommendation)

The IMT should consider implementing 'reactive' microbiological screening of all babies in the unit, and implement testing at regular intervals e.g. weekly, where appropriate.

(Category B recommendation)

There should be an agreed plan to direct patient screening and predefined actions dependent on screening results e.g. isolation and treatment, and a plan for stepping down reactive screening e.g. 2 weeks without any new positive screening results.

(Category C recommendation)

As per recommendations outlined in NIPCM literature review for incident and outbreaks in Scotland, the IMT may decide that staff screening is necessary to identify carriage or infection among staff groups. The decision to screen should be based on the need of one or more of the following:

- To characterise the epidemiology of the outbreak in terms of time, place and person;
- To identify the likely source and index case, with a view to control;
- To assist with interrupting the chain of transmission of an outbreak;
- To confirm eradication of an outbreak.

(Category B recommendation)

Staff screening should be undertaken by local Occupational Health Services and is a confidential process requiring staff consent.

(Mandatory)

Voluntary screening of parents/carers should be considered where an outbreak has persisted despite control measures, and there are potential epidemiological links to parents. Interviews regarding relevant symptoms or medical histories should be prioritised over microbiological screening.

(Category C Recommendation)

As part of the epidemiological investigation during an outbreak, microbiological sampling of environmental locations and equipment may be considered where:

- there is epidemiological information linking transmission to an environmental source;
- there is unexplained transmission ongoing;
- an environmental reservoir is suspected;
- there is a clinical isolate of *Pseudomonas aeruginosa* within the care area, which is indicative of an environmental source of colonisation/infection.

(Category B Recommendation)

For further guidance refer to 'Guidance for neonatal units (NNUs) (levels 1, 2 and 3), adult and paediatric intensive care units in Scotland to minimise the risk of *Pseudomonas aeruginosa* infection from water'.

What are the key measures to control incidents/outbreaks in NNUs and how should these be implemented in NHS Scotland?

If a healthcare infection incident/outbreak is suspected or confirmed, an immediate review of SICPs practice should be considered to identify areas for improvement and any potential sources of infection or transmission routes.

(Category B recommendation)

In addition to reviewing recent compliance monitoring reports, an audit and reinforcement of hand hygiene compliance and education among both staff and parents should be considered. A review of the management of equipment, the environment and the correct use of personal protective equipment (PPE) should also be considered.

(Category B recommendation)

Infected or colonised infants should be prioritised for isolation or cohorted in a designated area of the NNU, as outlined in Chapter 3 of the NIPCM. Equipment should be single-use or patient dedicated wherever possible. A documented risk assessment should be in place supporting ongoing assessment of the need for isolation.

(Mandatory)

An incubator is not considered a form of isolation.

(Category C recommendation)

There was insufficient evidence to support an informed recommendation regarding decolonisation of neonates for specific pathogens (*S. aureus*).

(No recommendation)

Consider assigning a dedicated team of staff to care for infected or colonised infants in isolation/cohort rooms/areas. This can only be implemented if there are sufficient levels of staff available. Where staff cohorting is not possible, a documented risk assessment should be put in place and reinforcement of strict application of SICPs and TBPs.

(Category B recommendation)

Transfers to other units during incidents or outbreaks should be avoided, where possible; however this should take into consideration the clinical needs of patients, and any practical or logistical issues for parents/carers.

(Category C recommendation)

Whilst closing the unit to new admissions should be considered, especially where cot capacity is exceeded or understaffing has been identified, this should not be carried out without conducting a risk assessment, in coordination with other NNUs in the network, taking account of other harms associated with unit closures.

(Category B recommendation)

Consider using hydrogen peroxide vapour (HPV) as an additional measure during enhanced cleaning, particularly if other measures implemented are failing to bring the incident under control and if multi-drug resistant or environmental organisms, such as *Serratia* spp. or *Pseudomonas* spp., are the cause of the incident.

(Category B recommendation)

How should NNU incidents/outbreaks be reported?

IPC Teams should conduct an initial assessment using the Healthcare Infection Incident Assessment Tool (HIIAT), and convene a Problem Assessment Group (PAG) and Incident Management Team (IMT), if required.

(Mandatory)

NHS Boards are required to communicate Healthcare Infection Incident Assessment Tool (HIIAT) assessments to ARHAI Scotland by completing the electronic Outbreak Reporting Tool (ORT) as outlined in Chapter 3 of the NIPCM.

(Mandatory)

The CNO National Support Framework may be invoked by the Scottish Government Health and Social Care Department (SGHSCD) or by an NHS Board to optimise patient safety during or following any healthcare infection incident.

(Mandatory)

Parents/carers of neonates should be informed promptly regarding any healthcare associated infection, infection risk, or associated adverse events, and support provided. This should be documented by the clinician.

(Mandatory)

During patient transfers, there should be open and frequent communication, in advance, between units and any transport services regarding ongoing incidents / outbreaks in NNUs, and all suspected and confirmed infection risks, where applicable.

(Category C recommendation)

Deaths associated with HAI should be recorded on the Medical Certificate of the Cause of Death (MCCD) and reported to the Infection Control Manager (ICM). A death which is considered to pose an acute and serious public health risk should be reported to the Procurator Fiscal when it has occurred as a result of an infection acquired while under medical/dental care, while on NHS premises.

(Mandatory)

How should a healthcare infection incident be 'closed, with lessons learned recorded and disseminated nationally?

In most circumstances, neonates should continue to be isolated/cohorted until discharge. Step-down of isolation/cohorting of neonates in NNU outbreaks should be agreed via the IMT with the local IPC team, using pathogen-specific guidance where available.

(Category B recommendation)

Once the incident is over, the PAG/IMT and NHS Boards should evaluate and report on the effectiveness and efficiency of the IMT using the Hot Debrief Tool.

(Category C recommendation)

Lessons learned should be captured through the Outbreak Reporting Tool (ORT) and IMT final report. Following agreement with the NHS Board, information and lessons learned should be shared with other NNUs via the Neonatal Network.

(Category C recommendation)

References

1. British Standards Institute. *Water Quality. Part 2: Risk assessments for* Pseudomonas aeruginosa *and other waterborne pathogens- Code of practice*. BS 8580-2:2022.

2. Wilson APR LD, Otter JA, Warren RE, Jenks P, Enoch DA et al. Prevention and control of multi-drug-resistant Gram-negative bacteria: recommendations from a Joint Working Party, (2016).

3. Independent Review of Incidents of Pseudomonas aeruginosa Infection in Neonatal Units in Northern Ireland. Final Report. 31 May 2012. The Regulation and Quality Improvement Authority., https://www.rqia.org.uk/RQIA/files/ee/ee76f222-a576-459f-900c-411ab857fc3f.pdf (accessed 01 Feb 2022).

4. Anthony M, Bedford-Russell A, Cooper T, et al. Managing and preventing outbreaks of Gram-negative infections in UK neonatal units. Archives of Disease in Childhood Fetal and Neonatal Edition 2013; 98: F549-553.

5. O'Connor C, Philip RK, Kelleher J, et al. The first occurrence of a CTX-M ESBL-producing Escherichia coli outbreak mediated by mother to neonate transmission in an Irish neonatal intensive care unit. BMC infectious Diseases 2017; 17: 16.

6. Chen JHK, So SYC, Wong SCY, et al. Whole-genome sequencing data-based modeling for the investigation of an outbreak of community-associated methicillin-resistant Staphylococcus aureus in a neonatal intensive care unit in Hong Kong. European Journal of Clinical Microbiology and Infectious Diseases 2019; 38: 563-573.

7. Zarrilli R, Di Popolo A, Bagattini M, et al. Clonal spread and patient risk factors for acquisition of extensively drug-resistant Acinetobacter baumannii in a neonatal intensive care unit in Italy. Journal of Hospital Infection 2012; 82: 260-265.

8. Deshpande A, Curran ET, Jamdar S, et al. Historical outbreak of Salmonella hadar. Journal of Hospital Infection 2015; 91: 171-175.

9. Sax H, Harbarth S, Touveneau S, et al. Control of a cluster of community-associated, methicillin-resistant Staphylococcus aureus in neonatology. Journal of Hospital Infection 2006; 63: 93-100.

10. Ali H, Nash JQ, Nixon Z, et al. Outbreak of a South West Pacific clone Panton-Valentine leucocidin-positive meticillin-resistant Staphylococcus aureus infection in a UK neonatal intensive care unit. Journal of Hospital Infection 2012; 80: 293-298.

11. Sanchini A, Monaco M, Pantosti A, et al. Outbreak of skin and soft tissue infections in a hospital newborn nursery in Italy due to community-acquired meticillin-resistant Staphylococcus aureus USA300 clone. Journal of Hospital Infection 2013; 83: 36-40.

12. Attman E, Korhonen P, Tammela O, et al. A Serratia marcescens outbreak in a neonatal intensive care unit was successfully managed by rapid hospital hygiene interventions and screening. Acta Paediatrica, International Journal of Paediatrics 2018; 107: 425-429.

13. Tsiatsiou O, Iosifidis E, Katragkou A, et al. Successful management of an outbreak due to carbapenem-resistant Acinetobacter baumannii in a neonatal intensive care unit. European Journal of Pediatrics 2015; 174: 65-74.

14. Dijk YV, Bik EM, Hochstenbach-Vernooij S, et al. Management of an outbreak of Enterobacter cloacae in a neonatal unit using simple preventive measures. Journal of Hospital Infection 2002; 51: 21-26.

15. Gopal Rao G, Batura R, Nicholl R, et al. Outbreak report of investigation and control of an outbreak of Panton-Valentine Leukocidin-positive methicillin-sensitive Staphylococcus aureus (PVL-MSSA) infection in neonates and mothers. BMC Infectious Diseases 2019; 19: 178.

16. Brown NM, Reacher M, Rice W, et al. An outbreak of meticillin-resistant Staphylococcus aureus colonization in a neonatal intensive care unit: use of a case-control study to investigate and control it and lessons learnt. Journal of Hospital Infection 2019; 103: 35-43.

17. Koningstein M GL, Geraat-Peters K, Lutgens S, Rietveld A, Jira P et al. The use of typing methods and infection prevention measures to a bullous impetigo outbreak on a neonatal ward. Antimicrobial Resistance and Infection Control 2012; 1.

18. Shimono N, Hayashi J, Matsumoto H, et al. Vigorous cleaning and adequate ventilation are necessary to control an outbreak in a neonatal intensive care unit. Journal of Infection and Chemotherapy 2012; 18: 303-307.

19. Song X, Cheung S, Klontz K, et al. A stepwise approach to control an outbreak and ongoing transmission of methicillin-resistant Staphylococcus aureus in a neonatal intensive care unit. American Journal of Infection Control 2010; 38: 607-611.

20. National Infection Prevention and Control Manual. ARHAI Scotland, https://www.nipcm.scot.nhs.uk/ (accessed 18 Jan 2022).

21. Infection Prevention and Control Standards For Health and Adult Social Care Settings. Health Improvement Scotland. 2022., https://www.healthcareimprovementscotland.org/his/idoc.ashx?docid=b32b9181-000b-4b44-aba4-dbb574f0b192&version=-1 (accessed 16 May 2022).

22. Neonatal Care in Scotland: A Quality Framework. Neonatal Expert Advisory Group. Scottish Government., (2013).

23. Toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae in Scottish acute settings. NHS National Services Scotland. Dec 2019., https://www.hps.scot.nhs.uk/web-resources-container/toolkit-for-the-early-detection-management-and-control-of-carbapenemase-producing-enterobacteriaceae-in-scottish-acute-settings/ (accessed 07 Jan 2022).

24. Protocol for CRA MRSA Screening National Rollout in Scotland. V.1.10. NHS National Services. Dec 2019.

25. Coia JE WJ, Bak A, Marsden GL, Shimonovich M, Loveday HP, Humphreys H, Wigglesworth N, Demirjian A, Brooks J, Butcher L. Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guidelines for the prevention and control of meticillin-resistant Staphylococcus aureus (MRSA) in healthcare facilities Journal of Hospital Infection 2021; 0195-6701.

26. Framework of actions to contain carbapenemase-producing Enterobacterales. Public Health England. Sep 2020.

27. David MD, Gossain S, Kearns AM, et al. Community-associated meticillin-resistant Staphylococcus aureus: nosocomial transmission in a neonatal unit. Journal of Hospital Infection 2006; 64: 244-250.

28. Otter JA, French GL, Klein JL, et al. Identification and control of an outbreak of ciprofloxacin-susceptible EMRSA-15 on a neonatal unit. Journal of Hospital Infection 2007; 67: 232-239.

29. Kato H, Ide K, Fukase F, et al. Polymerase chain reaction-based open reading frame typing (POT) method analysis for a methicillin-resistant Staphylococcus aureus (MRSA) outbreak through breast-feeding in the neonatal intensive care unit. IDCases 2018; 12: 1-3.

30. Moissenet D, Salauze B, Vu-Thien H, et al. Meningitis caused by Escherichia coli producing TEM-52 extended-spectrum beta-lactamase within an extensive outbreak in a

neonatal ward: Epidemiological investigation and characterization of the strain. Journal of Clinical Microbiology 2010; 48: 2459-2463.

31. Francis S, Khan H and Kennea NL. Infection control in United Kingdom neonatal units: variance in practice and the need for an evidence base. Journal of Infection Prevention 2012; 13: 158-162.

32. Cadot L, Bruguiere H, Jumas-Bilak E, et al. Extended spectrum beta-lactamase-producing Klebsiella pneumoniae outbreak reveals incubators as pathogen reservoir in neonatal care center. European Journal of Pediatrics 2019; 178: 505-513.

33. Giuffre M, Cipolla D, Bonura C, et al. Outbreak of colonizations by extended-spectrum beta-lactamase-producing Escherichia coli sequence type 131 in a neonatal intensive care unit, Italy. Antimicrobial Resistance and Infection Control 2013; 2: 8.

34. Milstone AM EA, Brady MT, Cox K, Fauerbach LL, Guzman-Cottrill JA, et al. Centers for Disease Control and Prevention. National Center for Emerging and Zoonotic Infectious Diseases. Division of Healthcare Quality Promotion. Recommendations for Prevention and Control of Infections in Neonatal Intensive Care Unit Patients: *Staphylococcus aureus.* Sep 2020., (2020).

35. Ergaz Z, Arad I, Bar-Oz B, et al. Elimination of vancomycin-resistant enterococci from a neonatal intensive care unit following an outbreak. Journal of Hospital Infection 2010; 74: 370-376.

36. Clinical Risk Assessment for Microbiological Screening of Neonates on Admission or Transfer. ARHAI Scotland. Aug 2019., https://www.nipcm.scot.nhs.uk/media/1453/2019-8-22-nnu-clinical-risk-assessment-v10-final.pdf (accessed 07 Jan 2022).

37. Health Building Note 09-03: Neonatal Units: planning and design. Guidance for the design of hospital neonatal units including special care, family spaces and specialist clinical rooms. UK Government Department of Health. 2013., https://www.england.nhs.uk/wp-content/uploads/2021/05/HBN_09-03_Final.pdf (accessed 07 Jan 2022).

38. Hosoglu S, Hascuhadar M, Yasar E, et al. Control of an Acientobacter baumannii outbreak in a neonatal ICU without suspension of service: A devastating outbreak in Diyarbakir, Turkey. Infection 2012; 40: 11-18.

39. Maragakis LL, Winkler A, Tucker MG, et al. Outbreak of multidrug-resistant Serratia marcescens infection in a neonatal intensive care unit. Infection control and hospital Epidemiology 2008; 29: 418-423.

40. Boehmer TK, Ghosh TS, Vogt RL, et al. Health care-associated outbreak of Salmonella Tennessee in a neonatal intensive care unit. American Journal of Infection Control 2009; 37: 49-55.

41. Alsubaie S, Bahkali K, Somily AM, et al. Nosocomial transmission of community-acquired methicillin-resistant Staphylococcus aureus in a well-infant nursery of a teaching hospital. Pediatrics International 2012; 54: 786-792.

42. Wisgrill L, Rittenschober-Bohm J, Berger A, et al. Outbreak of yersiniabactin-producing klebsiella pneumoniae in a neonatal intensive care unit. Pediatric Infectious Disease Journal 2019; 38: 638-642.

43. Laing A GA, McCallum A. Controlling an outbreak of MRSA in a neonatal unit: a steep learning curve. Review. Arch Dis Child Fetal Neonatal Ed 2008; 94: F307-F310.

44. Cantey JB, Jaleel M, Siegel JD, et al. Prompt control of an outbreak caused by extended-spectrum beta-lactamase-producing klebsiella pneumoniae in a neonatal intensive care unit. Journal of Pediatrics 2013; 163: 672.

45. Moffa M, Guo W, Li T, et al. A systematic review of nosocomial waterborne infections in neonates and mothers. International Journal of Hygiene and Environmental Health 2017; 220: 1199-1206.

46. Weng MK, Christensen BE, Moulton-Meissner H, et al. Outbreak investigation of Pseudomonas aeruginosa infections in a neonatal intensive care unit. American Journal of Infection Control 2019; 47: 1148-1150.

47. Kinsey CB, Koirala S, Solomon B, et al. Pseudomonas aeruginosa Outbreak in a Neonatal Intensive Care Unit Attributed to Hospital Tap Water. Infection Control & Hospital Epidemiology 2017; 38: 801-808.

48. Crivaro V, Di Popolo A, Caprio A, et al. Pseudomonas aeruginosa in a neonatal intensive care unit: Molecular epidemiology and infection control measures. BMC Infectious Diseases 2009; 9: 70.

49. Health Protection Scotland. Guidance for neonatal units (NNUs) (levels 1, 2 & 3), adult and paediatric intensive care units (ICUs) in Scotland to minimise the risk of Pseudomonas aeruginosa infection from water. 03 Sep 2018., https://www.nipcm.hps.scot.nhs.uk/media/1676/2018-08-pseudomonas-v23.pdf (accessed 09 Feb 2022).

50. Draft Pseudomonas aeruginosa routine water sampling in augmented care for NHSScotland. NHS National Services Scotland. V1.0: Sep 2018., https://hpspubsrepo.blob.core.windows.net/hps-website/nss/1989/documents/3_psuedomonas-water-testing-v1.0.pdf (accessed 10 Feb 2022).

51. Madani TA, James L, Eldeek BS, et al. Serratia marcescens-contaminated baby shampoo causing an outbreak among newborns at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Journal of Hospital Infection 2011; 78: 16-19.

52. Fournier S, Roze JC, Gras-Le Guen C, et al. Almond oil implicated in a Staphylococcus capitis outbreak in a neonatal intensive care unit. Journal of Perinatology 2007; 27: 713-717.

53. Narayan SA, Vakololoma M, Mejia A, et al. Investigation and control of an outbreak of enterobacter aerogenes bloodstream infection in a neonatal intensive care unit in Fiji. Infection Control and Hospital Epidemiology 2009; 30: 797-800.

54. Good infection prevention practice: using ultrasound gel. UK Government. Updated 12 Feb 2021.

55. Rahman ZA, Hasan H, Mohamed Z, et al. Contaminated parenteral nutrition solution causing a series of neonatal nosocomial infections by Serratia marcescens. Journal of Pediatric Infectious Diseases 2010; 5: 271-275.

56. Arslan U, Yuksekkaya S, Tuncer I, et al. Serratia marcescens sepsis outbreak in a neonatal intensive care unit. Pediatrics International 2010; 52: 208-212.

57. Neonatal parenteral nutrition. NICE guideline. 26 Feb 2020., www.nice.org.uk/guidance/ng154 (accessed 07 Jan 2022).

58. Complex nutrition care standards. Dec 2015. Healthcare Improvement Scotland, https://www.healthcareimprovementscotland.org/our_work/standards_and_guidelines/stnds/complex_nutrition_standards.aspx (accessed 07 Jan 2022).

59. Preventing infections when inserting and maintaining a neonatal Central Vascular Catheter. Health Protection Scotland. 13 Oct 2017., https://www.hps.scot.nhs.uk/web-resources-container/preventing-infections-when-inserting-and-maintaining-a-neonatal-central-vascular-catheter/ (07 Jan 2022).

60. Price E, Weaver G, Hoffman P, et al. Decontamination of breast pump milk collection kits and related items at home and in hospital: guidance from a Joint Working Group of the

Healthcare Infection Society and Infection Prevention Society. Journal of Hospital Infection 2016; 92: 213-221.

61. ARHAI Scotland. Standard Infection Control Precautions and Transmission Based Precautions Literature Review: Safe Management of the Care Environment (Environmental Decontamination). V.1.0 December 2020., https://www.nipcm.hps.scot.nhs.uk/media/1691/2020-12-sicp-tbp-lr-care-environment-v1.pdf.

62. Gillespie EE, Bradford J, Brett J, et al. Serratia marcescens bacteremia - an indicator for outbreak management and heightened surveillance. Journal of Perinatal Medicine 2007; 35: 227-231.

63. Weir E. Powdered infant formula and fatal infection with Enterobacter sakazakii. Canadian Medical Association Journal 2002; 166: 1570.

64. Safe preparation, storage and handling of powdered infant formula: guidelines. World Health Organisation, https://www.who.int/foodsafety/publications/micro/pif_guidelines.pdf (2007, accessed 07 Jan 2022).

65. Campbell JR, Hulten K and Baker CJ. Cluster of Bacillus species bacteremia cases in neonates during a hospital construction project. Infection Control and Hospital Epidemiology 2011; 32: 1035-1038.

66. Saunders A, Panaro L, McGeer A, et al. A nosocomial outbreak of community-associated methicillin-resistant Staphylococcus aureus among healthy newborns and postpartum mothers. Canadian Journal of Infectious Diseases and Medical Microbiology 2007; 18: 128-132.

67. Schmithausen RM, Sib E, Exner M, et al. The Washing Machine as a Reservoir for Transmission of Extended-Spectrum-Beta-Lactamase (CTX-M-15)-Producing Klebsiella oxytoca ST201 to Newborns. Applied and Environmental Microbiology 2019; 85.

68. Lister DM, Kotsanas D, Korman TM, et al. Outbreak of vanB vancomycin-resistant Enterococcus faecium colonization in a neonatal service. American Journal of Infection Control 2015; 43: 1061-1065.

69. Heinrich N, Mueller A, Bartmann P, et al. Successful management of an MRSA outbreak in a neonatal intensive care unit. European Journal of Clinical Microbiology and Infectious Diseases 2011; 30: 909-913.

70. Otter JA, Davies B, Menson E, et al. Identification and control of a gentamicin resistant, meticillin susceptible Staphylococcus aureus outbreak on a neonatal unit. Journal of Infection Prevention 2014; 15: 104-109.

71. Arnold SR, Hysmith ND, Buckingham SC, et al. Use of real-time semiquantitative PCR data in management of a neonatal intensive care unit adenovirus outbreak. Infection Control & Hospital Epidemiology 2018; 39: 1074-1079.

72. Gerber SI JR, Scott, MV, Price JS, Dworkin MS, Filippell MB et al. Management of Outbreaks of Methicillin-Resistant Staphylococcus aureus Infection in the Neonatal Intensive Care Unit: A Consensus statement. Infection Control & Hospital Epidemiology 2006; 27.

73. Tacconelli E CM, Dancer SJ, De Angelis G, Falcone M, Frank U et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect 2014; 20: 1-55.

74. ARHAI Scotland. Literature Review: Healthcare Infection Incidents and Outbreaks in Scotland. V1.0 Mar 2017, https://www.nipcm.hps.scot.nhs.uk/media/1644/2017-03-lr-chapter-3-literature-review-v1.pdf.

75. Calfee DP, Salgado CD, Milstone AM et al. Strategies to Prevent Methicillin-Resistant Staphylococcus aureus Transmission and Infection in Acute Care Hospitals: 2014 Update. Infection Control and Hospital Epidemiology. 35(7).

76. Guidelines for the Prevention and Control of Multi-drug resistant organisms (MDRO) excluding MRSA in the healthcare setting. Royal College of Physicians of Ireland in association with HSE Quality and Patient Safety. 2012.

77. Neylon O, McElligott F, Philip RK, et al. Neonatal staphylococcal scalded skin syndrome: Clinical and outbreak containment review. European Journal of Pediatrics 2010; 169: 1503-1509.

78. Buffet-Bataillon S, Bauer M, Rabier V, et al. Outbreak of Serratia marcescens in a neonatal intensive care unit: contaminated unmedicated liquid soap and risk factors. Journal of Hospital Infection 2009; 72: 17-22.

79. MacDonald TM, Allain K, Nelson G, et al. Serratia marcescens outbreak in a neonatal intensive care unit related to the exit port of an oscillator. Pediatric Critical Care Medicine 2011; 12: e282-e286.

80. National Infection Prevention and Control Manual. Chapter 3 - Healthcare Infection Incidents, Outbreaks and Data Exceedance, https://www.nipcm.scot.nhs.uk/chapter-3-healthcare-infection-incidents-outbreaks-and-data-exceedance/ (accessed 07 Jan 2022).

81. Ersoy Y, Otlu B, Turkcuoglu P, et al. Outbreak of adenovirus serotype 8 conjunctivitis in preterm infants in a neonatal intensive care unit. Journal of hospital Infection 2012; 80: 144-149.

82. HSS (MD) 17/2012. Guiding Principles for the Development of Decontamination Procedures for Infant Incubators and Other Specialist Equipment For Neonatal Care. Chief Medical Officer, Department of Health, Social Services and Public Safety. Northern Ireland Executive.

83. Sehulster LM CR, Arduino MJ, Carpenter J, Donlan R, Ashford D, Besser R, Fields B, McNeil MM, Whitney C, Wong S, Juranek D, Cleveland J. . Guidelines for environmental infection control in health-care facilities. Recommendations from CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Chicago IL; American Society for Healthcare Engineering/American Hospital Association; 2004.

84. Rutala WA, Weber DJ and Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for disinfection and sterilization in healthcare facilities, 2008, https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines-H.pdf (2008, accessed 15/04/2021).

85. ARHAI Scotland. Literature Review and Practice Recommendations: Existing and emerging technologies for decontamination of the health and care environment. Airborne Hydrogen Peroxide. V.2.0 Feb 2022, https://www.nss.nhs.scot/media/2200/2022-02-07-airborne-hydrogen-peroxide-v20.pdf.

86. Akinboyo IC ZK, Berg WM, Cantey JB, Huizinga B, Milstone AM. SHEA White Paper. SHEA neonatal intensive care unit (NICU) white paper series: Practical approaches to Staphylococcus aureus disease prevention. Infection Control & Hospital Epidemiology 2020; 41.

87. Health Protection Scotland. Interim Advice for the Diagnosis and Management of PVL-associated *Staphylococcus aureus* infections (PVL-*S. aureus*). Scottish Recommendations. May 2014.

88. National Infection Prevention and Control Manual. Responsibilities, https://www.nipcm.scot.nhs.uk/responsibilities/.

89. DL (2020) 01: NHSScotland Human Resources Policy Document. HAI: Guidance for Staff Screening during Healthcare Associated Infection Incidents and Outbreaks. Scottish Government. 31 Jan 2020.

90. Organisational Duty of Candour Guidance. Scottish Government. 2018, https://www.gov.scot/publications/organisational-duty-candour-guidance/ (accessed 01 Feb 2022).

91. The Duty of Candour Procedure (Scotland) Regulations 2018, https://www.legislation.gov.uk/ssi/2018/57/made/data.pdf (accessed 01 Feb 2022).

92. Inkster T CJ. Duty of candour and communication during an infection control incident in a paediatric ward of a Scottish hospital: how can we do better? J Med Ethics 2020; ePub ahead of print.

93. DL (2019) 23: Healthcare Associated Infection (HCAI) and Antimicrobial Resistance (AMR) Policy Requirements. Scottish Government. 23 Dec 2019.

94. Maternity and neonatal (perinatal) adverse event review process for Scotland. Operational guidance to supplement the HIS national framework. Scottish Government. Sep 2021., https://www.gov.scot/binaries/content/documents/govscot/publications/advice-and-guidance/2021/09/maternity-neonatal-perinatal-adverse-event-review-process-scotland/documents/maternity-neonatal-perinatal-adverse-event-review-process-scotland/maternity-neonatal-perinatal-adverse-event-review-process-scotland/govscot%3Adocument/maternity-neonatal-perinatal-adverse-event-review-process-scotland.pdf (accessed 01 Feb 2022).

95. MacCannell T UC, Agarwal RK, Lee I, Kuntz G, Stevenson KB, HICPAC Committee. Guideline for the Prevention and Control of Norovirus Gastroenteritis Outbreaks in Healthcare Settings. Healthcare Infection Control Practices Advisory Committee (HICPAC). Centers for Disease Control and Prevention., (2011).

Appendix 1: Supplementary Methodology

Due to the abundance of non-UK outbreak reports (observational studies); reports were only included if they made reference to any infection prevention or control measures including bundled measures, (for example, genetic analyses of outbreak strains were not included)

Additionally, for non-UK outbreak reports, these were required to include confirmation of cases via microbiological testing, such as phenotyping/genotyping etc. as a sufficient case definition.

Search strategies

V2.0 (current update):

Search performed on 02/06/2021 with date limits: 2000-current. Search findings were restricted using English language filter.

Medline/ Embase search:

1. (neonat* or NICU or newborn or preterm or premature).mp.
2. (outbreak adj3 prevent*).mp.
3. (outbreak adj3 manage*).mp.
4. (outbreak adj3 control).mp.
5. (outbreak adj3 report*).mp.
6. (outbreak adj3 investigat*).mp.
7. 2 or 3 or 4 or 5 or 6
8. 1 and 7
9. limit 8 to english language
10. limit 9 to human
11. limit 10 to yr="2000 -Current"

CINAHL search:

S1	(MH “Intensive Care,Neonatal” or “neonat*” orMH “Infant, Newborn”)
S2	Outbreak N3 prevent*
S3	Outbreak N3 manage*
S4	Outbreak N3 control
S5	Outbreak N3 report*
S6	Outbreak N3 investigat*
S7	S2 or S3 or S4 or S5 orS6

S8 S1 AND S7 Limiters – Published Date: 20000101-20211231; Exclude MEDLINE records

The following search strategies was applied in previous versions:

Version 1.0 search strategy:

Search performed on 24/10/2014 with date limits 2000-2014. Search findings were restricted using English language filter.

1. neonat*.mp.
2. newborn.mp.
3. (infant or preterm infant).mp.
4. (late onset sepsis or late-onset sepsis).mp.
5. infection.mp.
6. (colonisation or colonization).mp.
7. (routine screening or microbiological screening).mp.
8. routine culture.mp.
9. (skin culture or skin swab or skin sampling).mp.
10. mucosal culture.mp.
11. endotracheal aspirate.mp.
12. aspirate.mp.
13. 1 or 2 or 3
14. 4 or 5 or 6
15. 7 or 8 or 9 or 10 or 11 or 12
16. 16 13 and 14 and 15
17. 17 limit 16 to english language
18. 18 limit 17 to human
19. 19 limit 18 to yr="1999 -Current")
20. remove duplicates from 19

Search strategy:

1. neonat*.mp.
2. newborn.mp.
3. preterm infant.mp.

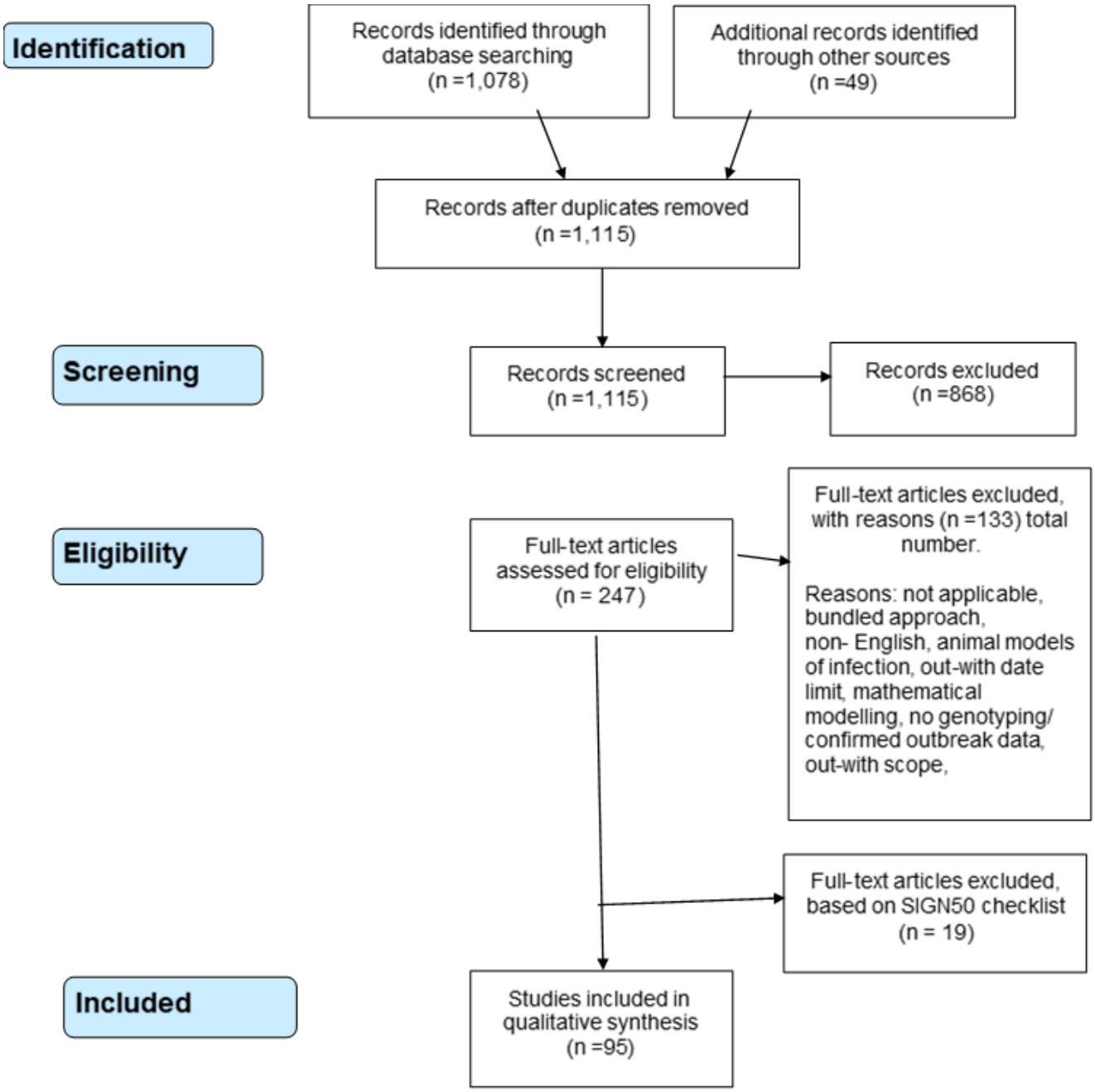
4. (late onset sepsis or late-onset sepsis).mp.
5. infection.mp.
6. (colonisation or colonization).mp.
7. outbreak.mp.
8. (screening or surveillance).mp.
9. culture.mp.
10. (skin culture or swab or skin sampling).mp.
11. mucosal culture.mp.
12. endotracheal aspirate.mp.
13. aspirate.mp.
14. 1 or 2 or 3
15. 4 or 5 or 6 or 7
16. 8 or 9 or 10 or 11 or 12 or 13
17. 14 and 15 and 16
18. limit 17 to yr="1999 -Current"
19. limit 17 to yr="1999 -Current"

Databases and resources searched

The databases and resources searched for this literature review are specified in the NIPCM methodology. The following online resources were searched additionally to identify any relevant policy or guidance documents or any significant grey literature:

- British Association of Perinatal Medicine
- Royal College of Obstetrics and Gynaecologists; Royal College of Midwives
- Royal College of Paediatrics And Child Health

Appendix 2: PRISMA diagram



Appendix 3: Grades of Recommendation

Final recommendations are given a grade to highlight the strength of evidence underpinning them, the NIPCM grades of recommendations are as follows:

Grade	Descriptor	Levels of evidence
Mandatory	Recommendations that are directives from government policy, regulations or legislation	N/A
Category A	Based on high to moderate quality evidence	SIGN level 1++, 1+, 2++, 2+, AGREE strongly recommend
Category B	Based on low to moderate quality of evidence which suggest net clinical benefits over harm	SIGN level 2+, 3, 4, AGREE recommend
Category C	Expert opinion, these may be formed by the NIPC groups when there is no robust professional or scientific literature available to inform guidance.	SIGN level 4, or opinion of NICP group
No recommendation	Insufficient evidence to recommend one way or another	N/A