Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI): An extension of the STROBE statement for neonatal infection research

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ABSTRACT

Neonatal infections are estimated to account for a quarter of the 2·8 million annual neonatal deaths, as well as approximately 3% of all DALYs. Despite this burden, data are limited on incidence, aetiology and outcomes, particularly regarding impairment. We aimed to develop guidelines for improved scientific reporting of observational and interventional neonatal infection studies, to increase comparability and to strengthen research in this area. This statement, *Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI)* is an extension of the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) checklist. STROBE-NI was developed following systematic reviews of published literature (1996-2015), compilation of over 130 potential reporting recommendations, and circulation of a survey to relevant professionals worldwide, eliciting responses from 147 professionals from 37 countries. An international consensus meeting of 18 participants (with expertise in infectious diseases, neonatology, microbiology, epidemiology and statistics) identified priority recommendations for reporting, additional to the STROBE statement. Implementation of these STROBE-NI recommendations, and linked checklist, aims to improve scientific reporting of neonatal infection studies, increasing data utility and allowing meta-analyses and pathogen-specific burden estimates to inform global policy and new interventions, including maternal vaccines.

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Background

Progress in improving child survival has been one of the greatest successes in international development.[1] However, there is an unfinished agenda,[2] since the mortality reduction has been slowest for neonates. Almost half (44%) of all child deaths now occur in the neonatal period (0-27 days),[3] with a substantial burden of mortality in the first few days after birth.[4] The "Every Newborn Action Plan" sets out a United Nations led platform, endorsed by all countries, to end preventable neonatal deaths, but requires data to implement and inform innovation.[2,5]

Estimates by the World Health Organisation (WHO), for 195 countries, suggest that infection accounts for around 680 000 deaths – a quarter of all neonatal deaths annually;[6] and half of all neonatal deaths in high neonatal mortality settings.[2] The closely linked 2·6 million annual stillbirths have an as yet poorly quantified infection burden.[7] Significant neurodevelopmental impairment affects approximately a quarter of neonates following meningitis, but impairment data are very limited worldwide, particularly for common infection syndromes such as sepsis and pneumonia.[8,9]

There are an estimated 6·9 million neonates with possible serious bacterial infection (pSBI) annually in Sub-Saharan Africa, South Asia and Latin America.[8] Approximately 84% of neonatal deaths attributed to infections could be averted by increasing coverage of prevention and access to treatment, yet currently the gap is high, especially in the poorest countries.[10] Recent large clinical trials have assessed the safety and efficacy of improving access to treatment through outpatient care, in cases where referral is not possible.[11–13]

Aetiology-specific data for neonatal infections are limited, and challenging to combine. Hospital-based studies suggest that *Staphylococcus aureus, Escherichia coli*, *Klebsiella* species and group B Streptococci (GBS) may be the most common pathogens globally.[14] As yet there are no community-based aetiological studies from Africa, and few from South Asia, which together carry over 75% of the burden. Hence, there is an urgent need to improve data on incidence (especially in the first days following birth), aetiology (bacterial, viral and fungal), antimicrobial sensitivity, and outcomes. These data are essential to understand the burden and risk factors, refine treatment algorithms, support potential interventions (eg. maternal vaccines for respiratory syncytial virus and Group B Streptococcus),[15–17] and mitigate antimicrobial resistance, which threatens current treatment strategies.[18–20]

Recording, reporting and interpreting neonatal infection data poses specific challenges. More than 95% of neonatal deaths occur in countries without adequate birth and death certification to capture cause-specific mortality,[2,6] let alone pathogen-specific surveillance. Systematic clinical assessment, with investigations providing microbiological data, are also limited.[8] Most available neonatal infection data are from tertiary referral hospitals, with recruitment bias, by missing those not accessing higher levels of care, or any care.[21] In population-based studies, which are extremely few in high burden settings,[22–24] even if women are recruited in pregnancy, the challenge remains that many newborns die within hours of birth before being assessed; meaning counting, investigations and treatment are missed.[25] In a population-based Bangladeshi cohort, 62% of neonates who died were never clinically assessed, with 59% of deaths occurring within 48 hours of birth.[22] Even when cases are captured in the numerator and denominator, case definitions are often inconsistent. Diagnosis is usually based on clinical expertise, or in settings with fewer health workers, on

simplified clinical algorithms designed to be highly sensitive. For example, the most commonly used WHO young infant pSBI algorithm is very sensitive (85%) and fairly specific (75%). [26–28] Additionally, unlike childhood infections, gestational age has a major effect on incidence, aetiology and outcomes of neonatal infections. Neonates of 25 and 35 week's gestation are both preterm, yet differentiation between the two is often missing in reported data, which is crucial for interpretation.

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[29] and Consolidated Standards of Reporting Trials (CONSORT)[30] statements were developed to improve scientific reporting. Several extensions of these statements have been published with additional recommendations for specialised fields of research, for example, the Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID)[31] and the Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION)[32] statement. These extensions build on the principles of STROBE and CONSORT but explicitly address additional, problematic methods or settings. There are reporting guidelines under development which are specific to child health trials (SPIRIT-C; CONSORT-C),[33] and for systematic reviews and meta-analyses (PRISMA-C; PRISMA-PC).[34] This paper aims to address the specific challenges in reporting neonatal infections, using the STROBE[29] model. If these recommendations are applied by upcoming epidemiological and interventional studies on neonatal infections, the value of new data will increase, avoiding "research waste".[35]

Aims of STROBE-NI

The purpose of these guidelines is to promote transparency, clarity and comparability of scientific reporting, specifically for neonatal infection research. We focus on observational studies (although many elements will be true for other study designs), and include detailed consideration of aetiological (bacterial, viral and fungal) data. Through improved reporting, we aim to facilitate reliable comparison of emerging newborn infection data across settings worldwide, and the synthesis of robust evidence to inform public health interventions. Our objectives were to assess current reporting components for neonatal infection in the literature, to list all potential reporting items, and to use an online survey and expert consensus process to develop the 'Strengthening Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI)' checklist. The STROBE-NI checklist is intended to guide authors, reviewers, publishers and funders of neonatal infection studies. We focussed on parameters that are not included in STROBE, or other extensions.

Development of the STROBE-NI checklist

The STROBE-NI checklist was developed using recommended methods.[36] The participants, processes and outputs are illustrated in Figure 1. Literature searches were undertaken to identify highly cited neonatal infection publications from different regions worldwide (1996-2015), and more recent (2011-2015) articles from high impact journals (see supplementary material for literature search criteria). Additional searches were carried out for reporting guidelines relevant to neonatal infections.

Through these reviews we identified a list of 133 reporting items, which was developed into an online survey (supplementary material). Respondents were asked to comment and/or rate the importance of each item in the list by selecting either 'unnecessary', 'sometimes useful', 'important for most studies', or 'essential for all studies'. Participants were also asked to identify definitions and classifications requiring discussion and clarification. The survey was disseminated to relevant investigator groups, corresponding authors of reviewed papers, and professional infectious disease and paediatrics networks worldwide (Figure 1). 147 experts replied, from 37 countries, with more than 41% from low/middle income counties (supplementary material).

In June 2015, a group of 18 international, multi-disciplinary experts (epidemiologists, statisticians, microbiologists, paediatricians, neonatologists) met in London to examine the literature reviews, potential reporting items and survey results and to draft the structure and content of the recommendations. Recommendations were aligned with STROBE items in one draft checklist, as a topic-specific implementation[36] of the STROBE statement. The structural relationship between STROBE-NI and STROBE[29] recommendations is illustrated in Figure 2.

The draft checklist was reviewed and revised by the expert group, disseminated to survey participants, and members of networks such as the Enhancing the Quality and Transparency of Health Research (EQUATOR) network, for further review and feedback, resulting in a final STROBE-NI Checklist (Table 1)

STROBE-NI Standards

The final STROBE-NI checklist is an extension of the 22 item STROBE list, with 28 additional parameters relating to neonatal infection. This includes a suggested flow diagram for both the recruitment and follow up of mothers and newborns, for which a template is provided in Figure 3. Below, we describe the additional recommendations for STROBE-NI that are not already outlined in detail in STROBE, or other extensions.

Methods: Study design

Clinical case definitions (STROBE-NI 4·1 – 4·4)

The individual clinical signs used in clinical case definition algorithms should be detailed, (STROBE-NI 4·1), making clear whether case ascertainment was through physician diagnosis or a clinical algorithm (eg. Young Infants Clinical Signs Study Group algorithm for pSBI). Definitions of neonatal infection syndromes (pneumonia, meningitis and sepsis) are important for consistency and comparability, however, they cannot be distinguished on clinical grounds alone. Where authors are reporting case definitions of specific syndromes, microbiological and/or laboratory and/or radiological criteria for diagnosis should be stated (STROBE-NI 4·1), differentiating between probable and confirmed cases. For meningitis, the indications for lumbar puncture should be described (STROBE-NI 4·1). Case definitions should be aligned to international standards, when available and ideally be clinically validated.[26] Clinical algorithms may introduce case ascertainment bias, and potential limitations of case definitions should be discussed.

Authors should state the criteria used to differentiate between new infection episodes and relapses (STROBE-NI 4·2). For example, new episodes may be considered when clinical signs develop more than 7 days after stopping treatment, versus a relapse, with reoccurrence of clinical signs within 7 days of stopping treatment. This is important for healthcare associated infections, and these should be explicitly differentiated from community-acquired infections, with reference to an international standard definition (STROBE-NI 4·3).[37] Where relevant, specific hospital acquired infections such as ventilator associated pneumonia and central line associated bloodstream infection should be defined, and presented separately.[37] Reporting whether the observed cases were part of an outbreak (see ORION statement)[32] is essential, and the definition used for outbreaks (STROBE-NI 4·4).

Microbiological sampling (STROBE-NI 4·5)

The microbiological sampling strategy for infections should be presented (STROBE-NI 4·5), such as samples being taken from all participants, or a subset meeting a case-definition (eg pSBI). This is important given that the positive and negative predictive values of tests differ according to the prevalence in those sampled. For instance if few cases of pSBI have lumbar punctures, then cases of meningitis may not be captured. Numbers from whom samples were taken, and sample type, should be provided, including sample volume ranges for

blood cultures, or minimum sample volume, as small volumes reduce sensitivity. It should be reported whether samples were taken prior to antimicrobial administration (which reduces sensitivity of testing) (STROBE-NI 4·5).

Microbiological methods (STROBE-NI 4·6 – 4·8)

Detailed reporting of laboratory methods is essential in order to assess implications and potential biases (STROBE-NI 4·6). To assess the extent of diagnostic investigation, a list of pathogens (or types of pathogen) being tested for, or likely to be identified by the methods used, should be available (including bacteria, viruses and fungi) (STROBE-NI 4·7). For diagnostic technologies using molecular methods, details of the assay should be given, describing any control samples used to determine clinical significance of detected organisms.[38–40] Antimicrobial susceptibility testing methodology should be reported according to an international standard (eg. Clinical and Laboratory Standards Institute) reporting the susceptibilities tested, and the criteria used to determine susceptibility to each antimicrobial (STROBE-NI 4·8). For molecular analyses, methods[41] should be explained (eg. for whole genome sequencing, details of mapping to reference genomes and quality assessment of sequences). Further details are in STROME-ID.[31]

Methods: Setting

Context and denominator (STROBE-NI 5·1 – 5·2)

Where possible, preterm, stillbirth, and neonatal mortality risks or rates at the study facility are helpful contextual information (STROBE-NI 5·1). This could be presented as the annual number of deaths, preterm births and stillbirths at the health facility, with live births (including the live birth definition used) or total births at the facility as the denominator.

When considering infection acquisition, stratification into 'inborn' or 'outborn' is not specific enough to be helpful, as multiple pathways to healthcare presentation exist; 'outborn' may reflect births at home or at another facility, and 'inborn' does not differentiate between those admitted from birth, and those returning to the facility following discharge. Alternative categories are 'admitted from birth at this facility', 'referred from another facility' or 'referred from home' (STROBE-NI 5·2). If specifying place of birth as a variable, similar categories of 'born at this facility', 'born at another facility' or 'born at home' could be used.

Community studies (STROBE-NI 5·3)

Community-based studies should report the surveillance strategy, including whether active or passive, and the methods used for defining and enumerating the population. Passive surveillance may underestimate disease, especially where care seeking is low (varying from 10 to 100%),[21] and an estimate of this should be made if possible. For active surveillance, if clinical algorithms are used by community health workers visiting homes, this should be documented, including visitation schedules. Active surveillance increases case ascertainment, particularly on days when visits are made.[42] In view of variation in adherence to referral, details on referral (including time from first presentation to treatment) are necessary, as well as loss to follow-up (STROBE-NI 5·3). This could be presented in a flow diagram (Figure 3).

Facility based studies (STROBE-NI 5·4 – 5·6)

Levels of neonatal and obstetric care differ greatly. The obstetric care available,[43] including the percentage of births that occur in a facility (versus the community) and the incidence of operative delivery, should be described (STROBE-NI 5·4). Details about the level of neonatal care in place are essential, including availability of basic neonatal care (eg. resuscitation, breastfeeding practices) and if there is intensive neonatal care such as ventilation (eg. invasive, non-invasive, oxygen), indwelling catheters, intravenous fluids, staffing (eg. nurse

to patient ratio), non-microbiological investigations (eg. biochemistry, radiology) and treatment (eg. antimicrobials available) (STROBE-NI 5·5). Where relevant, specific clinical infection control measures in place (and level of adherence), may be important contextual information to understand potential routes of infection acquisition and transmission.

The microbiology laboratory should be described, including location, facilities for different sample types and capacity for conventional and/or molecular microbiology. Laboratory quality control and quality assurance measures should be reported (STROBE-NI 5·6).

Methods: Participants

Neonatal age groups (STROBE-NI 6·1)

The 'neonatal' period is defined as <28 days (i.e. day 0 to 27·99) from birth. For babies born before 37 weeks gestation, noting gestational age at birth is essential to allow age correction**.** Disaggregating neonatal data from infants and children is important due to differing risk factors, aetiologies and outcomes (STROBE-NI 6·1).[44] Timing is crucial for neonatal infections as incidence rates for pathogens, such as Group B Streptococcus, vary by day.[45] The day of birth is best termed "day 0", as used in demographic work and most epidemiological studies (STROBE-NI 6·1). Time limits vary as to when 'day 0' becomes 'day 1' (eg. at midnight, or 24h after birth), and the method used should be stated.[4]

Methods: Variables

Clinical significance of pathogens (STROBE-NI 7·1)

Authors should be explicit about the clinical significance of the organisms detected. This may vary across settings (particularly organisms associated with indwelling devices, eg. coagulase negative staphylococci)[46] and the rationale for determining clinical significance should be stated, including control data, if available.[38–40] Publishing comprehensive lists of detected organisms, by sample type (eg. cerebrospinal fluid, blood), categorised as clinically significant, probably significant and clinically non-significant (the preferred term to "contaminant") are encouraged (STROBE-NI 7·1); as criteria for clinical significance may change over time.

Results: Participants

Flow diagram (STROBE-NI 13·1)

Figure 3 illustrates how the flow of eligibility, recruitment, sampling and diagnosis can be mapped in neonatal infection studies, including mothers and neonates (STROBE-NI 13·1).

Results: Descriptive data *(STROBE-NI 14·1 – 14·4)*

Maternal infections, and risk factors for infection, are important to report as maternal infections may result in vertical transmission and early onset neonatal infections, or stillbirth.[47,48] Results of antenatal screening tests (eg. for GBS, syphilis, HIV) when done, and risk factors at delivery (eg. prolonged rupture of membranes (>18h) fever, maternal urinary tract infection) (STROBE-NI 14·1), are important for identifying high risk groups and informing interventions.[49]

Neonatal characteristics, including sex, postnatal and gestational age categories (e.g. <28 weeks; 28 – <32 weeks; 32 – <37 weeks; ≥37 weeks)[50], birth weight categories (e.g. <=1500 grams; 1501-2500 grams; >2500 grams), place of birth (see above) and mode of feeding should be described, with ranges and medians stated for each numeric variable (STROBE-NI 14·2). Co-morbidities (eg. neonatal encephalopathy) should be reported, including any exclusion from analysis (STROBE-NI 14·2). Reporting of individual clinical signs is

encouraged (STROBE-NI 14·3),[8] allowing comparison with other studies and may be helpful in refining diagnostic algorithms.[2]
Details of treatment given before and after enrolment are important (STROBE-NI 14·4). Serum antimicrobial testing has shown that parents under-report antimicrobial administration;[22] and results of testing are preferable to report. Use of intrapartum antibiotic prophylaxis and its indication (eg. maternal risk factors versus positive GBS screening)[51] should be reported to inform interpretation of culture results (STROBE-NI 14·4).

Results: Outcome data

Microbiological results (STROBE-NI 15·1 – 15·2)

Microbiological results should be reported in the context of participants recruited, and the number and type of samples taken (STROBE-NI 15·1-2). For example, the number of those meeting clinical criteria for diagnostic lumbar puncture should be provided, as well as the cerebrospinal fluid results. The number and proportion of microbiologically proven clinical infections should be given, and incorporated within a flow diagram (Figure 3) (STROBE-NI 15·2).

Reporting all organisms detected (eg. as an appendix), including those considered clinically non-significant, is helpful. For molecular assays in particular, reporting thresholds for detection and the organisms detected in control samples supports clinical case interpretation.[38–40] Antimicrobial susceptibility data are essential to guide future antimicrobial policy development (STROBE-NI 15·1). It is helpful to provide raw antimicrobial susceptibility test result data (eg. minimum inhibitory concentrations), which can be analysed further in the future if international standards change.

Timing of infection (STROBE-NI 15·3)

Where categorisation into 'early-onset' (e.g. within 72 hours of birth) and 'late-onset' (e.g. after 72 hours of birth) disease is used, these terms should be clearly defined (STROBE-NI 15·3). Due to the changing aetiologies of neonatal disease, reporting infections by day, for the first week after birth (days 0-6) (STROBE-NI 15·3) is more informative than dichotomous categories, and may improve understanding of early and late onset disease.[45]

Mortality (STROBE-NI 15·4) and long-term outcomes

Mortality and other serious clinical outcomes should be reported (STROBE-NI 15·4), ideally by day (Figure 3). Sample size permitting, stratifying mortality by potential risk factors including sex, birthweight categories, gestational age groups,[50] infection syndromes, individual pathogens or antimicrobial resistance profiles, may highlight intervention opportunities for high risk groups.

Where studies are reporting other long-term outcomes, such as neurological impairment, an international standard approach should be used, including the timing of follow up and assessment.

Results: Main results

Incidence (STROBE-NI 16·1)

For incidence, the selection and source of the denominator should be explained (see above). For neonates it is usual to calculate incidence risk per 1000 live births (STROBE-NI 16·1), as the time period (28 days) is short.

Discussion: Limitations

Bias (STROBE-NI 19·1)

The first 12-48 hours after birth are critical, as the survival curve is steep,[4] and infectious aetiologies differ later after birth. These aetiologies may be systematically underestimated if there is recruitment bias arising from lack of access to care, or death before accessing care (STROBE-NI 19·1).[44] Identifying possible causes of recruitment and other biases in studies is therefore essential in interpreting findings.

For all denominators used, authors should state the source (eg. hospital data or census / registration data), commenting on possible bias (STROBE-NI 19·1).

Other information: *Ethics (STROBE-NI 23·1)*

Because of ethical issues around recruitment, consent, and sampling in neonates, approaches taken must be reported, including processes for requesting consent from young mothers (minors) (STROBE-NI 23·1).[52,53]

If the time frame for sample collection and obtaining consent is limited (eg. during delivery), a staged process of consent may be appropriate, to avoid exclusion of emergency cases (and reduce recruitment bias).[54]

Implications of STROBE-NI

The STROBE-NI checklist provides a tool for researchers, funders, reviewers and publishers to improve neonatal infection data, which have specific, previously unaddressed, requirements for scientific reporting. Building on the STROBE[29] statement and its related extensions, the checklist primarily targets observational studies.[29] However, STROBE-NI checklist items should also be considered for randomised controlled trials, alongside other guideline extensions.[33,34] To our knowledge, there are no other reporting guidelines specific to neonatal health research.[34] Whilst neonatal infections are a priority starting point, future re-iterations should also address other aspects of neonatal research, as well as maternal, and stillbirth outcomes. Only recommendations for reporting acute outcomes of infection were included in this checklist. However we recognise that other important long-term outcomes, such as neurological impairment, are increasingly being assessed, and are important to include.[55] Reporting guidance for impairment outcomes after neonatal infection as well as other common neonatal complications, such as preterm birth,[56] is an area for future development.

The STROBE-NI checklist guides minimum standards for high quality reporting but is not exhaustive; and certain research objectives or contexts may necessitate other details. For instance, new technologies, such as molecular investigations,[31,38] are likely to require additional descriptors.

This list was designed to be applicable to a wide range of settings, including those with limited resources and a high neonatal infection burden. To achieve this, we sought inputs from around the world through experts, and our online survey, as well as systematic literature reviews.

Uptake of the STROBE-NI checklist depends on dissemination through global research networks and meetings, and use by journals, funders and academics. Feedback and suggestions for improvement would be welcomed, as the STROBE-NI checklist will be updated periodically. Going forward, we intend to present 'explanation and elaboration' of this guidance (to build on that included in the supplementary material), develop abstract guidance for conference submissions, and evaluate the impact of STROBE-NI, as is recommended.[36]

The STROBE-NI checklist has been developed at a critical point in time for emerging opportunities in neonatal infection research. It is a demonstration of a new commitment towards reducing the unacceptable burden of mortality and morbidity from neonatal infection, and more broadly, as part of the movement to end preventable maternal and newborn deaths, and stillbirths.[5,57–59]

Author contributions:
EJAF, ACS, SV, MS, PTH and JEL coordinated the expert group and planned the expert meeting. EJAF, ACS and SV conducted the literature reviews and compiled the initial list of potential reporting items. SV, ACS, EJAF and JEL developed the online survey. ACS, SV, MS, PTH, SS, RA, AIA, RB, KB, HC, SC, GLD, NM, JP, SQ, SW, RW and JEL participated in the expert meeting and developed the STROBE-NI checklist, chaired by MS, SS, RB, HC, SC, and JEL, and coordinated by EJAF. EJAF, ACS and JEL wrote the first draft of the manuscript. ACS, SS and JEL developed the flow diagram with feedback from RW, PTH, RA and SJS. SV, MS, PTH, RA, AIA, ZAB, RB, HC, SC, GLD, SAM, ASM, NM, JP, SQ, SJS and BJS edited and contributed to successive versions of the paper.

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Figures

Figure 1: **Development process for the STROBE-NI checklist, showing participants, process and outputs**

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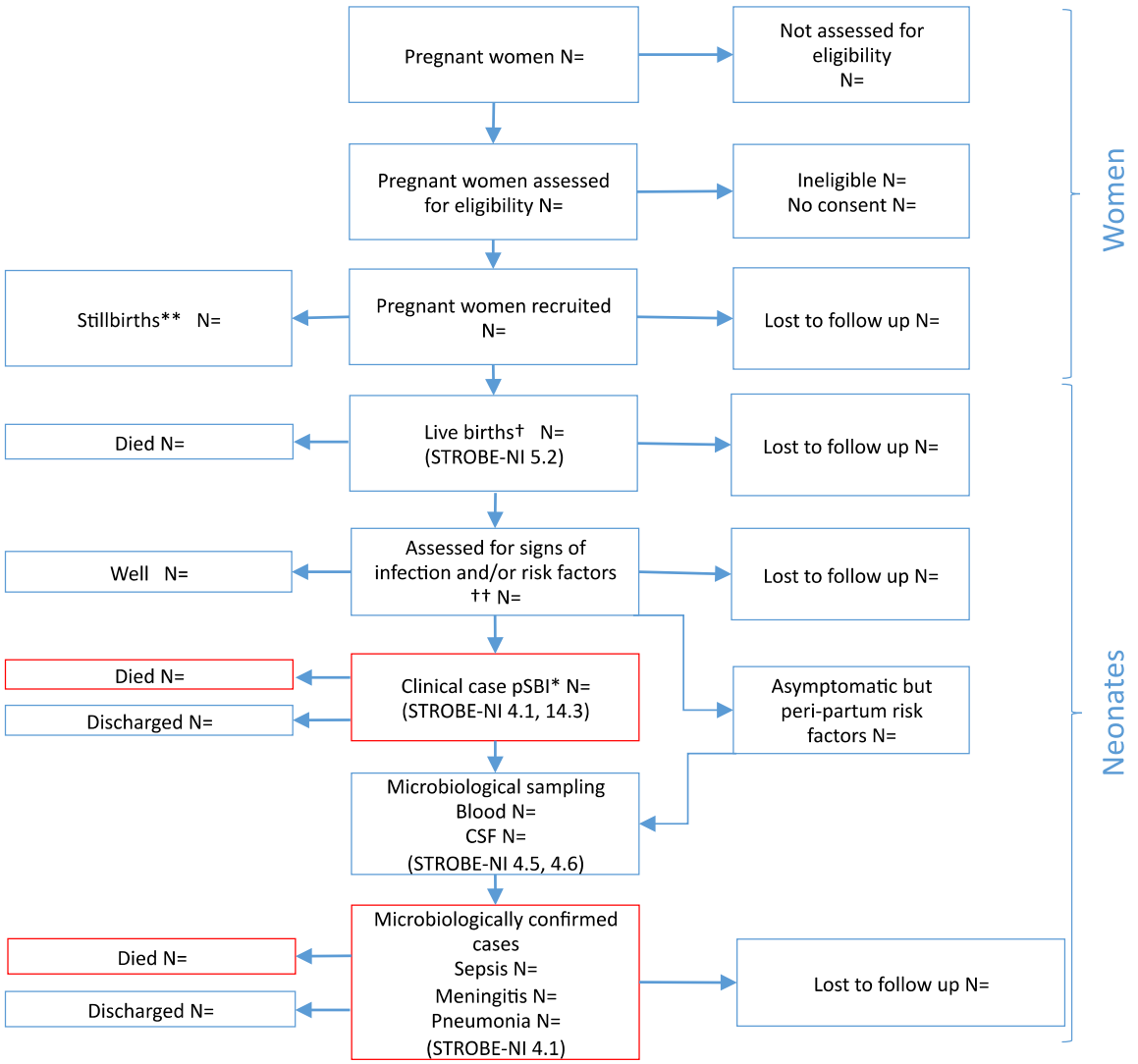
Figure 2: **Graphic showing structural relationship between STROBE[28] and STROBE-NI checklist items**

		STROBE	STROBE-NI
TITLE and ABSTRACT	Title and abstract	1(a)	
		1(b)	
INTRODUCTION	Background/rationale	2	
	Objectives	3	
METHODS	Study design	4	
			STROBE-NI-4·1
			STROBE-NI-4·2
			STROBE-NI-4·3
			STROBE-NI-4·4
			STROBE-NI-4·5
			STROBE-NI-4·6
			STROBE-NI-4·7
			STROBE-NI-4·8
	Setting	5	
			STROBE-NI-5·1
			STROBE-NI-5·2
			STROBE-NI-5·3
			STROBE-NI-5·4
			STROBE-NI-5·5
			STROBE-NI-5·6
	Participants	6(a)	
		6(b)	
	Variables		STROBE-NI-6·1
		7	STROBE-NI-7·1
	Data source/measurement	8	
	Bias	9	
	Study size	10	
	Quantitative variables	11	
	Statistical methods	12(a)	
		12(b)	
		12(c)	
		12(d)	
		12(e)	
RESULTS	Participants	13(a)	
		13(b)	
		13(c)	STROBE-NI-13·1
	Descriptive data	14(a)	STROBE-NI-14·1
			STROBE-NI-14·2
			STROBE-NI-14·3
			STROBE-NI-14·4
		14(b)	
		14(c)	
	Outcome data	15	STROBE-NI-15·1
			STROBE-NI-15·2
			STROBE-NI-15·3
			STROBE-NI-15·4
	Main results	16(a)	STROBE-NI-16·1
		16(b)	
		16(c)	
	Other analyses	17	
DISCUSSION	Key results	18	
	Limitations	19	STROBE-NI-19·1
	Interpretation	20	
	Generalisability	21	
OTHER INFORMATION	Funding	22	
	Ethics		STROBE-NI-23·1

Figure 3: **Strengthening Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI) recommended flow chart showing recruitment and participation in the study**



Give details by day where possible

*Give clinical algorithm used to define pSBI (STROBE-NI 4.1) and clinical signs for each neonate if possible (STROBE-NI 14.3)

** Give details of assessment, microbiological sampling if done.

†If live births are assessed for eligibility (rather than pregnant women), give numbers of live births assessed for eligibility and then recruited after this box.

††If neonates are assessed, for example at admission for care, give the numbers of neonates assessed and recruited. Differentiate between neonates born at home, at this facility or at another facility.

Table 1: **Strengthening Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI) Checklist: An extension of the STROBE statement for neonatal infection research**[29]

Section	Item No.	Recommendation
		TITLE AND ABSTRACT
	STROBE 1(a)	Indicate the study's design with a commonly used term in the title or abstract
	STROBE 1(b)	Provide in the abstract an informative and balanced summary of what was done and what was found
		INTRODUCTION
Background / rationale	STROBE 2	Explain the scientific background and rationale for the investigation being reported
Objectives	STROBE 3	State specific objectives, including any pre-specified hypotheses
		METHODS
Study design	STROBE 4	Present key elements of study design early in the paper
	STROBE-NI 4.1	Clearly state case ascertainment methods (eg. physician diagnosis, clinical algorithm), documenting individual clinical signs used for diagnosis of possible serious bacterial infection. Give microbiological and/or laboratory and/or radiological criteria for other infectious syndromes (eg. meningitis, sepsis, pneumonia). Include indications for clinical investigations (eg. lumbar puncture)
	STROBE-NI 4.2	Give criteria used to differentiate between new infection episodes and relapses
	STROBE-NI 4.3	For facility-based studies, indicate if the study is of community and/or hospital acquired infections (HAI), defining HAI using an international standard and presenting specific HAI clinical syndromes separately
	STROBE-NI 4.4	State whether this is an outbreak study, and if so define an outbreak, with reference to an international standard
	STROBE-NI 4.5	Describe sampling strategy (eg. clinical indication vs. routine surveillance) and sampling details, (eg. minimum volumes; timing in relation to antimicrobial administration)
	STROBE-NI 4.6	Describe conventional and/or molecular microbiological methods used, with details (eg. automation, enrichment steps), and the use of controls
	STROBE-NI 4.7	List pathogens that are likely to be identified by microbiological methods used, and criteria used to determine clinical significance
	STROBE-NI 4.8	Describe antimicrobial susceptibility tests and thresholds used, with reference to an international standard (eg. CLSI or EUCAST)
Setting	STROBE 5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
	STROBE-NI 5.1	Describe the study context in terms of incidence of neonatal mortality, stillbirth and preterm birth.
	STROBE-NI 5.2	Describe the population included eg. facility live births, referrals from home, referrals from another facility
	STROBE-NI 5.3	For community-based studies, describe care-seeking and adherence and time to referral
	STROBE-NI 5.4	For facility-based studies, describe obstetric care (basic or comprehensive), including proportion of births by caesarean section. Report annual number of live births per facility and state proportion of births in the study area that occur in hospital (vs. community)
	STROBE-NI 5.5	For facility-based studies, indicate if the facility is public or private, and give the number of health care staff and their training. Indicate the level of neonatal care available (eg. ventilatory support, indwelling catheters) and investigations available (eg. biochemistry, radiology). Report antimicrobial guidelines used for the empiric management of neonatal sepsis.
	STROBE-NI 5.6	State the laboratory location and capacity to process different sample types, and give quality control and assurance measures in place.

Participants	STROBE 6(a)	Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants
	STROBE 6(b)	Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case
	STROBE-NI 6.1	State age of participants (eg. 0-27 days defines neonates; 'day 0' as day of birth). Disaggregate neonatal data from that of older infants and from stillbirths
Variables	STROBE 7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
	STROBE-NI 7.1	State criteria used to define clinically significant organisms for each sample type
Data sources measurement	STROBE 8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	STROBE 9	Describe any efforts to address potential sources of bias
Study size	STROBE 10	Explain how the study size was arrived at
Quantitative variables	STROBE 11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	STROBE 12(a)	Describe all statistical methods, including those used to control for confounding
	STROBE 12(b)	Describe any methods used to examine subgroups and interactions
	STROBE 12(c)	Explain how missing data were addressed
	STROBE 12(d)	Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
	STROBE 12(e)	Describe any sensitivity analyses
		RESULTS
Participants	STROBE 13(a)	Report numbers of individuals at each stage of study—eg. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
	STROBE 13(b)	Give reasons for non-participation at each stage
	STROBE 13(c)	Consider use of a flow diagram
	STROBE-NI 13.1	See Figure 3 for suggested components of a flow diagram for neonatal infections
Descriptive data	STROBE 14(a)	Give characteristics of study participants (eg. demographic, clinical, social) and information on exposures and potential confounders
	STROBE-NI 14.1	Describe maternal infections (clinical or on screening, eg. GBS or HIV) or risk factors for infection (eg. PROM, peripartum fever).
	STROBE-NI 14.2	Describe key neonatal characteristics, including sex, postnatal and gestational age categories (range and median), birth weight categories (range and median), birth place, feeding (breast milk or other) and comorbidities

	STROBE-NI 14.3	Report data on occurrence of individual signs (eg. fast breathing), according to case definitions
	STROBE-NI 14.4	Give proportion of mothers and neonates with peripartum antibiotic exposure (+/- pre-admission exposure for neonates). Report details of antimicrobials (or supportive care) given during the study
	STROBE 14(b)	Indicate number of participants with missing data for each variable of interest
	STROBE 14(c)	Cohort study—Summarise follow-up time (eg. average and total amount)
Outcome data	STROBE 15	Cohort study—Report numbers of outcome events or summary measures over time Case-control study—Report numbers in each exposure category, or summary measures of exposure Cross-sectional study—Report numbers of outcome events or summary measures
	STROBE-NI 15.1	Report the number (+/- proportion) of samples microbiologically tested (including lumbar punctures for meningitis cases); the number (+/-proportion) that were positive (including thresholds for detection, where applicable); all isolates obtained (including clinically significant and non-significant); and antimicrobial susceptibilities of pathogens, where done.
	STROBE-NI 15.2	Report number (+/- proportion) of babies with microbiologically proven infection (and number of infections per baby), and include this in the flow chart (see Figure 3).
	STROBE-NI 15.3	Report infections by day, for days 0-6. State age categories, if used, defining 'early-onset' and 'late-onset' infection (eg. <72 hours and ≥ 72 hours respectively).
	STROBE-NI 15.4	Report deaths and any sub-analyses by risk groups
Main results	STROBE 16(a)	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg. 95% confidence interval). Make clear which confounders were adjusted for and why they were included
	STROBE 16(b)	Report category boundaries when continuous variables were categorized
	STROBE 16(c)	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
	STROBE-NI 16.1	For incidence, give risk per 1000 live births, or if alternative denominator used (eg. total births or bed days), define this clearly
Other analyses	STROBE 17	Report other analyses done—eg. analyses of subgroups and interactions, and sensitivity analyses
		DISCUSSION
Key results	STROBE 18	Summarise key results with reference to study objectives
Limitations	STROBE 19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
	STROBE-NI 19.1	Discuss sources of recruitment bias, particularly regarding the period of time shortly after birth. State source of denominator data and discuss possible related biases
Interpretation	STROBE 20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	STROBE 21	Discuss the generalisability (external validity) of the study results
		OTHER INFORMATION
Funding	STROBE 22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
Ethics	STROBE-NI 23.1	Report any ethical considerations, including the recruitment of young mothers (minors), and the consent process for early recruitment of neonates after delivery. Provide details of research ethics approval.

SUPPLEMENTARY MATERIAL

Strengthening Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI): An extension of the STROBE statement for neonatal infection research

Contents

SECTION 1: Literature Review and Preliminary List

1.A. Search strategy and selection criteria for neonatal infection articles

Search terms:

[All Fields] neonat* OR newborn* OR newborn infant* OR young infant* AND
[All Fields] infect* OR sepsis OR meningitis OR pneumonia OR tetanus OR omphalitis

Inclusion criteria:

- Papers presenting primary microbiological data on infections in neonates (0-27 days), including studies of infections in children who present separate neonatal data

Exclusion criteria:

- Studies with data **only** from very high risk neonatal populations (eg. very low birth weight, extremely premature)
- Studies focussing on HIV, TB, syphilis, malaria or other congenital infections

Search 1: Literature from seven Global Burden of Disease region

- SCOPUS database (which gives citation data)
- 1996 to February 2015 (last search 27th February 2015)
- Searches for literature with author affiliations to institutions in countries within each of seven Global Burden of Disease Regions[1] *and* presenting primary data from a country in that region
    i. Central Europe, Eastern Europe, and Central Asia
    ii. Latin American and Caribbean
    iii. North Africa and Middle East
    iv. South Asia
    v. Southeast Asia, East Asia and Oceania
    vi. Sub-Saharan Africa
    vii. High income countries – Asia-Pacific, North America, Western Europe, Australasia,
    viii. Southern Latin America
- All studies from each region ranked by number of citations per year
- Three studies, from each region, with the highest number of citations per year selected for review

Search 2: Recent literature from high impact infectious diseases and paediatric journals

(excluding journals not publishing neonatal infection articles eg. Journal of the American Academy of Child & Adolescent Psychiatry)

- Pubmed database
- 2011 to March 2015 (last search 15th March 15)
- Highest impact infectious disease journals searched:
    i. Lancet Infectious Diseases
    ii. Clinical Infectious Diseases
    iii. Emerging Infectious Diseases
    iv. Journal of Infectious Diseases
- Highest impact paediatric journals searched:
    i. Pediatrics
    ii. Archives of Pediatrics & Adolescent Medicine
    iii. Archives of Disease in Childhood – Fetal and Neonatal Edition
    iv. Journal of Pediatrics

Reference:

1 Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **6736**. DOI:10.1016/S0140-6736(15)60692-4.

1.B. Search results – papers selected for review

Table 1: Neonatal infection literature from seven global regions

Super-GBD Region	Title	Country	Authors	Year	Journal	Citations per year
South Asia	Population-Based Incidence and Etiology of Community-Acquired Neonatal Bacteremia in Mirzapur, Bangladesh: An Observational Study	Bangladesh	Darmstadt G.L., Saha S.K., Choi Y., Arifeen S.E., Ahmed N.U., Bari S., Rahman S.M., Mannan I., Crook D., Fatima K., Winch P.J., Seraji H.R., Begum N., Rahman N., Islam M., Rahman A., Black R.E., Santosham M., Sacks E., Baqui A.H.	2009	Journal of Infectious Diseases	4.8
	Multidrug resistant neonatal sepsis in Peshawar, Pakistan	Pakistan	Rahman S., Hameed A., Roghani M.T., Ullah Z.	2002	Archives of Disease in Childhood: Fetal and Neonatal Edition	4.0
	Early onset neonatal sepsis	India	Chacko B., Sohi I.	2005	Indian Journal of Pediatrics	3.9
Latin America & The Caribbean	A 10-year prospective surveillance of nosocomial infections in neonatal intensive care units	Brazil	Couto R.C., Carvalho E.A.A., Pedrosa T.M.G., Pedroso E.R., Neto M.C., Biscione F.M.	2007	American Journal of Infection Control	9.1
	Nosocomial infections in a neonatal intensive care unit: Incidence and risk factors	Brazil	Nagata E., Brito A.S.J., Matsuo T.	2002	American Journal of Infection Control	5.3
	Reduction in colonization and nosocomial infection by multiresistant bacteria in a neonatal unit after institution of educational measures and restriction in the use of cephalosporins	Brazil	Calil R., Marba S.T.M., von Nowakonski A., Tresoldi A.T.	2001	American Journal of Infection Control	4.1
North Africa & The Middle East	Neonatal nosocomial sepsis in a level-III NICU: Evaluation of the causative agents and antimicrobial susceptibilities	Turkey	Yalaz M., Cetin H., Akisu M., Aydemir S., Tunger A., Kultursay N.	2006	Turkish Journal of Pediatrics	3.3
	Changing spectrum of neonatal omphalitis	Oman	Sawardekar K.P.	2004	Pediatric Infectious Disease Journal	3.0
	A case control study of neonatal sepsis: Experience from Saudi Arabia	Saudi Arabia	Dawodu A., Al Umran K., Twum-Danso K.	1997	Journal of Tropical Pediatrics	1.4
	Nosocomial infection in a neonatal intensive care unit: A prospective study in Taiwan	Taiwan	Su B.-H., Hsieh H.-Y., Chiu H.-Y., Lin H.-C., Lin H.-C.	2007	American Journal of Infection Control	4.9

Southeast Asia, East Asia & Oceania	Neonatal enterovirus infections: Emphasis on risk factors of severe and fatal infections	Taiwan	Lin T.-Y., Kao H.-T., Hsieh S.-H., Huang Y.-C., Chiu C.-H., Chou Y.-H., Yang P.-H., Lin R.-I., Tsao K.-C., Hsu K.-H., Chang L.-Y.	2003	Pediatric Infectious Disease Journal	4.3
	Identification of febrile neonates unlikely to have bacterial infections	Taiwan	Chiu C.-H., Lin T.-Y., Bullard M.J.	1997	Pediatric Infectious Disease Journal	2.4
Sub-Saharan Africa	Viral etiology of severe pneumonia among Kenyan infants and children	Kenya	Berkley J.A., Munywoki P., Ngama M., Kazungu S., Abwao J., Bett A., Lassauniere R., Kresfelder T., Cane P.A., Venter M., Scott J.A.G., Nokes D.J.	2010	JAMA	21.4
	Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza- Tanzania	Tanzania	Kayange N., Kamugisha E., Mwizamholya D.L., Jeremiah S., Mshana S.E.	2010	BMC Pediatrics	8.2
	Bacteremia in febrile Malawian children: Clinical and microbiologic features	Malawi	Walsh A.L., Phiri A.J., Graham S.M., Molyneux E.M., Molyneux M.E.	2000	Pediatric Infectious Disease Journal	7.4
High Income Countries	Bacterial meningitis in the United States in 1995	USA	Schuchat A., Robinson K., Wenger J.D., Harrison L.H., Farley M., Reingold A.L., Lefkowitz L., Perkins B.A.	1997	New England Journal of Medicine	46.9
	Epidemiology of invasive group B streptococcal disease in the United States, 1999-2005	USA	Phares C.R., Lynfield R., Farley M.M., Mohle-Boetani J., Harrison L.H., Petit S., Craig A.S., Schaffner W., Zansky S.M., Gershman K., Stefonek K.R., Albanese B.A., Zell E.R., Schuchat A., Schrag S.J.	2008	JAMA - Journal of the American Medical Association	41.0
	Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis	USA	Schrag S.J., Zywicki S., Farley M.M., Reingold A.L., Harrison L.H., Lefkowitz L.B., Hadler J.L., Danila R., Cieslak P.R., Schuchat A.	2000	New England Journal of Medicine	39.9
Central Europe, Eastern Europe & Central Asia	Use of an alcohol-based hand rub and quality improvement interventions to improve hand hygiene in a Russian neonatal intensive care unit	Russia	Brown S.M., Lubimova A.V., Khrustalyeva N.M., Shulaeva S.V., Tekhova I., Zueva L.P., Goldmann D., O'Rourke E.J.	2003	Infection Control and Hospital Epidemiology	4.9
	Etiology of neonatal blood stream infections in Tbilisi, Republic of Georgia	Georgia	Macharashvili, N., Kourbatova, E., Butsashvili, M., Tsertsvadze, T., McNutt, L.-A., Leonard, M.K.	2009	International Journal of Infectious Diseases	3.3
	Group B streptococcus colonization of pregnant women and their children observed on obstetric and neonatal wards of the University hospital in krakow, Poland	Poland	Strus, M., Pawlik, D., Brzychczy-Włoch, M., Gosiewski, T., Rytlewski, K., Lauterbach, R., Heczko, P.B.	2009	Journal of Medical Microbiology	2.7

Table 2: Recent literature from high impact journals

	Title	Authors	Year	Journal	Journal Impact Factor
Infectious Disease Journals	Incidence of invasive group B streptococcal disease and pathogen genotype distribution in newborn babies in the Netherlands	Bekker V., Bijlsma M.W., van de Beek D., Kuijpers T.W., van der Ende A.	2014	Lancet ID	19.446
	Neonatal invasive haemophilus influenzae disease in England and Wales: Epidemiology, clinical characteristics, and outcome	Collins S., Litt D.J., Flynn S., Ramsay M.E., Slack M.P.E., Ladhani S.N.	2015	Clinical Infectious Diseases	9.416
	Incidence, etiology, and outcome of bacterial meningitis in infants aged <90 days in the United Kingdom and Republic of Ireland: Prospective, enhanced, national population-based surveillance	Okike I.O., Johnson A.P., Henderson K.L., Blackburn R.M., Muller-Pebody B., Ladhani S.N., Anthony M., Ninis N., Heath P.T.	2014	Clinical Infectious Diseases	7.327
Paediatric Journals	Early onset neonatal sepsis: The burden of group B streptococcal and E. coli diseases continues	Stoll B., Hansen N.I., Sanchez P.J., Faix R.G., Poindexter B.B., Van Meurs K.P., Bizzaro M.J., Goldberg R.N., Frantz I.D., Hale E.C., Shankaran S., Kennedy K., Carlo W.A., Watterberg K.L., Bell E.F., Walsh M.C., Schibler K., Laptook A.R., Shane A.L., Schrag S.J., Das A., Higgins R.D.	2011	Pediatrics	5.297
	Group B streptococcus late-onset disease: 2003-2010	Beradi A., Rossi C., Lugli L., Creti R., Reggiani M.L.B., Lanari M., Memo L., Pedna M.F., Venturelli C., Perrone E., Ciccia M., Tridapalli E., Piepoli M., Contiero R., Ferrari F.	2013	Pediatrics	5.297
	Trends in candida central line-associated bloodstream infections among NICUs, 1999-2009	Chitnis A.S., Magill S.S., Edwards J.R., Chiller T.M., Fridkin S.K., Lessa F.C.	2012	Pediatrics	5.297
	Changing epidemiology of bacteremia in infants aged 1 week to 3 months	Greenhow T.L., Hung Y-Y., Herz A.M	2012	Pediatrics	5.297
	Neonatal infections in China, Malaysia, Hong Kong and Thailand	Al-Taiar A., Hammoud M.S., Cuiqing L., Lee J.K., Lui K.M., Nakwan N., Isaacs D.	2013	Arch Dis Child: Fe Neonat Ed	3.861
	Seasonal variations in healthcare-associated infection in neonates in Canada.	Shah P.S., Yoon W., Kalapesi Z., Bassil K., Dunn M., Lee S.K.	2013	Arch Dis Child: Fe Neonat Ed	3.861
	Multi-drug resistant gram negative bacilli causing early neonatal sepsis in India	Viswanathan R., Singh A.K., Basu S., Chatterjee S., Sardar S., Isaacs D.	2012	Arch Dis Child: Fe Neonat Ed	3.861
	Neonatal infections in England: The NeonIN surveillance network	Vergnano S, Menson E, Kennea N, Embleton N, Russell AB, Watts T, Robinson MJ, Collinson A, Heath PT	2011	Archives of Disease in Childhood: Fetal and Neonatal Ed.	3.861

1.C. Preliminary ist of potential reporting items

Table 3. List of 133 potential reporting items derived from literature review			
Study Overview	1. Study purpose	a. Aim	
		b. Contribution to existing research	
		c. Primary outcomes	
		d. Secondary outcomes	
	2. Study design	a. Study type or description of surveillance network	(eg. cross-sectional, surveillance, case-control)
		b. Prospective vs. retrospective	
		c. Data collection dates (day, month, year)	
		d. Sample size calculations	
		e. Inclusion criteria	
		f. Exclusion criteria	
		g. Case finding method	(eg. systematic screening; active vs. passive surveillance)
		h. Method of randomisation	
		i. Ethical approval (name of board (s)/institution(s))	
		j. Funding source(s)	
		k. Source of demographic data	
	3. Recruitment	a. Number of eligible subjects	
		b. Number of subjects enrolled	
		c. Number of excluded subjects	
		d. Proportion of study subjects sampled	
		e. Description of comparison groups	(eg. size of groups; characteristics)
		f. Consent process	
	4. Statistical Methods	a. Software used	
		b. Descriptive statistics methods	
		c. Modelling methods	
Setting	5. Study site context	a. Facility or community based	
		b. Size of study site (catchment area or total population)	
		c. Annual number of live births in study catchment area	
		d. Neonatal mortality risk (per 1000 live births) in study area	
		e. Stillbirth risk (per 1000 births) in study area	
		f. Source of population denominator	(eg. vital registration or census data)
		g. Climate or seasonal change, where relevant	
		h. Healthcare staff (grade/qualification) looking after study patients	(eg. Community Health Workers, clinical officers, medical officers, paediatricians)
		i. Training (study specific) conducted	(eg. clinical algorithm to diagnose clinical possible severe bacterial infection)
		j. Geographical location	
		k. Endemic diseases	(eg. malaria)
		l. HIV testing strategy	
		m. Vaccination schedule	
		n. Vaccination coverage	
		o. Climate	(eg. seasonal rainfall)
	6. Health facility (where applicable)	a. Type of facility and which ward(s)/unit(s) included	(eg. First level health facility, district, referral hospital; neonatal intensive care unit, paediatric ward)
		b. Criteria for admission (+/- ward)	
		c. Annual admissions (+/- ward)	
		d. Level of care available	(eg. Level of respiratory support available: invasive ventilation, CPAP, oxygen, nil)
		e. Patients requiring ventilation, central lines, TPN and surgery, expressed as patient days (where relevant)	(eg. total central-line days)
		f. Cot occupancy	
		g. Infection control measures, availability of local guidelines, and adherence	(eg. space between cots, hand washing)
		h. Availability and use of kangaroo mother care	
		i. Size of health facility	
		j. Annual number of live births at the health facility	
		k. Annual number of admissions at the health facility	

		l. Outbreaks that occurred during the study	
		m. Classification of ventilation requirement	(eg. based on peak requirement vs. requirement at the time of data collection)
Clinical Information	7. Maternal demographic and clinical information	a. Maternal age	
		b. Parity	
		c. Mode of delivery	(eg. vaginal vs. elective caesarean vs. emergency caesarean)
		d. Complications during pregnancy / birth	(eg. Prolonged Rupture Of Membranes)
		e. Recent maternal illness	(eg. fever, UTI)
		f. Maternal co-morbidities	(eg. Anaemia, malaria)
		g. Definitions used for maternal co-morbidities	
		h. Antenatal screening for infections	(eg. GBS, HIV, syphilis, Hep B)
	8. Newborn demographic and clinical information	a. Sex	
		b. Postnatal age range (and mean / median) of study participants	(in hours or days)
		c. Time between admission/birth and infection	
		d. Gestational age range (and median) of study participants, including method of assessment and criteria used to define 'preterm' / 'very preterm'	
		e. Birth weight range (and mean / median) of study participants, including criteria used to define 'low birth weight' / 'very low birth weight'	
		f. Place of birth, defining terms such as 'inborn' and 'outborn'	
		g. Newborn comorbidities	(eg. congenital malformations, HIV)
		h. Definitions used for newborn comorbidities	
		i. Prognostic scores	(eg. 10 minute Apgar score, CRIB score)
	9. Clinical assessment	a. Physical examination and whether consistent	
		b. Blood tests other than culture	(eg. FBC)
		c. Measurement of vital signs	(eg. pulse oximetry, temperature)
		d. Radiological investigations	(eg. CXR)
		e. Method of documentation of case reports	(eg. standard data collection forms)
	10. Sampling strategy	a. Indication for sample collection	(eg. clinically indicated vs. routine surveillance)
		b. Sample collection method	(eg. whether aseptic technique used; clean catch vs. catheter for urine collection)
		c. Number of samples collected (from each subject)	
		d. Volume of sample collected	
		e. Methods for transfer/storage of clinical samples	
	11. Treatment	a. General case management	(eg. admission, IV fluid administration)
		b. Local empirical antimicrobial policy	
		c. Antimicrobial point prevalence survey data	
	12. Definitions of cases and denominators	a. Infectious syndromes definitions	(eg. sepsis, pneumonia, meningitis);
		b. Culture-proven infection definitions	
		c. HAI cases and outbreaks, definitions and duration of episode	(eg. criteria for HABSI, CLABSI);
		d. 'Early-onset' and 'late-onset' infection definitions	
		e. Denominator for incidence / mortality	(eg. patient days, live births, admissions)
		f. Stillbirth definitions, including subgroups	(eg. intrapartum (fresh) or Antepartum (macerated) stillbirth
		g. Morbidity or long-term impairment definitions	(eg. neurodisability)
	13. Antimicrobial use	a. Prior administration of antimicrobial (or anti-fungal) agents in the newborn, including type and timing and whether serum testing was done	
		b. Prior maternal use of antimicrobials (recent antenatal or intrapartum), including type and timing and whether for treatment or prophylaxis	
		c. Indications / rationale for antimicrobial use	(eg. empirical antibiotic policy)
		d. Number (+/- proportion) of study subjects who received antimicrobials, and type	(eg. proportion who received gentamicin or meropenem)
		e. Route, dose (per kg per day) and durations of antimicrobial administration	(eg. oral, intramuscular, intravenous)
Microbiology	14. Context	a. Location, description, and any accreditation of laboratory	
		b. Samples taken for culture, including number, type and collection methods	

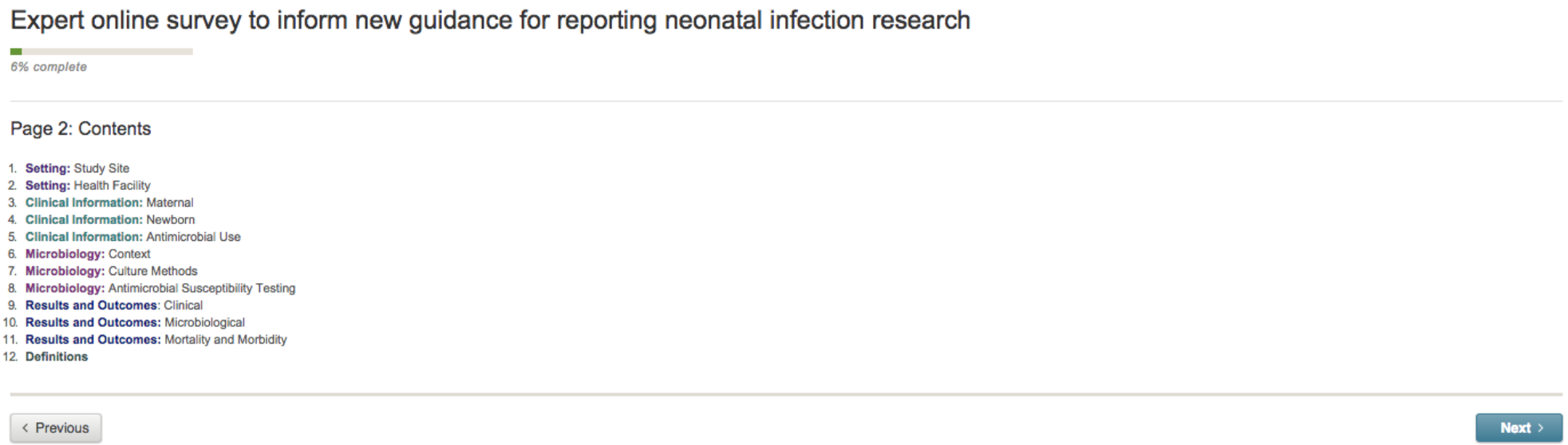
		c. Isolates defined as contaminants	
		d. Quality control and validation	(eg. whether any samples were externally validated; sensitivity or specificity of testing)
	15. Microbiological methods	a. Process for dealing with polymicrobial cultures	
		b. Conventional or molecular	
		c. Broth or direct plating	
		d. Gram staining or other method used	
		e. Method(s) of pathogen identification, including culture/sub-culture methods, automated or manual	(eg. biochemical testing, VITEK)
		f. Methods of DNA extraction, PCR and whole genome sequencing, including manufacturer of equipment used (where applicable))	(eg. quantitative, real-time, multiplex, 16s/18s, high throughput genome sequencing)
		g. Whether point of care tests were used and the type/brand	
	16. Antimicrobial susceptibility testing	a. Antimicrobial susceptibility testing methods	
		b. Antimicrobial testing standards	(eg. disc diffusion, e-test, MIC)
		c. Drugs tested	(eg. EUCAST/CLSI)
		d. Mechanisms of resistance tested for	
		Whether point of care tests were used and the type/brand	
Results & Outcomes	17. Microbiological results	a. Number (+/- proportion(s)) of positive cultures	
		b. Number (+/- proportion(s)) of isolates/pathogens	(eg. group B strep., klebsiella sp.)
		c. Number (+/-proportion(s)) of isolates susceptible, intermediate or resistant to each antimicrobial	(eg. PACCS, drug/bug combinations)
		d. Number (+/- proportion) of isolates classified as contaminants	
		e. Number (+/- proportions(s)) of isolates that were gram positive vs. gram negatives	
		f. Time between admission and positive culture	
	18. Clinical results	a. Number (+/- proportion) of babies meeting clinical case definition criteria	(eg. number with pSBI, pneumonia, meningitis)
		b. Number (+/- proportion) of babies with culture-proven infection	
		c. Number (+/- proportion(s)) of babies meeting criteria for hospital-acquired infection	(eg. HABSI, CLABSI)
		d. Incidence of infection cases (as per defined clinical and/or microbiological criteria)	(eg. per 1000 patient days, live births, admissions)
		e. Number (+/- proportion(s)) and/or incidence of cases by risk factors	(eg. by gestational age, postnatal age, birth weight)
		f. Trends in incidence risk	
	19. Mortality and morbidity	a. Overall mortality and/or case fatality risk, including timing	(eg. at 7 and 28 days)
		b. Subgroup mortality or CFR analysis by pathogen	(eg. GBS, E.Coli; resistant vs. sensitive)
		c. Subgroup mortality of CFR analysis by infection syndrome	(eg. sepsis vs. meningitis)
		d. Subgroup mortality or CFR analysis by risk group	(eg. by postnatal / gestational age, birth weight)
		e. Number (+/-proportion(s)) of stillbirths	(eg. of intrapartum vs antepartum stillbirths)
		f. Morbidity outcomes	(eg. long term neurological impairment)
		g. Morality trends	(eg. over months, years)
	20. Other	a. Estimates of burden	
		b. Cost analysis	
		c. Sources of recruitment bias	
		d. Sources of information bias	
		e. Factors affecting generalizability of results	

SECTION 2: Survey to rate potential reporting items
2.A Countries of survey respondents

Table 4.			n	% of total
Africa	Kenya		5	3.6%
	Nigeria		3	2.1%
	Ethiopia		2	1.4%
	Mozambique		1	0.7%
	Malawi		3	2.1%
	South Africa		4	2.9%
	Gambia		1	0.7%
	Egypt		1	0.7%
	Republic of Congo		1	0.7%
		Sub Total	21	15.0%
Asia	Cambodia		1	0.7%
	Bangladesh		2	1.4%
	India		22	15.7%
	Pakistan		2	1.4%
	Thailand		1	0.7%
	Hong Kong		1	0.7%
	Nepal		1	0.7%
		Sub Total	30	21.4%
North America	USA (see list of states)		27	19.3%
	Canada		1	0.7%
		Sub Total	28	20.0%
Europe	France		4	2.9%
	UK		29	20.7%
	Switzerland		4	2.9%
	Greece		4	2.9%
	Italy		3	2.1%
	Poland		1	0.7%
	Estonia		2	1.4%
	Netherlands		1	0.7%
		Sub Total	48	34.3%
Middle East	Qatar		1	0.7%
	UAE		1	0.7%
	Turkey		1	0.7%
	Oman		1	0.7%
		Sub Total	4	2.9%
Latin America	Peru		1	0.7%
	Venezuela		1	0.7%
	Guatemala		1	0.7%
	Brazil		2	1.4%
	Argentina		1	0.7%
		Sub Total	5	4.3%

Australasia	Australia	3	2.1%
	New Zealand	1	0.7%
	Sub Total	4	2.9%
(USA states)	Washington DC	4	2.9%
	Washington State	1	0.7%
	Massachusetts	4	2.9%
	New York	1	0.7%
	Indiana	1	0.7%
	Maryland	2	1.4%
	Georgia (US)	2	1.4%
	North Carolina	3	2.1%
	New Jersey	1	0.7%
	Ohio	2	1.4%
	Texas	2	1.4%
	Missouri	1	0.7%
	Philadelphia	1	0.7%
	Colorado	1	0.7%
	California	1	0.7%
	Sub Total	27	19.3%
	Number with country data	141	
	Number without country data	6	
	Total respondents	147	
	Total countries	37	

2.B. Survey Tool



Bristol Online Surveys: www.onlinesurveys.ac.uk

Q1 - Setting: Study Site

1 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Please select at least 9 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Facility or community based study	☐	☐	☐	☐	_
Size of study site catchment area or total population	☐	☐	☐	☐	_
Annual number of live births in study catchment area	☐	☐	☐	☐	_
Neonatal mortality rate in study area	☐	☐	☐	☐	_
Preterm birth rate in study area	☐	☐	☐	☐	_
Stillbirth rate in study area	☐	☐	☐	☐	_
Source of population denominator	☐	☐	☐	☐	eg. source of vital registration or survey data
Climate or seasonal change during study, where relevant	☐	☐	☐	☐	_
Type / grade and number of healthcare staff looking after study patients	☐	☐	☐	☐	eg. community health workers, neonatal nurses, paediatricians; nurse to patient ratio
Study specific training conducted	☐	☐	☐	☐	eg. clinical algorithm to diagnose possible bacterial infections
Obstetric care provided	☐	☐	☐	☐	eg. trained or untrained birth attendant; obstetric practices, infection control practices in the delivery room, availability of antenatal steroids

a Comments

Q2 - Setting: Health Facility

2 How important is it to report the following items in neonatal infection studies?

Please don't select more than 1 answer(s) per row.

Please select at least 8 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Type of facility and which ward(s)/unit(s) included	☐	☐	☐	☐	eg. first level health centres, district hospitals, referral hospital; neonatal intensive care unit, paediatric ward; private, public
Criteria for admission to the health facility (+/- ward)	☐	☐	☐	☐	-
Annual number of admissions to health facility (+/- ward)	☐	☐	☐	☐	_
Level of neonatal care available	☐	☐	☐	☐	eg. level of respiratory support offered: mechanical ventilation, continuous positive airway pressure, oxygen, none
Number of patients requiring interventions such as ventilation, central lines, TPN and surgery, expressed as patient days	☐	☐	☐	☐	_
Average cot occupancy rates	☐	☐	☐	☐	_
Infection control measures and adherence (including the delivery room)	☐	☐	☐	☐	eg. space between cots, audit data on hand washing
Availability and use of kangaroo mother care	☐	☐	☐	☐	_

a Comments

Q3 - Clinical Information: Maternal

3 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Please select at least 7 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Maternal age	☐	☐	☐	☐	–
Parity	☐	☐	☐	☐	–
Mode of delivery	☐	☐	☐	☐	eg. vaginal vs. elective caesarean vs. emergency caesarean
Complications during pregnancy / delivery	☐	☐	☐	☐	eg. prolonged or preterm rupture of membranes
Recent maternal illness	☐	☐	☐	☐	eg. fever, urinary tract infection
List of maternal comorbidities	☐	☐	☐	☐	eg. anaemia, malaria
Antenatal screening for infections	☐	☐	☐	☐	eg. GBS, HIV, syphilis, Hep B

a Comments

Q4 - Clinical Information: Newborn

4 How important is it to report the following items in neonatal infection studies?

Please don't select more than 1 answer(s) per row.

Please select at least 10 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Sex	☐	☐	☐	☐	_
Postnatal age range (and mean / median) of study participants (in hours or days)	☐	☐	☐	☐	_
Timing of infection, including proportion of cases occurring on the first day of life that were captured	☐	☐	☐	☐	_
Gestational age range (and median) of study participants, including method of assessment	☐	☐	☐	☐	_
Birth weight range (and mean / median) of study participants	☐	☐	☐	☐	_
Place of birth	☐	☐	☐	☐	eg. facility vs. home births; 'inborn' or 'outborn'
List of comorbidities	☐	☐	☐	☐	eg. congenital malformations, HIV
Prognostic scores	☐	☐	☐	☐	eg. 10 minute Apgar score, CRIB score
Methods of clinical assessment including examination performed, vital signs, blood tests (other than culture) and radiological investigations	☐	☐	☐	☐	eg. FBC, inflammatory markers
Supportive care available	☐	☐	☐	☐	eg. intravenous fluid administration, nasogastric feeds, phototherapy
Follow up period	☐	☐	☐	☐	eg. to discharge, to 28 days

a Comments

Q5 - Clinical Information: Antimicrobial Use

5 How important is it to report the following items in neonatal infection studies?

Please don't select more than 1 answer(s) per row.

Please select at least 5 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Prior administration of antimicrobials to the newborn, including type and timing	☐	☐	☐	☐	_
Use of maternal intrapartum antibiotic prophylaxis	☐	☐	☐	☐	_
Indications / rationale for antimicrobial use	☐	☐	☐	☐	eg. empirical antibiotic policy or criteria for starting antibiotics
Number (+/- proportion) of study subjects who received antimicrobials, and type	☐	☐	☐	☐	eg. proportion who received gentamicin or meropenem
Route, dose and duration of antimicrobial administration	☐	☐	☐	☐	eg. oral, intramuscular, intravenous

a Comments

Q6 - Microbiology: Context

6 How important is it to report the following items in neonatal infection studies?

Please don't select more than 1 answer(s) per row.

Please select at least 3 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Location and description, any accreditation of laboratory	☐	☐	☐	☐	–
Samples taken for culture, including type and collection methods	☐	☐	☐	☐	eg. blood or CSF; number and volume taken from each baby
Reason for sample collection	☐	☐	☐	☐	eg. routine surveillance, study requirement, clinical indication
Timing of sample collection in relation to antimicrobial administration	☐	☐	☐	☐	eg. samples taken before or after starting antibiotics
Quality control and validation	☐	☐	☐	☐	eg. whether samples were externally validated; sensitivity or specificity of testing

a Comments

Q7 - Microbiology: Culture Methods

7 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Please select at least 5 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Whether conventional or molecular methods used	☐	☐	☐	☐	_
Culture incubation	☐	☐	☐	☐	e.g BACTEC
Gram staining or other method used for early diagnosis	☐	☐	☐	☐	_
Method(s) of pathogen identification, including culture/sub-culture methods	☐	☐	☐	☐	eg. automated or manual, biochemical testing, VITEK
Methods of DNA extraction, PCR and whole genome sequencing, including manufacturer of equipment used, where applicable	☐	☐	☐	☐	eg. quantitative, real-time, multiplex, 16s/18s, high throughput genome sequencing

a Comments

Q8 - Microbiology: Antimicrobial Susceptibility Testing

8 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Please select at least 2 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Antimicrobial susceptibility testing methods, including whether automated or manual	☐	☐	☐	☐	eg. disc diffusion, e-test, minimum inhibitory concentration (MIC)
Antimicrobial testing policy	☐	☐	☐	☐	eg. EUCAST/CLSI

a Comments

Q9 - Results and Outcomes: Clinical

9 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Number (+/- proportion) of babies meeting clinical case definition criteria	☐	☐	☐	☐	eg. number with blood stream infections (BSI), pneumonia, meningitis
Number (+/- proportion) of babies with culture-proven infection	☐	☐	☐	☐	–
Number (+/- proportion) of babies meeting criteria for hospital acquired infection	☐	☐	☐	☐	–
Incidence of infection cases (as defined by clinical and/or microbiological criteria)	☐	☐	☐	☐	eg. per 1000 patient days, live births, admissions
Number (+/- proportion) and/or incidence of cases by perinatal and postnatal risk factors	☐	☐	☐	☐	eg. by gestational age, postnatal age, birth weight

Q10 - Results and Outcomes: Microbiological

10 **How important is it to report the following items in neonatal infection studies?**

Please don't select more than 1 answer(s) per row.

Please select at least 4 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Number (+/- proportion) of positive cultures	☐	☐	☐	☐	–
Number (+/- proportion) of isolates/pathogens	☐	☐	☐	☐	eg. group B strep., klebsiella pn.
Number (+/-proportion) of isolates susceptible, intermediate or resistant to each antimicrobial	☐	☐	☐	☐	eg. PACCS, drug/bug combinations
Number (+/- proportion) of isolates classified as contaminants	☐	☐	☐	☐	–

a Comments

Q11 - Results and Outcomes: Mortality and Morbidity

11 **How important is it to report the following items in neonatal infection studies (as applicable)?**

Please don't select more than 1 answer(s) per row.

Please select at least 7 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Overall mortality and/or case fatality risk (CFR), including timing	☐	☐	☐	☐	eg. at 7 and 28 days
Subgroup mortality or CFR analysis by pathogen	☐	☐	☐	☐	eg. group B strep., E.Coli; resistant vs. sensitive
Subgroup mortality of CFR analysis by infection syndrome	☐	☐	☐	☐	eg. blood stream infection vs. meningitis
Subgroup mortality or CFR analysis by risk group	☐	☐	☐	☐	eg. by post-natal age, gestational age, birth weight
Number (+/-proportion) of stillbirths (+/- subgroup analysis)	☐	☐	☐	☐	eg. antepartum or intrapartum stillbirths
Mortality trends, where possible	☐	☐	☐	☐	eg. over months, seasons, years
Morbidity outcomes	☐	☐	☐	☐	eg. number (+/- proportion) with long term neurological impairment

a Comments

Q12 - Definitions

12 **Clinical presentation and infection syndromes: How important is it that authors report their definitions or criteria for the following?**

Please don't select more than 1 answer(s) per row.

Please select at least 11 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies
Possible severe bacterial infection (pSBI)	☐	☐	☐	☐
Confirmed bloodstream infection (BSI)	☐	☐	☐	☐
Meningitis	☐	☐	☐	☐
Pneumonia (including VAP)	☐	☐	☐	☐
Hospital acquired infection	☐	☐	☐	☐
Central line associated infection	☐	☐	☐	☐
Outbreak	☐	☐	☐	☐
Contaminant isolate	☐	☐	☐	☐
Coagulase negative staphylococcus infection	☐	☐	☐	☐
Stillbirth	☐	☐	☐	☐
Onset of infection (eg. timing of early and late onset infection)	☐	☐	☐	☐
Duration of infection episode	☐	☐	☐	☐
Long term impairment (eg. neurodisability)	☐	☐	☐	☐

13 **Study population: How important is it that authors report their definitions or criteria for the following?**

Please don't select more than 1 answer(s) per row.

Please select at least 5 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Neonatal population	☐	☐	☐	☐	eg. 0-28 days vs. admissions to NICU
First day of life	☐	☐	☐	☐	eg. day 0, day 1
Birth weight categories	☐	☐	☐	☐	eg. VLBW, LBW
Gestational age categories	☐	☐	☐	☐	eg. late preterm, very preterm
Denominator	☐	☐	☐	☐	eg. 1000 live births, 1000 patient days, 1000 admissions

13 **Study population: How important is it that authors report their definitions or criteria for the following?**

Please don't select more than 1 answer(s) per row.

Please select at least 5 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Neonatal population	☐	☐	☐	☐	eg. 0-28 days vs. admissions to NICU
First day of life	☐	☐	☐	☐	eg. day 0, day 1
Birth weight categories	☐	☐	☐	☐	eg. VLBW, LBW
Gestational age categories	☐	☐	☐	☐	eg. late preterm, very preterm
Denominator	☐	☐	☐	☐	eg. 1000 live births, 1000 patient days, 1000 admissions

14 **Setting: How important is it that authors report their definitions and criteria for the following?**

Please don't select more than 1 answer(s) per row.

Please select at least 2 answer(s).

Having trouble with the format of this question? View in tableless mode

	Unnecessary	Sometimes useful	Important for most studies	Essential for all studies	
Place of birth	☐	☐	☐	☐	(eg. inborn vs. outborn)
Level of care	☐	☐	☐	☐	(eg. NICU I-III or SCBU, NHDU)

15 Comments

16 **Would reporting of neonatal infections be improved if the following had an agreed / recommended definition?**

Please don't select more than 1 answer(s) per row.

Please select at least 18 answer(s).

Having trouble with the format of this question? View in tableless mode

	No	Yes - but beyond the remit of SPRING	Yes - should be prioritised at the SPRING expert consensus meeting	
Possible severe bacterial infection (pSBI)	☐	☐	☐	_
Confirmed blood stream infection (BSI)	☐	☐	☐	_
Meningitis	☐	☐	☐	_
Pneumonia (including VAP)	☐	☐	☐	_
Hospital acquired infection	☐	☐	☐	_
Outbreak	☐	☐	☐	_
Contaminant isolate	☐	☐	☐	_
Coagulase negative stapylococcus infection	☐	☐	☐	_
Stillbirth	☐	☐	☐	eg. antepartum and intrapartum
Onset of infection	☐	☐	☐	eg. timing of early and late onset infection
Duration of infection episode	☐	☐	☐	_
Long-term impairment	☐	☐	☐	eg. neurodisability
Neonatal population	☐	☐	☐	eg. 0-28 days vs. admissions to NICU
First day of life	☐	☐	☐	eg. day 0, day 1
Birth weight categories	☐	☐	☐	eg. VLBW, LBW
Gestational age categories	☐	☐	☐	eg. late preterm, very preterm
Denominator	☐	☐	☐	eg. live births, patient days, admissions
Place of birth	☐	☐	☐	_
Level of care	☐	☐	☐	_

17 Comments

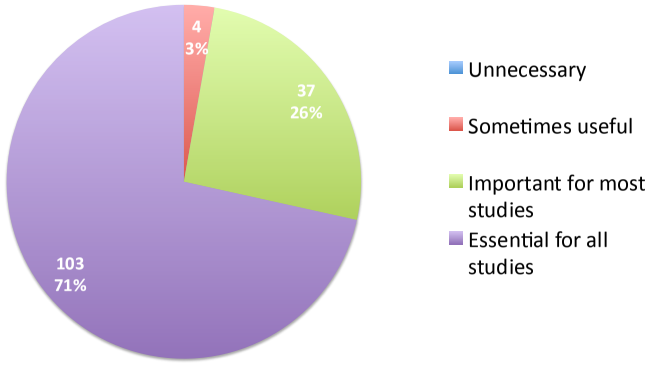
Online Survey Results

RESULTS:

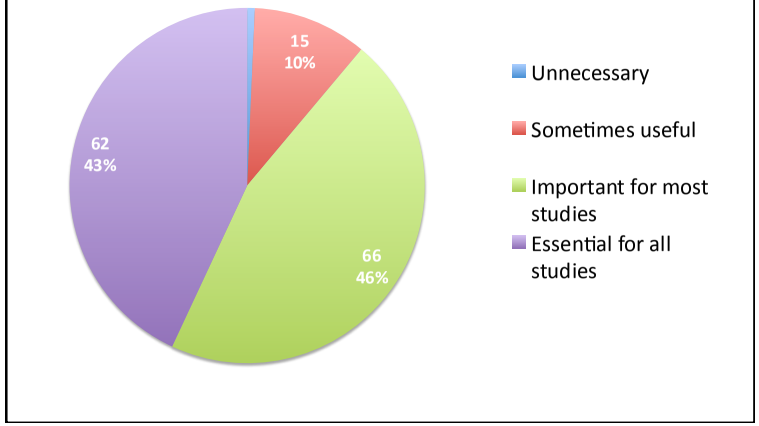
How important is it to report the following items in neonatal infection studies?

1. Setting: Study Site

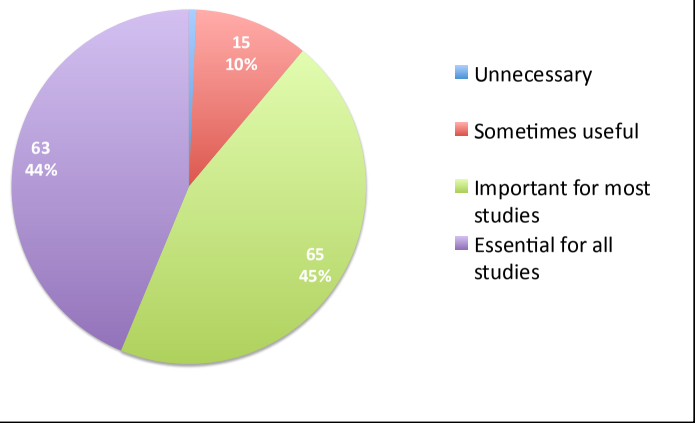
1.1. Facility or community based study



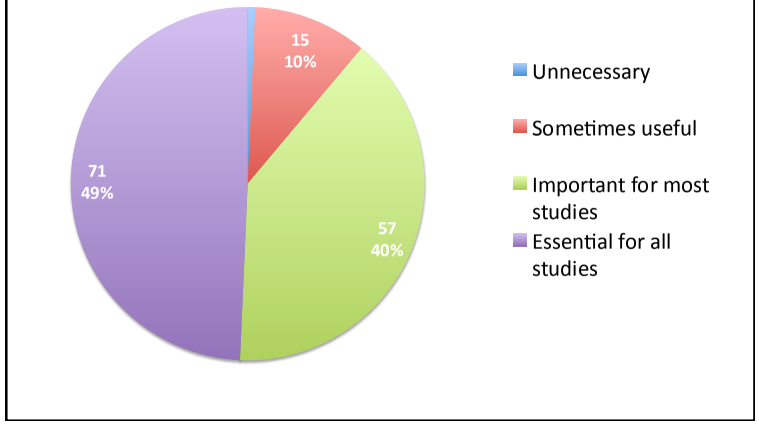
1.2. Size of study site catchment area or total population



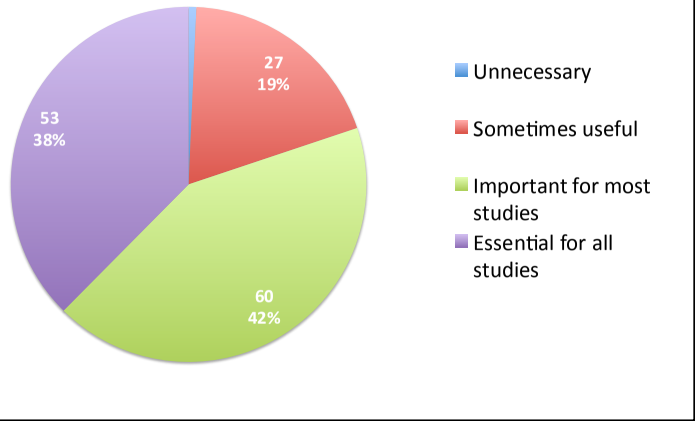
1.3. Annual number of live births in study catchment area



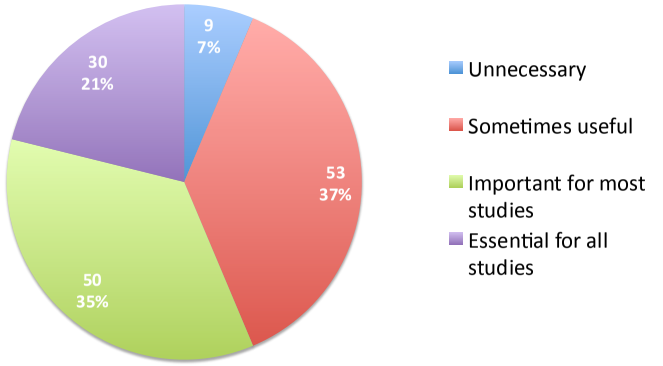
1.4. Neonatal mortality rate in study area



1.5. Preterm birth rate in study area

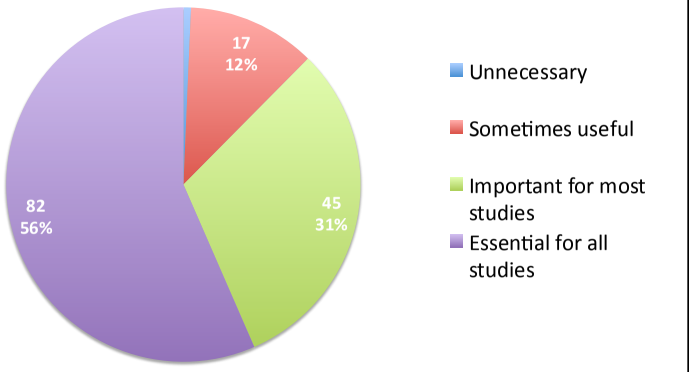


1.6. Stillbirth rate in study area

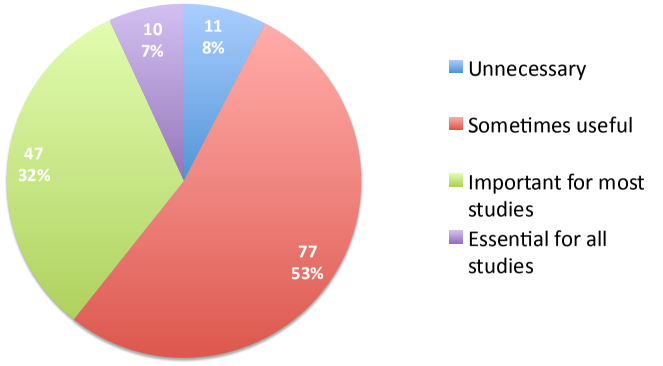


1.7. Source of population denominator

eg. source of vital registration or survey data

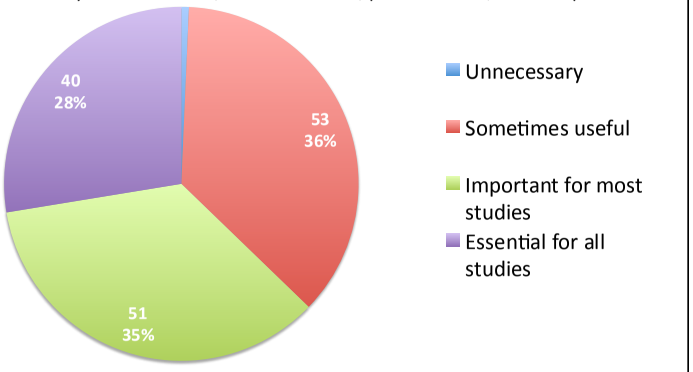


1.8. Climate or seasonal change during study, where relevant



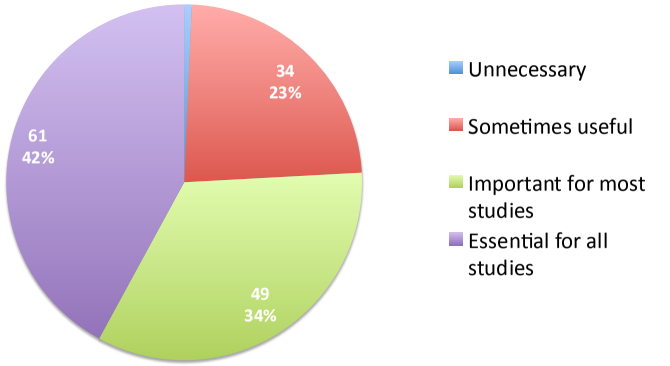
1.9. Type / grade and number of healthcare staff looking after study patients

eg. community health workers, neonatal nurses, paediatricians; nurse to patient ratio



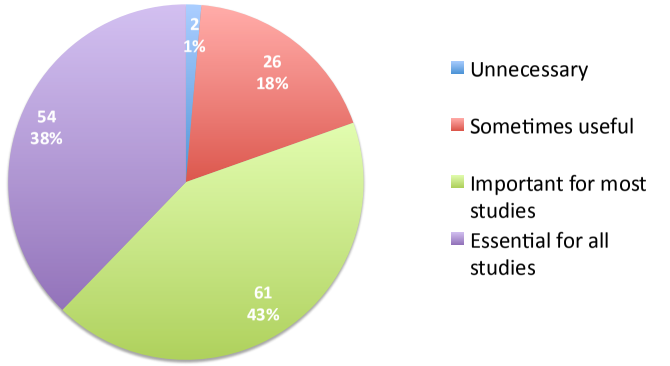
1.10. Study specific training conducted

eg. clinical algorithm to diagnose possible bacterial infections



1.11. Obstetric care provided

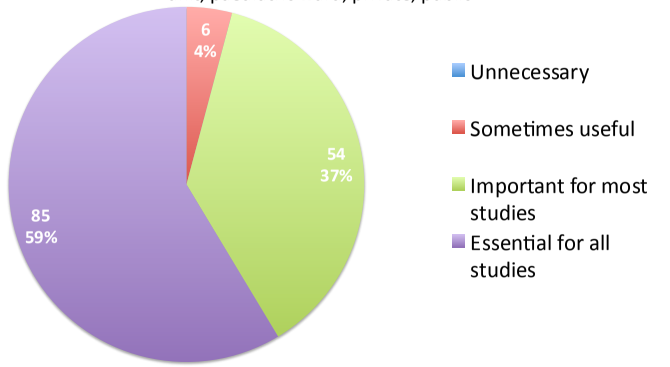
eg. trained or untrained birth attendant; obstetric practices, infection control practices in the delivery room, availability of antenatal steroids



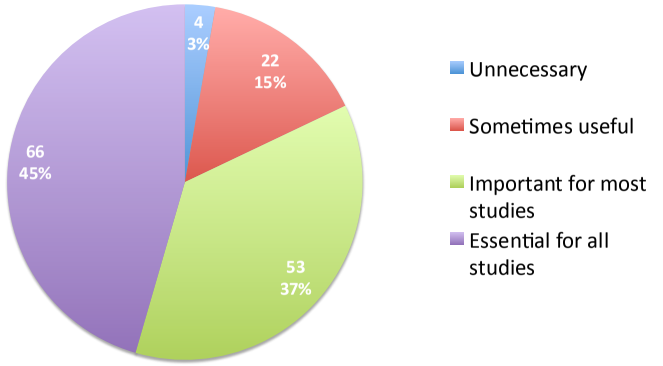
2. Setting: Health Facility

2.1. Type of facility and which ward(s)/ unit(s) included

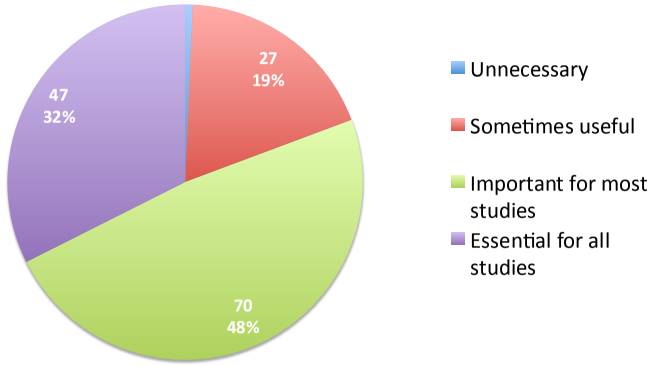
eg. first level health centres, district hospitals, referral hospital; neonatal intensive care unit, paediatric ward; private, public



2.2. Criteria for admission to the health facility (+/- ward)

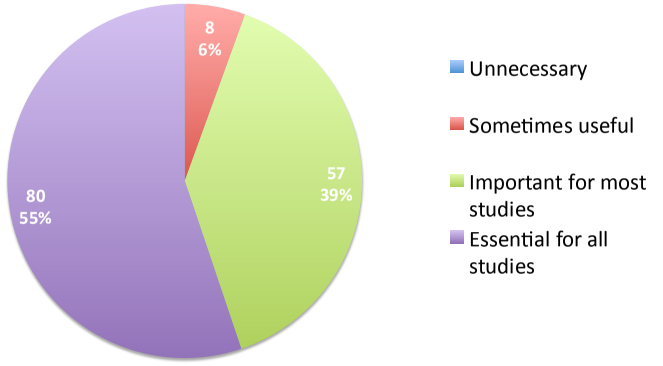


2.3. Annual number of admissions to health facility (+/- ward)



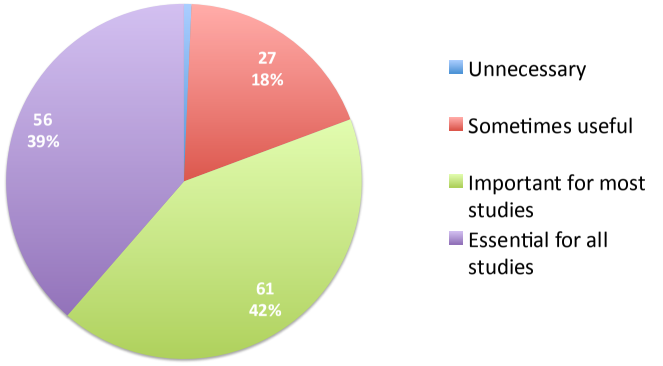
2.4. Level of neonatal care available

eg. level of respiratory support offered: mechanical ventilation, continuous positive airway pressure, oxygen, none

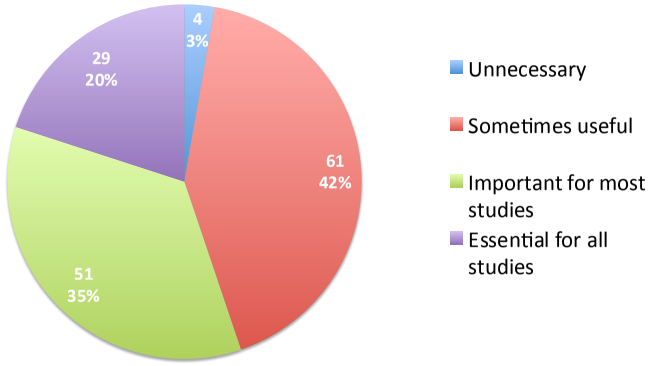


2.5. Number of patients requiring interventions

eg. ventilation, central lines, TPN and surgery, expressed as patient days

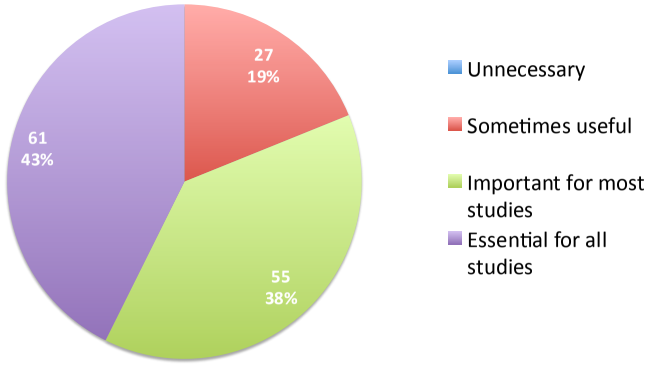


2.6. Average cot occupancy rates

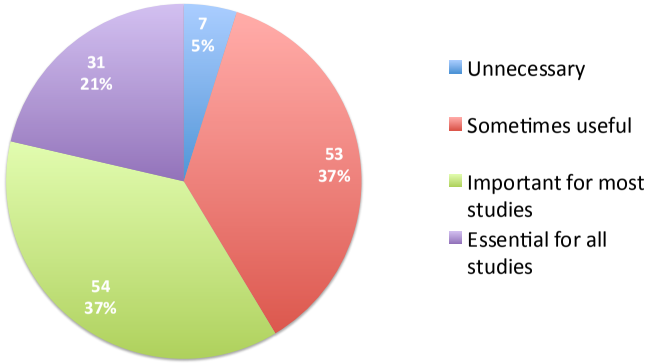


2.7. Infection control measures and adherence (including the delivery room)

eg. space between cots, audit data on hand washing

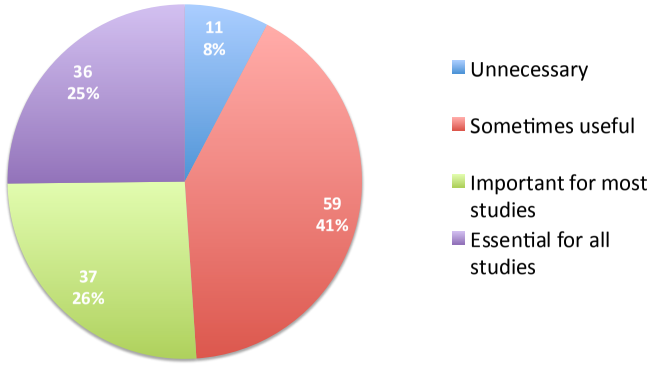


2.8. Availability and use of kangaroo mother care

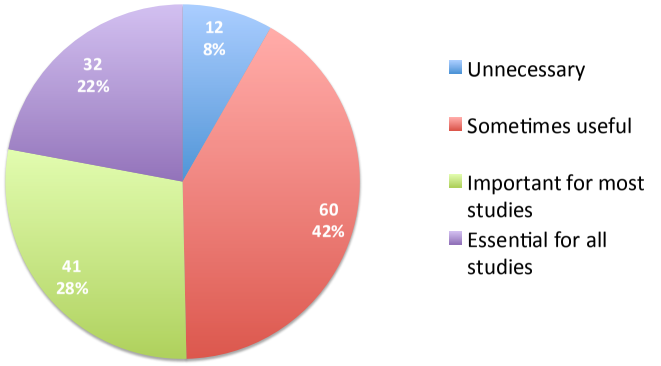


3. Clinical Information: Maternal

3.1. Maternal age

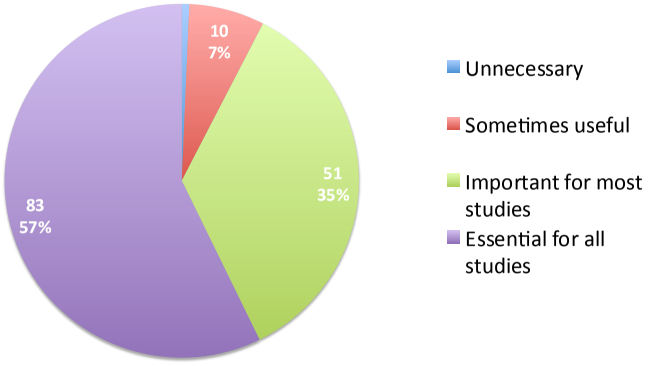


3.2. Parity



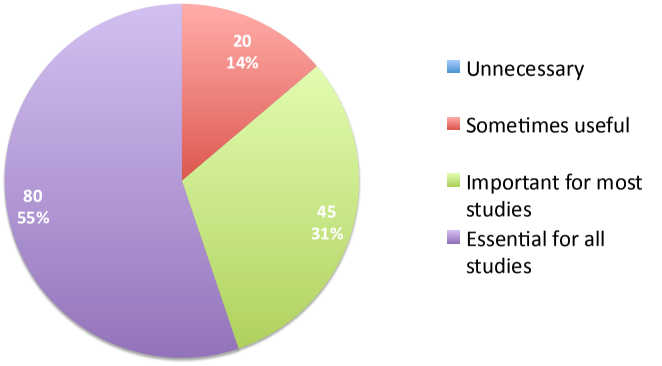
3.3. Mode of delivery

eg. vaginal vs. elective caesarean vs. emergency caesarean



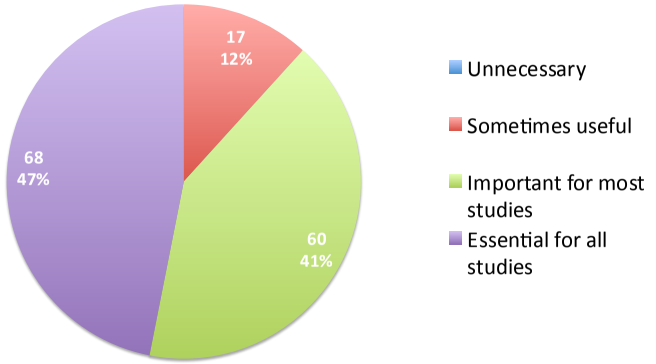
3.4. Complications during pregnancy or delivery

eg. prolonged or preterm rupture of membranes



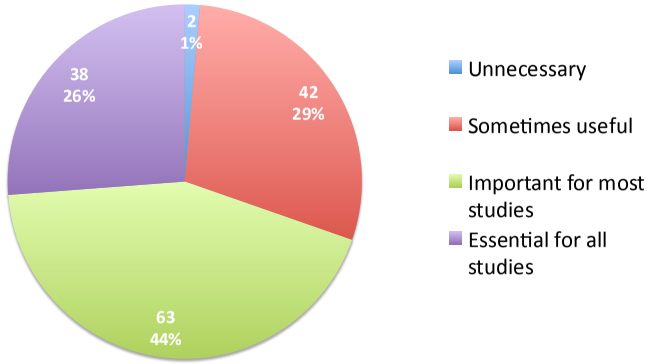
3.5. Recent maternal illness

eg. fever, urinary tract infection



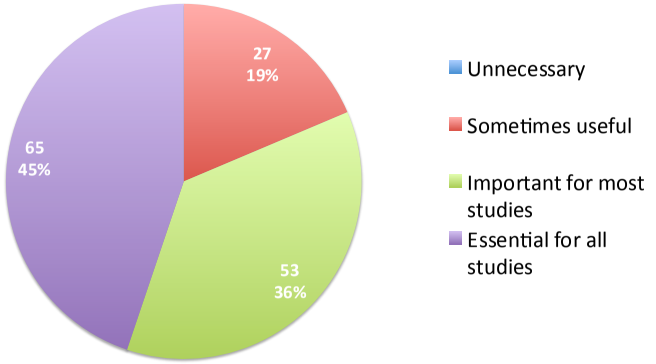
3.6. List of maternal comorbidities

eg. anaemia, malaria

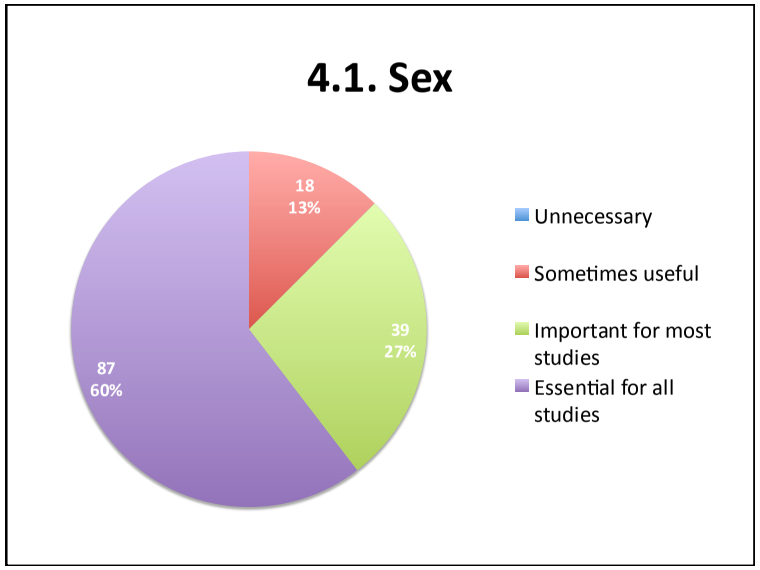


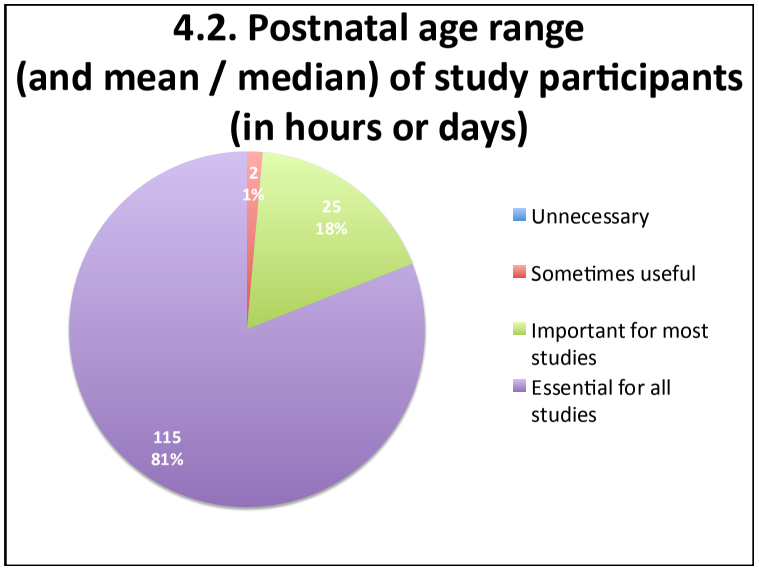
3.7. Antenatal screening for infections

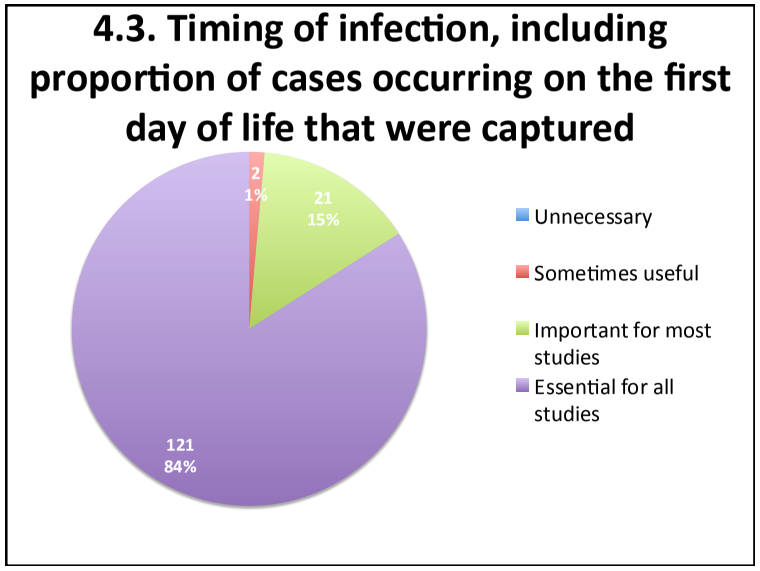
eg. GBS, HIV, syphilis, Hep B

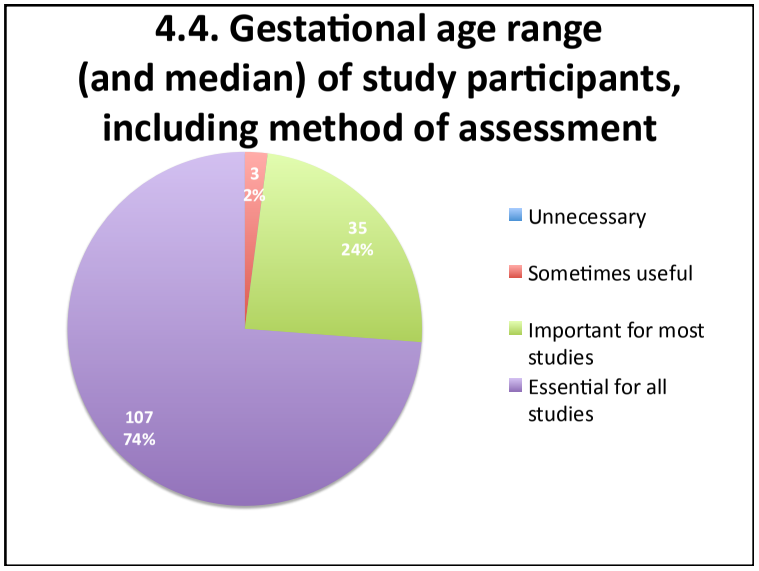


4. Clinical Information: Newborn

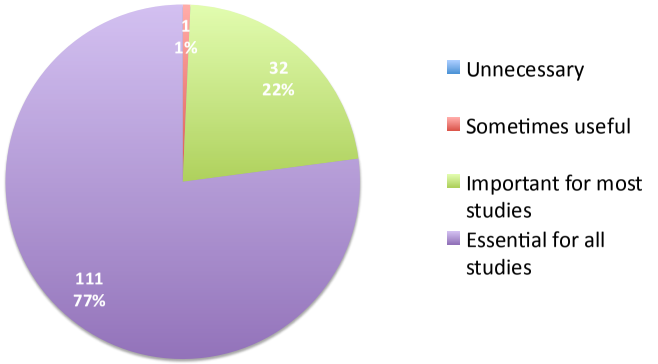

4.1. Sex
18
13%
39
27%
87
60%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies


4.2. Postnatal age range (and mean / median) of study participants (in hours or days)
2
1%
25
18%
115
81%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies


4.3. Timing of infection, including proportion of cases occurring on the first day of life that were captured
2
1%
21
15%
121
84%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies

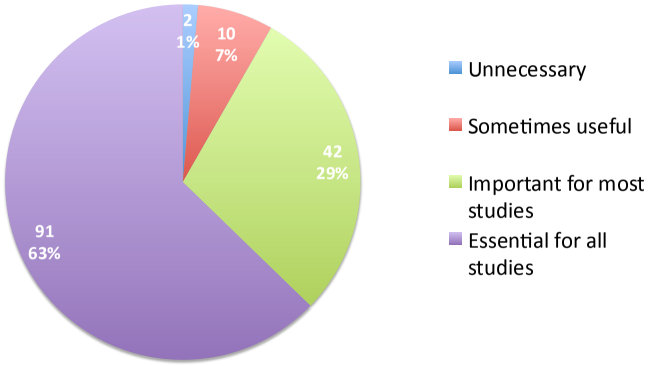

4.4. Gestational age range (and median) of study participants, including method of assessment
3
2%
35
24%
107
74%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies

4.5. Birth weight range (and mean / median) of study participants



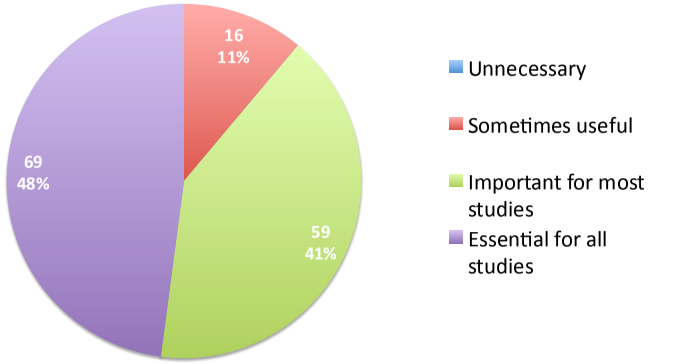
4.6. Place of birth

eg. facility vs. home births; 'inborn' or 'outborn'



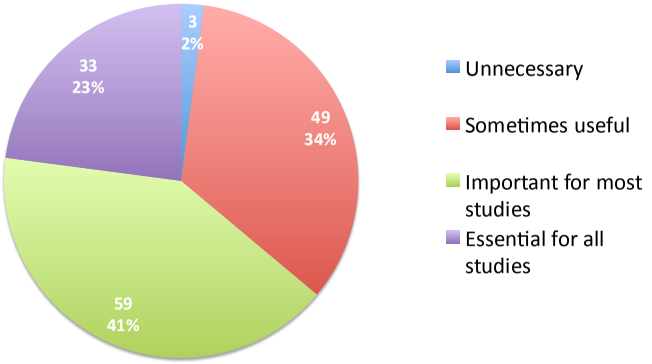
4.7. List of comorbidities

eg. congenital malformations, HIV



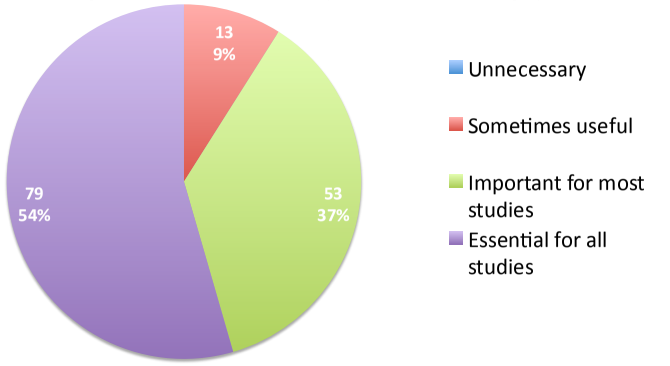
4.8. Prognostic scores

eg. 10 minute Apgar score, CRIB score



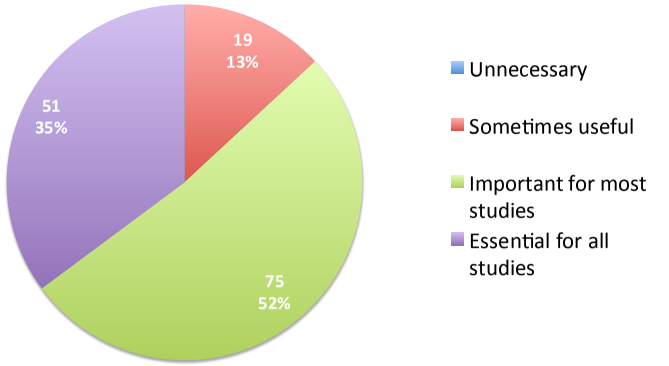
4.9. Methods of clinical assessment including examination performed, vital signs, blood tests (other than culture) and radiological investigations

eg. O2 sats, FBC, inflammatory markers, chest radiograph



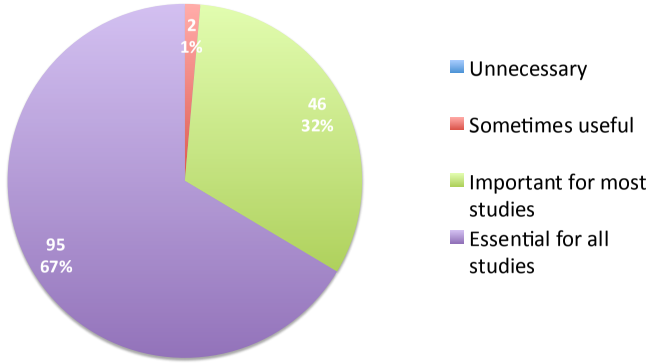
4.10. Supportive care available

eg. intravenous fluid administration, nasogastric feeds, phototherapy



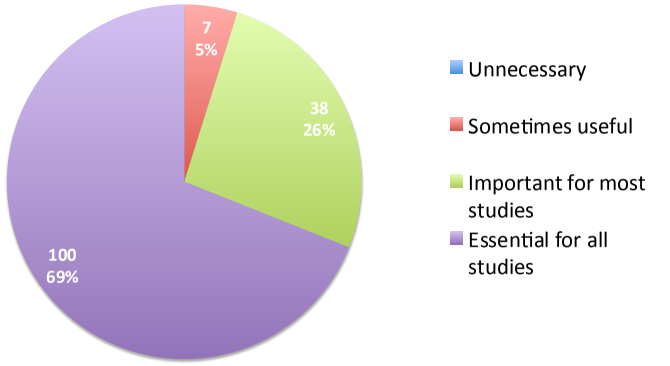
4.11. Follow up period

eg. to discharge, to 28 days

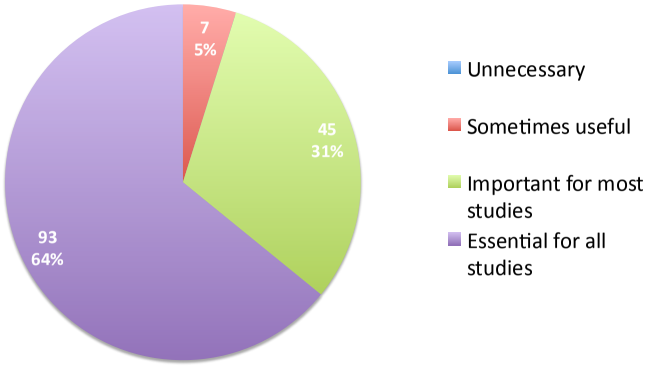


5. Clinical Information: Antimicrobial use

5.1. Prior administration of antimicrobials to the newborn, including type and timing

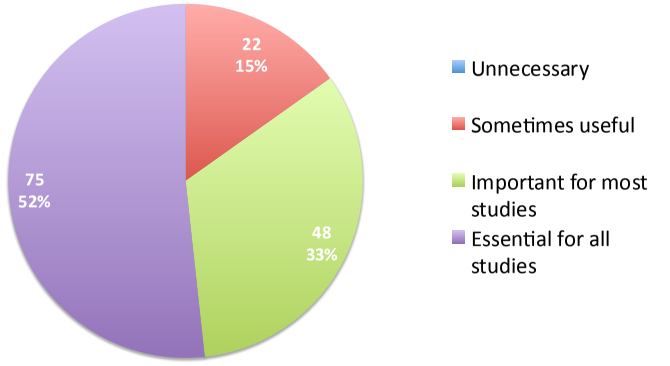


5.2. Use of maternal intrapartum antibiotic prophylaxis



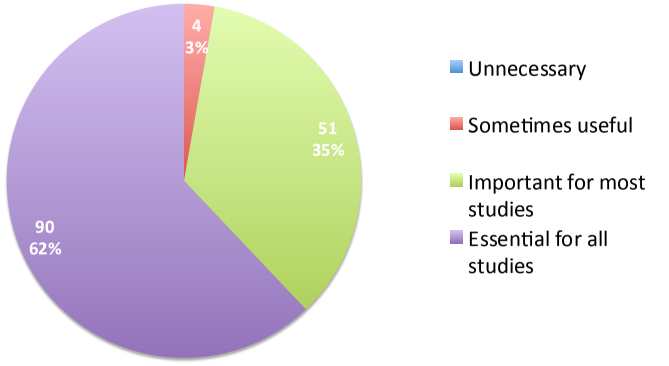
5.3. Indications / rationale for antimicrobial use

eg. empirical antibiotic policy or criteria for starting antibiotics



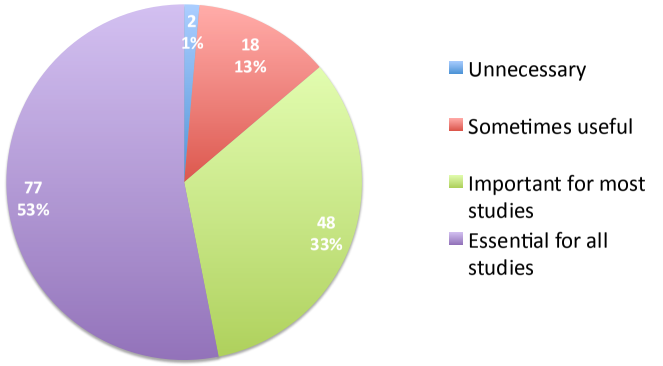
5.4. Number (+/- proportion) of study subjects who received antimicrobials, and type used

eg. proportion who received gentamicin or meropenem



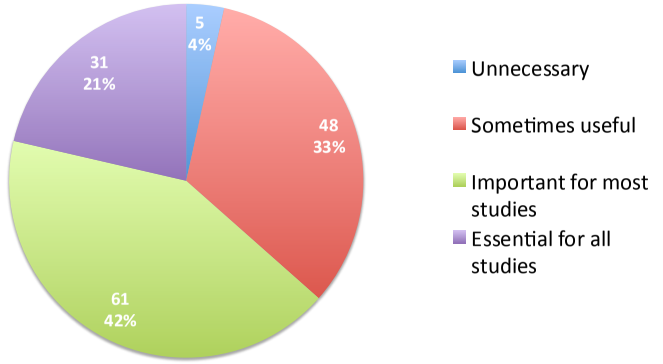
5.5. Route, dose and duration of antimicrobial administration

eg. oral, intramuscular, intravenous



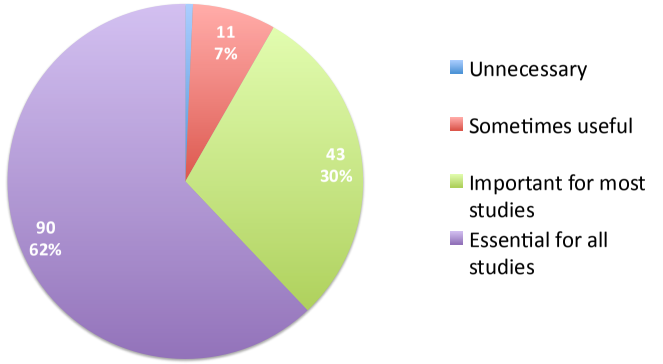
6. Microbiology: Context

6.1. Location, description, and any accreditation of laboratory



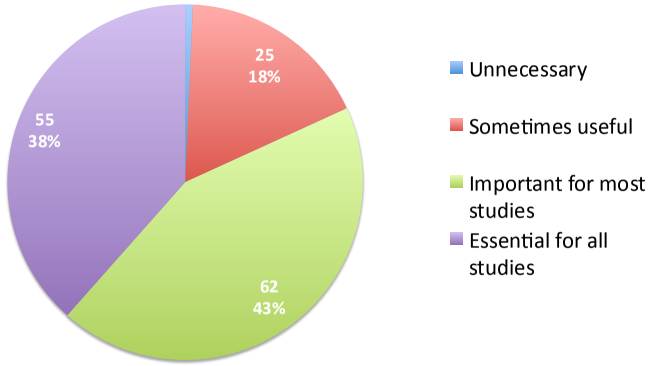
6.2. Samples taken for culture, including type and collection methods

eg. blood or CSF; number and volume taken from each baby



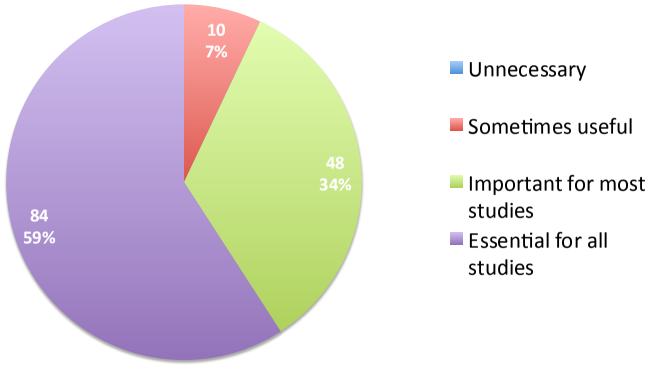
6.3. Reason for sample collection

eg. routine surveillance, study requirement, clinical indication



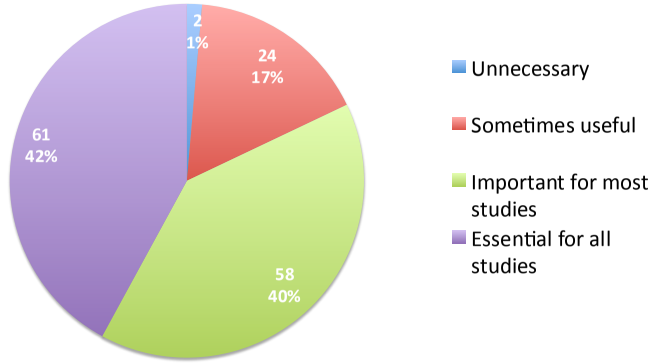
6.4. Timing of sample collection in relation to antimicrobial administration

eg. samples taken before or after starting antibiotics



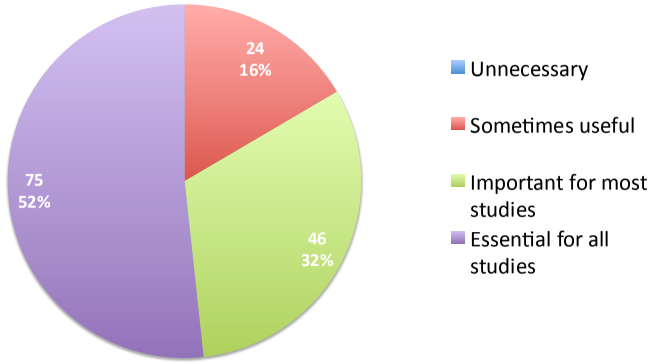
6.5. Quality control and validation

eg. whether samples were externally validated; sensitivity or specificity of testing



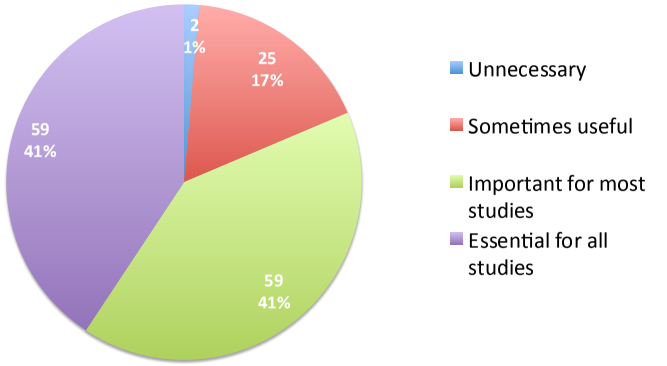
7. Microbiology: Culture Methods

7.1. Whether conventional or molecular methods used

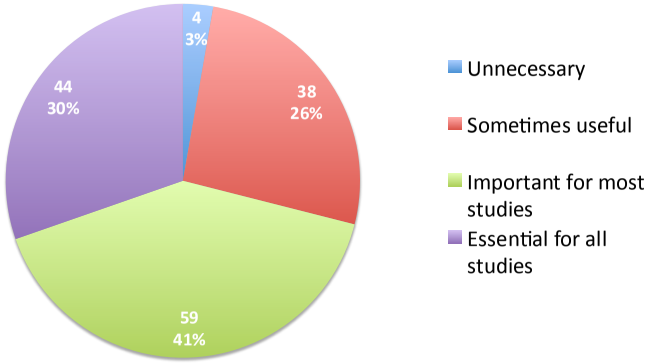


7.2. Culture incubation methods

eg. BACTEC

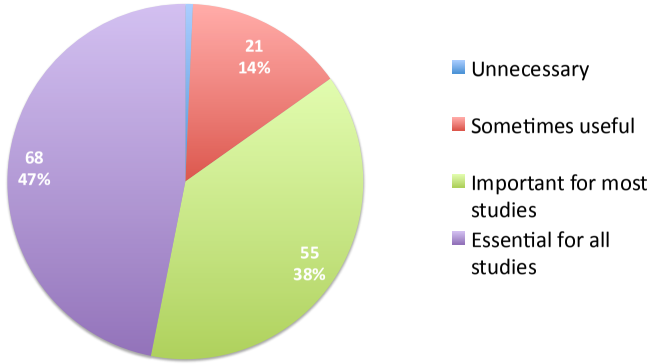


7.3. Gram staining or other method used for early diagnosis



7.4. Method(s) of pathogen identification, including culture/sub-culture methods

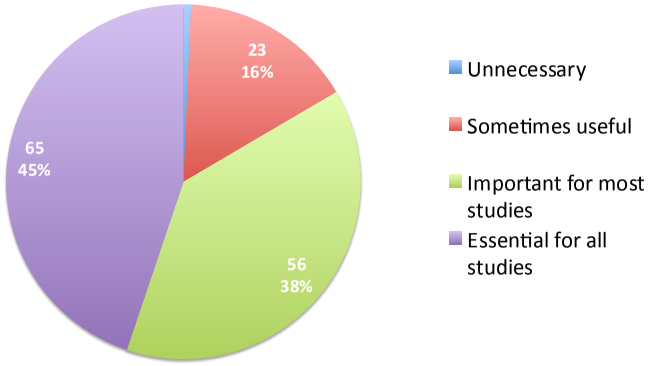
eg. automated or manual, biochemical testing, VITEK



8. Microbiology: Antimicrobial Susceptibility Testing

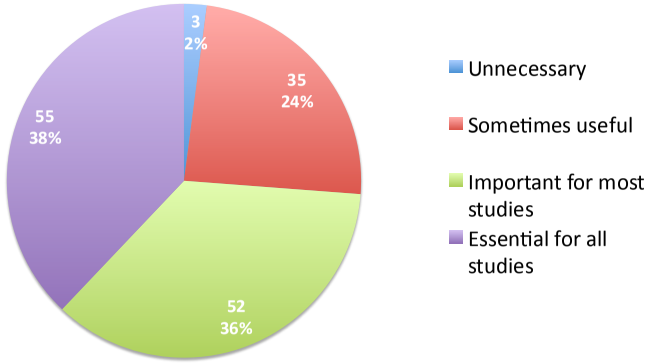
8.1. Antimicrobial susceptibility testing methods, including whether automated or manual

eg. disc diffusion, e-test, minimum inhibitory concentration (MIC)



8.2. Antimicrobial testing policy

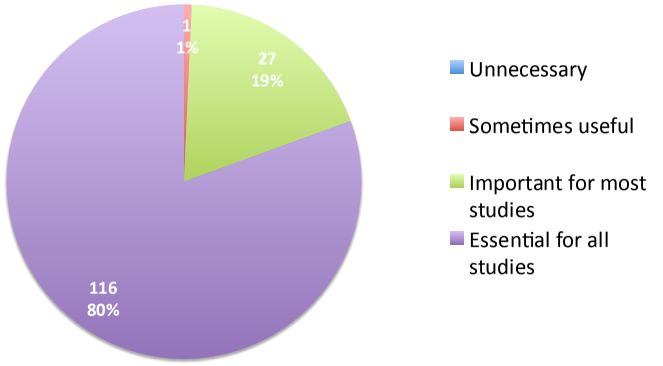
eg. EUCAST/CLSI



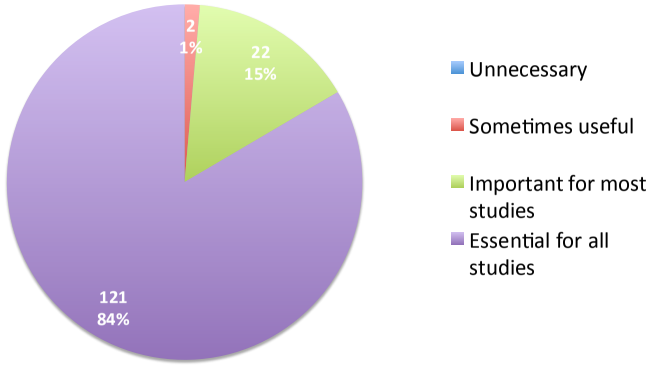
9. Results and Outcomes: Clinical

9.1. Number (+/- proportion) of babies meeting clinical case definition criteria

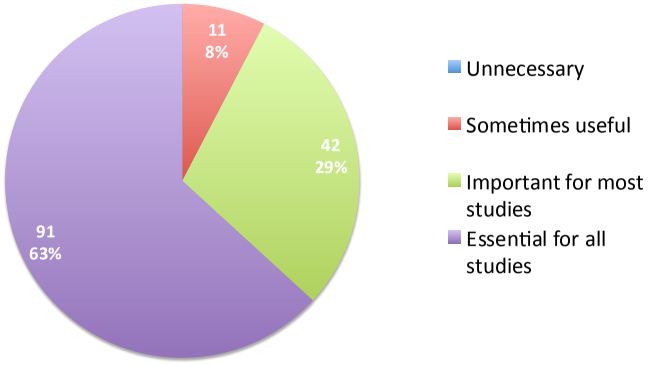
eg. number with blood stream infections (BSI), pneumonia, meningitis



9.2. Number (+/- proportion) of babies with culture-proven infection

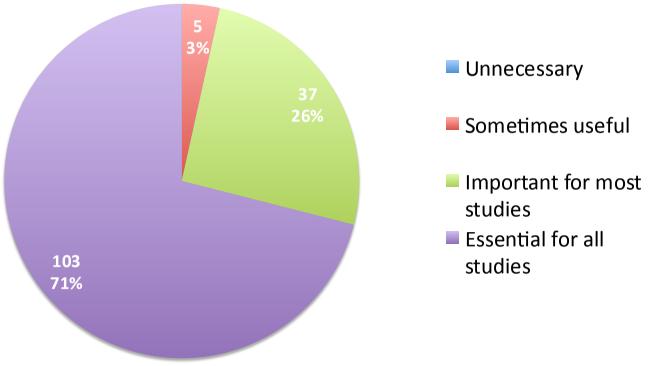


9.3. Number (+/- proportion) of babies meeting criteria for hospital acquired infection



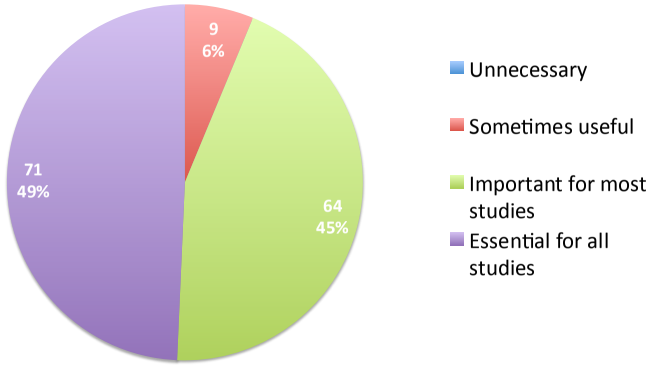
9.4. Incidence of infection cases (as defined by clinical and/or microbiological criteria)

eg. per 1000 patient days, live births, admissions



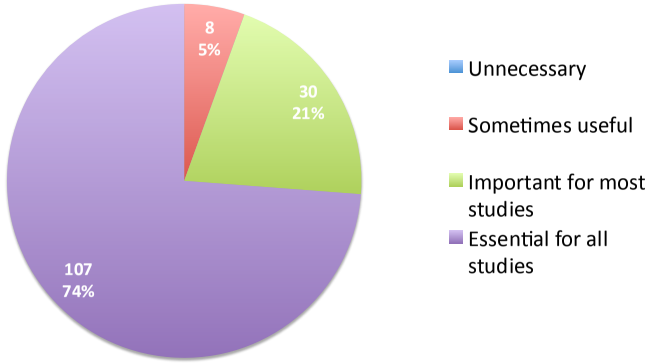
9.5. Number (+/- proportion) and/or incidence of cases by perinatal and postnatal risk factors

eg. by gestational age, postnatal age, birth weight



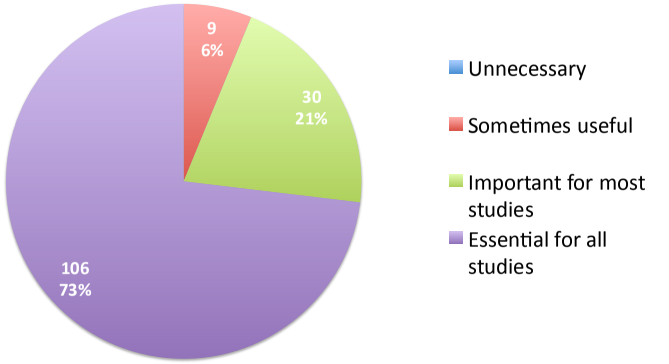
10. Results and Outcomes: Microbiological

10.1. Number (+/- proportion) of positive cultures



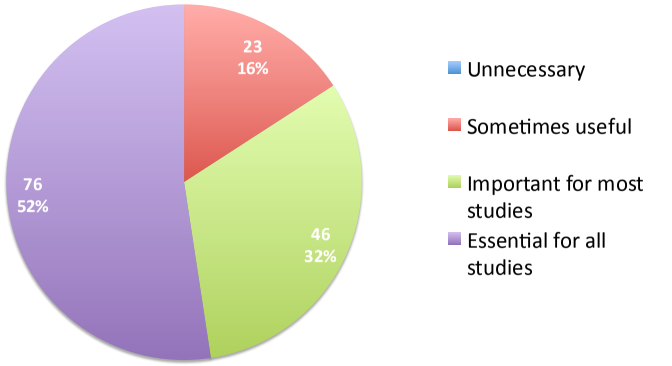
10.2. Number (+/- proportion) of isolates/ pathogens

eg. group B strep., klebsiella pn.

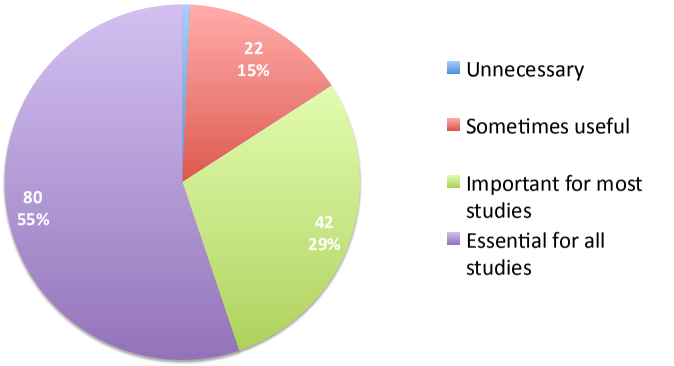


10.3. Number (+/-proportion) of isolates susceptible, intermediate or resistant to each antimicrobial

eg. PACCS, drug/bug combinations



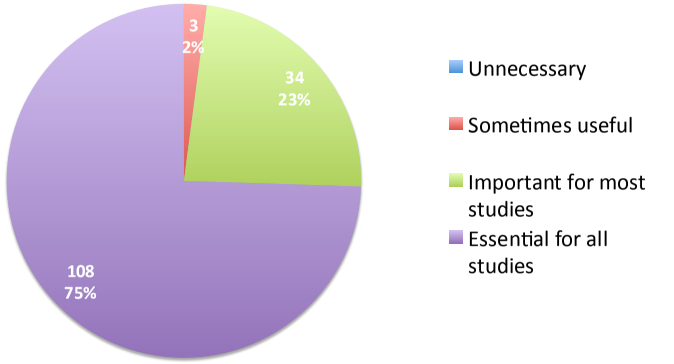
10.4. Number (+/- proportion) of isolates classified as contaminants



11. Results and Outcomes: Mortality and Morbidity

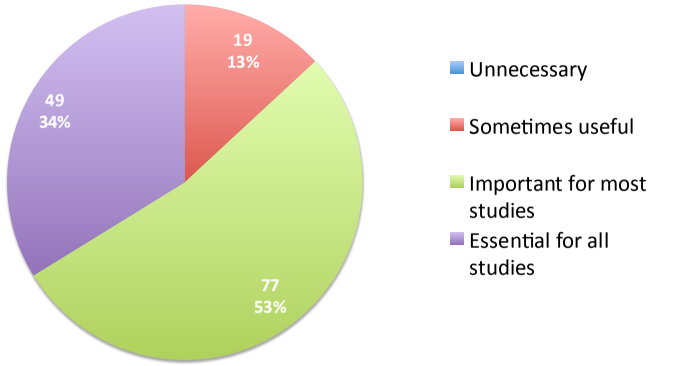
11.1. Overall mortality and/or case fatality risk (CFR), including timing

eg. at 7 and 28 days



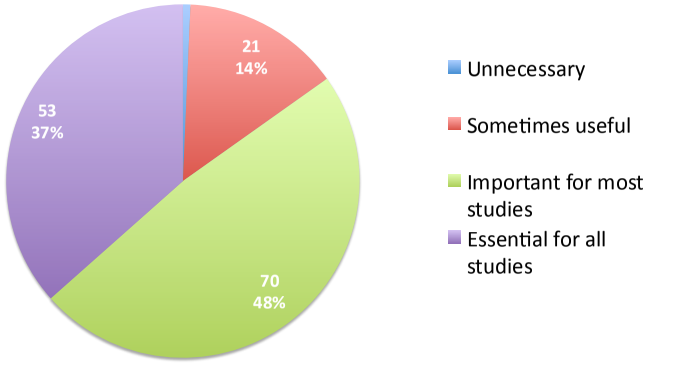
11.2. Subgroup mortality or CFR analysis by pathogen

eg. group B strep., E.Coli; resistant vs. sensitive



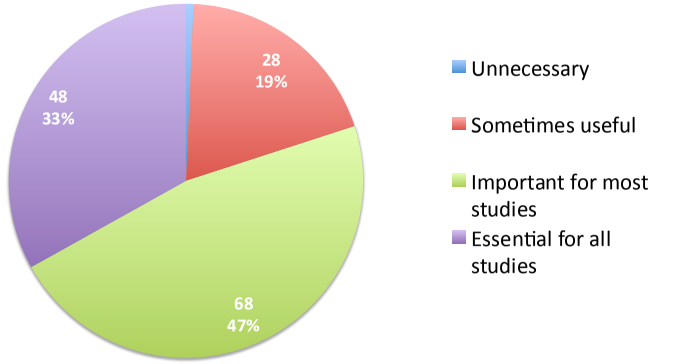
11.3. Subgroup mortality of CFR analysis by infection syndrome

eg. blood stream infection vs. meningitis



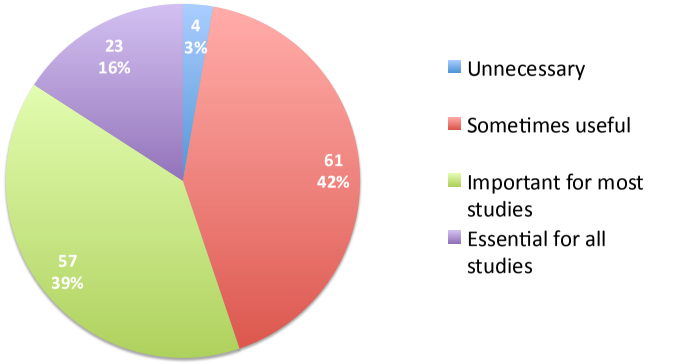
11.4. Subgroup mortality or CFR analysis by risk group

eg. by post-natal age, gestational age, birth weight



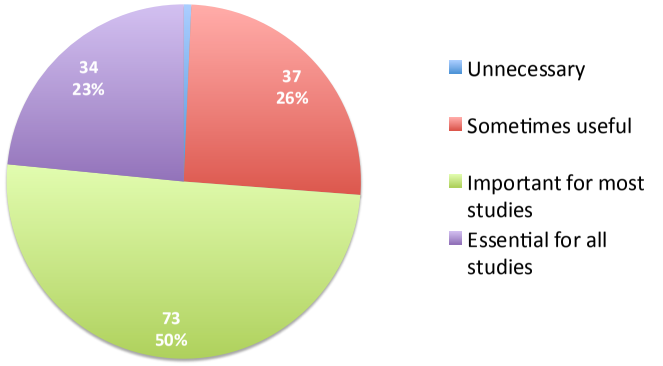
11.5. Number (+/-proportion) of stillbirths (+/- subgroup analysis)

eg. antepartum or intrapartum stillbirths



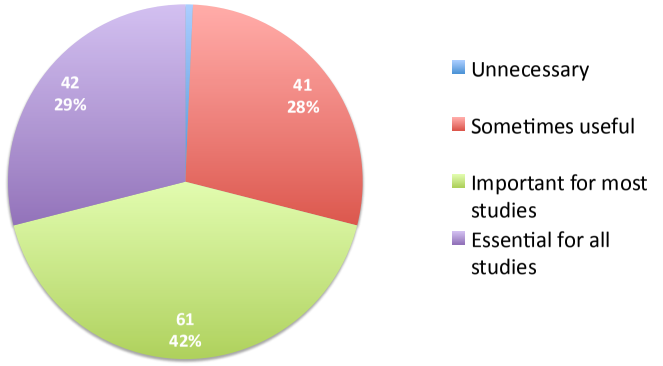
11.6. Mortality trends, where possible

eg. over months, seasons, years



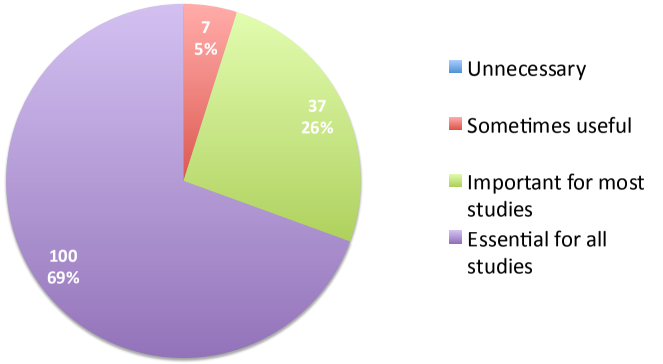
11.7. Morbidity outcomes

eg. number (+/- proportion) with long term neurological impairment

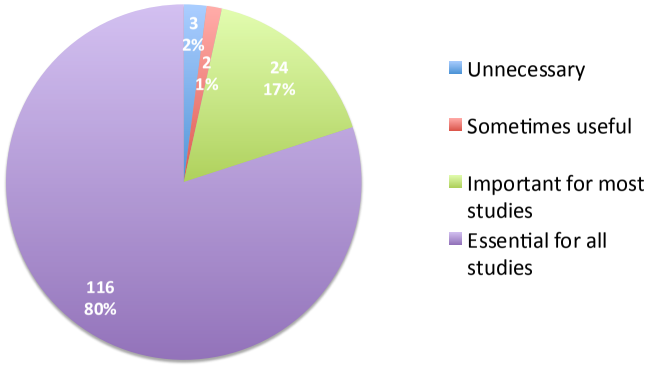


12. Definitions for authors to include when reporting neonatal infection research

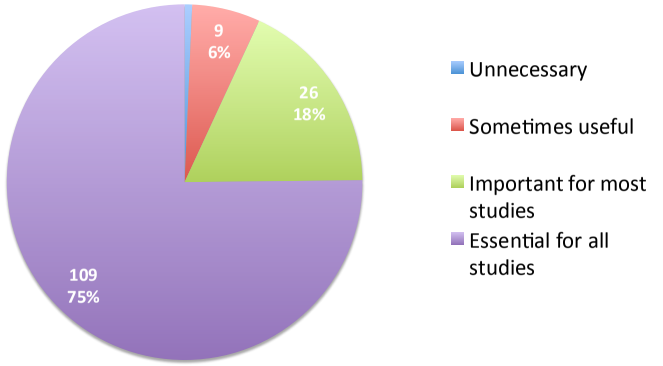
12.1. Possible severe bacterial infection (pSBI)



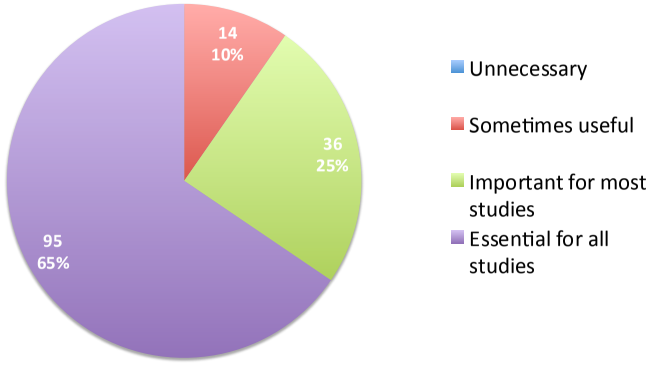
12.2. Confirmed bloodstream infection (BSI)



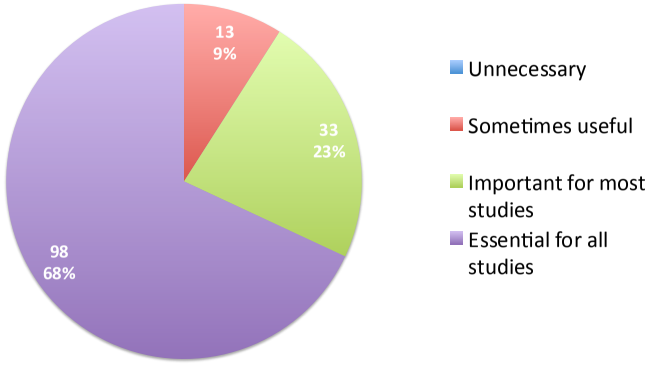
12.3. Meningitis



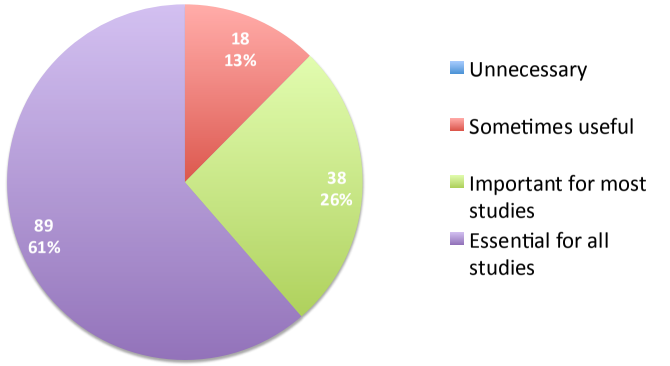
12.4. Pneumonia (including VAP)



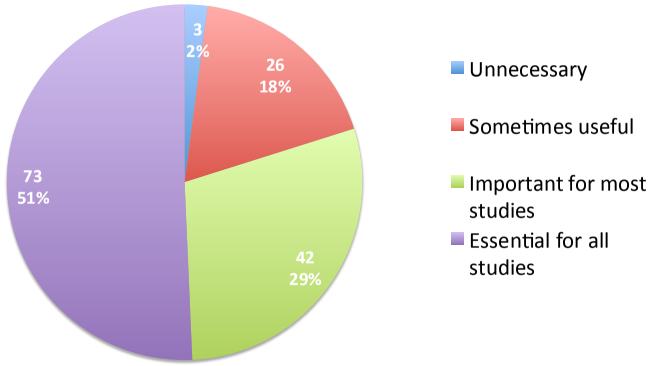
12.5. Hospital acquired infection



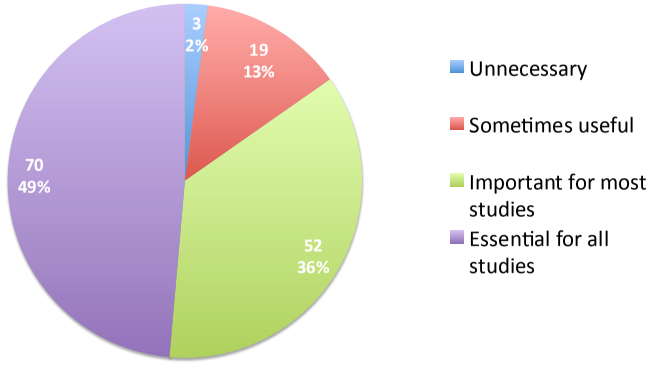
12.6. Central line associated infection



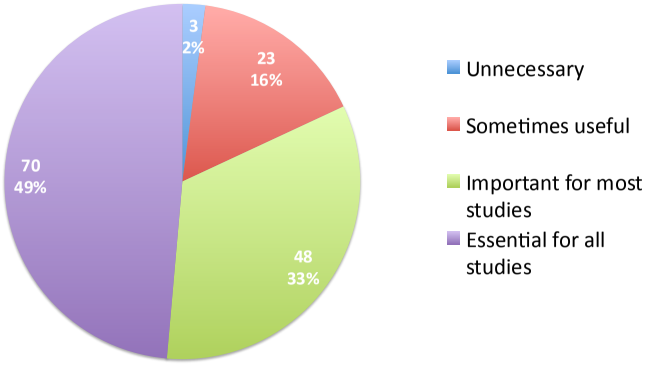
12.7. Outbreak



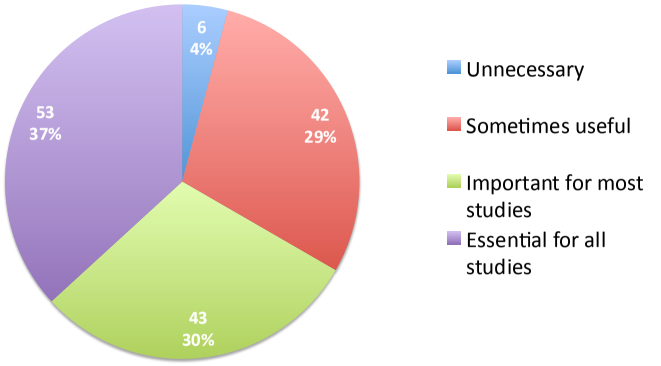
12.8. Contaminant isolate



12.9. Coagulase negative staphylococcus infection

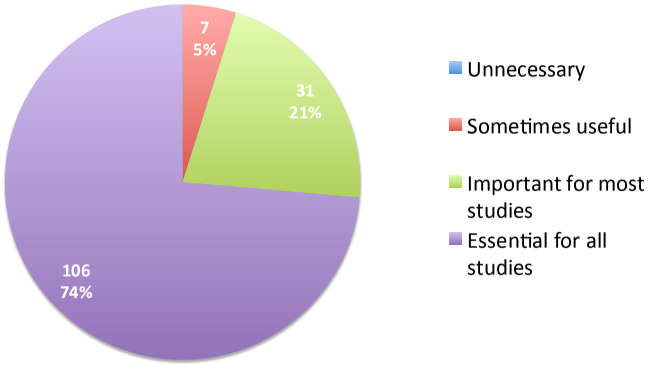


12.10. Stillbirth

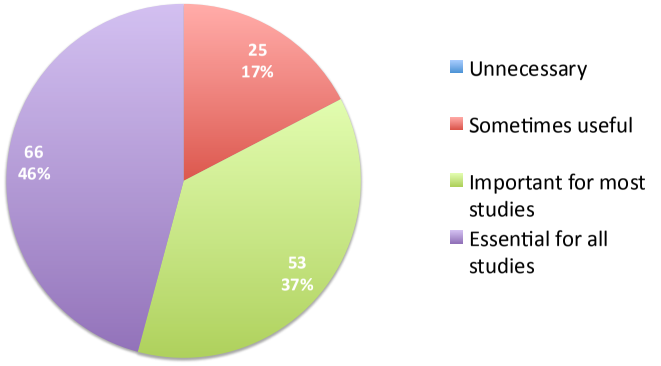


12.11. Onset of infection

(eg. timing of early and late onset infection)

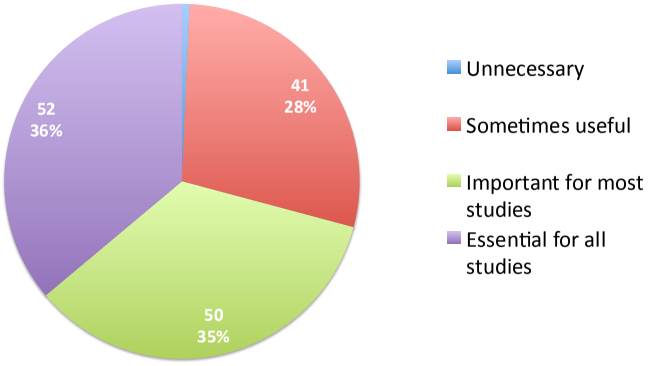


12.12. Duration of infection episode



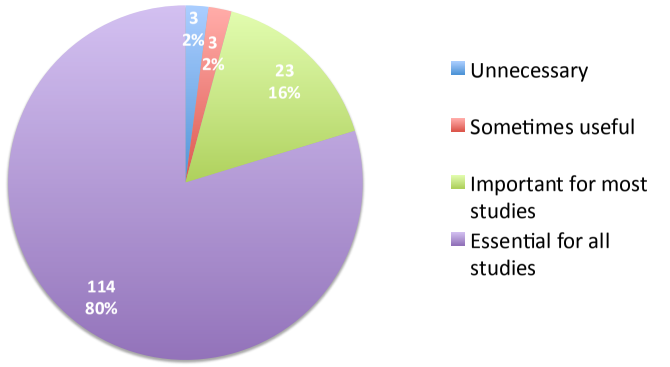
12.13. Long term impairment

(eg. neurodisability)



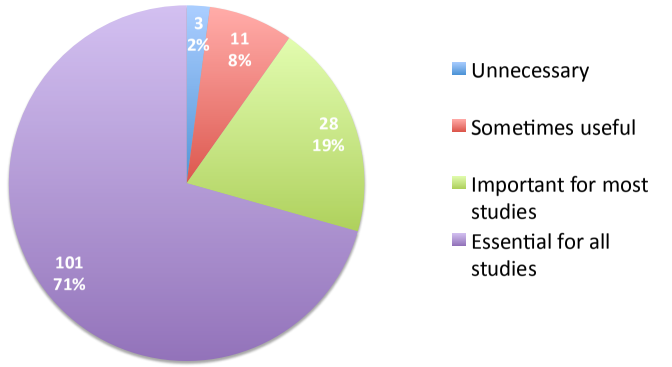
13.1. Neonatal population

eg. 0-28 days vs. admissions to NICU



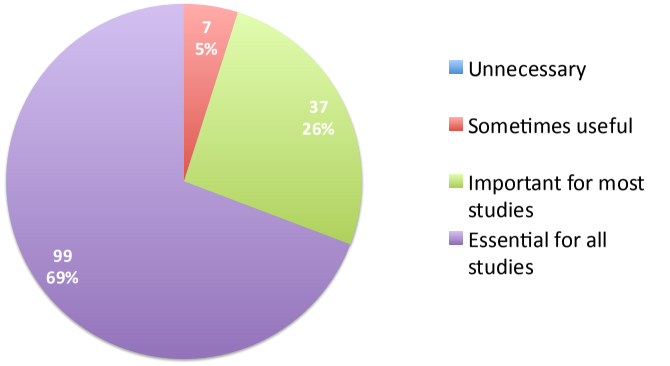
13.2. First day of life

eg. day 0, day 1



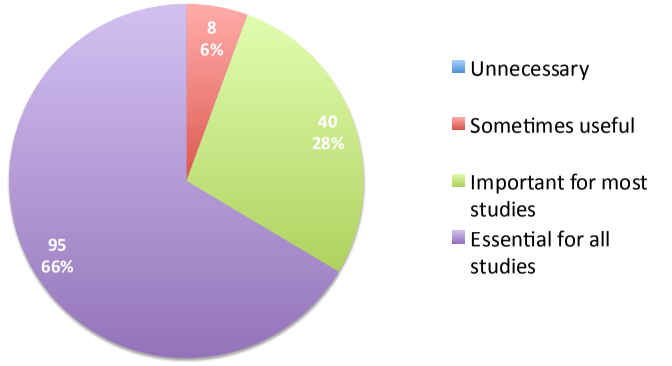
13.3. Birth weight categories

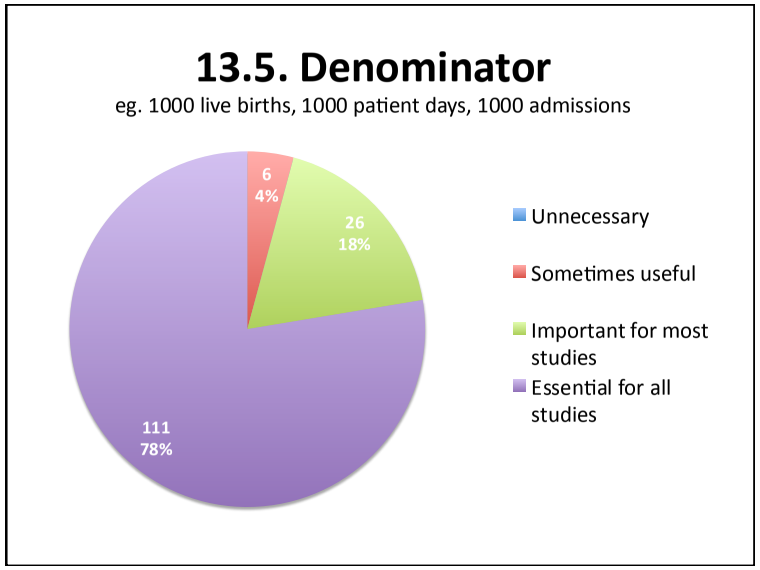
eg. VLBW, LBW

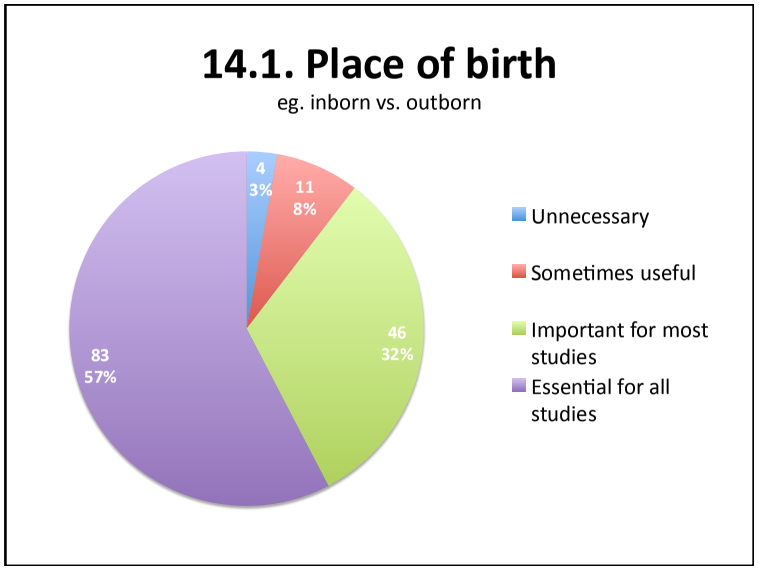


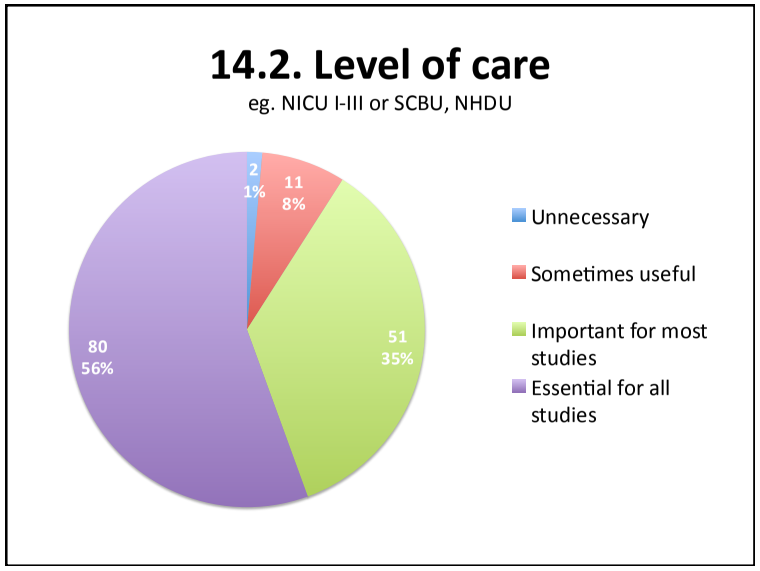
13.4. Gestational age categories

eg. late preterm, very preterm




13.5. Denominator
eg. 1000 live births, 1000 patient days, 1000 admissions
6
4%
26
18%
111
78%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies


14.1. Place of birth
eg. inborn vs. outborn
4
3%
11
8%
46
32%
83
57%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies


14.2. Level of care
eg. NICU I-III or SCBU, NHDU
2
1%
11
8%
51
35%
80
56%
Unnecessary
Sometimes useful
Important for most studies
Essential for all studies

3A. Figure 2b: Graphic showing structural relationship between STROBE[29], STROME-ID[31], and STROBE-NI

		STROBE	STROME-ID	STROBE-NI
TITLE and ABSTRACT		1(a)	STROME-ID 1.1	
		1(b)		
INTRODUCTION	Background/rationale	2	STROME-ID 2.1	
	Objectives	3	STROME-ID 3.1	
METHODS	Study design	4	STROME-ID 4.1	
			STROME-ID 4.2	
			STROME-ID 4.3	
				STROBE-NI-4.1
				STROBE-NI-4.2
				STROBE-NI-4.3
				STROBE-NI-4.4
			STROME-ID 4.4	STROBE-NI-4.5
				STROBE-NI-4.6
				STROBE-NI-4.7
				STROBE-NI-4.8
	Setting	5	STROME-ID 5.1	
				STROBE-NI-5.1
				STROBE-NI-5.2
				STROBE-NI-5.3
				STROBE-NI-5.4
				STROBE-NI-5.5
				STROBE-NI-5.6
	Participants	6(a)	STROME-ID 6.1	
		6(b)		
				STROBE-NI-6.1
	Variables	7		STROBE-NI-7.1
	Data source/measurement	8	STROME-ID 8.1	
	Bias	9	STROME-ID 9.1	
	Study size	10	STROME-ID 10.1	
	Quantitative variables	11		
	Statistical methods	12(a)	STROME-ID 12.1	
		12(b)	STROME-ID 12.2	
		12(c)		
		12(d)		
		12(e)		
RESULTS	Participants	13(a)	STROME-ID 13.1	
		13(b)	STROME-ID 13.2	
		13(c)		STROBE-NI-13.1
	Descriptive data	14(a)	STROME-ID 14.1	STROBE-NI-14.1
				STROBE-NI-14.2
				STROBE-NI-14.3
				STROBE-NI-14.4
		14(b)		
		14(c)		
	Outcome data	15		STROBE-NI-15.1
				STROBE-NI-15.2
				STROBE-NI-15.3
				STROBE-NI-15.4
	Main results	16(a)	STROME-ID 16.1	STROBE-NI-16.1
		16(b)		
		16(c)		
	Other analyses	17		
DISCUSSION	Key results	18		
	Limitations	19	STROME-ID 19.1	STROBE-NI-19.1
	Interpretation	20		
	Generalisability	21		
OTHER INFORMATION	Funding	22		
	Ethics		STROME-ID 23.1	STROBE-NI-23.1