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Feasibility of introducing pulse oximetry for identifying hypoxaemia among children with pneumonia in paediatric outpatient settings in Bangladesh:
Generating evidence and synthesising knowledge for influencing policy, programme planning and practice

By

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DECLARATION

I, Ahmed Ehsanur Rahman, hereby declare that this thesis has been composed by me and that it has not been submitted, in whole or in part, for any other degree or professional qualification. I confirm that the work submitted is my own, except where work which has formed part of jointly authored publications has been included. The contributions of myself and the other authors to this work have been clearly stated here. I confirm that appropriate credit has been given in this thesis where references to the work of others have been mentioned.

The work presented in Chapter 3 has been published as *"Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis"* in the Lancet Global Health by Ahmed Ehsanur Rahman (myself), Aniqa Tasnim Hossain, Harish Nair (co-supervisor), Mohammod Jobayer Chisti, David H Dockrell (co-supervisor), Shams El Arifeen (co-supervisor), and Harry Campbell (supervisor). AER and HC conceptualised, designed, and implemented the study. AER and ATH analysed and interpreted the data. AER wrote the first draft with guidance from HC and SEA. HN, DD, and MJC reviewed the drafts and provided inputs to all versions. All authors reviewed the final draft and agreed on its content and conclusions. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. AER and ATH accessed and verified the data.

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LIST OF ABBREVIATION

ABG	Arterial Blood Gas
ACPR	Associates for Community and Population Research
AFRINEST	African Neonatal Sepsis Trial
ALRI	Acute Lower Respiratory Infections
ANC	Antenatal Care
AOR	Adjusted Odds Ratio
BDHS	Bangladesh Demographic and Health Survey
BHFS	Bangladesh Health Facility Survey
BNF	Bangladesh Neonatal Federation
BPA	Bangladesh Paediatric Association
CC	Community Clinic
CHCP	Community Health Care Project
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CPAP	Continuous Positive Airway Pressure
CS	Civil Surgeon
DDFP	Deputy Director of Family Planning
DGDA	Directorate General of Drug Administration
DGFP	Directorate General of Family Planning
DGFP-MCRAH	Directorate General of Family Planning- Maternal, Child, Reproductive and Adolescent Health
DGHS	Directorate General of Health Services
DGHS-CBHC	Directorate General of Health Services-Community Based Health Care-Operational Plan
DGHS-HIS& e-Health	Directorate General of Health Services- Health Information System and e-Health- Operational Plan
DGHS-MNC&AH	Directorate General of Health Services-Maternal Newborn Child and Adolescent Health
DGHS-NNS	Directorate General of Health Services-National Nutrition Services-Operational Plan
DGHS-PMR	Directorate General of Health Services-Planning, Monitoring and Research-Operational Plan
DGMEd	Directorate General of Medical Education
DGNM	Directorate General of Nursing and Midwifery
DH	District Hospital
DHIS2	District Health Information Software - version 2
DNCC	Dhaka North City Corporation
DPM	Deputy Program Manager
DSCC	Dhaka South City Corporation
FWA	Family Welfare Assistant
FWV	Family Welfare Visitor
GAPPD	The integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea
GoB	Government of Bangladesh
HA	Health Assistant
Hib3	Haemophilus Influenzae Type B

HIV/AIDS	Human Immunodeficiency Virus Infection and Acquired Immune Deficiency Syndrome
HPNSP	Health Nutrition and Population Sector Program
ICD	International Classification of Diseases
icddr,b	International Centre for Diarrhoeal Disease Research, Bangladesh
IMCI	Integrated management of childhood illness
IPC	Infection Prevention and Control
IQR	Interquartile Range
KMC	Kangaroo Mother Care
LIST	The Lives Saved Tool
LMIC	Low- and Middle-Income Countries
MCE-IMCI	The Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact
MCWC	Mother & Child Welfare Centre
MDG	Millennium Development Goals
MIS	Management Information Systems
MOHFW	Ministry of Health and Family Welfare
NCD	Noncommunicable Diseases
NEMEW	National Electro Medical Equipment Maintenance Workshop
NIHR	National Institute for Health Research
NIPORT	National Institute of Population Research and Training
NNHP&IMCI	National Newborn Health Program & Integrated Management of Childhood Illness
OP	Operational Plan
PCR	Polymerase Chain Reaction
PCV	Pneumococcal Conjugate Vaccine
PERCH	Pneumonia Aetiology Research for Child Health
PNC	Postnatal Care
PO	Pulse Oximetry
PPT	Protect, Prevent, and Treat
PSBI	Possible Serious Bacterial Infection
RESPIRE	Global Health Research Unit on Respiratory Health
RMO	Resident Medical Officer
RSV	Respiratory Syncytial Virus
SACMO	Sub-Assistant Community Medical Officer
SATT	Simplified Antibiotic Therapy Trial
SCANU	Special Care Newborn Unit
SCI	Save the Children International
SCW	Special Care Ward
SDG	Sustainable Development Goals
SET	Signal Extraction Technology
SOP	Standard Operating Procedure
SpO_2	Saturation of Peripheral Oxygen
SWA	Sector-Wide Approach
TEMO	Transport and Equipment Management Organisation
UH&FWC	Union Health & Family Welfare Centre
UHC	Upazila Health Complex

UNICEF	United Nations International Children's Emergency Fund
UR	Uncertainty Range
VA	Verbal Autopsy
WHO	World Health Organization

LAY SUMMARY

Globally, pneumonia is the major killer of children under-5 years of age, and hypoxaemia, defined by low oxygen saturation in blood, is one of the strongest predictors of mortality among children with pneumonia. To address the crucial evidence gap, regarding the burden of hypoxaemia among children with pneumonia in low- and middle-income countries, I conducted a systematic review and meta-analysis. I found that overall prevalence of hypoxaemia to be very high, particularly among clinically severe or hospitalised children with pneumonia and moderately high prevalence was noticed among non-severe pneumonia cases. I further conducted a secondary analysis of data extracted from the routine clinical records of a secondary level hospital and found that the burden of hypoxaemia among children hospitalised with pneumonia is extremely high in Bangladesh. I also found that hypoxaemia was one of the strongest predictors of death or referral to a higher-level facility. Without rapid identification and prompt management of hypoxaemia, it will not be possible to substantially reduce pneumonia-related deaths. Therefore, countries with a high burden of childhood pneumonia should prioritise identification, referral, and management of hypoxaemia in their policy, programmes, and practice.

Bangladesh is one of the low- and middle-income countries that has declared its commitment to reduce under-5 mortality rates to ≤25 per 1,000 live births by 2030 and avert all preventable pneumonia-related deaths by 2025. I performed a secondary analysis of data from a population-based survey conducted with a nationally representative sample of households and my findings revealed that Bangladesh has a high burden of childhood pneumonia, causing approximately

24,000 under-5 deaths per year. After which I conducted another secondary analysis of data from a facility-based survey conducted with a nationally representative sample of health facilities in Bangladesh which showed that there were major gaps in the availability of pulse oximetry devices and oxygen delivery system in public hospitals and health facilities in Bangladesh. Almost none of the primary care health centres have pulse oximetry devices, though majority of children with pneumonia primarily seek care from such facilities. I also found critical gaps in the availability of oxygen sources and the oxygen delivery system in the surveyed facilities. This high burden of pneumonia, including hypoxaemia, combined with inadequate readiness of the health facilities for managing hypoxaemia, clearly shows the risk faced by children in this country, and reveals the evident disconnect between existing policy priorities and programme planning. The Government of Bangladesh should consider oxygen security as a strategic priority and invest in the oxygen delivery system ensuring rapid identification of hypoxaemia through point-of-care diagnostics and immediate management by appropriate oxygen therapy.

Bangladesh was one of the first countries to introduce the WHO recommended Integrated Management of Childhood Illness Strategy (commonly known as IMCI) in paediatric outpatient settings and nationally scaled-up the services. In Bangladesh, IMCI services are the first point of contact with the health system for most children with pneumonia, including hypoxaemia. The use of a point-of-care diagnostic tool, such as a pulse oximetry device, can improve the provision of hypoxaemia identification and the accuracy of pneumonia classification by the health service providers. Therefore, since 2014, WHO has recommended introducing pulse

oximetry in IMCI services where feasible. Unfortunately, until 2019, the Government of Bangladesh did not adopt the WHO recommendation regarding the use of pulse oximetry to identify and classify pneumonia. I was involved in a series of discussions with the national policymakers of Bangladesh to integrate pulse oximetry into the IMCI services. After successfully advocating for updating the National IMCI Guidelines, I engaged several national and district level stakeholders to update the National IMCI Implementation Package and develop a district model of implementation which adopted a health system strengthening approach. I further engaged the national and district level stakeholders in conceptualising and conducting an implementation research study through real-life demonstrations in selected public health facilities. The approach that I adapted for sensitising and engaging the stakeholders was comprehensive, context-driven, inclusive, resource-intensive and time-consuming. It required prioritisation and meticulous planning. The process was iterative as I had to repeatedly change and adapt the plan based on the changing context (including the COVID-19 pandemic) and respect the stakeholder's preferences and priorities. However, the stakeholder engagement process played a decisive role in ensuring government leadership, promoting multi-partner involvement, and creating a collective sense of ownership regarding introducing pulse oximetry in IMCI services in paediatric outpatient settings. Government leadership, partnership, and a sense of ownership among stakeholders are essential steps toward integrating pulse oximetry, scalability, and sustainability into the public health system. Lessons learnt from this exercise can help introduce pulse oximetry and relevant interventions in similar contexts and settings.

I implemented the district implementation model and demonstrated the introduction of pulse oximetry in 12 public facilities in a rural district and conducted a series of assessments to assess feasibility based on the WHO's implementation research framework. Furthermore, I conceptualised the questions based on the WHO recommended implementation outcome variables and found that the IMCI services providers are ready to accept pulse oximetry in their routine practice, can successfully conduct pulse oximetry assessments, and obtain a stable SpO_2 reading with minimum attempts and a relatively short time. However, I observed some variability in the pulse oximetry performance across several patient-related, provider-related and facility-related factors, and it was poorer among younger children, and a few providers performed the procedure less effectively. Although some of the IMCI service providers faced some difficulties and challenges, the caregivers of the children showed a positive attitude towards the use of this technology for assessing their children. These findings indicate the adequacy of the training package and district implementation model. They also emphasise the feasibility of introducing pulse oximetry in IMCI services in routine outpatient settings. The policymakers can capitalise on these encouraging findings and move ahead to scale up pulse oximetry in routine outpatient settings through a health system strengthening approach. The district implementation model will require context-specific adaptation and medication to overcome local barriers and health system challenges. Introducing pulse oximetry devices with advanced signal strengths in high-volume facilities can help overcome the challenges associated with motion artefacts, particularly among younger children. In training and routine

monitoring, health managers will need to emphasise adherence to standard operating procedures and infection prevention practices. Also, particular importance should be given to identify providers who would benefit from targeted monitoring and follow-up support. Future research should assess the effectiveness and impact of introducing pulse oximetry on managing childhood pneumonia and related mortalities.

Hypoxaemia is also common among several diseases and conditions other than pneumonia, such as chronic lung diseases, severe sepsis, meningitis, complications of prematurity, trauma, obstetric emergencies, and peri-operative care. Therefore, I strongly recommend introducing pulse oximetry in paediatric outpatient settings as well as all outpatient emergency and inpatient settings. This comprehensive approach will improve the accuracy of diagnosis and quality of management of pneumonia and other diseases associated with hypoxaemia. It will also address the need for regular monitoring of SpO_2 levels in hospital settings to use oxygen correctly and efficiently. Moreover, I also emphasise the importance of connecting pulse oximetry to a reliable oxygen source and a functioning oxygen delivery system.

The COVID-19 pandemic has added to the burden of hypoxaemia and revealed the pre-existing gaps in the preparedness and readiness of the oxygen system in health facilities and hospital settings, especially in low- and middle-income countries with limited resources. However, the urgency imposed by the COVID-19 pandemic has provided a unique opportunity for the Government of Bangladesh and other governments to consider oxygen security as one of the most pressing needs and

prioritise investments in pulse oximetry as a point of care diagnostics, reliable oxygen sources and functioning oxygen delivery systems to bolster the preparedness for the current pandemic and common conditions requiring oxygen therapy, such as childhood pneumonia.

ABSTRACT

Background

Pneumonia is the leading cause of childhood mortality, accounting for 16% of all under-5 deaths globally. Hypoxaemia is common among children with pneumonia and one of the strongest predictors of mortality. Since 2014, the World Health Organization has recommended introducing pulse oximetry for hypoxaemia identification and pneumonia classification in the Integrated Management of Childhood Illness (IMCI) services, which is a global strategy developed explicitly for outpatient management of common childhood illnesses, including pneumonia, in low-resource and high-burden settings by minimally trained health care providers. Unfortunately, there are few experiences of introducing pulse oximetry in paediatric outpatient settings and integrating it with IMCI services by adopting a health system strengthening approach.

Bangladesh is one of the South Asian countries with high burdens of childhood pneumonia and hypoxaemia. Although Bangladesh has adopted the IMCI strategy and scaled up it nationally, pulse oximetry is neither recommended nor routinely used in IMCI services in Bangladesh. Successful introduction of a generic recommendation, technology, or device, like pulse oximetry, in routine services, demands an in-depth understanding of the problem and the context, followed by context-specific adaptations, demonstrations, and feasibility assessments. Also, it requires strategic and extensive engagement with policymakers and stakeholders to

promote country ownership and government leadership, which are prerequisites for scalability and sustainability.

Objectives and method

The overall goal of my PhD is to improve the management of childhood pneumonia by introducing and integrating pulse oximetry in routine IMCI services in Bangladesh. Furthermore, the aim is to support the Government of Bangladesh in taking an evidence-based decision in this regard. Hence, I was engaged in a series of discussions with the policymakers of the Ministry of Health and Family Welfare of the Government of Bangladesh to understand their perspectives on the existing evidence gaps and research priorities for making informed decisions regarding pulse oximetry integration. Based on these consultations, I identified my PhD objectives. The following table summarises the objectives/research questions and proposed research methods.

Sl #	Objectives and research questions	Study design	Output
A	**Estimating the burden of hypoxaemia among children with pneumonia**		
1.	What is the burden of hypoxaemia among children with pneumonia globally?	Systematic review and meta-analysis	Article published in the *Lancet Global Health*
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?	Secondary analysis of routine health service data	Article published in the *Journal of Global Health*
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**		
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?	Secondary analysis of a national household survey	Article published in the *Journal of Global Health*
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?	Secondary analysis of a national health facility assessment survey	Article published in the *BMC Health Services Research*
C	**Assessing the Feasibility of introducing pulse oximetry in routine IMCI services in Bangladesh**		

Sl #	Objectives and research questions	Study design	Output
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?	Desk review, stakeholder engagement and cross-sectional survey	Article published in the *Journal of Global Health*
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?	Observational study-cross sectional survey	Article published in the *Journal of Global Health*
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?	Implementation Research -abstraction of data from routine registers, -observation, -re-assessment, -exit-interviews	Article accepted in the *Lancet eClinicalMedicine*

Results

A. Estimating the burden of hypoxaemia among children with pneumonia

I conducted a systematic review and meta-analysis by searching 11 bibliographic databases and citation indices. I reported pooled prevalence of hypoxaemia (SpO_2<90%) by classification of clinical severity and by clinical settings by using the random-effects meta-analysis models. I identified 2,825 unique records from the databases, of which 57 studies met the eligibility criteria: 26 from Africa, 23 from Asia, four from South America, and four from multiple continents. **The prevalence of hypoxaemia was 31% (95% CI, 26 to 36; 101,775 children) among all children with WHO-defined pneumonia, 41% (95% CI, 33 to 49; 30,483 children) among those with very severe or severe pneumonia, and 8% (95% CI, 3 to 16; 2,395 children) among those with non-severe pneumonia.** The prevalence was much higher in studies conducted in emergency and inpatient settings than those

conducted in outpatient settings. In 2019, we estimated that over 7 million children (95% UR, 5 to 8 million) were admitted to the hospital with hypoxaemic pneumonia.

I also conducted a secondary analysis of data obtained from icddr,b-Dhaka Hospital, a secondary level referral hospital located in Dhaka, Bangladesh. I included 2,646 children aged 2-59 months admitted with WHO-defined severe pneumonia during 2014-17**. On admission, the prevalence of hypoxaemia among children hospitalised with pneumonia was approximately 40% (95% CI, 38 to 42).** Hypoxaemia was the strongest predictor of mortality (AOR = 11.1; 95% CI, 7.3 to 16.9) and referral (AOR = 5.9; 95% CI, 4.3 to 17.0) among other factors such as age, sex, history of fever and cough or difficulty in breathing, and severe acute malnutrition. Among those who survived, the median duration of hospital stay was 7 days (IQR, 4 to 11) in the hypoxaemic group and 6 days (IQR, 4 to 9) in the non-hypoxaemic group, and the difference was significant at $p<0.001$.

B. Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh

I conducted a secondary analysis using data from the 2017-18 round of the Bangladesh Demographic and Health Survey (BDHS), which adopts a nationally representative sample of households. I included 456 deaths among children under-5 years of age in our analysis. Descriptive statistics were used to present the causes, timing, and places of death with uncertainty ranges (UR). **Pneumonia is the major killer (19%, 95% CI, 15.3 to 22.7), accounting for approximately 24,268 (UR, 21,626**

to 26,695) under-5 deaths per year. Among children aged 1-11 months, pneumonia accounts for approximately 43% of deaths.

I further conducted a secondary analysis of the Bangladesh Health Facility Survey-2017, which was conducted with a nationally representative sample including all administrative divisions and types of health facilities**. More than 90% of the district hospital and sub-district hospitals and three-fourths of primary level health centres provide IMCI-based pneumonia management services. Pulse oximetry was available in 27% of the district hospitals, 18% of the sub-district level hospitals and none of the primary level health centres**. Around 72% of the sub-district hospitals had the availability of one of any of the four oxygen sources (oxygen concentrators, filled oxygen cylinder with flowmeter, filled oxygen cylinder without flowmeter, and oxygen distribution system), followed by district hospitals (66%). Almost none of the primary level health centres had oxygen sources available on the day of the visit.

C. Assessing the feasibility of introducing pulse oximetry in routine IMCI services

Based on literature review and expert consultations, I developed a conceptual framework, which guided the planning and implementation of a 4-step stakeholder engagement process for introducing pulse oximetry in routine IMCI services in Bangladesh. In the first step, a comprehensive desk review and key informant interviews were conducted to identify stakeholder organisations and score them based on their power and interest levels regarding IMCI implementation in Bangladesh. In the second step, two national level, two district level and five sub-

district level sensitisation workshops were organised to orient all stakeholder organisations having high power or high interest regarding the importance of using pulse oximetry for pneumonia assessment and classification. In the third step, national and district level high power-high interest stakeholder organisations were involved in developing a joint action plan for introducing pulse oximetry in routine IMCI services. In the fourth step, led by a formal working group under the leadership of the Ministry of Health, we updated the National IMCI Implementation Package, including all guidelines, training manuals, services registers and referral forms in English and Bangla. **Our engagement process contributed to the national decision to introduce pulse oximetry in paediatric outpatient settings and update the National IMCI Implementation Package demonstrating country ownership, government leadership and multi-partner involvement, which are steppingstones towards scalability and sustainability.** However, our experience clearly delineates that stakeholder engagement is a context-driven, time-consuming, resource-intensive, iterative, and mercurial process that demands meticulous planning, prioritisation, inclusiveness, and adaptability.

Based on WHO's global recommendation in 2014, the National IMCI Programme of Bangladesh decided to introduce pulse oximetry in routine IMCI services in 2019 and developed a short training package for IMCI service providers. They decided to test the package in a relatively controlled setting for finalising the content and choice of pulse oximetry device before the demonstration in routine outpatient settings and subsequent scale-up. A cross-sectional study was conducted among children admitted to a rural district hospital. We employed 11 nurses and seven paramedics

as assessors who received a one-day training on pulse oximetry. Each assessor performed at least 30 pulse oximetry measurements on children with two types of handheld devices. **The assessors successfully established a stable SpO_2 reading in all attempts (n=1478) except one. The median time taken was 30 seconds (IQR, 22 to 42), and within 60 seconds, 92% of attempts were successful. The median time was significantly (p<0.0001) higher among assessments conducted with a Lifebox device (36 seconds, IQR, 25 to 50) than those with a Masimo device (27 seconds, IQR, 20 to 35).** Similarly, assessors aged >25 years are 4.8 (95% CI, 1.2 to 18.6) times more likely to obtain a stable reading within 60 seconds. Regarding patient-related factors, the odds of obtaining a stable SpO_2 reading was 2.6 (95% CI, 1.6 to 4.2) times higher among children aged 12-59 months than among children aged 2-11 months.

The National IMCI Programme of Bangladesh designed and developed a district implementation model for introducing pulse oximetry in IMCI services through stakeholder engagement and demonstrated the model in the Kushtia district by adopting a health system strengthening approach. Between December 2020 and June 2021, two assessment rounds were conducted based on WHO's implementation research framework and outcome variables in 12 facilities involving 22 IMCI service providers and 1860 children presenting with cough/difficulty in breathing in the IMCI consultation rooms. **We observed that IMCI service providers performed pulse oximetry on almost all eligible children, of which 99% of assessments were successful; 85% (95% CI, 83 to 87) in one attempt and 69% (95% CI, 67 to 71) within one minute.** The adherence to standards of procedures related to pulse oximetry was 92% (95% CI, 91 to 93), and agreement regarding identifying

hypoxaemia was 96% (95% CI, 95 to 97). The median performance time was 36 seconds (IQR, 20 to 75), which was longer among younger children (2-11 months: 44 seconds, IQR, 22 to 78; 12-59 months: 30 seconds, IQR 18 to 53, p<0.001) and among those classified as pneumonia/severe pneumonia than as no pneumonia (41 seconds, IQR, 22 to 70; 32 seconds, IQR, 20 to 62, p<0.001). We observed improvements in all indicators in the second round of assessments. Caregivers showed positive attitudes towards using this novel technology for the assessment of children.

Conclusion

Based on context-specific experience generated through these studies, the Government of Bangladesh decided to integrate pulse oximetry into routine IMCI services throughout Bangladesh. Furthermore, the learnings synthesised through these studies can also help convince the policymakers and managers of other LMICs with similar burdens and contexts to introduce pulse oximetry in routine settings providing outpatient-based paediatric services and contribute to achieving the target of averting all preventable childhood pneumonia deaths by 2025.

Chapter 1: INTRODUCTION

1.1 GLOBAL, REGIONAL AND NATIONAL BURDEN OF CHILDHOOD PNEUMONIA

Despite the remarkable progress in improving child survival in the past two decades, global efforts were not enough to reach the target of Millennium Development Goal (MDG) 4 which was two-thirds reduction of under-5 mortality by 2015 from the 1990 estimate (1, 2). Since the start of the MDG-era, the global under-5 mortality rate declined from 93 per 1,000 live births in 1990 to 39 per 1,000 live births in 2017 (3). Despite this progress and achievement, an estimated 5.4 million children died in 2017 before celebrating their fifth birthday with an uncertainty range (UR) of 5.2 to 5.8 million and the majority of these deaths were due to preventable causes (3, 4). Pneumonia is the leading cause of childhood mortality, accounting for 16% of all under-5 deaths globally (12.8% among children 1-59 months and 2.7% among neonates) (5, 6). In 2015, pneumonia caused an estimated 0.9 million (UR, 0.8 to 1.1) under-5 deaths, and the majority of these deaths occurred in low- and middle-income countries and mainly were preventable (6, 7). Sub-Saharan Africa and South-East Asia, where coverage of basic health services is low, service availability and readiness of health facilities are often inadequate, and quality of care is sub-optimum, contributed to more than three-fourths of these deaths from pneumonia (7, 8). In 2015, the cause-specific mortality among children under-5 years of age due to pneumonia was 6.6 per 1,000 live births, with a 95% confidence interval (CI) of 5.8 to 8.0 (7).

In addition to mortality, the incidence of pneumonia and its associated morbidities contribute significantly to the global burden of disease (4). Pneumonia also contributes indirectly to the global burden of disease through its sequalae. A systematic review was conducted (13 studies, 722 children) to estimate the risk of long term sequalae of childhood pneumonia and reported that the risk of developing at least one major sequelae (restrictive lung disease, obstructive lung disease, bronchiectasis) was 5.5% (95% CI, 2.8 to 8.3) among children with pneumonia who did not require hospitalization and 13.6% (95% CI, 6.2 to 21.1) among children with pneumonia who required hospitalization (9). The study also reported that the risk of developing at least one minor sequelae (chronic bronchitis, asthma, other abnormal pulmonary function, other respiratory disease) was 1.6% (95% CI, 1.0 to 8.5) among children with pneumonia who did not require hospitalization and 7.1% (95% CI, 1.0 to 13.4) among children with pneumonia who required hospitalization. The estimated annual incidence of clinical pneumonia in developing countries was 231 episodes per 1,000 children years of observation (95% CI, 144 to 377) in 2015, which declined from 329 episodes (95% CI, 201 to 537) in 2000 (7). The number of episodes of clinical pneumonia among children under-5 years was 138 million (UR, 86 to 226) in 2015, which decreased from 178 million (UR, 110 to 289) in 2000 (7). Around 16% of these pneumonia episodes were severe (presence of chest in-drawing as one of the danger signs) accounting for an estimated 22 million episodes (UR, 18 to 46) of severe pneumonia in 2015, a substantial reduction from 28 million episodes (UR, 14 to 36) in 2000 (7). There were 16.4 million children (UR, 9.8 to 28) who were

admitted to hospitals due to pneumonia in 2015, a marked increase from 5.7 million (UR, 3.5 to 9.5) in 2000 (7).

Although significant achievements have been made globally in reducing childhood pneumonia incidence and mortality in the past two decades, gaps remain regarding the availability, accessibility and quality of services for the management of pneumonia in countries with some of the highest burdens (7, 10). In 2009 and 2013, the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) published the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD) and set forth an ambitious goal of ending all preventable deaths due to pneumonia by 2025 (pneumonia specific mortality rate <3 deaths per 1,000 live births by 2025) (11). The GAPPD report recommended adopting an integrated approach and outlined a set of core interventions for prevention, protection and treatment of pneumonia and diarrhoea. However, there are substantial gaps in achieving high coverage of these core interventions in 15 high burden countries contributing 70% of all pneumonia and diarrhoea related deaths (10). Only 50% of children in these high burden countries had received exclusive breast feeding, 80% received vaccination against Haemophilus influenzae type b (Hib3) and 60% received vaccines against streptococcus pneumoniae (PCV). Among children with a suspected episode of pneumonia and 49% were taken to an appropriate health care provider (10, 12). In 2018, the median GAPPD pneumonia score (a composite indicator based on the coverage of core interventions) was 59% among these 15 countries, and none of these countries met the target of 84% (10). The GAPPD pneumonia score varied from 25% to 78% across these fifteen countries,

which reflect the existence of wide between-country-disparities (10). In addition, there were issues with inequity as the coverage of these key interventions varied significantly by gender, wealth, maternal education and residence (10). Without strategic focus, substantial investments and consorted efforts across the global health community, achieving the ambition 2025 target of ending preventable pneumonia death and 2030 Sustainable Development Goal (SDG) target of reducing child mortality to 12 and below per 1,000 live births will be challenging (10, 13).

Among the 75 countdown which accounted for more than 95% of global maternal, newborn and child deaths in 2015, Bangladesh was one of the few countries to have reached the MDG-4 target on time (14, 15). However, Bangladesh still suffers from one of the highest under-5 mortality rates in the world, which was 45 per 1,000 live births according to the latest Bangladesh Demographic and Health Survey conducted in 2017 (16). With more than 24,000 deaths in 2015, pneumonia accounted for around 19% of all under-5 deaths in Bangladesh (12). Pneumonia specific mortality among children under-5 was around 11.7 per 1,000 live births in 2015(12).

The estimated annual incidence of clinical pneumonia in Bangladesh was 277 episodes per 1,000 children years of observation (95% CI, 163 to 470) in 2015, which was a reduction from 361 episodes (95% CI, 218 to 601) in 2000 (7). It is estimated that there were more than 4 million episodes of clinical pneumonia among children under-5 years of age in Bangladesh in 2015, of which around 677,000 were severe pneumonia episodes (7). The burden of pneumonia and severe pneumonia episodes have declined by around 30% between 2000 and 2016 (7).

There are substantial gaps in achieving high coverage of core interventions for averting pneumonia burden in Bangladesh (10). Although the coverage of key vaccines was reasonably high (97% for Hib3 and 97% for PCV), only 55% of children had received exclusive breast feeding (10). Among children with a suspected episode of pneumonia, and only 42% were taken to an appropriate health care provider (10). In 2018, the median GAPPD pneumonia score was 64% in Bangladesh among these 15 countries, and the country failed to meet the global target of 84% (10).

A systematic review was conducted in 2013 to identify the risk factors in children under-5 years of age for severe acute lower respiratory infections (including pneumonia) (17). Low birth weight (odds ratio: 3.2; 95% CI, 1.0 to 9.9), indoor air pollution (odds ratio: 1.6; 95% CI, 1.1 to 2.3), lack of exclusive breast feeding (odds ratio: 2.7; 95% CI, 1.7 to 4.4), incomplete immunisation as defined by lack of immunisation for measles at the end of the first year of life (odds ratio: 1.8; 95% CI 1.3 to 2.5), crowding as defined by more 7 persons per household (odds ratio: 1.9; 95% CI, 1.5 to 2.5), underweight (weight for age <standard deviation) (odds ratio: 4.5; 95% CI, 2.1 to 9.5), stunting (height for age <2 standard deviation) (odds ratio: 2.6; 95% CI, 1.5 to 4.6), wasting (weight for height <2 standard deviation) (odds ratio: 2.8; 95% CI, 1.8 to 4.3) and HIV infection (odds ratio: 4.6; 95% CI 2.2 to 9.7) were reported to be definite risk factors in that review since they showed consistent associations with severe acute lower respiratory infections. Passive smoking, lack of maternal education, sex (being male), vitamin D deficiency, preterm birth, anaemia, zinc deficiency was reported to be among the risk factors since they showed associations in the majority of the studies. On the other hand, day care, birth interval

(<24 months), birth order (three or more), vitamin A deficiency and previous history of severe acute lower respiratory infections were reported to be possible risk factors since they showed sporadic associations across different studies.

Another systematic review was conducted in 2015 to evaluate risk factors for death from acute lower respiratory infections (ALRI) in children in low- and middle-income countries (18). Regarding host and disease characteristics, severe pneumonia according to WHO classification (odds ratio: 9.2; 95% CI, 6.4 to 13.9), age below 2 months (odds ratio: 5.2; 95% CI, 1.7 to 16.0), HIV/AIDS (odds ratio: 4.7; 95% confidence interval 3.7 to 5.9), and severe malnutrition (odds ratio: 4.3; 95% CI, 3.5 to 5.5) were reported to be strong risk factors for deaths among children with acute low lower respiratory infection. Regarding socio-economic and environmental factors, young maternal age (odds ratio: 1.84, 95% CI, 1.03 to 3.31), low maternal education (odds ratio: 1.43, 95% CI, 1.13 to 1.82), low socio-economic status (odds ratio: 1.62, 95% CI, 1.32 to 2.00), second-hand smoke exposure (odds ratio: 1.52, 95% CI, 1.20 to 1.93), indoor air pollution (odds ratio: 3.02, 95% CI, 2.11 to 4.31) and incomplete immunization (odds ratio: 3.02, 95% CI, 2.11 to 4.31) were reported to be prominent risk factors of deaths.

1.2 PNEUMONIA DEFINITIONS AND CLASSIFICATIONS

Hippocrates was the first scholar to describe pneumonia in 460-370 BC (19), but the clinical and pathological features of pneumonia was first outlined by Laennec in 1819 (20). The differentiation between lobal-pneumonia and broncho-pneumonia was first proposed by Rokitansky in 1842 (21). Today, the definition of pneumonia varies substantially based on affected site, clinical severity, aetiology, method of

diagnosis/classification, etc. (22). The International Classification of Diseases (ICD) lists pneumonia in seven codes (23). In addition, there are three separate codes for acute bronchitis, bronchiolitis and unspecified acute lower respiratory infections, which share similar clinical features with pneumonia.

According to *Harrison's Textbook of Internal Medicine* pneumonia is a form of acute infection on lung parenchyma caused by various organisms, which fills the alveoli with inflammatory cells and fluid, thus makes breathing difficult and limits intake of oxygen through respiration (24). Although the text book described the pathologic demarcation between lobar- and broncho-pneumonia, it recommends classifying pneumonia based upon the causative microorganism (aetiology) (24). However, aetiology specific diagnosis and classification of pneumonia will require invasive procedures and advanced laboratory support for relevant microbiological and serological tests (culture, C-Reactive Protein, PCR, etc); which will be difficult for health facilities in resource poor settings to introduce and sustain. Moreover, specific microbial aetiology remains unknown in majority of patients (24, 25). Cognisant of this reality, WHO recommends classifying pneumonia based on selected clinical signs and symptoms (history of cough or difficult breathing, breathing rate, chest indrawing, stridor, wheeze) (26, 27). In addition to this, WHO recommends other pneumonia classification based on chest radiograph findings (28) and the International Classification of Diseases (ICD) (23).

1.3 CURRENT STATUS AND TREND IN THE AETIOLOGY OF CHILDHOOD PNEUMONIA

A number of infectious agents including bacteria, virus and fungi can cause pneumonia. *Streptococcus pneumoniae and Haemophilus influenzae type b* (Hib) are the main bacterial causes of pneumonia (29-35). Among other bacterial causes *S. aureus,* non-typable *Haemophilus influenzae, Mycoplasma pneumonae, Moraxella catarrhalis, etc. are notable* (29, 32, 34, 36-38). Respiratory syncytial virus (RSV) is the main viral cause of pneumonia (including bronchiolitis), followed by rhino, adeno, influenza A and B, parainfluenza, corona, boca, human metapneumovirus and adenovirus (39-44). However, the majority of these estimates predates the introduction of pneumococcal conjugate vaccine (PCV) and Hib vaccine in countries with high burden of pneumonia.

The introduction of PCV in national immunization programmes resulted in significant reduction in incidence and severity of pneumonia in high-income countries and some of the Latin American countries (45-47). Subsequently, RSV and other viruses became the major pathogens causing pneumonia among children in these countries (48, 49). A study estimating the effect of PCV and Hib vaccine in developing countries through the LiST based modelling exercise reported 4% reduction of clinical pneumonia, 6% reduction of severe pneumonia and 18% reduction of radiologically confirmed pneumonia due to Hib vaccine, and 7% reduction of clinical pneumonia, 7% reduction of severe pneumonia and 26% reduction of radiologically confirmed pneumonia due to PCV (50). However, there is paucity of evidence regarding pneumonia aetiology after introduction of PCV and Hib vaccine in Africa and South

Asia, where majority of global pneumonia burden is concentrated in. Several studies are being conducted in some of high burden countries to address this key evidence gap. Of which, the most notable is the Pneumonia Aetiology Research for Child Health (PERCH) project which aims to evaluate the etiologic agents causing severe pneumonia in children from 7 developing countries with diverse contexts and settings (51). Although the final results of this multi-country study are yet to be published, a pilot study from one of the PERCH study sites reported bacterial and viral aetiology of children hospitalized with lower respiratory infection (pneumonia and bronchiolitis) (52). The pathogens were detected in nasopharyngeal specimens, induced sputum, blood, or urine. At least one pathogen was detected from 88% of cases. A bacterial pathogen was detected in 23% of cases and a viral pathogen was detected in 83% of cases. Out of all the pathogens detected in the pilot study, around 32% were RSV, and 24% were rhinovirus. Less than 2% pathogens were *Streptococcus pneumoniae and only 4% were Haemophilus influenzae.* Another study conducted in a South African site showed a high coverage of PCV and Hib vaccine. (53). RSV and Influenza (A, B and C) were reported to be the major contributor of pneumonia instead of Streptococcus *pneumoniae and Haemophilus influenzae. B. pertussis* was reported to be one the major bacterial pathogens in that study.

1.4 GLOBAL, REGIONAL AND NATIONAL STRATEGIES TO PREVENT, PROTECT AND TREAT CHILDHOOD PNEUMONIA

For outpatient management of common childhood illnesses, including pneumonia, the global recommendation is to adopt the Integrated Management of Childhood

Illness (IMCI) strategy in low-resource settings where the under-5 mortality rate is more than 40 per 1,000 live births (54, 55).

IMCI is a global strategy which was developed by the Department of Child Health and Development of World Health Organization (WHO) in collaboration with other WHO programmes and United Nations Children's Fund (UNICEF) in the mid-1990s to reduce the morbidity and mortality of under-5 children (56). IMCI is designed to address the major causes of childhood deaths (acute respiratory infections (ARI), diarrhoea, measles, malaria, malnutrition, etc.) through an integrated approach as sick children often present with signs and symptoms that are related to more than one condition or they have more than one condition (54, 55, 57). In health facilities, the IMCI strategy promotes the accurate identification of childhood illnesses in outpatient settings, ensuring appropriate combined treatment of all major illnesses, strengthening of the counselling of caretakers and the provision of preventive services, speeding up the referral of severely ill children and improving the quality of care of sick children at the referral level (26, 54, 55, 57, 58). In the home setting, it promotes appropriate care seeking behaviours, improved nutrition and preventive care, and the correct implementation of prescribed care (26, 54, 55, 57, 58). The following are the three basic pillars of the IMCI Strategy (59, 60):

- Improving skills of health workers through the provision of training, locally adapted case management guidelines and activities to promote their use;
- Strengthening health system's effective management of childhood illness, including supervision and supply;

- Improving family and community practices

The IMCI strategy focuses on improving quality of outpatient care at first-level health facilities by introducing an algorithm-based clinical classification and management system in settings where health service providers with minimum knowledge, training and experience must manage sick children with limited resources (26, 54, 55, 58). The clinical algorithm of IMCI guides a service provider to follow a step-by-step approach in history taking, clinical assessment, classification of the illness and treatment for a sick child (26).

Effective implementation of the IMCI guidelines has demonstrated an increase in the use of health services, improvements in health workers performance and quality of care, reduction in irrational use of drugs including antibiotics and decline of childhood mortality (13% to 70%) in countries with limited resources (61-69). It is now being implemented in more than 100 countries across all WHO-regions and continents, of which approximately two-thirds have achieved national coverage of more than 90% districts (58, 70). Although IMCI has been implemented in a large proportion of their districts in many countries, few have achieved full national scale up (58). Despite the high reported implementation in many of these countries, IMCI strategy is yet to benefit the children who are most in need as coverage of IMCI is the lowest in high mortality countries and settings (58).

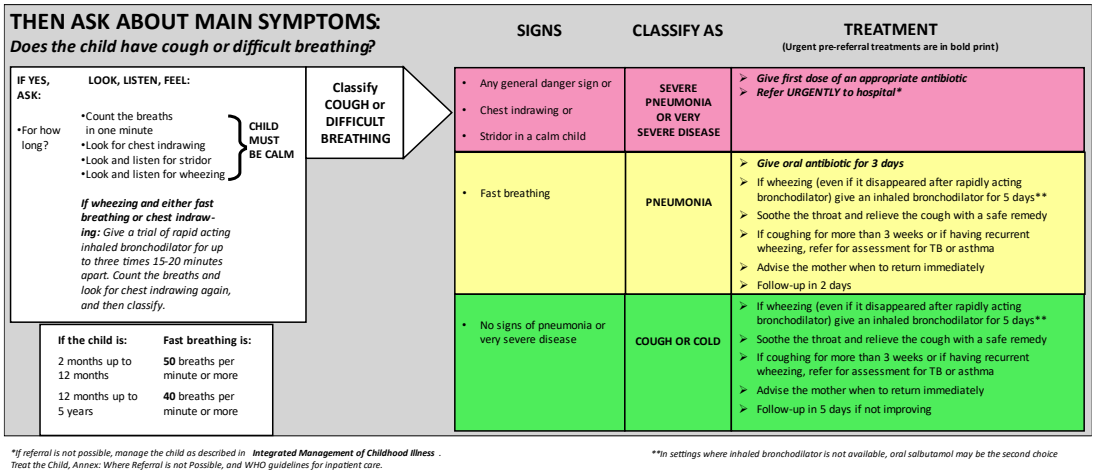
1.5 RECOMMENDATIONS FOR USING PULSE OXIMETRY IN CLASSIFICATION AND MANAGEMENT OF CHILDHOOD PNEUMONIA

The previous IMCI guidelines (published in 2008) recommend that any child presenting with cough or difficult breathing should be assessed clinically for the presence of any danger sign, chest indrawing, stridor, wheezing; and would be classified as one of the followings (Figure 1.1) (71):

1. 'Severe Pneumonia/Very Severe Disease'
2. 'Pneumonia'
3. 'Cough or Cold'

This implies that, according to the previous IMCI guidelines any child (2 months to 59 months) presenting with any danger sign or chest indrawing, or stridor would be classified as 'Severe Pneumonia/Very Severe Disease', and therefore, would be urgently referred to a hospital after giving the first dose of an appropriate antibiotic. According to the WHO Pocket Book of Hospital Care for Children, 'Severe Pneumonia/Very Severe Disease' cases would require inpatient care and should be treated with injectable antibiotics with other supportive care (27).

Figure 1.1: Assessment and classification of children aged 2-59 months presenting with cough or difficult breathing according to the IMCI guidelines 20 (adopted from IMCI Chart Booklet 2008)



Source: *http://apps.who.int/iris/bitstream/handle/10665/43993/9789241597289_eng.pdf?sequence=1*

The sensitivity of the previous definition of 'Severe Pneumonia/Very Severe Disease' was very high but it had issues with low specificity. This resulted in over referral of 'Severe Pneumonia/Very Severe Disease' cases to the hospital for inpatient care, which gave rise to the following concerns:

Firstly, in appropriate referral and inpatient care create additional health system burden for relevant logistics and supplies and substantially raises the cost of health care (72).

Secondly, over-referral contributes to over-crowding in referral facilities and may cause substantial delay for other severe cases to receive appropriate care. It may also cause disproportionate allocated and utilization of life saving commodities (antibiotics, oxygen, etc.), thus creating barriers to providing appropriate care to the more severe cases.

Thirdly, Injectable antibiotics may increase the risk of cannula sites of infections and transmission of infections through contaminated needles (73).

Lastly, children who have been referred for inpatient management might not reach the hospitals due to various demand-side barriers and challenges related to transportation (74, 75).

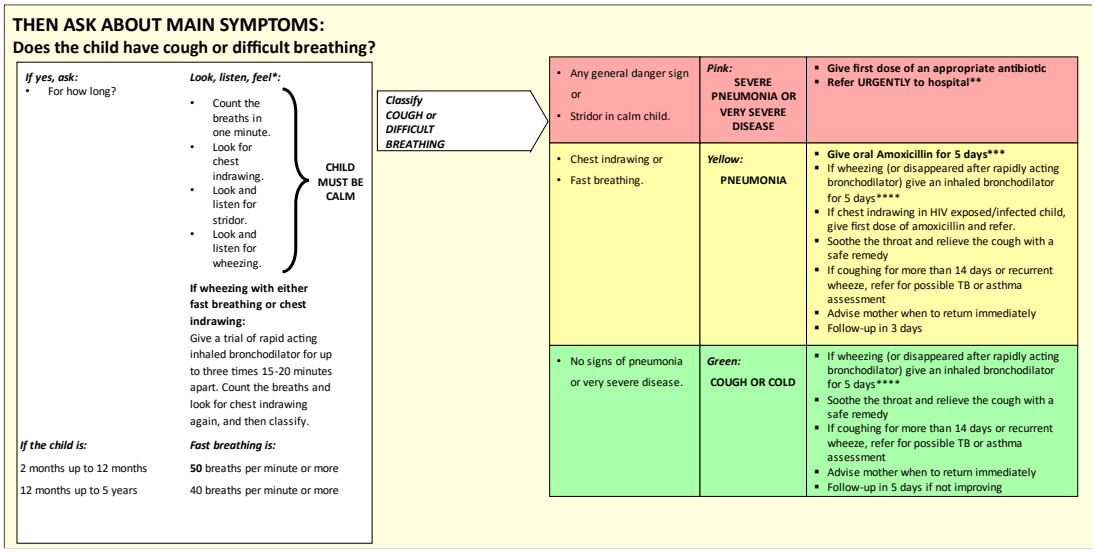
In order to address the above-mentioned challenges, it was imperative to reassess the validity of 'severe pneumonia' classification as outlined in the previous IMCI

guidelines (2008). Prognostic value and treatment options for different signs of 'severe pneumonia' including chest indrawing required a critical evaluation.

Addo-Yobo et al and Hazer et al. (NO-SHOTS Study) conducted a randomized controlled trial to evaluate the effectiveness of treating children with chest indrawing as the only sign of illness with home-based oral antibiotics. Although there are some concerns regarding the overall quality of these studies, both reported that the treatment failure rate among children who were treated with oral antibiotics was non-inferior to the treatment failure rate with parenteral antibiotics. Based on these two studies and other relevant evidence (76-80), WHO published an evidence summary regarding the classification and treatment options for pneumonia management (81, 82). Subsequently, IMCI guidelines were revised in 2014 through an expert consultation process (26).

The new IMCI guidelines (2014) recommends that any child (2 months to 59 months) presenting with fast breathing or chest indrawing (and no other danger signs) should be classified as 'Pneumonia', and would be treated through home-based management with oral antibiotics (amoxicillin for five days) (26) (Figure 1.2). In addition to other changes in the management to malnutrition, this was the most significant shift from the previous classification and treatment recommendation for pneumonia management (26, 71). Previously, any child with chest indrawing would be classified as 'Severe Pneumonia', therefore would have been urgently referred to the hospital (71).

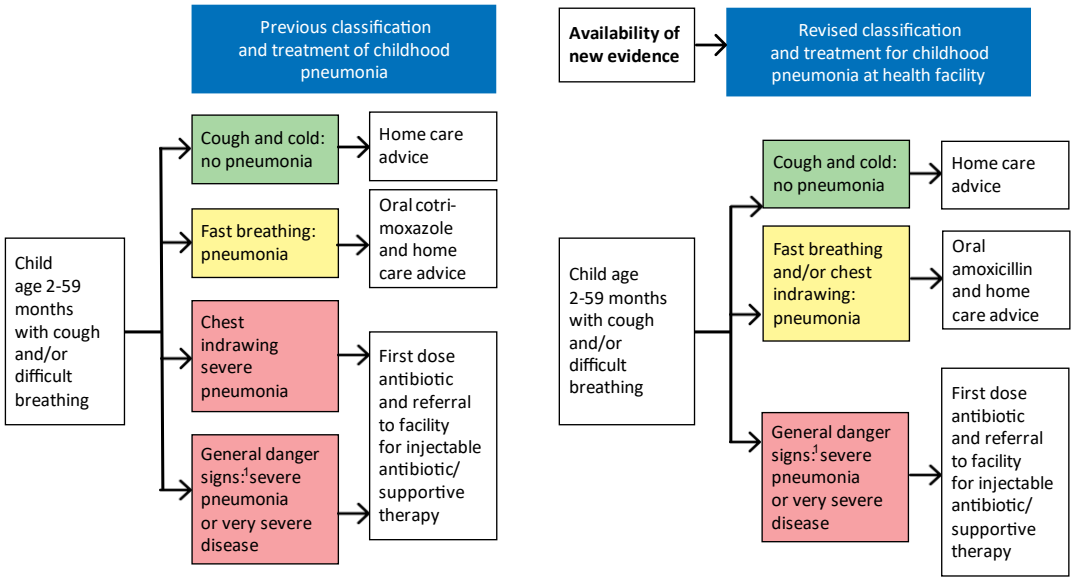
Figure 1.2: Assessment and classification of children age 2-59 months presenting with cough or difficult breathing according to the IMCI guidelines 20 (source: IMCI Chart Booklet 2008) Clinical assessment and classification of children age 2-59 months presenting with cough or difficult breathing according to the IMCI guidelines 2014 (adopted from IMCI Chart Booklet 2014)



Source: https://apps.who.int/iris/bitstream/handle/10665/104772/9789241506823_Chartbook_eng.pdf

An illustrative comparison of the 2008 and 2014 version of IMCI guidelines is presented in Figure 1.3.

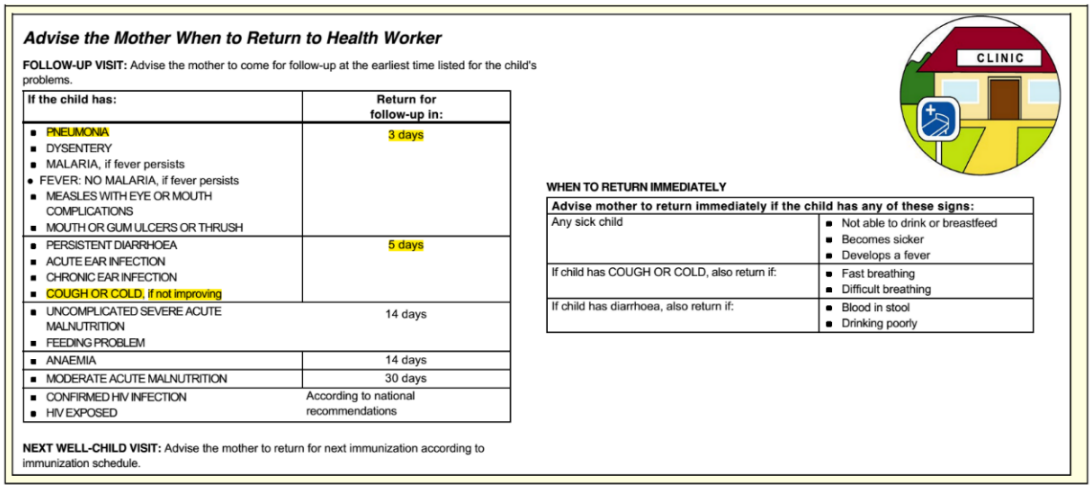
Figure 1.3: Difference in classification and treatment of children aged 2-59 months presenting with cough or difficult breathing according to the IMCI guidelines (2008 vs. 2014) (adopted from the WHO evidence summary)



Source: *https://apps.who.int/iris/bitstream/handle/10665/137319/9789241507813_eng.pdf*

According to the WHO (2014) and Bangladesh adapted IMCI guidelines (2017), the pneumonia cases should be managed through home-based treatment with oral antibiotics for five days. All locally managed 'Pneumonia' cases are asked to come back on day 3 for scheduled follow up visits (26, 83) (Figure 1.4). IMCI guidelines recommend that the service providers should advise the mother/primary care giver about danger signs and the need to return to the health facility with the child immediately if there is a reappearance of any danger sign within this period (Figure 1.4).

Figure 1.4: Instructions of the mother when to return to health worker (adopted from IMCI Chart Booklet 2008)



Advise the Mother When to Return to Health Worker

FOLLOW-UP VISIT: Advise the mother to come for follow-up at the earliest time listed for the child's problems.

If the child has:	Return for follow-up in:
▪ PNEUMONIA ▪ DYSENTERY ▪ MALARIA, if fever persists • FEVER: NO MALARIA, if fever persists ▪ MEASLES WITH EYE OR MOUTH COMPLICATIONS ▪ MOUTH OR GUM ULCERS OR THRUSH	3 days
▪ PERSISTENT DIARRHOEA ▪ ACUTE EAR INFECTION ▪ CHRONIC EAR INFECTION ▪ COUGH OR COLD, if not improving	5 days
▪ UNCOMPLICATED SEVERE ACUTE MALNUTRITION ▪ FEEDING PROBLEM	14 days
▪ ANAEMIA	14 days
▪ MODERATE ACUTE MALNUTRITION	30 days
▪ CONFIRMED HIV INFECTION ▪ HIV EXPOSED	According to national recommendations

NEXT WELL-CHILD VISIT: Advise the mother to return for next immunization according to immunization schedule.

CLINIC

WHEN TO RETURN IMMEDIATELY

Advise mother to return immediately if the child has any of these signs:	
Any sick child	▪ Not able to drink or breastfeed ▪ Becomes sicker ▪ Develops a fever
If child has COUGH OR COLD, also return if:	▪ Fast breathing ▪ Difficult breathing
If child has diarrhoea, also return if:	▪ Blood in stool ▪ Drinking poorly

Although the WHO has now recommended considering chest in-drawing (without any danger signs) as a sign of 'pneumonia' (instead of 'severe pneumonia') according to the 2014-IMCI Guidelines, a systematic review on management of severe pneumonia with chest in-drawing reported an average treatment failure rate of 8.5% on day 6 (95% CI, 5.9%-11.5%) (77, 80, 84-86). Around half of the treatment failure cases (4%) still had chest indrawing on day 6 (84). The treatment failure rates varied between as low as 6.4% in Ghana and as high as 18% in Pakistan among the different studies (77, 80, 84). This implies that some of the 'Pneumonia' cases with chest indrawing would require inpatient care with special support (as recommended by WHO in 2014), although it depends on the validity (mostly specificity) of treatment failure definitions.

There has been significant debate regarding the best prognostic factor including clinical signs and symptoms that can be used in routine care to assess the severity of pneumonia and identify children with a higher risk of morbidity and mortality due to pneumonia (17, 87-90). There are also issues regarding the validity of assessment by

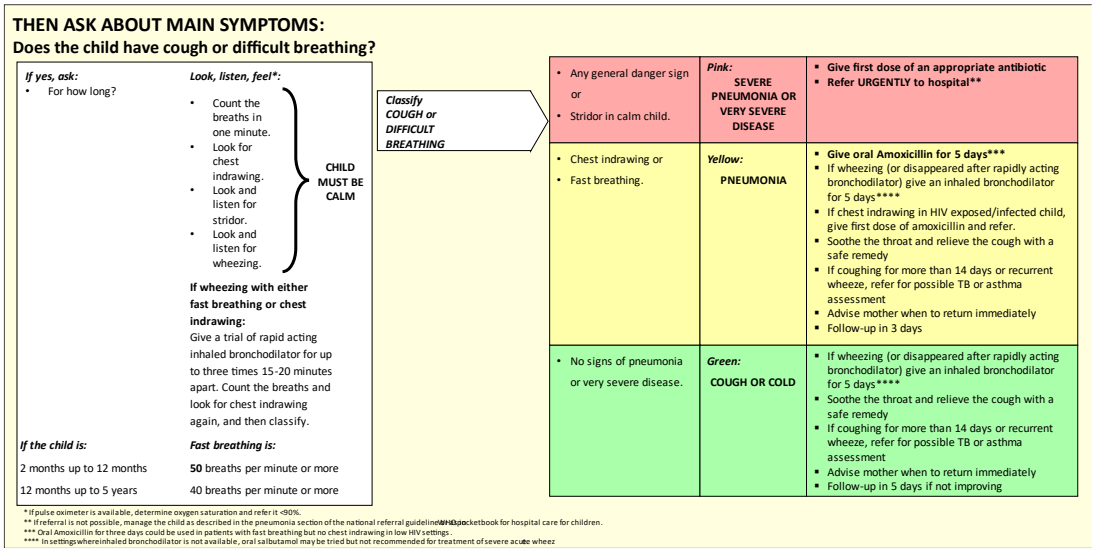
health service providers and recall by caregivers of sick children regarding these clinical sign and symptoms. IMCI classifications greatly depend on the clinical assessment skills of service providers. Different studies have reported that there can be subjective variations in assessment of different clinical signs (danger sings, fast breathing and chest indrawing) by IMCI trained service providers which subsequently may lead to misclassification (such as 'Severe pneumonia' classified as 'Pneumonia'), inappropriate referral (under or over referral) and eventually treatment failure for locally managed pneumonia cases (91-94). As IMCI is designed to be used in resource-limited outpatient settings through health care providers with minimum training and clinical experience, the risks of potential errors in clinical assessment and classification are substantial. Regarding the recall of pneumonia related clinical symptoms by caregivers, the validity (both sensitivity and specificity) is reported to be low (95). Therefore, identifying another valid and reliable prognostic factor which can be integrated into the routine IMCI services holds paramount importance.

Hypoxaemia (SpO_2<90%) is one of the strongest predictors of mortality due to acute lower respiratory infections including WHO classified pneumonia in comparison to other clinical signs. A systematic review (12 studies on 13,936 children) reported that hypoxaemia (SpO_2<90%) was associated with increased odds of death from acute lower respiratory infections (odds ratio 5.47, 95% confidence interval 3.93 to 7.63) (90, 96). The review also reported that among children with pneumonia according to the WHO classification, the odds of dying is also 5-times higher (odds ratio 5.06, 95% 95% confidence interval 3.79 to 6.76) among those who had hypoxaemia. Hypoxaemia is also common among children with pneumonia as another systematic

review conducted in 2008 (21 studies, more than 16,000 children) reported that 13% (IQR 9.3-37.5%) of all children with pneumonia according to the WHO classification (including pneumonia and severe pneumonia) had hypoxaemia (97). The prevalence of hypoxaemia ranged from 3·69% to 80·00% among severe cases and from 6·35% to 100% among very severe cases. The review also reported that hypoxaemia was present in 0.69 to 17.14% non-severe cases (97). Although specific estimates are not available among neonatal pneumonia cases, the prevalence of hypoxaemia ranged from 18% to 23% among neonates requiring hospitalization as reported in different studies (98-102). Another systematic review conducted in 2001 (17 studies, more than 4,000 children) reported that the prevalence of hypoxaemia was 43% among children with clinical pneumonia. It was much higher (73%) among children with radiologically confirmed pneumonia.

Integration of SpO_2 assessment in existing IMCI services can significantly improve the accuracy of assessment of hypoxaemia and increase the validity (accuracy) of pneumonia classification (90, 97). In response to the need and global evidence, WHO has recommended measuring SpO_2 in routine IMCI services (26, 82). According to the updated IMCI guidelines (2014), any sick child having SpO_2<90% should be immediately referred for inpatient management irrespective of the clinical classification (described in Figure 1.5) (26).

Figure 1.5: Addition of pulse oximetry to take referral decision in patients with cough or difficult breathing in the IMCI guideline 2014 (source: IMCI Chart Booklet 2008)



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1.6 PRINCIPLES OF PULSE OXIMETRY AND ITS ROLE IN DETECTION OF HYPOXAEMIA

The Gold Standard for measurement of oxygen saturation in blood is Arterial Blood Gas (ABG) analysis. However, this is invasive, painful, time-consuming and resource intensive. Therefore, it is not useful for point of care diagnostics and not feasible to integrate into primary care settings with a high volume of patients and limited resources. Use of respiratory and non-respiratory clinical signs as predictors of hypoxaemia is feasible in primary care settings but there are major concerns regarding the validity and reliability of these predictors. A systematic review reported that none of the clinical signs was a reliable predictor of hypoxaemia (103). The review reported that the specificity of fast breathing (>70 breaths per minute) was 70-100% but the sensitivity was only 4-57%. Reducing the cut-off to 60 or fewer breaths per minute may increase the sensitivity but it also reduces the specificity substantially. Similarly, the specificity of central cyanosis was higher than that of

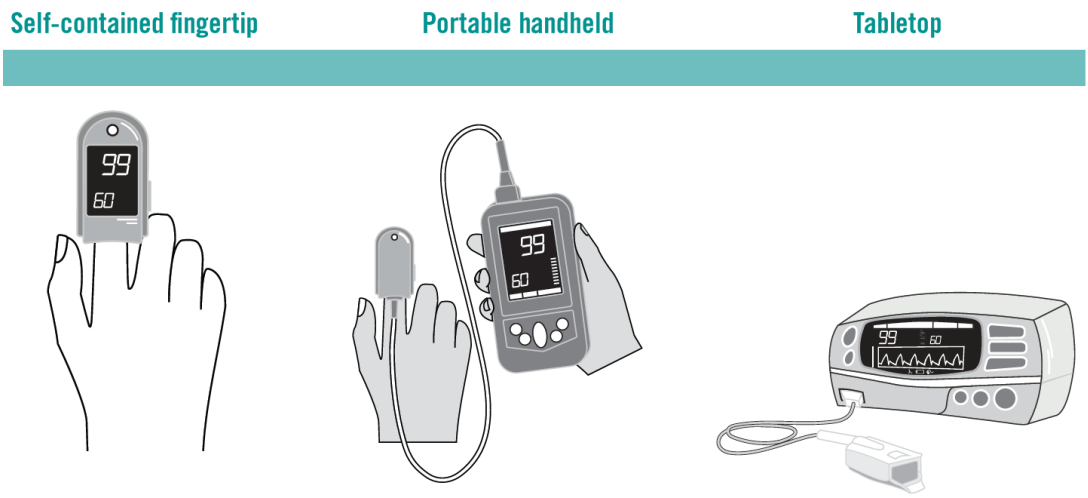
clinical signs, but its sensitivity was only 9-42%. Severe chest in drawing as a clinical sign was not found to be a reasonable predictor of hypoxaemia (103). On the other hand, pulse oximetry is a non-invasive device which can be used as a point of care diagnostics to obtain a reasonably accurate measurement of oxygen saturation of blood. Appropriate use of pulse oximetry along with reliable oxygen sources in district hospitals in developing countries can reduce pneumonia related mortality by 35% (104, 105). The Pneumonia Series published by the Lancet in 2013 outlined four opportunities for further acceleration of progress towards averting global pneumonia burden in low- and middle- income countries (106). Introduction of pulse oximetry in places with intermittent power was identified as one of the new products or technologies which could improve the diagnostics capacities and promote appropriate treatment of pneumonia. One of the other papers it the series identified pulse oximetry together with oxygen therapy with an assured oxygen supply from oxygen concentrators as one the potential cost effective intervention to address deaths due to children pneumonia (107).

Pulse oximetry estimates the oxygen saturation of haemoglobin in arterial blood through spectrophotometry. The sensor of the pulse oximetry has a light emitter diode, a photo-detector diode and a processor. The light emitter diode emits light of two wavelengths i.e., infrared 910-940 nm and red 650-660 nm. The photo-detector diode absorbs the infrared and red light. The processor estimates the oxygen saturation by measuring the quantity of infrared light and red light emitted from the light emitter diode and received by the photo-detector diode (108).

Pulse oximeters based on Aoyagi's theory are still used in modern times, albeit as conventional ones with certain drawbacks, such as difficulty monitoring moving or unstable patients (109). Furthermore, with low or inadequate perfusion, these traditional pulse oximeters misread patient monitoring. It has other drawbacks, such as interacting with visible and infrared light sources. To overcome these drawbacks, Masimo Corporation launched its next-generation Single Extraction Technology (SET) at the turn of the millennium, which is now wide-speeded and at the heart of modern-day pulse oximetry (110). Masimo's SET pulse oximetry now efficiently provides continuous monitoring of the patient's SpO_2 during demanding clinical situations of movement and poor tissue perfusion (111).

Self-contained fingertip, *Portable handheld*, and *Tabletop* pulse oximeters are the three types of pulse oximeters available considering their application. *Tabletop* pulse oximeters outperform the other two varieties in terms of reliability, validity, accuracy, and feasibility, and are recommended for secondary to tertiary level health facilities/clinical settings. Primary and secondary health centres, as well as outpatient departments, can benefit from *portable handheld* pulse oximeters which can be used for both spot checking as well as continuous monitoring of SpO_2. Whereas *self-contained fingertip* pulse oximeters can be used for spot checking of SpO_2 on adults or children, if a paediatric model for an appropriate weight range is used. However, World Health Organization (WHO) does not recommend using *self-contained fingertip* pulse oximeters on neonates (112). Based on the design and application, Figure 1.6 depicts three different types of pulse oximeters.

Figure 1.6: Three types of a pulse oximeters according to their application and design



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The sensor of the pulse oximetry is placed in a relatively translucent part of the body, such as a finger point or an ear lobe. The light emitter emits lights. The oxygenated haemoglobin allows red light to pass through, but absorbs infrared light, whereas deoxygenated haemoglobin allows infrared light to pass through but absorbs red light (108, 113, 114). The ratio of absorbed red to infrared light indicates the degree of oxygenation of the blood. With every cardiac beat (pulse), blood flow/volume to the artery increases, which in-turn increases the light absorption by a photo-detector diode, creating "waveform". Thus, the term "pulse oximetry" refers to the observation of this peak blood flow with each pulse. The oximetry displays the SpO_2 together with an audible signal for each pulse beat, a pulse rate and, in most recent models, a graphical display of the blood flow as it passes the probe.

The first device to measure the blood oxygen saturation using a non-invasive technique was built by Karl Matthes in 1935. The World War-II boosted the evolution of pulse oximetry as it was required to monitor the blood oxygen saturation level of

air-plane pilots flying at high altitudes (115). The first complete reading pulse oximetry was built by Robert Shaw in 1964, which was made commercially available by Hewlett-Packard in 1970. However, due to its large size and high cost, the use of this device was limited to highly sophisticated cardiac catheter laboratories (114). The next generation of pulse oximetry was built by Takuo Aoyagi and Michio Kishi in 1970 using dye-dilution techniques and through the development of photo-plethysmogram (114, 116). The first pulse oximetry suitable for both in-patient and out-patient use was built by Bill New in 1983 (115).

One of the major limitations of pulse oximetry was motion artefact as it led to an inaccurate estimation of blood oxygen saturation level. The earlier models of pulse oximetry devices could not also differentiate between venous and arterial blood during movements of the limb attached to the sensor, which resulted in an underestimation of SpO_2 (117, 118). In 1996 Masimo developed a pulse oximetry which could accurately estimate SpO_2 during low perfusion or periods of patient movement using the Signal Extraction Technology, which is now widely used globally in diverse settings (119, 120).

1.7 GAPS IN EVIDENCE OF USING PULSE OXIMETRY IN RESOURCE LIMITED SETTINGS

Handheld pulse oximetry has made a significant contribution to the non-invasive monitoring of SpO_2 in a wide variety of clinical situations (121). It allows for continuous, safe and reliable measurements of SpO_2 while avoiding the discomfort and risks of arterial puncture (108). However, service providers require specific

training and instructions regarding appropriate use of pulse oximetry in clinical settings.

Pulse oximetry as an intervention has great potential to reduce neonatal and childhood mortality by early detection of hypoxaemia (122, 123). However, the majority of global evidence related to the use of pulse oximetry is from high-income countries for a variety of clinical conditions. There is some evidence related to the use of pulse oximetry in resource poor-settings for improving the quality of paediatric services (124-129). One demonstration study conducted in two first-level referral facilities of Bangladesh showed that introduction of pulse oximetry for inpatient management of paediatric sepsis resulted in near universal adoption of pulse oximetry (assessment of SpO_2) by on-duty nurses, which substantially improved quality of care and treatment outcomes (124). Another study conducted in 18 health centres and among 38 community health workers in rural Malawi demonstrated that SpO_2 status was successfully obtained for 94% of children after introduction pulse oximetry (127). The study also reported that there was moderate agreement (weighted kappa=0.41) regarding measurement of SpO_2 between routine health service providers (comparator) and the paediatric pulmonologist (gold standard). Introduction of pulse oximetry in IMCI services resulted in significant reduction of misclassification of 'Pneumonia' as 69% of hypoxaemic (SpO_2<90%) children at the study centres would have been considered ineligible for referral in the absence of pulse oximetry (127). Health service providers participating in that study also reported several operational challenges regarding the use of pulse oximetry, of which maintenance of the pulse oximetry battery, probe size and fittings

and movement of children were the major issues. Similar operational barriers and challenges were reported by another qualitative study conducted in Bangladesh and Malawi (2016) (128). Another study conducted in Pakistan looked at the feasibility of introducing pulse oximetry in IMCI services (129). The study workers established stable SpO_2 readings within 1 minute among 95% of children assessed (median time 44 seconds). The study also explored the acceptability of introducing pulse oximetry among parents and guardians of children undergoing routine SpO_2 assessments in primary care centres. Almost all the parents/guardians reported that SpO_2 assessment was useful to check the status of their babies and they were satisfied with the routine SpO_2 assessment. Several other studies and reviews reported experiences and challenges associated with the use of pulse oximetry in different contexts (130, 131).

Although all these studies provide crucial evidence in support of introducing pulse oximetry in improving the quality of paediatric service in resource-poor settings, some of these studies predate the recent WHO recommendations regarding IMCI guidelines (2014) and most of these experiences are from resource-intensive demonstration projects, from controlled research environments or for inpatient paediatric care. None of these studies specifically looked at the feasibility and effectiveness of introducing pulse oximetry in IMCI services through routine providers.

There are several health systems barriers and operational challenges associated with introducing new technology (like pulse oximetry) in developing country settings.

Moreover, the characteristics of public health systems in each country are different and might present a unique set of context specific issues and challenges. Hence, feasibility testing plays an important role in the introduction and adaptation of new tools/technologies in routine services in public health settings (129, 132-134).

1.8 PUBLIC HEALTH SYSTEM IN BANGLADESH

The People's Republic of Bangladesh is a low-middle income country with per capita GDP of $1,516 (in 2017), and a land area of 147,547 square kilometres (135, 136). Currently, the country has around 160 million population and is one of the most densely populated countries in the world (1,174 people per square kilometre)(136). Administratively, the country is divided into seven divisions, which are further divided into 64 districts (*zila*s). The districts are divided into sub-districts (*Upazila*s), with a total of 492 sub-districts with an approximate population of 250,000 to 300,000 each). Sub-districts are divided into unions (total of about 4554 with approximate population 25,000 to 30,000 each), which consist of numerous wards and villages.

The health service in Bangladesh is governed by the Ministry of Health and Family Welfare (MOHFW) through two divisions: (i) Health Services Division and (ii) Medical Education and Family Welfare Division (137). Health Services Division is responsible for clinical and public health service delivery and related activities. Medical Education and Family Welfare Division is responsible for family planning services, nursing services, medical education services and services related to research and training for professional and service development. There are 5 regulatory bodies and 9 implementing agencies under MOHFW (137). The regulatory bodies are as follows:

Bangladesh Medical and Dental Council, Bangladesh Nursing Council, State Medical Faculty, Homeo, Unani and Ayurvedic Board, and Bangladesh Pharmacy Council. The implementing agencies are as follows: Directorate General of Health Services (DGHS), Directorate General of Family Planning (DGFP), National Institute of Population Research & Training (NIPORT), Directorate General of Drug Administration (DGDA), Directorate General of Health Economics Unit, Directorate General of Health Engineering Department, Directorate General of Nursing and Midwifery (DGNM), Transport & Equipment Maintenance Organization (TEMO), and National Electro-medical & Engineering Workshop (NEMEW) (137).

DGHS and DGFP are primarily responsible for providing health and family planning services in Bangladesh through different types of public health structures and health care providers. The healthcare infrastructure under MoHFW is in six tiers: national, divisional, district, Upazila (sub-district), union, and ward. At the national level and divisional levels, there are post-graduate institutes and undergraduate medical college hospitals (tertiary care referral hospitals). In each district, there is a district hospital which is a secondary level referral hospital with 100-200 in-patient beds. Each district hospital is staffed with Specialist Doctors (Senior and/or Junior Consultants for Medicine, Surgery, Gyn-Obs, Paediatrics, Eye, ETC, Radiology, etc.), Medical Officers and Nurses. In each sub-district, there is an Upazila Health Complex (UHC) which is the primary level referral hospital with 50 in-patient beds. Each UHC hospital is staffed with Specialist Doctors (Medicine, Survey, Gyn-Obs and Paediatrics-occasionally), Medical Officers and Nurses. At the union level, there are Union Health and Family Welfare Centres (UH&FWCs) which are primary care

facilities offering outpatient services only. Each UH&FWC is staffed with a Sub-Assistant-Community-Medical-Officers (SACMO) with 4 years of pre-service para-medic clinical training and a Family Welfare Visitor (FWV) with 18 months of pre-service reproductive health training. The SACMO is responsible for basic preventive and curative care for the general population including children. The FWV is responsible for basic reproductive and maternal health services. In addition, there is a large network (#13,907) of Community Clinics (CC) at the ward/village level with a catchment population of 6,000-10,000, which often serve as the first point of contact for the provision of primary care. The CCs are primarily served by a Community Health Care Provider (CHCP) with 3 months of in-service basic training and are mainly responsible for delivering primary healthcare services, treatment for common diseases (pneumonia, fever, cough, etc), basic family planning services and health education to the catchment population. Some of the community clinics have also started providing normal delivery services.

Apart from regular health services, MOHFW runs multiple projects for the development of the services under different agencies in collaboration with development partners. The 1st sector wide approach (SWAp) plan was started in 1998 replacing many isolated projects and vertical initiatives. The idea was to create a sustainable plan for developing a comprehensive healthcare service in Bangladesh which should be in alignment with the five-yearly development programme by Planning Commission and National Health Policy, and which would contribute to achieving the global commitments such as MDGs, SDGs. Currently, the 4th health sector programme 2017-2022 (Health Population and Nutrition Sector Program,

HPNSP) is underway. There are 29 Operation Plans in the 4th HPNSP which are distributed across different directorates (DGHS #14, DGFP #7, MOHFW #5 DGDA #1, DGNM #1, and NIPORT#1). Each Operation Plan is led by a Line Director and has a functional administrative structure, including staff, budget and infrastructure. There are two Operation Plans which are directly linked to improving child health services in Bangladesh, including IMCI services. One of the Operation Plans is led by DGHS and another one is led by DGFP. Figure 1.7, 1.8 and 1.9 present a more detailed description of the public health systems and structures in Bangladesh.

Figure 1.7: Public administrative structure in Bangladesh

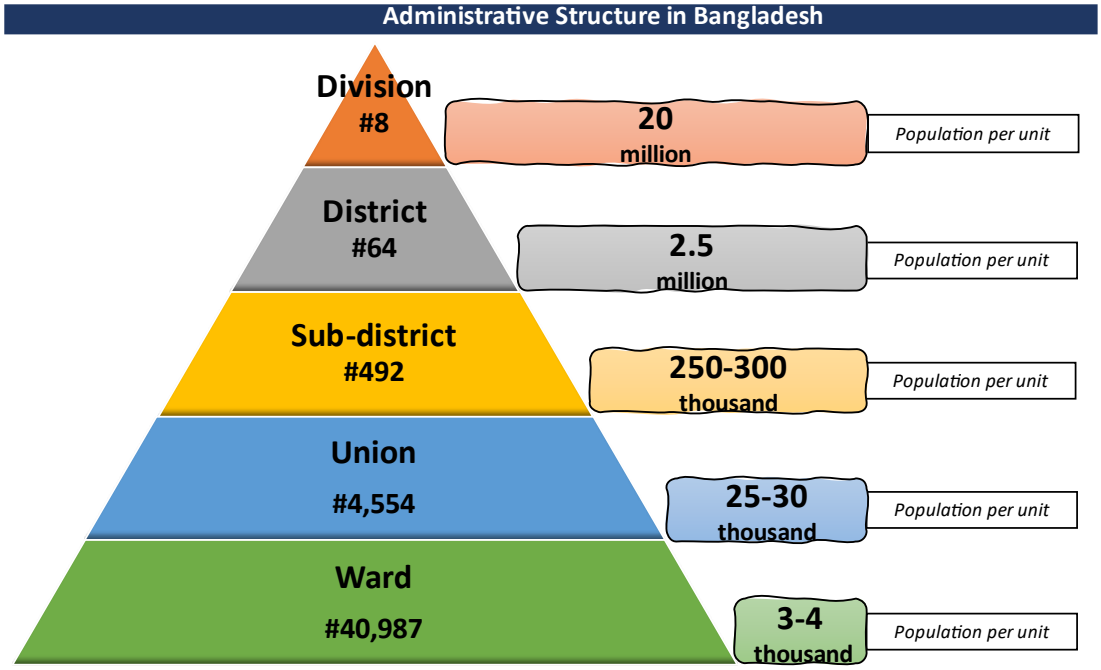
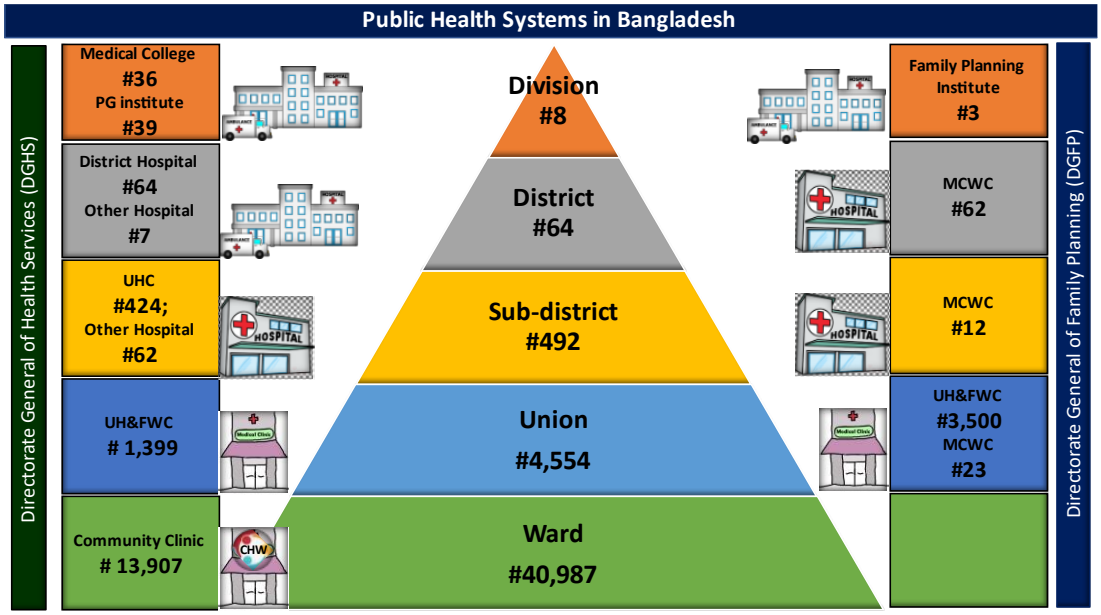
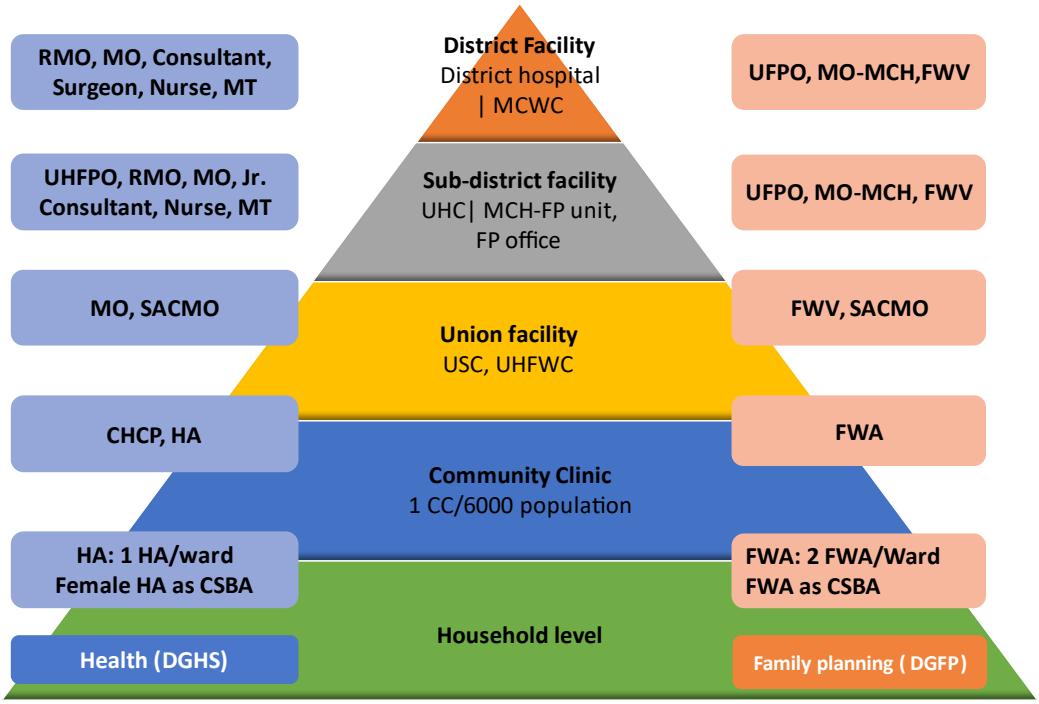


Figure 1.8: Public health service delivery system in Bangladesh



UHC: Upazila Health Complex; UH&FWC: Union Health & Family Welfare Centre; MCWC: Mother & Child Welfare Centre

Figure 1.9: Health service providers in public health service delivery system in Bangladesh



DGHS: Directorate General of Health Services; DGFP: Directorate General of Family Planning; RMO: Resident Medical Officer; MO: Medical Officer; MT: Medical trainee; UHFPO: Upazila Health and Family Planning Officer; SACMO: Sub-Assistant Community Medical Officer; CHCP: Community Heath Care Provider; HA: Health Assistant; CSBA: Community Skill Birth Attendance; UFPO: Upazila Family Planning Officer; MO-MCH: Medical Officer of Maternal and Child Health; FWA: Family Welfare Assistant; FWV: Family Welfare Visitors

Table 1.1: Bangladesh public health system structures, types of health facilities and health care providers

Levels	Health Systems Tiers	Health Facility	Types of Services	Health Service Provider
National	Tertiary Level-Referral	DGHS: Post Graduate Institute and Hospitals (#39)	Curative	Consultants, Medical Officers and Nurses
		DGFP: Family Planning Institutes (#3)	Curative	Consultants, Medical Officers, FWVs
Division (#8) Ave Pop: 22.5 million	Tertiary Level-Referral	DGHS: Medical College (# 36)	Curative	Consultants, Medical Officers and Nurses
		DGHS: Specialized Hospital (#28)	Curative	Consultants, Medical Officer and Nurses
District (#64) Ave Pop: 2.5 million	Secondary Level-Referral	DGHS: District Hospital (#64)	Curative	Consultants, Medical Officers Nurses
		DGHS: General Hospital (#9)	Curative	Consultants, Medical Officers and Nurses
		DGFP: MCWC (#62)	Curative	Medical Officers and FWVs
Sub-district/ Upazila (#492) Ave Pop: 320,000	Primary Level-Referral	DGHS: UHC (#424)	Curative	Consultants, Medical Officers, Nurses and SACMOs
		DGHS: Other Hospital at Upazila Level (#62)	Curative	Consultants, Medical Officers, Nurses and SACMOs
		DGFP: MCWC (#12)	Curative	Medical Officers and FWVs
Union (#4554) Ave Pop: 35,000	Primary Level-outpatient services only	DGHS: Union Sub-Centre (#1312)	Limited Curative	Medical Officers and SACMOs
		DGHS: UHFWC (#87)	Limited Curative	Medical Officers and SACMOs
		DGFP: UH&FWC (#3500)	Limited Curative	SACMOs and FWVs
		DGFP: MCWC (#23)	Curative	Medical Officers and FWVs
Ward (# 40,987)	Primary Level outpatient services only	DGHS: Community Clinic (#13,907)	Promotive, Preventive and Limited Curative	CHCPs
	Primary Level-Household	No facility	Promotive and Preventive	HAs (#20,908) FWAs (#21,083)

DGHS: Directorate General of Health Services; DGFP: Directorate General of Family Planning; RMO: Resident Medical Officer; MO: Medical Officer; MT: Medical trainee; UHFPO: Upazila Health and Family Planning Officer; SACMO: Sub-Assistant Community Medical Officer; CHCP: Community Heath Care Provider; HA: Health Assistant; CSBA: Community Skill Birth Attendance; UFPO: Upazila Family Planning Officer; MO-MCH: Medical Officer of Maternal and Child Health; FWA: Family Welfare Assistant; FWV: Family Welfare Visitors

1.9 IMCI IMPLEMENTATION AND PULSE OXIMETRY INTRODUCTION STATUS IN BANGLADESH

Bangladesh was one of the five countries where the WHO-led Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact (MCE-IMCI) study was implemented (138). In the last 2 years of the study in Bangladesh, the mortality rate was 13.4% lower in IMCI than in comparison areas (95% CI, 14.2 to 34.3) (62). The study also reported that successful implementation of the IMCI package led to improved health-worker skills, health-system support, and family and community practices, translating into increased care-seeking for illnesses (62). It also demonstrated a positive effect on exclusive breast feeding and stunting (62). Based on experience gained and evidence generated through this study and global recommendations, the Government of Bangladesh (GoB) adopted the IMCI strategy in 1998. After successful piloting of facility based IMCI in three Upazilas, IMCI was included in the Sector Investment Plan (SIP) of Health, Nutrition and Population Sector Programme (HNPSP) 2005-2010 as one of the priority strategic components to improve child health in Bangladesh and achieve MDG-4 targets. By the end of 2006, facility-based IMCI was scaled up in 174 upazilas. GoB in collaboration with UNICEF, WHO and other partners scaled up facility-based IMCI in 300 Upazilas (out of 464) in 25 districts in Bangladesh by the end of 2008. By 2014 facility-based IMCI was scaled-up in all districts (#64) and more than 420 Upazilas.

IMCI services are provided in all UHCs through a dedicated corner (IMCI corner) at the out-patient departments. IMCI trained doctors or SACMOs and nurses are responsible for providing services in these IMCI corners. In addition, the majority of

the UH&FWCs (primary care facilities with outpatient services only) are mandated to provide IMCI service through SACMOs. Health care providers (doctors, SACMOs and nurses) must participate in a specialised in-service (11 days) training before providing IMCI services. The routine IMCI services in Bangladesh neither have pulse oximetry for SpO_2 assessment nor have a supply of oxygen to manage hypoxaemia right now. The current health sector programme (2017-2022) envisions sustaining the high national coverage of IMCI services and improving quality of IMCI services through strengthening existing systems and innovations.

1.10 REFERENCE

1. UNICEF, WHO, World Bank Group, United Nations. Levels & Trends in Child Mortality-Report 2018: Estimates developed by the UN Inter-agency Group for Child Mortality Estimation. 2015.
2. United Nations. The Millennium Development Goals Report 2015. 2015.
3. UNICEF, WHO, World Bank Group, United Nations. Levels & Trends in Child Mortality-Report 2018: Estimates developed by the UN Inter-agency Group for Child Mortality Estimation. 2018.
4. Dicker D, Nguyen G, Abate D, Abate KH, Abay SM, Abbafati C, et al. Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. The lancet. 2018;392(10159):1684-735.
5. World Health Organization. Causes of child mortality: Global Health Observatory (GHO) Data 2015 [Available from: http://www.who.int/gho/child_health/mortality/causes/en/.
6. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2017;388(10063):3027-35.
7. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
8. Lim Y-W, Steinhoff M, Girosi F, Holtzman D, Campbell H, Boer R, et al. Reducing the global burden of acute lower respiratory infections in children: the contribution of new diagnostics. Nature. 2006;444(suppl 1):9-18.
9. Edmond K, Scott S, Korczak V, Ward C, Sanderson C, Theodoratou E, et al. Long term sequelae from childhood pneumonia; systematic review and meta-analysis. PLoS One. 2012;7(2):e31239.
10. Johns Hopkins Bloomberg School of Public Health. Pneumonia & Diarrhea Progress Report 2018. 2018.
11. World Health Organization. Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). 2013.
12. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.
13. United Nations. Sustainable Development Goals 2016 [Available from: http://www.un.org/sustainabledevelopment/.
14. Requejo JH, Bryce J, Barros AJ, Berman P, Bhutta Z, Chopra M, et al. Countdown to 2015 and beyond: fulfilling the health agenda for women and children. The Lancet. 2015;385(9966):466-76.
15. Victora CG, Requejo JH, Barros AJ, Berman P, Bhutta Z, Boerma T, et al. Countdown to 2015: a decade of tracking progress for maternal, newborn, and child survival. The Lancet. 2015.

16. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-Preliminary Report. Dhaka, Bangladesh and Calverton, Maryland, USA; 2018.

17. Jackson S, Mathews KH, Pulanić D, Falconer R, Rudan I, Campbell H, et al. Risk factors for severe acute lower respiratory infections in children–a systematic review and meta-analysis. Croatian medical journal. 2013;54(2):110-21.

18. Sonego M, Pellegrin MC, Becker G, Lazzerini M. Risk factors for mortality from acute lower respiratory infections (ALRI) in children under-five years of age in low- and middle-income countries: a systematic review and meta-analysis of observational studies. PloS one. 2015;10(1):e0116380.

19. Adams F. Hippocrates, The Genuine Works. New York: Printed for Sydenham Society; 1849.

20. Laennec RTH, Forbes J. A Treatise on the Diseases of the Chest, and on Mediate Auscultation: Samuel S. and William Wood; 1838.

21. Rokitansky C. Manual of Pathological Anatomy:Inflammations of the lungs (pneumoniae). London: Sydenham Society; 1852.

22. Mackenzie G. The definition and classification of pneumonia. Pneumonia. 2016;8(1):14.

23. World Health Organization. International Classfiication of Diseases (ICD)-11 2018 [Available from: https://www.who.int/classifications/icd/en/.

24. Levison M. Pneumonia, including necrotizing pulmonary infections (lung abscess). Harrison's principles of internal medicine. 1994.

25. McNally LM, Jeena PM, Gajee K, Thula SA, Sturm AW, Cassol S, et al. Effect of age, polymicrobial disease, and maternal HIV status on treatment response and cause of severe pneumonia in South African children: a prospective descriptive study. The Lancet. 2007;369(9571):1440-51.

26. World Health Organization, UNICEF. Integrated Management of Childhood Illness (Chart Booklet). Geneva: World Health Organization,; 2014.

27. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

28. World Health Organization. World Health Organization Pneumonia Vaccine Trial Investigators' Group: Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children2001.

29. Shann F. Etiology of severe pneumonia in children in developing countries. The Pediatric Infectious Disease Journal. 1986;5(2):247-52.

30. Adegbola RA, Falade AG, Sam BE, Aidoo M, Baldeh I, Hazlett D, et al. The etiology of pneumonia in malnourished and well-nourished Gambian children. The Pediatric infectious disease journal. 1994;13(11):975-82.

31. Forgie IM, O'neill KP, Lloyd-Evans N, Leinonen M, Campbell H, Whittle HC, et al. Etiology of acute lower respiratory tract infections in Gambian children: II. Acute lower respiratory tract infection in children ages one to nine years presenting at the hospital. The Pediatric infectious disease journal. 1991;10(1):42-7.

32. Shann F, Germer S, Hazlett D, Gratten M, Linnemann V, Payne R. Aetiology of pneumonia in children in Goroka hospital, Papua New Guinea. The Lancet. 1984;324(8402):537-41.

33. Kamiya Y, Mtitimila E, Graham S, Broadhead R, Brabin B, Hart C. Pneumocystis carinii pneumonia in Malawian children. Annals of Tropical Paediatrics. 1997;17(2):121-6.

34. Falade A, Mulholland E, Adegbola R, Greenwood B. Bacterial isolates from blood and lung aspirate cultures in Gambian children with lobar pneumonia. Annals of tropical paediatrics. 1997;17(4):315-9.

35. Jaiswal N, Singh M, Thumburu KK, Bharti B, Agarwal A, Kumar A, et al. Burden of invasive pneumococcal disease in children aged 1 month to 12 years living in South Asia: a systematic review. PLoS One. 2014;9(5):e96282.

36. Asghar R, Banajeh S, Egas J, Hibberd P, Iqbal I, Katep-Bwalya M, et al. Multicentre randomized controlled trial of chloramphenicol vs. ampicillin and gentamicin for the treatment of very severe pneumonia among children aged 2 to 59 months in low resource settings: a multicenter randomized trial (spear study). BMJ. 2008;336:80-4.

37. Graham SM, Molyneux EM, Walsh AL, Cheesbrough JS, Molyneux ME, Hart CA. Nontyphoidal Salmonella infections of children in tropical Africa. The Pediatric infectious disease journal. 2000;19(12):1189-96.

38. Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among children admitted to a rural hospital in Kenya. New England Journal of Medicine. 2005;352(1):39-47.

39. Weber MW, Weber MW, Mulholland EK, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. Tropical medicine & international health. 1998;3(4):268-80.

40. Simoes EA. Respiratory syncytial virus infection. The Lancet. 1999;354(9181):847-52.

41. Stensballe LG, Devasundaram JK, Simoes EA. Respiratory syncytial virus epidemics: the ups and downs of a seasonal virus. The Pediatric infectious disease journal. 2003;22(2):S21-S32.

42. Sinaniotis C. Viral pneumoniae in children: incidence and aetiology. Paediatric Respiratory Reviews. 2004;5:S197-S200.

43. JuvÉn T, Mertsola J, Waris M, Leinonen M, Meurman O, Roivainen M, et al. Etiology of community-acquired pneumonia in 254 hospitalized children. The Pediatric infectious disease journal. 2000;19(4):293-8.

44. Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. The Lancet. 2010;375(9725):1545-55.

45. Angoulvant F, Levy C, Grimprel E, Varon E, Lorrot M, Biscardi S, et al. Early impact of 13-valent pneumococcal conjugate vaccine on community-acquired pneumonia in children. Clinical Infectious Diseases. 2014;58(7):918-24.

46. Tregnaghi MW, Sáez-Llorens X, López P, Abate H, Smith E, Pósleman A, et al. Efficacy of pneumococcal nontypable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV) in young Latin American children: a double-blind randomized controlled trial. PLoS medicine. 2014;11(6):e1001657.

47. Simonsen L, Taylor RJ, Schuck-Paim C, Lustig R, Haber M, Klugman KP. Effect of 13-valent pneumococcal conjugate vaccine on admissions to hospital 2 years after its introduction in the USA: a time series analysis. The Lancet Respiratory Medicine. 2014;2(5):387-94.

48. Jain S, Williams DJ, Arnold SR, Ampofo K, Bramley AM, Reed C, et al. Community-acquired pneumonia requiring hospitalization among US children. New England Journal of Medicine. 2015;372(9):835-45.

49. Rhedin S, Lindstrand A, Hjelmgren A, Ryd-Rinder M, Öhrmalm L, Tolfvenstam T, et al. Respiratory viruses associated with community-acquired pneumonia in children: matched case–control study. Thorax. 2015;70(9):847-53.

50. Theodoratou E, Johnson S, Jhass A, Madhi SA, Clark A, Boschi-Pinto C, et al. The effect of Haemophilus influenzae type b and pneumococcal conjugate vaccines on childhood pneumonia incidence, severe morbidity and mortality. International journal of epidemiology. 2010;39(suppl_1):i172-i85.

51. Levine OS, O'brien KL, Deloria-Knoll M, Murdoch DR, Feikin DR, DeLuca AN, et al. The Pneumonia Etiology Research for Child Health Project: a 21st century childhood pneumonia etiology study. Clinical infectious diseases. 2012;54(suppl_2):S93-S101.

52. Mermond S, Zurawski V, D'Ortenzio E, Driscoll AJ, DeLuca AN, Deloria-Knoll M, et al. Lower respiratory infections among hospitalized children in New Caledonia: a pilot study for the Pneumonia Etiology Research for Child Health project. Clinical infectious diseases. 2012;54(suppl_2):S180-S9.

53. Zar HJ, Barnett W, Stadler A, Gardner-Lubbe S, Myer L, Nicol MP. Aetiology of childhood pneumonia in a well vaccinated South African birth cohort: a nested case-control study of the Drakenstein Child Health Study. The Lancet Respiratory medicine. 2016;4(6):463-72.

54. World Health Organization. IMCI information package. INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS (IMCI). Geneva; 1999.

55. Gove S. Integrated management of childhood illness by outpatient health workers: technical basis and overview. The WHO Working Group on Guidelines for Integrated Management of the Sick Child. Bulletin of the World Health Organization. 1997;75(Suppl 1):7.

56. Tulloch J. Integrated approach to child health in developing countries. The Lancet. 1999;354:SII16-SII20.

57. World Health Organization. Management of childhood illness in developing countries: Rationale for an integrated strategy: World Health Organization,; 1999.

58. World Health Organization. Integrated Management of Childhood Illness: Global Survey Report. 2017.

59. World Health Organization, UNICEF. IMCI Planning Guide: Gaining experience with the IMCI strategy in a country: World Health Organization; 1999.

60. World Health Organization. Planning National Implementation of IMCI: World Health Organization; 1999.

61. Sazawal S, Black RE, Group PCMT. Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials. The Lancet infectious diseases. 2003;3(9):547-56.

62. Arifeen SE, Hoque DE, Akter T, Rahman M, Hoque ME, Begum K, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. The Lancet. 2009;374(9687):393-403.

63. Chowdhury EK, El Arifeen S, Rahman M, Hoque DE, Hossain MA, Begum K, et al. Care at first-level facilities for children with severe pneumonia in Bangladesh: a cohort study. The Lancet. 2008;372(9641):822-30.

64. Schellenberg JRA, Adam T, Mshinda H, Masanja H, Kabadi G, Mukasa O, et al. Effectiveness and cost of facility-based Integrated Management of Childhood Illness (IMCI) in Tanzania. The Lancet. 2004;364(9445):1583-94.

65. Nguyen DTK, Leung KK, McIntyre L, Ghali WA, Sauve R. Does integrated management of childhood illness (IMCI) training improve the skills of health workers? A systematic review and meta-analysis. PloS one. 2013;8(6):e66030.

66. Gera T, Shah D, Garner P, Richardson M, Sachdev HS. Integrated management of childhood illness (IMCI) strategy for children under-five. Cochrane Database of Systematic Reviews. 2016(6).

67. Theodoratou E, Al-Jilaihawi S, Woodward F, Ferguson J, Jhass A, Balliet M, et al. The effect of case management on childhood pneumonia mortality in developing countries. International journal of epidemiology. 2010;39(suppl_1):i155-i71.

68. Rakha MA, Abdelmoneim A-NM, Farhoud S, Pièche S, Cousens S, Daelmans B, et al. Does implementation of the IMCI strategy have an impact on child mortality? A retrospective analysis of routine data from Egypt. BMJ open. 2013;3(1):e001852.

69. Kanyuka M, Ndawala J, Mleme T, Chisesa L, Makwemba M, Amouzou A, et al. Malawi and Millennium Development Goal 4: a Countdown to 2015 country case study. The Lancet Global Health. 2016;4(3):e201-e14.

70. Chopra M, Binkin NJ, Mason E, Wolfheim C. Integrated management of childhood illness: what have we learned and how can it be improved? Archives of disease in childhood. 2012;97(4):350-4.

71. World Health Organization, UNICEF. Integrated Management of Childhood Illness (Chart Booklet). Geneva: World Health Organization,; 2008.

72. Hoque DM, Rahman M, Billah SM, Savic M, Karim AR, Chowdhury EK, et al. An assessment of the quality of care for children in eighteen randomly selected district and sub-district hospitals in Bangladesh. BMC pediatrics. 2012;12(1):197.

73. Hauri AM, Armstrong GL, HUTiN YJ. Contaminated injections in health care settings. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors Geneva: World Health Organization. 2003.

74. Owais A, Sultana S, Stein AD, Bashir NH, Awaldad R, Zaidi AK. Why do families of sick newborns accept hospital care? A community-based cohort study in Karachi, Pakistan. J Perinatol. 2011;31(9):586-92.

75. Peterson S, Nsungwa-Sabiiti J, Were W, Nsabagasani X, Magumba G, Nambooze J, et al. Coping with paediatric referral—Ugandan parents' experience. The Lancet. 2004;363(9425):1955-6.

76. Straus WL, Qazi SA, Kundi Z, Nomani NK, Schwartz B, Group PC-tS. Antimicrobial resistance and clinical effectiveness of co-trimoxazole versus amoxycillin for pneumonia among children in Pakistan: randomised controlled trial. The Lancet. 1998;352(9124):270-4.

77. Addo-Yobo E, Anh DD, El-Sayed HF, Fox LM, Fox MP, MacLeod W, et al. Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the MASS study. Tropical Medicine & International Health. 2011;16(8):995-1006.

78. Atkinson M, Lakhanpaul M, Smyth A, Vyas H, Weston V, Sithole J, et al. A multicentre randomised controlled equivalence trial comparing oral amoxicillin and intravenous benzyl penicillin for community acquired pneumonia in children PIVOT Trial. Thorax. 2007.

79. Ayieko P, English M. Case management of childhood pneumonia in developing countries. The Pediatric infectious disease journal. 2007;26(5):432.

80. Bari A, Sadruddin S, Khan A, Khan A, Lehri IA, Macleod WB, et al. Community case management of severe pneumonia with oral amoxicillin in children aged 2–59 months in Haripur district, Pakistan: a cluster randomised trial. The Lancet. 2011;378(9805):1796-803.

81. World Health Organization. Revised WHO classification and treatment of pneumonia in children at health facilities: evidence summaries. 2014.

82. World Health Organization. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care. 2012.

83. Ministry of Health and Family Welfare- Government of Bangladesh. Integrated Management of Childhood Illness (Chart Booklet)-Bangladesh Adapted Version. Dhaka: Government of Bangladesh; 2017.

84. Fox MP, Thea DM, Sadruddin S, Bari A, Bonawitz R, Hazir T, et al. Low rates of treatment failure in children aged 2–59 months treated for severe pneumonia: a multisite pooled analysis. Clinical infectious diseases. 2012;56(7):978-87.

85. Addo-Yobo E, Chisaka N, Hassan M, Hibberd P, Lozano JM, Jeena P, et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. The Lancet. 2004;364(9440):1141-8.

86. Hazir T, Fox LM, Nisar YB, Fox MP, Ashraf YP, MacLeod WB, et al. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. The Lancet. 2008;371(9606):49-56.

87. Wonodi CB, Deloria-Knoll M, Feikin DR, DeLuca AN, Driscoll AJ, Moïsi JC, et al. Evaluation of risk factors for severe pneumonia in children: the Pneumonia Etiology Research for Child Health study. Clinical infectious diseases. 2012;54(suppl_2):S124-S31.

88. Nacul LC, Kirkwood BR, Carneiro AC, Pannuti CS, Magalhaes M, Arthur P. Aetiology and clinical presentation of pneumonia in hospitalized and outpatient children in Northeast Brazil and risk factors for severity. Journal of Health, Population and Nutrition. 2005:6-15.

89. Ruiz M, Ewig S, Torres A, Arancibia F, Marco F, Mensa J, et al. Severe community-acquired pneumonia: risk factors and follow-up epidemiology. American journal of respiratory and critical care medicine. 1999;160(3):923-9.

90. Reed C, Madhi SA, Klugman KP, Kuwanda L, Ortiz JR, Finelli L, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One. 2012;7(1):e27793.

91. Ahmed HM, Mitchell M, Hedt B. National implementation of Integrated Management of Childhood Illness (IMCI): policy constraints and strategies. Health policy. 2010;96(2):128-33.

92. Walter ND, Lyimo T, Skarbinski J, Metta E, Kahigwa E, Flannery B, et al. Why first-level health workers fail to follow guidelines for managing severe disease in children in the Coast Region, the United Republic of Tanzania. Bulletin of the World Health Organization. 2009;87(2):99-107.

93. Arifeen S, Bryce J, Gouws E, Baqui A, Black R, Hoque D, et al. Quality of care for under-fives in first-level health facilities in one district of Bangladesh. Bulletin of the World Health Organization. 2005;83:260-7.

94. Lange S, Mwisongo A, Mæstad O. Why don't clinicians adhere more consistently to guidelines for the Integrated Management of Childhood Illness (IMCI)? Social Science & Medicine. 2014;104:56-63.

95. Hazir T, Begum K, El Arifeen S, Khan AM, Huque MH, Kazmi N, et al. Measuring coverage in MNCH: a prospective validation study in Pakistan and Bangladesh on measuring correct treatment of childhood pneumonia. PLoS medicine. 2013;10(5):e1001422.

96. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.

97. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.

98. Duke T. Neonatal pneumonia in developing countries. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2005;90(3):F211-FF9.

99. Duke T, Blaschke A, Sialis S, Bonkowsky J. Hypoxaemia in acute respiratory and non-respiratory illnesses in neonates and children in a developing country. Archives of disease in childhood. 2002;86(2):108-12.

100. English M, Ngama M, Musumba C, Wamola B, Bwika J, Mohammed S, et al. Causes and outcome of young infant admissions to a Kenyan district hospital. Archives of disease in childhood. 2003;88(5):438-43.

101. Junge S, Palmer A, Greenwood BM, Kim Mulholland E, Weber MW. The spectrum of hypoxaemia in children admitted to hospital in The Gambia, West Africa. Tropical medicine & international health. 2006;11(3):367-72.

102. Weber MW, Carlin JB, Gatchalian S, Lehmann D, Muhe L, Mulholland EK, et al. Predictors of neonatal sepsis in developing countries. The Pediatric infectious disease journal. 2003;22(8):711-7.

103. Ayieko P, Graham S. In children aged 2-59 months with pneumonia, which clinical signs best predict hypoxaemia? J Trop Pediatr 2006.

104. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.

105. Duke T, Mgone J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea [oxygen therapy in children]. The International Journal of Tuberculosis and Lung Disease. 2001;5(6):511-9.

106. Chopra M, Mason E, Borrazzo J, Campbell H, Rudan I, Liu L, et al. Ending of preventable deaths from pneumonia and diarrhoea: an achievable goal. The Lancet. 2013;381(9876):1499-506.

107. Bhutta ZA, Das JK, Walker N, Rizvi A, Campbell H, Rudan I, et al. Interventions to address deaths from childhood pneumonia and diarrhoea equitably: what works and at what cost? The Lancet. 2013;381(9875):1417-29.

108. Schnapp LM, Cohen NH. Pulse oximetry: uses and abuses. Chest. 1990;98(5):1244-50.

109. Severinghaus JW. Takuo Aoyagi: discovery of pulse oximetry. Anesthesia & Analgesia. 2007;105(6):S1-S4.

110. Next-generation pulse oximetry. Focusing on Masimo's signal extraction technology. Health Devices. 2000;29(10):349-70.

111. Goldman JM, Petterson MT, Kopotic RJ, Barker SJ. Masimo signal extraction pulse oximetry. J Clin Monit Comput. 2000;16(7):475-83.

112. World Health Organization. WHO-UNICEF technical specifications and guidance for oxygen therapy devices. 2019.

113. Jubran A. Pulse oximetry. Critical Care. 2015;19(1):272.

114. Kamat V. Pulse oximetry. Indian J Anaesth. 2002;46(4):261-8.

115. Mechem CC. Pulse oximetry. UpTo-Date Waltham, MA: UpToDate Publishing. 2012.

116. Dresher RP, Mendelson Y, editors. Reflectance forehead pulse oximetry: Effects of contact pressure during walking. 2006 International Conference of the IEEE Engineering in Medicine and Biology Society; 2006: IEEE.

117. Barker SJ. "Motion-resistant" pulse oximetry: a comparison of new and old models. Anesthesia & Analgesia. 2002;95(4):967-72.

118. Hartmut Gehring M, ME HM, Schmucker P. The effects of motion artifact and low perfusion on the performance of a new generation of pulse oximeters in volunteers undergoing hypoxemia. Respiratory Care. 2002;47(1):48-60.

119. Jopling MW, Mannheimer PD, Bebout DE. Issues in the laboratory evaluation of pulse oximeter performance. Anesthesia and analgesia. 2002;94(1 Suppl):S62.

120. Shah N, Ragaswamy HB, Govindugari K, Estanol L. Performance of three new-generation pulse oximeters during motion and low perfusion in volunteers. Journal of clinical anesthesia. 2012;24(5):385-91.

121. Sherman B, Nisenboum JM, Jesberger BL, Morrow CA, Jesberger JA. Assessment of dysphagia with the use of pulse oximetry. Dysphagia. 1999;14(3):152-6.

122. Floyd J, Wu L, Burgess DH, Izadnegahdar R, Mukanga D, Ghani AC. Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Nature. 2015;528(7580):S53.

123. Duke T, Subhi R, Peel D, Frey B. Pulse oximetry: technology to reduce child mortality in developing countries. Annals of tropical paediatrics. 2009;29(3):165-75.

124. Rahman AE, Iqbal A, Hoque DE, Moinuddin M, Zaman SB, Rahman QS-u, et al. Managing Neonatal and Early Childhood Syndromic Sepsis in Sub-District Hospitals in Resource Poor Settings: Improvement in Quality of Care through Introduction of a Package of Interventions in Rural Bangladesh. PloS one. 2017;12(1):e0170267.

125. Garde A, Zhou G, Raihana S, Dunsmuir D, Karlen W, Dekhordi P, et al. Respiratory rate and pulse oximetry derived information as predictors of hospital admission in young children in Bangladesh: a prospective observational study. BMJ open. 2016;6(8):e011094.

126. Raihana S, Dunsmuir D, Huda T, Zhou G, Rahman QS-u, Garde A, et al. Development and internal validation of a predictive model including pulse oximetry for hospitalization of under-five children in Bangladesh. PloS one. 2015;10(11):e0143213.

127. McCollum ED, King C, Deula R, Zadutsa B, Mankhambo L, Nambiar B, et al. Pulse oximetry for children with pneumonia treated as outpatients in rural Malawi. Bulletin of the World Health Organization. 2016;94(12):893.

128. King C, Boyd N, Walker I, Zadutsa B, Baqui AH, Ahmed S, et al. Opportunities and barriers in paediatric pulse oximetry for pneumonia in low-resource clinical settings: a qualitative evaluation from Malawi and Bangladesh. BMJ Open. 2018;8(1):e019177.

129. Emdin CA, Mir F, Sultana S, Kazi A, Zaidi AK, Dimitris MC, et al. Utility and feasibility of integrating pulse oximetry into the routine assessment of young infants at primary care clinics in Karachi, Pakistan: a cross-sectional study. BMC pediatrics. 2015;15(1):141.

130. Ginsburg AS, Izadnegahdar R, Klugman KP. World Pneumonia Day 2016: pulse oximetry and oxygen. The Lancet Global Health. 2016;4(12):e893-e4.

131. Ginsburg AS, Van Cleve WC, Thompson MI, English M. Oxygen and pulse oximetry in childhood pneumonia: a survey of healthcare providers in resource-limited settings. Journal of tropical pediatrics. 2012;58(5):389-93.

132. King EM, Lieu C, Kasasa A, Ewer AK, Thangaratinam S. Pulse Oximetry as a Screening Tool to Detect Hypoxia Associated with Early-onset Sepsis in Asymptomatic Newborns: A Feasibility Study in a Low-income Country. 2014.

133. Resnicow K, Baranowski T, Ahluwalia JS, Braithwaite RL. Cultural sensitivity in public health: defined and demystified. Ethnicity & disease. 1999;9(1):10-21.

134. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. American journal of preventive medicine. 2009;36(5):452-7.

135. World Bank. GDP per capita (current US$): Bangladesh 2019 [Available from: https://data.worldbank.org/indicator/ny.gdp.pcap.cd?locations=bd.

136. Bangladesh Bureau of Statistics-Goverment of Bangladesh. Population and Household Census 2011 2019 [Available from: http://www.bbs.gov.bd/site/page/47856ad0-7e1c-4aab-bd78-892733bc06eb/-.

137. Directorate General of Health Services-Ministry of Health and Family Welfare- Government of Bangladesh. Bangladesh Health Bulletin 2017. Dhaka, Bangladesh Management Information System, ; 2018.

138. Bryce J, Victora CG, Habicht J-P, Black RE, Scherpbier RW. Programmatic pathways to child survival: results of a multi-country evaluation of Integrated Management of Childhood Illness. Health policy and planning. 2005;20(suppl_1):i5-i17.

Chapter 2: AIMS AND OBJECTIVES

2.1 GOALS AND AIMS

The overall **GOAL** is to improve the management of pneumonia by introducing pulse oximetry in routine IMCI services in Bangladesh at scale. The **AIM** of my PhD is to support the Government of Bangladesh in taking an evidence-based decision in this regard.

2.2 OBJECTIVES AND RESEARCH QUESTIONS

I was engaged in a series of discussions with the policymakers of Ministry of Health and Family Welfare of the Government of Bangladesh to understand their perspectives on the existing evidence gaps and research priorities for taking any decision regarding pulse oximetry integration. Based on these consultations, I identified my PhD objectives, which reflect the perspectives and priorities of the Government of Bangladesh. The following table summarises the objectives/research questions.

Table 2.1: General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia in LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

Chapter 3: BURDEN OF HYPOXAEMIA AMONG CHILDREN WITH PNEUMONIA IN LMICS

One of my general objectives was to estimate the burden of hypoxaemia among children with pneumonia. The specific research question 1 was to assess the burden of hypoxaemia among children with pneumonia in LMICs.

Table 3.1: General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh
3.	**What is the context of childhood pneumonia-related deaths in Bangladesh?**
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

The work presented in the chapter 3 was published in The Lancet Global Health in 2022.

Title: Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis

Authors: **Ahmed Ehsanur Rahman** (myself), Aniqa Tasnim Hossain, **Harish Nair** (co-supervisor), Mohammod Jobayer Chisti, **David H Dockrell** (co-supervisor), **Shams El Arifeen** (co-supervisor), and **Harry Campbell** (supervisor).

URL: https://www.thelancet.com/action/showPdf?pii=S2214-109X%2821%2900586-6

3.1 ABSTRACT

3.1.1 Background

Pneumonia accounts for around 16% of all deaths of children younger than 5 years globally. Most happen in resource-constrained settings and are potentially preventable. Hypoxaemia is one of the strongest predictors of these deaths. We present an updated estimate of hypoxaemia prevalence among children with pneumonia in low-income and middle-income countries.

3.1.2 Methods

We conducted a systematic review using the following key concepts “children under-5 years of age” AND “pneumonia” AND “hypoxaemia” AND “low- and middle-income countries” by searching in 11 bibliographic databases and citation indices. We included all articles published between Nov 1, 2008, and Oct 8, 2021, based on observational studies and control arms of randomised and non-randomised controlled trials. We excluded protocol papers, articles reporting hypoxaemia prevalence based on less than 100 pneumonia cases, and articles published before 2008 from the review. Quality appraisal was done with the Joanna Briggs Institute tools. We reported pooled prevalence of hypoxaemia (SpO_2<90%) by classification of clinical severity and by clinical settings by use of the random-effects meta-analysis models. We combined our estimate of the pooled prevalence of pneumonia with a previously published estimate of the number of children admitted to hospital due to pneumonia annually to calculate the total annual number of children admitted to hospital with hypoxaemic pneumonia.

3.1.3 Results

We identified 2825 unique records were identified from the databases, of which 57 studies met the eligibility criteria: 26 from Africa, 23 from Asia, four from South America, and four from multiple continents. The prevalence of hypoxaemia was 31% (95% CI, 26 to 36; 101775 children) among all children WHO-defined pneumonia, 41% (33-49; 30483 children) among those with very severe or severe pneumonia, and 8% (3-16; 2395 children) among those with non-severe pneumonia. The prevalence was much higher in studies conducted in emergency and inpatient settings than in studies conducted in outpatient settings. In 2019, we estimated that over 7 million children (95% CI, 5 to 8 million) were admitted to the hospital with hypoxaemic pneumonia. The studies included in this systematic review had high τ^2 (i.e., 0.17), indicating a high level of heterogeneity between studies, and a high I^2 value (i.e., 99.6%), indicating that the heterogeneity was not due to chance. This study is registered with PROSPERO, CRD42019126207.

3.1.4 Conclusion

The high prevalence of hypoxaemia among children with severe pneumonia, particularly among children who have been admitted to hospital, emphasises the importance of overall oxygen security within the health systems of low-income and middle-income countries, particularly in the context of COVID-19 pandemic. Even among children with non-severe pneumonia that is managed in outpatient and community settings, the high prevalence emphasises the importance of rapid

identification of hypoxaemia at the first point of contact and referral for appropriate oxygen therapy.

Research in context

Evidence before this study

A review paper by Lozano and colleagues in 2001 reported a hypoxaemia prevalence of 31% among children presenting with acute lower respiratory infection in emergency settings, 43% among children with clinical pneumonia, and 47% among children who were admitted to hospital with pneumonia. The previous global estimate of hypoxaemia prevalence is based on a systematic review conducted by Subhi and colleagues in 2009, which reported a median hypoxaemia prevalence of 13% (IQR 9·3–37·5) among young children with WHO-defined pneumonia requiring admission to hospital. A systematic review conducted by Lazzerini and colleagues in 2015 reported that hypoxaemia was associated with five-times higher odds of death from acute lower respiratory infections. This updated systematic review was done following WHO's revised clinical pneumonia classification for children in 2014, the introduction of pneumococcal and Haemophilus influenza vaccines into the routine childhood immunisation programmes of many low-income and middle-income countries, and concerns about oxygen security concerns in the context of the COVID-19 pandemic. We searched MEDLINE, Embase, Global Health via OVID, and Cochrane Central Register of Controlled Trials (CENTRAL) with the following search terms: “children under-5 years of age” AND “pneumonia” AND “hypoxaemia” AND “low-

and middle-income countries" AND "systematic review/meta-analysis" for studies published in English between Nov 1, 2008, and Oct 8, 2021.

Added value of this study

This Article reports an updated estimate of hypoxaemia prevalence among children with WHO-defined pneumonia in low-income and middle-income countries on the basis of searches of 11 bibliographic databases and citation indices. We identified 57 studies and presented both the pooled and median prevalence estimates on the basis of more than 100000 observations, whereas the previous estimate in 2009 was based on around 18000 observations. The estimates were further disaggregated by clinical severity classifications, clinical settings, hospitalisation status, and altitude levels.

Implications of all the available evidence

This study presents an estimated number of children who are admitted to hospital due to pneumonia with hypoxaemia annually. The high prevalence of hypoxaemia among children with WHO-defined severe pneumonia, reported in this systematic review, emphasises the importance of overall oxygen security within health systems, particularly in the context of COVID-19. The high prevalence of hypoxaemia among children with non-severe pneumonia accentuates the need for novel diagnostics, such as pulse oximetry, at the first point of contact and urgent referral for prompt management of children with hypoxaemia.

3.2 BACKGROUND

Pneumonia accounts for approximately 16% of all deaths in children younger than 5 years, and most of these deaths occur in low-income and middle-income countries (LMICs) (1-3). Cognisant of the high burden of mortality, WHO declared pneumonia a "forgotten killer of children" (4). Without effectively preventing and treating pneumonia, countries with a high burden of pneumonia will not reach the ambitious UN Sustainable Development Goal target of reducing the mortality rate of children younger than 5 years to less than or equal to 25 per 1000 live births by 2030 (5).

Hypoxaemia, defined as low oxygen saturation in arterial blood, (i.e., SpO_2<90%), is common among children with pneumonia and other acute lower respiratory infections, and is one of their strongest predictors of mortality (3, 6-11). WHO recommends measuring SpO_2 in routine practice, even in settings with limited resources, as it can substantially improve the accuracy of classification of pneumonia and other acute lower respiratory infections by clinical severity (12, 13).

Despite the high mortality risk, little is known about the prevalence of hypoxaemia among children with pneumonia in LMICs (14). The most recent global estimate is based on Subhi and colleagues' systematic review published in 2009, which reported a median hypoxaemia prevalence of 13.3% (IQR, 9.3–37.5) among young children with WHO-defined pneumonia requiring admission to hospital. The prevalence varied widely across countries, age groups, and classifications of clinical severity (8). Subhi and colleagues' systematic review predates the revised WHO pneumonia classifications of 2014, which included recommendations for assessing SpO_2 in routine practice (12, 13, 15). It is an appropriate time to update the systematic

review and meta-analysis to include children classified with WHO's 2014 pneumonia classification.

We aimed to report an updated prevalence of hypoxaemia among children younger than 5 years with WHO-defined pneumonia in LMICs, stratified by classifications of clinical severity, clinical-settings, and altitude levels, based on the basis of articles published between 2008 and 2021.

3.3 METHODS

3.3.1 Search strategy and selection criteria

In this systematic review and meta-analysis, we conducted an initial scoping review to help inform our search strategy. The search terms were "*children under-5 years of age*" **AND** "*pneumonia*" **AND** "*hypoxaemia*" **AND** "*low- and middle- income countries*". The detailed search strategy is presented in the (Supplementary table 3.1). The list of LMICs (Supplementary table 3.2) was obtained from the UN Statistics Division (16). We searched MEDLINE (via OVID), Embase (via OVID), Global Health (via OVID), Cochrane Central Register of Controlled Trials, Clinical Trial.Gov, Scopus, CINHAL, PubMed, Global Index Medicus, IndMED, Global Index Medicus by WHO, including African Index Medicus, the literature of Latin America and the Caribbean (AMRO/Pan American Health Organization), the Index Medicus for the Eastern Mediterranean Region (IMEMR/ EMRO), the Index Medicus for South-East Asia Region (IMSEAR/ SEARO), Western Pacific Region Index Medicus (WPRIM/ WPRO), Web of Science, and Social Sciences Citation Index (SCI index) for all studies published between Nov 1, 2008 and Oct 8, 2021, without any language restrictions.

We included studies with children younger than 5 years with WHO-defined pneumonia (i.e., assessed with the Integrated Management of Childhood Illness or WHO's Pocket Book) (12, 13). Hypoxaemia assessed by any health-service provider (e.g., doctors, nurses, paramedics and community health workers) through pulse oximetry and reported as a prevalence estimate was considered as the outcome (17, 18). We did not include any grey literature or any unpublished studies in our systematic review. Both observational studies and control groups of randomised and non-randomised controlled trials were included. We excluded articles reporting hypoxaemia prevalence based on less than 100 patients with pneumonia to minimise the error margin, and articles where pulse oximetry was used to identify a particular disease or condition (8). Finally, we excluded articles published before 2008 (i.e., the upper limit of the previous review by Subhi and colleagues) during the full-text review process (8). Here, we present our main findings based on the WHO-defined pneumonia cases. We also assessed the prevalence of hypoxaemia among non-WHO pneumonia cases to contextualise our results, and we present these results in the supplementary materials.

The review team consisted of topic experts in pneumonia and hypoxaemia (AER, HC, HN and DD), an epidemiologist (SEA), a statistician (ATH), and a librarian/systematic review expert (Marshall Dozier). After removing duplicates, two reviewers (AER and Sabrina Jabeen) independently screened the articles with a structured checklist (Supplementary table 3.3). Then two reviewers (AER and Shema Mhajabin) independently reviewed the full-text articles and abstracted data using another structured checklist (Supplementary table 3.4). The details of reviewed articles are

provided in the appendix (Supplementary table 3.5). The inclusion criteria were the same for the systematic review and the meta-analysis.

We adapted the tool developed by Joanna Briggs Institute for quality assessment of studies included for data abstraction, which was undertaken by two reviewers independently (Supplementary table 3.6 and Supplementary table 3.7) (19). In case of disagreement, a third reviewer was consulted.

3.3.2 Analysis plan

We abstracted data by use of a structured checklist (Supplementary table 3.4) and two reviewers independently entered data using a template designed in SPSS (version 19). Duplicate articles were primarily removed with EndNote (version 20), and afterwards duplicate data from the selected articles were removed through manual checks. We used Stata version 14 and R package (version 4.0.5) for statistical analysis. We calculated the pooled prevalence of hypoxaemia with 95% CIs using the random-effects models (20, 21). We also reported medians with IQR. The pooled estimates were stratified by classification of clinical severity (i.e., "very severe pneumonia" or "severe pneumonia" was stratified as "very severe or severe pneumonia" and "pneumonia" was stratified as "non-severe pneumonia" and "unclassified pneumonia" where the study used WHO classification but did not differentiate between severe and non-severe pneumonia), clinical-settings (i.e., indoor, emergency, or outdoor), and altitude-levels (i.e., high-altitude if at least 2400 m above sea-level) (12, 13). We could not report the hypoxaemia prevalence by ethnicity or sex as we could not extract such disaggregated data from the selected

articles. Publication bias was assessed with funnel plots by use of R package's funnel command (22, 23). We reported the τ^2 value as a measure of heterogeneity across studies and I^2 value to explain the proportion of heterogeneity that was not due to chance (Supplementary table 3.8).

We also estimated the total number of children admitted to hospital with hypoxaemic pneumonia annually by use of McAllister and colleagues' estimated number of children admitted to hospitals due to pneumonia annually and the pooled hypoxaemia prevalence among children admitted to hospital in LMICs reported in this systematic review (24).

We followed the Preferred Reporting Items for Systematic Reviews And Meta-Analyses guidelines for reporting (25). This protocol is registered at PROSPERO, CRD42019126207 (26).

3.4 RESULTS

We identified 4,275 records, of which 1,450 were duplicates (Supplementary table 3.9 and Figure 3.1). After title and abstract screening, 306 articles were selected for full-text review. 230 articles were excluded because they did not meet the eligibility criteria. Data were abstracted from 76 articles (two articles reported hypoxaemia among children with WHO-defined pneumonia and non-WHO-defined pneumonia), of which 57 studies reported hypoxaemia prevalence among children with WHO-defined pneumonia (with 61 prevalence estimates) and 101,775 children were involved (Supplementary table 3.10); the remaining articles (i.e., 21 articles) reported hypoxaemia prevalence among children with non-WHO-defined

pneumonia or acute lower respiratory infection. Among the 57 studies reporting hypoxaemia prevalence among children with WHO-defined pneumonia, 26 studies were from Africa, 23 from Asia, four from South America, and four from multiple continents (Figure 3.2).

Figure 3.1: Flow diagram of the study selection process

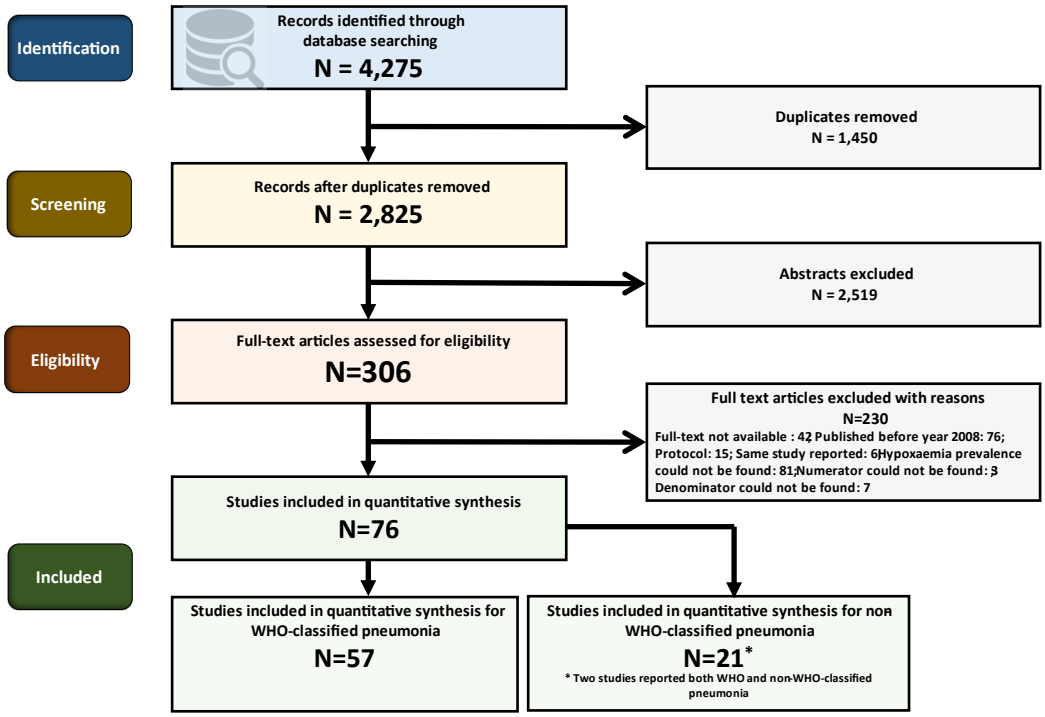
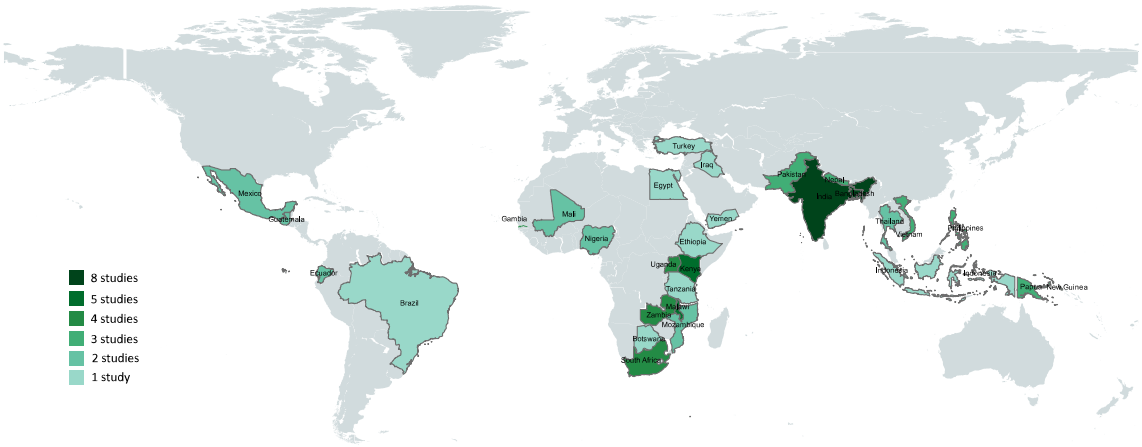


Figure 3.2: Distribution of countries and the number of studies reporting hypoxaemia prevalence among children with WHO-defined pneumonia (N=57)

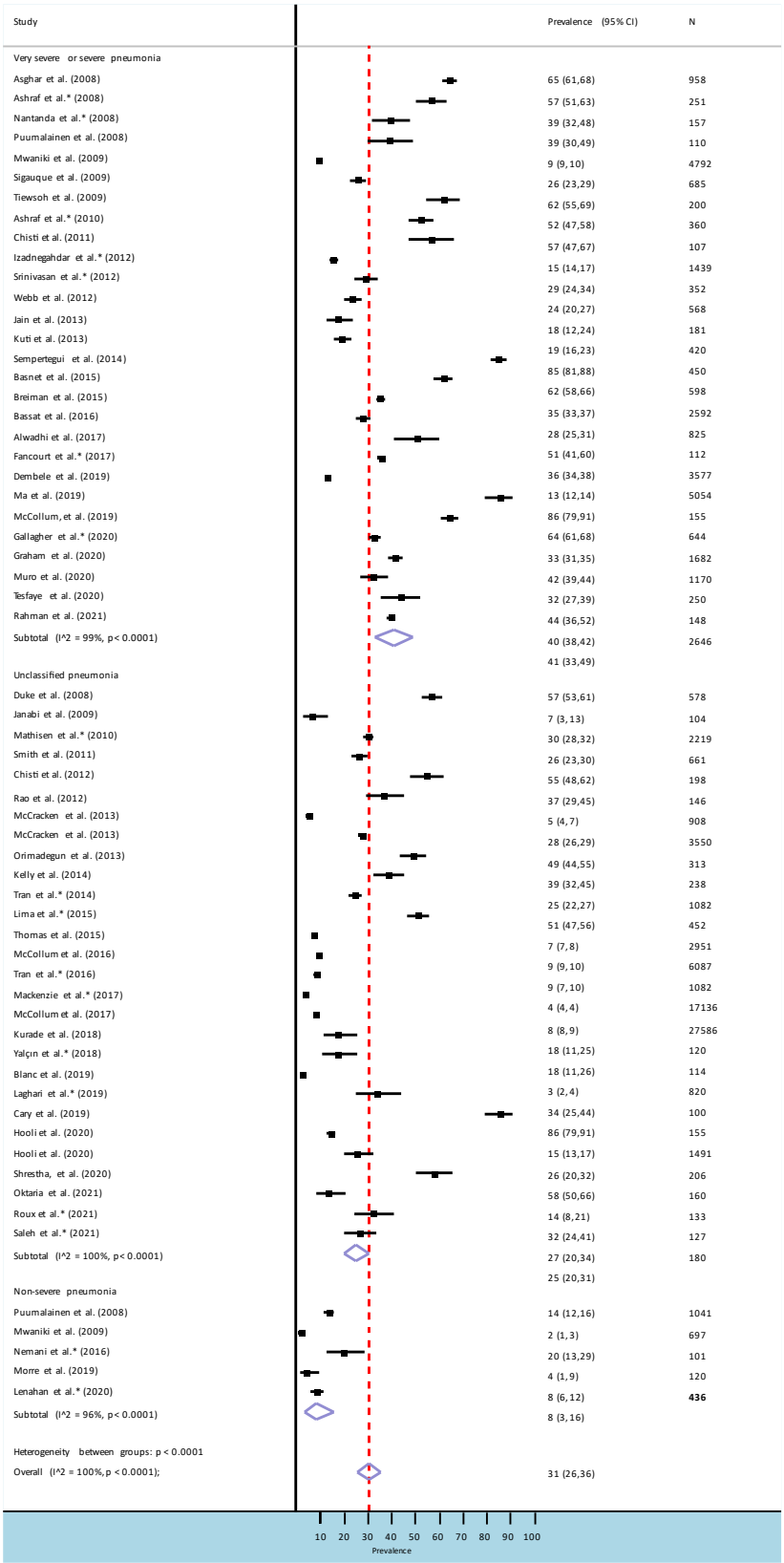


Five of 57 studies were conducted at high-altitude sites (Supplementary table 3.8). 30 studies were done in tertiary-level referral facilities, 12 studies were in primary-level or secondary-level referral facilities, six studies were in health centres, and six studies were in mixed settings. Facility information could not be extracted from three articles. Eight studies measured SpO_2 in the emergency setting, 32 studies in the in-patient setting, 12 studies in the outpatient setting, and five studies in mixed settings. 56 studies reported hypoxaemia prevalence (40 in hospitalised children, 12 in non-hospitalised children, and four in a mixed population of hospitalised and non-hospitalised children). We could not ascertain the patient status from one study. 28 studies reported hypoxaemia prevalence among children with WHO-defined very severe or severe pneumonia, and five studies reported prevalence among children with non-severe pneumonia. Classification of clinical severity was not explicitly mentioned in 28 studies, which are presented as unclassified pneumonia. 29 studies mentioned the type (i.e., table-top, handheld, fingertip), manufacturer, and models of the pulse oximetry devices used, and 13 studies explicitly mentioned use of a

paediatric probe. 38 studies used the WHO-recommended SpO_2 cut-off of less than 90%, 12 studies used less than 92%, two studies used less than 93%, one study used less than 94%, two studies used less than 95%, one study used less than 87% and one study used 90-93%.

Figure 3.3 presents the hypoxaemia prevalence among WHO-defined pneumonia by clinical severity. The pooled overall prevalence of hypoxaemia was 31% (95% CI, 26 to 36) among 101,775 children with WHO-defined pneumonia. The median overall prevalence was 29% (IQR, 15 to 49). The prevalence was 41% (95% CI, 33 to 49) among 30,483 children with very severe or severe pneumonia, 8% (95% CI, 3 to 16) among 2,395 children with non-severe pneumonia, and 25% (20-31) among 68,897 children with unclassified pneumonia. The studies included in this review had high τ^2 values (τ^2 = 0.18 for very severe or severe pneumonia, τ^2 = 0.06 for non-severe pneumonia, and τ^2 = 0.10 for unclassified pneumonia), indicating a high level of heterogeneity between studies and a high I^2 values (99.5% for very severe or severe pneumonia, 96.3% for non-severe pneumonia, and 99.5% for unclassified pneumonia), indicating the heterogeneity was not due to chance.

Figure 3.3: Hypoxaemia prevalence among children with WHO-defined pneumonia by clinical severity; presented in %



The broken red line shows the overall pooled prevalence of hypoxaemia.
*studies where SpO_2 cut-off is <90%

Figure 3.4 shows wide variations in hypoxaemia prevalence among WHO-defined pneumonia across different categories. Regarding classification of clinical severity, hypoxaemia prevalence was highest among children classified as severe pneumonia. Although the confidence intervals are overlapping, the point prevalence was higher among studies conducted in emergency (47%, 95% CI, 30 to 64) and inpatient (32%, 95% CI, 26 to 38) settings than among those conducted in outpatient settings (23%, 95% CI, 15 to 33). The estimates were not substantially different between regions (Asia 31%, 95% CI, 24 to 39; Africa 28%,95% CI, 22 to 34) or by hospitalisation status of children (33%, 95% CI, 27 to 39 in children admitted to hospital; 29%,95% CI, 19 to 40 in children not admitted to hospital). The overall estimate also did not vary between classifications before 2014 and classifications after 2014, but there were some differences in unclassified pneumonia estimates (Supplementary table 3.11). Median prevalence with IQR across different subgroups is found in supplementary table 3.12.

Figure 3.4: Hypoxaemia prevalence among children with WHO-defined pneumonia and comparison between random-effects pooled estimate across different subgroups; presented in %

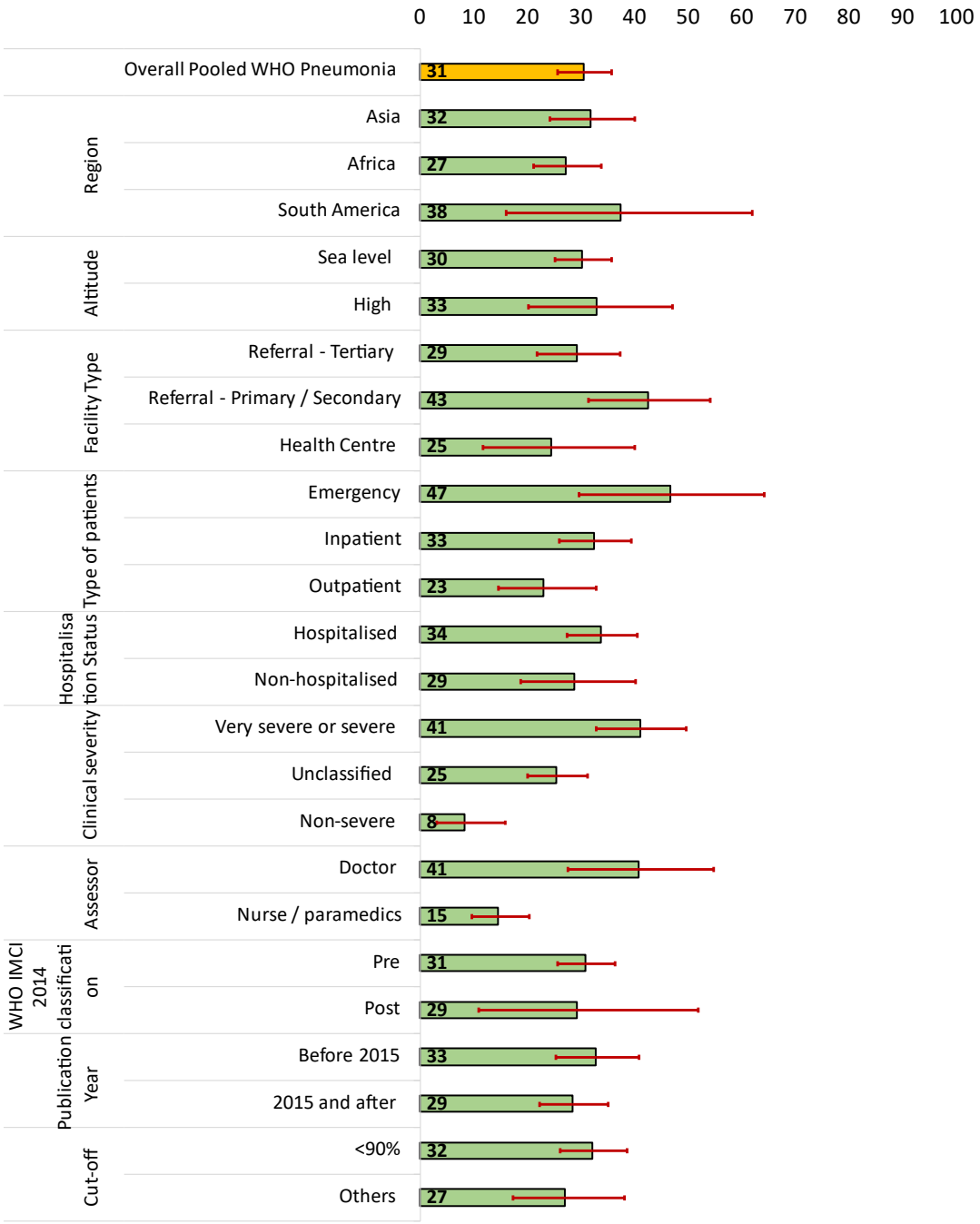
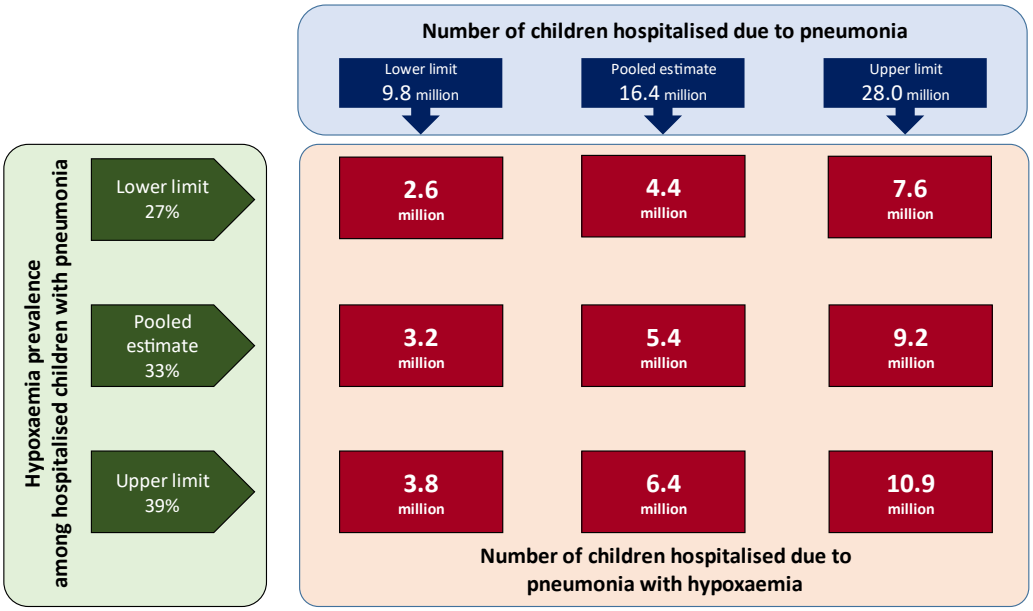


Figure 3.5 presents a scenario-based projection of the estimated number of children admitted to hospital due to pneumonia with hypoxaemia annually. On the basis of the estimated number (i.e., 16.4 million) of children admitted to hospital due to pneumonia annually reported by McAllister and colleagues, and hypoxaemia

prevalence (i.e., 33%) among children admitted to hospital with pneumonia reported in our systematic review, we estimate that approximately 5.4 million children were admitted to hospital due to pneumonia with hypoxaemia in 2015. If we consider the lower limits and upper limits of hypoxaemia prevalence (27-39%) based on our study, the estimated number was between 4.4 million and 6.4 million. Assuming an average annual growth rate of 7% over the period of 2000-15 and continued over the period 2015-19, hospitalisations due to hypoxaemic pneumonia would have been close to 7.2 million in 2019 (24).

Figure 3.5: Global estimated number of children admitted to hospital due to pneumonia with hypoxaemia annually, presented in million children



The hypoxaemia prevalence was 36% (95% CI, 26 to 46) among children with non-WHO classified clinical pneumonia (13 studies), 19% (11-29) among children with radiological pneumonia (six studies), and 33% (29-37) among organism-specific pneumonia (i.e., respiratory syncytial virus; two studies; supplementary figure 3.1).

During the screening and full-text review, we included only observational studies and control group of randomised and non-randomised controlled trials with adequate sampling size (≥100 participants). During the quality assessment, we found that the description regarding the sampling strategy was inadequate in two articles. Funnel plots assessing the publication bias of the selected articles can be found in the appendix (Supplementary figure 3.2, 3.3, and 3.4). Overall, the τ^2 value was 0.17, indicating a high level of heterogeneity between studies, and I^2 value was 99.6%, indicating that the heterogeneity was not due to chance.

3.5 DISCUSSION

This systematic review reports a high prevalence of hypoxaemia among children with WHO-defined pneumonia, which is one of the strongest predictors of mortality due to pneumonia (3, 6-10). Ensuring rapid identification of hypoxaemia through routine assessment of SpO_2 and immediate hospital admission for oxygen therapy with supportive care can substantially reduce pneumonia-related childhood mortality (27, 28). In this Article, we addressed a notable evidence gap by presenting the burden of hypoxaemia among children with pneumonia in LMICs. The pooled estimates included 57 studies with more than 100000 children with pneumonia, and reasonably represented different regions, facility types, patient types, hospitalisation status, and clinical severity based on WHO-classifications. The overall prevalence of hypoxaemia was high, particularly among patients with clinically severe pneumonia or those who were admitted to hospitals. We also found a moderately high prevalence among children with non-severe pneumonia.

The overall prevalence of hypoxaemia reported here is higher than that reported by Subhi and colleagues in 2009 but similar to that reported by Lozano in 2001 (8, 29). In our systematic review, the overall prevalence was 31% (95% CI, 26 to 36), and the prevalence was 33% (27-39) among hospitalised children and 47% (30-64) among children presenting in the emergency department. Lozano reported a prevalence of 31% among children with acute lower respiratory infection in emergency settings, 43% among children with clinical pneumonia, and 47% among hospitalised children with pneumonia. By contrast, Subhi and colleagues reported a much lower prevalence of 13% among young children who were admitted to hospital with pneumonia. The introduction of Pneumococcal and Haemophilus influenzae vaccines in the routine childhood immunisation programmes in many LMICs in the past decade is expected to reduce the community burden of pneumonia and severe pneumonia, including hypoxaemic pneumonia. However, during the same period, the increasing trend towards improving the socio-economic conditions, availability and access to health care, and provision and practice of SpO_2 assessment and oxygen security in health facilities might have led to better care-seeking practices and a higher-level of detection of hypoxaemia in lower-level health centres and in referral facilities than before (30-32). Another reason could be the proportional contribution of hospitalised children in our review. Of the 57 studies, eight reported measuring SpO_2 in emergency settings, whereas 32 reported measuring in inpatient settings. It is expected that these cases will be more severe and have a higher prevalence of hypoxaemia than those in outpatient settings (33). Moreover, Subhi and colleagues included children younger than 12 years, whereas we included only children younger

than 5 years. This difference in age might be one of the reasons explaining the difference in prevalence, as the prevalence of hypoxaemia is lower among older children than younger children (34). In our systematic review, the prevalence of hypoxaemia varied only slightly between the Asian and African regions, with overlapping confidence intervals, which is different from the large difference reported by Subhi and colleagues (8). One possible explanation is the larger sample size of our review than in Subhi and colleagues' review, which has contributed to generating more precise estimates with overlapping confidence intervals. The other explanation is the inclusion of more children with very severe or severe pneumonia among Asian studies and a differing spectrum of causes of pneumonia across different countries of Asia and Africa (35, 36). Moreover, Subhi and colleagues reported a hypoxaemia prevalence of less than 10% among children with pneumonia in the African-region, which was much lower than the prevalence estimates (i.e., 28-57%) reported in most studies from the same region (32, 37-42). Lastly, hypoxaemia can be a transient phenomenon, and SpO_2 status can change after initial stabilisation (37). The studies included in our review have exclusively reported hypoxaemia based on the basis of the initial contact with health systems. Since few studies have follow-up SpO_2 status, the pooled prevalence could be an overestimation of the actual burden.

We noted the hypoxaemia prevalence to be much higher among children who were admitted to hospital and studies conducted in inpatient and emergency settings than those that were conducted in outpatient and community settings. According to WHO, children presenting with clinical features of severe pneumonia require

admission to hospital with supportive care (43). Therefore, it is highly likely that the studies conducted among children who were admitted to hospital and in emergency and inpatient settings predominantly enrolled children with clinically severe pneumonia, for whom the prevalence of hypoxaemia is expected to be higher than in those managed as outpatients. The prevalence was also higher in emergency settings than in inpatient settings, possibly because hypoxaemia was measured after initial stabilisation in studies reporting the prevalence among children who were inpatients.

We estimate that the total number of children admitted to hospital due to pneumonia with hypoxaemia was 5.5 million in 2015 (24). Given the increase in the rate of hospitalisations during 2000-15, this estimate might be an underestimation of the current burden. If this rate of increase continued to apply over the period 2015-19, the estimated number of hypoxaemic pneumonia-related hospitalisations in young children would be close to 7.2 million in 2019 (24). This estimate does not include patients with hypoxaemic severe pneumonia who could not reach hospitals for appropriate care or died in the community or those who were classified with non-severe pneumonia.

In our systematic review, the prevalence of hypoxaemia among children with non-severe pneumonia was 8%, implying that some children with non-severe pneumonia (with no other danger signs) actually would require oxygen therapy with supportive care (44). This implication could potentially explain the findings of Fox and colleagues' systematic review, which reported that children with chest in-drawing

pneumonia who were treated with only oral antibiotics, on the basis of the 2014 WHO recommendations, had a high rate of non-response to treatment (43) (45-49).

It is important to consider the strengths and limitations of our systematic review and compare our search strategy and execution with the previous reviews. We conducted a scoping review to fine-tune the search strategy and keywords. In addition to international databases, we expanded our search to multiple national databases representing south Asia, the Middle East, Africa and Latin-America, which added robustness to our review with adequate sensitivity. Although our systematic review and meta-analysis had similar objectives to Subhi and colleagues and Lozano and colleagues, there were some differences in execution. Subhi and colleagues used around 18000 observations of children younger than 12 years, which included 12 published papers (up to November 2008) from three international databases and 12 unpublished studies. Lozano and colleagues included 17 published articles, involving around 4000 children from one database and covering January, 1966, to August, 1999. Our review was more comprehensive than these two reviews and included 57 published studies from 11 international and national bibliographic databases, covering the period of January, 2008 to October, 2021, and involved over 100000 children younger than 5 years with pneumonia. We did not include unpublished studies and Chinese databases, which could have influenced our estimates.

WHO changed its pneumonia classification in 2014, and our review included studies that were published from 2008 and onwards (43). In many instances, we could not determine the version of WHO pneumonia classifications that different studies had

adopted when reporting hypoxaemia prevalence. Although we did not have enough information regarding the presenting signs and symptoms to map the clinical severity classification on the basis of the 2014 WHO guidelines, we reported the pooled estimates by different clinical severity classifications separately. Additionally, different studies used different definitions of hypoxaemia and different SpO_2 cut-offs. However, these differences did not affect the overall estimate, since the difference was not notable between the studies that used the WHO recommended cut-off of less than 90% and those that used 90-95%. We struggled to extract prevalence estimates by different age bands, type of providers who measured SpO_2 (e.g., doctors, nurses, paramedics, community health workers, etc), type of training or orientation received, and type of pulse oximetry device and probes used for assessments. We could not report the validity and reliability of assessments by different providers with different types of pulse oximetry in various clinical settings. There could be some selection bias in the studies, but inadequate information existed to assess bias due to inconsistency when reporting hypoxaemia prevalence by various categories across different studies. We recommend a minimum set of standards to report hypoxaemia prevalence in future studies. Lastly, we acknowledge that we reported hypoxaemia prevalence on the basis of SpO_2 status measured by pulse oximetry devices, whereas the gold standard is arterial blood-gas analysis. Although several studies have reported a strong correlation between pulse oximetry and blood-gas analysis measures in controlled clinical-settings, pulse oximeter measures can be affected by various clinical, mechanical and device-

related factors (50-53). Unfortunately, we could not adjust our estimates for these variables.

Although we conducted a rigorous quality assessment by use of the checklist developed by Joanna Briggs Institute, which is specially designed for studies reporting prevalence or cumulative incidence, we acknowledge the potential effect of publication bias (19). Although we reported some extreme values in the funnel plot (Supplementary figure 3.2, 3.3, and 3.4), the individual prevalence estimates were widely dispersed in both directions (with no apparent skewing) from the pooled estimate. This dispersion could be explained by the large heterogeneity among these studies, indicated by high τ^2 and I^2 values (54). Therefore, we used the random-effects model to generate the pooled prevalence estimate. We also reported median (IQR) for all reporting categories to maintain comparability with previous estimates (8).

In addition to the high prevalence of hypoxaemia among children with WHO-defined pneumonia, we also reported somewhat similar prevalence among children with non-WHO-defined pneumonia. Hypoxaemia is also common among children admitted to hospital with asthma, meningitis or encephalitis, malnutrition, acute febrile encephalopathy, sepsis, or malaria and neonates with neonatal encephalopathy, prematurity, or sepsis (32, 55). Hence, hypoxaemia can be considered as a stand-alone danger sign among young children, irrespective of clinical classification. The use of pulse oximetry with appropriate oxygen therapy can reduce pneumonia-related mortality rates and length of hospital stay (56). Hence,

WHO recommends routine assessment of SpO_2, rapid identification of hypoxaemia, and immediate admission to hospital for oxygen therapy with other supportive care to avert these hypoxaemia-related deaths (43, 57, 58). However, there are gaps between policy and practices. The availability of pulse oximeters, the provision of oxygen therapy during referral, transportation and inpatient care, and the overall oxygen security are still inadequate in most LMICs (59-62). Therefore, urgent attention should be given to improving the access, provision and quality of care, including SpO_2 assessment and oxygen therapy in resource-poor settings (28). Although, pulse oximeters are reasonably valid, affordable, easy-to-use devices that identify hypoxaemia immediately, there are several health systems barriers and operational challenges associated with introducing pulse oximeters in LMICs (63-65). The characteristics of public health systems and the health service provider's skills and capacity in each country are different and might present a unique set of context-specific challenges. Further research studies on implementation are needed to understand the feasibility aspects, focusing on provider's capacity to measure SpO_2, choice of device, and time required for SpO_2 assessment. Emphasis should be given to training staff, building a culture of hypoxaemia assessment, and promoting judicial use of oxygen (44). National programmes should give increased attention and funding support to addressing these challenges, particularly in the context of the COVID-19 pandemic, as this support might improve the overall readiness and performance of health systems regarding emergency triage and management (66, 67).

3.6 CONCLUSION

In conclusion, the high prevalence of hypoxaemia among children with WHO-defined severe pneumonia, particularly among children who were admitted to hospital, emphasises the importance of oxygen security within LMIC health systems. Without the provision of rapid identification and prompt management of hypoxaemia, it will not be possible to substantially reduce pneumonia-related deaths. On the basis of the findings of this systematic review and the context of COVID-19 pandemic, we strongly recommend introducing pulse oximetry at the first point of contact after feasibility assessment and health systems integration of pulse oximetry, especially in resource-constrained settings. We also emphasise the need for regular monitoring SpO_2 levels in hospital settings in order to use oxygen correctly and efficiently.

3.7 SUPPLEMENTARY MATERIALS

3.7.1 Supplementary table

Supplementary table 3.1: Detailed search language with keywords and their synonyms

	1	BO	2	BO	3	BO	4
	Outcome		**Population**		**Population**		**Context**
Concepts	**hypoxaemia**		**pneumonia**		**children under-5 years of age**		**low- and middle-income countries**
Keywords	hypoxaemia/ hypoxaemia/ anoxia/ hypoxia/ oximetry/ oximeter/ oximetre/ oxymetry/ oxymeter/ oxymetre/ blood oxygen saturation/ arterial oxygen saturation/ blood gas monitoring/ blood gas analysis/ analysis blood gas/ SpO2/ SPO2	**AND**	pneumonia/ severe pneumonia/ severe disease/ very severe disease/ bronchiolitis/ acute respiratory infection/ ARI/ acute respiratory infections/ acute respiratory tract infection/ ARTI/ acute respiratory tract infections/ respiratory illness/ respiratory illnesses/	**AND**	child*/ infant*/ pediatric*/ paediatric*/	**AND**	developing countr*/ low-and middle income countr* LMIC*/ low income countr*/ middle income countr* / lower middle income countr*/ upper middle income countr*/ 'name of the country (supplementary table 3.2)'
	BO: Boolean Operator						

Supplementary table 3.2: List of low- and middle-income countries

Sl #	County
1	Afghanistan
2	Albania
3	Albania
4	American Samoa
5	Angola
6	Armenia
7	Azerbaijan
8	Bangladesh
9	Belarus
10	Belize
11	Benin
12	Bhutan
13	Bolivia
14	Bosnia and Herzegovina
15	Botswana
16	Brazil
17	Bulgaria
18	Burkina Faso
19	Burundi
20	Cabo Verde
21	Cambodia
22	Cameroon
23	Central African Republic
24	Chad
25	China
26	Colombia
27	Comoros
28	Democratic Republic of Congo OR DR Congo OR DRC OR the Congo
29	Congo, Rep.
30	Costa Rica
31	Côte d'Ivoire OR Ivory Coast
32	Cuba
33	Djibouti
34	Dominica
35	Dominican Republic
36	Ecuador
37	Egypt, Arab Rep.
38	El Salvador
39	Equatorial Guinea
40	Eritrea
41	Ethiopia
42	Fiji
43	Gabon
44	The Gambia
45	Georgia
46	Ghana
47	Grenada
48	Guatemala
49	Guinea
50	Guinea-Bissau or Guinea Bissau

Sl #	County
51	Guyana
52	Haiti
53	Honduras
54	India
55	Indonesia
56	Iran, Islamic Rep.
57	Iraq
58	Jamaica
59	Jordan
60	Kazakhstan
61	Kenya
62	Kiribati
63	Korea, Dem. People's Rep.
64	Kosovo
65	Kyrgyz Republic
66	Lao PDR
67	Lebanon
68	Lesotho
69	Liberia
70	Libya
71	Macedonia, FYR
72	Madagascar
73	Malawi
74	Malaysia
75	Maldives
76	Mali
77	Marshall Islands
78	Mauritania
79	Mauritius
80	Mexico
81	Micronesia, Fed. Sts.
82	Moldova
83	Mongolia
84	Montenegro
85	Morocco
86	Mozambique
87	Myanmar
88	Namibia
89	Nauru
90	Nepal
91	Nicaragua
92	Niger
93	Nigeria
94	Pakistan
95	Papua New Guinea
96	Paraguay
97	Peru
98	Philippines
99	Romania
100	Russian Federation
101	Rwanda

Sl #	County
102	Samoa
103	São Tomé and Principe OR Timor OR Timor-Liste OR Timor Liste
104	Senegal
105	Serbia
106	Sierra Leone
107	Solomon Islands
108	Somalia
109	South Africa
110	South Sudan
111	Sri Lanka
112	Saint Lucia
113	Vincent and the Grenadines
114	Sudan
115	Suriname
116	Swaziland
117	Syrian Arab Republic
118	Tajikistan
119	Tanzania
120	Thailand
121	Timor-Leste
122	Togo
123	Tonga
124	Tunisia
125	Turkey
126	Turkmenistan
127	Tuvalu
128	Uganda
129	Ukraine
130	Uzbekistan
131	Vanuatu
132	Venezuela, RB
133	Vietnam
134	West Bank and Gaza
135	Yemen, Rep.
136	Zambia
137	Zimbabwe

Supplementary table 3.3: Structured form for abstract screening

Reviewer Code				
Abstract ID				
Name of the journal				
Title				
First Author				
Last Author				
Language	1.English 2. French 3.Chinese	4.Spanish 5. German 6. ----------		
Study design	1. Cross sectional study 2. Cohort study	3. Non-randomized control trial 4. Randomized control trial		
Inclusion Criteria				
Population	Children under the age of five years	Yes	No	N/A
	Classified as pneumonia	Yes	No	N/A
Outcome	SpO_2 status measured with pulse oximetry	Yes	No	N/A
Context	Low- and middle-income countries	Yes	No	N/A
Year of publication	Any study published by Dec 2018	Yes	No	N/A
Exclusion Criteria				
Sample size	Less than hundred	Yes	No	N/A
Use of pulse oximeter	To identify a particular illness	Yes	No	N/A
Screening result				
	Included for data extraction	Yes	No	Need full text review
If not included, reason for exclusion				
Additional comments (if any)				

Supplementary table 3.4: Extraction of data from selected articles after screening

Sl #	Item	Option		
1	Study ID			
2	Study Title			
3	First Author Last Name			
4	Last Author Last Name			
5	Year of Publication			
6	Name of the Journal			
7	Type of Study	Cross Sectional		
		Case Control		
		Cohort		
		Individual RTC		
		Cluster RCT		
		Quasi-Experimental		
8	Study Settings-Region	Asia		
		Europe		
		Africa		
		South America		
		North America		
9	Study Settings-Clinical	Referral Hospital		
		Non-Referral Health Centres		
		Community		
10	Age group	2-11 months	Yes	No
		11-59 months	Yes	No
		>59 Months	Yes	No
11	Specific Classification Reported		Yes	No
12	Type of Classification Reported	Pneumonia	Yes	No
		Severe Pneumonia	Yes	No
		ARI	Yes	No
		Others, specify	Yes	No
13	PO use Reported		Yes	No
14	Type of PO Used, specify			
15	Hypoxaemia Reported		Yes	No
16	Prevalence of Hypoxaemia in %	Overall		
		2-11 months		
		11-59 months		
		>59 Months		
		Pneumonia		
		Severe Pneumonia		
		ARI		
		Others, specify		
		Referral Hospital		
		Non-Referral Health Centres		
		Community		
		Asia		
		Europe		
		Africa		
		South America		
		North America		
17	Specific SpO_2 Measurement Available		Yes	No
18	SpO_2 Status in %	Overall		
		2-11 months		

Sl #	Item	Option		
		11-59 months		
		>59 Months		
		Pneumonia		
		Severe Pneumonia		
		ARI		
		Others Classification		
		Referral Hospital		
		Non-Referral Health Centres		
		Community		
		Asia		
		Europe		
		Africa		
		South America		
		North America		
19	Type of Health Care Worker measuring SpO_2 reported		Yes	No
20	Type of Health Care Worker	Doctors	Yes	No
		Nurses	Yes	No
		Paramedics	Yes	No
		Community Health Worker	Yes	No
21	Oxygen Given for Hypoxaemia Reported		Yes	No
22	Type of Oxygen Given	High Flow		
		Low Flow		
23	Other Intervention Given for Hypoxaemia Reported		Yes	No
24	Other Intervention Given for Hypoxaemia Reported, specify			
25	Case Fatality Rate Reported among Hypoxaemia Cases (without intervention) Reported		Yes	No
26	Case Fatality Rate (death) among Hypoxaemia Cases (without intervention) in %	Overall		
		2-11 months		
		11-59 months		
		>59 Months		
		Pneumonia		
		Severe Pneumonia		
		ARI		
		Others, specify		
		Referral Hospital		
		Non-Referral Health Centres		
		Community		
		Asia		
		Europe		
		Africa		
		South America		
		North America		
27	Other Outcome Reported		Yes	No
28	Other Outcome Reported, please specific			

Supplementary table 3.5: Overview of the studies reporting the prevalence of hypoxaemia among WHO-defined pneumonia

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
Alwadhi et al.	2017	Indian Pediatrics	Asia	India	Low	Very severe or severe pneumonia	90	Ohmeda Biox 3700e pulse oximeter
Asghar et al.	2008	BMJ Open	Multiple Continent	Bangladesh, Ecuador, India, Mexico, Pakistan, Yemen and Zambia	Low	Very severe or severe pneumonia	90	Not mentioned
Ashraf et al.	2008	Archives of Disease in Childhood, BMJ	Asia	Bangladesh	Low	Very severe or severe pneumonia	95	Not mentioned
Ashraf et al.	2010	Pediatrics	Asia	Bangladesh	Low	Very severe or severe pneumonia	95	Not mentioned
Basnet et al.	2015	PLoS ONE	Asia	Nepal	High	Very severe or severe pneumonia	90	Nellcor Puritan Bennett NPB-40, Pleasanton, CA, USA
Bassat et al.	2016	Tropical Medicine & International Health	Africa	Southern Mozambique	Low	Very severe or severe pneumonia	90	Nellcor, Boulder, CO
Breiman et al.	2015	BMC Infectious Diseases	Africa	Kenya	Low	Very severe or severe pneumonia	90	Not mentioned
Chisti et al.	2011	PLoS ONE	Asia	Bangladesh	Low	Very severe or severe	90	Not mentioned

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
						pneumonia		
Dembele et al.	2019	Bmj Open	Asia	Phillipines	Low	Very severe or severe pneumonia	90	Handheld Pulse Oximeter PalmSAT 2500A with Finger
Fancourt et al.	2017	Journal of Paediatrics and Child Health	Multiple Continent	Kenya, The Gambia, Mali, Zambia, South Africa, Thailand, Bangladesh	Low	Very severe or severe pneumonia	92	Not mentioned
Gallagher et al.	2020	Clinical Infectious Diseases	Multiple Continent	Asia and Arfica	Mixed	Very severe or severe pneumonia	92	Not mentioned
Graham et al.	2020	EClinicalMedicine	Africa	Nigeria	Low	Very severe or severe pneumonia	90	Not mentioned
Izadnegahdar et al.	2012	Journal of Pediatric Infectious Diseases	Multiple Continent	Colombia, Ghana, India, Mexico, Pakistan, South Africa, Vietnam and Zambia	Low	Very severe or severe pneumonia	92	Nellcor N-20E, N-25 secsor, Pleasanton, CA, USA
Jain et al.	2013	Indian Pediatrics	Asia	India	Low	Very severe or severe pneumonia	90	Not mentioned
Kuti et al.	2013	ISRN Pediatrics	Africa	Gambia	Low	Very severe or severe	90	Nellcor N-200, USA

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
						pneumonia		
Ma et al.	2019	American Journal of Tropical Medicine and Hygiene	Africa	Uganda	Low	Very severe or severe pneumonia	90	Not mentioned
McCollum et al.	2019	Lancet Respir Med	Africa	Malawi	Low	Very severe or severe pneumonia	90	Rad5 Masimo, Irvine, CA, USA
Nantanda et al.	2008	Annals of Tropical Paediatrics	Africa	Uganda	Low	Very severe or severe pneumonia	92	Not mentioned
que et al.	2009	Journal of Tropical Pediatrics	Africa	Mozambican	Low	Very severe or severe pneumonia	90	Nellcor
Sempertegui et al.	2014	American Journal of Clinical Nutrition	South America	Ecuador	Low	Very severe or severe pneumonia	90	OxiMax N-65; Nellcor
Srinivasan et al.	2012	BMC medicine	Africa	Uganda	Low	Very severe or severe pneumonia	92	Ohmeda Biox 3700 Ohmeda GE healthcare, Pollards Wood Chalfont St. Giles Bucks HP8 4SP UK
Tesfaye et al.	2020	Bmj Open	Africa	Ethiopia	Low	Very severe or severe pneumonia	90	ADC Adimals 2150

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
Tiewsoh et al.	2009	BMC Pediatrics	Asia	India	Low	Very severe or severe pneumonia	90	Not mentioned
Webb et al.	2012	Journal of Pediatric Infectious Diseases	Africa	Kenya	Low	Very severe or severe pneumonia	90	Neclor USA
Blanc et al.	2019	PLoS One	Africa	PNG	Low	Unclassified pneumonia	90	Nellcor Pulse OxyMax N-20PA
Chisti et al.	2012	Tropical Medicine & International Health	Asia	Bangladesh	Low	Unclassified pneumonia	90	OxiMax N-600; Nellcor, Boulder, CO, USA
Duke et al.	2008	Lancet	Africa	Papua New Guinea	Low	Unclassified pneumonia	90	Not mentioned
Hooli et al.	2020	American Journal of Tropical Medicine and Hygiene	Africa	Malawi	Low	Unclassified pneumonia	90	Lifebox
Janabi et al.	2009	Iraqi Postgrad. Med. J.	Asia	Iraq	Low	Unclassified pneumonia	90	Kontron Medical B.P:7845
Kelly et al.	2014	Journal of the Pediatric Infectious Diseases Society	Africa	Bostwana	Low	Unclassified pneumonia	90	Not mentioned
Kurade et al.	2018	Journal of Tropical Pediatrics	Asia	India	Low	Unclassified pneumonia	90	Not mentioned
Laghari et al.	2019	Cureus	Asia	Pakistan	Low	Unclassified pneumonia	92	Not mentioned
Lima et al.	2015	Pediatric Health,	South	Brazil	Low	Unclassified	92	Not mentioned

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
		Medicine, and Therapeutics	America			pneumonia		
Ma et al.	2019	American Journal of Tropical Medicine and Hygiene	Africa	Uganda	Low	Unclassified pneumonia	90	Not mentioned
Mackenzie et al.	2017	Lancet Infectious Disease	Africa	Gambia	Low	Unclassified pneumonia	92	Nellcor N-65, Covidian, Boulder, CO, USA
Mathisen et al.	2010	Pediatric Infectious Disease Journal	Asia	Nepal	High	Unclassified pneumonia	93	Siemens MicroO2 ,Siemens Medical Systems Inc,Danvers, MA with Nellcor, Pleasnton,CA
McCollum et al.	2017	Plos One	Africa	Malawi	Low	Unclassified pneumonia	90	Masimo (R) Hospitals or Lifebox (R)
McCollum et al.	2016	Bulletin of the World Health Organization	Africa	Malawi	Low	Unclassified pneumonia	90	Lifebox
McCracken et al.	2013	American Journal of Tropical Medicine and Hygiene	South America	Guatemala	High	Unclassified pneumonia	90	Not mentioned
Orimadegun et al.	2013	Transactions of the Royal Society of Tropical Medicine and Hygiene	Africa	Nigeria	Low	Unclassified pneumonia	90	True Colour OLED fingertip oximeters
Rao et al.	2012	World Journal of Pediatrics	Asia	India	Low	Unclassified	90	Nellcor Puritan

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
						pneumonia		Bannet NPB-40
Shrestha et al.	2020	Plos One	Asia	Nepal	High	Unclassified pneumonia	90	Mini SpO_2, Criticare Systems, USA
Smith et al.	2011	Lancet	South America	Guatemala	High	Unclassified pneumonia	87	Not mentioned
Thomas et al.	2015	Tropical Medicine & International Health	Asia	Philippines	Low	Unclassified pneumonia	90	Not mentioned
Tran et al.	2016	Epidemiol Infect.	Asia	Vietnam	Low	Unclassified pneumonia	92	Siemens Micro Oe, Siemens Medical Systems Inc, USA
Tran et al.	2014	Journal of Medical Virology	Asia	Vietnam	Low	Unclassified pneumonia	92	Not mentioned
Yalçın et al.	2018	Indian Journal of Pediatrics	Asia	Turkey	Low	Unclassified pneumonia	93	PM-60, Mindray, China
Lenahan et al.	2020	Erj Open Research	Africa	Malawi	Low	Non-severe pneumonia	90	Not mentioned
Morre et al.	2019	Journal of Tropical Pediatrics	Africa	Papua New Guinea	Low	Non-severe pneumonia	90	Not mentioned
Mwaniki et al.	2009	Bulletin of the World Health Organization	Africa	Kenya	Low	Non-severe pneumonia	90	Nellcor Puritan Bennett NPB-40, USA
Nemani et al.	2016	Clinical Epidemiology and Global health	Asia	India	Low	Non-severe pneumonia	92	SHO 3002, Harsons, India

Author	Year	Journal	Region	Country	Altitude	Pneumonia classification	SpO_2	Pulse oximetry (maker and model)
Puumalainen et al.	2008	BMC Infectious Diseases	Asia	Philippines	Low	Non-severe pneumonia	90	BCI 3303 ximeter (Waukeha, USA)
Oktaria et al.	2021	PLoS One	Asia	Indonesia	Low	Unclassified pneumonia	90	Not mentioned
Rahman et al.	2021	Journal of Global Health	Asia	Bangladesh	low	Severe pneumonia	90	OxiMax N-600; Nellcor, Boulder, CO, USA
Roux et al.	2021	PLoS One	Africa	South Africa	low	Unclassified pneumonia	92	Not mentioned
Shrestha et al.	2020	PLOS ONE	Asia	Nepal	High	Radiological and non-radiological pneumonia	90	Mini SpO_2, Criticare Systems, USA
Muro et al.	2020	PLOS ONE	Africa	Tanzania	Low	Severe pneumonia	90	Not mentioned
Falade et al.	2020	Pediatr Infect Dis J.	South America	Paraguay	Low	Radiological	90	Not mentioned
Alfonso et al.	2021	Journal of Pharmaceutical Policy and Practice	South America	Colombia	Low	Bronchiolitis	90	Not mentioned
Stoiber et al.	2020	Journal of Medical Virology	Africa	Tunisia	Low	Other ARI	94	Not mentioned
Mahmoud et al.	2021	Padiatric Research	Africa	Egypt	Low	Unclassified pneumonia	94	Not mentioned

Supplementary table 3.6: Quality assessment of the studies reporting the prevalence of hypoxaemia among WHO-defined pneumonia

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
1	Alwadhi et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Asghar et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	Ashraf et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Ashraf et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	Basnet et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Bassat et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	Breiman et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Chisti et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9	Dembele et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10	Fancourt et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Gallagher et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12	Graham et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13	Izadnegahdar et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14	Jain et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
15	Kuti et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
16	Ma et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
17	McCollum et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
18	Nantanda et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
19	que et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
20	Semperte gui et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
21	Srinivasan et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
22	Tesfaye et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
23	Tiewsoh et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24	Webb et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
25	Blanc et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
26	Chisti et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
27	Duke et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
28	Hooli et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
29	Janabi et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
30	Kelly et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
31	Kurade et al.	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
32	Laghari et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
33	Lima et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
34	Ma et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
35	Mackenzie et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
36	Mathisen et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
37	McCollum et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
38	McCollum et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
39	McCracken et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
40	Orimadegun et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
41	Rao et al.	Unclear	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
42	Shrestha et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
43	Smith et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
44	Thomas et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
45	Tran et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
46	Tran et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
47	Yalçın et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
48	Lenahan et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
49	Morre et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
50	Mwaniki et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
51	Nemani et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
52	Puumalainen et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
53	Oktaria et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
54	Rahman et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
55	Roux et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
56	Shrestha et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
57	Muro et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Supplementary table 3.7: Quality assessment of the studies reporting the prevalence of hypoxaemia among other lab diagnosed pneumonia classification

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
1	Abdulkadir et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Araya et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	Benet et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Chisti et al.	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
5	Ciftci et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Fashanu et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	Kabir et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Nathan et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9	Nyawanda et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10	Pascoal et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Pervaiz et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12	Pukai et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13	Rani et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14	Reed et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
15	Ueno et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
16	Falade et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Serial	Author	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
17	Alfonso et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
18	Stoiber et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
19	Mahmoud et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Supplementary table 3.8: I2 and τ2 value for measure of heterogeneity across studies reporting the prevalence of hypoxaemia among WHO-defined pneumonia

Categories	Sub-categories	Heterogeneity statistic	DF	P-value	I^2	τ^2
Region	Asia	2722.26	23	0	99.16%	0.16
	Africa	6815.26	27	0	99.60%	0.13
	South America	1163.17	4	0	99.66%	0.32
	Multiple continent	649.64	3	0	99.54%	0.12
Altitude	High	736.45	5	0	99.32%	0.13
	Low	13687.19	53	0	99.61%	0.17
Facility type	Tertiary level referral facilities	3886.90	31	0	99.20%	0.21
	Primary or secondary referral facilities	1109.11	12	0	98.92%	0.11
	Health centres	604.13	5	0	99.17%	0.17
	Mixed setting	1794.99	5	0	99.72%	0.2
Type of patients	Emergency	476.44	7	0	98.53%	0.25
	Inpatient	4935.40	34	0	99.31%	0.15
	Outpatient	2270	12	0	99.47%	0.16
	Mixed	931.8	4	0	99.57%	0.04
Hospitalisation status	Hospitalised	6166.21	42	0	99.32%	0.18
	Non-hospitalised	2515.64	12	0	99.52%	0.19
	Mixed	918.55	3	0	99.67%	0.04
Clinical severity	Non-severe pneumonia	108.07	4	0	96.30%	0.06
	Unclassified pneumonia	5496.68	27	0	99.51%	0.1
	Very severe or severe pneumonia	5013.99	27	0	99.46%	0.18
Assessor	Doctor	2674.06	15	0	99.44%	0.32
	Nurse/paramedics	3691.52	12	0	99.67%	0.08
WHO IMCI 2014 classification	Pre	13470.43	47	0	99.65%	0.16
	Post	1261.32	12	0	99.05%	0.25
Publication Year	Before 2015	4087.45	27	0	99.34%	0.20
	2015 and after	9981.15	32	0	99.68%	0.15
SpO_2 Cut off	90%	10525.38	41	0	99.61%	0.18
	Others	5108.22	18	0	99.65%	0.24

DF: Degreed of freedom

Supplementary table 3.9: Number of articles using different database

Database	#
MEDLINE	425
EMBASE	807
GLOBAL HEALTH	130
Cochrane	153
Clinicaltrails.gov	85
SCOPUS	665
CINHAL	66
PubMed	907
Global Index Medicus (WHO)	376
IndMed (Advanced)	33
Web of Science (Advanced)	628
Total	4275

Supplementary table 3.10: Number of studies reporting the prevalence of hypoxaemia among WHO-defined pneumonia across various sub-groups

Categories	Sub-categories	Number of Studies (#57)
Region	Asia	23
	Africa	26
	South America	4
	Multiple continent	4
Altitude	High	5
	Low	51
	Mixed	1
Facility type	Tertiary level referral facilities	30
	Primary or secondary referral facilities	12
	Health centres	5
	Mixed setting	6
	Not reported	3
Type of patients	Emergency	8
	Inpatient	32
	Outpatient	12
	Mixed	5
Hospitalisation status	Hospitalised	40
	Non-hospitalised	12
	Mixed	4
	Not reported	1
Assessor	Doctor	15
	Nurse/paramedics	12
	Doctors/nurses/paramedics	2
	Non clinical	2
	Not mentioned	23
PO type mentioned	Yes	29
	No	28
PO probe type	Adult	1
	Paediatric	13
	Not reported	43
SpO_2 cut off	87%	1
	90%	38
	92%	12
	93%	2
	94%	1
	95%	2
	90-93%	1

Supplementary table 3.11: Prevalence of hypoxaemia among WHO-defined pneumonia before and after the change in pneumonia classification in 2014; presented in %

Pneumonia classification	IMCI classification version	Prevalence of hypoxaemia	Lower limit	Upper limit
		%	%	%
Very severe or severe	Pre 2014 (n = 24)	41	32	50
	2014 and after (n = 4)	40	37	43
Non-severe	Pre 2014 (n = 3)	10	2	24
	2014 and after (n = 2)	7	5	10
Unclassified	Pre 2014 (n = 21)	23	18	29
	2014 and after (n = 7)	32	9	60
Overall	Pre 2014 (n = 48)	31	26	36
	2014 and after (n = 13)	29	17	42

Lower Limit: Lower Limit of 96% Confidence Interval
Upper Limit: Upper Limit of 96% Confidence Interval

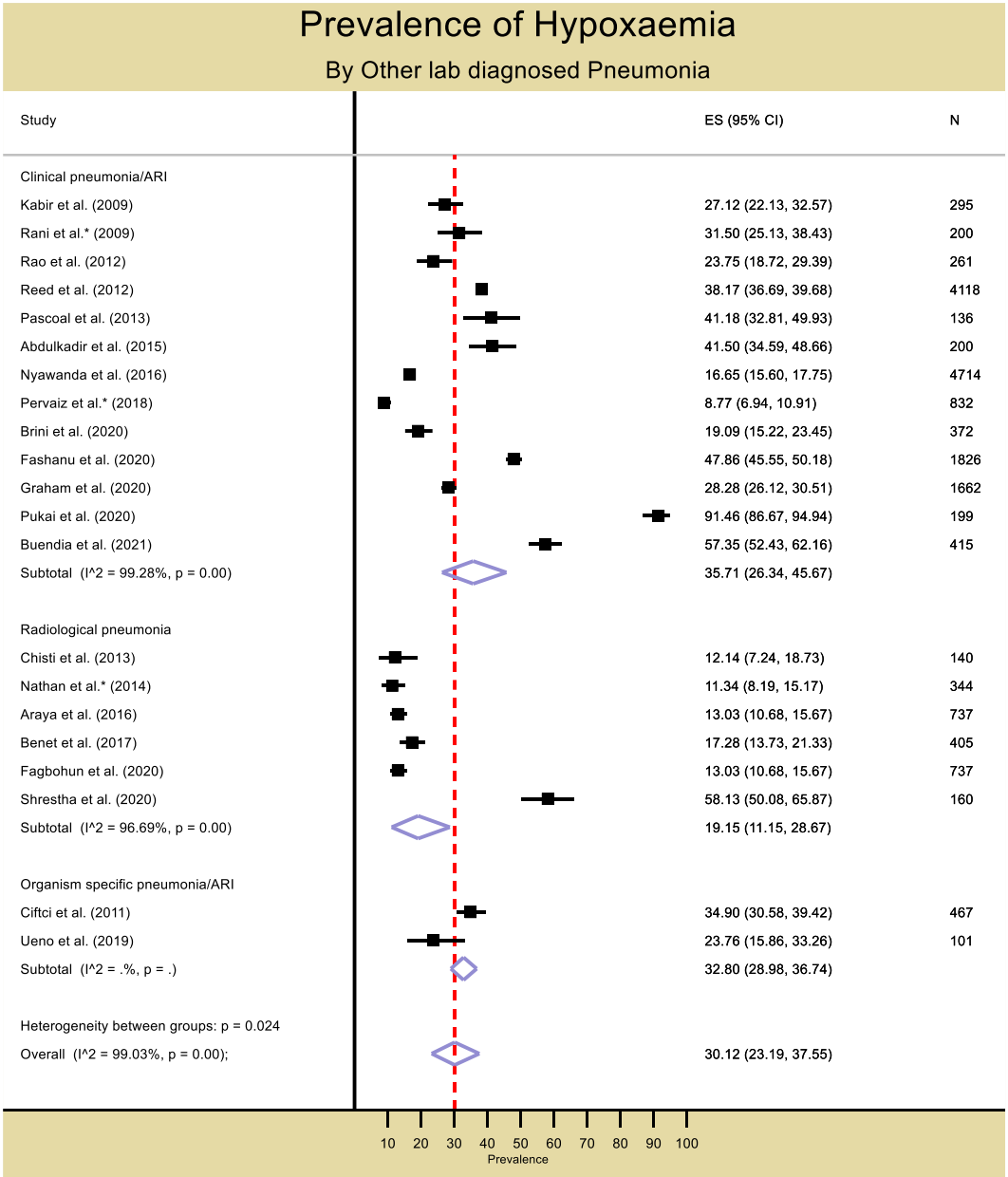
Supplementary table 3.12: Hypoxaemia prevalence among children with WHO-defined pneumonia across different subgroups, comparison between random-effects pooled estimate presented in % with 95% confidence interval and median with interquartile range

		Random Effects pooled estimate	Lower limit	Upper limit	Median	Q1	Q3
		%	%	%			
Region	Asia	31	24	39	32	16	54
	Africa	28	22	34	27	9	40
	South America	38	16	62	28	26	51
	Multiple continent	36	21	54	34	24	50
Altitude	High	33	20	47	29	26	58
	Low	30	25	35	28	14	49
Facility Type	Referral - Tertiary	29	22	36	28	15	44
	Referral - Primary / Secondary	42	33	51	40	28	57
	Health Centre	25	12	40	26	9	44
	Mixed setting	39	23	57	36	13	65
Type of patients	Emergency	47	30	64	50	33	60
	Inpatient	32	26	38	32	18	42
	Outpatient	23	15	33	26	7	35
	Mixed	17	11	24	16	8	18
Hospitalisation Status	Hospitalised	33	27	39	32	18	49
	Non-hospitalised	29	19	40	30	9	51
	Mixed	17	10	24	12	6	34
Clinical severity	Very severe or severe	41	33	49	39	27	57
	Unclassified	25	20	31	26	9	38
	Non-severe	8	3	16	8	4	14
Assessor	Doctor	41	28	55	39	23	58
	Nurse / paramedics	16	10	23	9	5	28
WHO IMCI 2014 classification	Pre	31	26	36	28	15	51
	Post	29	17	42	32	14	42
Publication Year	Before 2015	33	25	41	30	18	54
	2015 and after	29	23	35	28	13	42
SpO_2 Cut off	<90%	32	26	38	30	14	55
	Others	27	18	38	29	18	36
Overall		**31**	**26**	**36**	**28**	**14**	**50**

Lower Limit: Lower Limit of 96% Confidence Interval
Upper Limit: Upper Limit of 96% Confidence Interval
Q1: Quartile 1
Q3: Quartile 3

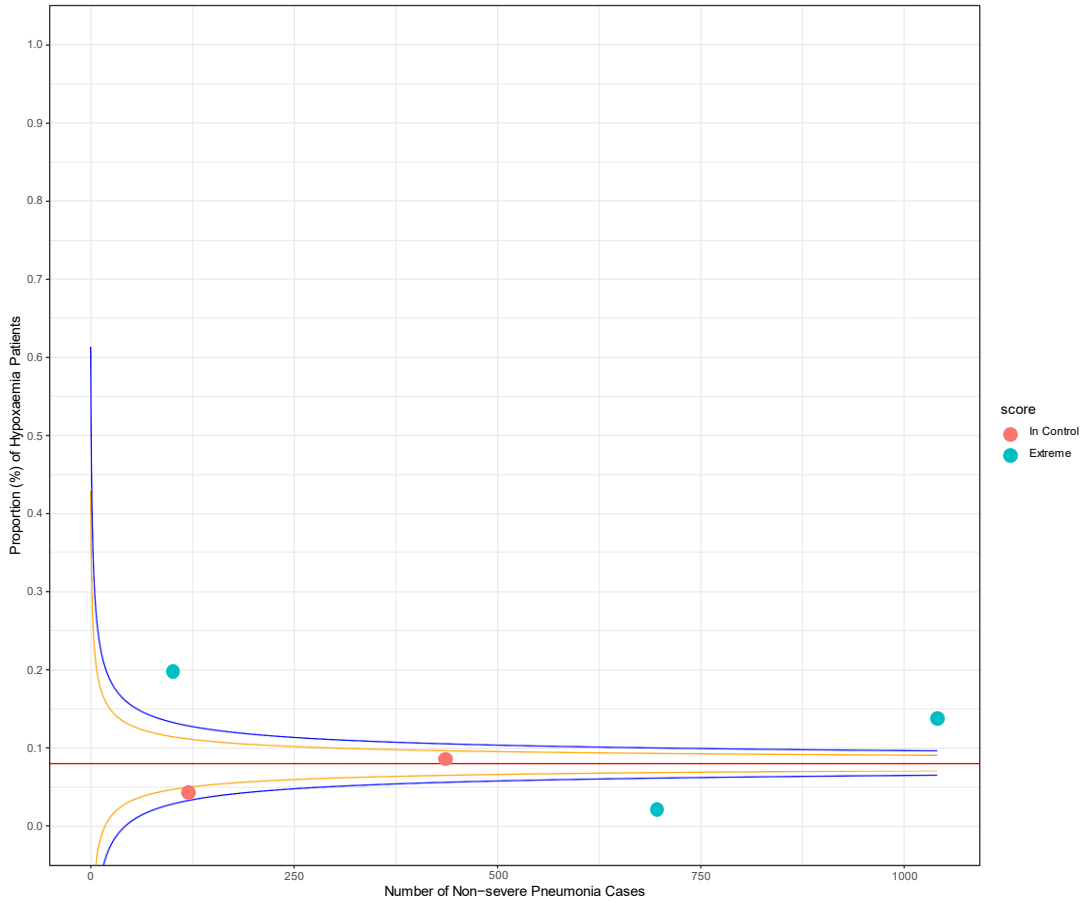
3.7.2 Supplementary figure

Supplementary figure 3.1: Hypoxaemia prevalence among children non-WHO-defined pneumonia; presented in %

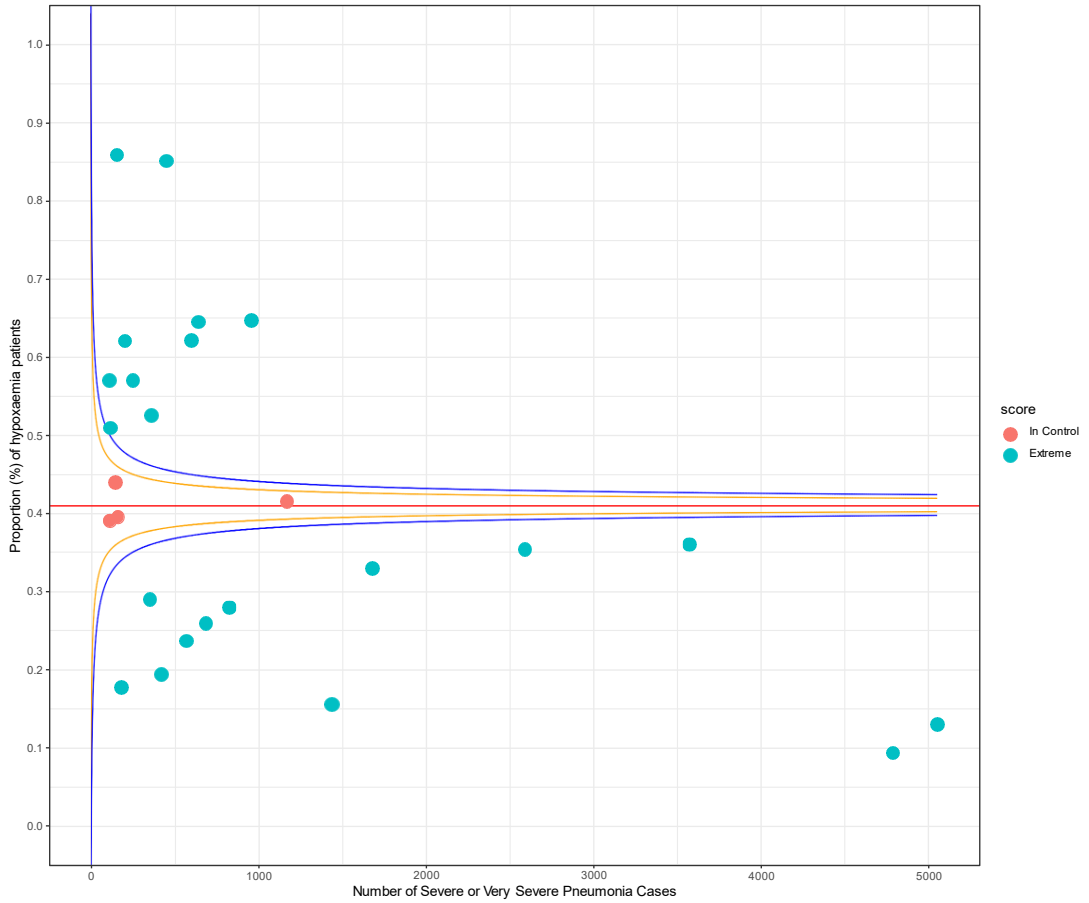


The broken red line shows the overall pooled prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

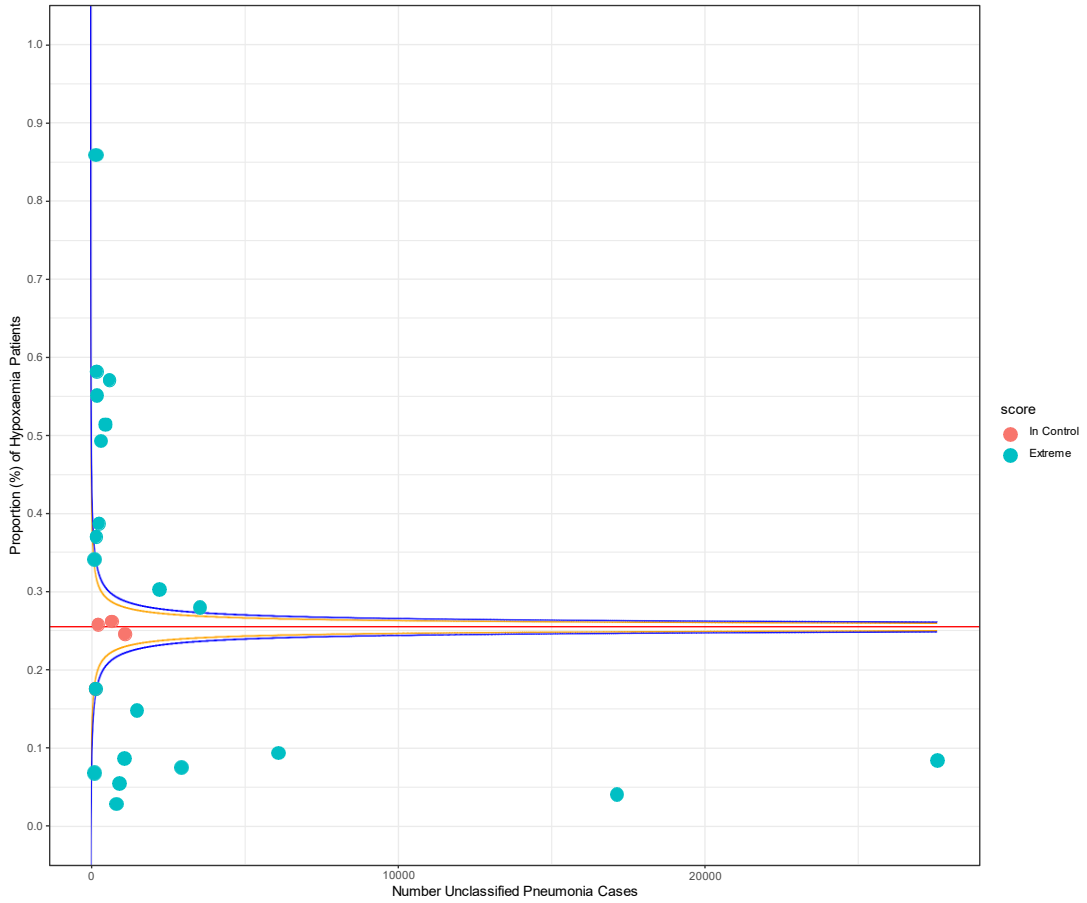
Supplementary figure 3.2: Funnel plot to assess bias in the studies which reported hypoxaemia prevalence among children with WHO-defined non-severe pneumonia



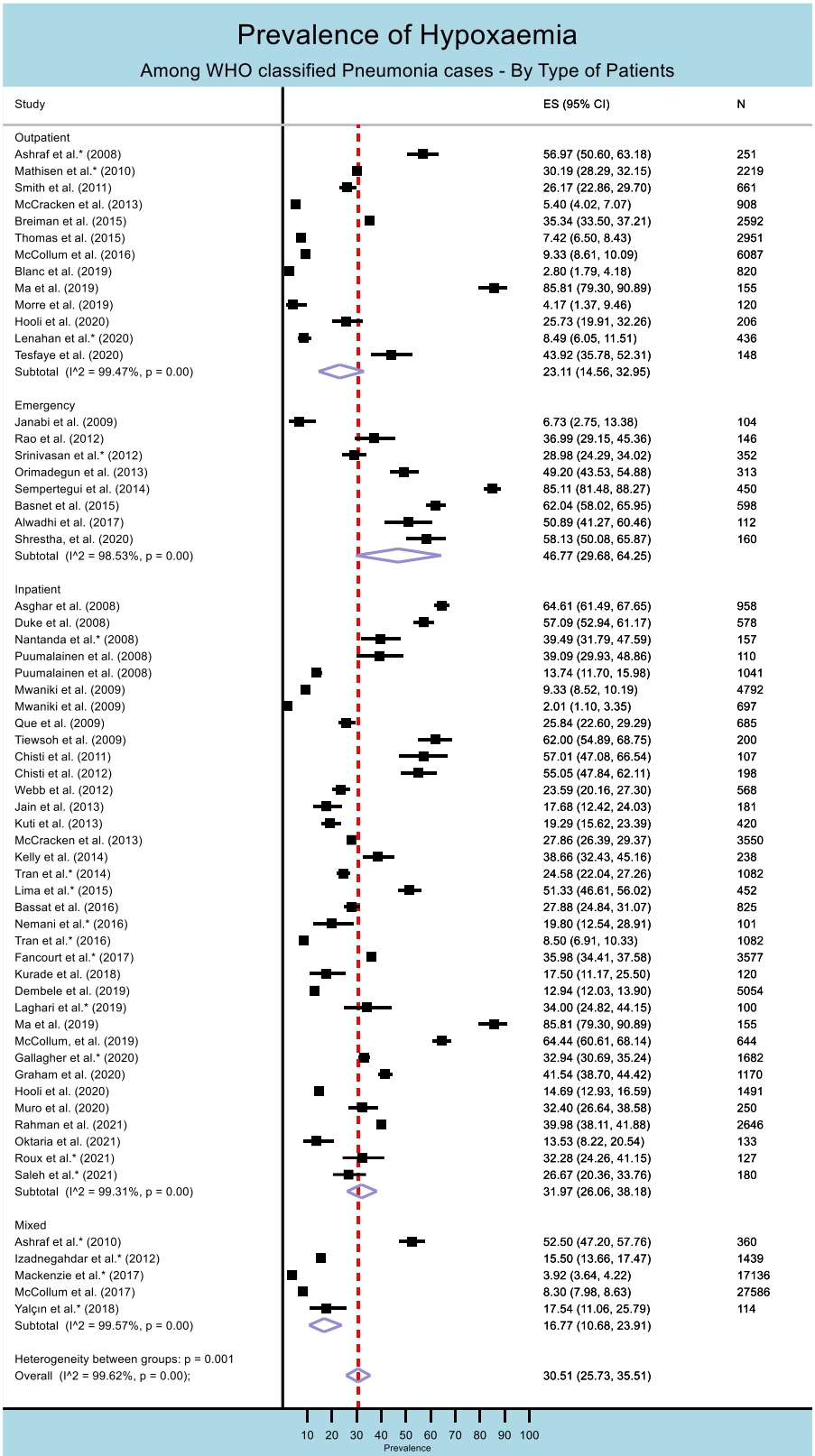
Supplementary figure 3.3: Funnel plot to assess bias in the studies which reported hypoxaemia prevalence among children with WHO-defined severe or very severe pneumonia



Supplementary figure 3.4: Funnel plot to assess bias in the studies which reported hypoxaemia prevalence among children with unclassified pneumonia

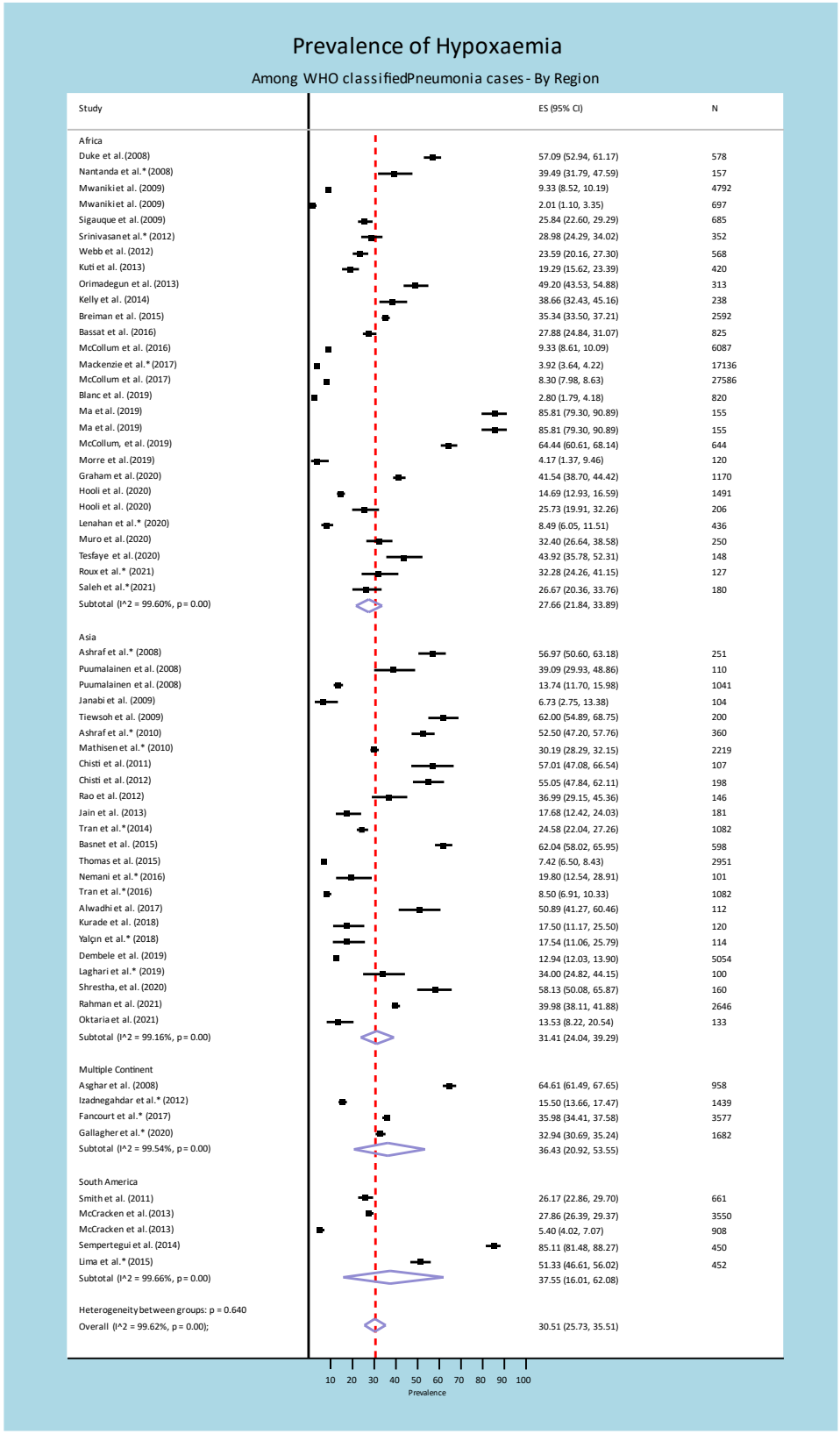


Supplementary figure 3.5: Hypoxaemia prevalence among children with WHO-defined pneumonia by type of patients; presented in %



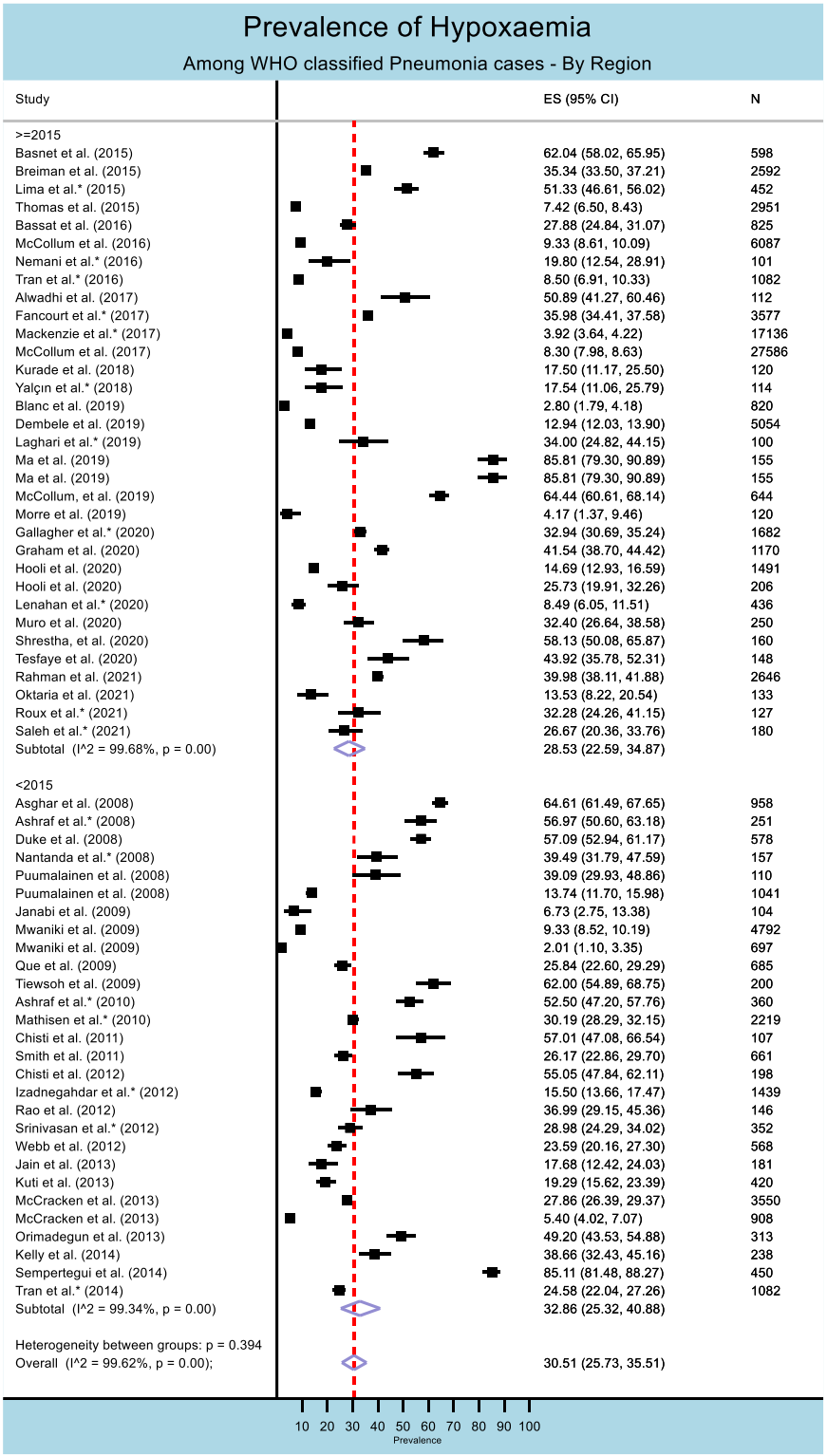
The broken red line shows the overall pooled prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

Supplementary figure 3.6: Hypoxaemia prevalence among WHO-defined pneumonia by region; presented in %



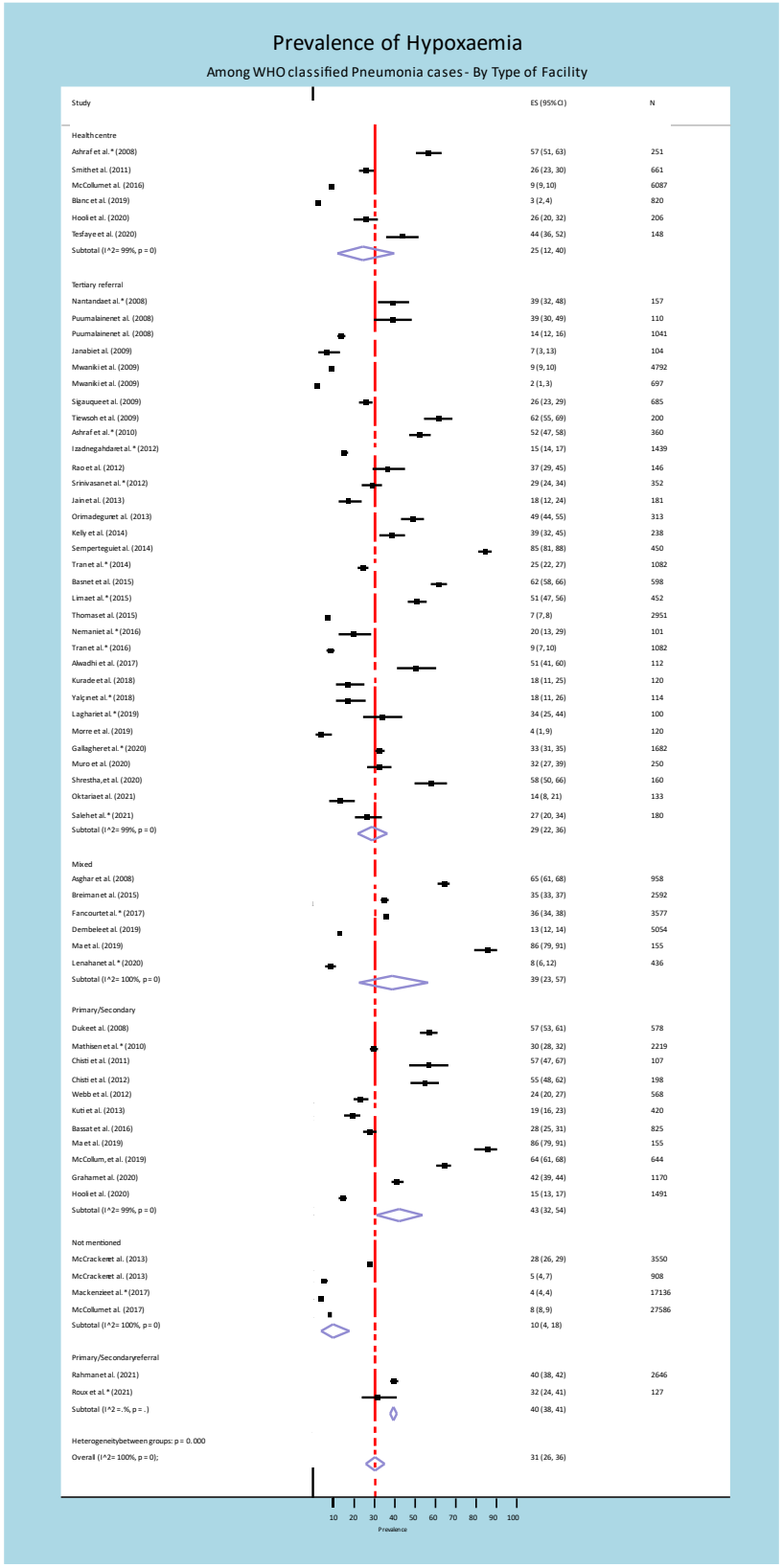
The broken red line shows the overall pooled estimate of prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

Supplementary figure 3.7: Hypoxaemia prevalence among children with WHO-defined pneumonia by publication year; presented in %



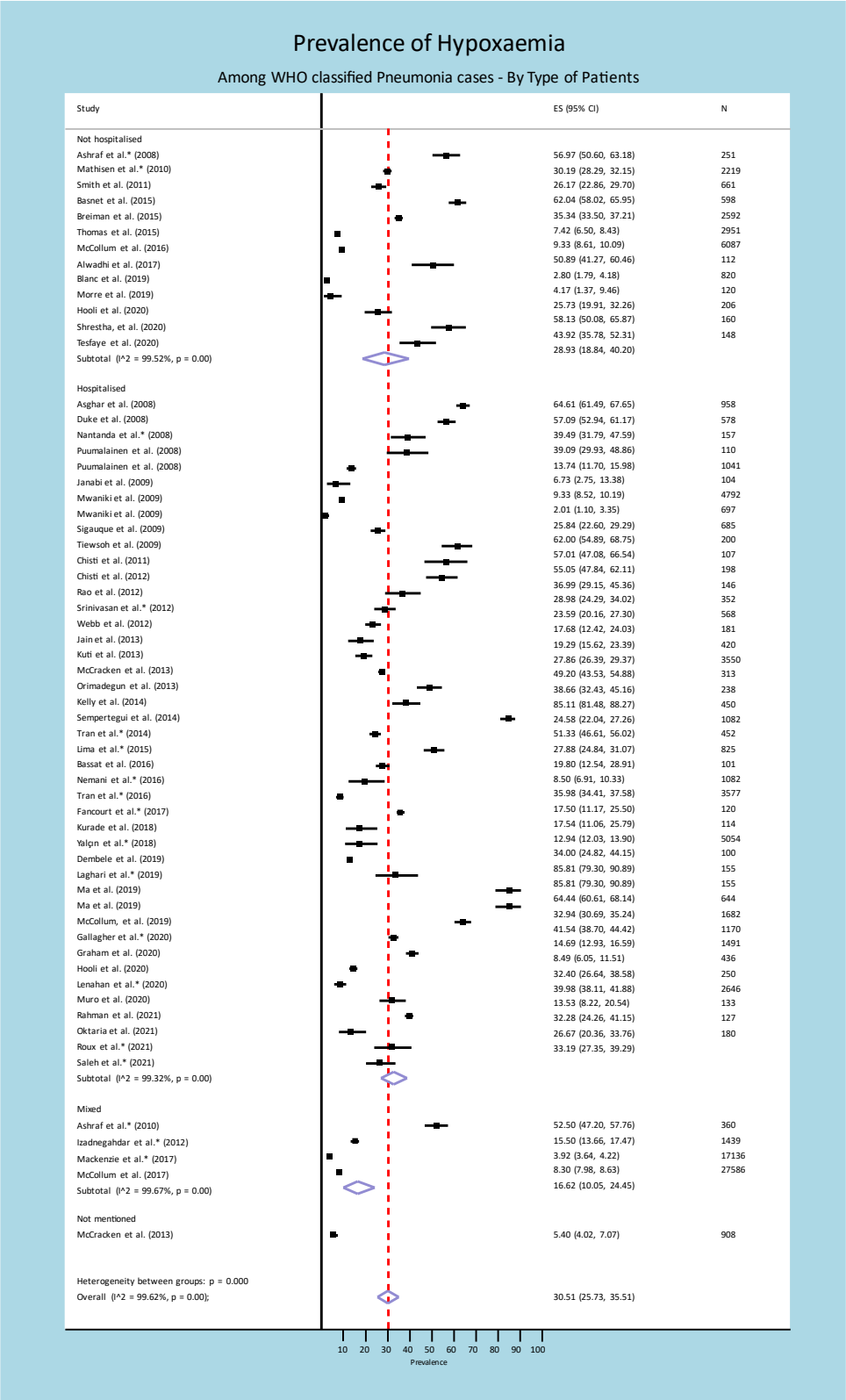
The broken red line shows the overall pooled prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

Supplementary figure 3.8: Hypoxaemia prevalence among WHO-defined pneumonia by facility type; presented in %



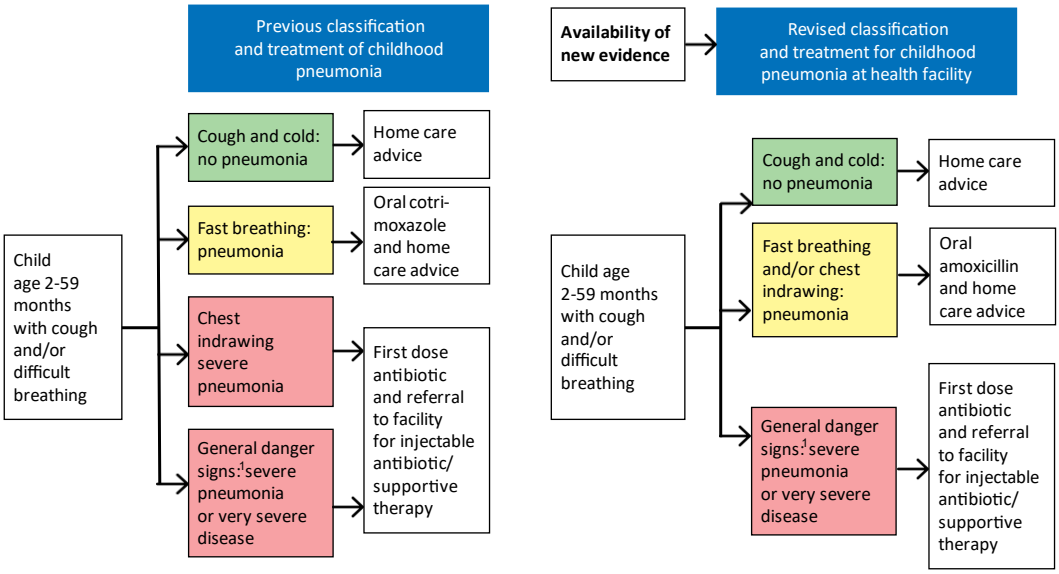
The broken red line shows the overall pooled prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

Supplementary figure 3.9: Hypoxaemia prevalence among WHO-defined pneumonia by patient status; presented in %



The broken red line shows the overall pooled prevalence of hypoxaemia.
*Studies where SpO_2 cut-off is >90%

Supplementary figure 3.10: Difference in classification and treatment of children age 2-59 months presenting with cough or difficult breathing according to the IMCI guidelines (2008 vs. 2014) (adopted from the WHO evidence summary)



† Not able to drink, persistent vomiting, convulsions, lethargic or unconscious, stridor in a calm child or severe malnutrition.

3.8 REFERENCE

1. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2016;388(10063):3027-35.
2. Lim Y-W, Steinhoff M, Girosi F, Holtzman D, Campbell H, Boer R, et al. Reducing the global burden of acute lower respiratory infections in children: the contribution of new diagnostics. Nature. 2006:9.
3. Oldenburg O, Wellmann B, Buchholz A, Bitter T, Fox H, Thiem U, et al. Nocturnal hypoxaemia is associated with increased mortality in stable heart failure patients. European heart journal. 2016;37(21):1695-703.
4. Wardlaw T, Johansson E, Hodge M. Pneumonia: The Forgotten Killer of Children. UNICEF's Division of Communication. New York: WHO Press; 2006.
5. United Nations. Sustainable Development Goals 2016 [Available from: http://www.un.org/sustainabledevelopment/.
6. Mower WR, Sachs C, Nicklin EL, Baraff LJ. Pulse oximetry as a fifth pediatric vital sign. Pediatrics. 1997;99(5):681-6.
7. Reed C, Madhi SA, Klugman KP, Kuwanda L, Ortiz JR, Finelli L, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One. 2012;7(1):e27793.
8. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.
9. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9).
10. Adebola O, Babatunde O, Bose O. Hypoxemia predicts death from severe falciparum malaria among children under-5 years of age in Nigeria: the need for pulse oximetry in case management. African health sciences. 2014;14(2):397-407.
11. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.
12. Integrated management of childhood illness (IMCI), World Health Organization. Integrated management of childhood illness (IMCI) chart booklet. Distance Learn Course. 2014:1-76.
13. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.
14. McCollum ED, Bjornstad E, Preidis GA, Hosseinipour MC, Lufesi N. Multicenter study of hypoxemia prevalence and quality of oxygen treatment for hospitalized Malawian children. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2013;107(5):285-92.

15. World Health Organization. Revised WHO classification and treatment of childhood pneumonia at health facilities. WHO. 2014.

16. The World Bank. World Bank Country and Lending Groups: World Bank Group; 2018 [Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519.

17. World Health Organization. Oxygen therapy for children. 2016.

18. World Health Organization, Unicef. Integrated Management of childhood Illness (chart booklet). 2008.

19. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. International journal of health policy and management. 2014;3(3):123.

20. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives of Public Health. 2014;72(1):39.

21. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Jama. 2000;283(15):2008-12.

22. Matthew Kumar. Funnel Plots for Proportion Data 2018 [Available from: https://cran.r-project.org/web/packages/funnelR/vignettes/introduction.html.

23. Begg CB, Berlin JA. Publication bias: a problem in interpreting medical data. Journal of the Royal Statistical Society: Series A (Statistics in Society). 1988;151(3):419-45.

24. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.

25. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology. 2009;62(10):e1-e34.

26. Rahman AE, Campbell H, Arifeen SE, Nair H, Dockrell D, Dozier M, et al. The prevalence of hypoxaemia among children with pneumonia in low- and middle-income countries: a systematic review and meta-analysis. PROSPERO 2019 CRD42019126207 [cited 2021 22 November 2021]. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019126207.

27. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.

28. Duke T, Graham S, Cherian M, Ginsburg A, English M, Howie S, et al. Oxygen is an essential medicine: a call for international action [Unresolved issues]. The International journal of tuberculosis and lung disease. 2010;14(11):1362-8.

29. Lozano J. Epidemiology of hypoxaemia in children with acute lower respiratory infection [oxygen therapy in children]. The international journal of tuberculosis and lung disease. 2001;5(6):496-504.

30. Graham H, Tosif S, Gray A, Qazi S, Campbell H, Peel D, et al. Providing oxygen to children in hospitals: a realist review. Bulletin of the World Health Organization. 2017;95(4):288.

31. Wahl B, O'Brien KL, Greenbaum A, Majumder A, Liu L, Chu Y, et al. Burden of Streptococcus pneumoniae and Haemophilus influenzae type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000–15. The Lancet Global Health. 2018;6(7):e744-e57.

32. Graham H, Bakare AA, Ayede AI, Oyewole OB, Gray A, Peel D, et al. Hypoxaemia in hospitalised children and neonates: a prospective cohort study in Nigerian secondary-level hospitals. EClinicalMedicine. 2019;16:51-63.

33. Zhang L, Mendoza-Sassi R, Santos J, Lau J. Accuracy of symptoms and signs in predicting hypoxaemia among young children with acute respiratory infection: a meta-analysis. The International journal of tuberculosis and lung disease. 2011;15(3):317-25.

34. Rahman AE, Hossain AT, Chisti MJ, Dockrell DH, Nair H, El Arifeen S, et al. Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh. Journal of global health. 2021;11.

35. Saha SK, Schrag SJ, El Arifeen S, Mullany LC, Islam MS, Shang N, et al. Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study. The Lancet. 2018;392(10142):145-59.

36. O'Brien KL, Baggett HC, Brooks WA, Feikin DR, Hammitt LL, Higdon MM, et al. Causes of severe pneumonia requiring hospital admission in children without HIV infection from Africa and Asia: the PERCH multi-country case-control study. The Lancet. 2019;394(10200):757-79.

37. Orimadegun AE, Ogunbosi BO, Carson SS. Prevalence and predictors of hypoxaemia in respiratory and non-respiratory primary diagnoses among emergently ill children at a tertiary hospital in south western Nigeria. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2013;107(11):699-705.

38. Ibraheem R, Abdulkarim A. Hypoxaemia in hospitalized under-five Nigerian children with pneumonia. 2014.

39. Bassat Q, Lanaspa M, Machevo S, O'Callaghan-Gordo C, Madrid L, Nhampossa T, et al. Hypoxaemia in Mozambican children <5 years of age admitted to hospital with clinical severe pneumonia: clinical features and performance of predictor models. Tropical Medicine & International Health. 2016;21(9):1147-56.

40. Tolla HS, Letebo M, Asemere YA, Belete AB, Tumbule TC, Feleke Z, et al. Use of pulse oximetry during initial assessments of children under-5 with pneumonia: a retrospective cross-sectional study from 14 hospitals in Ethiopia. J Glob Health Rep. 2019;3:e2019016.

41. Salah ET, Algasim SH, Mhamoud AS, Husian NEOSA. Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2015;19(4):203.

42. Wandeler G, Pauchard J, Zangger E, Diawara H, Gehri M. Which clinical signs predict hypoxaemia in young Senegalese children with acute lower respiratory tract disease? Paediatrics and international child health. 2015;35(1):65-8.

43. World Health Organization. Making fair choices on the path to universal health coverage: Final report of the WHO Consultative Group on Equity and Universal Health Coverage. 2014.

44. World Health Organization. Oxygen therapy for children. Geneva, Switzerland; 2016.

45. Fox MP, Thea DM, Sadruddin S, Bari A, Bonawitz R, Hazir T, et al. Low rates of treatment failure in children aged 2–59 months treated for severe pneumonia: a multisite pooled analysis. Clinical infectious diseases. 2012;56(7):978-87.

46. Addo-Yobo E, Anh DD, El-Sayed HF, Fox LM, Fox MP, MacLeod W, et al. Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the MASS study. Tropical Medicine & International Health. 2011;16(8):995-1006.

47. Addo-Yobo E, Chisaka N, Hassan M, Hibberd P, Lozano JM, Jeena P, et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. The Lancet. 2004;364(9440):1141-8.

48. Bari A, Sadruddin S, Khan A, Khan A, Lehri IA, Macleod WB, et al. Community case management of severe pneumonia with oral amoxicillin in children aged 2–59 months in Haripur district, Pakistan: a cluster randomised trial. The Lancet. 2011;378(9805):1796-803.

49. Hazir T, Fox LM, Nisar YB, Fox MP, Ashraf YP, MacLeod WB, et al. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. The Lancet. 2008;371(9606):49-56.

50. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. Respiratory medicine. 2013;107(6):789-99.

51. Sinex JE. Pulse oximetry: principles and limitations. The American journal of emergency medicine. 1999;17(1):59-66.

52. Zeserson E, Goodgame B, Hess JD, Schultz K, Hoon C, Lamb K, et al. Correlation of venous blood gas and pulse oximetry with arterial blood gas in the undifferentiated critically ill patient. Journal of intensive care medicine. 2018;33(3):176-81.

53. Chushkin M, Popova L, Shergina E, Krasnikova E, Gordeeva O, Karpina N. Comparative analysis of the arterial oxygen saturation (SaO2) and pulse oximetry measurements (SpO2) in patients with pulmonary tuberculosis. European Respiratory Society; 2020.

54. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I 2 in assessing heterogeneity may mislead. BMC medical research methodology. 2008;8(1):79.

55. Rahman AE, Iqbal A, Hoque DE, Moinuddin M, Zaman SB, Rahman QS-u, et al. Managing neonatal and early childhood syndromic sepsis in sub-district hospitals

in resource poor settings: improvement in quality of care through introduction of a package of interventions in rural Bangladesh. PloS one. 2017;12(1):e0170267.

56. Enoch AJ, English M, Shepperd S. Does pulse oximeter use impact health outcomes? A systematic review. Archives of disease in childhood. 2016;101(8):694-700.

57. World Health Organization. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care. 2012.

58. Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker JN. Reviewing the WHO guidelines for antibiotic use for sepsis in neonates and children. Paediatrics and international child health. 2018;38(sup1):S3-S15.

59. Ginsburg AS, Van Cleve WC, Thompson MI, English M. Oxygen and pulse oximetry in childhood pneumonia: a survey of healthcare providers in resource-limited settings. Journal of tropical pediatrics. 2012;58(5):389-93.

60. Arifeen S, Bryce J, Gouws E, Baqui A, Black R, Hoque D, et al. Quality of care for under-fives in first-level health facilities in one district of Bangladesh. Bulletin of the World Health Organization. 2005;83(4):260-7.

61. Anwar I, Kalim N, Koblinsky M. Quality of obstetric care in public-sector facilities and constraints to implementing emergency obstetric care services: evidence from high-and low-performing districts of Bangladesh. Journal of health, population, and nutrition. 2009;27(2):139.

62. Chowdhury S, Hossain SA, Halim A. Assessment of quality of care in maternal and newborn health services available in public health care facilities in Bangladesh. Bangladesh Medical Research Council Bulletin. 2009;35(2):53-6.

63. Baker K, Ward C, Maurel A, de Cola MA, Smith H, Getachew D, et al. Usability and acceptability of a multimodal respiratory rate and pulse oximeter device in case management of children with symptoms of pneumonia: A cross-sectional study in Ethiopia. Acta Paediatrica. 2021;110(5):1620-32.

64. Boyd N, King C, Walker IA, Zadutsa B, Bernstein M, Ahmed S, et al. Usability Testing of a Reusable Pulse Oximeter Probe Developed for Health-Care Workers Caring for Children <5 Years Old in Low-Resource Settings. Am J Trop Med. 2018;99(4):1096.

65. Baker K, Akasiima M, Wharton-Smith A, Habte T, Matata L, Nanyumba D, et al. Performance, Acceptability, and Usability of Respiratory Rate Timers and Pulse Oximeters When Used by Frontline Health Workers to Detect Symptoms of Pneumonia in Sub-Saharan Africa and Southeast Asia: Protocol for a Two-Phase, Multisite, Mixed-Methods Trial. JMIR research protocols. 2018;7(10):e10191.

66. World Health Organization. Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization; 2020.

67. World Health Organization. WHO-UNICEF technical specifications and guidance for oxygen therapy devices. 2019.

Chapter 4: BURDEN OF HYPOXAEMIA AMONG CHILDREN WITH PNEUMONIA IN BANGLADESH

One of my general objectives was to estimate the burden of hypoxaemia among children with pneumonia. The specific research question 2 was to assess the burden of hypoxaemia among children with pneumonia in Bangladesh.

Table 4.1 General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

The work presented in the chapter 4 was published in The Journal of Global Health in 2021.

Title: Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh

Authors: **Ahmed Ehsanur Rahman (myself)**, Aniqa Tasnim Hossain, Mohammod Jobayer Chisti, **David H Dockrell** (co-supervisor), **Harish Nair** (co-supervisor), **Shams El Arifeen** (co-supervisor), and **Harry Campbell** (supervisor).

URL: https://jogh.org/documents/2021/jogh-11-04053.pdf

4.1 ABSTRACT

4.1.1 Background

With an estimated 1 million cases per year, pneumonia accounts for 16% of all under-5 deaths globally, and hypoxaemia is one of the strongest predictors of mortality. Most of these deaths are preventable and occur in low- and middle-income countries. Bangladesh is among the six high burden countries with an estimated 4 million pneumonia episodes annually. There is a gap in updated evidence on the prevalence of hypoxaemia among children with severe pneumonia in high burden countries, including Bangladesh.

4.1.2 Methods

We conducted a secondary analysis of data obtained from icddr,b-Dhaka Hospital, a secondary level referral hospital located in Dhaka, Bangladesh. We included 2646 children aged 2-59 months admitted with WHO-defined severe pneumonia during 2014-17. The primary outcome of interest was hypoxaemia, defined as SpO_2<90% on admission. The secondary outcome of interest was adverse clinical outcomes defined as deaths during hospital stay or referral to higher-level facilities due to clinical deterioration.

4.1.3 Results

On admission, the prevalence of hypoxaemia among children hospitalised with severe pneumonia was 40%. The odds of hypoxaemia were higher among females (adjusted Odds ratio AOR=1.44; 95% CI, 1.22 to 1.71) and those with a history of cough or difficulty in breathing for 0-48 hours before admission (AOR=1.61; 95% CI,

1.28 to 2.02). Among all children with severe pneumonia, 6% died during the hospital stay, and 9% were referred to higher-level facilities due to clinical deterioration. Hypoxaemia was the strongest predictor of mortality (AOR=11.08; 95% CI, 7.28 to 16.87) and referral (AOR=5.94; 95% CI, 4.31 to 17) among other factors such as age, sex, history of fever and cough or difficulty in breathing, and severe acute malnutrition. Among those who survived, the median duration of hospital stay was 7 days (IQR 4-11) in the hypoxaemic group and 6 days (IQR 4-9) in the non-hypoxaemic group, and the difference was significant at $p<0.001$.

4.1.4 Conclusion

The high burden of hypoxaemia and its clinical outcomes call for urgent attention to promote oxygen security in low resource settings like Bangladesh. The availability of pulse oximetry for rapid identification and an effective oxygen delivery system for immediate correction should be ensured for averting many preventable deaths.

4.2 BACKGROUND

Pneumonia accounts for approximately 16% of all under-5 deaths, making it one of the leading causes of mortality in this age group globally (1). Most of these deaths are preventable and occur in low- and middle-income countries (LMICs) (2, 3). Considering the high morbidity and mortality burden, the World Health Organisation (WHO) and UNICEF declared it the major “forgotten killer of children” (4).

Hypoxaemia, defined as low oxygen saturation in arterial blood (peripheral capillary oxygen saturation (SpO_2<90%) by the World Health Organization, is a common complication of pneumonia and other acute lower respiratory infections (ALRIs) with wide variations in prevalence across different clinical severity classifications and geographical areas (5, 6). Hypoxaemia is one of the strongest predictors of mortality among children suffering from pneumonia and other ALRIs (7, 8). Most of the hypoxaemia-related deaths can be prevented by routine assessment, early detection, and rapid correction through appropriate oxygen therapy (9, 10).

Bangladesh is one of six high burden countries with an estimated 4 million episodes of clinical pneumonia and 677,000 episodes of severe pneumonia annually among children under-5 years of age (11). Like many other LMICs, pneumonia is the primary killer among this age group causing approximately 19% of all under-5 deaths in Bangladesh (12). Therefore, in addition to achieving high coverage of Pneumococcal Vaccine and Haemophilus Influenzae Type b for prevention and ensuring appropriate antibiotic therapy for treatment, timely management of hypoxaemia is essential to avert these preventable deaths and achieve the 2025 Global Action Plan for Pneumonia and Diarrhoea (GAPPD) target (13-15).

WHO recommends routine assessment of hypoxaemia at the first point of contact and ensuring oxygen therapy in inpatient care, but there are significant gaps between policy and actual clinical practices (16, 17). In Bangladesh, very few public and private hospitals have the provision for routine assessment of hypoxaemia among children presenting with pneumonia or other ALRIs (18). Hence, there are scant data regarding the current prevalence of hypoxaemia among children with pneumonia. This paper aims to assess the prevalence of hypoxaemia, disaggregated by background characteristics and clinical history, among children hospitalised with WHO-defined severe pneumonia in a non-government hospital in Bangladesh. We also explore the contribution of hypoxaemia as a predictor of death and referral due to clinical deterioration.

4.3 METHODS

4.3.1 Study design

We conducted a secondary analysis of data obtained from icddr,b-Dhaka Hospital, a non-government hospital located in Dhaka, Bangladesh's capital.

The icddr,b-Dhaka Hospital provides treatment to approximately 200,000 patients annually, of which more than half are children under-5 years of age (19). Most of these patients are from a low-socioeconomic background, principally residing in urban or peri-urban Dhaka. Diarrhoea is the primary entry point for admission to icddr,b-Dhaka Hospital; however, children with cough and respiratory distress receive treatment irrespective of their diarrhoea status. Most patients are treated through the short stay ward (less than 24 hours). They are admitted to the special

care ward (SCW) if severe complications, including pneumonia and other ALRI. The SCW of icddr,b treats on average 1200 under-5 children per year, and among which almost 50% are severe pneumonia cases. There are nine fixed beds in SCW. Extra beds are provided for sick children when there is a surge of severe patients, including pneumonia. This SCW has mechanical ventilators, non-invasive ventilation, piped oxygen, cardiac monitors, pulse oximetry, infusion pumps, syringe pumps, and inotropes and vasopressor drugs. All children with severe pneumonia and hypoxaemia used to receive (since August 2013) locally made low-cost bubble-continuous positive airway pressure (CPAP) as a part of the hospital standard of care.

In this secondary analysis, we included all children aged 2-59 months admitted to the SCW with WHO-defined severe pneumonia between 2014 and 2017.

All children admitted to SCW were seen by the attending physician, who performed a physical examination. The on-duty hospital nurses collected the background characteristics (including age) and the history of illness based on a standard form as a part of routine practice. In addition, they also measured the height and weight on admission. WHO reference value was used to calculate the z-score and classify the malnutrition level. The attending nurse also measured SpO_2 for all children presenting with cough and difficulty in breathing on admission. A portable pulse oximetry (OxiMax N-600; Nellcor, Boulder, CO, USA) with a paediatric probe was used for SpO_2 assessment. The clinical definition of the 2013 version of the WHO Pocketbook of Hospital Care for Children was used for pneumonia classification (20). Severe pneumonia was defined as children with a history of cough and difficulty in

breathing with central cyanosis or SpO_2<90% or severe respiratory distress defined as grunting or very severe chest indrawing or signs of pneumonia according to WHO Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses (20) (≥50 breaths per minute in a child aged 2-11 months, and ≥40 breaths per minute in a child aged 12-59 months), with any of the following danger signs: lethargy, unable to breastfeed or drink, convulsion, loss of consciousness. We extracted data from electronic individual patient records and included all children with WHO-defined severe pneumonia for this analysis.

Children admitted to the SCW with severe pneumonia received antibiotics and supportive care following the WHO-pocket book guidelines (20). Moreover, they received frequent monitoring by the clinical team and nutritional support (breast milk, micronutrients, zinc). In addition, all children with hypoxaemia received O2 supplementation through nasal prongs using the locally made bubble CPAP (21).

4.3.2 Analysis plan

We used Stata version 14.0 (22) for data analysis. The primary outcome of interest was hypoxaemia on admission, and we used the WHO recommended cut-off of SpO_2<90% (20, 23). The secondary outcome of interest was adverse clinical outcomes defined as deaths during hospital stay or referral to higher-level facilities due to clinical deterioration. We used descriptive statistics (proportion with 95% confidence intervals) to report the prevalence of hypoxaemia, which was disaggregated by background characteristics (age and sex), history of illness (number of days suffering from fever and cough or difficulty in breathing before admission)

and presence of comorbidities (severe acute malnutrition- as <−3z score of weight for age). We also presented the seasonal variations in hypoxaemia prevalence by quarter. The average annual rate of increase was estimated using the following equation: r=[ln(p2/p1)]/(t2-t1), where t1 is the first time-point, t2 is the last time-point, p1 is prevalence in t1 and p2 is prevalence in t2. We used multiple logistic regression to present the relationship of different risk factors (background characteristics such as age and sex, history of illness and comorbidities) with hypoxaemia status after adjusting for the effect of potential confounders and covariates. We followed a similar approach to present the relationship between hypoxaemia status and adverse hospital outcomes (death during hospitalisation or referral to higher-level facilities due to clinical deterioration separately and a composite indicator). The risks were presented with adjusted odds ratios (AORs) with 95% confidence intervals (CI). Among those who were alive at the end of their hospital stay, we estimated the median duration of hospital stay with the inter-quartile range (IQR). Those who died during the hospital stay or left the hospital against medical advice were treated as missing values for this analysis. The difference in the median duration of hospital stay by their hypoxaemia status on admission was assessed using the nonparametric equality of medians test since they were not normally distributed. Shapiro-Wilk and Shapiro-Francia tests were used for testing the normality of distribution.

4.3.3 Ethical considerations

We obtained routine health data from icddr,b-Dhaka hospital's patient records. The researchers were not directly involved with services and did not have any interaction

with the patients during the data collection. Ethical approval for this study was obtained from the Institutional Review Board of icddr,b (PR-18054).

4.4 RESULTS

A total of 2646 children met the inclusion criteria, and all were included in the analysis. Table 4.2 presents the background characteristics of the children who were included in this analysis. Around 70% of children were aged 2-11 months, and 65% were male. Approximately 60% of them had a history of fever, and 25% had a history of difficulty in breathing before admission. Around 42% of them had severe acute malnutrition.

Table 4.2: Background characteristics of children aged 2-59 months admitted to icddr,b-Dhaka Hospital with WHO-defined severe pneumonia between 2014-17; presented in %; N=2646

	N	%
Age		
2-11 months	1,895	72
12-59 months	751	28
Sex		
Male	1,707	65
Female	939	35
History of fever		
No fever	1,101	42
0-1 days	239	9
2-6 days	1,040	39
7 or more days	266	10
History of cough or difficulty in breathing		
No respiratory distress	1,949	74
0-48 hours	384	14
More than 48 hours	313	12
Severe Acute Malnutrition		
No	1,116	42
Yes	1,530	58
Total	**2,646**	**100**

Figure 4.1 represents the hypoxaemia prevalence disaggregated by background characteristics, clinical history, and comorbidities. On admission, the overall prevalence was 40% (95% CI, 38 to 42). The prevalence was higher among females (46%; 95% CI, 43 to 49) and those who had a history of fever for 0-1 days (47%; 95%

CI, 41 to 55) and cough or difficulty in breathing for 0-48 hours (53%, 95% CI, 48 to 58) before admission. Although not statistically significant, the prevalence of hypoxaemia was somewhat higher among the younger age group than that of older children (Supplementary figure 4.1)

Figure 4.1: Hypoxaemia prevalence among children aged 2-59 months admitted to icddr,b Dhaka Hospital with WHO-defined pneumonia between 2014-17 by background characteristics; presented in %; N=2646.

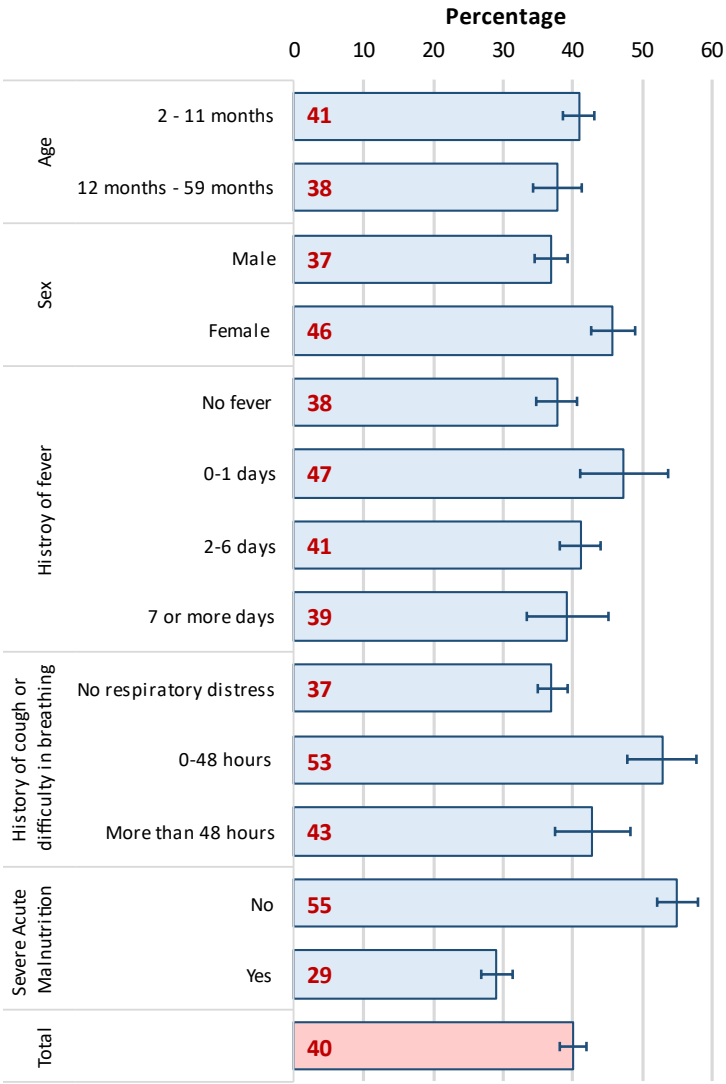
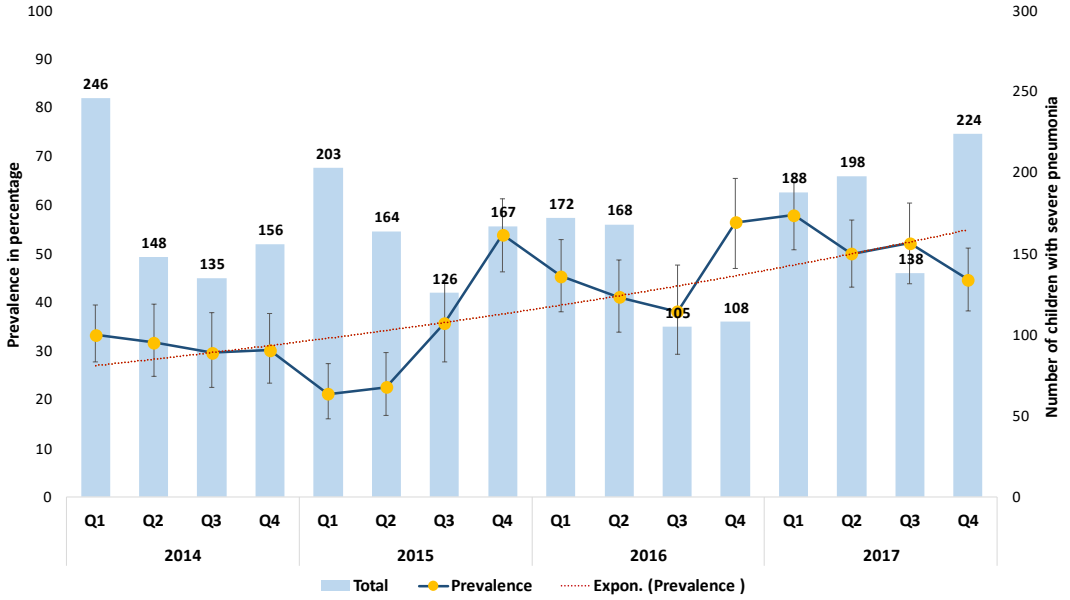


Figure 4.2 represents the seasonal variation in hypoxaemia prevalence between 2014 and 2017. Here the prevalence (%) is presented with the line-graph, and the number of children hospitalised with severe pneumonia is presented with the column-graphs. Although no notable seasonal pattern was observed, the average annual prevalence increased from 32% in 2014 to 51% in 2018. The average annual rate of increase was around 19%.

Figure 4.2: Hypoxaemia prevalence among children aged 2-59 months admitted to icddr,b Dhaka Hospital with WHO-defined pneumonia between 2014-17 by quarters; presented in %; N=2646



Q_i: Quarter$_i$, Expon: Exponential

Table 4.3 represents the relationship of various risk factors with the hypoxaemia status of children. The odds of hypoxaemia were higher among females (AOR=1.44; 95% CI, 1.22 to 1.71). It was also higher among children who had a history of cough or difficulty in breathing for 0-48 hours on admission (AOR=1.61; 95% CI, 1.28 to 2.02).

Table 4.3: Association between various risk factors and hypoxaemia status of children aged 2-59 months admitted to icddr,b-Dhaka Hospital with WHO-defined severe pneumonia between 2014-17; presented in odds ratio and adjusted odds ratio with 95% confidence interval ; N=2646

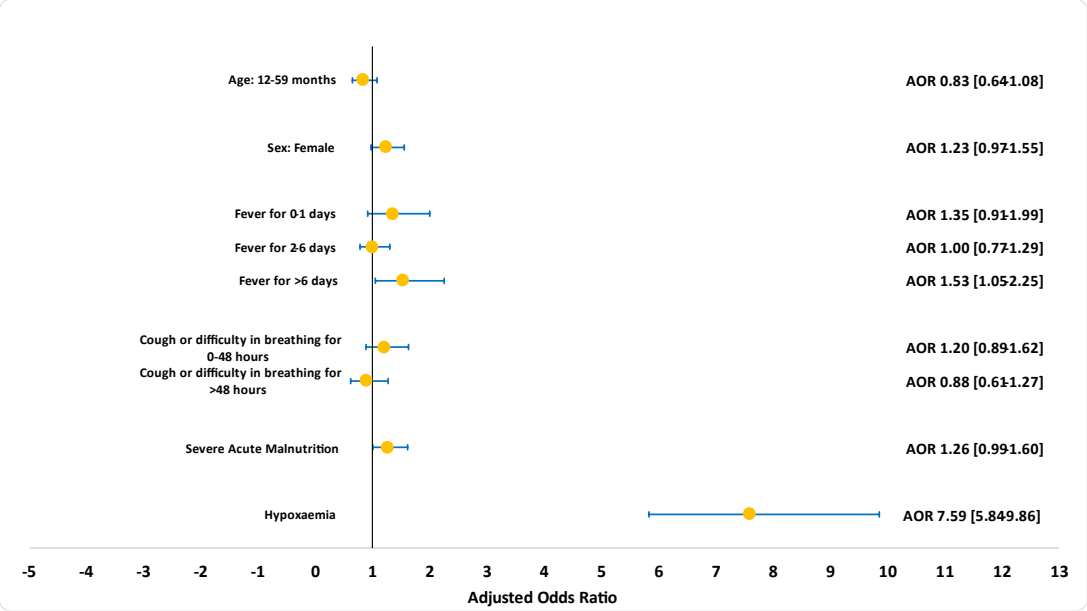
	Prevalence (%)	OR (95% CI)	AOR (95% CI)
Age			
2-11 months	41	Reference	Reference
12 months-59 months	38	0.88 (0.74,1.05)	0.85 (0.71,1.02)
Sex			
Male	37	Reference	Reference
Female	46	1.45 (1.23,1.7)	1.44 (1.22,1.71)
History of fever			
No fever	38	Reference	Reference
0-1 days	47	1.48 (1.12,1.96)	1.3 (0.97,1.75)
2-6 days	41	1.15 (0.97,1.37)	1.04 (0.87,1.25)
7 or more days	39	1.06 (0.81,1.4)	1.1 (0.82,1.46)
History of cough or difficulty in breathing			
No respiratory distress	37	Reference	Reference
0-48 hours	53	1.91 (1.53,2.38)	1.61 (1.28,2.02)
More than 48 hours	43	1.27 (1,1.62)	1.1 (0.86,1.42)
Severe Acute Malnutrition			
No	55	Reference	Reference
Yes	29	0.34 (0.29,0.39)	0.35 (0.3,0.41)
Total	**40**		

OR: Odds Ratio
AOR: Adjusted Odds Ratio
95% CI: 95% confidence interval

Among all children admitted with WHO-defined severe pneumonia, 79% were discharged with medical advice, 6% died during admission, 9% were referred to a higher-level facility due to clinical deterioration, and another 6% left the hospital against medical advice. Among the children with hypoxaemia, a higher proportion (13%) died during the hospital stay or referred to a higher-level facility (17%), in comparison to those who did not have hypoxaemia (dead 2%, referred 4%) (Supplementary figure 4.2). The overall case-fatality rate was 7.5% over the study period, which was significantly ($p<0.01$) higher among the children who had hypoxaemia on admission (17.1%), compared to those who did not (2.1%). Supplementary figure 4.3 present the trend in case-fatality rate by years.

Figure 4.3 presents the association between hypoxaemia status and adverse clinical outcomes (death or referrals to a higher-level facility due to deterioration in the patient's condition). Hypoxaemia is the strongest predictor of adverse clinical outcomes (AOR=7.59; 95% CI, 5.84 to 9.86). History of fever for more than 7 days (AOR=1.53; 95% CI, 1.05 to 2.25) was another significant predictor of adverse outcomes. Hypoxaemia was also the strongest predictor of mortality (AOR=11.08; 95% CI, 7.28 to 16.87) and referral (AOR=5.94; 95% CI, 4.31 to 8.17) independently. The details of the multivariable regression model are presented in supplementary table 4.1, 4.2, and 4.3.

Figure 4.3: Association of adverse clinical outcomes with hypoxaemia, other background characteristics and history of illness among children aged 2-59 months admitted to icddr,b Dhaka Hospital with WHO-defined severe pneumonia between 2014-17; presented in adjusted odds ratio with 95% confidence interval; N=2646.

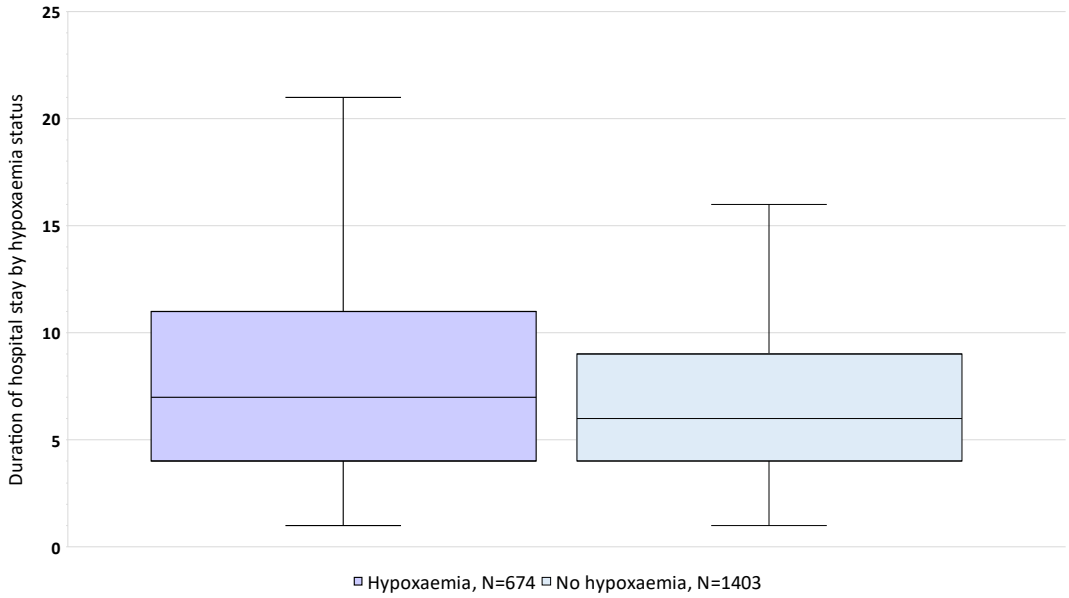


AOR: Adjusted Odds Ratio
95% CI: 95% Confidence Interval

Figure 4.4 presents the difference in median duration for hospital stay by hypoxaemia status on admission. The median duration was 7 (IQR, 4 to 11) days

among those who had hypoxaemia and 5 (IQR, 4 to 9) days among those who did not have hypoxaemia. The difference was significant at *P*<0.001.

Figure 4.4: Box plot of the duration of hospital stay by hypoxaemia status on admission among those who were alive at the end of hospital stay; presented in median days with interquartile range (N=2646)



4.5 DISCUSSION

We found that the prevalence of hypoxaemia among children hospitalised with severe pneumonia was 40% on admission. The odds of hypoxaemia were higher among females and those with a history of cough or difficulty in breathing. Hypoxaemia was the strongest predictor of death or referral to a higher-level facility among other covariates such as age, sex, history of fever and cough or difficulty in breathing and malnutrition. The median duration of hospital stay was significantly higher in the hypoxaemic group than in the non-hypoxaemic group.

Hypoxaemia is common among children with pneumonia and requires aggressive correction with oxygen therapy to prevent mortality and long-term consequences. Data to derive the local prevalence of hypoxaemia and its adverse consequences are

crucial for the health care providers to appreciate the importance of routine assessment of hypoxaemia and for policymakers to prioritise relevant interventions in programme planning. We report the most up-to-date estimate of the prevalence of hypoxaemia and its adverse clinical outcomes in Bangladesh.

The hypoxaemia prevalence (40%) reported in our study is somewhat similar to the systematic review conducted by Lozano et al. in 2001 but much higher than the one conducted by Subhi et al. in 2009 (5, 6). However, the 2009 review also reported wide variations between clinical severity classifications as the prevalence of hypoxaemia ranged from 9% to 39% among pneumonia cases in Asia. Moreover, the 2009-review followed the pre-2013 WHO-classification, including chest indrawing as a sign of severe pneumonia. Chest indrawing is a common sign of pneumonia but a relatively weak predictor of its clinical severity (24-26). On the contrary, we included only hospitalised children with severe pneumonia and followed the 2013 WHO-classification, which dropped chest indrawing as a sign of severe pneumonia (20). Moreover, the hypoxaemia prevalence reported in this paper is within the ranges of several other conducted in some South-Asian (17% to 57%) and African countries (18% to 57%) and published after 2009 (27-33).

The hypoxaemia prevalence reported in this paper is based on children admitted in icddr,b-Dhaka hospital, a non-government hospital located in Bangladesh's capital. We acknowledge that the results are not representative of all types (public and private) and levels (health centre, primary, secondary, and tertiary) of health facilities in Bangladesh. However, icddr,b mainly deals with primary cases of

pneumonia and serves as the primary point for contact for severe and relatively complicated cases to its catchment population due to its good reputation for pneumonia care in the catchment communities. It provides all services free of cost, and the majority of patients receiving care from icddr,b-Dhaka hospital is from a low-socioeconomic background. Hence, it is comparable to the district- and upazila- (sub-district level public hospitals where people with access to less financial resources predominately seek free-of-cost services. Another important consideration is the issue of selection bias. Although the icddr,b-Dhaka hospital is specialised for treating diarrhoea, all children meeting the criteria for hospitalisation based on the WHO-pneumonia-classifications were offered admission irrespective of their diarrhoea status and other comorbid conditions (20). All eligible children admitted to the special care ward were included in this analysis. Hence, we are confident that the prevalence estimate is not majorly influenced by selection bias. Lastly, the accuracy and reliability of hypoxaemia measurements are critical to the internal validity of the relevant estimates. In our study, SpO_2 assessment was included as a part of the routine assessment on admission, and trained nurses measured the SpO_2 status with handheld pulse oximetry with an appropriate paediatric probe. The clinical assessment and physical examination were conducted by trained doctors, which added additional value to the validity of relevant measurements. Moreover, our study was conducted immediately after completing the randomised control trial on bubble CPAP in icddr,b-Dhaka hospital (21). Therefore, the knowledge, skill, and behaviour of the clinical team responsible for the management of pneumonia were optimum, resulting in almost universal assessment and documentation of

hypoxaemia status among all children admitted with a history of cough or difficulty in breathing. It explains the unusually low level of data missingness regarding hypoxaemia status on admission in our study.

We found that hypoxaemia on admission was associated with a short history of cough or difficulty in breathing, as reported by the parents. The association was less strong with a relatively long history. The severity of complications on admission can explain this. Parents are more likely to seek care from a hospital with a short history of acute respiratory complaints if they perceive it as more severe or the condition deteriorates rapidly. Gender preference in care-seeking practices can explain the difference observed in hypoxaemia prevalence among boys and girls. A survey with a nationally representative sample in Bangladesh found that boys were more likely than girls to be taken to a health facility or provider (46% and 31%, respectively) for acute respiratory infections (12). Similarly, other studies based in hospital settings demonstrated a sex-based disparity in the severity of pneumonia and deaths among children admitted to hospitals in Bangladesh (34-37). Therefore, it is highly likely that the female children included in our analysis were brought to the hospital in a more critical stage than their male counterparts. We found that hypoxaemia on admission was strongly associated with the nutritional status. Although we found a negative association, another study conducted in similar settings did not find any significant associations between nutritional status and hypoxaemia (38).

We present the hypoxaemia prevalence disaggregated by 16 quarters between 2014 and 2017. Although we did not find any notable seasonal variation, the hypoxaemia

prevalence increased at an average annual rate of around 19% during this period. The introduction of PCV and Hib vaccine in the national immunisation programmes in several countries, including Bangladesh, resulted in a significant reduction in bacterial pneumonia, which has consequently made RSV and other viruses the common pathogens causing pneumonia among children (39-43). This change in the pneumonia aetiology may shift clinical features, including hypoxaemia, as approximately 20% of the hospitalised children with Respiratory Syncytial Virus-Acute Lower Respiratory Infections (RSV-ALRI) have hypoxaemia (44). This may explain the change in hypoxaemia prevalence that we observed during the study duration. Another potential explanation could be the pneumonia care-seeking practice in Bangladesh. According to the Bangladesh Demographic and Health surveys, care-seeking for parents reported acute respiratory infection from the medically trained provider had increased from 20% in 2004 to 40% in 2017, implying that the parents are more aware of pneumonia-related symptoms and complications (12). Hence, appropriate care-seeking practices from health facilities and formal health care providers may have contributed to better capturing the more complicated cases, including hypoxaemia, through hospital-based assessments.

There is significant debate regarding clinical prognostic factors, in addition to SpO_2 status, that can be used in routine care to assess the severity of pneumonia and mortality (7, 45). Our analysis also found that several background characteristics, clinical history, and other comorbid conditions such as severe acute malnutrition are associated with hypoxaemia status on admission. This finding is consistent with another Gambian study which reported a rapid respiratory rate, grunting, and

absence of a history of fever were the best independent predictors of hypoxaemia among children aged 2-33 months (46). Further studies are necessary to draw insight into the association between hypoxaemia and severe acute malnutrition. However, it is challenging to develop a predictive model based on these signs and symptoms, which can reliably and accurately identify hypoxaemia. A systematic review reported that several clinical signs alone or in combination have high sensitivity but very low specificity of predicting hypoxaemia, which substantially minimises its usability in clinical settings (47). There are also major issues regarding the validity and reliability of clinical assessment by health service providers (48-51). Regarding the recall of pneumonia-related clinical symptoms by caregivers, both the sensitivity and specificity were poor (52).

In our study, the case fatality rate of children hospitalised with severe pneumonia was around 7.5%. A large retrospective observational study in Malawi estimated the case fatality rate of 6.6% based on more than 100,000 hospitalised pneumonia cases from 40 hospitals (53). Another study conducted in a multi-speciality referral hospital in Chennai also reported a case fatality rate of around 8% among clinical pneumonia cases (54). Although the rates reported in these two studies are similar to the rate reported in our study, there is a potential difference in the case-mix. The Malawian study used the pre-2013 WHO-pneumonia classification, which included both severe and non-severe cases, whereas we used the 2013 WHO-pneumonia classification. The Malawian study also reported a higher case fatality rate (12%) among children with very severe pneumonia than that of our study. This may be because Malawi has a high burden of HIV. Moreover, after the successful bubble CPAP trial, icddr,b-Dhaka

hospital introduced routine assessment of hypoxaemia on admission and use of bubble CPAP for hypoxaemia management as the standard of care (21). The overall clinical knowledge and pneumonia management skills of icddr,b-Dhaka hospital staff also improved due to the rigorous implementation of the bubble CPAP trial and its follow up roll-out in routine practice. The high level of awareness and sensitivity regarding pneumonia and hypoxaemia management may have reduced severe pneumonia-related deaths in this clinical setting.

We report that hypoxaemia is a powerful predictor of adverse clinical outcomes defined as death during the hospital stay or clinical deterioration requiring referral to a higher-level facility independently or in combination. Other studies have also mentioned hypoxaemia as a strong predictor of mortality in children with WHO-defined pneumonia in lower and middle-income countries (55). However, the odds of adverse outcomes estimated in our study is relatively higher than the pooled estimate reported by a systematic review conducted by Lazzerini et al. in 2015 (56). Lazzerini et al. found that, among children with WHO-defined pneumonia, the odds of dying are 5-times higher among those who had hypoxaemia, while it was approximately eight times higher in our study. Variations in the enrolment criteria and severity classifications may explain the difference between these two estimates. Our analysis included only those children who were hospitalised with WHO-defined severe pneumonia, whereas Lazzerini et al. included all children with WHO-defined clinical pneumonia, which may also include non-severe pneumonia who required hospitalisation for other complications. Therefore, the hypoxaemia status among the more severe cases included in our study is expected to have a greater prognostic

value in predicting the adverse outcomes. Moreover, Lazzerini et al. conducted sensitivity analysis and reported confidence intervals (95% CI, 2.55 to 8.61) after adjusting for potential confounders, which marginally overlaps with the confidence interval (95% CI, 5.84 to 9.86) reported in our study after adjusting for potential confounders and covariates.

In addition to pneumonia, hypoxaemia is common among hospitalised children with several other complications like bronchiolitis, asthma, sepsis, malaria, meningitis, etc. (29, 57). Hence, hypoxaemia can be considered a stand-alone danger sign among young children irrespective of clinical classification, especially in low resource settings. The gold standard for measuring oxygen saturation in the blood is arterial blood gas (ABG) analysis. However, this is invasive, painful, time-consuming and resource intensive. Therefore, it is not helpful for point of care diagnostics and not feasible to integrate into primary care settings with a high volume of patients and limited resources. On the other hand, a pulse oximetry is a non-invasive device used as a point of care diagnostics to obtain a reasonably accurate measurement of blood's oxygen saturation. Appropriate use of pulse oximetry and reliable oxygen sources in developing countries can substantially reduce pneumonia-related mortality (9, 10, 55). Duke et al. reported that the introduction of an effective oxygen system could reduce 35% of severe pneumonia deaths, even in resource-poor settings. The locally made bubble CPAP reduced severe pneumonia mortality by 75% compared to the WHO standard low flow oxygen therapy (21).

The Pneumonia Series published by The Lancet in 2013 outlined the introduction of pulse oximetry as one of the four opportunities for further accelerating progress towards averting the global pneumonia burden in LMICs (58). Although WHO now recommends routine assessment of SpO_2 for rapid identification of hypoxaemia and immediate hospitalisation for oxygen therapy with other supportive care, there are significant gaps between policy and actual clinical practice due to insufficient provision for SpO_2 assessment and inadequate oxygen security in LMIC contexts (17, 59-62). Therefore, urgent attention should be given to improving access, provision, and quality of care regarding overall oxygen security (63, 64).

In this paper, we report the prevalence of hypoxaemia based on retrospective data extracted from individual patient records of routine hospital services. We acknowledge that the quality and oversight during routine clinical assessments are not comparable with controlled environments of clinical trials. However, the icddr,b-Dhaka hospital maintains a high clinical standard by adhering to the national and global guidelines. After the bubble CPAP trial, icddr,b Dhaka hospital introduced routine assessment of hypoxaemia on admission and the use of bubble CPAP for hypoxaemia management as the standard of care. The high level of sensitivity regarding pneumonia and hypoxaemia management may have contributed to the almost universal assessment of hypoxaemia and relevant documentation practices. We also acknowledge the limitation in the availability of detailed clinical information regarding study subjects since the data were obtained from routine clinical records. Therefore, the provision for adjusting for other comorbid conditions such as cyanosis, ability to feed, head nodding, respiratory rate >70/min and

unresponsiveness/impaired reusability, crepitations in lung auscultation, nasal flaring as potential confounders (65) and their interaction effects while exploring the effect of hypoxaemia on adverse clinical outcomes was somewhat limited.

The hypoxaemia prevalence reported in this paper is four years of data, which has helped to overcome the potential effect of seasonal variations. Furthermore, the analysis included a reasonably large sample size in reporting hypoxaemia prevalence with an acceptable error margin. We also adjusted for possible confounders in our analysis to give robust estimates of risk factors.

4.6 CONCLUSION

Hypoxaemia is common among children hospitalised with WHO-defined severe pneumonia in Bangladesh. It is also one of the strongest predictors of adverse clinical outcomes, among other background characteristics and history of illnesses. We reinforce the need for pulse oximetry availability and recommend ensuring an effective oxygen delivery system in low- and middle-income countries to avert these preventable deaths.

4.7 SUPPLEMENTARY MATERIALS

4.7.1 Supplementary tables

Supplementary table 4.1: Predictors of adverse outcomes as either death during hospital stay or referral to higher level facility for clinical deterioration among children admitted in icddr,b hospital with WHO-defined pneumonia, presented in odds ratio and adjusted odds ratio with 95% confidence interval

Background Characteristics	N	%	OR	P	LL	UL	AOR	P	LL	UL
Age										
2 - 11 months	308	16.3								
12 months - 59 months	102	13.6	0.80	0.08	0.63	1.03	0.83	0.16	0.64	1.08
Sex										
Male	238	13.9								
Female	172	18.3	1.39	0.00	1.12	1.72	1.23	0.08	0.97	1.55
H/O Fever										
No fever	155	14.1								
0-1 days	48	20.1	1.55	0.02	1.08	2.22	1.35	0.14	0.91	1.99
2-6 days	156	15	1.06	0.63	0.83	1.35	1.00	0.99	0.77	1.29
7 or more days	51	19.2	1.46	0.04	1.03	2.00	1.53	0.03	1.05	2.25
H/O Cough or difficulty breathing										
No respiratory distress	283	14.5								
0-48 hours	81	21.1	1.56	0.00	1.18	2.05	1.20	0.23	0.89	1.62
More than 48 hours	46	14.7	1.00	0.99	0.71	1.41	0.88	0.50	0.61	1.27
Severe Acute Malnutrition										
No	205	18.4								
Yes	205	13.4	0.72	0.00	0.58	0.89	1.26	0.06	0.99	1.60
Hypoxaemia										
No	91	5.7								
Yes	319	30.1	7.30	0.00	5.68	9.37	7.59	0.00	5.84	9.86
Total	410	15.5								

OR: Odd Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

Supplementary table 4.2: Predictors of death during hospital stay among children admitted in icddr,b hospital with WHO-defined pneumonia between 2014-17; presented in odds ratio and adjusted odds ratio with 95% confidence interval

Background Characteristics	N	%	OR	P	LL	UL	AOR	P	LL	UL
Age										
2 - 11 months	128	6.8								
12 months - 59 months	41	5.5	0.78	0.18	0.54	1.12	0.84	0.36	0.57	1.23
Sex										
Male	91	5.3								
Female	78	8.3	1.65	0.00	1.20	2.26	1.45	0.03	1.04	2.02
H/O Fever										
No fever	70	6.4								
0-1 days	19	7.9	1.36	0.26	0.80	2.31	1.28	0.39	0.73	2.25
2-6 days	57	5.5	0.86	0.41	0.60	1.23	0.84	0.36	0.57	1.23
7 or more days	23	8.6	1.46	0.14	0.89	2.40	1.50	0.13	0.89	2.56
H/O Cough or difficulty breathing										
No respiratory distress	124	6.4								
0-48 hours	21	5.5	0.92	0.73	0.57	1.49	0.74	0.25	0.45	1.23
More than 48 hours	24	7.7	1.19	0.45	0.76	1.89	1.05	0.84	0.65	1.71
Severe Acute Malnutrition										
No	75	6.7								
Yes	94	6.1	0.90	0.53	0.66	1.24	1.65	0.01	1.17	2.33
Hypoxaemia										
No	30	1.9								
Yes	139	13.1	9.64	0.00	6.43	14.46	11.08	0.00	7.28	16.87
Total	**169**	**6.4**								

OR: Odd Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

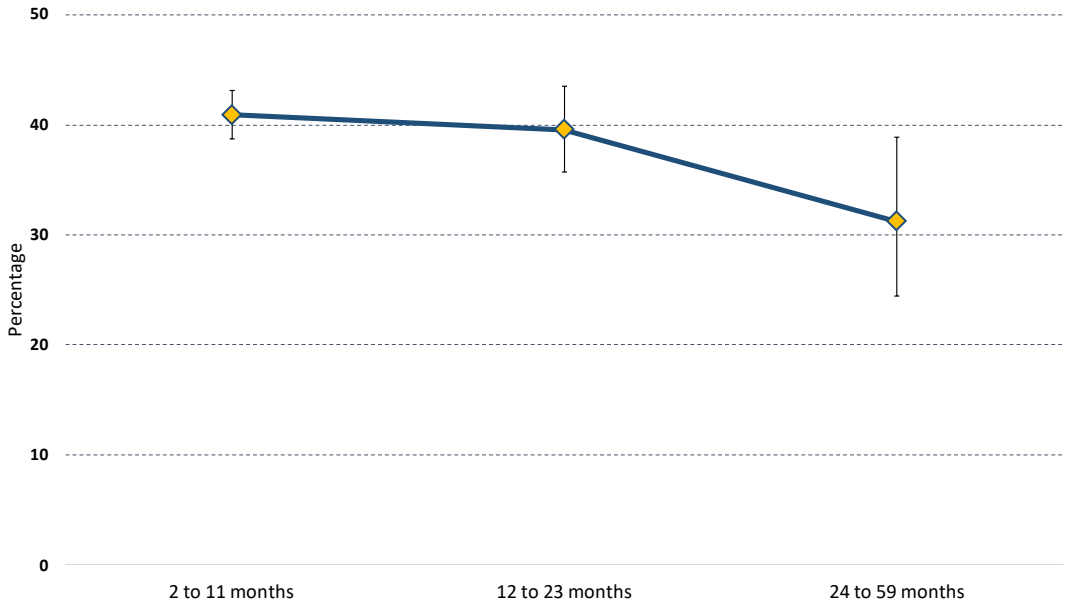
Supplementary table 4.3: Predictors of referral to higher level facility for clinical deterioration among children admitted in icddr,b hospital with WHO-defined pneumonia between 2014-17, presented in odds ratio and adjusted odds ratio with 95% confidence interval

Background Characteristics	N	%	OR	P	LL	UL	AOR	P	LL	UL
Age										
2 - 11 months	180	9.5								
12 months - 59 months	61	8.1	0.82	0.21	0.61	1.12	0.84	0.29	0.61	1.16
Sex										
Male	147	8.6								
Female	94	10	1.23	0.14	0.93	1.62	1.09	0.54	0.82	1.46
H/O Fever										
No fever	85	7.7								
0-1 days	29	12.1	1.71	0.02	1.09	2.68	1.36	0.21	0.85	2.19
2-6 days	99	9.5	1.23	0.19	0.91	1.67	1.13	0.45	0.82	1.56
7 or more days	28	10.5	1.46	0.10	0.93	2.30	1.56	0.07	0.97	2.52
H/O Cough or difficulty breathing										
No respiratory distress	159	8.2								
0-48 hours	60	15.6	2.05	0.00	1.48	2.83	1.54	0.01	1.09	2.18
More than 48 hours	22	7	0.85	0.51	0.54	1.36	0.75	0.24	0.46	1.21
Severe Acute Malnutrition										
No	130	11.6								
Yes	111	7.3	0.62	0.00	0.47	0.80	1.07	0.65	0.80	1.44
Hypoxaemia										
No	61	3.8								
Yes	180	17	6.14	0.00	4.53	8.33	5.94	0.00	4.31	8.17
Total	**241**	**9.1**								

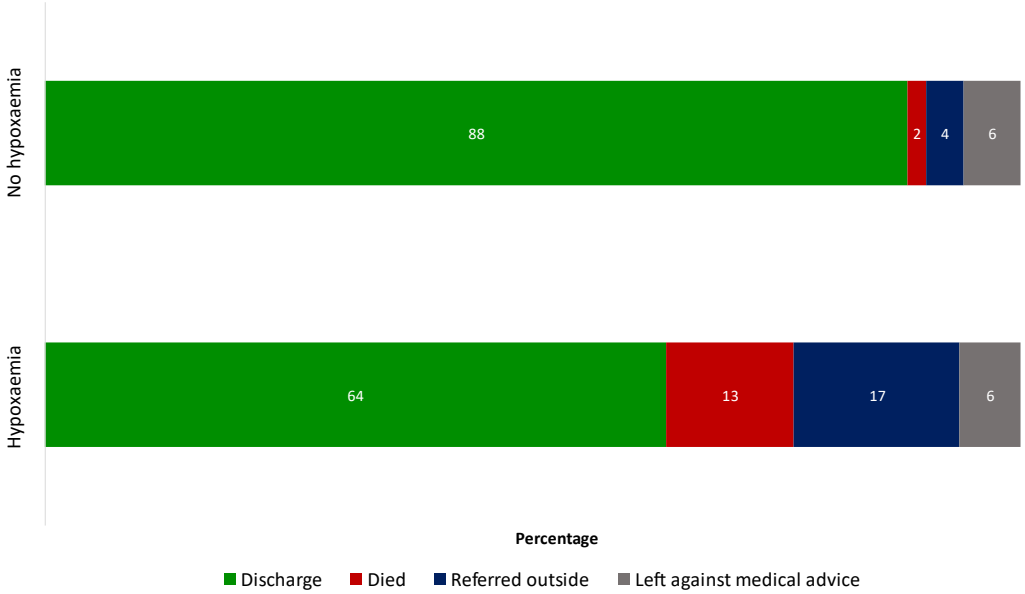
OR: Odd Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

4.7.2 Supplementary figures

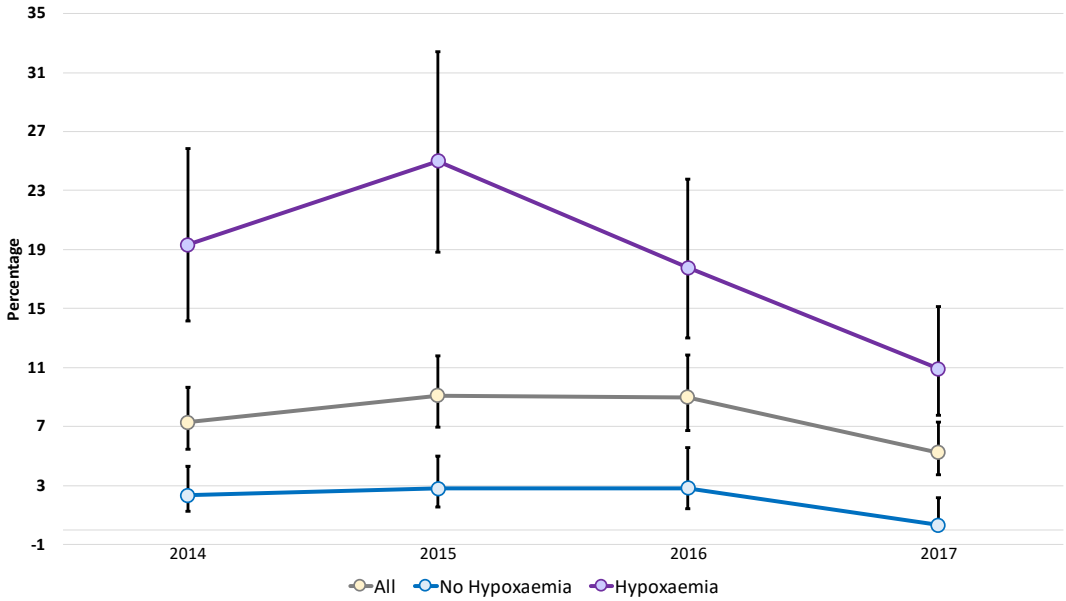
Supplementary figure 4.1: Hypoxaemia prevalence among children aged 2-59 months admitted to icddr,b Dhaka Hospital with WHO-defined pneumonia between 2014-17 by age groups; presented in %; N=2646.



Supplementary figure 4.2: Distribution of hospital outcomes of children aged 2-59 months admitted to icddr,b-Dhaka Hospital with WHO-defined clinical pneumonia between 2014-17; presented in percentage by hypoxaemia status on admission.



Supplementary figure 4.3: Trend in the case fatality rates of children aged 2-59 months admitted to icddr,b-Dhaka Hospital with WHO-defined clinical pneumonia between 2014-17 by hypoxaemia status on admission and disaggregated by the year; presented in %



Supplementary figure 4.4: Risk of adverse hospital outcomes among children aged 2-59 months admitted to icddr,b Dhaka Hospital with WHO-defined pneumonia with hypoxaemia between 2014-17; presented in adjusted odds ratio with 95% confidence internal; N=2646.

4.8 REFERENCE

1. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2016;388(10063):3027-35.
2. Lim Y-W, Steinhoff M, Girosi F, Holtzman D, Campbell H, Boer R, et al. Reducing the global burden of acute lower respiratory infections in children: the contribution of new diagnostics. Nature. 2006:9.
3. Oldenburg O, Wellmann B, Buchholz A, Bitter T, Fox H, Thiem U, et al. Nocturnal hypoxaemia is associated with increased mortality in stable heart failure patients. European heart journal. 2016;37(21):1695-703.
4. Wardlaw T, Johansson E, Hodge M. Pneumonia: The Forgotten Killer of Children. UNICEF's Division of Communication. New York: WHO Press; 2006.
5. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.
6. Lozano J. Epidemiology of hypoxaemia in children with acute lower respiratory infection [oxygen therapy in children]. Int J Tuberc Lung Dis. 2001;5(6):496-504.
7. Reed C, Madhi SA, Klugman KP, Kuwanda L, Ortiz JR, Finelli L, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One. 2012;7(1):e27793.
8. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9).
9. Enoch AJ, English M, Shepperd S. Does pulse oximeter use impact health outcomes? A systematic review. Archives of disease in childhood. 2016;101(8):694-700.
10. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.
11. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
12. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.
13. World Health Organization, UNICEF. End preventable deaths by 2025: The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). France; 2013.

14. United Nations. Sustainable Development Goals 2016 [30 March 2020]. Available from: http://www.un.org/sustainabledevelopment/.

15. Johns Hopkins Bloomberg School of Public Health. Pneumonia & Diarrhea Progress Report 2018. 2018.

16. World Health Organization, UNICEF. Integrated Management of Childhood Illness (Chart Booklet). Geneva: World Health Organization,; 2014.

17. World Health Organization. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care. 2012.

18. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2017. Dhaka, Bangladesh; 2019.

19. icddr b. icddr,b Annual Report 2019. 2020.

20. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

21. Chisti MJ, Salam MA, Smith JH, Ahmed T, Pietroni MA, Shahunja K, et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. The Lancet. 2015;386(9998):1057-65.

22. Stata. Stata 2021 [cited 2021 3 April 2020]. Available from: https://www.stata.com/.

23. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet: World Health Organization; 2014.

24. Addo-Yobo E, Anh DD, El-Sayed HF, Fox LM, Fox MP, MacLeod W, et al. Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the MASS study. Tropical Medicine & International Health. 2011;16(8):995-1006.

25. Atkinson M, Lakhanpaul M, Smyth A, Vyas H, Weston V, Sithole J, et al. A multicentre randomised controlled equivalence trial comparing oral amoxicillin and intravenous benzyl penicillin for community acquired pneumonia in children PIVOT Trial. Thorax. 2007;62 (12):1102–6.

26. Bari A, Sadruddin S, Khan A, Khan A, Lehri IA, Macleod WB, et al. Community case management of severe pneumonia with oral amoxicillin in children aged 2–59 months in Haripur district, Pakistan: a cluster randomised trial. The Lancet. 2011;378(9805):1796-803.

27. Orimadegun AE, Ogunbosi BO, Carson SS. Prevalence and predictors of hypoxaemia in respiratory and non-respiratory primary diagnoses among emergently ill children at a tertiary hospital in south western Nigeria. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2013;107(11):699-705.

28. Ibraheem R, Abdulkarim A. Hypoxaemia in hospitalized under-five Nigerian children with pneumonia. 2014.

29. Graham H, Bakare AA, Ayede AI, Oyewole OB, Gray A, Peel D, et al. Hypoxaemia in hospitalised children and neonates: a prospective cohort study in Nigerian secondary-level hospitals. EClinicalMedicine. 2019;16:51-63.

30. Bassat Q, Lanaspa M, Machevo S, O'Callaghan-Gordo C, Madrid L, Nhampossa T, et al. Hypoxaemia in Mozambican children <5 years of age admitted to hospital with clinical severe pneumonia: clinical features and performance of predictor models. Tropical Medicine & International Health. 2016;21(9):1147-56.

31. Tolla HS, Letebo M, Asemere YA, Belete AB, Tumbule TC, Feleke Z, et al. Use of pulse oximetry during initial assessments of children under-5 with pneumonia: a retrospective cross-sectional study from 14 hospitals in Ethiopia. J Glob Health Rep. 2019;3:e2019016.

32. Salah ET, Algasim SH, Mhamoud AS, Husian NEOSA. Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2015;19(4):203.

33. Wandeler G, Pauchard J, Zangger E, Diawara H, Gehri M. Which clinical signs predict hypoxaemia in young Senegalese children with acute lower respiratory tract disease? Paediatrics and international child health. 2015;35(1):65-8.

34. Mahmud I, Das S, Khan SH, Faruque A, Ahmed T. Gender disparity in care-seeking behaviours and treatment outcomes for dehydrating diarrhoea among under-5 children admitted to a diarrhoeal disease hospital in Bangladesh: an analysis of hospital-based surveillance data. BMJ open. 2020;10(9):e038730.

35. Naheed A, Breiman RF, Islam MS, Saha SK, Tabassum Naved R. Disparities by sex in care-seeking behaviors and treatment outcomes for pneumonia among children admitted to hospitals in Bangladesh. PloS one. 2019;14(3):e0213238.

36. Nair H, Simões EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JSF, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. The Lancet. 2013;381(9875):1380-90.

37. Nair H, Campbell H, Park J, Brondi L, Shi T, Olsson S, et al. Common childhood infections and gender inequalities: a systematic review. UNICEF Maternal, Newborn and Child Health Working Papers New York, NY. 2015.

38. Chisti MJ, Duke T, Robertson CF, Ahmed T, Faruque AS, Ashraf H, et al. Clinical predictors and outcome of hypoxaemia among under-five diarrhoeal children with or without pneumonia in an urban hospital, Dhaka, Bangladesh. Tropical Medicine and International Health. 2011;17(1):106-11.

39. Angoulvant F, Levy C, Grimprel E, Varon E, Lorrot M, Biscardi S, et al. Early impact of 13-valent pneumococcal conjugate vaccine on community-acquired pneumonia in children. Clinical Infectious Diseases. 2014;58(7):918-24.

40. Tregnaghi MW, Sáez-Llorens X, López P, Abate H, Smith E, Pósleman A, et al. Efficacy of pneumococcal nontypable Haemophilus influenzae protein D conjugate

vaccine (PHiD-CV) in young Latin American children: a double-blind randomized controlled trial. PLoS medicine. 2014;11(6):e1001657.

41. Simonsen L, Taylor RJ, Schuck-Paim C, Lustig R, Haber M, Klugman KP. Effect of 13-valent pneumococcal conjugate vaccine on admissions to hospital 2 years after its introduction in the USA: a time series analysis. The Lancet Respiratory Medicine. 2014;2(5):387-94.

42. Jain S, Williams DJ, Arnold SR, Ampofo K, Bramley AM, Reed C, et al. Community-acquired pneumonia requiring hospitalization among US children. New England Journal of Medicine. 2015;372(9):835-45.

43. Rhedin S, Lindstrand A, Hjelmgren A, Ryd-Rinder M, Öhrmalm L, Tolfvenstam T, et al. Respiratory viruses associated with community-acquired pneumonia in children: matched case–control study. Thorax. 2015;70(9):847-53.

44. Shi T, McAllister DA, O'Brien KL, Simoes EA, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. The Lancet. 2017;390(10098):946-58.

45. Jackson S, Mathews KH, Pulanić D, Falconer R, Rudan I, Campbell H, et al. Risk factors for severe acute lower respiratory infections in children–a systematic review and meta-analysis. Croatian medical journal. 2013;54(2):110-21.

46. Usen S, Weber M, Mulholland K, Jaffar S, Oparaugo A, Omosigho C, et al. Clinical predictors of hypoxaemia in Gambian children with acute lower respiratory tract infection: prospective cohort study. Bmj. 1999;318(7176):86-91.

47. Ayieko P, Graham S. In children aged 2-59 months with pneumonia, which clinical signs best predict hypoxaemia? J Trop Pediatr 2006;52(5):307-10.

48. Ahmed HM, Mitchell M, Hedt B. National implementation of Integrated Management of Childhood Illness (IMCI): policy constraints and strategies. Health policy. 2010;96(2):128-33.

49. Walter ND, Lyimo T, Skarbinski J, Metta E, Kahigwa E, Flannery B, et al. Why first-level health workers fail to follow guidelines for managing severe disease in children in the Coast Region, the United Republic of Tanzania. Bulletin of the World Health Organization. 2009;87(2):99-107.

50. Arifeen S, Bryce J, Gouws E, Baqui A, Black R, Hoque D, et al. Quality of care for under-fives in first-level health facilities in one district of Bangladesh. Bulletin of the World Health Organization. 2005;83:260-7.

51. Lange S, Mwisongo A, Mæstad O. Why don't clinicians adhere more consistently to guidelines for the Integrated Management of Childhood Illness (IMCI)? Social Science & Medicine. 2014;104:56-63.

52. Hazir T, Begum K, El Arifeen S, Khan AM, Huque MH, Kazmi N, et al. Measuring coverage in MNCH: a prospective validation study in Pakistan and Bangladesh on measuring correct treatment of childhood pneumonia. PLoS medicine. 2013;10(5):e1001422.

53. Lazzerini M, Seward N, Lufesi N, Banda R, Sinyeka S, Masache G, et al. Mortality and its risk factors in Malawian children admitted to hospital with clinical

pneumonia, 2001–12: a retrospective observational study. The Lancet Global health. 2016;4(1):e57-e68.

54. Ramachandran P, Nedunchelian K, Vengatesan A, Suresh S. Risk factors for mortality in community-acquired pneumonia among children aged 1–59 months admitted in a referral hospital. Indian pediatrics. 2012;49(11):889-95.

55. Duke T, Mgone J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea [oxygen therapy in children]. Int J Tuberc Lung Dis. 2001;5(6):511-9.

56. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.

57. Rahman AE, Iqbal A, Hoque DE, Moinuddin M, Zaman SB, Rahman QS-u, et al. Managing neonatal and early childhood syndromic sepsis in sub-district hospitals in resource poor settings: improvement in quality of care through introduction of a package of interventions in rural Bangladesh. PloS one. 2017;12(1):e0170267.

58. Chopra M, Mason E, Borrazzo J, Campbell H, Rudan I, Liu L, et al. Ending of preventable deaths from pneumonia and diarrhoea: an achievable goal. The Lancet. 2013;381(9876):1499-506.

59. Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker JN. Reviewing the WHO guidelines for antibiotic use for sepsis in neonates and children. Paediatrics and international child health. 2018;38(sup1):S3-S15.

60. Arifeen S, Bryce J, Gouws E, Baqui A, Black R, Hoque D, et al. Quality of care for under-fives in first-level health facilities in one district of Bangladesh. Bulletin of the World Health Organization. 2005;83(4):260-7.

61. Anwar I, Kalim N, Koblinsky M. Quality of obstetric care in public-sector facilities and constraints to implementing emergency obstetric care services: evidence from high-and low-performing districts of Bangladesh. Journal of health, population, and nutrition. 2009;27(2):139.

62. Chowdhury S, Hossain SA, Halim A. Assessment of quality of care in maternal and newborn health services available in public health care facilities in Bangladesh. Bangladesh Medical Research Council Bulletin. 2009;35(2):53-6.

63. Duke T, Graham S, Cherian M, Ginsburg A, English M, Howie S, et al. Oxygen is an essential medicine: a call for international action [Unresolved issues]. Int J Tuberc Lung Dis. 2010;14(11):1362-8.

64. Bhutta ZA, Das JK, Walker N, Rizvi A, Campbell H, Rudan I, et al. Interventions to address deaths from childhood pneumonia and diarrhoea equitably: what works and at what cost? The Lancet. 2013;381(9875):1417-29.

65. Zhang L, Mendoza-Sassi R, Santos J, Lau J. Accuracy of symptoms and signs in predicting hypoxaemia among young children with acute respiratory infection: a meta-analysis. Int J Tuberc Lung Dis. 2011;15(3):317-25.

Chapter 5: CONTEXT OF CHILDHOOD PNEUMONIA-RELATED DEATHS IN BANGLADESH

One of my general objectives was to understand the context of managing children with pneumonia, including hypoxaemia in Bangladesh. The specific research question 3 was to assess the context of childhood pneumonia deaths in Bangladesh.

Table 5.1 General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

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Title: Child mortality in Bangladesh-why, when, where and how? a national survey-based analysis

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URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8442576/pdf/jogh-11-04052.pdf

5.1 ABSTRACT

5.1.1 Background

Updated information on the cause of childhood mortality is essential for developing policies and designing programmes targeting the major burden of disease. There is a paucity of evidence regarding the current estimates of the cause of death in Bangladesh, which is essential for reinvigorating the current policies and reshaping existing strategies to avert preventable deaths. This paper aims to address this critical evidence gap and report the cause, timing and place of death among children under-5 years of age using a nationally representative sample.

5.1.2 Methods

The present study was undertaken to provide updated estimates of causes of death among children under-5 years of age using data from the 2017-18 round of the Bangladesh Demographic and Health Survey (BDHS). The verbal autopsy (VA) questionnaire of the 2017-18 BDHS was adapted from the standardised WHO 2016 instruments. Specially trained physicians reviewed the responses of the VA questionnaire and assigned the cause of death based on the online-2016-version of the International Classification of Diseases (ICD-10). We included 456 deaths among children under-5 years of age in our analysis. Descriptive statistics were used to present the causes, timing and places of death with confidence interval (CI).

5.1.3 Results

Pneumonia is the major killer (19%), accounting for approximately 24,268 (UR, 21,626 to 26,695) under-5 deaths per-year. It is followed by birth asphyxia (16%),

prematurity and low-birth-weight (11%), serious infections including sepsis (8%) causing 20,882 (UR, 18,608 to 22,970), 14,956 (UR, 13,327 to 16,452), and 10,723 (UR, 9,555 to 11,795) deaths per-year, respectively. Drowning (8%) caused 10,441 (UR, 9,304 to 11,485) deaths and congenital anomaly (7%) resulted in 8,748 (UR, 7,795 to 9,623) deaths per-year. Around 29% of all deaths occurred on the first day, 52% within the first week, and 66% within the first month of life. Around 70% of birth asphyxia, prematurity, and low birth weight-related deaths happen on the day of birth. Approximately 43% of pneumonia-related deaths occur in age 1-11 months, and around 51% of drowning related deaths happen in age 12-23 months.

5.1.4 Conclusion

Pneumonia with other serious infections, birth asphyxia, prematurity and low-birth-weight are responsible for more than half of all deaths among children under-5 years of age. Strengthening the existing maternal, neonatal and child health programmes may be helpful in averting the majority of these preventable deaths. A multisectoral approach is required for the prevention of childhood deaths, especially drowning-related fatalities. Special measures need to be taken to prevent and control emerging public health challenges like birth defects and congenital anomalies.

5.2 BACKGROUND

The rapid decline in childhood mortality observed in Bangladesh during the first two decades since the 1990s came to an apparent stalling in the 2010s (1, 2). Today, far too many of these children die due to preventable causes. According to the Bangladesh Demographic and Health Survey, the neonatal mortality rate was 28 per 1,000 live births in 2014 and 30 per 1,000 live births in 2017 (1, 2). Similarly, the under-5 mortality rate was 46 per 1,000 live births in 2014 and 45 per 1,000 live births in 2017 (1, 2). The Government of Bangladesh (GoB) needs to critically review the existing policies, strategies and programmes to identify possible gaps related to newborn and child health and identify strategies to avert preventable deaths.

Prioritising interventions targeting the major causes of death can provide fresh impetus for accelerating the reduction in mortality rates. In high-income settings, the civil registration system is the most common and valid source of data as it systematically documents vital statistics related to deaths and their causes (3). Unfortunately, there are substantial gaps in coverage and quality of birth and death reporting in low- and middle-income settings (3). In Bangladesh, the coverage of birth registration is around 54%, and death registration is approximately 13% (4) (5). Moreover, about 70% of deaths take place outside health facilities with minimum to no information regarding the cause of death (6). Out of the facility deaths, very few have medical certification of the cause of death, as the programme is in its early roll-out phase (6). The Bangladesh Bureau of Statistics runs surveillance with a nationally representative sample to track key demographic indicators. However, information regarding the cause of death is not systematically collected by adopting a globally

accepted standard (7). icddr,b, an international health research organisation based in Bangladesh, manages several demographic surveillance sites throughout Bangladesh and collects information on the cause of death using the WHO recommended verbal autopsy tools (8). Although these demographic surveillance sites offer a rich source of data on the cause of death patterns and trends over time, the estimates are not nationally representative. In this regard, the last national estimate was based on the verbal autopsy conducted among under-5 deaths in the 2011 round of the Bangladesh Demographic and Health Survey (BDHS) (9). Although another round of BDHS was conducted in 2014, it did not include the verbal autopsy component. Therefore, there is a paucity of evidence regarding the current national estimates of the cause of death, which is essential for reinvigorating the current policies and reshaping existing strategies to avert child deaths.

This paper aims to address this critical evidence gap and report the timing, place, and cause of death among children under-5 years of age with a nationally representative sample.

5.3 METHODS

5.3.1 Study design

We analysed publicly available data from the 2017-18 round of BDHS. BDHS uses a nationally representative sample, and the 2017-18 round collected information on the cause of death through verbal autopsy. The verbal autopsy tool was adapted from the standardised and validated WHO 2016 and 2011 BDHS verbal autopsy instruments (2). The tool was adapted to Bangladesh's context based on expert

review and translated to Bangla, the most commonly spoken language in Bangladesh. The 2017-18 tool had a separate questionnaire for neonatal deaths (age 0-28 days) and child deaths (age 29 days to 59 months). The questionnaires included both open-ended and close-ended questions and were pretested in two rural clusters in Manikgonj district and two urban clusters in Dhaka before finalisation. A national advisory committee constituted by verbal autopsy experts supervised the country adaptation, translation and pretesting processes for finalisation.

Mitra and Associate collected the data under the leadership of NIPORT (2). The verbal autopsy data collection team had trained interviewers and field editors. The data collection team, the supervisors and the quality controllers received one-week training from icddr,b on the VA questionnaire before data collection. During the survey, four review meetings were organised to discuss the quality of data collection and address specific problems faced by interviewers. The VA data collection team conducted in-person interviews with the next of kin or the primary caregivers of all children under-5 years of age who died within five years of the survey in the surveyed areas. All interviews were successfully completed except one where the respondent refused to participate.

icddr,b was responsible for assigning the cause of death through physician review. Three physicians, with a degree of Bachelor in Medicine and Surgery (MBBS), were recruited by icddr,b and received a training for four consecutive weeks on the verbal autopsy instruments and cause of death assignment based on the online-2016-version of the International Classification of Diseases (ICD-10) (10). The physicians

were trained by master trainers who were previously involved with 2011 BDHS, 2013 Bangladesh Urban Health Survey and 2016 Bangladesh Maternal Mortality Survey.

Each questionnaire was independently reviewed by two physicians and each physician assigned a cause of death (direct, underlying and contributory). When the two physicians agreed on the underlying cause, it was considered the final cause of death. In case of disagreement, an additional review was conducted by a third physician. If the underlying causes were agreed upon by any two of three physicians, it was considered the final cause of death. The cause of death was recorded as "undetermined" if no agreement was reached after the third physician review. In a few cases, where two physicians had assigned identical sets of causes of deaths but disagreed on whether these were immediate or underlying causes, a discussion was arranged to reconcile the differences in the presence of a trained verbal autopsy expert. The review process is summarised in supplementary figure 5.1.

5.3.2 Analysis plan

We used Stata version 14 for data analysis (11). We used descriptive statistics to report the cause, timing and place of death. We grouped similar ICD-10 codes and presented the cause of death in 16 broad categories. Supplementary table 5.1 shows the ICD-10 codes that were grouped under each broad category of cause of death. We reported the proportional distribution of the cause of death among all under-5 deaths, neonates (0-28 days) and post-neonatal children (29 days-59 months). We used the under-5 mortality rates and the cause-specific mortality fractions to estimate the cause-specific mortality rates. The uncertainty range (UR) was

calculated using the confidence intervals obtained for the reported mortality rate among children under-5 years of age in 2017-18 BDHS. The cause-specific mortality rates were also disaggregated by sex, birth order, father and mother's education, residence (rural-urban), and wealth (lowest and highest quintile). The sample size was not enough to check for statistically significant difference in the cause specific mortality rates by disaggregating variables. Hence, we considered a difference 'substantial' if the difference was ≥25% (relative) by disaggregating variables. We also projected the number of deaths for each of the broad categories using the adjusted population size in 2015 (12), crude birth rate from the 2015 Sample Vital Registration System report (13) and the cause-specific mortality rates reported in our paper. The detailed calculations are presented in supplementary table 5.2.

The overall timing of death was presented by age in months. Also, we showed the timing of death in days for neonatal (0-28 days) mortality. Place of death was categorised as home, facility (public or private) and during transportation. We also presented the timing of death and place of death disaggregated by the cause of death. The time variable has been further disaggregated to present the cause of death by the following categories: Day 0, Day 1-6, Day 7-28, 1-11 months, 12-23 months, 24-35 months, 36-47 months and 48-59 months.

All analysis presented in this paper were weighted for the overall sampling frame of 2017-18 BDHS.

5.3.3 Ethical considerations

This study used secondary dataset collected by National Institute of Population Research and Training (NIPORT), Bangladesh, and Monitoring and Evaluation to Assess and Use Results Demographic and Health Surveys (MEASURE DHS). We got approval from the DHS program for utilising the applicable datasets for this study.

5.4 RESULTS

We included all 456 deaths among children under-5 years of age in our analysis.

Figure 5.1 presents the percent distribution of the cause of death among all children under-5 years of age. Pneumonia is the major killer (9% during the neonatal and 10% during the post-neonatal periods), followed by birth asphyxia (16% exclusively during the neonatal period), prematurity and low-birth-weight (11% during the neonatal and one during the post-neonatal periods), serious infections including sepsis (8% during the neonatal period and 1% during the post-neonatal period), drowning (8% exclusively during the post-neonatal period), congenital anomaly (4% during the neonatal and 3% during the post-neonatal periods) and birth injuries (4% during the neonatal period). Although less than 1% of deaths were directly attributable to malnutrition, it was associated with 13% of all under-5 deaths (not presented in the figure).

Figure 5.1: Distribution of cause of death among children under-5 years of age; presented in percent distribution; N=456

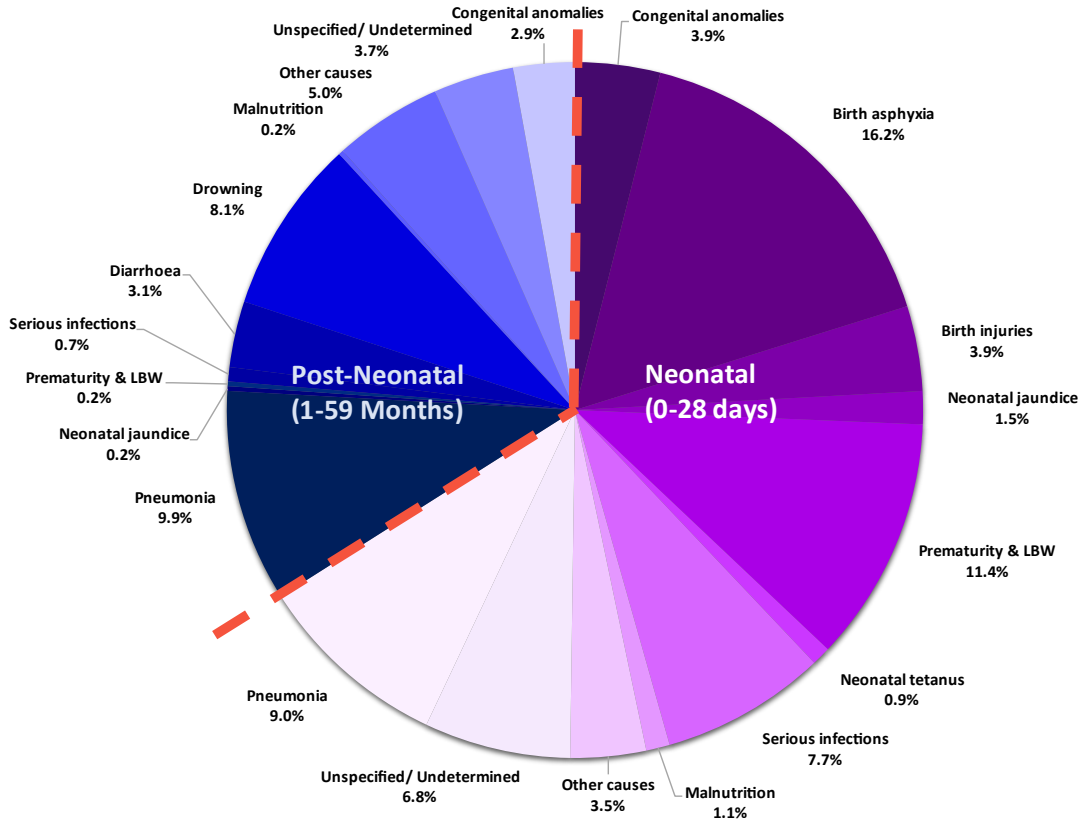


Figure 5.2 presents the cause-specific mortality rates by background characteristics. The cause-specific mortality rate was 8.5 per 1,000 live births for pneumonia (95% CI, 7.6 to 9.3), 7.3 per 1,000 live births for birth asphyxia (95% CI, 6.5 to 8.0), 5.5 per 1,000 live births for prematurity and low-birth-weight (95% CI, 4.7 to 5.8), 3.8 per 1,000 live births for serious infections (95% CI, 3.3 to 4.1), 3.7 per 1,000 live births for drowning (95% CI, 3.3 to 4.0), 3.1 per 1,000 live births for the congenital anomaly (95% CI, 2.7 to 3.4), 1.8 per 1,000 live births for birth injuries (95% CI, 1.6 to 2.0) and 1.4 per 1,000 live births for diarrhoea (95% CI, 1.2 to 1.5). We did not observe any substantial difference by gender across the mortality rates for different causes, except serious infection, where it was higher among female children. While the

cause-specific mortality rates for birth asphyxia, congenital anomaly and birth injury were higher among the first-born children, we observed lower rates (in the same group) for pneumonia, drowning and diarrhoea. For most of the categories, the cause-specific mortality rates were higher among both mothers and fathers who did not have any formal education than those with ten or more years of schooling. The cause-specific mortality rates for pneumonia, birth asphyxia, prematurity and low birth weight, congenital anomaly and birth injury were higher in urban areas. However, the cause-specific mortality for serious infection was higher in rural areas. We did not observe any notable difference in the cause-specific mortality rates for drowning and diarrhoea based on the deceased children's residence status. The cause-specific mortality rates for pneumonia, birth asphyxia, prematurity and low birth weight, serious infection, drowning, and diarrhoea were higher among the poorest than the richest. On the contrary, the cause-specific mortality rate for the congenital anomaly was higher among the richest than the poorest. Supplementary table 5.3 presents more disaggregated estimates of cause specific mortality rates. Supplementary figure 5.2 compares the major causes of death between 2011 BDHS and 2017-18 BDHS by cause-specific mortality rates.

Figure 5.2: Cause specific mortality by background characteristics; presented in deaths per 1,000 live births

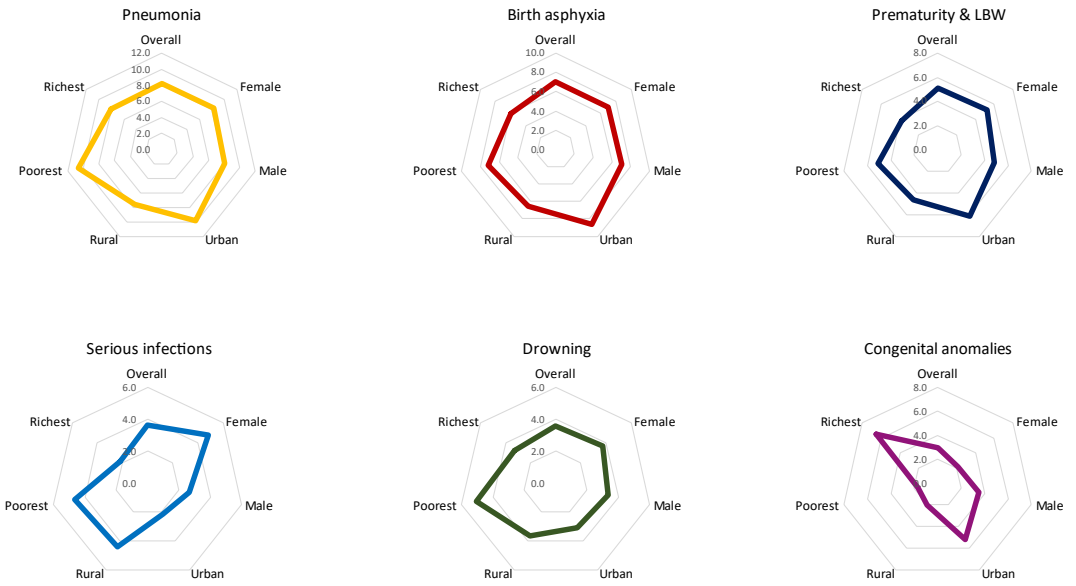


Figure 5.3 summarises the estimated number of deaths among children under-5 years of age in 2015 by causes. Pneumonia caused an estimated 24,268 (UR, 21,626 to 26,695) deaths, and birth asphyxia caused approximately 20,882 (UR, 18,608 to 22,970) deaths. Approximately 15,000 (UR, 18,608 to 22,970) children died of prematurity and low-birth-weight. Serious infections including sepsis caused 10,723 deaths (UR, 9,555 to 11,795) and drowning were responsible for about 10,441 (UR, 9,304 to 11,445) deaths. Birth defects and congenital anomalies were responsible for around 8,748 (UR, 7,795 to 9,623) deaths. Around 5,079 (UR, 4,526 to 5,587) deaths were attributable to birth injuries and close to 3,951 (UR, 3,520 to 4,436) deaths were due to diarrhoea.

Figure 5.3: Estimated number of under-5 deaths in 2015 by the causes of deaths; presented in 1,000 deaths

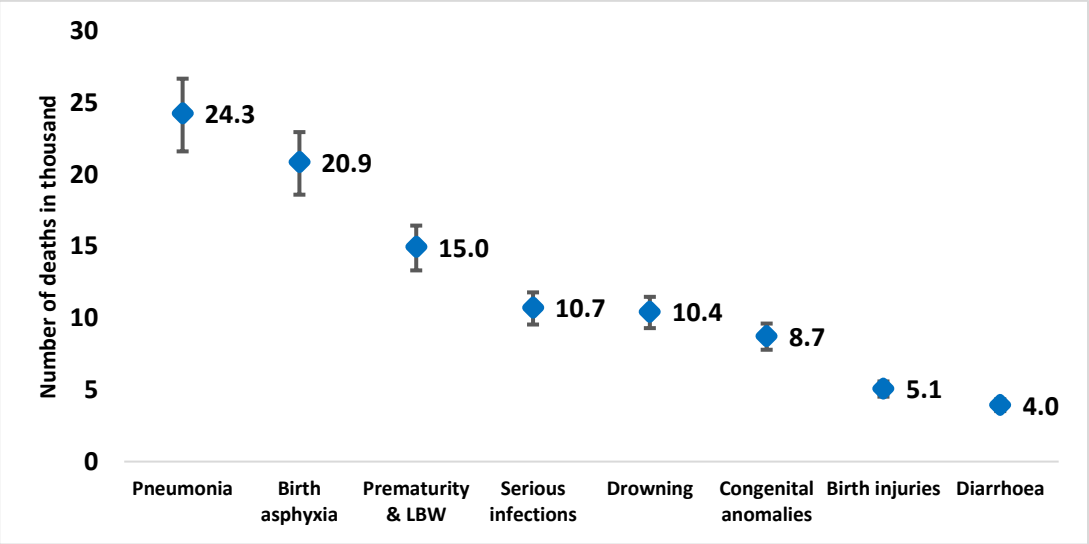


Figure 5.4 shows the timing of death where the primary vertical axis presents the number of deaths, and the secondary vertical axis presents the cumulative percentage. Around 29% of all deaths occurred on the day of birth, 52% died within the first week, 66% in the first month and 85% within the first year.

Figure 5.4: Timing of under-5 deaths; presented in numbers and cumulative %; N=456

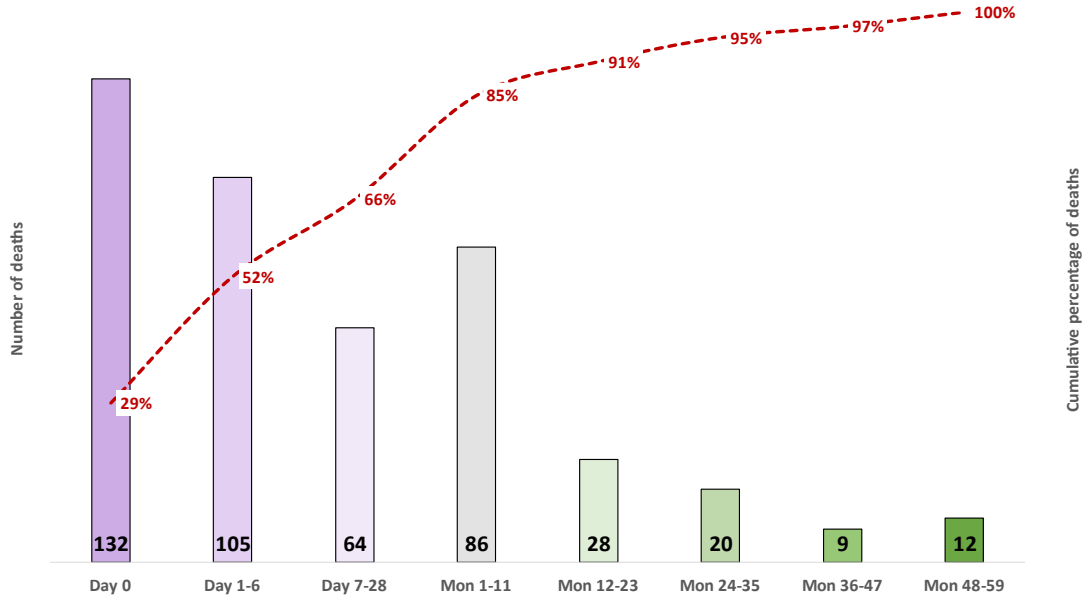


Figure 5.5 presents the percent distribution of the timing of under-5 deaths by causes. Close to half of the pneumonia-related deaths happened in the first month of life, and 43% between month 1 and month 11. Less than 10% of the pneumonia-related deaths occurred after the infancy period (0-11 months). Among those who died due to birth asphyxia, approximately 70% died on the day of birth, 26% died between day 1 and 6, and the rest died within the first one month. Similarly, 72% of all prematurity and low birth weight-related deaths occurred on the day of birth, and another 13% died between day 1 and day 6. The risk of serious infection-related death was the highest between day 7 and day 28 (39%), followed by day 1 and day 6 (34%) and the day of birth (18%). On the contrary, all deaths due to drowning occurred after the infancy period, particularly between months 12 and 23 (51%). Another 24% of drowning-related deaths happened between month 24 and month 35.

Figure 5.5: Timing of under-5 deaths by the causes of deaths; presented in percent distribution

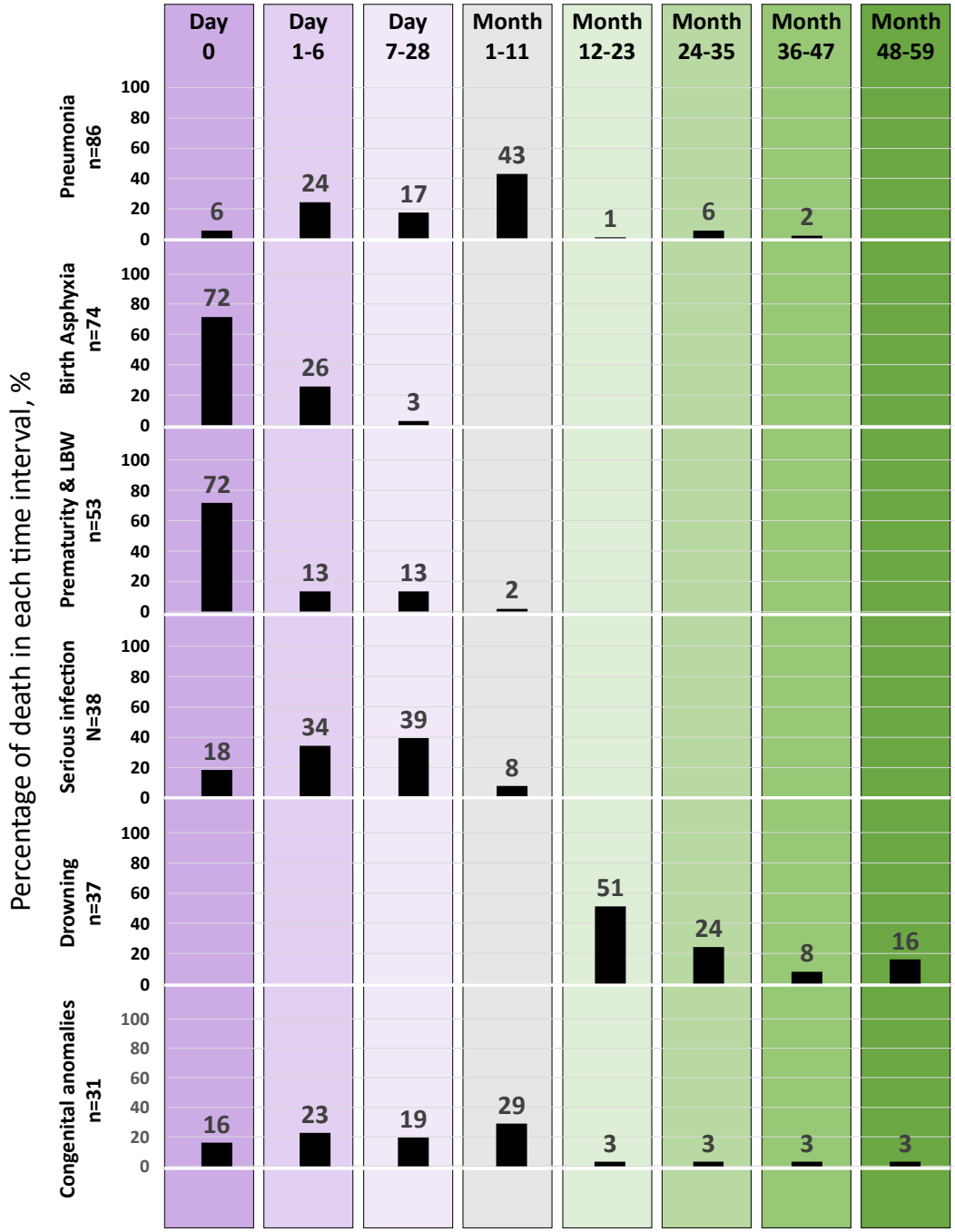


Figure 5.6 presents the percent distribution of place of death by causes. Out of all deaths among children under-5 years of age, 53% occurred at home, 39% at hospitals or health facilities and 8% during transit. Among the pneumonia deaths, 48% happened at home, 44% at hospitals and 8% during transit. 58% of deaths due to

birth asphyxia and 72% of the deaths due to birth injuries occurred at hospitals. On the contrary, 69% of the deaths due to serious infections and 76% of the deaths due to drowning took place at home. Among the deaths attributable to diarrhoea, 36% happened during transit.

Figure 5.6: Place of under-5 deaths by the causes of deaths; presented in percent distribution; N=456

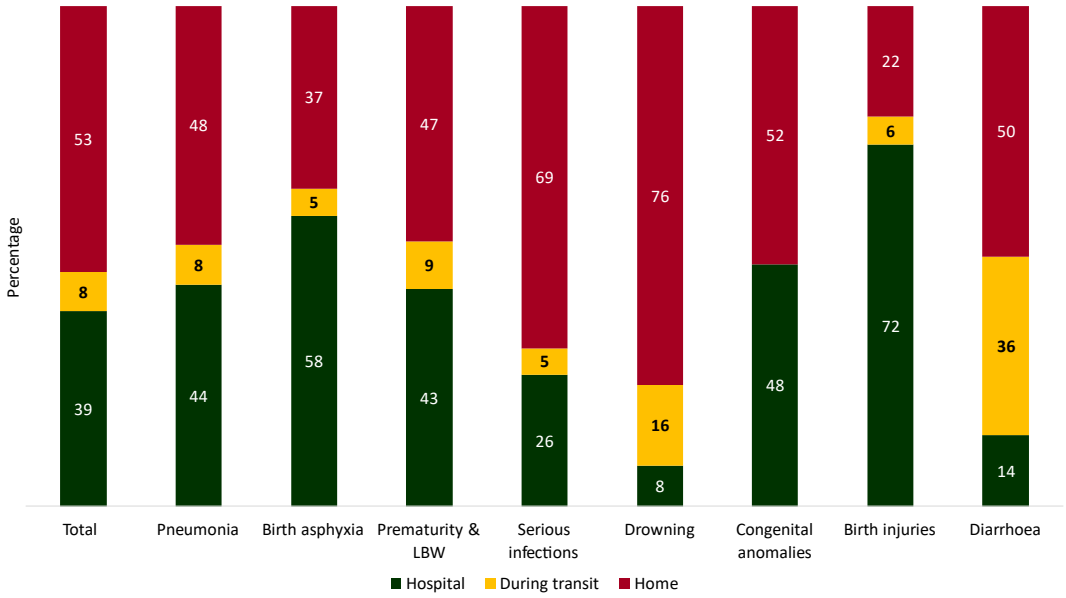
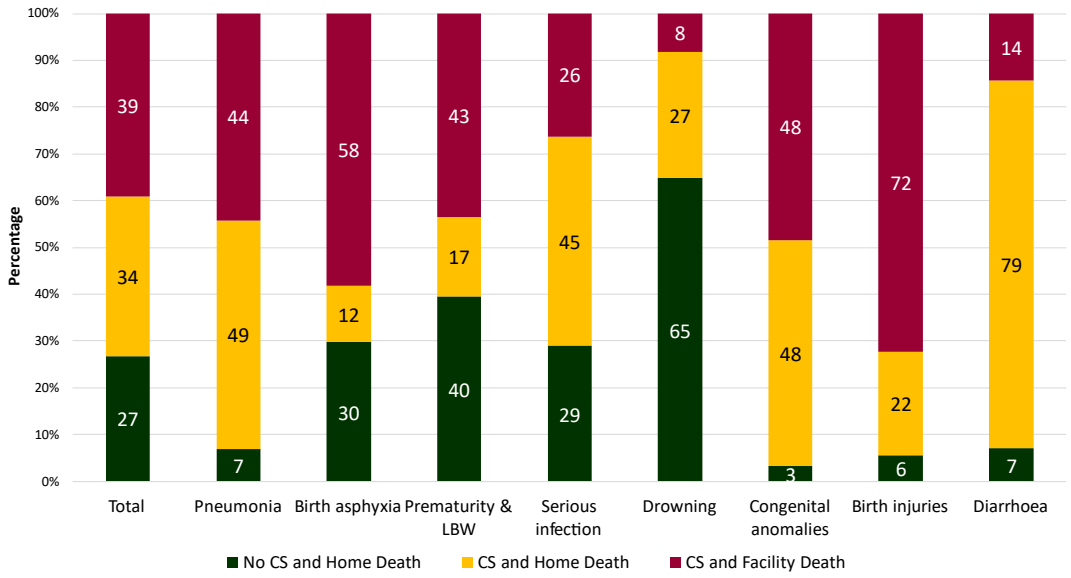


Figure 5.7 summarises the care-seeking practice before death among children under-5 years of age. Among the pneumonia deaths, 7% did not seek care, and another 49% died at home after seeking care. Regarding deaths due to prematurity and low birth weight, 40% did not seek care, and 17% died at home after seeking care. Similarly, 7% of the deaths due to diarrhoea did not seek care at all, and another 79% died at home after seeking care from outside the home.

Figure 5.7: Care seeking practice of under-5 deaths by the causes of deaths; presented in percent distribution by causes; N=456



Among the deaths due to pneumonia, around 20% of the parents had doubts about whether medical care was required, 45% received injectable antibiotics, 11% reported problems with hospital admission/medical treatment/getting medication/medical tests and 50% reported that the total cost of care prohibited other household payments.

Among the deaths due to birth asphyxia, around half had facility birth, and 70% had vaginal births. Similarly, 62% of the birth injury-related deaths had facility births, and 85% had vaginal births. Regarding deaths attributable to prematurity and low birth weight, 77% had facility births, and 81% had vaginal births.

Among the deaths due to serious infections, 34% were born premature (as reported by the parents), 13% of the parents had doubts whether medical care was required, 21% received injectable antibiotics, 13% reported problems with hospital

admission/medical treatment/getting medication/medical tests and 37% reported that the total cost of care prohibited other household payments.

Regarding deaths due to diarrhoea, 43% of the parents had doubts whether medical care was required and 14% did not receive any oral rehydration saline.

5.5 DISCUSSION

Bangladesh has made remarkable progress in health and development since the 1990s (14). However, the recent phase of apparent stalling in reducing neonatal and child morality essentially exposes the disconnect between the fast-changing landscape of child health and the gaps in prioritisation and programme planning (2, 15). This calls for reshaping the existing policies, redirecting the current strategic focus based on updated evidence, and targeting the most pressing health needs. This paper addresses a key evidence gap related to the cause and context of child mortality in Bangladesh. This can aid in reinvigorating the programmes and make course corrective measures to achieving the ambitious Sustainable Development Goal (SDG) targets of reducing neonatal mortality rate to ≤12 per 1,000 live births and under-5 mortality rate to ≤25 per 1,000 live births and by 2030 (16).

We found that the cause-specific mortality rate due to pneumonia was 8.5 per 1,000 live birth in 2017-18, making it the largest killer among children under-5 years of age in Bangladesh. The current rate is much higher than the global average of 6.6 per 1,000 live births in 2015. It is also higher than the average rate of 7.4 per 1,000 live births among developing countries and other neighbouring countries like India and Nepal (17). Although the cause-specific mortality rate decreased by 27% between

2011 and 2017-18 in Bangladesh, pneumonia still causes approximately 24,000 deaths per year (9). The majority of these deaths can be prevented by adopting the WHO recommended *prevent, protect and treat strategy* and by scaling up low-cost interventions (18). However, there are substantial gaps in the coverage and quality of priority interventions outlined in WHO's *prevent, protect and treat strategy (19, 20)*. In 2020, the median GAPPD pneumonia score was 81 % in Bangladesh against the global target of 90% (21). GAPPD scores are calculated as the average of 7 relevant indicators, which are as follows: pneumonia specific indicators such as exclusive breastfeeding, MCV1 coverage, DTP3 coverage, Hib3 coverage, PCV3 coverage, appropriate care seeking, antibiotic treatment. Although the coverage of key vaccines was reasonably high (98% for Hib3 and 97% for PCV), only 65% of children received exclusive breastfeeding (2). Among children with a suspected episode of pneumonia, only 46% were taken to an appropriate health care provider, and 65% received antibiotics (2, 21). Our analysis found that the awareness of parents, care-seeking practice, and antibiotic coverage were even lower among the deceased children. The WHO recommended IMCI is one of the key strategies adopted by the Government of Bangladesh for managing pneumonia (22). The success of IMCI services will greatly influence Bangladesh's progress towards achieving the GAPPD target of preventing all avoidable pneumonia-related deaths by 2025 (18). Although ensuring the service availability and readiness of health facilities is critical to managing pneumonia through IMCI services effectively, there are substantial gaps, particularly in rural facilities (23). Unfortunately, two-thirds of the designated facilities in Bangladesh do not have an ARI timer or watch with second

timing (24). Approximately half of the facilities do not have an appropriate weighing scale which is essential for prescribing proper dosages of medicines (including antibiotics for pneumonia management) (24, 25). There are substantial gaps regarding the availability of antibiotics such as amoxicillin, which is essential for managing pneumonia (24, 25). Hypoxaemia is common among children with pneumonia and is one of the strongest predictors of mortality due to pneumonia (26-28). Less than one-tenth of the facilities in Bangladesh have pulse oximeters (24). The availability of pulse oximeters was not optimal even in referral hospitals as less than one-third of the district hospitals and one-fifth of the sub-district hospitals have readiness in this regard (24). Moreover, one-third of the district hospitals and one-fourth of the sub-district hospitals do not have a reliable oxygen source which is essential for managing severe pneumonia with hypoxaemia (24, 29). Unfortunately, these critical gaps in readiness related to pneumonia management did not change between 2014 and 2017, as reported by two national surveys (24, 30). This can also explain the apparent stalling in the overall child mortality rate, which was observed in the corresponding period (1, 2). In addition to ensuring the adequate readiness of equipment, drugs, and logistics essential for managing pneumonia, strategic investment should be made to ensure universal assessment of hypoxaemia with pulse oximetry and supportive care with oxygen therapy (31, 32).

In our review, the cause-specific mortality rate due to birth asphyxia was 7.3 per 1,000 live birth, making it the second-largest killer among children under-5 years of age and the major contributor among all neonatal deaths. Around three-fourths of them died on the day of birth, emphasising the importance of delivering the

intervention within a short window of opportunity. Prevention and management of birth asphyxia requires specialised skills and services, which are more conducive to be arranged and ensured among facility births. A systematic review reported facility birth as one of the strongest interventions to avert birth asphyxia related deaths (33). Although facility births have been increasing substantially and consistently in Bangladesh since 2000, we did not observe any notable difference in the cause-specific mortality rate due to birth asphyxia since 2010 (9). We found that more than half of the deaths due to birth asphyxia had a facility birth. The apparent gaps in facility readiness and quality of obstetric care prevailing in public and private health facilities in Bangladesh can potentially explain these contradictory trends. The latest national survey conducted in 2017 reported that less than 5% of the facilities offering normal delivery services in Bangladesh met the WHO recommended minimum readiness criteria. The condition remained unchanged from the 2014 estimate (24, 30). Other studies have reported major gaps in the provision and experience of care related to childbirth in both public and private health facilities in Bangladesh (34-36). Moreover, around two-thirds of the facilities offering normal delivery services did not have a suction apparatus, and approximately half of the facilities did not have a bag-mask in the delivery corner, only one-third of providers received in-service training on newborn resuscitation which is essential for the management of birth asphyxia (24, 37). It is also important to note that around half of the babies who died due to birth asphyxia had a home birth. Since more than one-third of the total births happen at home, primarily with untrained birth attendants, particular strategies should be taken to promote facility birth with optimum quality of care.

Complications related to prematurity and low birth weight cause approximately 15,000 lives per year in Bangladesh, making them the third most significant contributor of deaths among children under-5 years of age and the second major contributor among all neonatal deaths. Kangaroo Mother Care (KMC) is an evidence-based, cost-effective and high-impact intervention that can significantly reduce the risk of death due to prematurity and low birth weight (38). The Government of Bangladesh adopted the WHO-recommended KMC services as the primary approach for averting prematurity-related deaths through the Promise Renewed Declaration in 2013 (39, 40). However, there are substantial gaps between the policy and practice. According to the national guideline, any stable newborn with a birth weight of less than 2000g should receive KMC. Each year an estimated 573,000 babies are born prematurely, and 192,000 babies have low birth weight (less than 2000 gram) in Bangladesh (41). Only 193 facilities offer KMC services in Bangladesh, which reveals the prominent gap in care provision. In 2020, approximately 5700 babies received KMC services from these facilities, implying that the coverage was extremely poor at below 5% (42). This is consistent with our findings, where none of the deceased children included in our analysis reported having received KMC. Also, the average duration of stay in KMC facilities was around three days, against the minimum recommendation of 10-14 days (42, 43). It highlights the substantial gap in quality, which deters achieving effective coverage with this life-saving intervention. We also found that around three-fourths of the deaths due to prematurity and low birth weight occurs on the date of birth. Since the rate of facility birth is increasing rapidly in Bangladesh, identifying prematurity and low birth weight at birth and

introducing KMC immediately after birth can be a low hanging fruit to increase the coverage (2, 44) efficiently. These gaps in provision, coverage and quality of KMC services are not unique to Bangladesh, as the majority of the low-and middle-income countries practicing KMC face similar barriers and challenges (44). In addition to health systems bottlenecks, there are issues related to community awareness, acceptability, access and other demand-side barriers. The operational plan for the current health sector programme does not have any specific initiatives addressing these demand-side barriers (45). It is important to adopt a multipronged approach including health systems strengthening, monitoring and mentoring as well as strong community engagement and participation to achieve high and effective coverage of KMC and avert preventable deaths.

Antenatal corticosteroids, given to women in preterm labour, is a safe, effective and low-cost intervention that can significantly reduce the deaths due to prematurity, primarily reducing the risk of respiratory distress syndrome. A Cochrane review and meta-analysis found that antenatal corticosteroid can reduce death by 31% and incidence of respiratory distress syndrome by 34% (46). Another meta-analysis found that antenatal corticosteroids can have a more significant impact in low-resource settings without the provision of advanced intensive care (47). The Government of Bangladesh decided to incorporate the use of antenatal corticosteroid in the national programme in 2013 (39). However, the programme implementation plan did not identify specific actions and allocate resources for the capacity development of healthcare workers and ensuring the availability of essential logistics (22, 45). Hence, this promising intervention could not significantly impact prematurity-related

mortality due to the extremely low coverage. Such gaps in the overall policy prioritisation, programme planning, implementation can explain the apparent increase in prematurity and low birth weight specific mortality rates that was observed between 2011 and 2017-18 (2, 9).

We report that the cause-specific mortality rate due to serious infections (primarily sepsis) was 3.8 per 1,000 live births, making it the fourth-largest killer among children under-5 years of age. Around 90% of these deaths happened during the neonatal period emphasising the importance of focusing on this age group with appropriate programme planning and targeted interventions. The cause-specific mortality rate reduced by almost two-thirds between 2011 and 2017-18. The primary reason for this decline could be the pervasive use of broad-spectrum antibiotics, especially by informal care providers in rural settings who are widely available, accessible, and affordable (48-53). The national neonatal health programme also changed its policy and programme approach to improve accessibility and increase treatment coverage. Until 2015, the WHO recommended inpatient hospital care for managing possible severe bacterial infections with multi-drug multi-dose injectable antibiotics for 7-10 days (54). Based on the evidence from the SATT and AFRINEST studies, WHO changed its guideline in 2015 and recommended treating the clinically less severe possible bacterial severe infections through outpatient care with simplified antibiotic regimens where referral is not feasible (55) (56-58). The Government of Bangladesh adopted the WHO recommendation, changed the existing guidelines and took initiatives to scale up sepsis management nationally with the simplified antibiotic regimens (59). This could

also explain the decline in serious infection-related mortality in Bangladesh. Besides these achievements, there are programme implementation gaps in ensuring the availability of essential drugs and logistics, adhering to the clinical management guidelines by health care providers, completing the antibiotic course by the caregivers and quality of care received at the referral hospitals (59). We also found that almost all of those who died due to serious infections received antibiotics and around one-third were born prematurely. It indicates that these cases were more complicated and required more specialised and advanced care at referral hospitals (29). There are substantial gaps in the quality of inpatient care, including diagnostics, antibiotics and supportive care, in primary and secondary level referral hospitals in Bangladesh (60, 61). Unfortunately, the current national neonatal and child health programme does not have any specific activity for strengthening and monitoring the provision and quality of inpatient care in referral facilities. Without strategic focus and substantial investment in inpatient care, it will be difficult to further reduce the serious infections specific mortality in Bangladesh.

Drowning is among the top five causes of death in Bangladesh. Around half of these deaths happen in the third year of life, making it the largest killer among children after passing their first year of life. Although the cause-specific mortality has declined slightly between 2011 and 2017-18, the national child health programme does not have any specific activity for promoting awareness and prevention in this regard (9, 22). The lack of adequate childcare while parents are working may be among the main reasons for these deaths. A large scale intervention trial conducted in seven rural sub-districts in Bangladesh found that creches are effective for preventing

childhood drowning as the incidence rate declined 87 per 100,000 population per year at baseline to 43 per 1,000 population per year in the post-implementation period (62). Although the evidence is encouraging, it will require substantial investments and a multisectoral approach to adopt, introduce, and scale up this intervention, primarily in the districts with high drowning-related mortality burden. In addition, other interventions focusing on education and information, blocking access to water bodies by employing barriers and regulations, provision of supervision, and acquisition of survival skills can be contextualised and tested to add impetus to the drowning prevention efforts (63).

Complications related to birth defects and congenital anomalies are responsible for around 6% of all deaths under-5 years of age in Bangladesh, making it an emerging public health concern (2). Although several referral hospitals have recently started birth defects screening and surveillance, most of these facilities are situated in urban areas, mainly clustered in bigger cities. The programme coverage and clinical support to managing the complications of birth defects and congenital anomalies are sub-optimum and require strategic focus with significant investments. Moreover, reducing the mortality burden of birth defects and congenital anomalies will substantially depend on the prevention strategy and effective delivery of interventions adopting a life course approach (64). Bangladesh needs to develop and implement an integrated plan for the prevention and control of common birth defects involving public health programmes like maternal, newborn and child health, nutrition, immunisation, and other stakeholders.

Lastly, around 40% of all deaths under-5 years of age in Bangladesh happen in health facilities, in contrast to only 15% among adults. This has important implications for the public health programmes as it indicates the changing dynamic of care-seeking from formal health care providers and health facilities for fatal childhood illnesses. Proper investments should be made in improving the provision and quality of emergency and inpatient care for averting preventable deaths. Simultaneously, it is also important to note that more than half of the deaths still happen at home, and some after seeking care from formal health care providers. The context and challenges faced by the parents of these children can be very different from those who effectively sought care. It is important to understand the context and investigate the care-seeking challenges these communities face for developing a people-centred, participatory and responsive health system.

The major causes of death presented in this paper have been analysed using the most recently published nationally representative Bangladesh Health and demographic Survey 2017-18 (2). This survey includes samples from all administrative divisions of Bangladesh and has appropriate representation from urban and rural areas and across different population's socio-demographic characteristics. Therefore, our results can be generalised to the overall population of Bangladesh. The data were collected using the validated WHO Standard Verbal Autopsy Tool, which was adapted to the country context before finalisation. The physicians received a month-long training on assigning the causes of death based on the ICD codes. The authors of this paper were heavily involved in the training of the data collectors and physicians. They were also an integral part of the data quality

monitoring team, which adds to the quality and authenticity of the data used in this analysis.

Although the survey used a nationally representative sample, the sample size was not enough for providing disaggregated estimates by different background characteristics with an acceptable level of precision. We acknowledge the limitation of the sample size in reporting the difference in cause-specific mortality rates by disaggregating variables with appropriate statistical significance. We also acknowledge the issues with recall error and, recall bias as the past information was collected from a close family member of the deceased person. Moreover, the tools had questions regarding clinical details, which could be intimidating and inappropriate for the respondents to recall and report accurately. We also acknowledge that the cause of deaths was assigned by physicians, which may have issues with misclassification bias due to the variations in subjective interpretations. However, the physicians were extensively trained and documented detailed justification for assigning the cause of deaths based on a structured checklist. These measures have contributed in minimising the misclassification bias. Lastly, we used data from the most recent national survey (2017-18), but the anchoring year was 2015.

5.6 CONCLUSION

Accurate and reliable Information on the cause of childhood mortality is essential for developing policies and designing programmes targeting the major burden of disease. Around half of all deaths among children under-5 years of age happen in the neonatal period, emphasising the importance of prioritising neonatal health

interventions and initiatives. Pneumonia with other serious infections, birth asphyxia and prematurity, and low birth weight are responsible for more than half of all deaths of children under-5 years of age. Strengthening of existing maternal, neonatal and child health programmes may be helpful in averting the majority of these preventable deaths. We recommend special measures to prevent and control emerging public health challenges like birth defects and congenital anomalies.

5.7 SUPPLEMENTARY MATERIALS

5.7.1 Supplementary tables

Supplementary table 5.1: Summery matrix of ICD-10 codes used to present the causes of deaths in categories

Broad Category	ICD-10 Code
1. Neonatal tetanus	A33
2. Congenital abnormality	Q00.0, Q02, Q03, Q03.9, Q24.9, Q42.3, Q43.9, Q74.9, Q75.9, Q76.9, Q79.5, Q89.9
3. Drowning	W70, W73
4. Birth asphyxia	P20.9, P21.9, P22.9, P24.0, P24.3, P24.9
5. Birth injury	P12.9, P13.1, P13.9, P15.9
6. Measles	
7. Diarrhoea	A05.9, A09.0
8. Pneumonia	J17.1, J18.9,
9. Meningitis	
10. Neonatal jaundice	P59.9, R17
11. Pre-term birth	P07.1, P07.3
12. Possible serious infection	A41.9, P36.9, P90
13. Malnutrition	E46,
14. Other causes	C26.0, C95.9, D56.9, D77, F89, G40.9, I51.9, K13.7, K76.9, N13.3, N17.9, N20.9, O75.9, P00.9, P01.2, P02.7, P51, P51.9, P70.2, P76.9, P91.7, R10.0, R50.9, R56, R56.0, R56.8, T63.0, W19, W87, Y09, Y65.2
15. Unspecified	P96.9, R99
16. Undetermined	Undetermined

Supplementary table 5.2: Projected number of deaths for each of the broad categories using the adjusted population size in 2015.

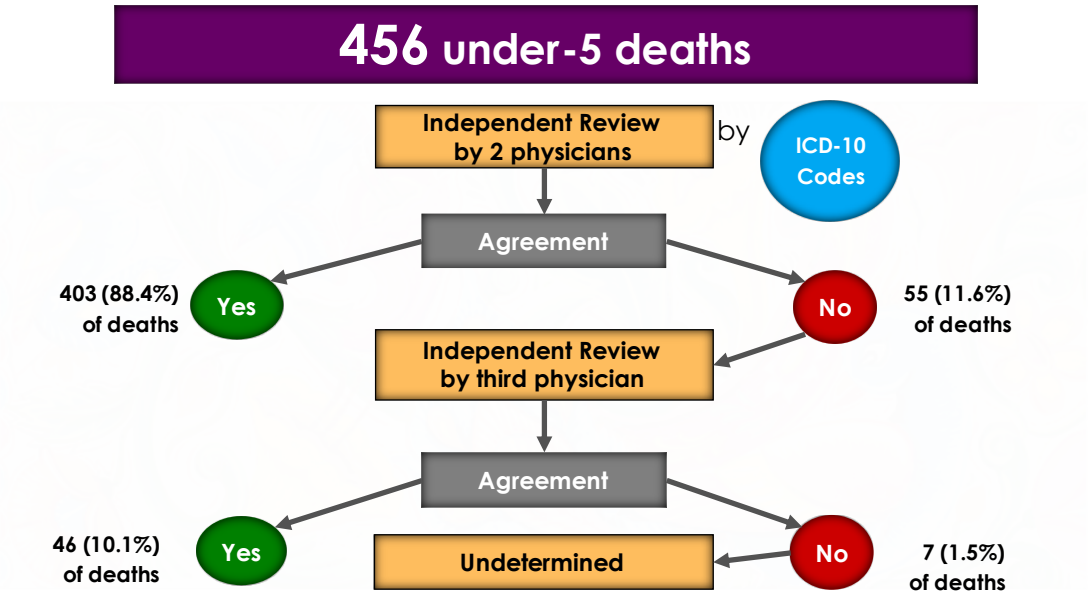
Population 2011 from census 2011	144043697			
Growth rate from census 2011	1.37%			
CBR 2015 from SVRS 2015	18.8			
Projected population 2015	152100991.6			
Projected live birth in 2015	2859499			
Percent distributions for top eight causes				
Under-5 mortality	45			
Lower interval: Under-5 mortality	40.1			
Upper interval: Under-5 mortality	49.5			
Number of under-5 death	128677			
Lower limit: Number of under-5 death	114666			
Upper limit: Number of under-5 death	141545			
Percent distributions for top eight causes	**Percent**	**Number of deaths**	**Lower limit**	**Upper limit**
Pneumonia	18.9	24268	21626	26695
Birth asphyxia	16.2	20882	18608	22970
Prematurity & LBW	11.6	14956	13327	16452
Serious infections	8.4	10723	9555	11795
Drowning	8.1	10441	9304	11485
Congenital anomalies	6.8	8748	7795	9623
Birth injuries	3.9	5079	4526	5587
Diarrhoea	3.1	3951	3520	4346

Supplementary table 5.3: Cause specific mortality rates of the major causes of deaths by background characteristics; presented in number of deaths per 1,000 live births

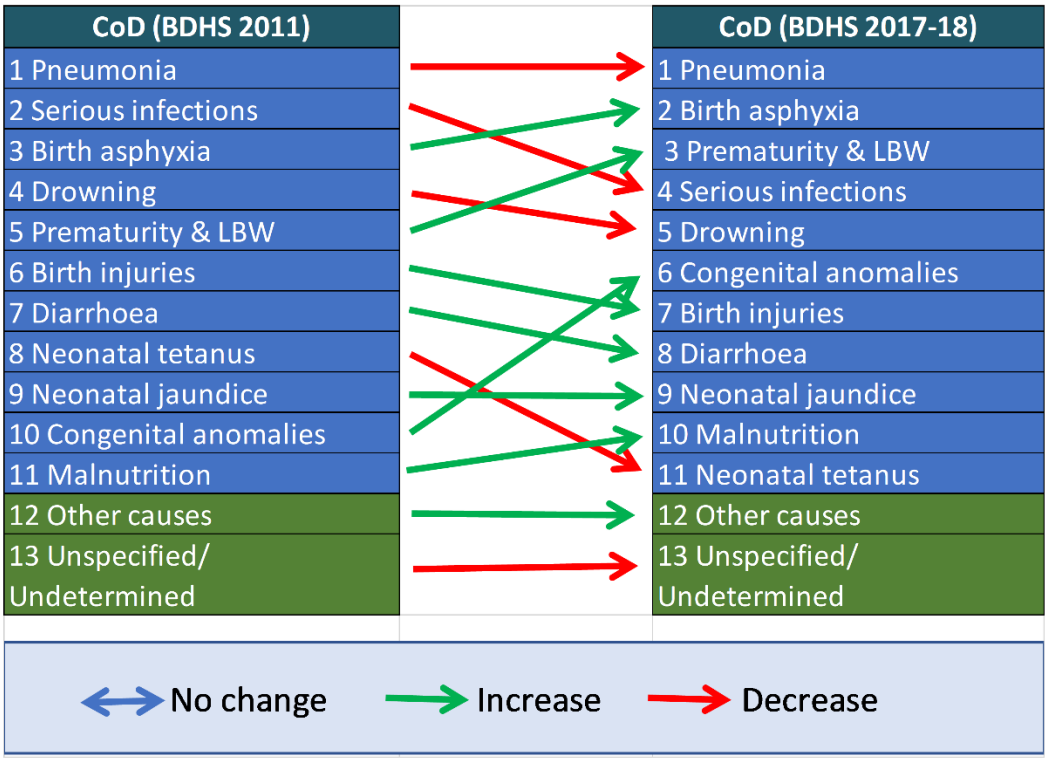
		Pneumonia	Birth asphyxia	Prematurity & LBW	Serious infections	Drowning	Congenital anomalies	Birth injuries	Diarrhoea
Sex	**Female**	8.3	7.0	5.2	4.8	3.7	2.2	1.7	1.7
	Male	8.0	7.0	4.8	2.7	3.3	3.5	1.7	1.0
Birth Order	**1**	8.1	9.6	5.6	4.0	2.0	4.5	3.5	0.5
	2 or more	11.1	7.4	6.4	4.5	5.8	2.7	0.8	2.5
Mother Education	**No education**	12.4	5.5	9.7	4.1	8.3	0.0	0.0	4.1
	Primary Incomplete	9.9	8.9	6.9	6.9	2.5	2.0	2.5	3.0
	Primary Complete	11.7	4.2	5.0	4.2	2.5	5.0	2.5	1.7
	Secondary Incomplete	7.5	7.8	4.6	2.5	4.1	3.7	0.9	0.7
	Secondary Complete or More	5.0	6.5	3.0	2.5	2.0	2.5	3.0	0.0
Father Education	**No education**	8.9	7.7	4.7	7.1	3.5	2.4	1.2	3.5
	Primary Incomplete	10.3	4.0	6.2	4.5	3.6	2.2	1.8	1.3
	Primary Complete	8.1	7.5	3.4	4.7	4.7	3.4	1.4	0.7
	Secondary Incomplete	7.1	7.9	6.6	2.1	3.7	3.3	2.9	1.2
	Secondary Complete or More	6.4	8.6	3.9	1.7	2.1	3.9	1.3	0.4
Residence	**Urban**	9.8	8.6	6.1	2.1	3.1	5.2	3.1	1.2
	Rural	7.6	6.5	4.7	4.4	3.7	2.0	1.1	1.4
Wealth	**Lowest**	10.6	7.2	5.1	4.7	5.1	1.7	1.3	3.4
	Second	6.1	7.1	6.6	4.7	2.8	1.4	0.9	0.9
	Middle	8.1	6.7	3.8	3.8	2.9	4.3	2.9	0.0
	Fourth	8.3	8.8	6.2	2.6	3.1	1.5	2.1	1.5
	Highest	8.1	6.0	3.8	2.2	3.2	6.5	1.6	0.5
Total		**8.5**	**7.3**	**5.2**	**3.8**	**3.7**	**3.1**	**1.8**	**1.4**

5.7.2 Supplementary figures

Supplementary figure 5.1: Physician review process of assigning the causes of deaths



Supplementary figure 5.2: Comparison of cause-specific mortality rates of the major causes of deaths between 2011 BDHS and 2017-18 BDHS.



5.8 REFERENCE

1. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2014. Dhaka, Bangladesh and Calverton, Maryland, USA; 2016.
2. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.
3. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, De Savigny D, Lozano R, et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. The Lancet. 2015;386(10001):1395-406.
4. United Nations Children Fund. Childinfo: Monitoring the situation of children and women. Under-five Mortality (U5MR) 2009 [April 4, 2021]. Available from: URL: http://www.childinfo.org/mortality_underfive.php.
5. Office of Registrar General. [cited 2020 October 30, 2020]. Available from: http://180.211.213.83/brisreport/ReportPage.aspx?rpno=7.
6. World Health Organization. Revealing the toll of COVID-19: a technical package for rapid mortality surveillance and epidemic response. 2020.
7. Amouzou A, Kante A, Macicame I, Antonio A, Gudo E, Duce P, et al. National Sample Vital Registration System: A sustainable platform for COVID-19 and other infectious diseases surveillance in low- and middle-income countries. Journal of global health. 2020;10(2).
8. Organization WH. Verbal autopsy standards: ascertaining and attributing cause of death: World Health Organization; 2007.
9. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2011. Dhaka, Bangladesh and Calverton, Maryland, USA; 2013.
10. Jetté N, Quan H, Hemmelgarn B, Drosler S, Maass C, Oec D-G, et al. The development, evolution, and modifications of ICD-10: challenges to the international comparability of morbidity data. Medical care. 2010:1105-10.
11. STATA. STATA 2020 [1 December 2020]. Available from: https://www.stata.com/.
12. Bangladesh Bureaur of Statistics. Bangladesh Population and Housing Census 2011. 2011.
13. Bangladesh Bureaur of Statistics. Sample Vital Registration System. 2015.
14. Chowdhury AMR, Bhuiya A, Chowdhury ME, Rasheed S, Hussain Z, Chen LC. The Bangladesh paradox: exceptional health achievement despite economic poverty. The Lancet. 2013;382(9906):1734-45.
15. Ahsan KZ, Streatfield PK, Ijdi R-E-, Escudero GM, Khan AW, Reza M. Fifteen years of sector-wide approach (SWAp) in Bangladesh health sector: an assessment of progress. Health policy and planning. 2016;31(5):612-23.
16. United Nations. The Sustainable Development Goals Report 2016. 2016.

17. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.

18. World Health Organization, UNICEF. End preventable deaths by 2025: The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). France; 2013.

19. Johns Hopkins Bloomberg School of Public Health. Pneumonia & Diarrhea Progress Report 2018. 2018.

20. Johns Hopkins Bloomberg School of Public Health. Pneumonia & Diarrhea Progress Report 2019. 2019.

21. Johns Hopkins Bloomberg School of Public Health. Pneumonia & Diarrhea Progress Report 2020. 2020.

22. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Neonatal, Child, & Adolescent Health (MNC&AH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

23. World Health Organization. Integrated Management of Childhood Illness: Global Survey Report. 2017.

24. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2017. Dhaka, Bangladesh; 2019.

25. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet: World Health Organization; 2014.

26. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.

27. Reed C, Madhi SA, Klugman KP, Kuwanda L, Ortiz JR, Finelli L, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One. 2012;7(1):e27793.

28. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.

29. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

30. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2014. Dhaka, Bangladesh; 2016.

31. Duke T, Subhi R, Peel D, Frey B. Pulse oximetry: technology to reduce child mortality in developing countries. Annals of tropical paediatrics. 2009;29(3):165-75.

32. Graham H, Tosif S, Gray A, Qazi S, Campbell H, Peel D, et al. Providing oxygen to children in hospitals: a realist review. Bull World Health Organ. 2017;95:288-302.

33. Igboanugo S, Chen A, Mielke JG. Maternal risk factors for birth asphyxia in low-resource communities. A systematic review of the literature. Journal of Obstetrics and Gynaecology. 2020;40(8):1039-55.

34. Billah SM, Chowdhury MAK, Khan ANS, Karim F, Hassan A, Zaka N, et al. Quality of care during childbirth at public health facilities in Bangladesh: a cross-sectional study using WHO/UNICEF 'Every Mother Every Newborn (EMEN)'standards. BMJ open quality. 2019;8(3):e000596.

35. Perkins J, Rahman AE, Mhajabin S, Siddique AB, Mazumder T, Haider MR, et al. Humanised childbirth: the status of emotional support of women in rural Bangladesh. Sexual and reproductive health matters. 2019;27(1):228-47.

36. Winter R, Yourkavitch J, Wang W, Mallick L. Assessment of health facility capacity to provide newborn care in Bangladesh, Haiti, Malawi, Senegal, and Tanzania. Journal of global health. 2017;7(2).

37. Organization WH. Guidelines on basic newborn resuscitation. 2012.

38. Boundy EO, Dastjerdi R, Spiegelman D, Fawzi WW, Missmer SA, Lieberman E, et al. Kangaroo mother care and neonatal outcomes: a meta-analysis. Pediatrics. 2016;137(1):e20152238.

39. Ministry of Health and Family Welfare GotPsRoB. Committing to Child Survival: A Promise Renewed Declaration 2013. Dhaka, Bangladesh; 2013.

40. UNICEF. Committing to child survival: a promise renewed. eSocialSciences; 2015.

41. Blencowe H, Krasevec J, de Onis M, Black RE, An X, Stevens GA, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. The Lancet Global Health. 2019;7(7):e849-e60.

42. Directorate General of Health Services (DGHS). District Health Information System (DHIS2) Dhaka, Bangladesh2020 [cited 2020 1 November 2020]. Available from: https://centraldhis.mohfw.gov.bd/dhismohfw/dhis-web-visualizer/.

43. World Health Organization. Kangaroo mother care: Practical guide, 2003 Geneva: Department of Reproductive Health and Research, WHO

44. Seidman G, Unnikrishnan S, Kenny E, Myslinski S, Cairns-Smith S, Mulligan B, et al. Barriers and enablers of kangaroo mother care practice: a systematic review. PloS one. 2015;10(5):e0125643.

45. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Child, Reproductive, & Adolescent Health (MCRAH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

46. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane database of systematic reviews. 2017(3):CD004454.

47. Mwansa-Kambafwile J, Cousens S, Hansen T, Lawn JE. Antenatal steroids in preterm labour for the prevention of neonatal deaths due to complications of preterm birth. International journal of epidemiology. 2010;39(suppl_1):i122-i33.

48. Mahmood SS, Iqbal M, Hanifi SMA, Wahed T, Bhuiya A. Are 'Village Doctors' in Bangladesh a curse or a blessing? BMC International Health and Human Rights. 2010;10(1):18.

49. Rahman MH, Agarwal S, Tuddenham S, Peto H, Iqbal M, Bhuiya A, et al. What do they do? Interactions between village doctors and medical representatives in Chakaria, Bangladesh. International Health. 2014;7(4):266-71.

50. Darmstadt GL, Syed U, Patel Z, Kabir N. Review of domiciliary newborn-care practices in Bangladesh. J Health Popul Nutr. 2006;24(4):380-93.

51. Chowdhury SK, Billah SM, Arifeen SE, Hoque DME. Care-seeking practices for sick neonates: Findings from cross-sectional survey in 14 rural sub-districts of Bangladesh. PLoS One. 2018;13(9):e0204902.

52. Ahmed S, Sobhan F, Islam A, Barkat e K. Neonatal morbidity and care-seeking behaviour in rural Bangladesh. J Trop Pediatr. 2001;47(2):98-105.

53. Shah R, Mullany LC, Darmstadt GL, Talukder RR, Rahman SM, Mannan I, et al. Determinants and pattern of care seeking for preterm newborns in a rural Bangladeshi cohort. BMC Health Serv Res. 2014;14:417.

54. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources. Geneva, Switzerland.; 2011.

55. World Health Organization. Guideline: Managing possible serious bacterial infection in young infants when referral is not feasible. Geneva: World Health Organization; 2015.

56. Baqui AH, Saha SK, Ahmed ANU, Shahidullah M, Quasem I, Roth DE, et al. Safety and efficacy of alternative antibiotic regimens compared with 7 day injectable procaine benzylpenicillin and gentamicin for outpatient treatment of neonates and young infants with clinical signs of severe infection when referral is not possible: a randomised, open-label, equivalence trial. The Lancet Global health. 2015;3(5):e279-e87.

57. Tshefu A, Lokangaka A, Ngaima S, Engmann C, Esamai F, Gisore P, et al. Simplified antibiotic regimens compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomised, open-label, equivalence trial. The Lancet. 2015;385(9979):1767-76.

58. Tshefu A, Lokangaka A, Ngaima S, Engmann C, Esamai F, Gisore P, et al. Oral amoxicillin compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with fast breathing when referral is not possible: a randomised, open-label, equivalence trial. The Lancet. 2015;385(9979):1758-66.

59. Rahman AE, Herrera S, Rubayet S, Banik G, Hasan R, Ahsan Z, et al. Managing possible serious bacterial infection of young infants where referral is not possible:

Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. PloS one. 2020;15(5):e0232675.

60. Rahman AE, Iqbal A, Hoque DE, Moinuddin M, Zaman SB, Rahman QS-u, et al. Managing Neonatal and Early Childhood Syndromic Sepsis in Sub-District Hospitals in Resource Poor Settings: Improvement in Quality of Care through Introduction of a Package of Interventions in Rural Bangladesh. PloS one. 2017;12(1):e0170267.

61. Rahman AE, Hossain AT, Zaman SB, Salim N, Ashish K, Day LT, et al. Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy childbirth. 2021;21(1):1-17.

62. Alonge O, Bishai D, Wadhwaniya S, Agrawal P, Rahman A, Dewan Hoque EM, et al. Large-scale evaluation of interventions designed to reduce childhood Drownings in rural Bangladesh: a before and after cohort study. Injury epidemiology. 2020;7:1-12.

63. Leavy JE, Crawford G, Leaversuch F, Nimmo L, McCausland K, Jancey J. A review of drowning prevention interventions for children and young people in high, low- and middle income countries. Journal of community health. 2016;41(2):424-41.

64. Organization WH. Prevention and control of birth defects in South-East Asia region: Strategic framework (2013-2017). WHO Regional Office for South-East Asia; 2013.

Chapter 6: STATUS OF FACILITY READINESS REGARDING THE AVAILABILITY OF PULSE OXIMETRY FOR MANAGING CHILDHOOD PNEUMONIA IN BANGLADESH

One of my general objectives was to understand the context of managing children with pneumonia, including hypoxaemia in Bangladesh burden of hypoxaemia among children with pneumonia. The specific research question 4 was to assess the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh.

Table 6.1 General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	**What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?**
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	Can minimally trained health personnel perform pulse oximetry in hospital settings?
7.	Can IMCI service providers perform pulse oximetry in routine outpatient settings in rural Bangladesh?

The work presented in the chapter 6 was published in the Journal of BMC Health Service Research in 2021.

Title: Managing pneumonia through facility-based integrated management of childhood management (IMCI) services: an analysis of the service availability and readiness among public health facilities in Bangladesh

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URL:https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-021-06659-y

6.1 ABSTRACT

6.1.1 Background

With an estimated 24,000 deaths per year, pneumonia is the single largest cause of death among young children in Bangladesh, accounting for 19% of all under-5 deaths. The Government of Bangladesh adopted the WHO recommended Integrated Management of Childhood Illness (IMCI) strategy in 1998 for outpatient management of pneumonia, which was scaled-up nationally by 2014. This paper reports the service availability and readiness related to pneumonia management through IMCI services in Bangladesh.

6.1.2 Methods

We conducted a secondary analysis of the Bangladesh Health Facility Survey-2017, which was conducted with a nationally representative sample including all administrative divisions and types of health facilities. We limited our analysis to District Hospitals (DHs), Maternal and Child Welfare Centres (MCWCs), Upazila (sub-district) Health Complexes (UHCs), and Union Health and Family Welfare Centres (UH&FWCs), which are mandated to provide IMCI services. Readiness was reported

based on 10 items identified by national experts as 'essential' for pneumonia management.

6.1.3 Results

More than 90% of DHs and UHCs, and three-fourths of UH&FWCs and MCWCs provide IMCI-based pneumonia management services. Less than two-third of the staff had ever received IMCI-based pneumonia training. Only one-third of the facilities had a functional ARI timer or a watch able to record seconds on the day of the visit. Pulse oximetry was available in 27% of the district hospitals, 18% of the UHCs and none of the UH&FWCs. Although more than 80% of the facilities had amoxicillin syrup or dispersible tablets, only 16% had injectable gentamicin. IMCI service registers were not available in nearly one-third of the facilities and monthly reporting forms were not available in around 10% of the facilities. Only 18% of facilities had a high-readiness (score 8-10), whereas 20% had a low-readiness (score 0-4). The readiness was significantly poorer among rural and lower level facilities ($p<0.001$). Seventy-two percent of the UHCs had availability of one of any of the four oxygen sources (oxygen concentrators, filled oxygen cylinder with flowmeter, filled oxygen cylinder without flowmeter, and oxygen distribution system) followed by DHs (66%) and MCWCs (59%).

6.1.4 Conclusion

There are substantial gaps in the readiness related to pneumonia management through IMCI services in public health facilities in Bangladesh. Since pneumonia remains a major cause of child death nationally, Bangladesh should make a

substantial effort in programme planning, implementation and monitoring to address these critical gaps to ensure better provision of essential care for children suffering from pneumonia.

6.2 BACKGROUND

Bangladesh was one of the few high burden countries with limited resources which achieved the ambitious MDG-4 target of reducing the under-5 mortality rate by two-thirds) ahead of 2015 (1, 2). Despite this commendable accomplishment, Bangladesh still suffers one of the highest under-5 mortality rates in the world (3). According to the latest Demographic and Health Survey conducted in 2017, the under-5 mortality in Bangladesh was 45 per 1,000 live births, indicating an apparent stalling in the rate of reduction from the 2014 estimates of 46 per 1,000 live births (2, 3). With an estimated 24,000 deaths per year, pneumonia accounted for 19% of all under-5 deaths, making it the single largest cause of death among young children (4). Therefore, achieving the ambitious 2030-SDG target of reducing the under-5 mortality to 25 per 1,000 live births or below will require strategic focus, substantial investments and concerted efforts by all stakeholders by prioritisation of pneumonia at every stage (5, 6).

Cognizant of the high burden of pneumonia morbidity and mortality in the majority of Low- and Middle-Income Countries (LMICs), the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) set forth an ambitious goal to end all preventable deaths due to pneumonia by 2025 (5). Bangladesh declared its commitment to reduce the pneumonia specific mortality rate among children less than 5 years of age from eight deaths per 1,000 live births to three deaths per 1,000 live birth by 2025 by implementing WHO and UNICEF's Global Action Plan for Pneumonia and Diarrhoea (GAPPD) (5).

Ensuring timely and appropriate management of pneumonia through outpatient and inpatient care is one of the key components of GAPPD's 'prevent-protect-treat' strategy (5). For outpatient management of common childhood illnesses, including pneumonia, the global recommendation is to adopt the Integrated Management of Childhood Illness (IMCI) strategy in high-burden and low-resource settings (7, 8). IMCI has demonstrated a positive impact in improving health worker's performance and quality of care as well as reducing childhood mortality, including pneumonia in settings with limited resources (9-16). However, success depends on the effective implementation of the three basic pillars outlined in the IMCI strategy, which include improving health worker's skills, improving the health system to ensure supplies of essential items to provide quality services, and improving family and community practices (17-20). Ensuring the service availability and readiness of health facilities are among the first steps towards strengthening the health systems (17, 18). They are also fundamental to ensuring the provision of care, which is one of the core components of WHO's Quality of Care Framework (21, 22).

The Government of Bangladesh (GoB) adopted the IMCI strategy in 1998, and facility-based IMCI was scaled up in all districts (64) and more than 90% of all sub-districts (420) by 2014 (16, 23). According to the current programme implementation model, IMCI services are provided through a dedicated corner (i.e. IMCI corner) at the outpatient departments in all district and sub-district level hospitals (24, 25). At the sub-district level, IMCI services are provided through union-level health centres. Doctors, nurses or paramedics (locally known as SACMOs) with special in-service training are responsible for providing IMCI services (24, 25). Unfortunately, there is

little evidence regarding the current status of service availability, readiness and quality of care rendered through IMCI services in Bangladesh. Such information, particularly those that are related to pneumonia management, is critical for understanding the health systems bottlenecks and taking course corrective measures to achieve the ambitious 2025-GAPPD and 2030-SDG targets.

This paper attempts to address this critical evidence gap by presenting the status of IMCI services, explicitly focusing on the service availability and readiness related to IMCI-based pneumonia management in Bangladesh, stratified by rural-urban, administrative division and type of health facilities.

6.3 METHODS

6.3.1 Study design

We conducted a secondary analysis of the Bangladesh Health Facility Survey (BHFS), which was conducted in 2017 with a nationally representative sample of health facilities (26). The survey included all types of public hospitals and health centres as well as some private and NGO hospitals with at least 20 inpatient beds. The survey was carried out by the National Institute of Population Research and Training (NIPORT) with technical assistance from ICF International (USA) and the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). Data were collected by Associates for Community and Population Research (ACPR), Dhaka, a private research agency appointed by NIPORT for this survey.

Bangladesh is divided into eight administrative divisions (Barisal, Chittagong, Dhaka, Khulna, Rajshahi, Rangpur, Sylhet, and Mymensingh), which are subdivided into 64

districts (zilas), and further divided into 485 sub-districts (upazilas). The public health systems in Bangladesh has three tiers of referral hospitals and two types of health centres. At the district level, there are Medical College Hospitals as tertiary level referral hospitals, District Hospitals (DHs) as secondary level referral hospitals with 250-500 beds. At the sub-district level, there are Upazila Health Complexes (UHCs) as primary level referral hospitals with 50 beds. Below the sub-district level, there are Union Health and Family Welfare Centres (UH&FWCs) and Community clinics (CCs) and) as health centres. In addition, there are Maternal and Child Welfare Centres (MCWCs) in all districts and few sub-districts with 10 beds. DHs have a catchment population of around 2-3 million, while it is 250,000-300,000 for UHCs, 25,000-30,000 for UH&FWCs and 6,000-10,000 for CCs.

The survey adopted a stratified random sampling procedure where the health facilities were stratified according to their administrative units and type of facilities. All divisions and the following types of health facilities were included in the survey: DHs, MCWCs, UHCs, UH&FWCs, CCs, and private hospitals and NGO clinics with at least 20 beds. In BHFS-2017, data were successfully collected from 1,524 health facilities (95% response rate). From each facility, an average of eight health care providers, who provided the range of services being assessed, were selected for interviews. In facilities with less than eight health care providers, all providers present on the day of the visit were interviewed. A total of 5,400 providers were interviewed (26).

BHFS 2017 used two types of questionnaires for data collection: a facility inventory questionnaire and a health care provider interview questionnaire. The facility inventory questionnaire was used to collect data related to the service availability and readiness of each priority services. The health care provider interview questionnaire was used to collect information related to the level of education, training, clinical experience, and supervision received by a sample of health care providers from each facility.

The data collection team consisted of 40 medical doctors and 40 paramedics who received three weeks of training from 09 July to 27 July 2017 in Dhaka. Data were collected between 30 July and 19 October 2017. Additional details are available in the BHFS-2017 report (26).

6.3.2 Analysis plan

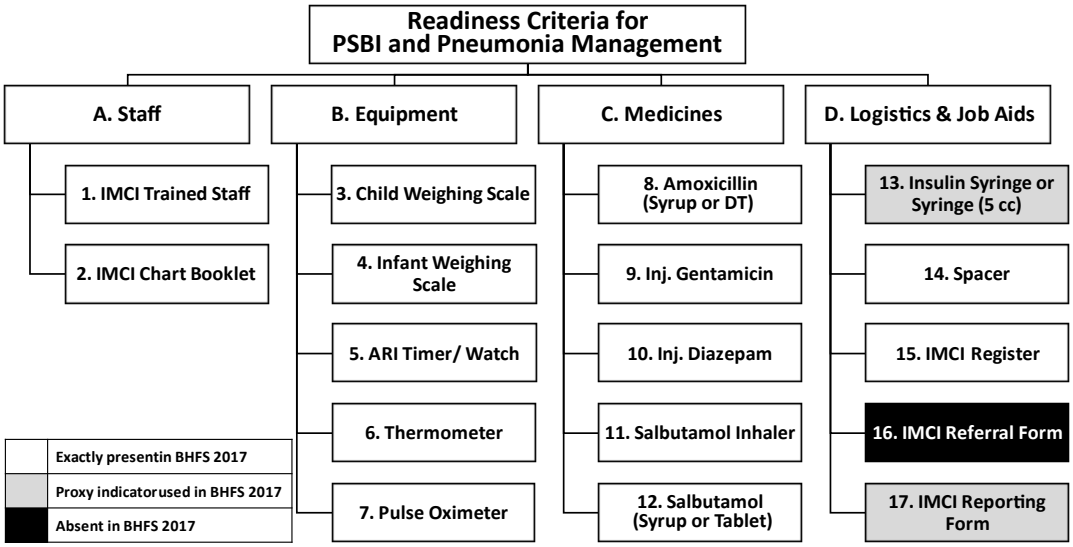
Data were analysed using Stata version 14 (StataCorp, College Station, TX).

According to the national IMCI programme, all DHs, MCWCs, UHCs and UH&FWCs are mandated to provide facility-based IMCI services through outpatient departments (24, 25). Therefore, in this paper, we limited our analysis to DHs (n=62), UHCs (n=141), UH&FWCs (n=677), and MCWCs (n=90), which were consistently used as denominators throughout the analysis

The National Newborn Health Programme and IMCI (NNHP&IMCI) of Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MoH&FW), Bangladesh has an approved list of essential equipment, drugs and logistics for IMCI services in Bangladesh. A consultative workshop was organised with

the national experts under the leadership of IMCI Programme to review the IMCI-list and identify items ‘required’ for pneumonia management based on the facility-based IMCI guidelines. The national experts identified 17 items as ‘required’, which was categorised into four domains: A. staff, B. equipment, C. medicines and D. logistics & job aids. Out of these 17 items, 14 were available, and three were absent in the BHFS-2017 tool. However, we identified proxy items (disposable syringe instead of Insulin syringe or 5cc syringe; monthly reporting form instead of IMCI reporting form) in the tool for two of the absent items. The national experts also identified 10 items from the list of 17 required items as essential for managing pneumonia based on facility-based IMCI guidelines. Supplementary table 6.1 presents the list of essential items. A ten-point scoring system was developed to measure the minimum pneumonia management readiness of designated health facilities. The availability of each of the essential item was given an equal score of one**.** Then, the facilities were categorised as 'poor readiness: score 0-4, 'moderate readiness: score 5-7 and 'high readiness: score 8-10. The scoring system was developed in consultation with national experts and IMCI programme management team. Figure 6.1 summarises the items identified by the Technical Committee and their availability in BHFS 2017 tool.

Figure 6.1: Items required for managing pneumonia based on facility-based IMCI guidelines



Service availability was defined as facilities offering curative childcare and reporting to provide the service based on facility-based IMCI guidelines. Readiness was defined as the presence of required items listed in Figure 6.1 on the day of the visit. Supplementary table 6.2 present the operational definition of readiness for each of the required items. Descriptive statistics (proportions) were used to report availability and readiness for each item. The estimates were stratified by facility type (DHs, UHCs, UH&FWCs, MCWCs), location (rural and urban) and administrative division.

In addition to the required and essential items, we present the readiness of IMCI facilities regarding the oxygen system. In addition to pulse oximetry (which was already included as a required item), the following items were included for presenting oxygen system readiness: availability of oxygen concentrator, availability of oxygen cylinder with flow meter, availability of oxygen cylinder without flow meter, and availability of oxygen distribution system.

4.1.1 Ethical considerations

This study used secondary dataset of Bangladesh Health Facility Survey (BHFS) collected by National Institute of Population Research and Training (NIPORT), Bangladesh. We got approval from the NIPORT for utilising the applicable datasets for this study.

6.4 RESULTS

Table 6.2 describes the background characteristics of the public health facilities, which are mandated to provide facility-based IMCI services in Bangladesh and included in this analysis. All of the DHs and the majority (79%) of the MCWCs were situated in urban areas. Regarding UHCs, around half were located in urban areas. In contrasts, almost all the UH&FWCs were located in rural areas. Among all the facilities, around one-fifth were in Barisal and Chittagong divisions each while rest of the divisions, contributed around 10% each.

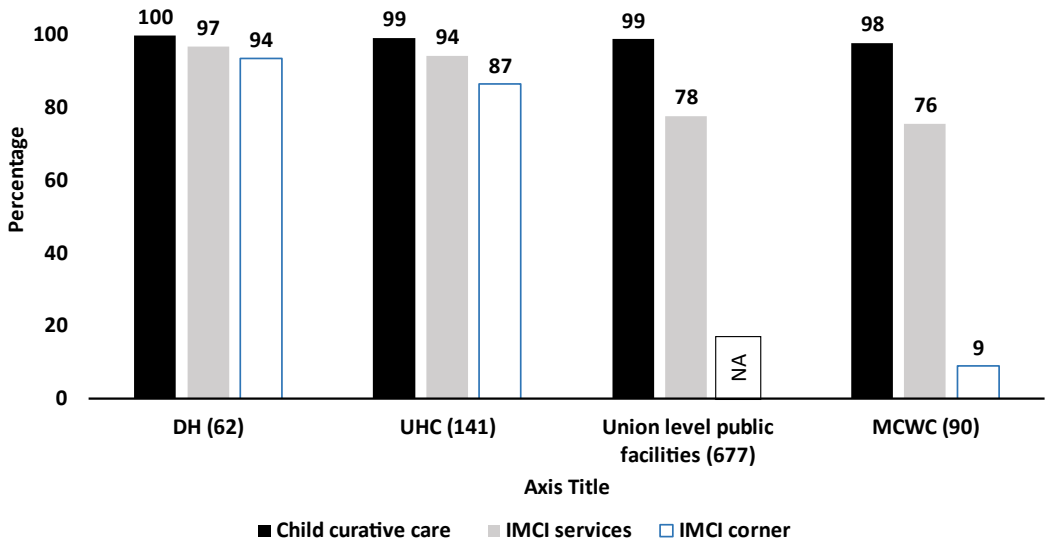
Table 6.2: Background characteristics of the facilities mandated to provide facility-based IMCI services in Bangladesh, presented in frequency and column percentage

	DH		UHC		UH&FWC		MCWC		Total	
	n	%	n	%	n	%	n	%	n	%
Location										
Urban	62	100%	77	55%	6	1%	71	79%	216	22%
Rural	0	0%	64	45%	671	99%	19	21%	754	78%
Division										
Barisal	6	10%	26	18%	141	21%	10	11%	183	19%
Chittagong	11	18%	25	18%	151	22%	18	20%	205	21%
Dhaka	14	23%	15	11%	67	10%	14	16%	110	11%
Khulna	10	16%	14	10%	57	8%	13	14%	94	10%
Rajshahi	7	11%	17	12%	61	9%	13	14%	98	10%
Rangpur	7	11%	14	10%	58	9%	12	13%	91	9%
Sylhet	4	6%	18	13%	90	13%	6	7%	118	12%
Mymensingh	3	5%	12	9%	52	8%	4	4%	71	7%
Total	62	100%	141	100%	677	100%	90	100%	970	100%

DH: District Hospital
UHC: Upazila Health Complex
UHFWC: Union Health and Family Welfare Centres
MCWC: Mother & Child Welfare Centre

Figure 6.2 summarises the service availability related to pneumonia management in public health facilities mandated to provide facility-based IMCI services in Bangladesh. Curative child care is almost universally available across all types of facilities. More than 90% of DHs and UHCs reported providing IMCI services (including pneumonia management), whereas such services were available in three-fourths of UH&FWCs and MCWCs. Around 90% of DHs and UHCs had IMCI corners. However, the availability was extremely low (9%) in MCWCs. UH&FWCs were not mandated to establish specific corners for providing IMCI services; therefore, the findings for this facility have been presented as 'not applicable'.

Figure 6.2: Service availability of IMCI services (including pneumonia management) in different types of public health facilities mandated to provide facility-based IMCI services in Bangladesh; presented in %



DH: District Hospital
UHC: Upazila Health Complex
UHFWC: Union Health and Family Welfare Centres
MCWC: Mother & Child Welfare Centre

Figure 6.3 illustrates the readiness related to the management of pneumonia in different types of public health facilities mandated to provide facility-based IMCI services in Bangladesh. The availability (on the day of the visit) is presented for each of the items (presented in Figure 6.3) required for managing pneumonia according to facility-based IMCI guidelines. Around 57% of the facilities had a staff ever trained in facility-based IMCI guidelines, and 44% had a copy of the IMCI chart booklet on the day of the visit. Regarding equipment, the thermometer was available in 82% of facilities. Weighing scales (child or infant) were available in half of the facilities. Only one-third of the facilities had an ARI timer or a watch that can record time in seconds on the day of the visit. Pulse oximetry was available in only 6% of facilities. More than 80% of the facilities had amoxicillin syrup or dispersible tablets on the day of

the visit. However, the availability of injection gentamicin was only 16%. An Insulin syringe or disposable 5 cc syringe was available in 77% of facilities. Although monthly reporting forms were available in 88% of facilities, around one-third of the facilities did not have an IMCI service register to document their care practices.

Figure 6.3: Availability of the items required for managing pneumonia in public health facilities mandated to provide facility-based IMCI services in Bangladesh; presented in %; N=970

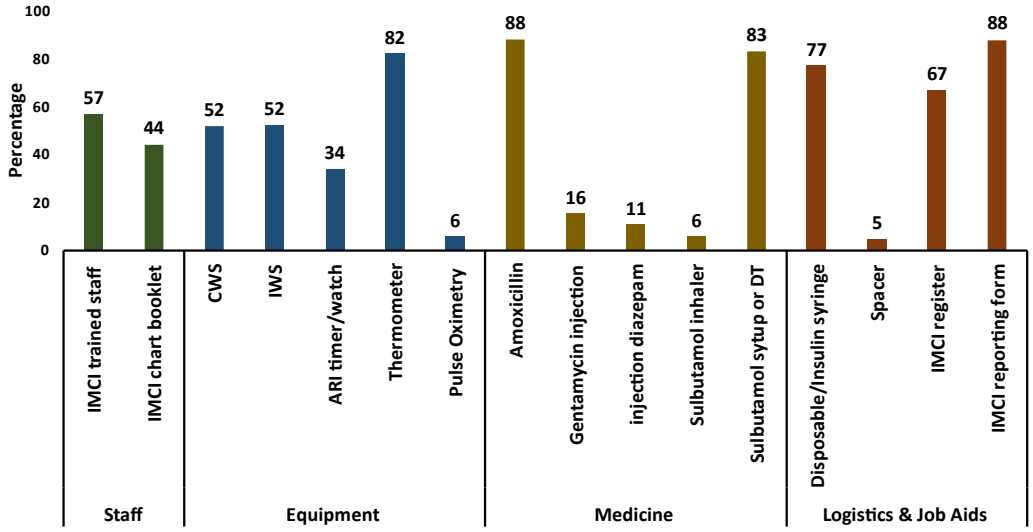


Table 6.3 presents the readiness (availability of required items on the day of the visit) related to the management of pneumonia in public health facilities mandated for providing facility-based IMCI services in Bangladesh, disaggregated by facility type, location and division for each of the readiness items. DHs and UHCs demonstrated higher levels of readiness than UH&FWCs for the majority of the items. The readiness of UH&FWCs was particularly low (less than half of DHs) for IMCI chart booklet, weighing scale, ARI timer, pulse oximeter, injection gentamicin, injection diazepam and IMCI register. Similarly, the readiness was higher among urban-facilities than that of rural-facilities across all items. Pulse oximetry was available in only 27% of the district hospitals and 18% of the UHCs. None of the UH&FWCs had a pulse

oximeter on the day of the visit. No obvious pattern was observed regarding the readiness across different divisions. More than two-thirds of UHCs had both IMCI trained staff and guideline, but around a quarter of MCWCs and union facilities had both. Similar gaps were identified of all other domains.

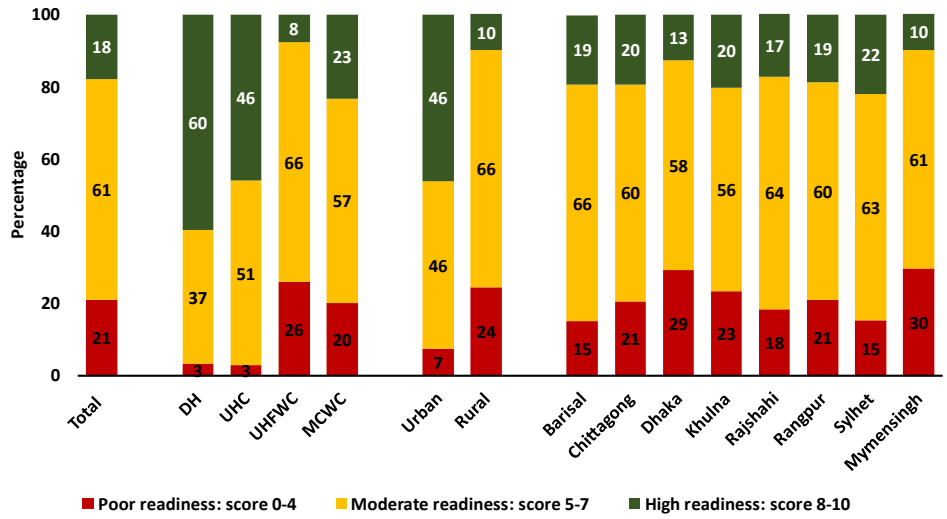
Table 6.3: Availability of the items required for managing pneumonia in public health facilities mandated to provide facility-based IMCI services in Bangladesh by facility type, location and division; presented in %

	Staff and guideline			Equipment						Medicines						Logistics				
	1. IMCI TS	2. IMCI CB	All	3. CWS	4. IWS	5 ARI or TW	6. Th	7. PO	All	8. Amox	9. Inj. G	10. Inj. D	11. SI	12. SS/ST	All	13. IS	14. Sp	15. IMCI R	16. IMCI	All
Type																				
DH	79	69	53	71	69	45	87	27	11	94	44	61	31	92	11	73	23	94	97	16
UHC	85	72	63	73	69	46	92	18	5	89	41	31	17	92	4	75	17	89	97	14
Union level public facilities	57	37	24	45	48	29	79	0	0	87	8	1	2	81	0	77	1	61	87	0
MCWC	59	37	23	57	61	47	86	17	3	93	10	23	1	81	0	83	7	59	79	2
Location																				
Urban	78	61	49	69	66	49	90	22	7	92	34	40	17	89	5	76	15	80	90	11
Rural	58	40	27	47	50	30	80	1	0	87	10	3	3	81	0	77	2	63	87	1
Division																				
Barisal	72	51	37	50	59	36	89	6	2	85	19	8	4	79	1	81	4	70	91	3
Chittagong	56	41	29	49	54	39	84	4	2	89	23	8	3	91	2	78	5	58	89	2
Dhaka	68	48	35	43	30	29	71	6	0	82	10	16	15	71	2	75	6	69	91	5
Khulna	64	40	31	59	60	31	78	11	3	92	16	16	7	81	0	76	5	70	87	4
Rajshahi	58	35	25	40	57	37	87	7	1	89	11	14	7	83	2	79	6	75	91	6
Rangpur	62	44	34	62	62	30	82	7	1	93	8	17	4	87	3	67	6	69	82	4
Sylhet	61	42	27	63	55	38	86	5	3	89	14	8	5	85	2	88	5	63	80	2
Mymensingh	59	54	37	58	48	21	68	3	0	90	10	7	4	85	0	61	1	70	90	1

1.IMCI TS: IMCI trained staff	9. Inj. G: Injection Gentamicin
2. IMCI CB: IMCI chart booklet	10. Inj. D: Injection Diazepam
3. CWS: Child weighing scale	11. SI: Salbutamol inhaler
4. IWS: Infant weighing scale	12. SS/ST: Salbutamol syrup/tablet
5. ARI TW: ARI Timer or watch able to record seconds hand	13. IS: Insulin syringe or disposable 5 cc syringe
6. TH: Thermometer	14. S: Spacers
7. PO: Pulse oximeter	15. IMCI R: IMCI registers
8. Amox: Amoxicillin Dispersible Tablets or syrup	16. IMCI RF: IMCI reporting form

Figure 6.4 presents the readiness based on ten essential items for managing pneumonia in public health facilities mandated to provide facility-based IMCI services in Bangladesh. The score denotes the number of items available on the day of the visit. Out of the facilities surveyed, only 18% had a high level of readiness with an overall readiness score of 8-10, whereas 20% had a low level of readiness with an overall score of 0-4. When stratified by facility type, DH and UHC showed a higher level of readiness than that of UH&FWCs (60% for DHs, 46% for UHCs and 8% for UH&FWCs, p<0.001). Facilities located in urban areas had a much higher level of high readiness (46%) than facilities located in rural areas (10%) (p<0.001). The readiness patterns were similar across all administrative divisions. Supplementary figure 6.1 illustrates that none of the facilities had all of the ten essential items available on the day of the visit. Around 5 percent of the DHs and UHCs had all essential items, whereas only 1 percent of MCWCs and no union facilities had all essential items.

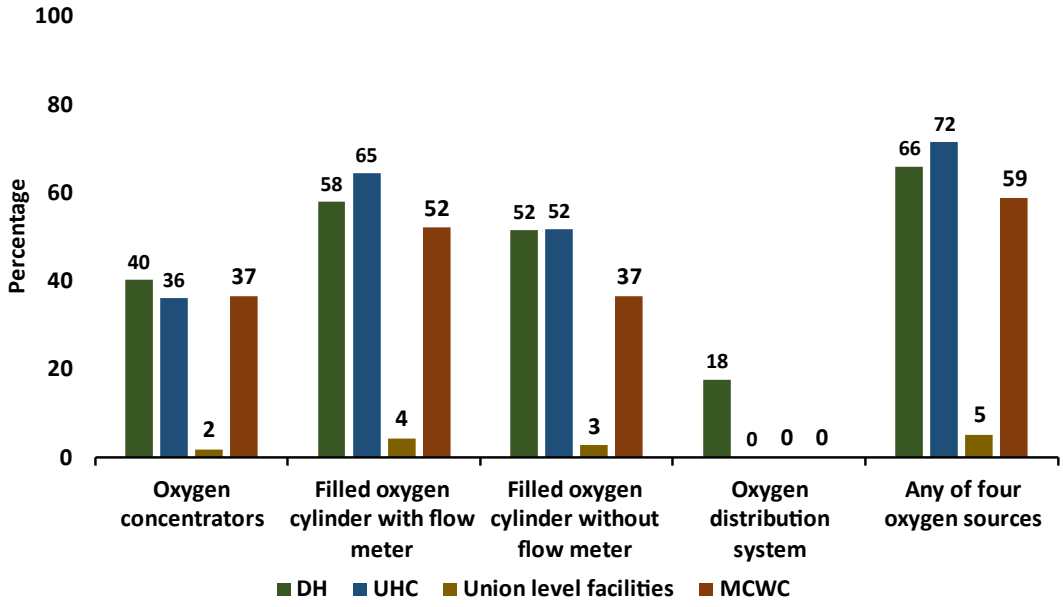
Figure 6.4: Availability of items essential for managing pneumonia in public health facilities mandated to provide facility-based IMCI services in Bangladesh by facility type, location and administrative division; presented in % based on a ten-point readiness score



DH: District Hospital; UHC: Upazila Health Complex; UHFWC: Union Health and Family Welfare Centres; MCWC: Mother & Child Welfare Centre

Figure 6.5 illustrates the readiness related to oxygen sources in public health facilities in Bangladesh. Around 40% of the DHs and one-thirds of the UHCs and MCWCs had a functioning oxygen concentrator on the day of the visit. More than half (52%-65%) of the DHs, UHCs and MCWCs had oxygen cylinders with flow meters. Besides, around half of the DHs and UHCs, and one-third of the MCWCs had oxygen cylinders without flowmeters on the day of the visit. Around 18% of the district hospitals had an oxygen distribution system, but none of UHCs, UH&FWC and MCWCs had this. The availability of any of the four oxygen sources was the highest in UHCs (72%) followed by DHs (66%) and MCWCs (59%). Oxygen availability was particularly low (5%) in UH&FWCs.

Figure 6.5: Availability of oxygen sources in different types of public facilities in Bangladesh; presented in %



DH: District Hospital
UHC: Upazila Health Complex
MCWC: Mother & Child Welfare Centre

6.5 DISCUSSION

Pneumonia is the largest killer of children under-5 years of age in Bangladesh, and IMCI is one of the key strategies adopted by the Government of Bangladesh for managing pneumonia (3, 24, 25). The success of IMCI services will greatly influence Bangladesh's progress towards achieving the GAPPD target of preventing all avoidable pneumonia-related deaths by 2025 (5). Ensuring the service availability and readiness of health facilities are the stepping stones for health systems strengthening and critical to promoting the quality of care rendered through IMCI services (27). This is the first study to report the service availability and readiness related to IMCI-based pneumonia services in Bangladesh through a nationally representative sample. This study identified that there were substantial gaps in staff trained in IMCI services, availability of essential items like functional ARI timer or watch that can record time in seconds, pulse oximeter, registers and reporting forms for documentation, and necessary medicines for providing IMCI-based pneumonia management. Moreover, there were critical gaps in the availability of oxygen sources in the surveyed facilities.

WHO developed the IMCI strategy in the mid-1990s, which incorporated key lessons from WHO's Global Acute Respiratory Infection Control Programme launched in 1980s (27). The Government of Bangladesh adopted the IMCI strategy immediately after that, and the process of health systems integration and national scale-up were completed through its inclusion in the National Health Sector Programme 2011-16 and Essential Service Package (28, 29). According to the current National Health Sector Programme 2017-22, all types of public facilities (DH, UHCs, UH&FWCs and

MCWCs) are mandated to provide curative child care through IMCI services (24, 25). Our analysis reveals that almost all facilities offer child curative services, but there are substantial gaps regarding the availability of IMCI services in UH&FWCs and MCWCs. The divide between the two directorates of the Ministry of Health and the differences in their strategic focus can potentially explain such contrasting pictures. All DHs and UHCs are under the DGHS, however, the majority of the UH&FWCs and all MCWCs are under the Directorate General of Family Planning (DGFP) (24, 25). Historically, DGHS was involved in the introduction and scale-up of IMCI services in Bangladesh, and they have a specific programme named after IMCI (NNHP&IMCI). On the other hand, the prime mandate of DGFP is to promote and provide family planning services. Child curative care was incorporated into DGFP's mandate as an expansion of the existing family planning services. Also, there are gaps in coordination between the IMCI programme of DGHS and the child health programme of DGHS.

According to the current health sector programme, all DHs, UHCs and MCWCs are supposed to prioritise IMCI services by maintaining a dedicated corner in the outpatient department (24, 25). IMCI corners require dedicated staff (IMCI trained), equipment and logistics, which helps operationalising outpatient services and retaining the skills of the service providers. The IMCI corners also help in managing the high-volume patient flow in DHs, UHCs and MCWCs, and act as a referral link for children who are referred from UH&FWCs. Contrary to the policy outlined in the health sector programme, 6% of DHs, 13% of UHCs, and more than 90% of MCWCs do not have dedicated IMCI corners. The lack of a strategic focus and programmatic

investments by DGFP regarding IMCI services can potentially explain the low availability of IMCI corners in MCWCs. In addition to the IMCI corners, different programmes have recommended maintaining various other corners like ANC corner, PNC corner, KMC corner, SCANU corner, NCD Corner, Breast Feeding corner, VIA corner etc. in DHs and UHCs (24, 25, 29). The competing interests of various corners can, which were established as a horizontal integration of various services, be another explanation for the gaps in the availability of IMCI corners in facilities with limited resources.

IMCI adopts a syndromic management approach, where the service provider has to follow various clinical algorithms to classify and treat childhood illnesses (30). It requires continuous in-service training and supportive supervision to retain the knowledge and skills of the service provider and ensure the quality of IMCI services (20). Unfortunately, almost half of the surveyed facilities do not have an IMCI trained staff and a copy of the chart booklet. The situation is particularly worse in UH&FWCs and MCWCs. Although DHs and UHCs demonstrate a comparatively higher level of readiness regarding the availability of a service provider ever trained in IMCI only around 31% of the DHs and approximately one-third of the UHCs have a service provider who received IMCI training within the past 24 months (26). It raises a critical concern regarding the quality of IMCI services, including management of pneumonia rendered through the service provider without appropriate training and supervision. It reveals the apparent gaps in national programme planning and implementation.

The survey (BHFS) was conducted in 2017, which is just after the completion of the previous National Health Sector Programme 2011-16 (26, 28). IMCI training organised by the IMCI programme in the last sector programme implementation period was not adequate to the needs of the country. Since 2017, the Ministry of Health is implementing the current National Health Sector Programme 2011-16 (31). The provision and resource allocation for IMCI training in the operation plan of the current health sectors programme is also inadequate and insufficient (24, 25). Moreover, in the first two years of the current sector programme implementation period (2017-19), the IMCI programme did not organise any IMCI training for the old and newly recruited service providers. One of the core components of IMCI strategy is to improve the case-management skills of service providers through the provision of locally adapted IMCI-guidelines and through activities to promote their use. Unfortunately, more than half of the surveyed facilities do not have a copy of the chart booklet. Moreover, the latest version of Bangladesh adapted version of the IMCI chart booklet is based on WHO's 2008-edition (32, 33). In 2014, WHO released another version of IMCI chart booklet with major updates regarding pneumonia classification, treatment recommendations and referral criteria (30, 34). During the implementation periods of the previous health sector programme (2011-16) and the first two years of the current health sector programme (2017-22), the IMCI programme could not take proper initiatives to update the IMCI chart booklet based on WHO's recent recommendations as well as print and distribute them to the IMCI service delivery points in DHs, UHCs, UH&FWCs and MCWCs. This could substantially

affect the safety of treatment and quality of care, particularly for pneumonia and sepsis management.

IMCI is designed for settings with minimum diagnostic capacity. Therefore, the availability of some basic equipment and medicine must be ensured for proper clinical assessment and treatment according to the guidelines (30). Assessment of respiratory rate is one of the most important steps in IMCI-based pneumonia classification, which eventually determines the management plan, referral decision and treatment outcomes (34-36). Unfortunately, two-thirds of the designated facilities in Bangladesh do not have a functional ARI timer or watch that is able to record time in seconds. Moreover, around half of the facilities do not have an appropriate weighing scale which is important for prescribing medicines (including antibiotics of pneumonia management) with appropriate dosages (30). The majority of these essential equipment are not costly and are readily available in the local market. Therefore, the observed gaps in their availability reflect the apparent lack of effective programme planning, coordination and monitoring.

The IMCI-based pneumonia management requires the availability of oral amoxicillin and injectable gentamicin as the first-line treatment for severe pneumonia and possible serious bacterial infection of young infants (37, 38). For more severe cases, the availability of both amoxicillin and gentamicin together is essential for prereferral treatment and outpatient-based management (when applicable) (39). Although the availability of oral amoxicillin was reasonably high among all types of facilities, there are substantial gaps regarding the availability of injectable

gentamicin. Such critical gaps in readiness regarding the first-line antibiotics essentially reduce the level of effective coverage, may compromise the level of adherence to guidelines and potentially result in avertable pneumonia-related deaths (40). Besides the availability of the IMCI medicines, the choice of antibiotics recommendations by IMCI services providers may be influenced by external factors. Several studies conducted in Bangladesh reported that there are substantial gaps regarding health care provider's adherence to guidelines since many of them prefer higher general antibiotics over the first-line recommended antibiotics (41-44).

Documentation is one of the most important parts of IMCI services. The IMCI service register is designed to capture essential details on clinical assessments, disease classifications, treatments, and referral decisions. It acts as a job aid to assist the provider in adhering to the guideline and prepare monthly reports efficiently (45). Registers are also linked to the overall monitoring and supervision framework laid out for IMCI services, as well as the overall accountability structure (20, 45). Although registers are almost universally available in DHs and UHCs, one-third of UH&FWCs and MCWCs do not have them, according to our analysis. The lack of availability of IMCI registers also raises questions regarding the validity of data in monthly reports, which is the basis of effective programme planning and monitoring for health managers.

Based on the multi-country evaluation of IMCI, which ran from 1999 to 2007, WHO released a position paper with a strong recommendation for health systems strengthening by ensuring the availability of skilled health workers, essential

medicines, and supplies as a comprehensive package in all IMCI service delivery points (46). The lack of comprehensive readiness, including essential equipment, drugs and logistics adversely affect the performance of the IMCI service provider and result in the poor quality of care (47, 48). A global survey conducted by WHO found that the countries with a comprehensive implementation status of IMCI were 3.6 times were more likely to achieve MDG-4 target than other countries who could not adopt a comprehensive approach (27). It is imperative to ensure comprehensive readiness of facilities for providing IMCI services, including pneumonia management, by learning lessons from this global evidence. We report substantial gaps regarding the overall readiness of public facilities in Bangladesh pertaining to pneumonia management. The readiness of private facilities regarding IMCI services is equally poor in Bangladesh (26). Less than 1% of the private facilities were identified to be ready for providing child curative services. Only 20% of private facilities had an IMCI trained staffs. Without addressing these gaps, it will not be possible to adhere to the WHO quality of care standards related to the provision of care and experience of care (22). The lack of comprehensive readiness, including essential equipment, drugs and logistics adversely affect the performance of the IMCI service provider and result in the poor quality of care (47, 48). The readiness is much worse in lower-level facilities and facilities located in rural areas. The lower level facilities (UH&FWCs) are mostly located in rural areas and serve as the first point of contacts for the poorer and more disadvantaged sections of the population. Thus, the lower level of overall readiness in these facilities further contributes to the existing inequity in access to and utilisation of appropriate health services in Bangladesh and other low- and

middle-income countries (2, 49-51). According to Bangladesh Demographic Health Survey 2017-18, only 20% of the under-5 children with symptoms of acute respiratory infections sought care from public health facilities (52). The poor level of readiness of public facilities may explain the low care-seeking practice from public health facilities.

Hypoxaemia is common among children with pneumonia and is one of the strongest predictors of mortality due to acute lower respiratory infections (53-55). Integration of SpO_2 assessment in existing IMCI services can significantly improve the accuracy of hypoxaemia assessment and increase the validity (accuracy) of pneumonia classification (89, 96). In response to the need and global evidence, WHO recommended measuring SpO_2 in routine IMCI services (23, 81). In addition, oxygen security is a vital concern in the context of the COVID-19 pandemic. The Government of Bangladesh adopted the WHO recommendation and decided to introduce pulse oximetry in IMCI services for SpO_2 assessment (38). Although the survey predates the Government of Bangladesh's policy adoption regarding SpO_2 assessment in IMCI services, it is helpful to understand the baseline situation of the country in this regard. Less than one-tenth of the facilities have pulse oximetry. The availability of pulse oximetry was not optimal even in referral hospitals as less than one-third of the DHs and one-fifth of the UHCs have readiness in this regard. This is similar to the status of many other low- and middle countries with limited resources (56). To achieve the universal availability of pulse oximetry in all IMCI services contact points, the Government of Bangladesh needs to prioritise its procurement and efficiently manage its distribution. In addition to ensuring the availability of pulse oximetry, it

is equally important to ensure the availability of oxygen in referral hospitals to aggressively correct and manage hypoxaemia (57, 58). Unfortunately, one-third of the DHs and one-fourth of the UHCs do not have a reliable oxygen source which is essential for managing children with hypoxaemia. Effective oxygen therapy requires not only prompt and accurate detection of hypoxaemia but also appropriate administration of oxygen, combined with good clinical evaluation and management of the underlying condition. Bangladesh can learn from other low- and middle-income countries that have strategically invested in oxygen security in referral hospital and effectively reduced the burden of mortality due to pneumonia (59, 60). Experience from four decades of 'oxygen projects' shows that effective improvement of oxygen systems in low-resource settings is possible but is complex and requires context-specific technical, clinical, and managerial solutions (61).

It is important to discuss some of the strengths and limitation of this study. BHFS-2017 was conducted with a nationally representative sample allowing us to generate specific estimates by facility types, locations and divisions. Moreover, the data collection tool used in BHFS-2017 was validated and adapted to the national context through expert consultations. The survey presents a snapshot of the service availability and readiness of the surveyed facilities since it only considered the availability of services and items on the day of the visit. Information regarding service availability is based on the self-reported status of the facility. Regarding readiness, the data collectors physically verified the availability of required and essential items and assessed their functionality where applicable. Although there were no globally validated criteria for assessing the service availability and readiness related to

pneumonia management, we went through an expert consultation process under the leadership of IMCI programme in the Ministry of Health and Family Welfare to develop the service availability and readiness criteria for Bangladesh. The experts identified the lists of required and essential items as well as the scoring system based on consensus and under the leadership of the national IMCI programme. Although the lists and the scoring system are not validated externally, they reflect the national programme priorities. Lastly, we acknowledge that the gaps in service availability and readiness may be resulting from broader health systems building blocks issues such as health financing and governance. The availability of data did not allow us to explore and present such root causes, which needs to be explored through future research in this field.

6.6 CONCLUSION

Our study findings reported low to moderate level of readiness for providing IMCI-based pneumonia management in public health facilities in Bangladesh. The readiness was significantly poorer among rural and lower-level facilities. Achieving the ambitious target of averting all preventable pneumonia-related mortality by 2025 will require effective coverage of pneumonia management with appropriate quality of care from the governments and supports from global level partners. Ensuring the service availability and readiness of health facilities is the first step towards promoting effective coverage and is integral to WHO's quality of care framework. There are substantial gaps in the availability of IMCI services and readiness of essential items required for pneumonia management in public health facilities in Bangladesh. The situation is significantly worse in the lower level and

rural facilities. Bangladesh should make substantial efforts to improve programme planning, implementation, and monitoring to address these critical gaps to ensure better provision of care for children suffering from pneumonia. Moreover, as IMCI has been scaled up in Bangladesh, there is a need for research on improving delivery strategies and overcoming barriers to implementation.

6.7 SUPPLEMENTARY MATERIALS

6.7.1 Supplementary tables

Supplementary table 6.1: List of core items required for pneumonia management services

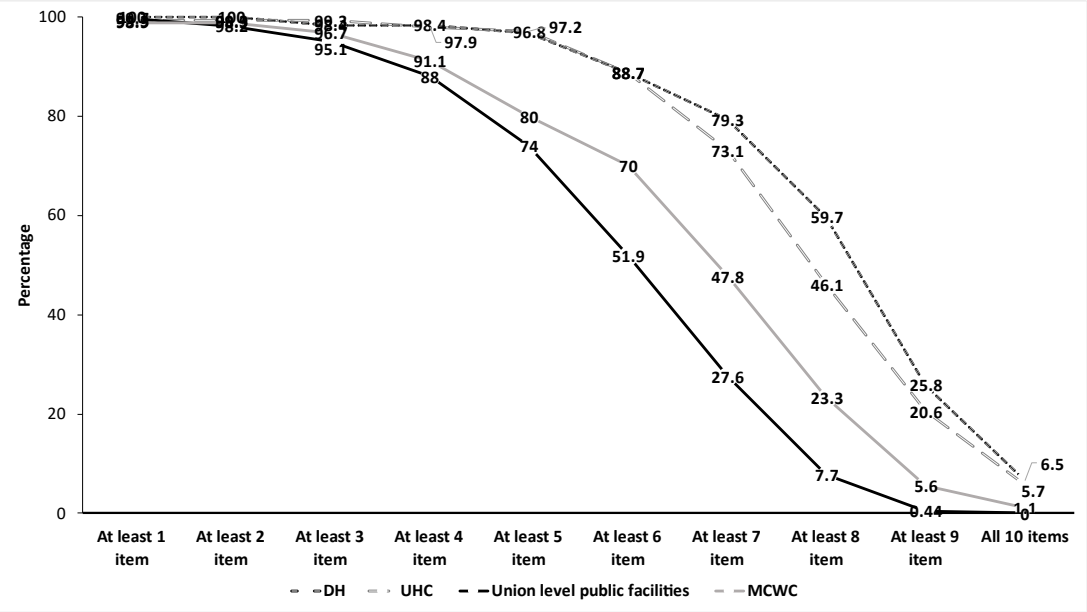
Essential items	
i.	1. IMCI trained staff
ii.	3. CWS OR 4. IWS
iii.	5. ARI Timer or watch able to record seconds hand
iv.	6. Thermometer
v.	8. Amoxicillin DT or syrup
vi.	9. Injection Gentamycin
vii.	10. Injection Diazepam
viii.	11. & 12. Salbutamol inhaler/syrup/tablet
ix.	13. Syringe (5 cc)
x.	15. IMCI register

Supplementary table 6.2: Definition of readiness for all pneumonia readiness items

	Items	Readiness definition
1.	IMCI trained staff	Availability of staff who received IMCI training ever
2.	IMCI Chart booklet	Observed availability of IMCI chart booklet in the facility
3.	Child weighing scale	Observed availability and functionality of child weighing scale in the facility
4.	Infant weighing scale	Observed availability and functionality of infant weighing scale in the facility
5.	ARI Timer or watch able to record seconds hand	Observed availability and functionality of ARI Timer or watch able to record seconds hand in the facility
6.	Thermometer	Observed availability and functionality of thermometer in the facility
7.	Pulse oximeter	Observed availability and functionality of pulse oxymeter in the facility
8.	Amoxicillin DT or syrup	Observed availability of at least one valid Amoxicillin dispersible tablet or syrup in the facility
9.	Inj Gentamycin	Observed availability of at least one valid injection gentamycin in the facility
10.	Inj Diazepam	Observed availability of at least one valid injection Diazepam in the facility
11.	Sulbutamol inhaler	Observed availability of at least one valid Sulbutamol inhaler in the facility
12.	Sulbutamol syrup/tablet	Observed availability of at least one valid Sulbutamol syrup/ tablet in the facility
13.	Insulin syringe or disposable 5cc syringe	Observed availability of insulin syringe or disposable 5cc syringe in the facility
14.	Spacers	Observed availability of spacers in the facility
15.	IMCI register	Observed availability of IMCI register in the facility
16.	IMCI referral form	Observed availability of IMCI referral form in the facility

6.7.2 Supplementary figures

Supplementary figure 6.1: Availability of core items required for managing pneumonia in public health facilities mandated to provide facility-based IMCI services in Bangladesh; presented in %; N=970



DH: District Hospital
UHC: Upazila Health Complex
UHFWC: Union Health and Family Welfare Centres
MCWC: Mother & Child Welfare Centre

6.8 REFERENCE

1. United Nations. The Millennium Development Goals Report 2015. 2015.
2. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2014. Dhaka, Bangladesh and Calverton, Maryland, USA; 2016.
3. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.
4. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
5. World Health Organization, UNICEF. End preventable deaths by 2025: The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). France; 2013.
6. United Nations. The Sustainable Development Goals Report 2016. 2016.
7. World Health Organization. IMCI information package. INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS (IMCI). Geneva; 1999.
8. Gove S. Integrated management of childhood illness by outpatient health workers: technical basis and overview. The WHO Working Group on Guidelines for Integrated Management of the Sick Child. Bulletin of the World Health Organization. 1997;75(Suppl 1):7.
9. Sazawal S, Black RE, Group PCMT. Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials. The Lancet infectious diseases. 2003;3(9):547-56.
10. Chowdhury EK, El Arifeen S, Rahman M, Hoque DE, Hossain MA, Begum K, et al. Care at first-level facilities for children with severe pneumonia in Bangladesh: a cohort study. The Lancet. 2008;372(9641):822-30.
11. Schellenberg JRA, Adam T, Mshinda H, Masanja H, Kabadi G, Mukasa O, et al. Effectiveness and cost of facility-based Integrated Management of Childhood Illness (IMCI) in Tanzania. The Lancet. 2004;364(9445):1583-94.
12. Nguyen DTK, Leung KK, McIntyre L, Ghali WA, Sauve R. Does integrated management of childhood illness (IMCI) training improve the skills of health workers? A systematic review and meta-analysis. PloS one. 2013;8(6):e66030.
13. Gera T, Shah D, Garner P, Richardson M, Sachdev HS. Integrated management of childhood illness (IMCI) strategy for children under-5. Cochrane Database of Systematic Reviews. 2016(6).
14. Rakha MA, Abdelmoneim A-NM, Farhoud S, Pièche S, Cousens S, Daelmans B, et al. Does implementation of the IMCI strategy have an impact on child mortality? A retrospective analysis of routine data from Egypt. BMJ open. 2013;3(1):e001852.

15. Kanyuka M, Ndawala J, Mleme T, Chisesa L, Makwemba M, Amouzou A, et al. Malawi and Millennium Development Goal 4: a Countdown to 2015 country case study. The Lancet Global Health. 2016;4(3):e201-e14.

16. Arifeen SE, Hoque DE, Akter T, Rahman M, Hoque ME, Begum K, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. The Lancet. 2009;374(9687):393-403.

17. World Health Organization, UNICEF. IMCI Planning Guide: Gaining experience with the IMCI strategy in a country: World Health Organization; 1999.

18. World Health Organization. Planning National Implementation of IMCI: World Health Organization; 1999.

19. Ahmed HM, Mitchell M, Hedt B. National implementation of Integrated Management of Childhood Illness (IMCI): policy constraints and strategies. Health policy. 2010;96(2):128-33.

20. World Health Organization, UNICEF. Handbook: IMCI Integrated Management of Childhood Illness: World Health Organization; 2005.

21. World Health Organization. Standards for improving quality of maternal and newborn care in health facilities. 2016.

22. World Health Organization. Standards for improving the quality of care for children and young adolescents in health facilities. 2018.

23. Bryce J, Victora CG, Habicht J-P, Black RE, Scherpbier RW. Programmatic pathways to child survival: results of a multi-country evaluation of Integrated Management of Childhood Illness. Health policy and planning. 2005;20(suppl_1):i5-i17.

24. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Child, Reproductive, & Adolescent Health (MCRAH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

25. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Neonatal, Child, & Adolescent Health (MNC&AH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

26. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2017. Dhaka, Bangladesh; 2019.

27. World Health Organization. Integrated Management of Childhood Illness: Global Survey Report. 2017.

28. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. Health, Population and Nutrition Sector Development Program (2011-2016) (HPNSDP): Project Implementation Plan (PIP). Dhaka: Government of Bangladesh; 2011.

29. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. Bangladesh Essential Service Package (BESP). Dhaka; 2016.

30. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet: World Health Organization; 2014.

31. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. Health, Nutrition and Population Sector Program (2017-2022) (HPNSP): Project Implementation Plan (PIP). 2017.

32. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet. Geneva: World Health Organization,; 2008.

33. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. Integrated Management of Childhood Illness (IMCI)-Chart Booklet Bangladesh Adapted Version. Dhaka: Government of Bangladesh; 2009.

34. World Health Organization. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care. 2012.

35. World Health Organization. Revised WHO classification and treatment of pneumonia in children at health facilities: evidence summaries. 2014.

36. Boonstra E, Lindbæk M, Ngome E. Adherence to management guidelines in acute respiratory infections and diarrhoea in children under-5 years old in primary health care in Botswana. International Journal for Quality in Health Care. 2005;17(3):221-7.

37. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet. 2014.

38. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. Integrated Management of Childhood Illness (IMCI)-Chart Booklet Bangladesh Adapted Version. Dhaka: Government of Bangladesh; 2020.

39. World Health Organization. Guideline: Managing possible serious bacterial infection in young infants when referral is not feasiblele. 2015. Report No.: 9241509260.

40. Izudi J, Anyigu S, Ndungutse D. Adherence to Integrated Management of Childhood Illnesses Guideline in Treating South Sudanese Children with Cough or Difficulty in Breathing. International journal of pediatrics. 2017;2017.

41. Rahman AE, Herrera S, Rubayet S, Banik G, Hasan R, Ahsan Z, et al. Managing possible serious bacterial infection of young infants where referral is not possible: Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. PloS one. 2020;15(5):e0232675.

42. Rahman AE, Iqbal A, Hoque DE, Moinuddin M, Zaman SB, Rahman QS-u, et al. Managing Neonatal and Early Childhood Syndromic Sepsis in Sub-District Hospitals in Resource Poor Settings: Improvement in Quality of Care through Introduction of a Package of Interventions in Rural Bangladesh. PloS one. 2017;12(1):e0170267.

43. Rahman AE, Hossain AT, Zaman SB, Salim N, Ashish K, Day LT, et al. Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy childbirth. 2021;21(1):1-17.

44. Billah SM, Hoque DE, Rahman M, Christou A, Mugo NS, Begum K, et al. Feasibility of engaging "Village Doctors" in the Community-based Integrated Management of Childhood Illness (C-IMCI): experience from rural Bangladesh. Journal of global health. 2018;8(2).

45. Pandya H, Slemming W, Saloojee H. Health system factors affecting implementation of integrated management of childhood illness (IMCI): qualitative insights from a South African province. Health Policy and Planning. 2018;33(2):171-82.

46. Mason E, Scherpbier R, Lawe-Davies O. WHO position statement on IMCI. The Lancet. 2009;374(9692):782-3.

47. Huicho L, Dávila M, Campos M, Drasbek C, Bryce J, Victora CG. Scaling up integrated management of childhood illness to the national level: achievements and challenges in Peru. Health policy and planning. 2005;20(1):14-24.

48. Pariyo GW, Gouws E, Bryce J, Burnham G. Improving facility-based care for sick children in Uganda: training is not enough. Health policy and planning. 2005;20(suppl_1):i58-i68.

49. Huda TM, Tahsina T, El Arifeen S, Dibley MJ. The importance of intersectoral factors in promoting equity-oriented universal health coverage: a multilevel analysis of social determinants affecting neonatal infant and under-five mortality in Bangladesh. Global health action. 2016;9:29741.

50. Målqvist M, Singh C, Kc A. Care seeking for children with fever/cough or diarrhoea in Nepal: equity trends over the last 15 years. Scandinavian Journal of Public Health. 2017;45(2):195-201.

51. Humphreys D, Kalyango JN, Alfven T. The impact of equity factors on receipt of timely appropriate care for children with suspected malaria in eastern Uganda. 2020.

52. National Institute of Population Research and Training (NIPORT), ICF International. Bangladesh Demographic and Health Survey 2017-18: Key indicators. Dhaka, Bangladesh, and Rockville, Maryland, USA; 2019.

53. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.

54. Reed C, Madhi SA, Klugman KP, Kuwanda L, Ortiz JR, Finelli L, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One. 2012;7(1):e27793.

55. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.

56. Ginsburg AS, Van Cleve WC, Thompson MI, English M. Oxygen and pulse oximetry in childhood pneumonia: a survey of healthcare providers in resource-limited settings. Journal of tropical pediatrics. 2012;58(5):389-93.

57. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

58. World Health Organization. Oxygen therapy for children. 2016.

59. Duke T, Mgone J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea [oxygen therapy in children]. The International Journal of Tuberculosis and Lung Disease. 2001;5(6):511-9.

60. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.

61. Graham H, Tosif S, Gray A, Qazi S, Campbell H, Peel D, et al. Providing oxygen to children in hospitals: a realist review. Context. 2017;95(4).

Chapter 7: PROCESS OF INTEGRATING PULSE OXIMETRY IN THE NATIONAL IMCI IMPLEMENTATION PACKAGE

One of my general objectives was to assess the feasibility of introducing pulse oximetry in routine IMCI services. The specific research question 5 was to assess the process of integrating pulse oximetry in the national IMCI implementation package of pulse oximetry for managing childhood pneumonia in Bangladesh.

Table 7.1: General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

The work presented in the chapter 7 was published in The Journal of Global Health in 2022.

Title: Introducing pulse oximetry in routine IMCI services in Bangladesh: a context-driven approach to influence policy and programme through stakeholder engagement

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URL: https://jogh.org/2022/jogh-12-06001

7.1 ABSTRACT

7.1.1 Background

Pneumonia is the leading cause of under-5 child deaths globally and in Bangladesh. Hypoxaemia or low (<90%) oxygen concentration in the arterial blood is one of the strongest predictors of child mortality from pneumonia and other acute respiratory infections. Since 2014, the World Health Organization recommends using pulse oximetry devices in IMCI services (outpatient child health services), but it was not routinely used in most health facilities in Bangladesh until 2018. This paper describes the stakeholder engagement process embedded in an implementation research study to influence national policy and programmes to introduce pulse oximetry in routine IMCI services in Bangladesh.

7.1.2 Methods

Based on literature review and expert consultations, we developed a conceptual framework, which guided the planning and implementation of a 4-step stakeholder engagement process. Desk review, key informant interviews, consultative workshops and onsite demonstration were the key methods to involve and engage a wide range of stakeholders. In the first step, a comprehensive desk review and key informant interviews were conducted to identify stakeholder organisations and scored them based on their power and interest levels regarding IMCI

implementation in Bangladesh. In the second step, two national level, two district level and five sub-district level sensitisation workshops were organised to orient all stakeholder organisations having high power or high interest regarding the importance of using pulse oximetry for pneumonia assessment and classification. In the third step, national and district level high power-high interest stakeholder organisations were involved in developing a joint action plan for introducing pulse oximetry in routine IMCI services. In the fourth step, led by a formal working group under the leadership of the Ministry of Health, we updated the national IMCI implementation package, including all guidelines, training manuals, services registers and referral forms in English and Bangla. Subsequently, we demonstrated its use in real-life settings involving various levels of (national, district and sub-district) stakeholders and worked alongside the government leaders towards carefully resuming activities despite the COVID-19 pandemic.

7.1.3 Results

Our engagement process contributed to the national decision to introduce pulse oximetry in routine child health services and update the national IMCI implementation package demonstrating country ownership, government leadership and multi-partner involvement, which are steppingstones towards scalability and sustainability. However, our experience clearly delineates that stakeholder engagement is a context-driven, time-consuming, resource-intensive, iterative, mercurial process that demands meticulous planning, prioritisation, inclusiveness, and adaptability. It is also influenced by the expertise, experience, and positionality of the facilitating organization.

7.1.4 Conclusion

Our experience has demonstrated the value and potential of the approach that we adopted for stakeholder engagement. However, the approach needs to be conceptualised coupled with the allocation of adequate resources and time commitment to implement it effectively.

7.2 BACKGROUND

Pneumonia is the leading cause of childhood mortality, accounting for around 16% of 5.2 million under-5 deaths globally (1-3). In addition to mortality, childhood pneumonia contributes significantly to the global burden of disease through morbidities and long-term complications (4, 5). Moreover, most of these deaths and morbidities occur in low- and middle-income countries (LMICs) (1, 2). In Bangladesh, childhood pneumonia causes approximately 24,300 deaths per year, making it the leading cause of death in children younger than five years (6, 7).

Hypoxaemia, defined by low (<90%) oxygen saturation in the arterial blood, is common among children with pneumonia and is one of the strongest predictors of mortality caused by pneumonia and other lower acute respiratory tract infections (8-12). Early identification of hypoxaemia and timely administration of oxygen therapy can avert a significant portion of hypoxaemia-related deaths (8, 10). Pulse oximetry is an easy, non-invasive, and low-cost procedure used to measure and monitor the oxygen saturation level of arterial blood (SpO_2) (13). In high-income countries, pulse oximetry device is almost universally available as a standard for paediatric care but is rarely available and used in LMICs, particularly in routine outpatient services (11). However, in 2014, the World Health Organization (WHO) revised its guidelines for routine outpatient services, i.e., Integrated Management of Childhood Illness (IMCI), recommending the introduction and use of pulse oximetry in the early detection of hypoxaemia and referral decisions even in low-resource settings (12, 14-16).

Bangladesh was one of the sites in the Multi-Country Evaluation of IMCI coordinated by WHO (17). Based on the evidence generated from this study and global recommendations, the Government of Bangladesh adopted the IMCI strategy in 1998 as its primary approach to delivering outpatient-based services for sick children, including those with pneumonia. A decade later, by 2008, health facility-based IMCI was scaled up in all 64 districts and 420 of the 483 sub-districts (locally known as Upazilas) (18). However, despite this progress, the use of pulse oximetry was still not recommended in routine IMCI services until 2018, as the assessment for pneumonia was primarily based on clinical history taking and physical examinations (19). Therefore, an implementation research study was initiated in 2018 to assess the feasibility of introducing pulse oximetry in routine IMCI services in Bangladesh. The National Newborn Health and IMCI Programme of the Ministry of Health and Family Welfare led the study with technical support and facilitation from icddr,b (an international health research institute based in Bangladesh, which was formally known as International Centre for Diarrhoeal Disease Research, Bangladesh), and funding from the NIHR Global Health Research Unit on Respiratory Health (RESPIRE) through the University of Edinburgh, UK (20, 21). The implementation research was conducted in one district hospital, five sub-district hospitals (locally known as the Upazila Health Complexes) and five primary care health centres (locally known as Union Health and Family Welfare Centres) in Kushtia, a rural district in Bangladesh. The National Newborn Health and IMCI Programme in consultation with icddr,b selected Kushtia as the demonstration site as the under-5 and neonatal mortality rates of the district were close to the average national estimates (22). The objective

of the study was to incorporate the recommendations for using pulse oximetry in routine IMCI services in national policy and programme documents, and assess the usability, acceptability, fidelity and utility based on WHO's implementation research guideline (23).

Engaging a wide range of stakeholders is a key step for ensuring the relevance of research studies and improving the utilisation of research findings in local health systems settings (24, 25). As a result, health research funding agencies are increasingly promoting stakeholder engagement as an important step towards achieving impact (26). Unfortunately, there is a dearth of evidence regarding the process of conceptualization, planning, implementation as well as mitigating challenges associated with stakeholder engagement in real-life settings. One of the main objectives of our implementation research was to promote context-specific solutions to implementation, participatory approach, government leadership, country ownership, scalability and sustainability by engaging key stakeholders at every stage of design, development, implementation and decision-making (25). In this paper, we describe the rationale, strategy and process of influencing the policy and programme through a context-driven stakeholder engagement approach.

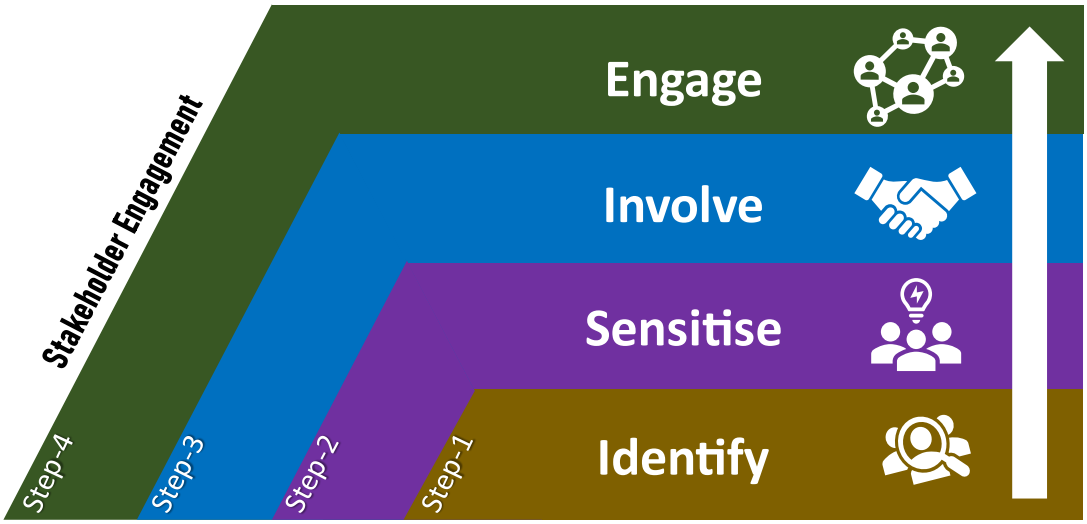
7.3 METHODS

7.3.1 Study design

Stakeholders are individuals, organisations, or communities that can influence or are affected by a project's process and outcomes, research or policy (27). Stakeholder engagement is an iterative process of actively soliciting interested and influential

individual's knowledge, experience, and values to create a shared understanding, mutually agree on outcomes, and make relevant, transparent, and effective decisions. Essentially, a bi-directional relationship between the stakeholders and the researchers results in informed decision-making about the prioritisation, implementation, and use of research findings (28). The literature on stakeholder engagement in health research points towards various processes and approaches, primarily derived from priorities, opportunities and contexts (24, 28-30). Guided by the literature, consultations with policymakers and experts, and based on practical experiences in implementing development projects in the context of Bangladesh, we adapted a conceptual framework to guide the stakeholder engagement related activities in our study (Figure 7.1). This framework proposes four steps. **Step-1:** Identification and prioritisation of stakeholders for subsequent sensitisation, involvement and engagement. **Step-2:** Sensitising the majority of stakeholders regarding the context, rationale, importance and process of the proposed research to build interest, confidence and trust. **Step-3:** Involving key stakeholders in planning, ensuring agreement regarding the implementation process and solidifying commitments for shared responsibilities. **Step-4:** Engaging the stakeholders at every stage of design, development, implementation and evaluation.

Figure 7.1: Conceptual framework adapted to guide the stakeholder engagement process to integrating pulse oximetry in routine IMCI services in Bangladesh



Step 1: Identifying stakeholders for sensitisation, involvement, and engagement

In Bangladesh, health services are provided by two directorates under the Ministry of Health and Family Welfare. They are the Directorate General of Health Services and Directorate General of Family Planning. Each directorate has a dedicated programme for child health, which manages the child health services, including IMCI services in Bangladesh. In addition, several other programmes are also related to child health services. Besides the government programmes, several development partners and professional societies support the Government of Bangladesh in managing and implementing child health services, including IMCI services. The National Newborn Health and IMCI Programme under the Directorate General of Health Services of the Ministry of Health and Family Welfare is responsible for coordinating with all partners and ensuring the delivery of IMCI services in Bangladesh.

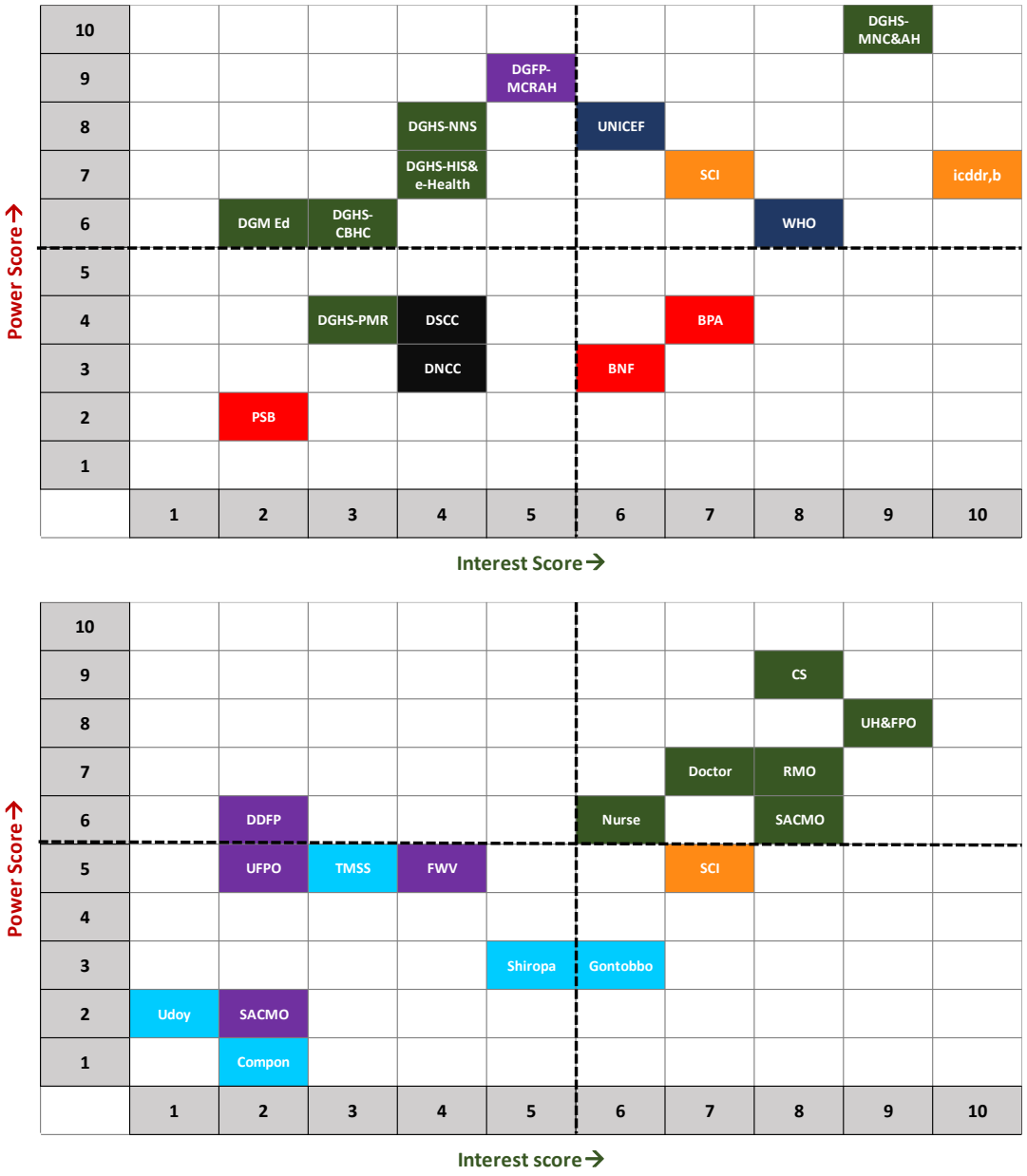
First, comprehensive desk review was conducted on IMCI related documents and eight key informant interviews to identify national and district level stakeholders related to IMCI implementation in Bangladesh (Supplementary table 7.1 and 7.2). We purposively selected the key informants based on their former and current involvement with the IMCI programme in Bangladesh. After reaching reasonable level of data saturation, we identified 16 national-level and 16 district-level stakeholder organisations ranging from government health programmes, professional societies, UN agencies, local, national, and international non-government organisations (NGO), health service providers, etc. As Kushtia was our demonstration district, we identified the IMCI related stakeholder organisations exclusively working in Kushtia district.

We primarily focused on influencing the policy and guidelines to introduce and integrate pulse oximetry in routine IMCI services in Bangladesh. We also wanted to maximise the use of limited resources by prioritising a few stakeholder organisations that we would engage with. Hence, we organised a consultative workshop with the Programme Manager and all of the five Deputy Programme Managers of the National Newborn Health and IMCI Programme, where we used the Power-Interest matrix for stakeholder prioritisation (31).

At the workshop, the participants scored each stakeholder organisation on their level of power and interest regarding IMCI implementation in Bangladesh based on a 10-point Likert scale where one was regarded as the lowest and ten was considered the highest (Supplementary table 7.3) (32). We then plotted each stakeholder

organisation (identified through desk review and key informant interview) in the Power-Interest matrix based on their average scores allotted by the workshop participants (Figure 7.2). Any stakeholder organisation with an average interest score of 6 and above was considered to have high interest. Similarly, any stakeholder organisation having an average power score of 6 and above was considered to have high power. Thus, of the 16 stakeholder organisations identified at the national level, five were categorised in the high power-high interest group, five in the high power-low interest and two low power-high interest groups, while four stakeholders were classed into the low power-low interest group. The 16 district-level stakeholder organisations were categorised similarly, with six prioritised as having high power-high interest. We decided to inform (described in step 2) all the stakeholders with high power or high interest but focus our attention on stakeholders with high power-high interest during the involve (described step 3) and engage (described in step 4) phases.

Figure 7.2: Power-Interest mapping of national and district level stakeholder organisations related to IMCI implementation in Bangladesh



BNF-Bangladesh Neonatal Federation, **BPA**-Bangladesh Pediatric Association, **PSB**- Perinatal Society of Bangladesh, **DGFP-MCRAH**- Directorate General of Family Planning- Maternal, Child, Reproductive and Adolescent Health, **DGHS-CBHC**- Directorate General of Health Services-Community Based Health Care-Operational Plan, **DGHS-HIS& e-Health**- Directorate General of Health Services- Health Information System and e-Health- Operational Plan, **DGHS-MNC&AH**- Directorate General of Health Services-Maternal Newborn Child and Adolescent Health, **DGHS-NNS**- Directorate General of Health Services-National Nutrition Services- Operational Plan, **DGHS-PMR**- Directorate General of Health Services-Planning, Monitoring and Research- Operational Plan, **SCI**- Save the Children, **UNICEF**- United Nations International Children's Emergency Fund, **WHO**- World Health Organization, **DNCC**- Dhaka North City Corporation, **DSCC**- Dhaka South City Corporation, **DGMEd**- Directorate General of Medical Education, **icddr,b**- International Centre for Diarrhoeal Disease Research **CS**-Civil Surgeon, **DDFP**-Deputy Director Family Planning, **FWV**-Family Welfare Visitor, **RMO**-Residential Medical Officer, **SACMO**- Assistant Community Medical Officer, **TMSS**- Thengamara Mohila Sobuj Sangha, **UFPO**- Upazila Family Planning Officer, **UH&FPO**- Upazila Health and Family Planning Officer.

Directorate general of health services
Directorate general of family planning
Professional body
City corporation

UN organization
National/ International NGO
Local NGO

Step 2: Sensitising stakeholders for awareness building and understanding

Two sensitisation workshops were conducted with national-level stakeholders prioritised in the previous step. In the first workshop, we invited 40 participants from stakeholder organisations representing the high power-high interest, high power-low interest, and high interest-low power groups. The Programme Manager of the National Newborn Health and IMCI Programme chaired the workshops to promote country ownership and government leadership. In the first workshop, the research team of icddr,b presented the burden of hypoxaemia among children suffering from pneumonia, the importance of using pulse oximetry in hypoxaemia assessment and the updated WHO recommendation for introducing pulse oximetry in routine assessment and classification of pneumonia. In the second workshop, the invitation was limited to 19 participants from five organisations representing the high power-high interest group (14, 15, 33, 34). The participants discussed both the technical and operational feasibility of introducing pulse oximetry in routine IMCI services in Bangladesh.

A sensitisation workshop was conducted in Kushtia, with 32 participants from all district level stakeholder organisations, including the district health manager (locally known as Civil Surgeon, i.e. CS), district level family planning manager (locally known as Deputy Director Family Planning, i.e. DDFP), all (five) sub-district health managers (locally known as Upazila Health and Family Planning Officers, i.e. UH&FPO) and all sub-district level family planning managers (Upazila Family Planning Officers, i.e. UFPO). In addition, managers from the National Newborn Health and IMCI Programme attended the event. They presented the importance of identifying

hypoxaemia in pneumonia assessment and classification and discussed the operational feasibility of introducing pulse oximetry in real-life settings.

Subsequently, we organised five such sensitisation workshops in each sub-district, with 14 participants in each workshop, including IMCI service providers such as doctors, nurses and paramedics (locally known as Sub-assistant Community Medical Officers, i.e., SACMO) and their respective supervisors. For each sub-district level workshop, the respective sub-district health managers gave the keynote presentation.

Lastly, 71 enlisted national and local level NGOs actively working in Kushtia district were identified, of which 21 had strong community acceptance and health-related activities. We organised another sensitisation workshop with representatives from these 21 organisations. The district health manager gave the keynote presentation, and all the sub-district managers contributed to the subsequent discussions. All participating NGO partners agreed to raise awareness regarding pneumonia and hypoxaemia and promote appropriate care-seeking practices in the local communities.

Step 3: Involving stakeholders in joint planning and sharing responsibilities

Like the previous sensitisation phase, we organised workshops at the national, district, and sub-district levels to involve stakeholder organisations representing the high power and high-interest group, discuss a strategy, and develop a mutually agreed plan for introducing pulse oximetry in routine IMCI services of Bangladesh. At the national level, the Programme Manager of the National Newborn Health and

IMCI Programme chaired the workshop. All the participants discussed and developed a national action plan to introduce pulse oximetry in routine IMCI services in Bangladesh. The roles of all key stakeholder organisations were clarified and defined in this comprehensive action plan. The National Newborn Health and IMCI Programme agreed to lead this process, and WHO, UNICEF, Save the Children and icddr,b committed to providing technical assistance and implementation support. The National Newborn Health and IMCI Programme also decided to update the National IMCI Implementation Package based on the updated WHO recommendations, including introducing pulse oximetry in pneumonia assessment and classification. This National IMCI Implementation Package consists of guidelines, registers, referral forms, reporting forms, job aids, monitoring checklist, list of essential equipment, medicine and logistics and training manuals. It was also decided that the development partners will be initially responsible for the procurement and supply of pulse oximetry devices in some demonstration facilities. The National Newborn Health and IMCI Programme declared to include pulse oximeters in the national procurement plan if the demonstration is successful.

A small working group was formed with technical experts from each stakeholder organisation with high power-high interest to update the implementation package. The small working group recommended assessing the feasibility of implementing the updated implementation package (including pulse oximetry) through an implementation research study. icddr,b volunteered to lead this implementation research study in Kushtia district. The working group members identified the evidence gaps and finalised key research questions for the implementation research

through a consultative process. Further, at this workshop, it was also decided that the experience gathered through this implementation research would assist the Government of Bangladesh in taking evidence-based decisions for a national scale-up.

A planning workshop was organised in Kushtia district headquarter, which was chaired by the district health manager and attended by all sub-district health managers. At this workshop, the participating stakeholders decided that the implementation research would include all types of health facilities providing IMCI services. Hence, the Kushtia District Hospital, all five Upazila Health Complexes and one Union Health and Family Welfare Centre from each sub-district were selected as demonstration sites for the implementation research study. A district-level action plan was jointly developed outlining the roles of different district level stakeholders and the key activities, including training, distribution of pulse oximetry device, revised IMCI registers, referral forms and reporting forms, supportive supervision visits and assessments. Subsequently, a planning workshop was organised in each sub-district with the supervisors of IMCI service providers. The respective sub-district managers chaired this event and shared guidance on developing a sub-district level implementation plan for introducing pulse oximetry. A preparatory and planning meeting followed in each demonstration facility with IMCI service providers, respective supervisors, and facility managers, leading to the finalisation of a facility-specific implementation plan (with a timeline) to introduce pulse oximetry minimally impacting their routine services and existing practices.

Step 4: Engaging stakeholders in design, development, and implementation

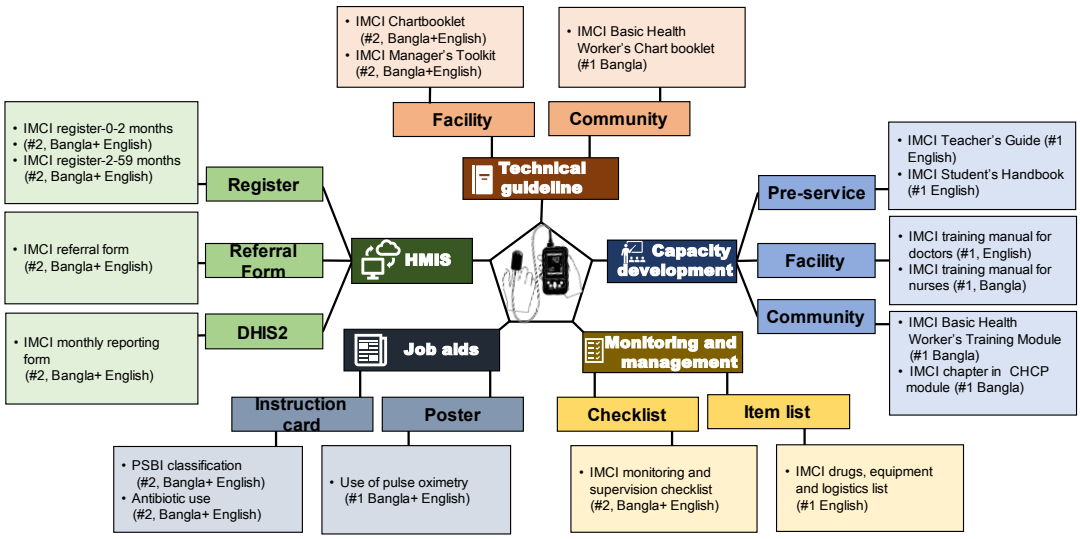
In this stage, National Newborn Health and IMCI Programme and icddr,b worked closely with the high power-high interest stakeholders on the following steps to update the IMCI implementation package and implement it in the demonstration facilities in real-life settings.

i. ***Formation of a working group:*** The Line Director of Maternal, Newborn, Child and Adolescent Health Programme of the Ministry of Health and Family Welfare formed a small working group with 13 IMCI experts representing the five high power-high interest groups to review and update the National IMCI Implementation Package (Supplementary table 7.4). The Programme Manager of the National Newborn Health and IMCI Programme chaired this group and icddr,b provided secretarial support. The group agreed to review the current availability of pulse oximetry devices in public health facilities and the overall oxygen delivery system in the country in addition to incorporating the recommendations and instruction to use pulse oximetry in the national IMCI implementation package.

ii. **Updating the National IMCI Implementation Package:** The working group reviewed the National IMCI Implementation Package, which was based on the previous WHO guideline in 2009 and compared them with the updated WHO guidelines in 2014 (15, 35) (Supplementary table 7.5). In addition to the new guidance on using pulse oximetry in pneumonia assessment and classification, WHO recommended other major changes in the assessment,

classification and management of possible serious bacterial infection (among children aged 0-59 days), pneumonia (among children aged 2-59 months), diarrhoea, dehydration and malnutrition. The working group discussed these changes and decided to incorporate them in the national IMCI guidelines based on the country context, rationale, and operational feasibility. Based on these decisions, the working group also updated the national IMCI chart booklet of Bangladesh. The key changes that are incorporated in the National IMCI chart booklet and summarised in Supplementary table 7.6. Subsequently, relevant training manuals were updated for IMCI services providers (doctors, nurses, and paramedics), community health workers and medical students (pre-service training). The working group also updated the IMCI-related service register, referral form, reporting form and job aids. Additional implementation materials such as the essential list of IMCI-related equipment, drugs and logistics, and monitoring checklists were also updated. All the National IMCI Implementation Package documents were developed in English and Bangla (the official language of Bangladesh). It took the working group a total of thirteen meetings (each lasting from three to five hours) to review and update all the documents in the IMCI implementation package (Figure 7.3).

Figure 7.3: Documents in the National IMCI Implementation Package updated to incorporate the recommendation for using pulse oximetry in routine IMCI services



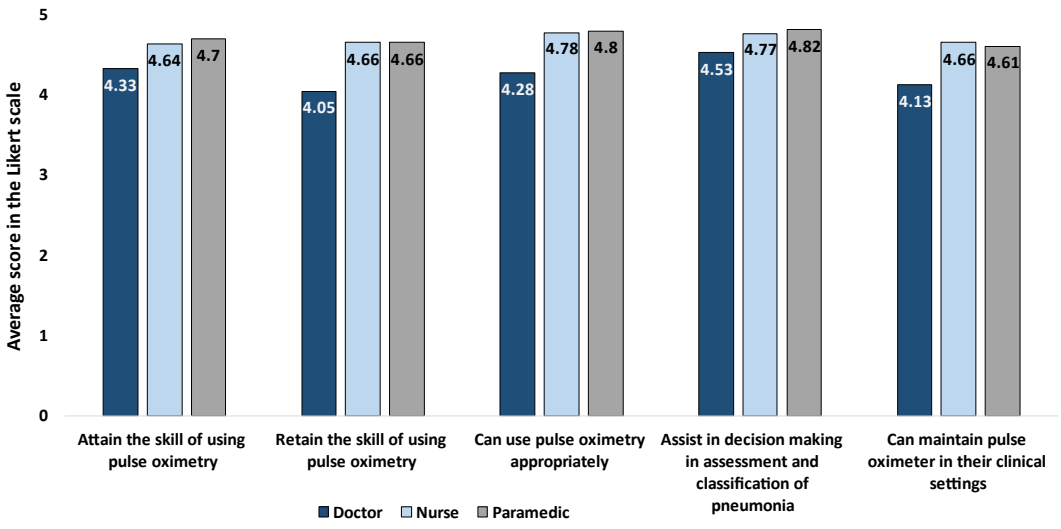
DHIS- DistrictHealth Information System, **HMIS**- Health Management Information System, **PSBI**- PossibleSerious BacterialInfection, **CHCP**- Community Health Cre Provider

iii. **Orientation training of national IMCI master trainers and pre-testing with IMCI service providers:** We organised a workshop to orient the national IMCI master trainers to the updated National IMCI Implementation Package, including the use of pulse oximetry in pneumonia assessment and classification. The master trainers reviewed the updated documents (primarily the chart booklet and training manuals) and shared their feedback.

Afterwards, the updated training package was pre-tested among IMCI service providers, including doctors, nurses, and paramedics. The National Newborn Health and IMCI Programme organised the training, the national master trainers facilitated the sessions, and icddr,b conducted assessment and evaluations. A total of 40 doctors, 91 nurses and 67 paramedics received training in 10 batches. We collected feedback from the IMCI providers on the

National IMCI Implementation Package, including the training manuals, registers, job aids and reporting forms. Figure 7.4 shows the response of the IMCI service providers regarding the perceived importance, acceptance and confidence of using pulse oximetry in a five-point Likert scale, which were collected after the end of the training. The average Likert scale score was more than four across all response categories. We also did not find any significant difference (ANOVA test) across the three types of providers for any of the response categories.

Figure 7.4: Response of IMCI service providers regarding perceived importance, acceptance and confidence of conducting pulse oximetry assessments after receiving training with the updated implementation package; presented in average score in a five-point Likert scale, doctors=40, nurses =91, paramedics=67



Likert scale scoring: 1= Strongly disagree, 2= Disagree, 3= Neither agree nor disagree, 4= Agree, 5= Strongly agree

iv. **Finalisation of the National IMCI Implementation Package:** Following the training workshops with master trainers and IMCI service providers, the working group updated the national implementation package based on their feedback. Then National Newborn Technical Working Committee for Newborn Health and the National IMCI Technical Working Committee, the highest-level technical committees regarding newborn and child health in

Bangladesh, reviewed the updated package and shared feedback. The National IMCI Implementation Package was finalised after incorporating their feedback and inputs.

v. **Incorporation of the use of pulse oximetry and hypoxaemia in the national health service records:** Over a series of six consultative workshops, the National Newborn Health and IMCI Programme convinced the Management Information System (MIS) department of the Directorate General of Health Services to update the national IMCI dataset (maintained in the national DHIS2) based on the updated monthly reporting form (including updated pneumonia classification and hypoxaemia status). icddr,b provided technical assistant and secretarial support in organising these events.

vi. **Involving national-level stakeholders in the implementation research:** A co-design and co-creation approach was adopted to develop the implementation research protocol. icddr,b led the process and engaged the National Newborn Health and IMCI Programme and other stakeholder organisations representing the high-power and high-interest group to prioritise research questions and finalise the research design, data collection methods, and data collection instruments. Additionally, one of the Deputy Programme Managers of the National Newborn Health and IMCI Programme joined the research team as a Co-Investigator.

vii. **Local-level involvement in the implementation research:** A district advisory committee was formed to guide the implementation research study in Kushtia-district. The district health manager chaired the committee, and all the sub-district level health managers were included as members. First, the advisory committee was oriented regarding the research questions and study design. Later, the committee developed a macro plan to introduce pulse oximetry in the selected facilities and conduct quantitative and qualitative assessments as outlined in the research protocol. Subsequently, a planning meeting was organised in each facility with respective IMCI

service providers and their supervisors to review the macro plan and develop a micro plan with a timeline. A dissemination meeting was organised with the district advisory committee after the baseline and each round of data collection. icddr,b provided technical assistance and secretarial support throughout the process.

viii. **Resuming study activities during the COVID-19 pandemic:** The Government of Bangladesh declared a nationwide lockdown in the last week of March 2020 to prevent the surge of COVID-19 infections and deaths. Unfortunately, all the implementation research-related activities were suspended due to the strict restrictions imposed during the lockdown period. In August 2020, the government started to reduce restrictions. The National Newborn Health and IMCI Programme issued an official order to resume the research activities with appropriate infection prevention and control measures. A series of meetings were organised in Kushtia-district with the district health manager and sub-district health managers to resume the suspended activities and revise the implementation plan (both macro plan and micro plan) accordingly.

7.3.2 Resources required for stakeholder engagement

Desk Review: A total of 37 documents with approximately 2507 pages were reviewed to identify the stakeholders and update the National IMCI Implementation Package. It required around 120 person-days of effort by medical graduates with basic IMCI training.

Resource person interview: A total of eight interviews and a group discussion was organised with IMCI experts to identify and prioritise the stakeholder organisations, requiring ten person-hours for interviewing and an additional 30 person-hours for transcribing and analysis.

Document development, editing and formatting: The National IMCI Implementation Package containing 24 documents with 1685 pages were updated, which required approximately 140 person-days of reviewing, editing and formatting to prepare the final versions.

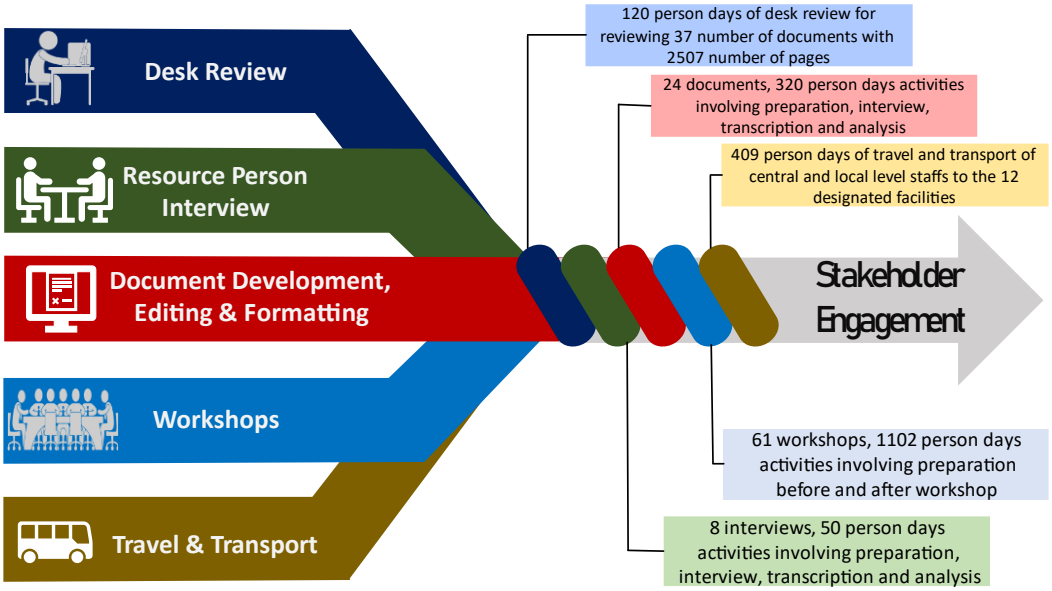
Workshops: At the national level, 30 workshops were organised to sensitise (step 2), involve (step 3) and engage (step 4) the stakeholders, requiring approximately 416 person-days of involvement by IMCI experts and stakeholders. In addition, about 42 person-days of investment was needed from icddr,b for taking preparation and organising the events. Furthermore, around 30 person-days was required to prepare and approve the meeting notes for official documentation.

At the district level, 45 meetings were organised, requiring approximately 183 person-days of involvement by IMCI service providers, 86 person-days by their clinical supervisors, and 101 person-days by district, sub-district and facility managers.

Travel and transport: To sensitise (step 2), involve (step 3) and engage (step 4) stakeholders at the district level, extensive travel and transport were required. A total of 97 person-days of travel and transportation were needed from central-level staff and 312 person-days from local-level staff to organise and participate in the stakeholder engagement related events

Figure 7.5 summarises the resource required for undertaking the above-mentioned stakeholder engagement related activities.

Figure 7.5: Resources required and invested for stakeholder engagement activities



7.3.3 Timeline

Step 1-Identify: This process began in October 2018 and continued till December 2018.

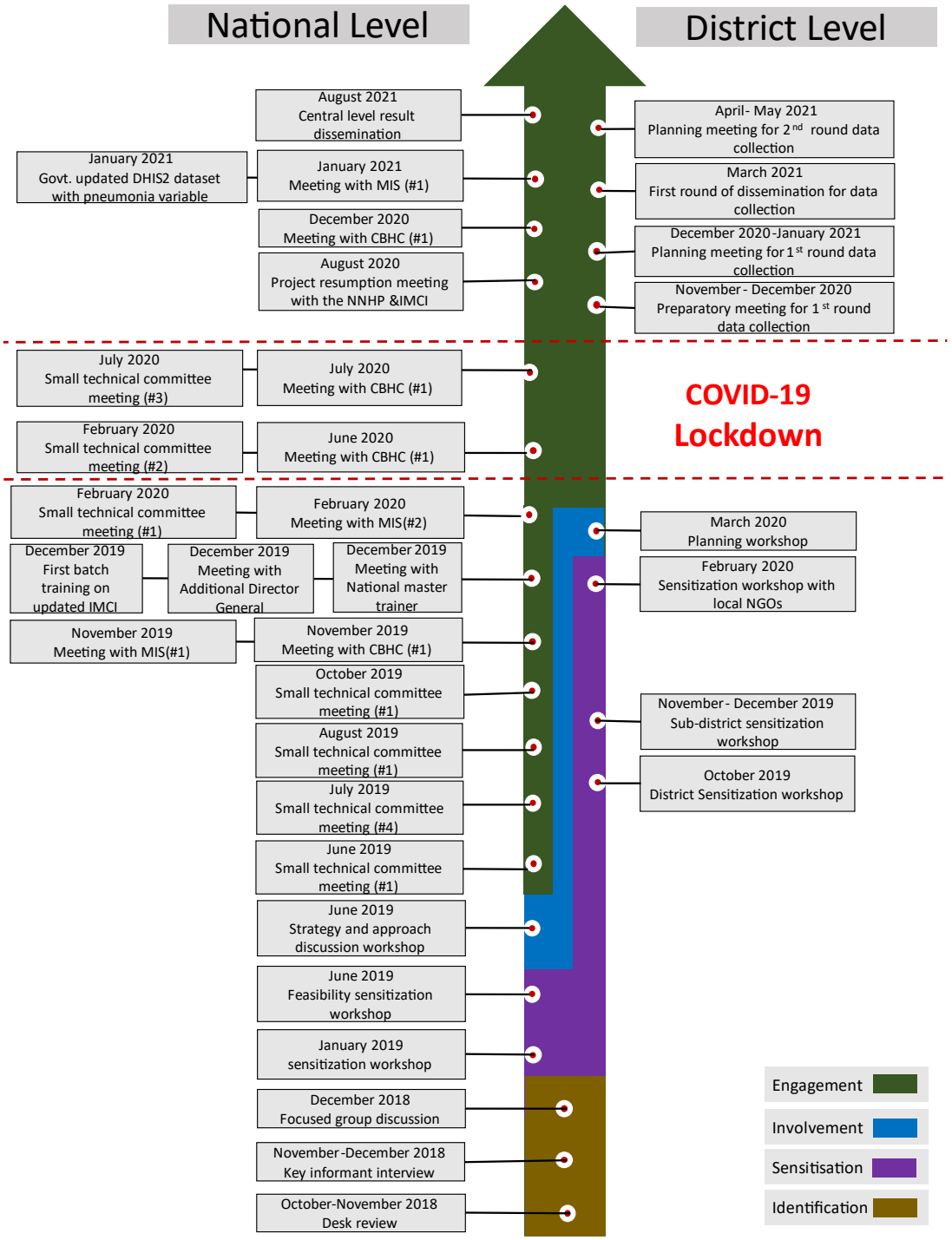
Step 2- Sensitise: At the national level, the sensitisation process started in January 2019 and continued till the end of that year, while at the district level, the sensitisation activities went on from October 2019 till February 2020.

Step-3-Involve: At the national level, the involvement process took place in June 2019 and at the district level, the process took place in March 2020.

Step 4-Engage: The national-level engagement process started in June 2019 and ended in January 2021. The district-level engagement process began in December 2020 and ended in July 2021.

Figure 7.6 presents the timeline of major stakeholder engagement related activities

Figure 7.6: Milestones and timeline of stakeholder engagement activities



DHIS2: District Health Information Software 2

MIS: Management Information System

NNHP&IMCI: National Newborn Health Program & Integrated Management of Childhood Illness

CBHC: Community Based Health Care

7.4 RESULTS

7.4.1 Impact of the stakeholder engagement process

CHANGE IN NATIONAL POLICY AND STRATEGY

The Government of Bangladesh and all the key stakeholders acknowledged the importance of identifying hypoxaemia through SpO_2 assessment for improving pneumonia assessment, classification, and management. As a result, the Government of Bangladesh decided to introduce pulse oximetry in routine IMCI services in Bangladesh.

CHANGE IN THE NATIONAL PROGRAMME

The National Newborn Health and IMCI Programme formed a national-level working committee with high power-high interest stakeholder organisations related to IMCI implementation in Bangladesh. This high-level working committee updated the National IMCI Implementation package including the chart booklet, register, referral form, reporting form, monitoring checklist and training manuals and incorporated specific recommendations to use pulse oximetry in relevant sections. Further, three hypoxaemia related indicators were included in the national IMCI dataset in DHIS2. The Government of Bangladesh trained 4872 IMCI service providers from across the country based on the updated National IMCI Implementation Package.

Progress towards scalability and sustainability

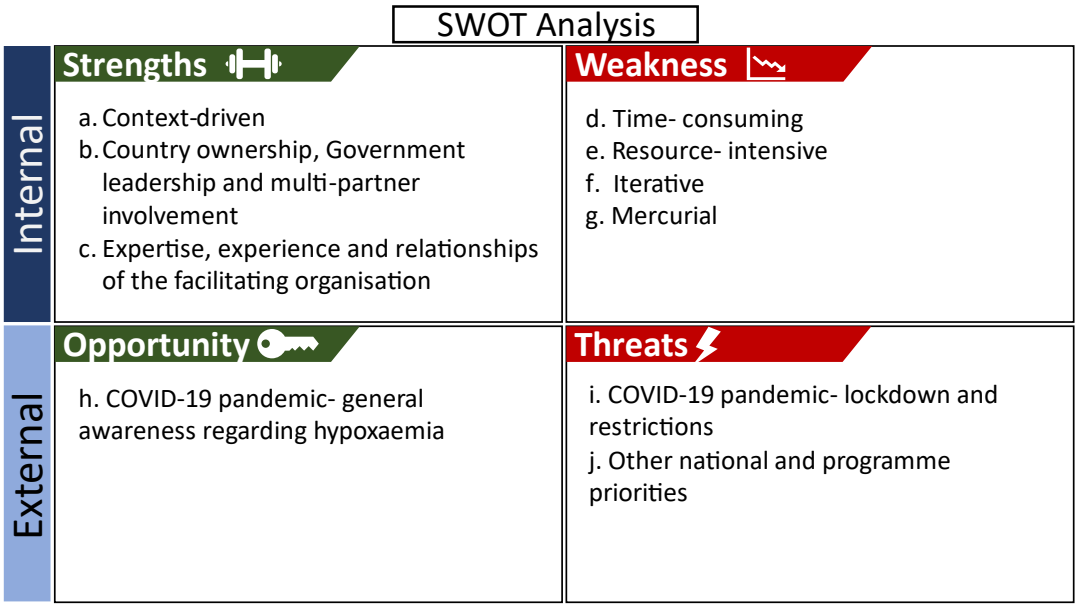
The Government of Bangladesh decided to scale up the use of pulse oximetry in routine IMCI services in a phased manner. As a result, the National Newborn Health

and IMCI Programme revised its existing plan and decided to procure pulse oximetry devices for the IMCI corners in approximately 200 Upazila health complexes. In the next phase, the National Newborn Health and IMCI Programme is planning to procure pulse oximetry devices for the remaining of the IMCI corners in the Upazila Health Complexes (approximately 250) and other union-level facilities (approximately 5000). Additionally, UNICEF has committed to support the Government of Bangladesh's national scale-up endeavour by introducing pulse oximetry in eight districts. icddr,b has committed to support in two districts, and Save the Children in one district. Moreover, WHO has supported the government by printing the updated IMCI registers for all facilities.

7.4.2 Lessons learned

We present the key learnings from the stakeholder engagement activities based on the SWOT analysis approach (36, 37). The summary of the SWOT analysis is presented in Figure 7.7.

Figure 7.7: Strength, weakness, opportunity, and threat analysis of the stakeholder engagement process



7.4.3 Strength

a. **Context-driven:** Our implementation research study primarily aimed to influence the national policy and programmes. Based on the context and prior experience, we adopted a framework with four steps for stakeholder engagement and prioritised only the high power-high interest stakeholder organisations. The framework guided the whole process and all related activities, and the prioritisation helped maximise the use of limited resources. Therefore, any implementation research study aiming to engage stakeholders need to adapt and modify the framework based on the objective and context.

b. **Country ownership, government leadership and multi-partner involvement:** The Government of Bangladesh demonstrated leadership in forming and leading the national working group, chairing the workshops,

developing the strategic plans, and bringing multiple partners together for building national consensus on introducing pulse oximetry in routine IMCI services in Bangladesh. All the major non-government organisations and development partners related to IMCI implementation in Bangladesh committed to using the updated National IMCI Implementation Package in their respective health system strengthening initiatives.

c. **Expertise, experience and relationships of the facilitating organisation:** The technical expertise and experience of icddr,b in the introduction and scale-up of IMCI services in Bangladesh and pre-existing relationships with other high power-high interest stakeholder organisations substantially contributed to the identification, sensitisation, involvement, and engagement of other high power-high interest stakeholder organisations. Moreover, the communication, and organising skills of icddr,b contributed to facilitating the stakeholder engagement process efficiently. Therefore, the positionality of implementing organisations needs to be considered before adopting a particular approach for engaging stakeholders.

7.4.4 Weakness

d. **Time consuming:** It took more than two and a half years to implement the stakeholder engagement related activities and achieve the objective of incorporating the use of pulse oximetry in national policy and programme. Numerous workshops were organised based on the availability of all high power-high interest stakeholders, which was difficult considering their busy

schedules, especially during ongoing COVID-19 pandemic. Extensive deskwork and preparations were necessary before organising these workshops, which called for several days or weeks of preparation. Hence, engaging the stakeholders effectively is time-consuming and will require patience and commitment by the facilitating organisation.

e. **Resource intensive:** The initial stage involved reviewing a significant number of documents to identify stakeholders and update the National IMCI Implementation Package, which required a substantial amount of person-time involvement of project staff. In addition, organising workshops at national, district and sub-district levels required numerous person-days of involvement from IMCI experts, managers, service providers and project staff. It also required extensive travelling by the project staff. Since stakeholder engagement is a resource-intensive process, it is important to have a planning and specific budgetary allocation for stakeholder engagement at the outset of any project.

f. **Iterative:** Reviewing, editing, and formatting several lengthy documents were essential for updating the National IMCI Implementation Package. Some of these documents required numerous rounds of editing and formatting to address and incorporate the feedback of all the stakeholders across the national, district and sub-district levels before finalisation. For example, IMCI chart booklet had 23 rounds of iteration and IMCI registers had 19 rounds of iteration before finalisation. Hence, the facilitating

organisation need to have dedication and attention to details to effectively steer the stakeholder engagement process.

g. **Mercurial:** The power-interest matrix of the stakeholders does not stay static and could change at any given time. For example, during the engagement process, one of the stakeholders with high power and low interest unexpectedly turned into a high power-high interest actor and started posing a risk to the process. Therefore, some part of the stakeholder engagement process was adapted based on the agenda of that particular stakeholder. In addition, during the stakeholder engagement process, there can be changes in leadership positions. For example, the National Newborn Health and IMCI Programme manager was changed twice, and the district health manager was changed three times during the engagement process, owing to administrative transfers. It required investing additional time and efforts to sensitise the new stakeholders and garnering their active buy-in to introduce pulse oximetry in routine IMCI services. Hence, stakeholder engagement is an adaptive process and will require flexibility in revising, updating and changing the plan based on the context and circumstances.

7.4.5 Opportunity

h. **COVID-19 pandemic- general awareness regarding hypoxaemia:** The COVID-19 pandemic has raised awareness among the health care provider and care receiver for using pulse oximetry in measuring the oxygen saturation level

and assessing the severity of pneumonia. This opportunity has facilitated the implementation process more easily.

7.4.6 Threats

i. **COVID-19 Pandemic- lockdown and restrictions:** The stakeholder engagement related activities and plans required extensive modification and revision due to the COVID-19 pandemic. During the first lockdown period between March and August 2020, all project-related activities were suspended. The team advocated with the National Newborn Health and IMCI Programme to resume project activities after the COVID-19 related restrictions were eased.

j. **Other national and programme priorities:** The engagement process and project-related activities were also interrupted by unanticipated events, such as implementing the national Measles-Rubella campaign, which kept the district and sub-district health managers and IMCI service providers occupied during February and March 2021. Therefore, the potential impact of an emerging threat on the overall outcome and timeline of the stakeholder engagement process must be acknowledged and should have the flexibility of modifying the plan to take course corrective measures.

7.5 CONCLUSION

Our experience has demonstrated the value and potential of the approach that we adopted for stakeholder engagement. Our engagement process contributed to the national decision to introduce pulse oximetry in routine IMCI services and update

the national implementation package, which are steppingstones towards scalability and sustainability. However, our experience also reveals that stakeholder engagement is a context-driven, time-consuming, resource-intensive, iterative, mercurial process that demands planning, prioritisation, inclusiveness and adaptability. It is also influenced by the expertise, experience and positionality of the facilitating organisation. However, the approach needs to be conceptualised coupled with the allocation of adequate resources and time commitment to replicate its impact and implement it effectively in other settings.

7.6 SUPPLEMENTARY MATERIALS

7.6.1 Supplementary tables

Supplementary table 7.1: List of documents reviewed for updating the IMCI implementation package

Si no	Name of the document	Number of pages
1.	IMCI chart booklet WHO 2014	80
2.	IMNCI Sick Young Infant chart booklet WHO 2019	36
3.	Bangladesh adopted IMCI chart booklet 2018	43
4.	IMCI training manual - 1. introduction	32
5.	IMCI training manual - 2. assess & classify	201
6.	IMCI training manual - 3. identify treatment	50
7.	IMCI training manual - 4. treatment	145
8.	IMCI training manual - 5. counselling	53
9.	IMCI training manual - 6. management of young infants aged up to 2 months	70
10.	IMCI training manual - 7. follow-up	54
11.	IMCI monthly reporting Form	1
12.	Case recording form (Age up to 2months)	2
13.	Case recording form (Age 2 months to 5 years)	2
14.	IMCI referral form	2
15.	IMCI teacher's guide – (English)	77
16.	IMCI student's handbook – (English)	180
17.	IMCI chart booklet for basic health workers (Bangla)	26
18.	IMCI training module for basic health workers (Bangla)	130
19.	IMCI manager's toolkit (Bangla)	88
20.	IMCI job aids (English)	6
21.	IMCI job aids (Bangla)	6
22.	Pre & post-test tools	2
23.	Supervision checklist	1
24.	Training schedule	4
25.	Community health care provider training module	328
26.	Operationalising management of sick young infants with possible serious bacterial infection (PSBI) when referral is not feasible in the context of existing maternal, newborn, and child health programmes	70
27.	WHO pulse oximeter	24
28.	WHO pocketbook	438
29.	WHO guideline for malaria treatment 2015	317
30.	Integrated Management of Childhood Illness (IMCI) in Bangladesh: early findings from a cluster-randomised study	7
31.	Community-based treatment of severe childhood pneumonia	2
32.	Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial	10
33.	Care at first-level facilities for children with severe pneumonia in Bangladesh: a cohort study	8
34.	Treating severe pneumonia in children: we can do better	1
35.	Reducing child mortality: can public health deliver?	5
36.	Treating severe pneumonia in children: we can do better	1
37.	Reducing child mortality: can public health deliver?	5

Supplementary table 7.2: List of interviewed informants, formerly and currently involved in the IMCI programme.

Sl no	Designation	Organisation
1.	Programme Manager, National Newborn Health Programme and IMCI	Directorate General of Health Services (DGHS)
2.	Ex-Programme Manager, National Newborn Health Programme and IMCI	Directorate General of Health Services (DGHS)
3.	Deputy Programme Manager, Training and child injury, National Newborn Health Programme and IMCI	Directorate General of Health Services (DGHS)
4.	Deputy Programme Manager, Newborn Health, National Newborn Health Programme and IMCI	Directorate General of Health Services (DGHS)
5.	National Professional Officer - Making Pregnancy Safer and Healthy Aging	World Health Organisation (WHO)
6.	Advisor, Pneumonia Sentinel Commitment (PCC) Project	Save the Children International (SCI)
7.	Health Specialist (Newborn Health)	UNICEF
8.	Senior Director and Senior Scientist, Maternal and Child Health Division	icddr,b

Supplementary table 7.3: List of acronyms for the Power matrix mapping figure (Figure- 7.2).

Sl no	Type	Acronym	Stakeholder	Power	Interest
1.	National	BNF	Bangladesh Neonatal Federation	6	3
2.	National	BPA	Bangladesh Paediatric Association	7	4
3.	National	PSB	Perinatal Society of Bangladesh	2	2
4.	National	DGFP-MCRAH	Directorate General of Family Planning-Maternal, Child, Reproductive and Adolescent Health	5	9
5.	National	DGHS-CBHC	Directorate General of Health Services-Community Based Health Care- Operational Plan	3	6
6.	National	DGHS-HIS& e-Health	Directorate General of Health Services- Health Information System and e-Health- Operational Plan	4	7
7.	National	DGHS-MNC&AH	Directorate General of Health Services-Maternal Newborn Child and Adolescent Health	9	10
8.	National	DGHS-NNS	Directorate General of Health Services-National Nutrition Services- Operational Plan	4	8
9.	National	DGHS-PMR	Directorate General of Health Services-Planning, Monitoring and Research-Operational Plan	3	4
10.	National	SCI	Save the Children	7	7
11.	National	UNICEF	United Nations International Children's Emergency Fund	6	8
12.	National	WHO	World Health Organization	8	6
13.	National	DNCC	Dhaka North City Corporation	4	3
14.	National	DSCC	Dhaka South City Corporation	4	4
15.	National	DGMEd	Directorate General of Medical Education	2	6
16.	National	icddr,b	International Centre for Diarrhoeal Disease Research	10	7
17.	District	CS	Civil Surgeon	8	9
18.	District	DDFP	Deputy Director Family Planning	2	6
19.	District	FWV	Family Welfare Visitor	4	5
20.	District	RMO	Residential Medical Officer	8	7
21.	District	SACMO	Sub-Assistant Community Medical Officer-DGHS	8	6
22.	District	SACMO	Sub-Assistant Community Medical Officer-DGFP	2	2
23.	District	TMSS	Thengamara Mohila Sobuj Sangha	3	5
24.	District	UFPO	Upazila Family Planning Officer	2	5
25.	District	UH&FPO	Upazila Health and Family Planning Officer	9	8
26.	District	Udoy	Local Non-Government Organisation	1	2
27.	District	Compon	Local Non-Government Organisation	2	1
28.	District	Shiropa	Local Non-Government Organisation	5	3
29.	District	Gontobbo	Local Non-Government Organisation	6	3
30.	District	Doctor	Local Non-Government Organisation	7	7
31.	District	Nurse	Local Non-Government Organisation	6	6
32.	District	SCI	Save the Children	7	5

Supplementary table 7.4: Team composition and terms of references of IMCI small working group.

Sl no	Designation	Organisation
1.	DPM, Monitoring and Data Quality, NNHP & IMCI	DGHS
2.	DPM, Training and Child Injury, NNHP & IMCI	DGHS
3.	DPM, Newborn Health, NNHP & IMCI	DGHS
4.	Focal Point, NNHP Cell, NNHP & IMCI, MNCAH	DGHS
5.	NPO-Making Pregnancy Safer and Healthy Aging	WHO
6.	Health Specialist	UNICEF
7.	Program Director, MAMONI MNCSP	Save the Children
8.	Advisor, MAMONI MNCSP	Save the Children
9.	Senior Scientist	icddr,b
10.	Associate scientist	icddr,b
11.	Deputy Project Coordinator	icddr,b
12.	Research Investigator	icddr,b
13.	Research Investigator	icddr,b

Supplementary table 7.5: List of the documents of IMCI implementation package

Sl no.	List of Documents	Number of Pages
1.	IMCI chart booklet (English)	52
2.	IMCI chart booklet (Bangla)	52
3.	IMCI register for 0- 59 days (English)	1
4.	IMCI register for 0-59 days (Bangla)	8
5.	IMCI register for 2 months - 5 years (English)	1
6.	IMCI register for 2 months - 5 years (Bangla)	7
7.	IMCI referral form (English)	1
8.	IMCI referral form (Bangla)	1
9.	IMCI monthly reporting form (English)	1
10.	IMCI monthly reporting form (Bangla)	8
11.	IMCI training manual (English)	428
12.	IMCI training manual (Bangla)	425
13.	IMCI monitoring and supervision checklist (English)	1
14.	IMCI monitoring and supervision checklist (Bangla)	1
15.	IMCI teacher's guide (English)	75
16.	IMCI student's handbook (English)	196
17.	IMCI manager's toolkit (English)	111
18.	IMCI manager's toolkit (Bangla)	101
19.	IMCI basic health worker's chart booklet (Bangla)	25
20.	IMCI basic health worker's training module (Bangla)	147
21.	IMCI chapter of CHCP training module (Bangla)	34
22.	IMCI job aids (English)	3
23.	IMCI job aids (Bangla)	3
24.	IMCI drugs, equipment and logistics list	3

Supplementary table 7.6: List of major changes in the updated IMCI chart booklet 2019 in Bangladesh

0-2 months of age		
1.	Integration of PSBI Classification	'Possible Serious Bacterial Infection (PSBI)' classification was merged with 'Very Severe Disease Classification' and a new 6 category classification given for **'Very Severe Diseases'**
2.	Update of injectable antibiotics regimen	• Omission of Injectable Ampicillin • Addition of Injectable Gentamicin in the treatment of ***'Very Severe Disease- Critical Illness', 'Very Severe Disease- Clinical Severe Illness'***, and ***'Very Severe Disease- Fast Breathing Pneumonia'*** • Reduction of Gentamycine 7 band doses in 3 ban doses based on the bodyweight of the children
3.	Update of oral antibiotics regimen	• Omission of Tablet Cotrimoxazole • Addition of dispersible tablet of oral Amoxicillin • Increase of Amoxicillin 2 band doses in 3 ban doses based on the bodyweight of the children
4.	Update the classification of Feeding Problem or Low Weight for Age	2 groups classification updated to 3 groups by addition of ***'Very Low Weight for Age'*** category to the Classification
5.	Addition of dehydration management for sick young infant	Addition of Plan A: Treat Diarrhoea at Home, Plan B: Treat Some Dehydration with Oral Rehydration Salt (ORS) and Plan C: Treat Severe Dehydration Quickly for young infant of 0-2 months
6.	Other changes	• Addition of follow-up schedule for PSBI classification • Update of the list of symptoms that requires an immediate return to the healthcare facility
2- 59 months of age		

1.	Update of Pneumonia classification	• ***'Very Severe Disease or Severe Pneumonia'***
		  ○ Addition of the sign 'Oxygen saturation (SpO_2) <90%'
		  ○ Dropping of 'chest indrawing'
		  ○ Addition of 'convulsing now' and 'hypoxia' in general danger sign
		• ***'Pneumonia'***
		  ○ Addition of the sign 'chest indrawing'

2.	Update of Pneumonia management	• The previous first line of treatment drug oral Cotrimoxazole has been replaced by Amoxicillin • Addition of bronchodilator and diazepam in the treatment of ***'Very Severe Disease or Severe Pneumonia'***
3.	Update the treatment of 'Very Severe Febrile Disease and Malaria'	• Omission of Injectable Quinine • Addition of Co-artemether therapy, Chloroquine and Primaquine in the Malaria treatment regime
4.	Other changes*	• Updated immunisation schedule in coordination with the national EPI schedule • Update of deworming treatment by integration of tablet Albendazole along with tablet Mebendazole and initiation of deworming program from 6 months of age instead of 1 year of age
** All updates are endorsed by the relevant Program of Directorate General of Health Services of Bangladesh*		

Supplementary table 7.7: Terms of Reference for the small technical working committee responsible to updating the national IMCI guidelines and implementation package

	Terms of reference
1.	To review the existing status of availability of pulse oximetry and oxygen delivery system in public hospitals and health facilities in Bangladesh.
2.	To review the existing IMCI Guideline, IMCI Training Manual and IMCI Case Recording Form of Bangladesh to identify areas for including instructions related to use of pulse oximetry in assessment, classification and management of pneumonia.
3.	To review the training manuals and instructions developed by WHO and other technical agencies on the use of pulse oximetry for assessment of SpO_2 among children.
4.	To develop an implementation toolkit for introduction of pulse oximetry in IMCI services in Bangladesh. The implementation toolkit will include the followings: • *Revised IMCI Guidelines* to use of SpO_2 status measured by pulse oximetry in pneumonia classification and management decisions • *Revised IMCI Training Manual* with instruction on the use of pulse oximetry and its maintenance. • *Revised IMCI Case Recording and Reporting Forms* to document and report SpO_2 status of children • Recommendations for integration of pulse oximetry in the national HMIS/*DHIS2*.

7.7 REFERENCE

1. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet. 2016;388(10063):3027-35.

2. World Health Organization. Causes of child mortality: Global Health Observatory (GHO) Data 2015 [06 September, 2021]. Available from: http://www.who.int/gho/child_health/mortality/causes/en/.

3. UNICEF. Annual Report 2020: Turning research into action for children and young people 2020 [06 September, 2021]. Available from: https://reliefweb.int/report/world/unicef-annual-report-2020-turning-research-action-children-and-young-people/.

4. Dicker D, Nguyen G, Abate D, Abate KH, Abay SM, Abbafati C, et al. Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1684-735.

5. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. Lancet Glob Health. 2019;7(1):e47-e57.

6. The National Institute of Population Research and Training (NIPORT) MoHaFWD, The DHS Program, ICF. Bangladesh Demographic and Health Survey 2017-18 2017-18 [06 September, 2021]. Available from: https://dhsprogram.com/pubs/pdf/PR104/PR104.pdf.

7. Rahman AE, Hossain AT, Siddique AB, Jabeen S, Chisti MJ, Dockrell DH, et al. Child mortality in Bangladesh–why, when, where and how? A national survey-based analysis. J Glob Health. 2021;11.

8. Duke T, Mgone J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea [oxygen therapy in children]. Int J Tuberc Lung Dis

2001;5(6):511-9.

9. Rahman AE, Hossain AT, Chisti MJ, Dockrell DH, Nair H, El Arifeen S, et al. Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh. J Glob Health. 2021;11.

10. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.

11. McCollum ED, King C, Colbourn T, Graham H, Bernstein M, Wilson IH, et al. Pulse oximetry in paediatric primary care in low-income and middle-income countries. Lancet Respir Med. 2019;7(12):1001.

12. World Health Organization. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and

delivery, common causes of fever, severe acute malnutrition and supportive care 2012 [Available from: https://apps.who.int/iris/bitstream/handle/10665/44774/9789241502825_eng.pdf;sequence=1.

13. Rahamn AE, Mhajabin S, Dockrell D, Nair H, El Arifeen S, Campbell H. Managing pneumonia through facility-based integrated management of childhood management (IMCI) services: an analysis of the service availability and readiness among public health facilities in Bangladesh. BMC health services research. 2021;21(1):1-13.

14. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization 2013 [cited 2021 06 September, 2021]. Available from: http://apps.who.int/iris/bitstream/handle/10665/43206/9241546700.pdf;sequence=1.

15. World Health Organization. Integrated Management of Childhood Illness (Chart Booklet) 2014 [06 September, 2021]. Available from: https://www.who.int/publications/i/item/9789241506823.

16. World Health Organization. Revised WHO classification and treatment of pneumonia in children at health facilities: evidence summaries 2014 [Available from: https://apps.who.int/iris/bitstream/handle/10665/137319/9789241507813_eng.pdf;sequence=1.

17. Arifeen SE, Hoque DE, Akter T, Rahman M, Hoque ME, Begum K, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. Lancet. 2009;374(9687):393-403.

18. Government of the Peoples' Republic of Bangladesh MoHaFW. Health Bulletin 2019 [Available from: https://dghs.gov.bd/images/docs/Publicaations/Health%20Bulletin%202019%20Print%20Version%20(2)-Final.pdf.

19. National Institute of Population Research and Training (NIPORT) II. Bangladesh Health Facility Survey 2017 2019 [cited 2021 24 October]. Available from: https://dhsprogram.com/pubs/pdf/SPA28/SPA28.pdf.

20. icddr b. icddr,b [cited 2021 24 October, 2021]. Available from: https://www.icddrb.org/.

21. The University of Edinburgh. NIHR Global Health Research Unit on Respiratory Health (RESPIRE) [24 October, 2021]. Available from: https://www.ed.ac.uk/usher/respire/acute-respiratory-disorders/pulse-oximetry-bangladesh.

22. National Institute of Population Research and Training (NIPORT) ME. Bangladesh District Level Socio-demographic and Health Care Utilization Indicators 2019 [24 October, 2021]. Available from: http://rdm.icddrb.org/wp-content/uploads/2020/04/Bangladesh-District-Level-Socio-demographic-and-Health-Care-Utilization.pdf.

23. Peters DH, Tran NT, Adam T. Implementation research in health: a practical guide: World Health Organization; 2013 [25 October, 2021]. Available from: https://apps.who.int/iris/bitstream/handle/10665/91758/9789241506212_eng.pdf;jsessionid=582156F0C85F443FDBAECA87DCF7BB15?sequence=1.

24. Boaz A, Hanney S, Borst R, O'Shea A, Kok MJHrp, systems. How to engage stakeholders in research: design principles to support improvement. Health Res Policy Syst. 2018;16(1):1-9.

25. Huzzard T. Achieving impact: Exploring the challenge of stakeholder engagement. European Journal of Work and

Organizational Psychology. 2020:1-11.

26. Kok MO, Gyapong JO, Wolffers I, Adjei DO, J R. Which health research gets used and why? An empirical analysis of 30 cases. Health research policy and

systems. 2016;14(1):1-18.

27. Deverka PA, Lavallee DC, Desai PJ, Esmail LC, Ramsey SD, Veenstra DL, et al. Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. J Comp Eff Res. 2012;1(2):181-94.

28. Concannon TW, Fuster M, Saunders T, Patel K, Wong JB, Leslie LK, et al. A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. J Gen Intern Med. 2014;29(12):1692-701.

29. Concannon TW, Grant S, Welch V, Petkovic J, Selby J, Crowe S, et al. Practical guidance for involving stakeholders in health research. J Gen Intern Med. 2019;34(3):458-63.

30. Coretta Mallery DG, Jessica Fernandez, Lauren Smeeding, Sandra Robinson, Marilyn Moon. Innovative Methods in Stakeholder Engagement: An Environmental Scan: American Institutes for Research 2021 [06 September, 2021]. Available from: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/stakeholders-engagement-others_research-2012-1.pdf.

31. National Health Service (NHS) Institute for Innovation and Improvement. The organising for quality and value: Delivering improvement programme. 2009.

32. Joshi A, Kale S, Chandel S, Pal DK. Likert scale: Explored and explained. Current Journal of Applied Science and Technology. 2015;7(4):396.

33. Floyd J, Wu L, Hay Burgess D, Izadnegahdar R, Mukanga D, Ghani AC. Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Nature. 2015;528(7580):S53-9.

34. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. Lancet Infect Dis. 2009;9(4):219-27.

35. World Health Organization. Integrated Management of Childhood Illness (Chart Booklet). 2009 [06 September, 2021]. Available from: https://www.who.int/publications/i/item/9789241506823.

36. Helms MM, Nixon J. Exploring SWOT analysis–where are we now? A review of academic research from the last decade. Journal of strategy and management. 2010.

37. Namugenyi C, Nimmagadda SL, Reiners T. Design of a SWOT analysis model and its evaluation in diverse digital business ecosystem contexts. Procedia Computer Science. 2019;159:1145-54.

Chapter 8: ADEQUACY OF THE TRAINING PACKAGE DEVELOPED FOR INTRODUCING PULSE OXIMETRY IN ROUTINE IMCI SERVICES

One of my general objectives was to assess the feasibility of introducing pulse oximetry in routine IMCI services. The specific research question 6 was to assess minimally trained health personnel's performance of pulse oximetry in hospital settings.

Table 8.1 General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

The work presented in the chapter 8 was published in The Journal of Global Health in 2022.

Title: Success and time implications of SpO_2 measurement through pulse oximetry among hospitalised children in rural Bangladesh: Variability by various device-, provider- and patient-related factors

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8.1 ABSTRACT

8.1.1 Background

Hypoxaemia is one of the strongest predictors of mortality among children with pneumonia. It can be identified through pulse oximetry instantaneously, which is a non-invasive procedure but can be influenced by factors related to the specific measuring device, health provider and patient. Following WHO's global recommendation in 2014, Bangladesh decided to introduce pulse oximetry in paediatric outpatient services, i.e., the Integrated Management of Childhood Illness (IMCI) services in 2019. A national committee updated the existing IMCI implementation package and decided to test it by assessing the pulse oximetry performance of different types of assessors in real-life inpatient settings.

8.1.2 Methods

We adopted an observational design and conducted a technology assessment among children admitted to a rural district hospital. Eleven nurses and seven paramedics received one-day training on pulse oximetry as assessors. Each assessor performed at least 30 pulse oximetry measurements on children with two types of

handheld devices. The primary outcome of interest was obtaining a successful measurement of SpO_2, defined as observing a stable (±1%) reading for at least 10 seconds. Performance time, i.e., time taken to obtain a successful measurement of SpO_2 was considered the secondary outcome of interest. In addition, we used Generalized Estimating Equation to assess the effect of different factors on the pulse oximetry performance.

8.1.3 Results

The assessors obtained successful measurements SpO_2 in all attempts (n=1478) except one. The median time taken was 30 seconds (IQR, 22 to 42), and within 60 seconds, 92% of attempts were successful. The odds of obtaining a successful measurement within 60 seconds were 7.3 times (95% CI, 3.7 to 14.2) higher with a Masimo device than a Lifebox device. Similarly, assessors aged >25 years were 4.8 times (95% CI, 1.2 to 18.6) more likely to obtain a successful measurement within 60 seconds. The odds of obtaining a successful measurement were 2.6 times (95% CI, 1.6 to 4.2) times higher among children aged 12-59 months compared to 2-11 months.

8.1.4 Conclusion

Our study indicated that assessors could achieve the necessary skills to perform pulse oximetry successfully in real-life inpatient settings through a short training module, with some effect of device-, provider- and patient-related factors. The National IMCI Programme of Bangladesh can use these findings for finalizing the

national IMCI training modules and implementation package incorporating the recommendation of using pulse oximetry for childhood pneumonia assessment.

8.2 BACKGROUND

Each year, approximately 24,000 children under-5 years of age die due to pneumonia in Bangladesh, making it the major killer among this age group (1, 2). In addition to mortality, the morbidity-burden associated with childhood pneumonia is also remarkably high in Bangladesh as it causes around 4 million episodes of illness every year, of which around one million are severe episodes, and approximately half a million require hospitalisations (3, 4). Many other low- and middle-income countries (LMICs) suffer from a similarly high burden of childhood pneumonia, where the majority of the deaths can be prevented by appropriate management and immediate treatment (3). Hypoxaemia, defined as low (<90%) oxygen saturation (SpO_2) in arterial blood, is common among children with pneumonia and is regarded as one of the strongest predictors of adverse clinical outcomes, including treatment failure and mortality (5-8). Early identification of hypoxaemia and prompt management with oxygen therapy can significantly avert deaths due to pneumonia (9, 10). Thus, strengthening the health system for early identification and management of hypoxaemia can play a crucial role in achieving the Sustainable Development Goals (SDG) target of reducing under-5 mortality to 25 per 1,000 live births or below by 2030 and the Integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD) target of reducing pneumonia specific under-5 mortality rate to 3 per 1,000 live births or below by 2025 (11-13).

Pulse oximetry is an indirect, simple and non-invasive procedure to measure SpO_2 using a pulse oximetry device and identify hypoxaemia instantaneously (14). Initially, its use was limited to monitoring SpO_2 during anaesthesia and almost exclusively in resource-intensive settings such as Intensive Care Units (ICUs) (15-18). However, the size and the cost of pulse oximetry devices have significantly decreased due to technological advancements in the last couple of decades (19, 20). Hence, pulse oximetry has become the standard of care in outpatient, emergency and inpatient settings, mainly in high-income countries. Due to the high burden of hypoxaemia among children with pneumonia and the potential impact of introducing pulse oximetry on child survival, the World Health Organization (WHO) has recommended introducing pulse oximetry in paediatric outpatient services, i.e., Integrated Management of Childhood Illness (IMCI) services since 2014 (4, 20-22). In 2019, the National IMCI Programme of the Government of Bangladesh decided to introduce pulse oximetry in routine IMCI services to identify hypoxaemia among children presenting with cough and difficulty breathing (23, 24). The National IMCI programme formed a high-level committee with IMCI experts to integrate the recommendation of using pulse oximetry in the National IMCI training modules and implementation package (24). The committee incorporated a short (one day) module on pulse oximetry into the existing IMCI training package (24).

Various factors influence pulse oximetry performance, particularly related to obtaining successful measurements and the time required for that (25-30). These factors can be divided into three broad categories: device-related factors, patient-related factors, and provider-related factors. Unfortunately, most of the evidence in

this regard is from resource-rich environments and high-income country settings and is predominantly based on qualitative explorations (31-36). There is a dearth of quantifiable evidence regarding the success and time implications for performing pulse oximetry and their variability by various factors in resource-limited settings, particularly in the context of Bangladesh. Hence, the National IMCI Programme of Bangladesh decided to test the newly developed training module in a paediatric inpatient setting and assess the pulse oximetry performance of different types of assessors by different types of devices before finalising the training modules and implementation package and feasibility assessment through demonstration in outpatient-based routine IMCI services (24). In this paper, we present key findings from the pre-implementation testing, which guided programme planning, and implementation in real-life settings.

8.3 METHODS

8.3.1 Study design

We conducted a technology assessment adopting an observational design, where study recruited assessors received training based on the updated module on pulse oximetry and used handheld pulse oximetry devices to assess SpO_2 status among children hospitalised in a rural district hospital in Bangladesh.

The study was conducted in Kushtia district, which is situated approximately 200 kilometres west of Dhaka city, the capital of Bangladesh. The Government of Bangladesh decided to conduct this study and subsequent feasibility assessment through field demonstration in this district as the under-5 mortality rate of Kushtia

was somewhat similar to the average under-5 mortality rate in Bangladesh (37). We conducted the assessments in the paediatric inpatient unit of Kushtia District Hospital, which is the highest-level referral facility (secondary level with 250 inpatient beds) in the Kushtia district. The paediatric inpatient unit of Kushtia District Hospital provides inpatient services to approximately 3,000 under-5 children per year. The majority of the admissions are due to pneumonia, sepsis, prematurity related complications, and perinatal birth asphyxia. Pulse oximetry was not routinely used in Kushtia District Hospital at the time of this study.

We included children aged 2-59 months who were admitted to the paediatric inpatient unit and whose parents consented to participate in the study. Exclusion criteria included unconsciousness, active bleeding and drowning at the time of assessment as they required urgent medical interventions, which were not directly dependent on SpO_2 assessment. In government settings, routine IMCI services are primarily provided by trained nurses and paramedics. Hence, we recruited study nurses and paramedics (graduates from Medical Assistant Training School) who received a one-day long training based on the newly developed IMCI training module on pulse oximetry. The training included the basic pathophysiology of hypoxaemia, the function of a pulse oximetry device and its parts, steps of performing pulse oximetry and instructions for the maintenance of the device.

The primary outcome of interest was obtaining a successful measurement of SpO_2 through pulse oximetry. Since we did not have any previous estimate from Bangladesh, we considered the maximum variance, i.e., a success rate of 50%. In

order to address the cluster effect (each assessor as a cluster), we adjusted the sample size with a design effect of 1.25. We also considered a non-response rate of 10%. The final adjusted sample size was 534 eligible children. We employed 11 nurses and seven paramedics as assessors. We wanted to enrol an equal number of participants per assessor. Hence, each assessor was responsible for performing at least 30 pulse oximetry assessments among hospitalised children. We adopted a time sampling approach as all children admitted to the inpatient department were approached and enrolled during the data collection period based on the inclusion and exclusion criteria. It took around 2-3 days per assessor to achieve the required target. On the day the required sample size (minimum of 30 children) was reached for each assessor, they continued enrolment and data collection until the end of their shifts.

We collected data between 29 October 2020 to 03 April 2021. Data collection methods included data extraction from routine hospital records, structured observation of pulse oximetry by study nurses and paramedics, and structured survey of the study nurses and paramedics on the challenges of using pulse oximetry on hospitalised children. Information regarding the children's basic demographic and clinical characteristics, such as age, sex, weight and diagnosis at admission, was extracted from hospital inpatient case recording forms using a structured form. The assessors performed pulse oximetry on each child immediately after admission using two types of handheld devices (i.e., Lifebox AH-M1, and Masimo Rad- 5V) with adequately fitted paediatric probes. The national committee selected the pulse oximetry devices based on technical specifications and in consultation with technical

experts (23). Additional technical details and specifications regarding pulse oximetry devices are summarised in Supplementary table 8.1. Independent observers assessed the pulse oximetry performance of study nurses and paramedics using a structured observation tool. A measurement was considered successful if the signal strength was shown adequate (four or more out of five) and a stable (±1%) SpO_2 reading was observed for at least 10 seconds. A measurement was considered unsuccessful if the signal strength was inadequate and they could not establish a stable SpO_2 reading within three minutes. Performance time was calculated from placing the probe onto the fingertip to obtaining a successful measurement using a digital stopwatch. After completion of the structured observation, the assessors completed a self-administered survey tool on the challenges of performing pulse oximetry on hospitalised children. The self-administered survey tool consisted of five-scale Likert scale statements with the following options: very easy, easy, neither easy nor challenging, challenging and very challenging. A medical graduate with prior experience in using pulse oximetry devices received IMCI training and monitored the data collection process as an on-site clinical supervisor. These supervisors provided feedback to the data collectors to improve the data quality. No additional refresher training was organised for the assessors during the data collection process in order to follow the exact procedure that applies for the government appointed IMCI service providers.

8.3.2 Analysis plan

We used the statistical software package Stata version 14.0 for data analysis (38).

Descriptive statistics (frequencies and percentages) were used to present the basic demographic and clinical characteristics (age, sex, weight for age and diagnosis on admission) of the children and background characteristics (age, sex and designation) of the assessors. Weight for age was calculated from WHO's z-score and categorised into not-underweight (weight for age score ≥-2 standard deviation), underweight (weight for age score is <-2 standard deviations), and severely underweight (weight for age score <-3 standard deviation)(39).

Obtaining a successful measurement of SpO_2 was considered as the primary outcome of interest. At first, we presented the success rates for different cut off time points: within 20 seconds, within 30 seconds, within 40 seconds, within 50 seconds, within 60 seconds, within 90 seconds, within 120 seconds and within 180 seconds.

Performance time, defined by the time taken to obtain a successful measurement of SpO_2, was considered the secondary outcome of interest. We checked the normality of the distribution of timing by device-related factors (type of pulse oximetry device), provider-related factors (age, sex and designation of assessor) and patient-related factors (age, sex, weight for age of the children, on-admission diagnosis/classification) using the Shapiro–Wilk test (Supplementary table 8.2) (40). Since they were non-normally distributed, we presented the median estimates with an interquartile range through boxplots. We used the Wilcoxon Signed Rank test (for paired observations) to check the differences in performance time by type of pulse oximetry devices and the Ranksum test (for non-paired observations) to check the differences for other provider-related and patient-related factors. We also reported

the median time taken by each assessor using radar plots. We used the Kruskal Wallis test to assess whether they were any differences in the median time taken by each assessor.

The National IMCI Programme, in consultation with IMCI experts, set an a-priori cut-off of obtaining a successful measurement of SpO_2 within 60 seconds as a feasible and acceptable performance time in a real-life setting. We used the Generalized Estimating Equation regression model to assess the effect of different device-related, provider-related, and patient-related factors on successful measurement of SpO_2 within 60 seconds. The unadjusted and adjusted odds ratios were presented with 95% confidence intervals (CI). The model adequacy was assessed using Wald Statistics.

We used the prevalence-and bias-adjusted kappa (PABAK) statistics for reporting the agreement of identifying hypoxaemia (SpO_2<90%) using Lifebox and Masimo devices, by various provider- and patient-related factors and by individual assessor (41). The agreement levels were presented with point estimates (percentage) with 95% confidence intervals.

We have reported the percentage of people reporting very easy, easy, neither easy nor challenging, challenging and very challenging for each statement using a bar graph.

We reported all differences or associations as significant at $p<0.05$.

8.3.3 Ethical considerations

Ethical approval for this study was obtained from the Institutional Review Board of icddr,b (PR-18054). We took informed and written consent from the primary caretaker/parents of the children and the assessors. We also obtained administrative approval from the Ministry of Health (IMCI Programme of Directorate General of Health Services) to conduct the study in Kushtia District Hospital.

8.4 RESULTS

A total of 739 children were enrolled in the study. Table 8.2 summarises the background characteristics of the children. Approximately 62% of the children were male, and around 52% were aged 2-11 months. Study nurses assessed around 61% of the children, and the remaining were assessed by the paramedics. Among the assessors, 14 (78%) were aged 25 years or below; seven (39%) were male, and 11 (61%) were females; 11 (61%) were nurses, and seven (39%) were paramedics. Supplementary table 8.3 presents the number of pulse oximetry performed by each assessor.

The assessors obtained a successful measurement of SpO_2 in all attempts except one.

Table 8.2: Background characteristics of the children hospitalised in Kushtia District Hospital and enrolled in the study; presented in %; N=739

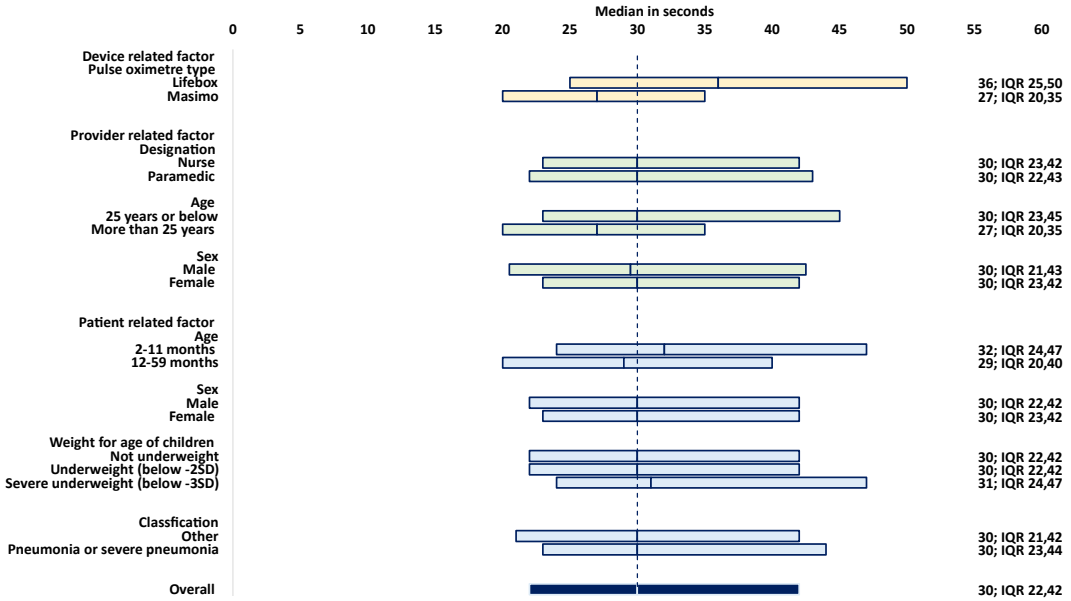
Characteristics	Category	n	%
Age	2-11 months	386	52
	12- 59 months	353	48
Sex	Male	457	62
	Female	282	38
Weight for Age	Not underweight	539	75
	Underweight (below -2SD)	102	14
	Severely underweight (below -3sD)	81	11
	Missing	17	
Diagnosis	Severe pneumonia or pneumonia	407	55
	Others	332	45

Type of assessor	Nurse	451	61
	Paramedic	288	39

SD: Standard Deviation

Figure 8.1 presents the median performance time by various device-, provider-and patient-related factors. The median time taken to obtain a successful measurement was 30 seconds (IQR 22, 42). The median time was significantly (Wilcoxon Signed Rank test for paired observations, p<0.0001) higher among children who were assessed with a Lifebox device (36 seconds) than those who were assessed with a Masimo device (27 seconds). Similarly, the assessors aged more than 25 years required significantly (p<0.0001) less time than assessors who were aged 25 years or less (median time 27 seconds vs 30 seconds). Moreover, the median time was more (p<0.0001) among children aged 2-11 months (32 seconds) than that of children aged 12-59 months (29 seconds). We did not observe any significant difference (p=0.296) between assessments conducted by nurses (median 30 seconds, IQR, 23 to 42) and paramedics (median 30 seconds, IQR 22 to 43).

Figure 8.1: Performance time to obtain a successful measurement of SpO_2 by device-, assessor- and patient-related factors; presented in median time taken in seconds; N=1478



IQR: Interquartile Range

SD: Standard Deviation

Figure 8.2 illustrates the median performance time by each assessor and proportion of successfully conducting pulse oximetry assessments within 60 seconds. The median performance time was less than 60 seconds for all assessors. The median time taken by the nurses was 30 seconds which varied between 40 seconds (highest) and 25 seconds (lowest) among individual nurses (chi-squared = 105.7, df=10 df, $p<0.0001$). Similarly, the median time taken by paramedics was 30 seconds which varied between 43 seconds (highest) and 24 seconds (lowest) among individual paramedics (chi-squared = 105.6, df= 10, $p<0.0001$).

The overall proportion of the successful assessments of pulse oximetry within 60 seconds is 92% for both nurse and paramedics. However, there exists variation on this proportion within the group of different assessors. Among the nurses and paramedics, the heterogeneity statistics I-squared are 85% and 80% and tau-squared are 46.01 and 33.5 respectively.

Figure 8.2: Performance time to obtain a successful measurement of SpO_2 and proportion of pulse oximetry assessments successfully conducting within 60 seconds by individual assessors, presented in median time taken in seconds and in % respectively

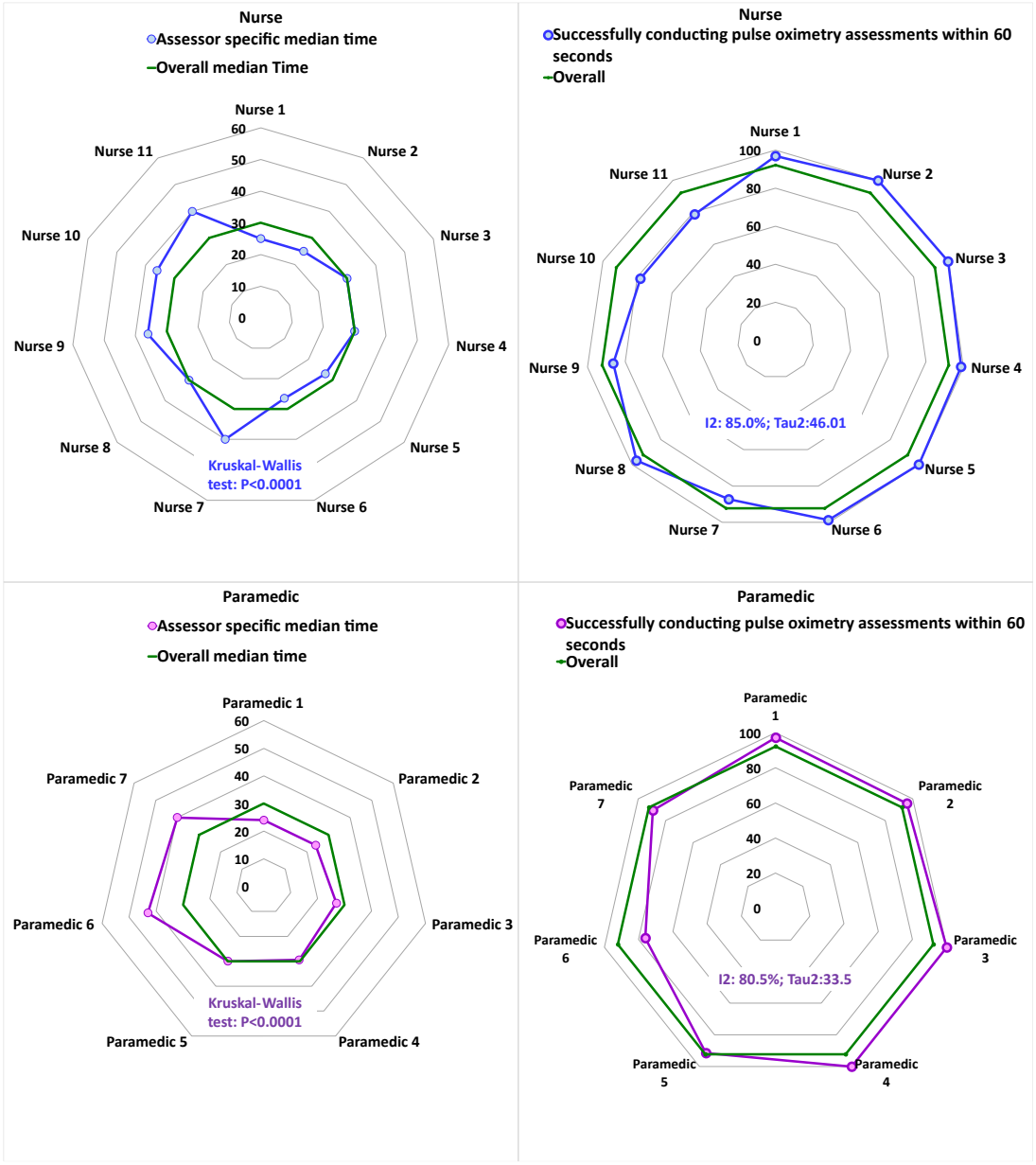


Figure 8.3 presents the rates of obtaining a successful measurement at various cut-off time points by pulse oximetry device type, assessor type and age of the children. The assessors obtained a successful measurement within 30 seconds among 54% of children. It was 92% within 60 seconds and 99% within 120 seconds. The assessors

obtained a successful measurement within 60 seconds among almost all children using a Masimo device, which was around 87% among children assessed with a Lifebox device. The assessors could successfully measure SpO_2 within 60 seconds among more than 90% of children for both younger (2-11 months) and older (12-59 months) age groups.

Figure 8.3: Rates of obtaining a successful measurement of SpO_2 by different cut-off time points, and by pulse oximetry device type, assessor type and age of the children, presented in %; N=1478

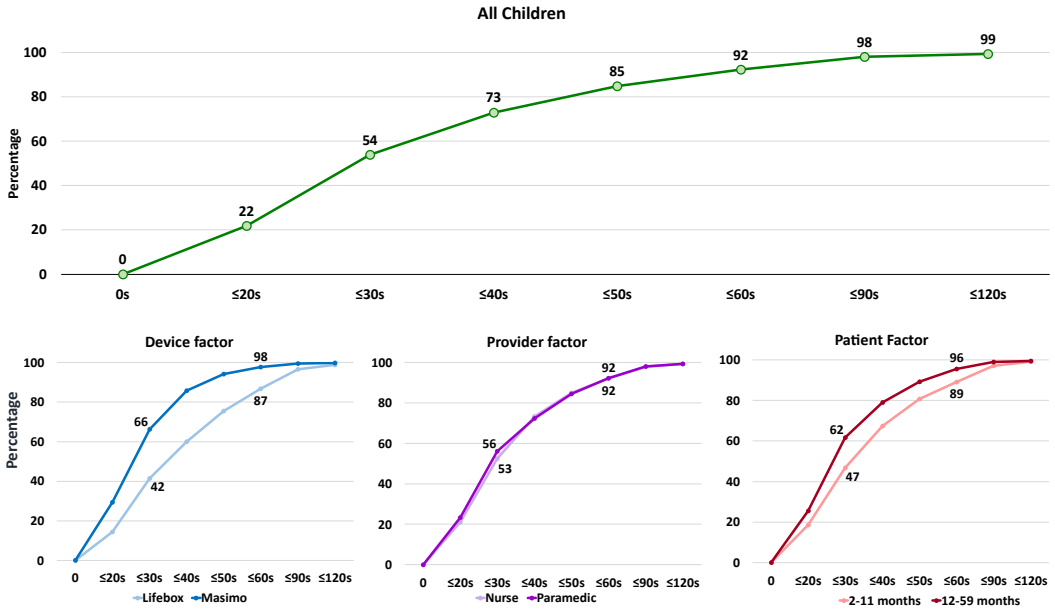
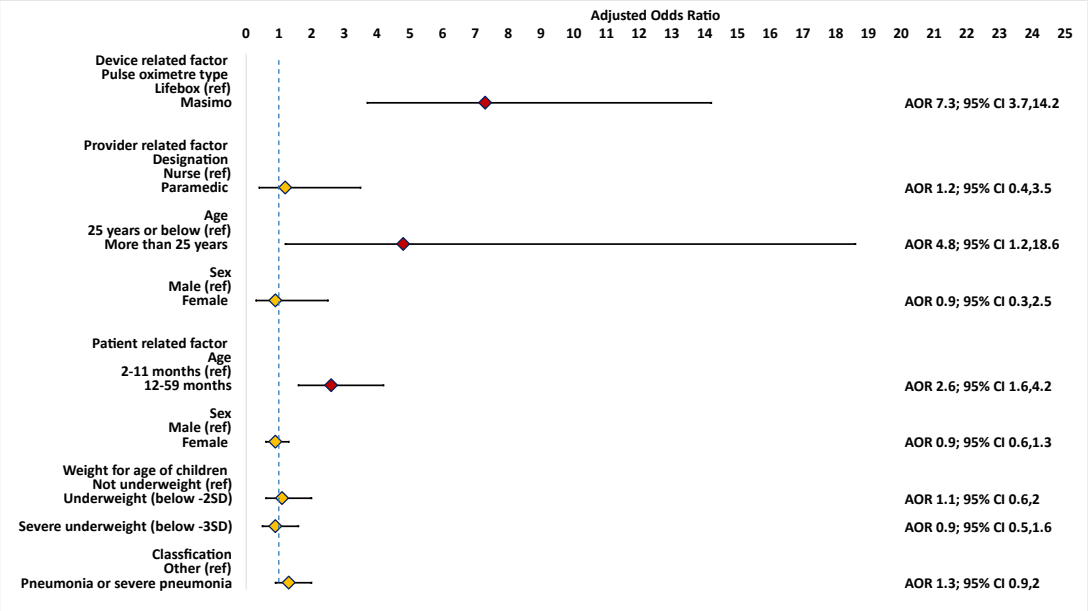


Figure 8.4 presents the effect of various device-, provider-, and patient-related factors on performance time to obtain a successful measurement of SpO_2 within 60 seconds after controlling for covariates and confounders. The odds to obtaining a successful measurement of SpO_2 within 60 seconds were 7.3 (95% CI 3.7, 14.2, $p<0.0001$) times higher when the assessments were conducted with a Masimo device than that of a Lifebox device. Similarly, assessors aged >25 years were 4.8 (95% CI, 1.2 to 18.6, $p=0.03$) times more likely to obtain a successful measurement of SpO_2 within 60 seconds. Regarding patient-related factors, the odds to obtaining a successful measurement of SpO_2 within 60 seconds were 2.6 (95% CI, 1.6 to 4.2,

p<0.001) times higher among children aged 12-59 months than among children aged 2-11 months. The Wald Statistics 49.14 (p<0.0001) obtained from the model demonstrated that the model was adequately fitted. Additional details are available in Supplementary table 8.4.

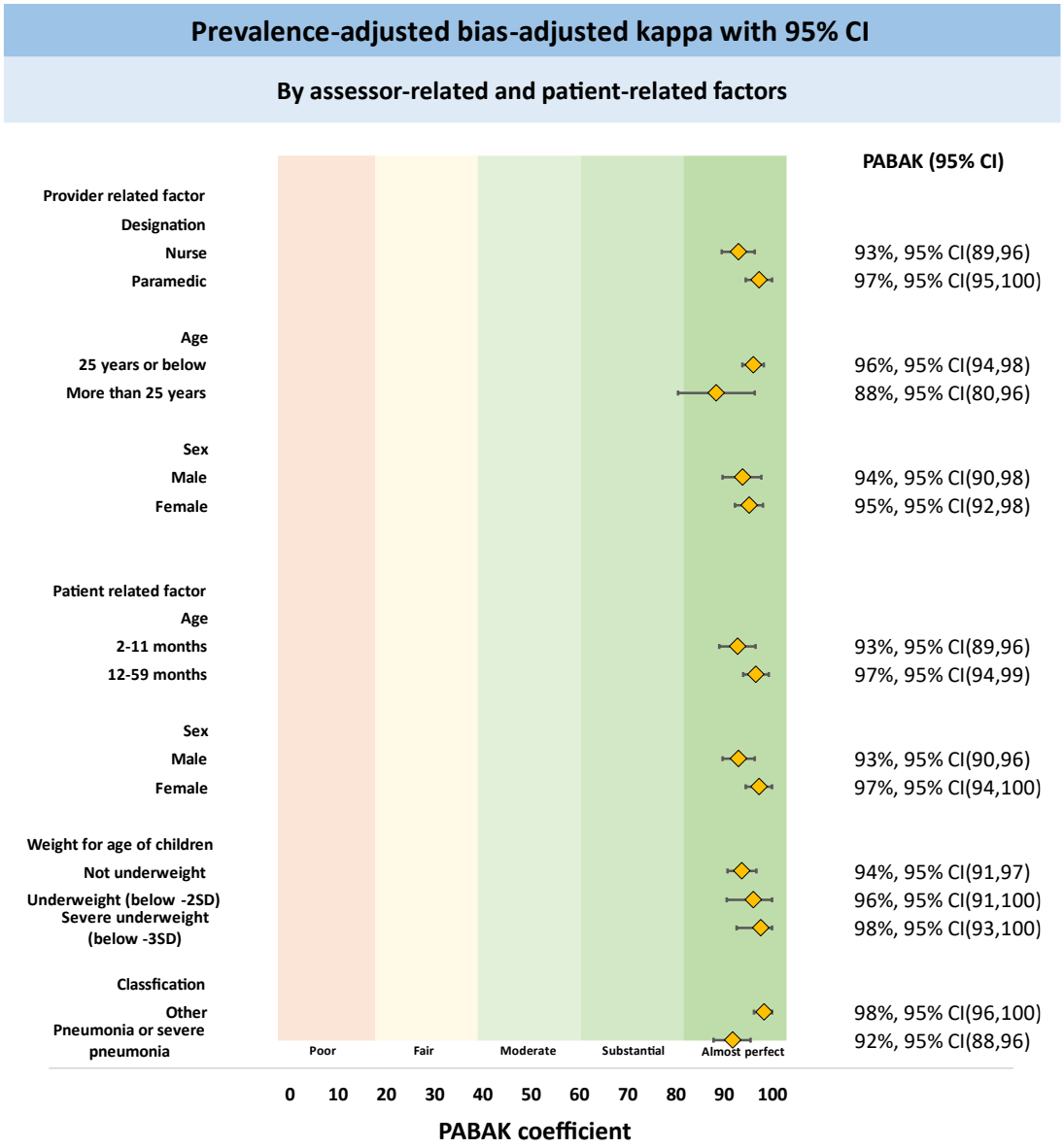
Figure 8.4: Associations between obtaining a successful measurement of SpO_2 within 60 seconds and various device-, assessor- and patient-related factors; presented in adjusted odds ratio using a Generalised Estimating Equation (GEE) regression model; N=1474



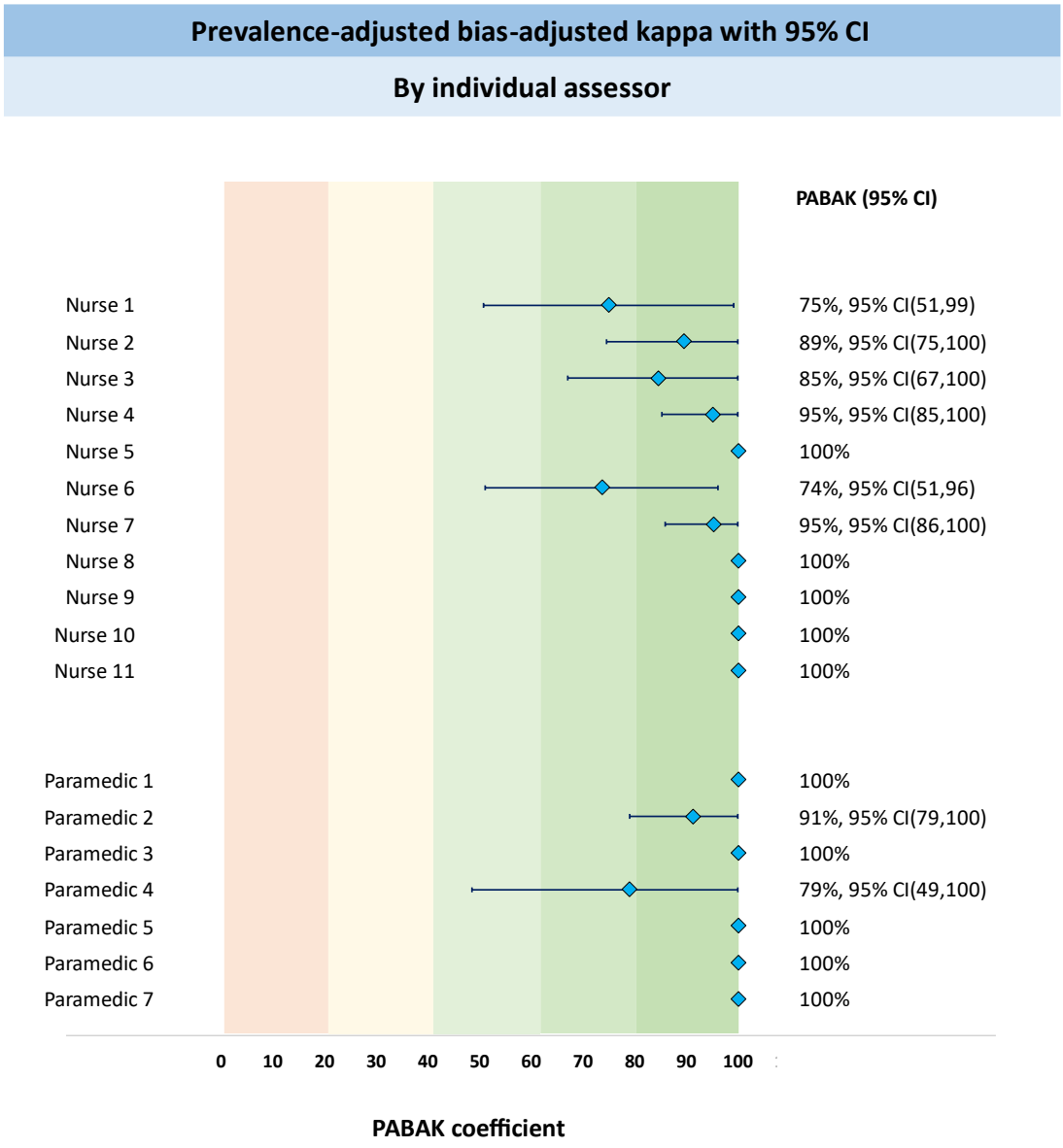
AOR: Adjusted Odds Ratio
CI: 95% Confidence Interval
SD: Standard Deviation
Ref: Reference

Figure 8.5 presents the agreement of identifying hypoxaemia using Lifebox and Masimo devices, by provider- and patient-related factors and by individual assessor. We observed almost perfect level of agreement by various factors. The agreement levels were between moderate to almost perfect among assessors.

Figure 8.5: Agreement of identifying hypoxaemia using Lifebox and Masimo devices by provider- and patient-related factors; presented through prevalence-adjusted and bias-adjusted kappa (PABAK) in % with 95% confidence interval



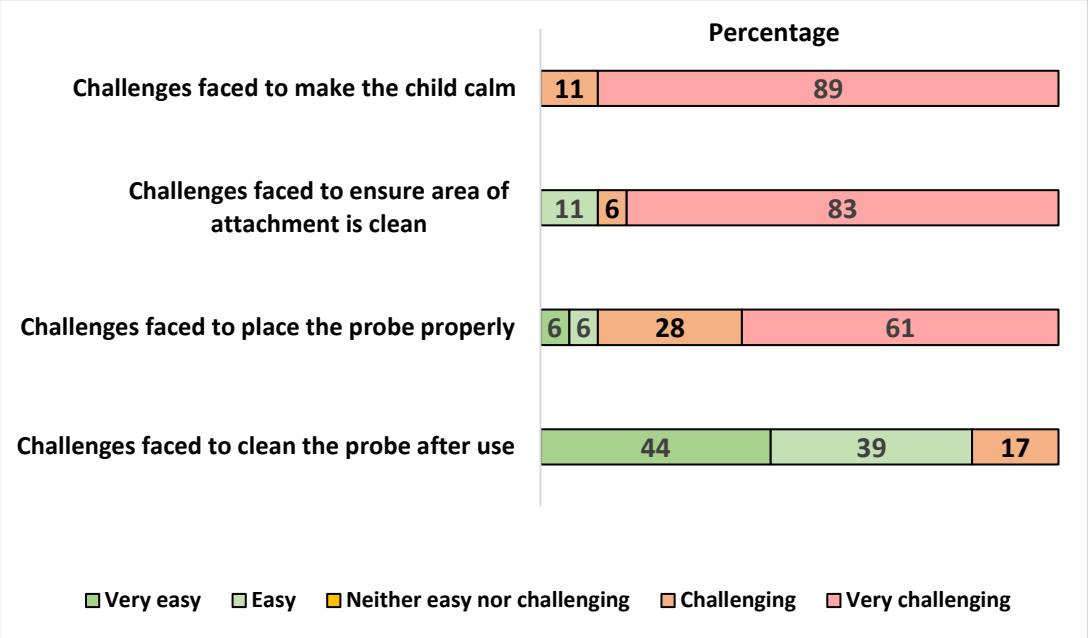
CI: 95% Confidence Interval



CI: 95% Confidence Interval

Figure 8.6 presents the result of the self-administered survey on the challenges of performing pulse oximetry on hospitalised children. All the assessors reported that they found it either very challenging or challenging to keep the baby was calm during performing pulse oximetry. Almost half of the assessors also reported that they found it very challenging to place the probe properly.

Figure 8.6: Feedback on challenges of performing pulse oximetry on children by assessors; presented as % of assessors reporting very easy, easy, neither easy or challenging, challenging and very challenging for each statement; N=18



8.5 DISCUSSION

The Government of Bangladesh decided to introduce pulse oximetry in routine IMCI services based on the WHO recommendation in 2014 and in-country consultation with IMCI experts and stakeholders (23). Hence, the IMCI Programme of the Government of Bangladesh warranted this study to test the newly developed training module and measure the influence of various device-related, provider-related, and patient-related factors on pulse oximetry performance. Our study showed that the assessors could successfully use handheld pulse oximetry devices with relatively short training. The results of this study address some of the key evidence gaps related to the feasibility of adopting a short training and choice of pulse oximetry devices in the Bangladesh context.

We found that the minimally trained assessors obtained a successful measurement of SpO_2 among more than 90% of the hospitalised children within 60 seconds. This is similar to findings reported by another study conducted in primary care clinics of rural Pakistan, which also employed study recruited personnel for pulse oximetry (42). The results indicate that the study nurses and paramedics without previous experience of using a pulse oximetry device achieved necessary skills based on the short training module developed by the national committee. It is important considering the context of Bangladesh, where most of the IMCI service providers are nurses and paramedics and do not have any prior exposure to performing pulse oximetry in outpatient or emergency settings. The short training package is also programmatically more implementable and scalable in a resource-constrained high pneumonia-burden setting like Bangladesh (1, 3, 23). Since more than 90% of the assessments were completed within 60 seconds, recommending pulse oximetry while assessing the respiratory rate for one minute will add minimum additional workload on the IMCI services providers even in high-volume facilities.

We compared the performance time taken by Masimo and Lifebox devices to obtain a successful measurement of SpO_2. This information is crucial for the uptake of pulse oximetry in high-volume facilities. We found that the performance time was significantly shorter with a Masimo device. This finding is consistent with another study conducted by King et al., who found that Masimo and Lifebox device's performance time was equivalent within ±7 seconds of one another (43). Some studies also reported that the performance of Masimo devices was better than several other commercially available handheld pulse oximetry devices (28, 30).

Masimo uses advanced Signal Extraction Technology (SET), which allows it to obtain a stable SpO_2 reading faster even in challenging conditions such as patient movement and low perfusion (28, 30). The technical superiority of a Masimo device over most other handheld devices may be an important consideration for the Government of Bangladesh to select it for national scale-up, particularly in high-volume referral hospitals like district hospitals and sub-district hospitals. However, Masimo devices are almost twice as expensive as Lifebox devices (44). Although the median performance time was more (9 seconds) with a Lifebox device, around 87% of the assessments were completed within one minute. In Bangladesh, the majority of the IMCI services are provided through the Union Health and Family Welfare Centres, which are primary care centres with a catchment population of around 25,000. Most of the Union Health and Family Welfare Centres are low-volume facilities and primarily deal with less severe cases. Considering the relative advantage of a Lifebox device over a Masimo device in price and the high rate of obtaining a successful measurement of SpO_2 reading within 60 seconds, introducing Lifebox devices in Union Health and Family Welfare Centres and low volume sub-district hospitals can be a cost-effective investment for the Government of Bangladesh.

Nurses and paramedics provide the majority of the IMCI services in Bangladesh. Our study recruited nurses and paramedics as assessors to perform pulse oximetry. We did not observe any notable difference in their success rate or performance time. Therefore, the feasibility of conducting pulse oximetry by nurses and paramedics as routine IMCI service providers looks promising. Our study also suggested that older

assessors were more likely to obtain a successful measurement of SpO_2 within 60 seconds. This may be explained by the maturity and experience of the assessors, which are expected to gain with age. Younger and relatively inexperienced providers may require additional attention during initial training and post-training monitoring for standardising and ensuring quality. During training and monitoring, special attention should be given to ensure that the assessors are aware of the factors that might affect SpO_2 readings, including anaemia, peripheral vasoconstriction, dark skin tone and skin discolouration of children (45).

Regarding patient-related factors, we found that obtaining a successful measurement of SpO_2 among younger children takes significantly more time. The results are similar to a large multi-site study (29). The healthcare workers interviewed in Bangladesh and Malawi also reported difficulties conducting pulse oximetry among smaller and younger children (35). Pulse oximetry readings are significantly affected by patient movement and appropriateness of the probe size (28, 30). Hence, it is recommended to stabilise the child before and during the assessment. During pulse oximetry assessments, younger children requiring admission in the district hospital are expected to be more severe and less likely to be calm and stable. This can be one of the explanations for requiring additional time to obtain a successful measurement of SpO_2 among younger children in our study. The other explanation is the design and appropriateness of the probe size. Although we used paediatric probes for both the devices, there could be issues with appropriate fit as around one-fifth of the children in rural Bangladesh are underweight, and one-third were stunted (46). Hence, ensuring the availability of

appropriate probe size is an important consideration for introducing pulse oximetry in routine IMCI services in Bangladesh and other LMICs with high burden of malnutrition.

Our study has several strengths and weaknesses. We included a reasonably large sample size ensuring 30-60 assessments per assessor, which allowed us to assess the pulse oximetry performance of each assessor separately. It was conducted in a district hospital. The results may not be nationally or regionally representative. However, Bangladesh is essentially a homogeneous country. There are minimal variations in the background characteristics and clinical profile of children admitted in secondary level public hospitals. We also acknowledge that we conducted the study among hospitalised children, who may not represent the children receiving IMCI services in busy outpatient settings. However, the number of irascible children among these hospitalised children are supposed to be higher than the children in outpatient (47). Therefore, obtaining a successful measurement of SpO_2 among relatively more severe hospitalised children is expected to be more difficult than children receiving IMCI services. Hence, the results of this study are still relevant for programme planning to introduce pulse oximetry in routine IMCI services. Furthermore, this study was conducted in a relatively controlled environment with study nurses and paramedics recruited and trained as part of a research study. Although we adopted the pulse oximetry training module developed by the national committee, our staff may have shown better performance than government employed health service providers in routine IMCI services due to the higher level of motivation and enthusiasm (23, 48). Regarding data collection, we extracted

information regarding the children's background characteristics and clinical information from routine hospital records. Therefore, the provision for presenting disaggregated estimates and adjusting for various comorbid conditions, such as specific diagnosis and spectrum of pathologies, while exploring the factors affecting the performance of pulse oximetry use was somewhat limited. Moreover, there can be issues with the validity of this information since documentation of paediatric inpatient care has always been a challenge in LMICs like Bangladesh (49). Regarding analysis, performance time was non-normally distributed in our analysis (Supplementary figure 8.1). Hence, we had to conduct non-parametric tests, which are less efficient and robust than parametric tests. However, we tried to choose the most relevant and appropriate tests (eg. Signed Rank test, Ranksum test, Kruskal Wallis test) based on the distribution of data and specific questions. Lastly, each assessor had two (Masimo and Lifebox) measurements of SpO_2 on each child. Therefore, to account for the effect of intra-assessor correlation, we performed Generalised Estimating Equation regression to measure the effect of different patient-related, provider-related, and device-related factors on the time taken to obtain a stable SpO_2 reading.

8.6 CONCLUSION

Our study indicated that minimally trained assessors could obtain a successful measurement of SpO_2 with handheld devices within 60 seconds in hospital inpatient settings with some effect of various device-, provider- and patient-related factors. The National IMCI Programme can use these findings for finalising the IMCI training modules and implementation package related to pulse oximetry. The feasibility and

implementation challenges of introducing pulse oximetry in routine IMCI service needs to be further evaluated in real-life settings.

8.7 SUPPLEMENTARY MATERIALS

8.7.1 Supplementary tables

Supplementary table 8.1: Lifebox vs Masimo model, technical specification and price comparison.

	Lifebox A-care AH-M1	Masimo Rad-5v®
Price	USD 200	USD 500
General specifications		
For adults, children and neonates	Yes	Yes
For all skin pigmentations	No data found	No data found
Weight range for each patient category	No data found	No data found
SpO_2 detection to include the range: 70–100%	Yes, 0-100%	Yes, 1-100%
SpO_2 resolution: 1% or less.	1%	1%
SpO_2 accuracy within ±3% for all patients and perfusion/movement conditions.	70%-100%: ± 2%; 0%-69%: not defined	2% with no motion low perfusion adults/paediatrics. 3% with motion and low perfusion neonates
Pulse rate range: 30–240 bpm.	25-250 bpm	25-240 bpm
Pulse rate resolution: 1 bpm or less	1 bpm	1 bpm
Pulse rate accuracy within ±3 bpm.	±2 bpm	3 bpm with no motion and in low perfusion, 5 bpm with motion
Audio specifications		
Audible and visual alarms for low/high saturation and pulse rate, threshold set by user	Yes	Yes
Audible and visual alarms for sensor error or disconnected, system errors, low battery	Yes	Yes
Probe specifications		
Capable of working with, and supplied with, adult, paediatric and neonatal reusable probes	Yes	Yes
Battery specifications		
Operated by replaceable battery power supply, either rechargeable or single use	Li-ion rechargeable battery or, 3 AA batteries	4XAA Alkaline batteries
Display specifications		
%SpO_2	Yes	Yes
Pulse rate	Yes	Yes
Plethysmographic waveform	Yes	Yes
Alarm messages	Yes	Yes
Battery state indication	Yes	Yes
Others	No	Perfusion Index, Signal IQ (SIQ) bar
Other specifications		
Internal data storage for patient trends and event log	Yes; 1-99 ID and 300 records for each ID	The Rad-5 can store 72 hours of SpO_2 and Pulse Rate and Perfusion Index trend data, captured at 2 second intervals. This trend data can then be

	Lifebox A-care AH-M1	Masimo Rad-5v®
		transferred to a PC for evaluation. Trend data is stored in non-volatile memory, so it is not erased when the device is shut off or when the batteries are replaced
FDA/CE Approved	Yes	Yes

Supplementary table 8.2: Performance time to obtain a successful SpO_2 measurement by device-, provider- and patient-related factors, presented in median in seconds with interquartile range

	Min	Q1	Median	Q3	Max	Test of Choice for equality of distribution	P-value
Device-related factor							
Pulse oximetry type							
Lifebox	10	25	36	50	182	Wilcoxon signrank test	0.001
Masimo	5	20	27	35	140		
Provider-related factor							
Designation							
Nurse	5	23	30	42	182	Wilcoxon ranksum test	0.297
Paramedic	8	22	30	43	140		
Age							
25 and below	5	23	30	45	182	Wilcoxon ranksum test	0.001
Above 25 years	10	20	27	35	120		
Sex							
Male	8	20.5	30	42.5	140	Wilcoxon ranksum test	0.155
Female	5	23	30	42	182		
Patient-related factor							
Age							
2-11 months	5	24	32	47	182	Wilcoxon ranksum test	0.001
12-59 months	5	20	29	40	181		
Sex							
Male	5	22	30	42	182	Wilcoxon ranksum test	0.508
Female	6	23	30	42	130		
Weight for age							
Not underweight	5	22	30	42	181	Kruskal-Wallis	0.376
Underweight (below -2SD)	5	22	30	42	182		
Severely underweight (below -3SD)	8	24	31	47	120		
Diagnosis							
Pneumonia or severe pneumonia	5	21	30	42	126	Wilcoxon ranksum test	0.0441
Other	5	23	30	44	182		
All	**5**	**22**	**30**	**42**	**182**		

Q1: Quartile 1
Q2: Quartile 3

Supplementary table 8.3: Number of assessments by assessor type.

Type of assessor	Number of assessments
Nurse 1	64
Nurse 2	76
Nurse 3	78
Nurse 4	82
Nurse 5	74
Nurse 6	76
Nurse 7	86
Nurse 8	96
Nurse 9	80
Nurse 10	96
Nurse 11	94
Paramedic 1	104
Paramedic 2	92
Paramedic 3	76
Paramedic 4	38
Paramedic 5	94
Paramedic 6	88
Paramedic 7	84

Supplementary table 8.4: Generalised estimating equation (GEE) regression to assess the association between time taken to obtain a successful measurement of SpO_2 within 60 seconds and different characteristics of participants; presented in adjusted odds ratio and 95% confidence interval; N=1474

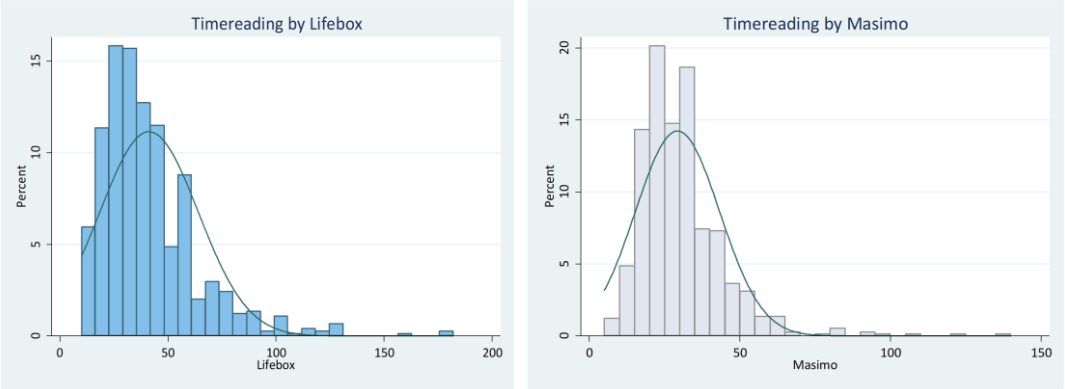
	%	Crude Odds Ratio	95% CI Lower limit	95% CI Upper limit	P value	Adjusted Odds Ratio	95% CI Lower limit	95% CI Upper limit	P value
Device-related factor									
Pulse oximetry type									
Lifebox	87	Ref				**Ref**			
Masimo	98	6.97	3.41	14.25	0.00	**7.29**	3.74	14.20	0.00
Provider-related factor									
Designation									
Nurse	92	Ref				**Ref**			
Paramedic	92	0.98	0.31	3.07	0.98	**1.19**	0.41	3.44	0.75
Age									
25 years and below	91	Ref				**Ref**			
Above 25	98	5.86	0.63	54.46	0.12	**4.75**	1.21	18.58	0.03
Sex									
Male	92	Ref				**Ref**			
Female	92	1.06	0.34	3.32	0.91	**0.85**	0.30	2.45	0.76
Patient-related factor									
Age									
2-11 months	89	Ref				**Ref**			
12- 59 months	96	2.07	1.32	3.24	0.00	**2.64**	1.64	4.24	0.00
Sex									
Male	92	Ref				**Ref**			
Female	92	0.92	0.63	1.36	0.69	**0.87**	0.58	1.32	0.52
Weight for age of child									
Not Under-Weight	93	Ref				**Ref**			
Underweight (below -2SD)	92	1.06	0.60	1.86	0.84	**1.09**	0.60	1.98	0.78
Severely underweight (below -3SD)	89	0.87	0.49	1.57	0.65	**0.87**	0.48	1.57	0.64
Classification									
Other	92	Ref				**Ref**			
Pneumonia or severe pneumonia	93	1.13	0.76	1.67	0.55	**1.33**	0.87	2.04	0.19

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

8.7.2 Supplementary figures

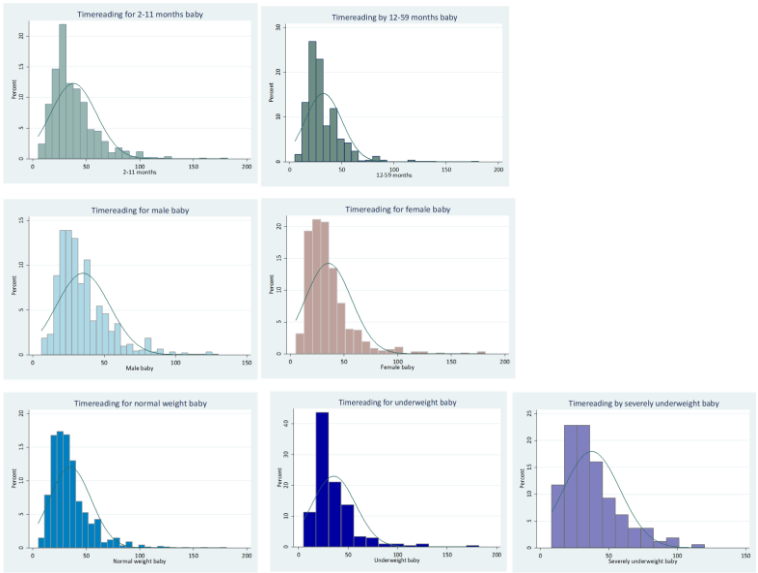
Supplementary figure 8.1: Histograms of time-reading for obtaining a successful measurement of SpO_2 by groups to assess normality.

Device factor



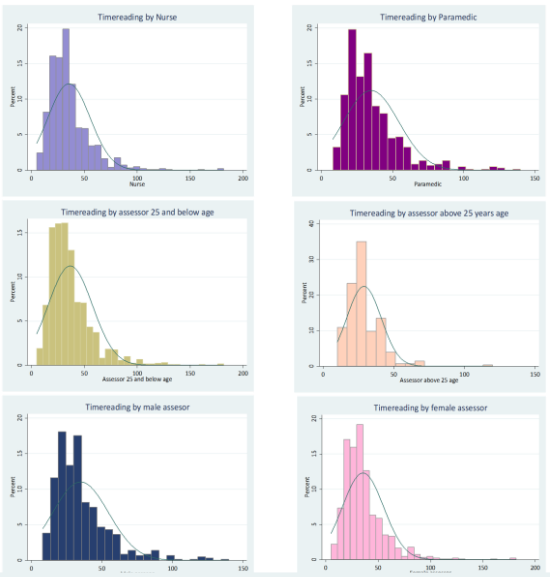
Shapiro-Wilk test for normality has been performed. P<0.001, hence the timing by each category is not normal

Children factors



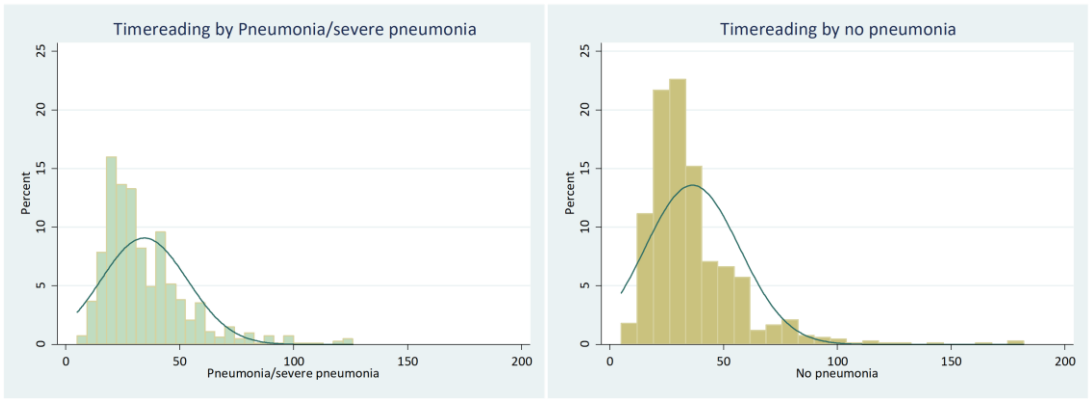
Shapiro-Wilk test for normality has been performed. P<0.001, hence the timing by each category is not normal

Assessor factors



Shapiro-Wilk test for normality has been performed. P<0.001, hence the timing by each category is not normal

Diagnosis



Shapiro-Wilk test for normality has been performed. P<0.001, hence the timing by each category is not normal

8.8 REFERENCE

1. Rahman AE, Hossain AT, Siddique AB, Jabeen S, Chisti MJ, Dockrell DH, et al. Child mortality in Bangladesh–why, when, where and how? A national survey-based analysis. Journal of global health. 2021;11.
2. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18: Final Report. Dhaka, Bangladesh and Calverton, Maryland, USA; 2019.
3. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
4. Rahman AE, Hossain AT, Nair H, Chisti MJ, Dockrell D, Arifeen SE, et al. The prevalence of hypoxaemia among children with pneumonia in low- and middle-income countries: a systematic review and meta-analysis. Lancet Glob Health.in press.
5. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.
6. Rahman AE, Hossain AT, Chisti MJ, Dockrell DH, Nair H, El Arifeen S, et al. Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh. Journal of global health. 2021;11.
7. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.
8. Rahman AE, Hossain AT, Nair H, Chisti MJ, Dockrell D, El Arifeen S, et al. Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Global Health. 2022;10(3):e348-e59.
9. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328-33.
10. Graham H, Bakare AA, Ayede AI, Oyewole OB, Gray A, Peel D, et al. Hypoxaemia in hospitalised children and neonates: a prospective cohort study in Nigerian secondary-level hospitals. EClinicalMedicine. 2019;16:51-63.
11. Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. Lancet. 2013;381(9875):1405-16.
12. United Nations. Take Action for the Sustainable Development Goals 2021 [cited 2021 28 November 2021]. Available from: https://www.un.org/sustainabledevelopment/sustainable-development-goals/.
13. World Health Organization. Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). 2013.

14. Gillor A, Schickendantz S, Heiner K, Mennicken U. Noninvasive determination of oxygen saturation using pulse oximetry in pediatric cardiology. Monatsschr Kinderheilkd. 1988;136(2):71-5.

15. Kamat V. Pulse oximetry. Indian J Anaesth. 2002;46(4):261-8.

16. Funk LM, Weiser TG, Berry WR, Lipsitz SR, Merry AF, Enright AC, et al. Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. Lancet. 2010;376(9746):1055-61.

17. Louw A, Cracco C, Cerf C, Harf A, Duvaldestin P, Lemaire F, et al. Accuracy of pulse oximetry in the intensive care unit. Intensive Care Med. 2001;27(10):1606-13.

18. Payne JP, Severinghaus JW. Pulse oximetry: Springer; 1986.

19. Varshini R. A Review on Design and Development of IoT Based Pulse Oximeter. Journal of Research Proceedings. 2021;1(2):1-10.

20. Floyd J, Wu L, Burgess DH, Izadnegahdar R, Mukanga D, Ghani AC. Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Nature. 2015;528(7580):S53-S9.

21. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

22. IMCI WHO. integrated management of childhood illness (IMCI) chart booklet. Distance Learn Course. 2014:1-76.

23. Rahman AE, Jabeen S, Genevie F, Banik G, Islam J, Ameen S, et al. Introducing pulse oximetry in routine IMCI services in Bangladesh: a context-driven approach to influence policy and programme through stakeholder engagement. J Glob Health. 2021;in press.

24. Meeting notes of consultative workshop on developing the implementation for the project "Assessing the feasibility and effectiveness of introducing pulse oximetry in IMCI services to manage acute respiratory infections at first level health facilities of Bangladesh. Date: 13 June 2019 [press release]. 2019.

25. Enoch AJ, English M, Network CI, McGivern G, Shepperd S. Variability in the use of pulse oximeters with children in Kenyan hospitals: a mixed-methods analysis. PLoS Med. 2019;16(12):e1002987.

26. Trivedi NS, Ghouri AF, Shah NK, Lai E, Barker SJ. Effects of motion, ambient light, and hypoperfusion on pulse oximeter function. J Clin Anesth. 1997;9(3):179-83.

27. Yamaya Y, Bogaard HJ, Wagner PD, Niizeki K, Hopkins SR. Validity of pulse oximetry during maximal exercise in normoxia, hypoxia, and hyperoxia. J Appl Physiol. 2002;92(1):162-8.

28. Sola A, Chow L, Rogido M, editors. Pulse oximetry in neonatal care in 2005. A comprehensive state of the art review. Anales De Pediatria (Barcelona, Spain: 2003); 2005.

29. Boyd N, King C, Walker IA, Zadutsa B, Bernstein M, Ahmed S, et al. Usability Testing of a Reusable Pulse Oximeter Probe Developed for Health-Care Workers Caring for Children <5 Years Old in Low-Resource Settings. Am J Trop Med. 2018;99(4):1096.

30. Baquero H, Alviz R, Castillo A, Neira F, Sola A. Avoiding hyperoxemia during neonatal resuscitation: time to response of different SpO2 monitors. Acta Paediatr. 2011;100(4):515-8.

31. Ramanathan R, Durand M, Larrazabal C. Pulse oximetry in very low birth weight infants with acute and chronic lung disease. Pediatrics. 1987;79(4):612-7.

32. Ewer AK, Middleton LJ, Furmston AT, Bhoyar A, Daniels JP, Thangaratinam S, et al. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. Lancet. 2011;378(9793):785-94.

33. Anderson CG, Benitz WE, Madan A. Retinopathy of prematurity and pulse oximetry: a national survey of recent practices. J Perinatol. 2004;24(3):164-8.

34. Brouillette RT, Morielli A, Leimanis A, Waters KA, Luciano R, Ducharme FM. Nocturnal pulse oximetry as an abbreviated testing modality for pediatric obstructive sleep apnea. Pediatrics. 2000;105(2):405-12.

35. King C, Boyd N, Walker I, Zadutsa B, Baqui AH, Ahmed S, et al. Opportunities and barriers in paediatric pulse oximetry for pneumonia in low-resource clinical settings: a qualitative evaluation from Malawi and Bangladesh. BMJ Open. 2018;8(1):e019177.

36. Mallory MD, Shay DK, Garrett J, Bordley WC. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. Pediatrics. 2003;111(1):e45-e51.

37. National Institute of Population Research and Training (NIPORT), International Centre for Diarrhoeal Disease Research Bangladesh, MEASURE Evaluation. Bangladesh District Level Socio-demographic and Health Care Utilization Indicators. Dhaka, Bangladesh, and Chapel Hill, NC, USA: NIPORT, icddr,b, and MEASURE Evaluation; 2019.

38. Stata. Stata 2021 [cited 2022 1 January 2022]. Available from: https://www.stata.com/.

39. World Health Organization. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development: World Health Organization; 2006.

40. Razali NM, Wah YB. Power comparisons of shapiro-wilk, kolmogorov-smirnov, lilliefors and anderson-darling tests. Journal of statistical modeling and analytics. 2011;2(1):21-33.

41. Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. J Clin Epidemiol. 1993;46(5):423-9.

42. Emdin CA, Mir F, Sultana S, Kazi A, Zaidi AK, Dimitris MC, et al. Utility and feasibility of integrating pulse oximetry into the routine assessment of young infants at primary care clinics in Karachi, Pakistan: a cross-sectional study. BMC Pediatr. 2015;15(1):1-11.

43. King C, Mvalo T, Sessions K, Wilson I, Walker I, Zadutsa B, et al. Performance of a novel reusable pediatric pulse oximeter probe. Pediatr Pulmonol. 2019;54(7):1052-9.

44. Salyer JW. Neonatal and pediatric pulse oximetry. Respir Care. 2003;48(4):386-98.

45. Myatt R. Measuring peak expiratory flow rate: what the nurse needs to know. Nursing. 2017;31(20):40-4.

46. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.

47. Carlson GA, Potegal M, Grover PJ. Helping children hospitalized for rages. Psychiatr Times. 2009;26(7):38.

48. Andaleeb SS. Public and private hospitals in Bangladesh: service quality and predictors of hospital choice. Health Policy Plan. 2000;15(1):95-102.

49. Rahman AE, Hossain AT, Zaman SB, Salim N, Ashish K, Day LT, et al. Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy childbirth. 2021;21(1):1-17.

Chapter 9: FEASIBILITY OF INTRODUCING PULSE OXIMETRY IN ROUTINE IMCI SERVICES IN OUTPATIENT SETTINGS IN RURAL BANGLADESH

One of my general objectives was to assess the feasibility of introducing pulse oximetry in routine IMCI services. The specific research question 7 was to assess IMCI service provider's performance of pulse oximetry in routine outpatient settings in rural Bangladesh.

Table 9.1: General objectives and specific research questions

Sl #	Objectives and Research Questions
A	**Estimating the burden of hypoxaemia among children with pneumonia**
1.	What is the burden of hypoxaemia among children with pneumonia LMICs?
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?
B	**Understanding the context of managing children with pneumonia, including hypoxaemia in Bangladesh**
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?
C	**Assessing the feasibility of introducing pulse oximetry in routine IMCI services**
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?
6.	What is the adequacy of the training package developed for introducing pulse oximetry in routine IMCI services in Bangladesh?
7.	What is the feasibility of implementing the district model for introducing pulse oximetry in routine IMCI services in Bangladesh?

The work presented in the chapter 9 has been accepted in the Lancet e-Clinical Medicine in 2022.

Title: Introducing pulse oximetry for outpatient management of childhood pneumonia: An implementation research adopting a district implementation model in selected rural facilities in Bangladesh

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9.1 ABSTRACT

9.1.1 Background

Pulse oximetry has enormous potential for identifying hypoxaemic pneumonia and reducing under-5 deaths in low- and middle-income country (LMIC) settings. However, there are few examples of introducing pulse oximetry in resource-constrained paediatric outpatient settings, i.e., Integrated Management of Childhood Illness (IMCI) services.

9.1.2 Methods

The National IMCI programme of Bangladesh designed and developed a district implementation model for introducing pulse oximetry in routine IMCI services through stakeholder engagement and demonstrated the model in Kushtia district adopting a health system strengthening approach. Between December 2020 and June 2021, two rounds of assessment were conducted based on WHO's implementation research framework and outcome variables, involving 22 IMCI service providers and 1680 children presenting with cough/difficulty-in-breathing in 12 health facilities. The data collection procedures included structured observations, re-assessments, interviews, and data extraction by trained study

9.1.3 Results

We observed that IMCI service providers conducted pulse oximetry assessments on all eligible children in routine outpatient settings, of which 99% of assessments were successful; 85% (95% CI, 83 to 87) in one attempt, and 69% (95% CI, 67 to 71) within one minute. The adherence to standard operating procedure related to pulse oximetry was 92% (95% CI, 91 to 93), and agreement regarding identifying hypoxaemia was 97% (95% CI, 96 to 98). The median performance time was 36 seconds (IQR, 20 to 75), which was longer among younger children (2-11 months: 44 seconds, IQR, 22 to 78; 12-59 months: 30 seconds, IQR, 18 to 53, $p<0.01$) and among those classified as pneumonia/severe pneumonia than as no pneumonia (41 seconds, IQR, 22 to 70; 32 seconds, IQR, 20 to 62, $p<0.01$). We observed improvements in almost all indicators during the round-2 of assessments. The IMCI service providers and caregivers showed positive attitudes towards using this novel technology for assessing their children.

9.1.4 Conclusion

This implementation research study demonstrated the adoption, feasibility, fidelity, appropriateness, acceptability, and sustainability of pulse oximetry introduction in routine IMCI services in resource-poor settings. The learning may inform the evidence-based scale-up of pulse oximetry linked with an oxygen delivery system in Bangladesh and other LMICs.

9.2 BACKGROUND

Pneumonia is the leading cause of childhood mortality, accounting for approximately 16% of under-5 deaths globally (1). The majority of these deaths occur in low- and middle-income countries (LMICs) and most are preventable (1-3). It takes more lives than any other causes in post-neonatal periods, especially in low-resource settings (4). In Bangladesh, it causes approximately one million episodes of severe-illness and 24,000 under-5 deaths every year (5, 6). Around 30% children with pneumonia suffer from hypoxaemia, defined by low oxygen saturation in arterial blood (SpO_2), and is a strong predictor of hospitalisations and deaths (7, 8). Pulse oximetry is an accurate and non-invasive procedure to measure SpO_2 at point of care (9). It can significantly improve childhood pneumonia classification through hypoxaemia identification and substantially reduce deaths in low- and middle-income country (LMIC) settings (9).

In 2014, the World Health Organization (WHO) updated its outpatient-based child-curative care guidelines, i.e., Integrated Management of Childhood Illness (IMCI) and recommended introducing pulse oximetry for pneumonia assessment (10). Several health system challenges are associated with integrating a new technology/device like pulse oximetry in LMIC settings (11). Although there is some published experience of introducing pulse oximetry in low-resource settings, most predates the 2014-WHO recommendations (12-14).

Successful introduction of a generic recommendation, technology or device in routine services demands context-specific adaptations, demonstration and feasibility assessments (15-17). In 2019, the National IMCI Programme of the Government of Bangladesh (GoB) decided to introduce pulse oximetry in routine

IMCI services (18). A national technical committee was formed, which updated the National IMCI Implementation Package by incorporating recommendations to conduct pulse oximetry assessments on all children presenting with cough/difficulty-in-breathing for pneumonia assessments (18, 19). The National IMCI Programme also decided to demonstrate the updated package in a district setting to inform evidence-based scale-up. Here, we present the experience and learning synthesised during the demonstration phase.

9.3 METHODS

9.3.1 Study design

An implementation research study was conducted, where the National IMCI Programme designed, developed, and demonstrated a district implementation model to introduce pulse oximetry in routine IMCI services. icddr,b, an international health research organisation based in Bangladesh, provided implementation facilitation support and assessments.

This study was conducted in Kushtia district (zila), approximately 200 kilometres from Dhaka, which was selected as the demonstration site as its under-5 mortality rate was close to the national average and the IMCI services were functioning relatively well (17). The IMCI Programme, in consultation with the district manager (Civil Surgeon) and sub-district managers (Upazila Health and Family Planning Officers), selected one district hospital (secondary referral), all five sub-district hospitals (primary referral) and six union-based facilities (health centres) as

demonstration facilities (additional details in supplementary table 9.1 & supplementary figure 9.1).

The **IMCI programme** designed and developed a district implementation model through stakeholder engagement and adopted a health systems approach to strengthening the overall IMCI services, including the introduction of pulse oximetry in demonstration facilities (additional details in supplementary figure 9.2). It had four components, which are as follows:

i) Sensitisation of district- and sub-district managers and IMCI service providers through workshops and involve them in planning and implementation

ii) Capacity development of IMCI service providers, supervisors, data officers and district- and sub-district managers

iii) Health system strengthening to improve IMCI service readiness and distribution of pulse oximetry devices through the routine distribution channel

iv) Follow-up support to IMCI service providers through routine monitoring, supportive supervision and performance appraisal workshops

The demonstration study started in October-2019, was suspended in March-2020 due to COVID-19, resumed in October-2020, and ended in October-2021.

i. Sensitisation and Planning

The National IMCI Programme organised a district-level workshop with the district- and sub-district managers of Kushtia to sensitise them regarding the importance of

introducing pulse oximetry in routine IMCI services and develop a high-level plan for implementing the updated IMCI implementation package in the selected health facilities. Following that, a workshop was organised in each sub-district with the respective sub-district health managers, IMCI service providers and their clinical supervisors for further sensitisation and developing facility-specific micro-plans. Then, a workshop was also organised in each of the selected health facilities with IMCI services providers and their supervisors to introduce pulse oximetry officially. These workshops were organised between October and December 2019. Unfortunately, the implementation was suspended in March 2020 due to the COVID-19 pandemic. The **IMCI programme** decided to resume the activities in September 2020. Between October and November 2020, another round of district- and sub-district-level workshops were organised to update the high-level as well as the facility-specific micro plans.

ii. CAPACITY BUILDING

Between December 2019 and February 2020, the IMCI Programme organised a series of training for IMCI service providers from across the country based on the updated IMCI implementation package as a part of their routine programme activities. The National IMCI master trainers facilitated the sessions, and all IMCI service providers from the selected health facilities of Kushtia received the training. The updated IMCI training manual had a module on pneumonia assessment and pulse oximetry adapted from the pulse oximetry training manual of WHO. The module had information and instructions on the pathophysiology of hypoxaemia; function, types

and parts of a pulse oximetry device; steps of conducting pulse oximetry assessments; and maintenance of the device. Half a day was dedicated to pulse oximetry which included both theoretical ad practical sessions. In addition, an orientation session was organised in Kushtia for the district- and sub-district managers, IMCI clinical supervisors, and data officers to discuss the basics of pulse oximetry and inclusion of SpO_2 status and hypoxaemia reporting in the IMCI service register and monthly reporting form

iii. DISTRIBUTION OF PULSE OXIMETERS

icddr,b surveyed the selected health facilities in December 2019 and identified the gaps in the availability of equipment, drugs, and logistics required for managing pneumonia based on the updated IMCI guidelines. The **IMCI programme** addressed these gaps through the existing procurement and distribution channel. In addition, icddr,b supported the **IMCI programme** to procure and distribute Masimo Rad-5v handheld pulse oximeters to the selected health facilities. The specific model was chosen by the national technical committee (mentioned earlier) based on the superiority in technical specifications and expert consultations. The distribution of pulse oximeters and other logistics were done between January and February 2020. In addition, batteries of the pulse oximetry devices were replaced through the existing procurement and distribution channel throughout the implementation period. In general, batteries were replaced after 15-25 days in the district hospitals, 30-40 days in sub-district hospitals and 60-70 days in health centres.

iv. MONITORING, SUPERVISION AND PERFORMANCE REVIEW WORKSHOPS

National, district and sub-district managers were responsible for monitoring and supervising the pulse oximetry related implementation in Kushtia. Representatives from the **IMCI programme** conducted several field visits during the implementation period. They also conducted online meetings with the district- and sub-district managers to review the progress and discuss implementation quality and challenges. In addition, the district and sub-district managers conducted at least one supervisory visit to each selected facility during the implementation period. The observations from these supervisory visits were discussed in the routine monthly meetings. Moreover, a review workshop was organised in March 2021 with all IMCI service providers in the presence of national-, district- and sub-district managers and clinical supervisors to discuss the achievements and gaps identified through the first round of assessments. A similar review workshop was also organised in October 2021 after completing the second round of assessments.

We adapted WHO's implementation research framework and implementation outcome variables for this study (20). The National IMCI Programme of Bangladesh and icddr,b jointly conducted a series of workshops with district- and sub-district managers to finalise the research questions based on WHO's framework and set a benchmark for successful demonstration for each outcome variable (additional details in supplementary table 9.2) (18). The primary research questions are outlined in table 9.2.

Table 9.2: Research questions and benchmarks for successful demonstration; adapted from WHO's implementation outcome variables and finalised through stakeholder consultations

WHOs' framework	Research questions	Proposed indicator	Benchmark for success
a) Adoption	Use: Do IMCI service providers conduct pulse oximetry assessments?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device	>90%
b) Feasibility	Success: Can IMCI service providers successfully conduct pulse oximetry assessments?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device and obtain a stable SpO_2 reading	>80%
	Usability by attempt: Can IMCI service providers successfully conduct pulse oximetry assessments in the first attempt?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device and obtain a stable SpO_2 reading in one attempt	>75%
	Usability by time: Can IMCI service providers successfully perform pulse oximetry in one minute?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device and obtain a stable SpO_2 reading in one minute	>66%
c) Fidelity	Adherence: Do IMCI service providers follow Standard Operating Procedure (SoP) while conducting pulse oximetry assessments?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service provider with a pulse oximetry device by putting the probe in appropriate position and direction and taking measures to keep the child calm during the procedure	>75%
	Agreement: Can IMCI service providers identify hypoxaemia through pulse oximetry?	Level of observed agreement between IMCI service providers and study nurses regarding hypoxaemia identification through pulse oximetry	>90%
d) Appropriateness	Experience: Do IMCI service-providers conduct pulse oximetry assessments with reasonably low barriers and challenges?	Proportion of IMCI service providers reporting an average challenge level of <80% or less regarding conducting pulse oximetry assessments in routine outpatient settings	>80%

WHOs' framework	Research questions	Proposed indicator	Benchmark for success
e) Acceptability	Usefulness: Do IMCI service providers perceive pulse oximetry as useful?	Proportion of IMCI service providers reporting that pulse oximetry is useful for identifying hypoxaemia and pneumonia classification	>80%
	Importance: Do the caregivers perceive pulse oximetry as important?	Proportion of caregiver of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device reporting that pulse oximetry was important for assessing their children	>80%
	Satisfaction: Are the caregivers satisfied with pulse oximetry introduction in routine IMCI services?	Proportion of children presenting with cough/difficulty-in-breathing assessed by IMCI service providers with a pulse oximetry device reporting that they will allow conducting pulse oximetry assessments on their children in future visits.	>80%
f) Sustainability	Sustainability: Does the pulse oximetry performance of IMCI service providers sustain over time (rounds)?	Proportions of the above-mentioned indicators representing adoption, feasibility, fidelity, appropriateness and acceptance of pulse oximetry demonstrating equal or better performance round-2 than that of round-1	>80%

Children aged 2-59 months presenting with cough/difficulty-in-breathing and receiving IMCI services at selected health facilities and government employed IMCI service providers (doctors, nurses, and paramedics) providing those services were the study population.

We calculated the sample size for each of the primary research questions based on the benchmark set for successful demonstration (Table 9.2). The maximum variance (67%) was expected for the usability-time indicator. The adjusted sample size was 639 children presenting with cough/difficulty-in-breathing per round. There were 22

IMCI service providers in the selected facilities. We aimed to assess the pulse oximetry performance of all IMCI service providers by observing and re-assessing at least 30 children presenting with cough/difficulty-in-breathing per provider, per round. We approached all children presenting with cough/difficulty-in-breathing on the day of assessment, and it required 3-7 days per provider per round to achieve the required sample size. On the day the required sample size (30 children) was reached for each IMCI service provider, we continued enrolment and data collection until the end of business hours.

We conducted two rounds of assessment: round-1 in December 2020-February 2021; round-2 in March-May 2021. The data collection procedures included structured observation of IMCI service providers conducting pulse oximetry assessments during routine consultations by study nurses, re-assessment (history taking, clinical assessment and pulse oximetry) of children (after IMCI consultation) by study nurses, exit-interviews of the caregivers by study paramedics, data extraction from IMCI-registers by data collectors, and structured-interviews with IMCI service providers by study paramedics (Supplementary table 9.3). We assessed the pulse oximetry performance of the same IMCI service providers in both rounds. All forms/questionnaires were pretested separately on at least five participants. The construct/framing of some of the questions and skip logics were updated based on the pre-tests. Data collection was conducted by means of a specially designed android-app, which had the provision to capture each pulse oximetry step with time stamping (21). The data collection team received extensive training and refresher training on IMCI guidelines, pulse oximetry principles and process, data collection

forms/questionnaires and the data-collection app. All tools were developed based on the extensive literature review and the structured interview and exit interview tool for the IMCI service providers on barriers and operational challenges were developed based on qualitative exploration. All tools were field-tested and pre-tested before finalisation.

i. Enrolment

A non-medical study staff approached all children in the waiting room/area of selected health facilities and enrolled children aged 2-59 presenting with cough/difficulty-in-breathing before receiving consultation from the IMCI service providers.

ii. Structured observation

Trained study nurses conducted structured observations of IMCI service providers conducting pulse oximetry assessments on children presenting with cough/ difficulty-in-breathing. The observers collected information on the following outcomes: use, success, usability by attempts, usability by time and performance time. The observers received ten days of training before data collection (five days on IMCI, one day on pulse oximetry, two days on using the data collection app based on the structured observation tool, and two days of field practice). Three days of refresher training was organised before the second round of data collection.

iii. Re-assessment

A separate group of trained study nurses conducted re-assessments of the enrolled children in a separate room after the structured observation. The assessors collected

data on the history of illness, conducted clinical assessments based on the IMCI guideline, and conducted pulse oximetry assessments using a device of the same model. The assessors received ten days of training before data collection (five days on IMCI, one day on pulse oximetry, two days on the re-assessment tool, and two days for field practice). Three days of refresher training was organised before the second round of data collection.

iv. Exit-interview

A separate group of trained paramedics conducted exit-interviews of the caregivers of the enrolled children after re-assessment. The interviewers used an interviewer-administered structured-questionnaire (translated in Bangla) to collect data on the acceptability and perceived importance of pulse oximetry. The interviewers received five days of training before data collection (one day on pulse oximetry, two days on the exit-interview questionnaire and two days of field practice). One day of refresher training was organised before the second round of data collection.

v. Data extraction

Trained data collectors extracted data from the IMCI services register of those children who were enrolled in this study. The data collectors took snapshots of the IMCI registers after service hours on the day of assessment (additional details in supplementary figure 9.3a). We obtained administrative approval from national **IMCI programme** of Directorate General of Health Services of Bangladesh for conducting this study including the approval for taking snapshots of register. We also received approval from district-level health manager at Kushtia district. Furthermore, we have conducted facility level sensitisation, preparatory and

planning meeting in presence of the IMCI service providers, respective supervisors and facility managers. A dedicated team of data operators used a desktop-based application that was specially developed for this study and entered all available information, including SpO_2 and hypoxaemia status reported in the IMCI registers. The data operators received two days of training on IMCI registers and the desktop-based application. A data entry supervisor checked the data extraction process and conducted re-extraction and re-entry of 5% observations. There were very few cases where we identified minor issues, which we rectified by checking the source documents (snapshots).

vi. Structured interviews

The interviewers who conducted the exit-interviews of the caregivers also conducted structured interviews with IMCI services providers at the end of round two. The interviewers used a structured questionnaire with a five-point Likert scale and collected data on the perceived utility of introducing pulse oximetry in routine IMCI services and barriers and challenges faced while conducting pulse oximetry in routine practice.

vii. Monitoring and supervision

A medical graduate directly supervised the data collection team. During the data collection period, the supervisor conducted regular monitoring visits meetings and organised weekly meetings with the data collection team to discuss data quality issues and specific gaps.

9.3.2 Analysis plan

The following indicators were selected as primary outcomes of interest: adoption-use, feasibility-success, feasibility-usability by attempt, feasibility-usability by time, fidelity-SoP adherence, fidelity-agreement, appropriateness-experience, acceptability-usefulness, acceptability-importance, and acceptability-satisfaction (Table 9.2).

Adoption was operationally defined as conducting pulse oximetry assessments on children presenting with cough/difficulty in breathing. A pulse oximetry assessment was considered successful if a stable (±1%) SpO_2 reading was observed for at least 10 seconds with adequate signal strength. Performance time was defined by the time taken (in seconds) from placing the probe to obtaining a stable reading. Adherence to standard operating procedures (SoP-adherence) was defined as putting the probe in the appropriate position and direction and taking measures to keep the baby calm before conducting pulse oximetry assessments. The agreement was reported on identifying hypoxaemia through pulse oximetry by IMCI service providers and re-assessment study nurses. We used a SpO_2 cut-off of <94% to operationally define hypoxaemia (22). Regarding experience, the IMCI service providers reported barriers and challenges on a five-point Likert scale for 12 device-, patient-, environment-, and user-related factors.

Relationships between patient- (age, sex, weight-for-height, clinical features, and pneumonia status), provider- (age, sex, and designation), facility-related (types) factors and assessment rounds, and primary outcomes of interest (Table 9.2) were

considered as the secondary outcomes of interest (Supplementary material 9.2). We also reported median performance time and infection prevention and control (IPC) practice, defined as cleaning the probe or attachment site of the child before conducting pulse oximetry assessments, as secondary outcomes of interest.

For categorical variables as outcomes of interest, we presented point estimates with 95% confidence intervals (CI). We used prevalence-adjusted and bias-adjusted kappa (PABAK) to report the agreement between IMCI service providers and re-assessment study nurses (23). We used Generalised Estimating Equation (GEE) models and reported crude and adjusted odds ratios (with 95% CI and p-value) to assess the adjusted effect of various factors and assessment rounds on these indicators. Wald statistics were used for checking the adequacy of the models. We used radar-plots to present the variations by each IMCI service provider and reported the heterogeneity with I^2 and Tau^2 statistics. The statistical significance of the estimates have been reported at 5% level of significance.

For performance time, we checked the normality distribution using Shapiro-Wilk test (Supplementary figure 9.4). As they were non-normally distributed, we presented medians with interquartile ranges (IQRs) and used Mood's non-parametric equality of medians test to check for significant differences in various factors and assessment rounds. Barrier and challenge experiences were presented as means with standard deviations (SDs).

We used Stata version 15.0 for data analysis. More details regarding the analysis plan are available in the supplementary material (Supplementary table 9.2).

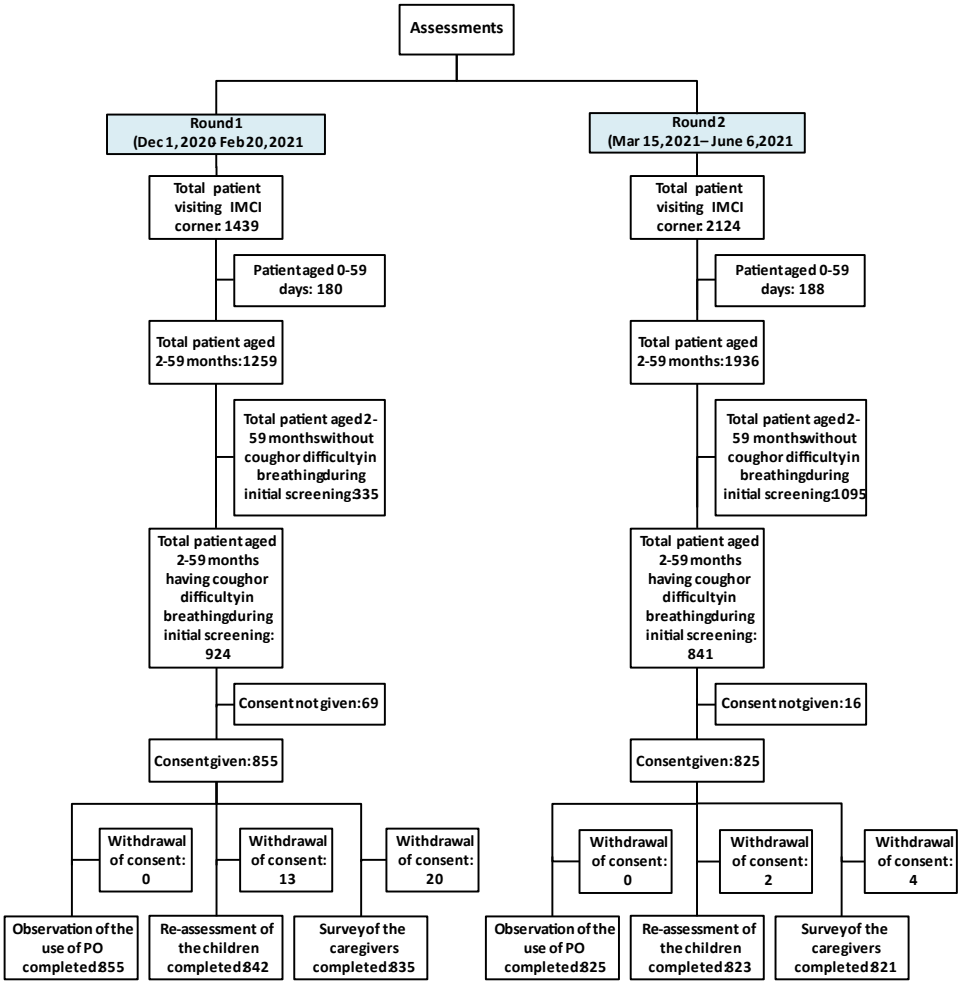
9.3.3 Ethical considerations

Ethical approval of the study was obtained from the Institutional Review Board of icddr,b (Protocol Number: PR-18054). Research Governance of The University of Edinburgh declared the study does not need any UK based ethical opinion as it was categorised as minimal risk.

9.4 RESULTS

We assessed the pulse oximetry performance of five doctors, five nurses and twelve paramedics as IMCI service providers in both rounds (additional details in supplementary table 9.4). During the two rounds of assessment, 3563 children received IMCI services from the selected facilities, of which 3195 (90%) were aged 2-59 months, 1765 (49%) had cough/difficulty-in-breathing, and 1680 (47%) were enrolled for assessments (Figure 9.1). Around one percent (0.9%) enrolled children were not re-assessed, and 1.4% caregivers could not be interviewed.

Figure 9.1: Sample size by each round of assessments

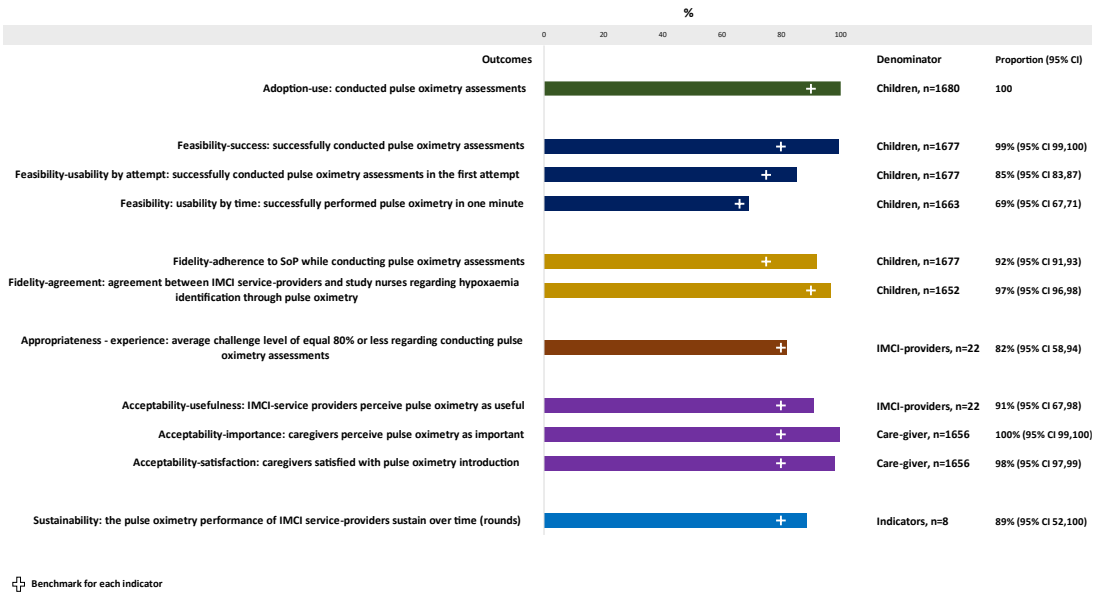


Of the enrolled children, 729 (43%) were aged 2-11 months, 164 (10%) were wasted/severely-wasted, and 220 (13%) were classified as pneumonia/severe pneumonia (Supplementary table 9.5, 9.6, and 9.7).

During our assessment, the IMCI service providers conducted pulse oximetry assessments (adoption-use) on all children presenting with cough/difficulty-in-breathing, of which 99% of assessments were successful (feasibility-success); 85% (95% CI, 83 to 87) in one attempt (feasibility-usability by attempt) and 69% (95% CI, 67 to 71) within one minute (feasibility-usability by time) (Figure 9.2). The adherence

to SoPs was 92% (95% CI, 91 to 93) (fidelity-SoP-adherence), and the agreement was 97% (95% CI, 96 to 98) (fidelity-agreement). All IMCI service providers reported that pulse oximetry was useful for identifying hypoxaemia and pneumonia classification (acceptability-usefulness). Almost all (98%) caregivers felt that it was an important diagnostic for assessing their children (acceptability-importance) and all of them would allow conducting it on their children during future visits (acceptability-satisfaction). The indicators representing adoption, feasibility, fidelity, appropriateness, and acceptance demonstrated equal or better performance in round-2 (sustainability).

Figure 9.2: Performance of conducting pulse oximetry assessments by IMCI service providers among children presenting with cough/difficulty-in-breathing in paediatric outpatient settings; presented in % with 95% confidence interval; N=1680



CI: 95% Confidence Interval

Table 9.3 summarises the effect of various factors and assessment rounds on feasibility- and fidelity-related indicators. The highlighted cells indicate the statistically significant odds ratio. The odds of successfully conducting pulse oximetry

assessments in one attempt was significantly higher among older (aged 12-59 months) (AOR 2.19, 95% CI, 1.65 to 2.92) and male (AOR 1.54, 95% CI, 1.16 to 2.04) children (Wald statistics 44.71, p<0.01). They were also more likely to successfully conduct pulse oximetry assessments within one minute on older children (AOR 2.05, 95% CI, 1.65 to2.55) (Wald statistics 59.98, p<0.01). Older, female, and sub-district hospital- and health centre-based providers were less likely to adhere to pulse oximetry SoPs (Wald statistics 100.14, p<0.01). Substantial improvement was observed in round-2 regarding most of these indicators. More details about the models are available in supplementary table 9.8, 9.9, 9.10, and 9.11.

Table 9.3: Influence of patient-, provider- and facility-related factors on the performance of conducting pulse oximetry assessments by IMCI service providers; presented in adjusted odds ratios; N=1680

	Feasibility-usability: Success at first attempt	Feasibility-performance time: Success within 60 seconds	Fidelity-adherence: Adherence to SoP of PO use	Fidelity-agreement: Observed agreement
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Patient-related factors				
Age				
2-11 months	Ref	Ref	Ref	Ref
12-59 months	2.2 (1.65,2.93)	2.05 (1.65,2.55)	1.06 (0.69,1.61)	1.19 (0.67,2.11)
Sex				
Female	Ref	Ref	Ref	Ref
Male	1.54 (1.16,2.04)	1.21 (0.98,1.5)	0.69 (0.46,1.05)	1.07 (0.6,1.89)
Z-score (weight for height)				
Not wasted (-2SD and above)	Ref	Ref	Ref	Ref
Wasted (below -2SD)	0.82 (0.47,1.43)	0.79 (0.51,1.24)	0.75 (0.29,1.94)	1.46 (0.36,5.95)
Severely wasted (below -3SD)	0.8 (0.41,1.55)	0.89 (0.52,1.53)	1.59 (0.33,7.72)	0.75 (0.21,2.59)
Fever				
No	Ref	Ref	Ref	Ref
Yes	0.99 (0.52,1.91)	0.79 (0.49,1.27)	0.5 (0.18,1.36)	0.92 (0.3,2.84)
Fast breathing				
No	Ref	Ref	Ref	Ref

	Feasibility-usability: Success at first attempt	Feasibility-performance time: Success within 60 seconds	Fidelity-adherence: Adherence to SoP of PO use	Fidelity-agreement: Observed agreement
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Yes	1.03 (0.3,3.56)	1.08 (0.4,2.91)	0.6 (0.07,5.43)	1 (0.16,6.15)
Chest indrawing				
No	Ref	Ref	Ref	Ref
Yes	0.68 (0.28,1.65)	0.9 (0.44,1.84)	0.81 (0.19,3.55)	1.35 (0.33,5.53)
IMCI classification				
No pneumonia	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	1.06 (0.3,3.78)	0.88 (0.32,2.42)	1.32 (0.14,12.1)	0.38 (0.06,2.4)
Provider-related factors				
Age				
≤ 35 years	Ref	Ref	Ref	Ref
> 35 years	1.08 (0.72,1.62)	1.17 (0.9,1.53)	0.29 (0.15,0.53)	1.1 (0.27,4.44)
Sex				
Female	Ref	Ref	Ref	Ref
Male	0.88 (0.54,1.44)	1.05 (0.78,1.43)	2.98 (1.34,6.63)	0.72 (0.1,5.31)
Designation				
Doctors	Ref	Ref	Ref	Ref
Nurse	0.6 (0.34,1.05)	1.03 (0.73,1.45)	0.42 (0.16,1.1)	0.49 (0.06,4.17)
Paramedics	0.82 (0.46,1.45)	0.77 (0.55,1.08)	1.88 (0.55,6.43)	0.3 (0.04,2.12)
Facility-related factors				
District Hospital	Ref	Ref	Ref	Ref
Sub-District Hospital	0.91 (0.49,1.72)	1.06 (0.72,1.55)	0.03 (0,0.25)	1.33 (0.15,11.38)
Health Centre	0.76 (0.36,1.62)	0.81 (0.51,1.29)	0 (0,0.05)	4.97 (0.36,68.53)
Assessments				
Round				
Round 1	Ref	Ref	Ref	Ref
Round 2	0.98 (0.74,1.3)	1.3 (1.05,1.62)	28.62 (11.03,74.29)	1.76 (0.96,3.23)

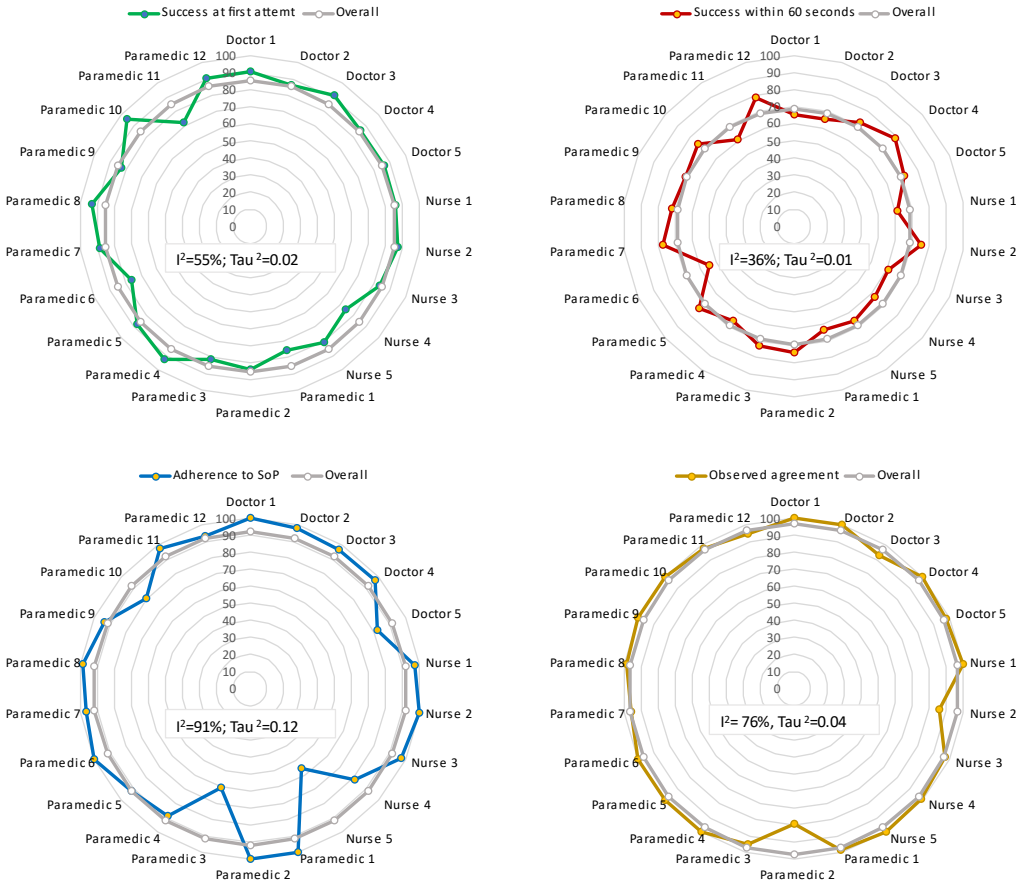
AOR: Adjusted Odds Ratio

95% CI: Confidence Interval

Regarding performance by individual IMCI service providers, we observed minimum variability in successfully conducting pulse oximetry assessment in one attempt

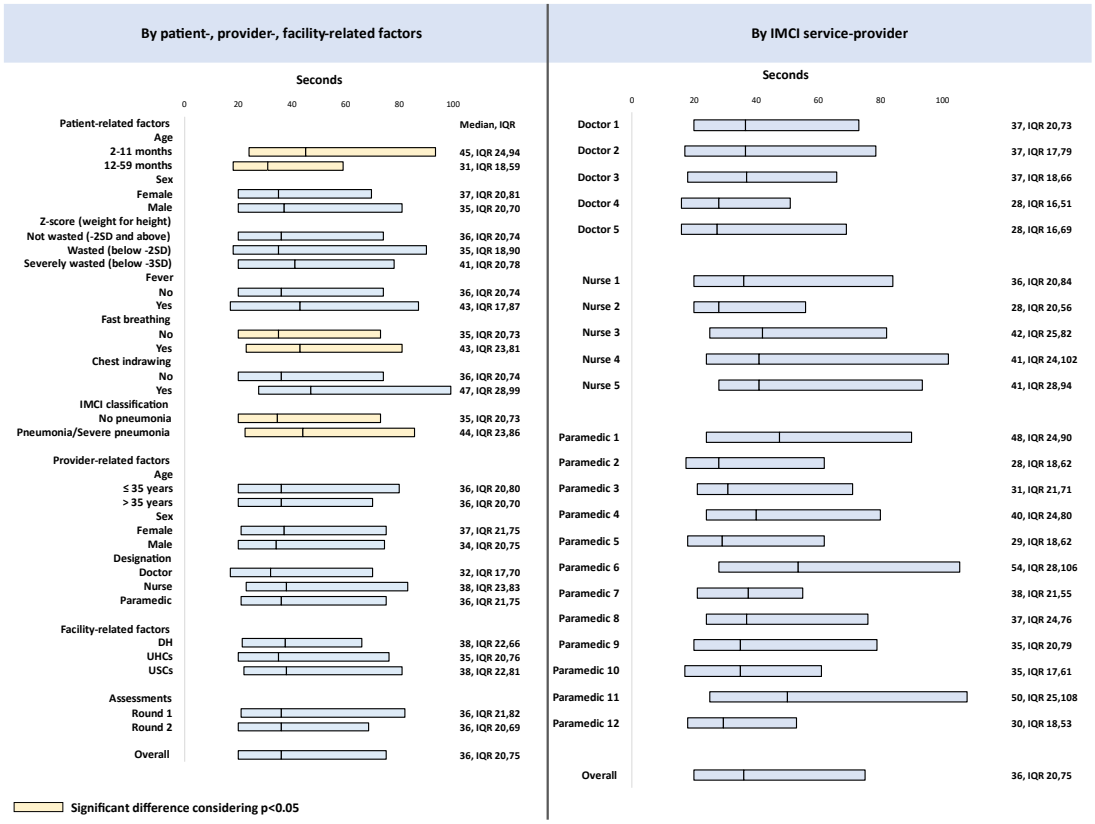
(I^2=55%; Tau^2=0.02), within one minute (I^2=36%; Tau^2=0.01), SoP-adherence (I^2=91%; Tau^2=0.12) and agreement (I^2=76%, Tau^2=0.04) (Figure 9.3).

Figure 9.3: Variability in performance of conducting pulse oximetry assessments by individual IMCI service providers; presented in %



The median performance time was 36 seconds (IQR 20,75) (Figure 9.4). The performance time was significantly (p<0.01) longer among younger children (aged 2-11 months; 44 seconds, IQR, 22 to 78) than older children (30 seconds, IQR, 18 to 53). Similarly, it took significantly (p<0.01) more time among children classified as pneumonia/severe pneumonia (41 seconds, IQR 22 to 70) than those who were classified as no pneumonia (32 seconds, IQR 20 to 62). There was wide variability among IMCI service providers regarding the timing (Pearson chi^2= 38.0240; p<0.01).

Figure 9.4: Performance time for conducting pulse oximetry assessment by patient-, provider-, and facility-related factors and by individual IMCI service providers; presented in median seconds with inter quartile range

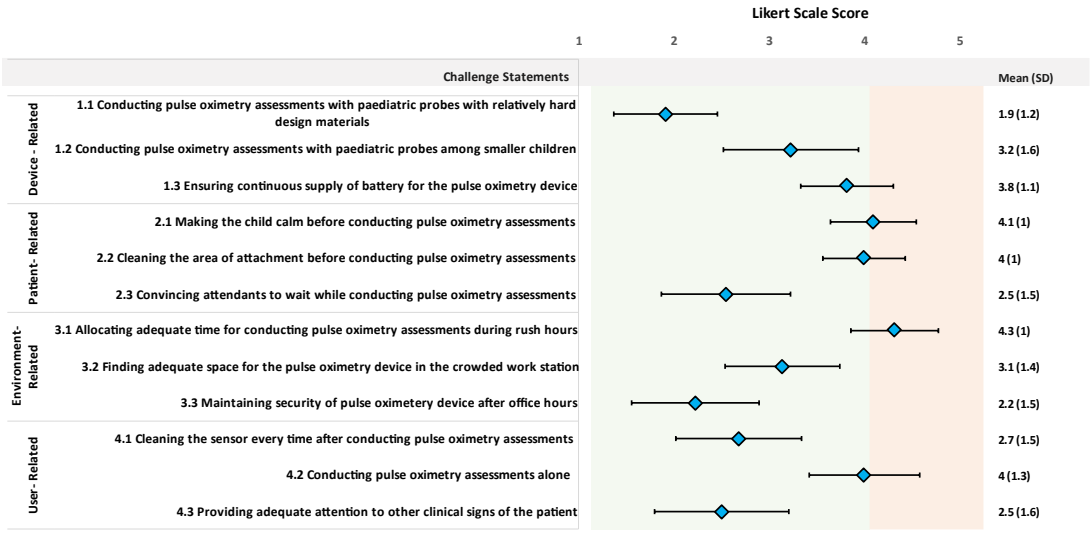


IQR: Interquartile Range

Figure 9.5 presents the barriers and challenges (appropriateness-experience) reported by the IMCI service providers while conducting pulse oximetry assessments based on a five-point Likert scale. Regarding patient-related factors, the highest (mean 4.1, 95% CI, 3.6 to 4.5) challenge was faced in making the child calm before conducting pulse oximetry assessments, which was closely followed by cleaning the area of attachment before placing the probe (mean 4.0, 95% CI, 3.6 to 4.4). Regarding environment-related factors, providers reported a high level of challenge in allocating adequate time for pulse oximetry during the period of peak service use

(mean 4.3, 95% CI, 3.9 to 4.8) and performing pulse oximetry alone (mean 4.0, 95% CI, 3.4 to 4.6).

Figure 9.5: Device-, patient-, environment- and user-related barriers and challenges faced by the IMCI service providers during pulse oximetry assessments; presented in mean score with SD based on a five-point Likert Scale; N=22



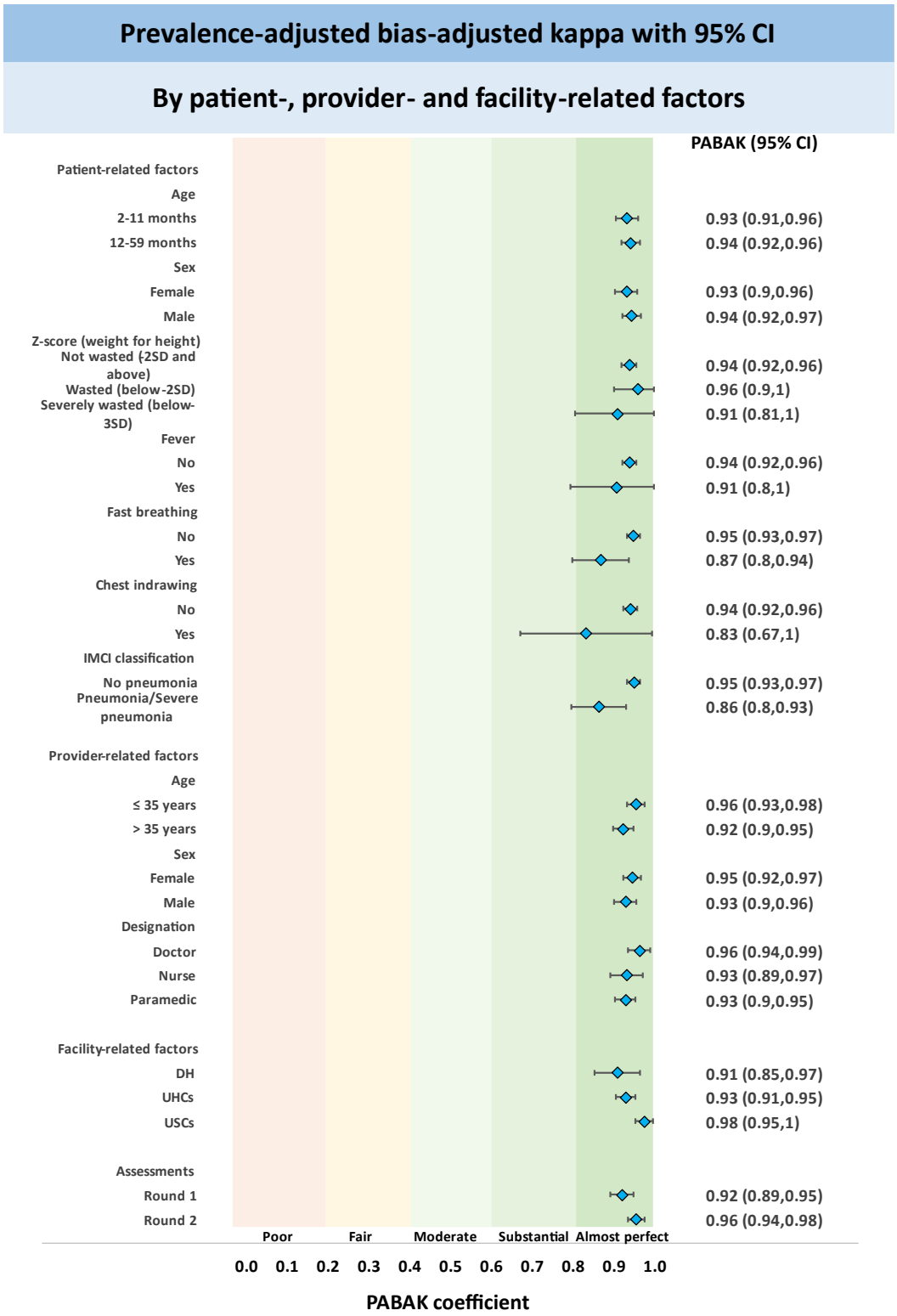
SD: Standard Deviation

The IMCI service providers maintained optimum IPC practice during 72% (95% CI, 70 to 74) of assessments (Supplementary table 9.12). This was significantly better among paramedics (AOR 2.6, 95% CI, 1.8 to 3.8) and nurses (AOR 1.8, 95% CI, 1.2 to 2.7) compared to doctors providing IMCI services, and in sub-district hospitals (AOR 20.3, 95% CI, 13.1 to 31.6) and health centres (AOR 7.0, 95% CI, 4.1, 11.7) compared to the district hospital. It was also substantially improved in round-2 (AOR 4.8, 95% CI 3.7, 6.3).

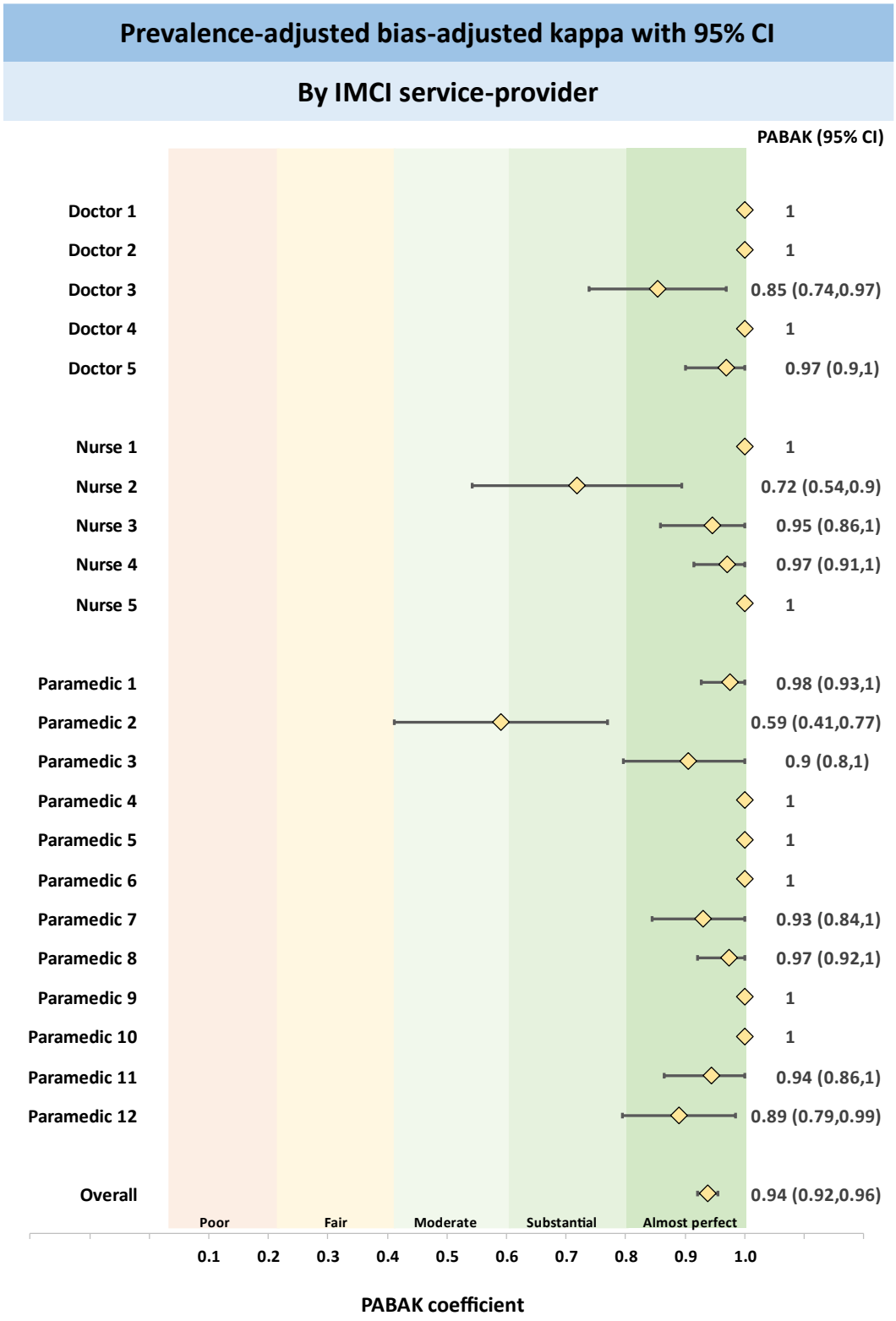
Figure 9.6 presents the agreement between IMCI service providers and study appointed nurses using prevalence-adjusted and bias-adjusted kappa (PABAK). The overall PABAK was 0.94; a very high level of agreement. We did not observe

significant variation by patient-, provider-, and facility-related factors and by individual IMCI service providers.

Figure 9.6: Agreement between IMCI service providers and study appointed nurses using prevalence-adjusted and bias-adjusted kappa (PABAK) by patient-related, provider-related and facility-related factors and by individual IMCI service providers; presented as coefficient with 95% confidence interval



CI: Confidence Interval



CI: 95% confidence interval

9.5 DISCUSSION

Pulse oximetry has enormous potential for maximising the impact of IMCI in LMIC settings with high burdens of childhood pneumonia and hypoxaemia (8, 13). This is one of the novel studies which adopted a health system strengthening approach and district model of implementation. To the best of our knowledge, this is the first study to report most of the WHO implementation outcome variables which include adoption, feasibility, fidelity, appropriateness, acceptability and sustainability. We observed that IMCI service providers almost universally conducted pulse oximetry assessments on almost all eligible children, and can successfully measure SpO_2 with minimum attempts, within a relatively short time and without major challenges. Their assessments were accurate, and performance was sustained or generally improved between two rounds. Also, caregivers were very positive towards introducing this technology for assessing their children.

Understanding the adoption and feasibility of introducing a new technology/device into routine systems is crucial to inform policy and programme (20). We observed high-level of use, success, and usability in conducting pulse oximetry assessment by IMCI service providers. Although there are some differences in the context, case-mix and assessor characteristics, our findings are comparable to studies conducted in Ethiopia, Malawi, UK, Bangladesh, and Pakistan (12, 13, 24, 25). These findings from diverse contexts reinforce the likelihood of adoption and feasibility of introducing pulse oximetry in resource-constrained outpatient settings. We have undertaken an inclusive approach of involving stakeholders, including IMCI service providers, in various stages of planning and implementation. We have also ensured their

continuous engagement through training, support supervision and performance appraisal workshops. This stakeholder engagement process may have contributed to the sense of ownership and acquisition of necessary skills, potentially explaining the encouraging findings related to adoption and feasibility (18). The first wave of the COVID-19 pandemic started a few months before the round-1 assessments. Although the pandemic created barriers in delivering many essential health services, it positively influenced the awareness of health care providers regarding hypoxaemia and attitude towards pulse oximetry and may have contributed as an unexpected enabler in this study (26, 27).

Fidelity of implementation is integrally linked to achieving the intended benefit of an intervention (20). In our study, we observed a high-level of SoP-adherence by IMCI service providers, similar to a study in rural Ethiopia (24). A systematic review reported that communicating through multiple approaches can significantly improve SoP-adherence among healthcare providers (28). We also adopted multiple approaches, such as emphasising the importance of calming the child and correct probe placement, along with ensuring availability of job-aids/visual aids in IMCI consultation rooms, which may have promoted such practice. However, we observed some issues related to IPC practices. Although probe cleaning procedures were not associated with successfully conducting pulse oximetry assessments, they represent an indispensable element of infection control, particularly in the COVID-19 context (29).

Regarding identifying hypoxaemia through pulse oximetry, we observed a high-level of agreement between IMCI service providers and study nurses. According to the WHO, fast breathing/chest-in-drawing as the only sign of pneumonia can be treated through outpatient management (10). However, around one in 10 such cases experience treatment failure, suggesting the presence of some 'severe cases' among apparently 'non-severe' cases of pneumonia (30). Hypoxaemia is one of the strongest predictors of adverse clinical outcomes, and its accurate identification can help reduce the misclassification of non-severe pneumonia (7, 31, 32). The high-level of agreement should give confidence to policymakers and families regarding the accuracy of SpO_2 measurement by minimally trained providers and thus their ability to identify the severe cases, even in routine settings.

We did not find any significant effect of provider- or facility-related factors on adoption and feasibility, suggesting that, with health systems inputs, such as training and post-training follow-up support through supervision and performance appraisal, different types of IMCI service providers can achieve necessary pulse oximetry skills in all kinds of facilities. Regarding patient-related factors, similar to a multi-country trial, we observed that success and usability were significantly poorer among younger children, with performance time decreasing with increasing age (25). The providers interviewed in our study and several other studies also reported facing difficulties in conducting pulse oximetry among younger and smaller children (11, 33). Pulse oximetry readings are significantly affected by patient movement (motion artefacts) and the appropriateness of the probe size (34). Younger children are expected to be more restless during pulse oximetry. Although we used Masimo

paediatric probes of same size in this study, the size, design and material used for these probes may need specific adaptations, especially in settings with high burdens of both pneumonia and malnutrition, which is the case for Bangladesh (25). Around a third of the children are underweight or stunted in Bangladesh (35). For the undernourished children it requires further adaptation for the best fit of the probes. We also found that success in one attempt was higher among male children, despite there being no notable differences in the clinical presentation of the children by sex. Although this requires more exploration, some studies have reported the presence of implicit gender bias among healthcare professionals while rendering care in routine settings (36).

With regard to fidelity, we observed that the male and younger IMCI service providers adhered to SoPs more than their counterparts. This may be because they have more access to new technology/devices in such contexts (37). Another reason could be that the average year of experience was higher among male providers. However, it requires further exploration and understanding. On facility-related factors, we observed that IMCI service providers at higher-level facilities are more likely to adhere to SoPs. Service providers in the district hospital usually receive more monitoring and supervision from the national and district health managers. These variations in programme inputs may explain this difference.

Pulse oximetry performance was better in round-2 assessments across most indicators. This strengthens the notion of sustainability of pulse oximetry practice and highlights the importance of allowing an intervention to mature and reach

optimum adoption and efficiency. Post-training follow-up support provided through supportive supervision and performance appraisal workshops (after round-1 assessments) possibly played a catalytic role in sustaining and improving the performance over time. The performance of a few providers was somewhat poorer than others, emphasising the importance of identifying weaker performers during the initial training and providing follow-up support through targeted monitoring and supervision.

There are several barriers and challenges to performing pulse oximetry in real-life settings. In our study, IMCI service providers reported difficulties during peak hours of attendance at health facilities. In Bangladesh, most IMCI services are provided through union-level health centres (> # 3500) and sub-district hospitals (~# 482), which have a relatively lower patient load than district hospitals (# 62). Hence, the peak-hour related challenges are primarily a concern for district hospitals and some high-volume sub-district hospitals. The IMCI service providers also reported facing major difficulties in keeping the child calm during pulse oximetry, which is mainly a concern for high volume facilities. Pulse oximetry devices with advanced Signal Extraction Technology (SET) require a shorter performance time, even in challenging conditions such as patient movement and low perfusion (34, 38). Although relatively more expensive ($300-500), it will require less than USD 250,000 to procure SET pulse oximetry devices for all high-volume IMCI consultation rooms in Bangladesh. We believe that this is affordable for a country like Bangladesh, as the overall national **IMCI programme** under the Maternal, Neonatal, Child & Adolescent Health (MNC&AH) Operation Plan of Bangladesh has a total of around 50 million USD

allocated for its activities. We believe, it is worth the investment to avert preventable pneumonia deaths by 2025 (39). In addition to enhancing the capacity of IMCI service providers through training and distributing toys to divert the attention of the child, active involvement of the caregivers has been shown to be effective in reducing the movement of the child during the procedure (11).

We conceptualised this study based on the WHO framework and implementation outcome variables (20). Although we contextualised the research questions by involving national- and local-level stakeholders, our reliance on WHO's implementation outcome variables limited the opportunities of capturing unexpected drivers and unintended consequences of pulse oximetry introduction in these settings (18). Moreover, we acknowledge that the time interval between the two rounds of assessments were not sufficient to allow for firm conclusions to be made regarding the sustainability. Furthermore, the COVID-19 pandemic may have confounded some of our findings as it significantly impacted Bangladesh's health systems awareness, attitude, readiness, response, and practices related to oxygen security. Similarly, the capacity, experience, and positionality of icddr,b as an implementation facilitation partner was a strong enabler and a potential confounder in this demonstration (17, 40).

We acknowledge the fact that we did not randomly select Kushtia as our demonstration site. Therefore, the result may not be applicable for the whole country. In Bangladesh, there are geographical variations which have impact on access to health care as well as service availability and readiness regarding various

health services. Kushtia predominantly belongs to the plain land which is not representative of the hard-to-reach areas. Based on our findings of this study, pulse oximetry can be introduced in most parts of Bangladesh except the hard-to-reach areas. We also acknowledge that we have selected a district with reasonably well functioning IMCI services. The results would have been more generalisable if we could have included one low performing district which we could not include due to implementation cost challenges.

We employed the same team in both rounds of assessment and used a specially designed and tested android-app for capturing multiple events with time-stamps through structured observations (21). These measures, we believe, reduced observation and measurement bias, increasing the validity and reliability of measurements, especially the performance time recording. While the presence of study nurses as independent observers may have introduced a surveillance bias, spending considerable time in building rapport with the IMCI service providers and observing each of them for 3-7 days are expected to minimise this bias (i.e., Hawthorne effect) (41). Finally, the hospitals had set-up temporary fever-clinics during the pandemic, which screened and redirected all symptomatic patients to dedicated COVID-19 services. It changed the overall case-mix of children receiving IMCI services, which may explain the relatively smaller number of hypoxaemia cases identified during the assessment period. Lastly, we acknowledge that the data collection tools used in this study for structured observation, re-assessment, exit-interview and IMCI service provider interview were not validated. Since we were conducting a novel study based on the WHO recommended implementation

outcome variables, we did not find any validated tools. Therefore, we conducted extensive desk review to construct the data collection tools. We also conducted qualitative explorations for understanding the major issues related to acceptance, barriers and challenges, which helped us preparing the exit-interview and IMCI service provider interview tools. We conducted field-testing and pretesting of each tool before finalisation. We believe that these measures have contributed in improving the content and construct validity of tools that were used in this study.

9.6 CONCLUSION

This implementation research study demonstrated the feasibility of introducing and integrating pulse oximetry in routine IMCI services in Bangladesh, adopting a district implementation model and using a health system strengthening approach. We are confident in our conclusion as we saw evidence of the programme maturing and improving over time and almost no influence of patient-, provider- and facilities-related factors on SpO_2 measurement, except that it was poorer among younger children, and a few providers performed the procedure less effectively. Introducing SET pulse oximetry devices in high-volume facilities can help overcome the challenges associated with motion artefacts, particularly among younger children. Special emphasis can be given to identifying providers who would benefit from targeted monitoring and follow-up support. Routine programmes will need to emphasise adherence to SoPs and IPC practices in training and routine monitoring. The policymakers can capitalise on these encouraging findings and ratify the integration of pulse oximetry with respiratory rate assessment in routine outpatient settings. Moreover, we also highlight the importance of connecting pulse oximetry

to a functioning oxygen delivery system and ensuring timely, adequate and appropriate oxygenation. We recommend future studies to assess the feasibility of pulse oximetry at community settings of Bangladesh. We also recommend further study on post-implementation follow-up to assess the sustainability and research looking at feasibility, effectiveness and impact over wider interval. The experience gained through this demonstration and the learning synthesised in this implementation research can help inform evidence-based decisions relating to the introduction and scale-up of pulse oximetry in Bangladesh and other LMICs, as these countries aim to avert all preventable deaths due to childhood pneumonia mortality by 2025.

9.7 SUPPLEMENTARY MATERIALS

9.7.1 Supplementary tables

Supplementary table 9.1: Type, staffing pattern, service availability and IMCI service utilisation of health facilities selected for introducing pulse oximetry and implementing the district model

Name	Type of Health Facility	Indoor service	Separate paediatric indoor	Emergency service	Outdoor service	IMCI service	Separate IMCI corner	IMCI utilisation								
								All children aged 2-59 months			Severe Pneumonia			Pneumonia		
								2019	2020	2021	2019	2020	2021	2019	2020	2021
Kushtia DH	DH	Yes, 250-bedded	Available	Available	Available	Available	Available	20,294	12,299	13,656	3,218	697	52	3,888	744	408
Kumarkhali UHC	UHC	Yes, 50-bedded	Not Available	Available	Available	Available	Available	18,495	6,636	8,891	367	227	267	655	309	307
Beharamara UHC	UHC	Yes, 50-bedded	Not Available	Available	Available	Available	Available	5,066	3,150	5,355	32	2	8	877	379	443
Mirpur UHC	UHC	Yes, 50-bedded	Not Available	Available	Available	Available	Available	9,072	4,386	4,610	16	4	0	16	1	11
Khoksa UHC	UHC	Yes, 50-bedded	Not Available	Available	Available	Available	Available	10,820	6,578	4,815	128	31	1	3,039	610	42
Daulatpur UHC	UHC	Yes, 50-bedded	Not Available	Available	Available	Available	Available	6,349	4,262	3,465	505	313	171	672	654	293
Shelaidaha USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	1,129	1,913	750	0	0	36	151	218	77
Saota USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	1,274	932	798	0	0	57	30	92	148
Bahadurpur USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	1,469	1,009	1,103	24	178	17	623	193	63
Dharampur USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	2,784	877	955	0	0	0	1,094	311	0
Amla USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	490	888	618	0	0	0	0	40	214
Khalishakundi USC	USC	Not Available	Not Applicable	Not Available	Available	Available	Not Available	444	299	747	12	0	0	407	247	3

DH: District Hospital
USC: Union Sub-Centre
UHC: Upazila Health complex

Supplementary table 9.2: Primary and secondary research questions and analysis plan

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
Primary Research Questions			
a) Adoption	**I.** Use: Do IMCI service providers conduct pulse oximetry assessments?	Percentage	Rates presented using percentage.
b) Feasibility	**II.** Success: Can IMCI service- providers successfully conduct pulse oximetry assessments?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	III. Usability by attempt: Can IMCI service providers successfully conduct pulse oximetry assessments at the first attempt?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	IV. Usability by time: Can IMCI service providers successfully conduct pulse oximetry assessments within one minute?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
c) Fidelity	**V.** Adherence: Do IMCI serviceproviders follow Standard Operating Procedure (SoP) while conducting pulse oximetry assessments?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	VI. Agreement: Can IMCI service providers identify hypoxaemia through pulse oximetry?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
d) Appropriateness	**VII.** Experience: Do IMCI service providers conduct pulse oximetry assessments with reasonably low barriers and challenges?	Mean score from 5-point Likert scale with 95% confidence interval	Mean score with confidence interval reported to present the barriers and challenges of performing pulse oximetry to present the central tendency and dispersion of the Likert statement scores.
e) Acceptability	**VIII.** Usefulness: Do IMCI service providers	Percentage with 95% Confidence Interval	Rates presented using percentage

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
	perceive pulse oximetry as useful?		and confidence interval.
	IX. Importance: Do the caregivers perceive pulse oximetry as important?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	X. Satisfaction: Are the caregivers satisfied with pulse oximetry introduction in routine IMCI services?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
f) Sustainability	**XI.** Sustainability: Does the pulse oximetry performance of IMCI service providers sustain over time (rounds)?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
Secondary Research Questions			
Feasibility	**XII.** Can IMCI service providers successfully conduct pulse oximetry assessments in two attempts?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XIII. Can IMCI service providers successfully conduct pulse oximetry in three attempts?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XIV. Do various patient-, provider- and facility-related factors influence successfully conducting pulse oximetry assessments at the first attempt?	Percentage with 95% Confidence Interval	We assume correlation within the assessments by each assessor. Therefore, GEE has been performed for accounting for this correlation in analysis. Wald statistics used for checking adequacy of model.
	XV. Is there any variation in successfully conducting pulse oximetry assessments at the first attempt by individual IMCI service providers?	Proportion with heterogeneity statistics across individual assessors (i.e., I2 an Tau2 statistics)	We assumed random variation within assessments by each assessor. Heterogeneity statistics I^2 was used to report the proportion of between assessor variability which is not due to chance

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
			and Tau^2 has been reported to report the actual between assessor variability.
	XVI. Can IMCI service providers successfully conduct pulse oximetry assessment in three minutes?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XVII. Can IMCI service providers successfully conduct pulse oximetry assessment in five minutes?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XVIII. Do various patient-, provider-, and facility-related factors influence successfully conducting pulse oximetry assessments within one minute?	Generalized Estimating Equation reporting odds ratios with 95% confidence interval	We assume correlation within the assessments by each assessor. Therefore, GEE has been performed for accounting for this correlation in analysis. Wald statistics used for checking adequacy of model.
	XIX. Is there any variation in successfully conducting pulse oximetry assessments within one minute by individual IMCI service providers?	Proportion with heterogeneity statistics across individual assessors (i.e. I2 an Tau2 statistics)	We assumed random variation within assessments by each assessor. Heterogeneity statistics I^2 was used to report the proportion of between assessor variability which is not due to chance and Tau^2 has been reported to report the actual between assessor variability.
	XX. What is the performance time for successfully conducting pulse oximetry assessments?	Median with Interquartile range (IQR)	Shapiro-Wilk test presented the non-normality of the distribution of the time taken for measurement of SpO_2 . Hence, median times were reported with IQR.

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
	XXI. Do various patient-, provider-, and facility-related factors influence performance time for successfully conducting pulse oximetry assessments?	Mood's Median Test	Shapiro-Wilk test presented the non-normality of the distribution of the time taken for measurement of SpO_2. Hence, median times were reported with IQR and non-parametric equality of median tests have been performed.
	XXII. Is there any variation in performance time for successfully conducting pulse oximetry assessments by individual IMCI service providers?	Mood's Median Test	Shapiro-Wilk test presented the non-normality of the distribution of the time taken for measurement of SpO_2. Hence, median times were reported with IQR and non-parametric equality of median tests have been performed.
Fidelity	**XXIII.** Do IMCI service providers ensure the baby was calm before conducting pulse oximetry assessments?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XXIV. Do they place the probe appropriately before conducting pulse oximetry assessments?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XXV. Do various patient-, provider-, and facility-related factors influence adhering to Standard Operating Procedure (SoP) while conducting pulse oximetry assessments?	Generalized Estimating Equation reporting odds ratios with 95% confidence interval	We assume correlation within the assessments by each assessor. Therefore, GEE has been performed for accounting for this correlation in analysis. Wald statistics used for checking adequacy of model.
	XXVI. Is there any variation in adhering to Standard	Proportion with heterogeneity	We assumed random variation

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
	Operating Procedure (SoP) while conducting pulse oximetry assessment by individual IMCI service providers?	statistics across individual assessors (i.e. I2 an Tau2 statistics)	within assessments by each assessor. Heterogeneity statistics I^2 was used to report the proportion of between assessor variability which is not due to chance and Tau^2 has been reported to report the actual between assessor variability.
	XXVII. Do IMCI service providers adhere to cleanliness practices before conducting pulse oximetry assessments?	Percentage with 95% Confidence Interval	Rates presented using percentage and confidence interval.
	XVIII. Do various patient-, provider-, and facility-related factors influence adhering to cleanliness practices while conducting pulse oximetry assessments?	Generalized Estimating Equation reporting odds ratios with 95% confidence interval	We assume correlation within the assessments by each assessor. Therefore, GEE has been performed for accounting for this correlation in analysis. Wald statistics used for checking adequacy of model.
	XXIX. Is there any variation in adhering to cleanliness practices while conducting pulse oximetry assessments by individual IMCI service providers?	Proportion with heterogeneity statistics across individual assessors (i.e. I2 an Tau2 statistics)	We assumed random variation within assessments by each assessor. Heterogeneity statistics I^2 was used to report the proportion of between assessor variability which is not due to chance and Tau^2 has been reported to report the actual between assessor variability.
	XXX. Do various patient-, provider-, and facility-related factors influence agreement of	Generalized Estimating Equation reporting odds	We assume correlation within the assessments by each assessor.

WHO's Implementation Outcome Variable	Research questions for performing pulse oximetry in routine outpatient settings	Statistical test	Rationale and details
	hypoxaemia identification (SpO_2<94%) thorough pulse oximetry?	ratios with 95% confidence interval	Therefore, GEE has been performed for accounting for this correlation in analysis. Wald statistics used for checking the adequacy of model.
	XXXI. Is there any variation in agreement of hypoxaemia identification (SpO_2<94%) through pulse oximetry by individual IMCI service providers?	Proportion with heterogeneity statistics across individual assessors (i.e., I2 and Tau2 statistics)	We assumed random variation within assessments by each assessor. Heterogeneity statistics I^2 was used to report the proportion of between assessor variability which is not due to chance and Tau^2 has been reported to report the actual between assessor variability.

Supplementary table 9.3: Background characteristics of the data collection team

Data collector	Data collection type	Age (in years)	Sex	Educational qualification	Experience (in years)
Nurse 1	Observation	24	Female	Diploma in Nursing & Midwifery	3
Nurse 2	Observation	22	Female	Diploma in Nursing & Midwifery	2
Nurse 3	Re-assessment	24	Female	Diploma in Nursing & Midwifery	2
Nurse 4	Re-assessment	23	Male	Diploma in Nursing & Midwifery	1
Paramedic 1	Exit interview	28	Male	Diploma in Medical Faculty	7
Paramedic 2	Exit interview	24	Female	Diploma in Medical Faculty	6
Data extractor 1	Data Extraction	30	Male	Master of Social Science	6
Data extractor 2	Data Extraction	31	Male	Master of Arts	3

Supplementary table 9.4: Background characteristics of the IMCI service providers by rounds of assessment; presented in %

	Round 1		Round 2		All rounds	
Service provider characteristics	n	%	n	%	n	%
Age						
≤ 35 years	10	46	10	46	10	46
> 35 years	12	55	12	55	12	55
Sex						
Male	10	46	10	46	10	46
Female	12	55	12	55	12	55
Designation						
Doctor	5	23	5	23	5	23
Nurse	5	23	5	23	5	23
Paramedic	12	55	12	55	12	55
Facility type						
District Hospital	3	14	3	14	3	14
Sub-District Hospital	13	59	13	59	13	59
Union-level Health Centre	6	27	6	27	6	27
Total	22	100	22	100	22	100

Supplementary table 9.5: Background characteristics of the children presenting with cough/difficulty-in-breathing by rounds of assessment

Patient characteristics	Round 1		Round 2		All rounds	
	n	%	n	%	n	%
Age						
2-11 months	355	42	374	45	729	43
12-59 months	500	59	451	55	951	57
Sex						
Male	455	53	453	55	908	54
Female	400	47	372	45	772	46
Z-score (weight for height)						
Not wasted (-2SD and above)	775	92	725	88	1500	90
Wasted (below -2SD)	36	4	62	8	98	6
Severely wasted (below -3SD)	30	4	36	4	66	4
Missing	14		2		16	
Fever						
No	811	95	765	93	1576	94
Yes	44	5	60	7	104	6
Fast breathing						
No	734	88	726	88	1460	88
Yes	102	12	97	12	199	12
Missing	19		2		21	
Chest indrawing						
No	823	98	793	96	1616	97
Yes	18	2	30	4	48	3
Missing	14		2		16	
IMCI classification						
No pneumonia	727	86	717	87	1444	87
Pneumonia/Severe pneumonia	114	14	106	13	220	13
Missing	14		2			
Total	855	51	825	49	1680	100

SD: Standard Deviation

Supplementary table 9.6: Number of children assessed by background characteristics of the IMCI service providers by rounds of assessment; presented in %

Provider characteristics	Round 1		Round 2		All rounds	
	n	%	n	%	n	%
Age						
≤ 35 years	374	44	363	44	737	44
> 35 years	481	56	462	56	943	56
Sex						
Male	388	45	385	47	773	46
Female	467	55	440	53	907	54
Designation						
Doctor	199	23	198	24	397	24
Nurse	190	22	177	22	367	22
Paramedic	466	55	450	55	916	55
Facility characteristics						
District Hospital	132	15	119	14	251	15
Sub-District Hospital	515	60	504	61	1019	61
Union-level Health Centre	208	24	202	25	410	24

Supplementary table 9.7: Number of assessments by IMCI service providers by round of assessments

	Number of assessments		
	Round 1	Round 2	All rounds
Doctor 1	45	40	85
Doctor 2	45	40	85
Doctor 3	41	42	83
Doctor 4	35	42	77
Doctor 5	33	34	67
Nurse 1	43	42	85
Nurse 2	33	32	65
Nurse 3	44	34	78
Nurse 4	33	37	70
Nurse 5	37	32	69
Paramedic 1	41	42	83
Paramedic 2	45	41	86
Paramedic 3	31	32	63
Paramedic 4	35	35	70
Paramedic 5	36	35	71
Paramedic 6	34	34	68
Paramedic 7	47	43	90
Paramedic 8	36	40	76
Paramedic 9	42	38	80
Paramedic 10	34	32	66
Paramedic 11	38	34	72
Paramedic 12	47	44	91

Supplementary table 9.8: Influence of several patient-, provider-, and facility-related factors on successfully conducting pulse oximetry assessments at the first attempt by IMCI service providers; presented in adjusted odds ratios with 95% confidence interval; N=1680

		Success at first attempt								
	N	%	OR	LL	UL	P value	AOR	LL	UL	P value
Patient characteristics										
Age										
2-11 months	582	79.80	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
12-59 months	847	89.30	2.15	1.63	2.83	0.00	2.20	1.65	2.93	0.00
Sex										
Female	634	82.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	795	87.70	1.51	1.15	1.98	0.00	1.54	1.16	2.04	0.00
Chest indrawing										
No	1384	85.60	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	38	79.20	0.59	0.30	1.19	0.14	0.68	0.28	1.65	0.40
Fast breathing										
No	1250	85.60	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	169	84.90	0.94	0.62	1.42	0.77	1.03	0.30	3.56	0.96
Fever										
No	1346	85.40	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	83	82.20	0.77	0.46	1.30	0.33	0.99	0.52	1.91	0.99
IMCI classification										
No pneumonia	1236	85.60	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	186	84.50	0.91	0.62	1.35	0.66	1.06	0.30	3.78	0.93
Z-score (weight for height)										
Not wasted (-2SD and above)	1287	85.80	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Wasted (below -2SD)	81	82.70	0.80	0.46	1.37	0.41	0.82	0.47	1.43	0.48
Severely wasted (below -3SD)	54	81.80	0.75	0.40	1.43	0.39	0.80	0.41	1.55	0.50
Service provider characteristics										
Age										
≤ 35 years	625	84.90	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
> 35 years	804	85.40	1.05	0.70	1.57	0.81	1.08	0.72	1.62	0.72
Sex										
Female	774	85.40	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	655	85.00	0.98	0.65	1.46	0.90	0.88	0.54	1.44	0.61
Designation										
Doctor	349	88.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Nurse	302	82.50	0.64	0.36	1.12	0.12	0.60	0.34	1.05	0.07
Paramedic	778	85.00	0.77	0.47	1.26	0.30	0.82	0.46	1.45	0.49
Facility characteristics										
District Hospital	221	88.00	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sub-District Hospital	863	84.90	0.77	0.42	1.41	0.39	0.91	0.49	1.72	0.78
Health Centre	345	84.10	0.73	0.37	1.42	0.35	0.76	0.36	1.62	0.48
Assessments										
Round 1	727	85.30	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Round 2	702	85.10	0.98	0.75	1.28	0.89	0.98	0.74	1.30	0.89

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

Supplementary table 9.9: Influence of several patient-, provider-, and facility-related factors on successfully conducting pulse oximetry assessments within one minute by IMCI service providers; presented in adjusted odds ratios with 95% confidence interval; N=1680

		Success within one minute								
	N	%	OR	LL	UL	P value	AOR	LL	UL	P value
Patient characteristics										
Age										
2-11 months	439	61	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
12-59 months	709	75	1.95	1.58	2.41	0.00	2.05	1.65	2.55	0.00
Sex										
Female	509	67	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	639	71	1.20	0.97	1.48	0.09	1.21	0.98	1.50	0.08
IMCI classification										
No pneumonia	998	70	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	144	66	0.82	0.61	1.11	0.20	0.88	0.32	2.42	0.81
Chest indrawing										
No	1112	69	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	30	63	0.69	0.38	1.25	0.22	0.90	0.44	1.84	0.77
Fast breathing										
No	1009	70	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	131	66	0.84	0.62	1.15	0.29	1.08	0.40	2.91	0.89
Fever										
No	1083	69	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	65	65	0.81	0.53	1.23	0.32	0.79	0.49	1.27	0.33
Z-score (weight for height)										
Not wasted (-2SD and above)	1036	70	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Wasted (below -2SD)	62	65	0.80	0.52	1.23	0.31	0.79	0.51	1.24	0.30
Severely wasted (below -3SD)	44	67	0.86	0.51	1.46	0.58	0.89	0.52	1.53	0.67
Service provider characteristics										
Age										
≤ 35 years	488	67	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
> 35 years	660	71	1.18	0.92	1.51	0.19	1.17	0.90	1.53	0.23
Sex										
Female	608	67	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	540	71	1.18	0.92	1.51	0.20	1.05	0.78	1.43	0.74
Designation										
Doctor	276	70	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Nurse	237	65	0.78	0.55	1.11	0.17	0.77	0.55	1.08	0.13
Paramedic	635	70	0.98	0.72	1.32	0.88	1.03	0.73	1.45	0.86
Facility characteristics										
District Hospital	177	71	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sub-District Hospital	701	70	0.95	0.65	1.38	0.78	1.06	0.72	1.55	0.78
Health Centre	270	67	0.83	0.55	1.26	0.39	0.81	0.51	1.29	0.38
Assessments										
Round 1	560	67	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Round 2	588	72	1.26	1.02	1.55	0.03	1.30	1.05	1.62	0.02

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

Supplementary table 9.10: Influence of several patient-, provider-, and facility-related factors on adhering to SoPs while conducting pulse oximetry assessments by IMCI service providers; presented in adjusted odds ratios with 95% confidence interval; N=1680

		Adherence to SoP of PO use								
	N	%	OR	LL	UL	P value	AOR	LL	UL	P value
Patient characteristics										
Age										
2-11 months	674	92.50	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
12-59 months	868	91.60	0.99	0.72	1.36	0.95	1.06	0.69	1.61	0.80
Sex										
Female	719	93.30	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	823	90.80	0.81	0.59	1.12	0.20	0.69	0.46	1.05	0.09
Z-score (weight for height)										
Not wasted (-2SD and above)	1378	91.90	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Wasted (below -2SD)	91	92.90	1.04	0.53	2.05	0.91	0.75	0.29	1.94	0.55
Severely wasted (below -3SD)	64	97.00	1.86	0.64	5.37	0.25	1.59	0.33	7.72	0.56
Chest indrawing										
No	1488	92.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	45	93.80	0.79	0.33	1.88	0.59	0.81	0.19	3.55	0.79
Fast breathing										
No	1349	92.40	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	179	89.90	0.66	0.43	1.03	0.07	0.60	0.07	5.43	0.65
Fever										
No	1452	92.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	90	89.10	0.65	0.37	1.16	0.15	0.50	0.18	1.36	0.17
IMCI classification										
No pneumonia	1334	92.40	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	199	90.50	0.68	0.44	1.04	0.08	1.32	0.14	12.10	0.81
Service provider characteristics										
Age										
≤ 35 years	686	93.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
> 35 years	856	91.00	0.74	0.22	2.49	0.63	0.29	0.15	0.53	0.00
Sex										
Female	813	89.70	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	729	94.60	2.09	0.64	6.76	0.22	2.98	1.34	6.63	0.01
Designation										
Doctor	377	95.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Paramedic	846	92.50	0.62	0.12	3.22	0.57	1.88	0.55	6.43	0.31
Nurse	319	87.20	0.36	0.06	2.04	0.25	0.42	0.16	1.10	0.08
Facility characteristics										
District Hospital	243	96.80	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sub-District Hospital	943	92.80	0.39	0.03	4.79	0.46	0.03	0.00	0.25	0.00
Health Centre	356	86.80	0.21	0.02	2.67	0.23	0.00	0.00	0.05	0.00
Assessments										
Round 1	725	85.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Round 2	817	99.00	15.98	5.67	45.00	0.00	28.62	11.03	74.29	0.00

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

Supplementary table 9.11: Influence of several patient-, provider-, and facility-related factors on agreement of identifying hypoxaemia through pulse oximetry between IMCI service providers and study nurses; presented in adjusted odds ratios with 95% confidence interval; N=1680

		Observed agreement (SpO_2<94%)								
	N	%	OR	LL	UL	P value	AOR	LL	UL	P value
Patient characteristics										
Age										
2-11 months	696	96.7	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
12-59 months	905	97.1	1.23	0.71	2.13	0.47	1.19	0.67	2.11	0.55
Sex										
Female	733	96.6	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	868	97.2	1.01	0.59	1.75	0.97	1.07	0.60	1.89	0.82
IMCI classification										
No pneumonia	1396	97.5	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	205	93.2	0.41	0.21	0.80	0.01	0.38	0.06	2.40	0.30
Chest indrawing										
No	1557	97.1	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	44	91.7	0.58	0.16	2.12	0.41	1.35	0.33	5.53	0.68
Fast breathing										
No	1412	97.4	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	186	93.5	0.42	0.21	0.84	0.01	1.00	0.16	6.15	1.00
Fever										
No	1518	97	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	83	95.4	0.78	0.26	2.36	0.67	0.92	0.30	2.84	0.89
Z-score (weight for height)										
Not wasted (-2SD and above)	1443	96.9	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Wasted (below -2SD)	95	97.9	1.52	0.37	6.15	0.56	1.46	0.36	5.95	0.60
Severely wasted (below -3SD)	63	95.5	0.75	0.22	2.55	0.65	0.75	0.21	2.59	0.64
Service provider characteristics										
Age										
≤ 35 years	711	97.8	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
> 35 years	890	96.2	0.67	0.15	2.92	0.60	1.10	0.27	4.44	0.89
Sex										
Female	867	97.3	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	734	96.5	0.84	0.20	3.49	0.81	0.72	0.10	5.31	0.75
Designation										
Doctor	384	98.2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Nurse	346	96.6	0.48	0.05	5.15	0.55	0.49	0.06	4.17	0.51
Paramedic	871	96.5	0.52	0.06	4.42	0.55	0.30	0.04	2.12	0.23
Facility characteristics										
District Hospital	232	95.5	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sub-District Hospital	970	96.5	1.30	0.23	7.42	0.77	1.33	0.15	11.38	0.80
Health Centre	399	98.8	3.69	0.29	47.41	0.32	4.97	0.36	68.53	0.23
Assessments										
Round 1	801	96	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Round 2	800	97.8	1.82	1.00	3.30	0.05	1.76	0.96	3.23	0.07

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

Supplementary table 9.12: Influence of several patient-, provider-, and facility-related factors on optimum cleanliness practices by IMCI service providers; presented in adjusted odds ratios with 95% confidence interval; N=1680

	N	%	OR	LL	UL	P value	AOR	LL	UL	P value
Patient characteristics										
Age										
2-11 months	555	76.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
12-59 months	651	68.70	0.69	0.55	0.86	0.00	0.66	0.51	0.85	0.00
Sex										
Female	566	73.40	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	640	70.60	0.87	0.70	1.08	0.21	0.92	0.71	1.18	0.49
IMCI classification										
No pneumonia	1038	71.90	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pneumonia/Severe pneumonia	160	72.70	1.04	0.76	1.43	0.80	1.17	0.34	3.98	0.81
Chest indrawing										
No	1166	72.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	32	66.70	0.77	0.42	1.42	0.41	0.48	0.21	1.12	0.09
Fast breathing										
No	1050	71.90	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	145	72.90	1.05	0.75	1.46	0.78	0.90	0.27	3.00	0.86
Fever										
No	1138	72.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	68	67.30	0.79	0.52	1.22	0.29	0.59	0.34	1.02	0.06
Z-score (weight for height)										
Not wasted (-2SD and above)	1074	71.60	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Wasted (below -2SD)	75	76.50	1.29	0.80	2.09	0.29	1.04	0.59	1.81	0.90
Severely wasted (below -3SD)	49	74.20	1.14	0.65	2.01	0.64	1.45	0.74	2.85	0.28
Service provider characteristics										
Age										
≤ 35 years	569	77.30	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
> 35 years	637	67.70	0.61	0.49	0.77	0.00	1.07	0.79	1.46	0.66
Sex										
Female	645	71.20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	561	72.80	1.08	0.87	1.34	0.48	0.33	0.23	0.46	0.00
Designation										
Doctor	253	63.90	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Paramedic	669	73.10	1.54	1.19	1.98	0.00	2.63	1.82	3.79	0.00
Nurse	284	77.60	1.96	1.42	2.70	0.00	1.77	1.17	2.69	0.01
Facility characteristics										
District Hospital	91	36.30	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sub-District Hospital	823	81.00	7.50	5.55	10.13	0.00	20.34	13.10	31.60	0.00
Health Centre	292	71.20	4.35	3.11	6.08	0.00	6.96	4.14	11.73	0.00
Assessments										
Round 1	512	60.10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Round 2	694	84.10	3.52	2.79	4.44	0.00	4.82	3.68	6.32	0.00

OR: Odds Ratio
AOR: Adjusted Odds Ratio
LL: Lower Limit of 95% Confidence Interval
UL: Upper Limit of 95% Confidence Interval

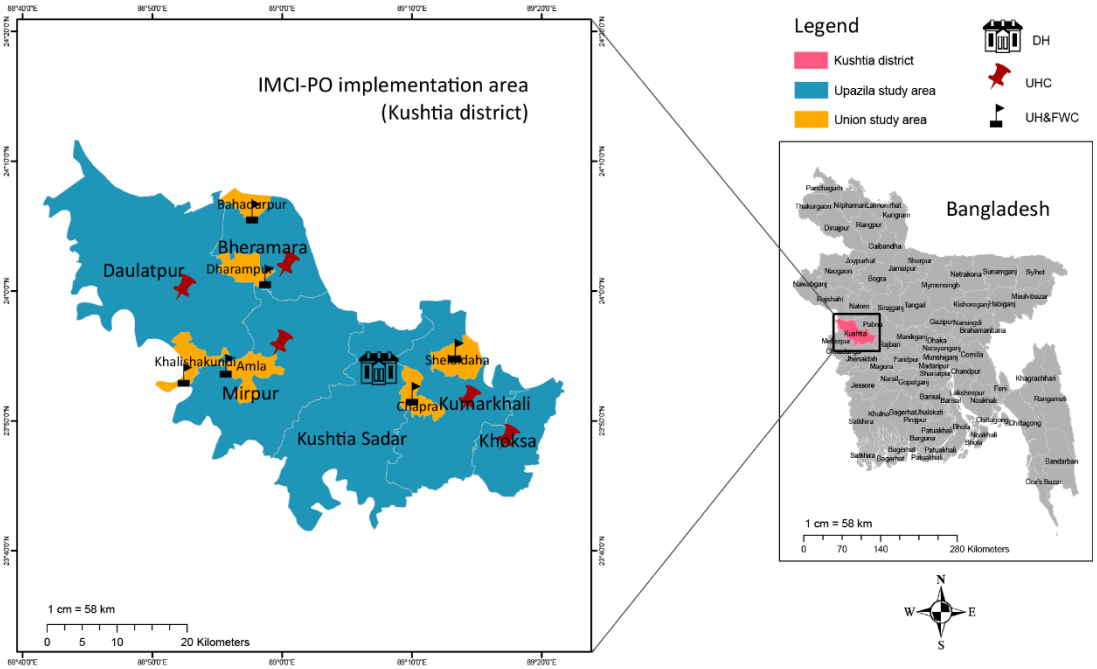
Supplementary table 9.13: Summary of findings on the secondary research questions

Outcome		Secondary Research Questions	Answers
Feasibility	1	Can they successfully conduct pulse oximetry assessments in two attempts?	96%, (95% CI, 95 to 97)
	2	Can they successfully conduct pulse oximetry assessments in three attempts?	99%, (95% CI, 98 to 99)
	3	Do various patient-, provider- and facility- factors influence successfully conducting pulse oximetry assessments at the first attempt?	Supplementary material 9.13
	4	Is there any variation in successfully conducting pulse oximetry assessments at the first attempt by individual IMCI service providers?	Figure-9.3
	5	Can IMCI service providers successfully conduct pulse oximetry assessments in three minutes?	94%, (95% CI, 92 to 95)
	6	Can MCI service providers successfully conduct pulse oximetry assessments in five minutes?	98%, (95% CI, 97 to 98)
	7	Do various patient-, provider-, and facility- factors influence successfully conducting pulse oximetry assessments within one minute?	Supplementary material 9.14
	8	Is there any variation in successfully conducting pulse oximetry assessments within one minute by individual IMCI service providers?	Figure-9.3
	9	What is the performance time for successfully conducting pulse oximetry assessments?	Figure-9.4
	10	Do various patient-, provider-, and facility-related factors influence performance time for successfully performing pulse oximetry	Figure-9.4
	11	Is there any variation in performance time for successfully performing pulse oximetry by individual IMCI service providers?	Figure-9.4
Fidelity	12	Do the IMCI service providers ensure the baby was calm before conducting pulse oximetry assessment?	93%, (95% CI, 91 to 94)
	13	Do the IMCI service providers place the probe appropriately while conducting pulse oximetry assessments?	99%, (95% CI, 98 to 99)
	14	Do various patient-, provider-, and facility-level factors influence adhering to Standard Operating Procedure (SoP) while conducting pulse oximetry assessments?	Supplementary material 9.15
	15	Is there any variation in adhering to Standard Operating Procedure (SoP) while conducting pulse oximetry assessments by individual IMCI service providers?	Figure-9.3
	16	Do the IMCI service providers adhere to cleanliness practices before conducting pulse oximetry assessments?	72%, (95% CI, 70 to 74)
	17	Do various patient-, provider-, and facility-level factors influence adhering to cleanliness practices before conducting pulse oximetry assessments?	Supplementary material 9.17

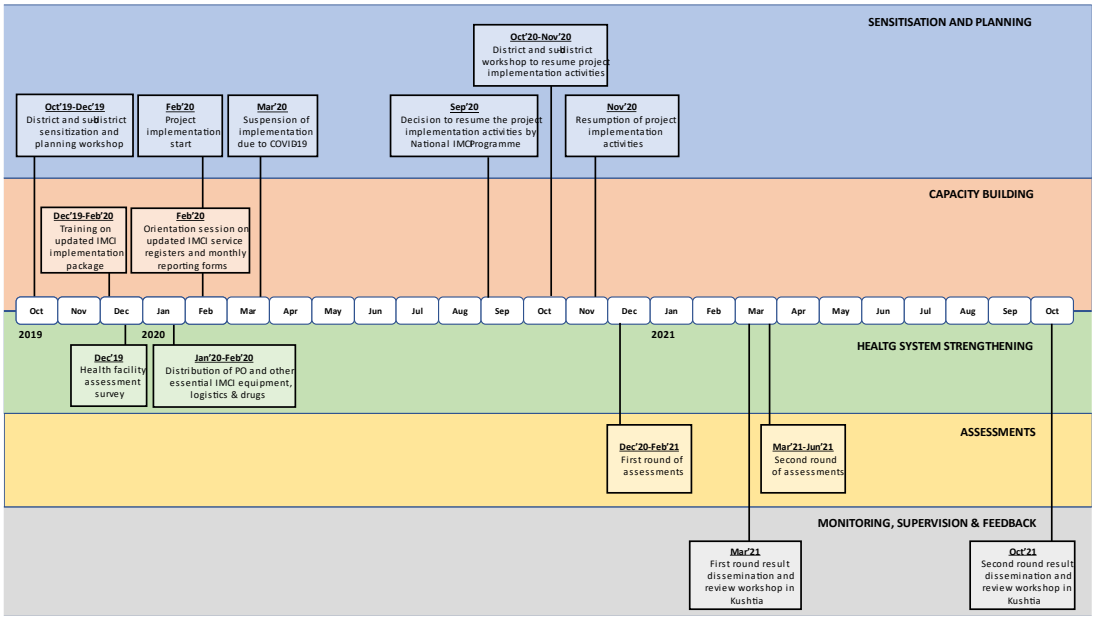
Outcome		Secondary Research Questions	Answers
	18	Is there any variation in adhering to cleanliness practices before conducting pulse oximetry assessment by individual IMCI service providers?	Supplementary material 9.19
	19	Do various patient-, provider-, and facility-related factors influence agreement of hypoxaemia identification (SpO_2<94%) through pulse oximetry?	Supplementary material 9.16
	20	Is there any variation in agreement of hypoxaemia identification (SpO_2<94%) through pulse oximetry by individual IMCI service providers?	Figure-9.3

9.7.2 Supplementary figures

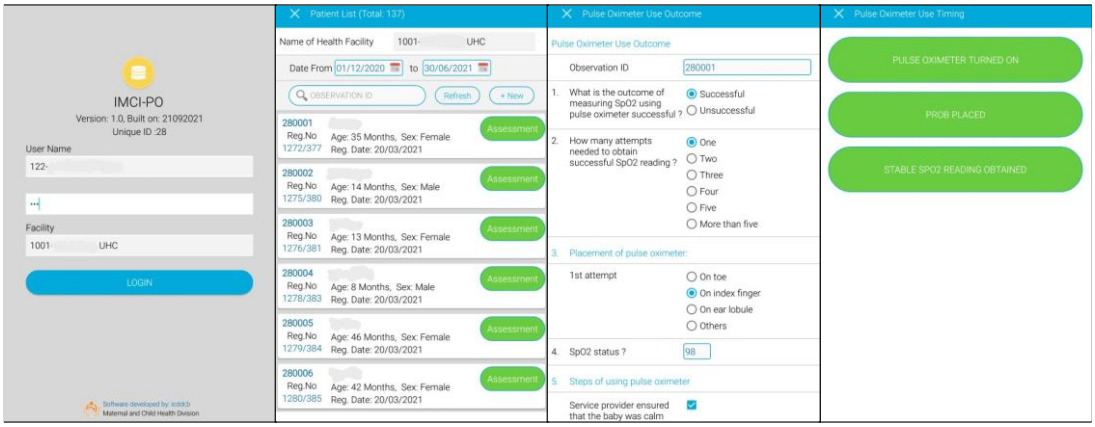
Supplementary figure 9.1: Study site and health facilities selected for introducing pulse oximetry in Kushtia, Bangladesh



Supplementary figure 9.2: Important milestones for the design, development, and demonstration of the district implementation model

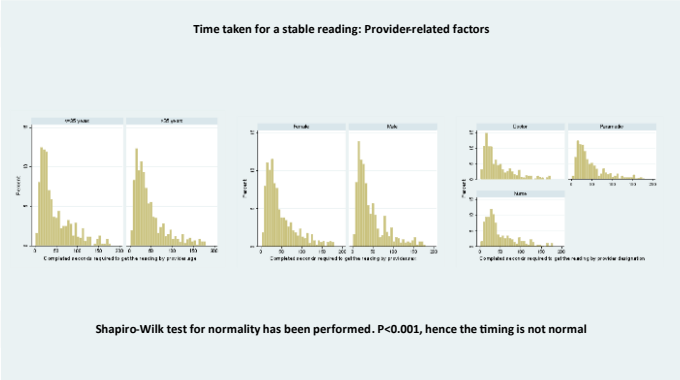


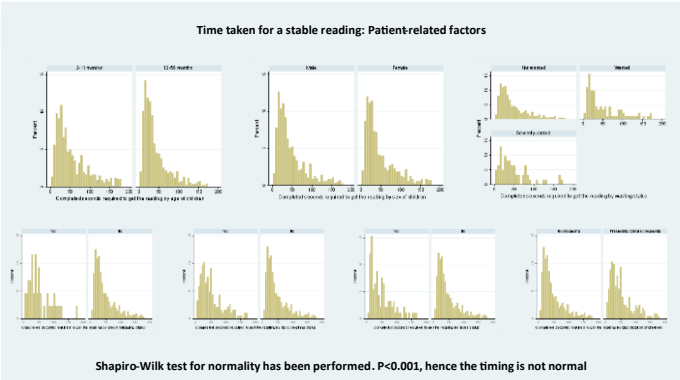
Supplementary figure 9.3: Snapshots of the survey app

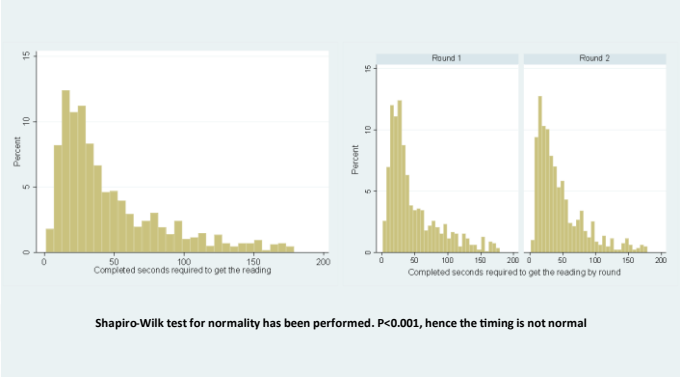


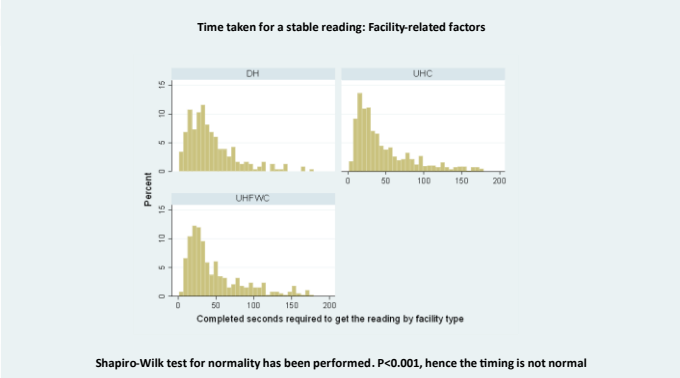
a. Log-in page **b. Patient list** **c. Observation checklist** **d. Time-stamping option for pulse oximetry timing**

Supplementary figure 9.4: Distribution of performance time for conducting pulse oximetry assessment, using the Shapiro–Wilk test









9.8 REFERENCE

1. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2016;388(10063):3027-35.
2. Oldenburg O, Wellmann B, Buchholz A, Bitter T, Fox H, Thiem U, et al. Nocturnal hypoxaemia is associated with increased mortality in stable heart failure patients. European heart journal. 2016;37(21):1695-703.
3. Wang X, Li Y, O'Brien KL, Madhi SA, Widdowson M-A, Byass P, et al. Global burden of respiratory infections associated with seasonal influenza in children under-5 years in 2018: a systematic review and modelling study. Lancet Global Health. 2020;8(4):e497-e510.
4. Marangu D, Zar HJ. Childhood pneumonia in low-and-middle-income countries: An update. Paediatric respiratory reviews. 2019;32:3-9.
5. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
6. Rahman AE, Hossain AT, Siddique AB, Jabeen S, Chisti MJ, Dockrell DH, et al. Child mortality in Bangladesh–why, when, where and how? A national survey-based analysis. Journal of global health. 2021;11.
7. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.
8. Rahman AE, Hossain AT, Nair H, Chisti MJ, Dockrell D, El Arifeen S, et al. Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Global Health. 2022;10(3):e348-e59.
9. Floyd J, Wu L, Burgess DH, Izadnegahdar R, Mukanga D, Ghani AC. Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Nature. 2015;528(7580):S53.
10. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet: World Health Organization; 2014.
11. King C, Boyd N, Walker I, Zadutsa B, Baqui AH, Ahmed S, et al. Opportunities and barriers in paediatric pulse oximetry for pneumonia in low-resource clinical settings: a qualitative evaluation from Malawi and Bangladesh. BMJ Open. 2018;8(1):e019177.
12. McCollum ED, King C, Deula R, Zadutsa B, Mankhambo L, Nambiar B, et al. Pulse oximetry for children with pneumonia treated as outpatients in rural Malawi. Bulletin of the World Health Organization. 2016;94(12):893.
13. Emdin CA, Mir F, Sultana S, Kazi A, Zaidi AK, Dimitris MC, et al. Utility and feasibility of integrating pulse oximetry into the routine assessment of young infants at

primary care clinics in Karachi, Pakistan: a cross-sectional study. BMC pediatrics. 2015;15(1):141.

14. King EM, Lieu C, Kasasa A, Ewer AK, Thangaratinam S. Pulse Oximetry as a Screening Tool to Detect Hypoxia Associated with Early-onset Sepsis in Asymptomatic Newborns: A Feasibility Study in a Low-income Country. 2014.

15. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. American journal of preventive medicine. 2009;36(5):452-7.

16. Brakema EA, van der Kleij RM, Poot CC, Le An P, Anastasaki M, Crone MR, et al. Mapping low-resource contexts to prepare for lung health interventions in four countries (FRESH AIR): a mixed-method study. The Lancet Global Health. 2022;10(1):e63-e76.

17. Rahman AE, Herrera S, Rubayet S, Banik G, Hasan R, Ahsan Z, et al. Managing possible serious bacterial infection of young infants where referral is not possible: Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. PloS one. 2020;15(5):e0232675.

18. Rahman AE, Jabeen S, Genevie F, Banik G, Islam J, Ameen S, et al. Introducing pulse oximetry in routine IMCI services in Bangladesh: a context-driven approach to influence policy and programme through stakeholder engagement. J Glob Health. 2021;in press.

19. World Health Organization, UNICEF. Integrated Management of Childhood Illness (Chart Booklet). Geneva: World Health Organization,; 2014.

20. Peters DH, Tran NT, Adam T. Implementation research in health: a practical guide. Geneva: World Health Organization; 2013.

21. Ruysen H, Rahman AE, Gordeev VS, Hossain T, Basnet O, Shirima K, et al. Electronic data collection for multi-country, hospital-based, clinical observation of maternal and newborn care: EN-BIRTH study experiences. BMC pregnancy and childbirth. 2021;21(1):1-15.

22. McCollum ED, King C, Ahmed S, Hanif AA, Roy AD, Islam AA, et al. Defining hypoxaemia from pulse oximeter measurements of oxygen saturation in well children at low altitude in Bangladesh: an observational study. BMJ open respiratory research. 2021;8(1):e001023.

23. Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. J Clin Epidemiol. 1993;46(5):423-9.

24. Baker K, Ward C, Maurel A, de Cola MA, Smith H, Getachew D, et al. Usability and acceptability of a multimodal respiratory rate and pulse oximeter device in case management of children with symptoms of pneumonia: A cross-sectional study in Ethiopia. Acta Paediatrica. 2021;110(5):1620-32.

25. Boyd N, King C, Walker IA, Zadutsa B, Bernstein M, Ahmed S, et al. Usability Testing of a Reusable Pulse Oximeter Probe Developed for Health-Care Workers Caring for Children <5 Years Old in Low-Resource Settings. Am J Trop Med. 2018;99(4):1096.

26. Shapira G, Ahmed T, Drouard SHP, Amor Fernandez P, Kandpal E, Nzelu C, et al. Disruptions in maternal and child health service utilization during COVID-19:

analysis from eight sub-Saharan African countries. Health policy and planning. 2021;36(7):1140-51.

27. Rahamn AE, Mhajabin S, Dockrell D, Nair H, El Arifeen S, Campbell H. Managing pneumonia through facility-based integrated management of childhood management (IMCI) services: an analysis of the service availability and readiness among public health facilities in Bangladesh. BMC health services research. 2021;21(1):1-13.

28. Silva MT, Galvao TF, Chapman E, da Silva EN, Barreto JOM. Dissemination interventions to improve healthcare workers' adherence with infection prevention and control guidelines: a systematic review and meta-analysis. Implementation Science. 2021;16(1):1-15.

29. World Health Organization. Care, cleaning and disinfection of pulse oximeters and patient monitors devices 2021 [Available from: https://www.who.int/publications/m/item/care-cleaning-and-disinfection-of-pulse-oximeters-and-patient-monitors-devices.

30. Fox MP, Thea DM, Sadruddin S, Bari A, Bonawitz R, Hazir T, et al. Low rates of treatment failure in children aged 2–59 months treated for severe pneumonia: a multisite pooled analysis. Clinical infectious diseases. 2013;56(7):978-87.

31. Tesfaye SH, Gebeyehu Y, Loha E, Johansson KA, Lindtjørn B. Pulse oximeter with integrated management of childhood illness for diagnosis of severe childhood pneumonia at rural health institutions in Southern Ethiopia: results from a cluster-randomised controlled trial. BMJ open. 2020;10(6):e036814.

32. Colbourn T, King C, Beard J, Phiri T, Mdala M, Zadutsa B, et al. Predictive value of pulse oximetry for mortality in infants and children presenting to primary care with clinical pneumonia in rural Malawi: a data linkage study. PLoS Med. 2020;17(10):e1003300.

33. Ginsburg AS, Van Cleve WC, Thompson MI, English M. Oxygen and pulse oximetry in childhood pneumonia: a survey of healthcare providers in resource-limited settings. Journal of tropical pediatrics. 2012;58(5):389-93.

34. Sola A, Chow L, Rogido M, editors. Pulse oximetry in neonatal care in 2005. A comprehensive state of the art review. Anales De Pediatria (Barcelona, Spain: 2003); 2005.

35. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.

36. FitzGerald C, Hurst S. Implicit bias in healthcare professionals: a systematic review. BMC medical ethics. 2017;18(1):1-18.

37. Li S, Glass R, Records H. The influence of gender on new technology adoption and use–mobile commerce. Journal of Internet Commerce. 2008;7(2):270-89.

38. Baquero H, Alviz R, Castillo A, Neira F, Sola A. Avoiding hyperoxemia during neonatal resuscitation: time to response of different SpO2 monitors. Acta Paediatr. 2011;100(4):515-8.

39. World Health Organization, UNICEF. End preventable deaths by 2025: The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). France; 2013.

40. Arifeen SE, Hoque DE, Akter T, Rahman M, Hoque ME, Begum K, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. The Lancet. 2009;374(9687):393-403.

41. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. Journal of clinical epidemiology. 2014;67(3):267-77.

Chapter 10: EXTENDED DISCUSSION

Pulse oximetry has enormous potential for improving the accuracy of pneumonia classification and the quality of pneumonia management, particularly in settings with limited resources (1). The primary objective of my thesis was to generate evidence and synthesise knowledge so that the policymakers in Bangladesh can understand the importance of identifying hypoxaemia among children with pneumonia and make informed decisions to introduce pulse oximetry in paediatric outpatient settings, i.e., IMCI services in Bangladesh. Therefore, I was engaged in a series of formal and informal consultations with the Ministry of Health policymakers, national IMCI programme managers and experts to discuss the country context and the current evidence gaps that need to be addressed for integrating pulse oximetry in routine IMCI services. These consultations helped me prioritise the objectives and finalise the research questions based on the Government of Bangladesh's strategic direction and programme priorities. Table 10.1 outlines my PhD project's objectives, research questions, study designs, and key outputs.

Table 10.1: Summary of objective, research questions, study designs and key scientific outputs of the PhD project

Sl #	Objectives and research questions	Study design	Output
A	**Estimating the BURDEN of hypoxaemia among children with pneumonia**		
1.	What is the burden of hypoxaemia among children with pneumonia in LMICs?	Systematic review and meta-analysis	Article published in *The Lancet Global Health*
2.	What is the burden of hypoxaemia among children with pneumonia in Bangladesh?	Secondary analysis of routine health service data	Article published in the *Journal of Global Health*
B	**Understanding the CONTEXT of managing children with pneumonia, including hypoxaemia in Bangladesh**		
3.	What is the context of childhood pneumonia-related deaths in Bangladesh?	Secondary analysis of a national household survey	Article published in the *Journal of Global Health*

Sl #	Objectives and research questions	Study design	Output
4.	What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?	Secondary analysis of a national health facility assessment survey	Article published in the *BMC Health Services Research*
C	**Assessing the FEASIBILITY of introducing pulse oximetry in routine IMCI services**		
5.	What is the process of integrating pulse oximetry in the national IMCI implementation package?	Desk review, stakeholder engagement and cross-sectional survey	Article published in the *Journal of Global Health*
6.	Can health care personnel perform pulse oximetry in hospital inpatient settings?	Observational study-cross sectional survey	Article published in the *Journal of Global Health*
7.	Can IMCI service providers perform pulse oximetry in routine outpatient settings in rural Bangladesh?	Implementation Research -abstraction of data from routine registers, -observation, -re-assessment, -exit-interviews	Article accepted in *The Lancet eClinicalMedicine*

I conducted several studies adopting various study designs and methods to answer the above-mentioned research questions. I presented the context, rationale, methods, results, and discussion in chapters 3, 4, 5, 6, 7, 8, and 9. In this chapter, I critically examine some additional issues related to the study design, sample size and sampling, measurements, and analysis, and outline specific recommendations for future research.

10.1 ESTIMATING THE BURDEN OF HYPOXAEMIA AMONG CHILDREN WITH PNEUMONIA

The first evidence gap identified through stakeholder consultation was related to the global burden of hypoxaemia in childhood pneumonia (Table 10.1). The second evidence gap that was identified through stakeholder consultation was related to the burden of hypoxaemia among children with pneumonia in Bangladesh (Table 10.1).

10.1.1What is the burden of hypoxaemia among children with pneumonia in LMICs?

The previous estimate regarding the burden of hypoxaemia was based on a systematic review conducted by Subhi et al. in 2009 and there was an urgent need to update the estimate (2). To address this, I conducted a systematic review and meta-analysis, which included more than 100,000 children with pneumonia or severe pneumonia from 57 studies, and represented different regions, facility types, patient types, hospitalisation status, and clinical severity based on WHO classifications (3). The pooled prevalence was 31%, with a confidence interval of 26-36 (95% CI).

I aimed to generate an updated estimate of the hypoxaemia burden, which will be representative of LMICs. I searched in 11 bibliographic databases and citation indices, which included several regional databases such as IndMED, Global Index Medicus by WHO, including African Index Medicus, the literature of Latin America and the Caribbean (AMRO/Pan American Health Organization), the Index Medicus for the Eastern Mediterranean Region (IMEMR/ EMRO), the Index Medicus for South-East Asia Region (IMSEAR/ SEARO), Western Pacific Region Index Medicus (WPRIM/ WPRO). Of the 57 studies included in this review, 26 were from Africa, 23 from Asia, four from South America, and four from multiple continents. I believe that the inclusion of regional databases substantially increased the sensitivity of the search strategy and the overall representativeness of the findings to LMICs, where the majority of childhood pneumonia episodes and deaths happen (4). Although I did not include any language restrictions in the search, I could not search any Chinese

language databases due to the language barrier. The number of studies conducted in China has been increasing exponentially over the past decade, and positive results are more likely to be published in English language journals and databases than in Chinese language journals and databases (5, 6). Hence, although excluding the Chinese databases may have introduced some language bias and indexing bias in our search strategy, several studies have reported that exclusion of Chinese databases did not substantially affect their overall results (7, 8). I also reported the prevalence of hypoxaemia by regions (i.e., Asia, Africa and South America). Therefore, the effect of the language bias and indexing bias will have minimum impact on the estimates generated for Africa and South America. Moreover, the studies included in our meta-analysis have a good representation of the rest of Asia (except China). The pooled prevalence of hypoxaemia in Asia did not vary substantially from that of Africa and South America.

Another important limitation of our study is the exclusion of unpublished studies, which is different from the approach adopted by Subhi et al. in their review (9). Restricting our meta-analysis to published studies may have introduced a publication bias in the overall estimate (10, 11). However, including the unpublished studies, could also increase the risk of bias, as they are not peer reviewed like other published papers. Thus, it would have minimised the validity of the overall estimate. Several studies have also found that exclusion of unpublished studies or grey literature changed the treatment effect in only a small number of systematic reviews and rarely impacted the overall results and conclusions (12, 13). Lastly, the impact of language bias, indexing bias, and publication bias on the pooled estimate is more

relevant for studies adopting an experimental design and reporting treatment/intervention effects. Most of the studies included in our meta-analysis were observational in design, and those that reported the prevalence of hypoxaemia. Hence, considering the complexity in finalising the search strategy in grey literature databases as well as time and resource constraints, I opted to limit my systematic review to published articles only.

I conducted risk of bias assessments of the studies included for full-text review. The primary objective of the systematic review was to report the hypoxaemia prevalence through descriptive statistics, and most of the studies included in the full-text review were observational in nature. On the other hand, the majority of the risk of bias assessment tools were designed and developed for experimental trials (14). I found that there are a few tools, such as the JBI critical appraisal checklists for studies reporting prevalence data, the agency for healthcare research and quality (AHRQ) methodology checklist and Crombie's items, which are relevant or specific to observational studies (15-17). Among these, I adopted the JBI tools for risk of bias assessment, which has a specific checklist for studies reporting descriptive statistics, such as the prevalence of a disease or a condition. The JBI tools also have specific checklists for randomised and non-randomised experimental studies. Therefore, using the JBI tools helped me standardise the risk of bias assessment across the studies adopting different designs and methods. However, I acknowledge that this checklist does not have any numeric scoring system.

I also assessed the extent of publication bias in our systematic review. Although there are several methods/tools for assessing the publication bias, such as Doi plot, Begg and Mazumdar, and Egger regression, I adopted the funnel plots since it is most commonly used and the outputs are relatively easy to interpret (18-20). I found a large dispersion among the prevalence estimates of individual studies included in the meta-analysis (high I^2 and tau^2 value), but I did not observe any asymmetry in the funnel plots. It implies that the pooled hypoxaemia-related estimates generated through our analysis are less likely to be significantly affected by the publication bias of the included studies. I acknowledge our limitation of not conducting the sensitivity analysis between high-precision (wide confidence intervals) and low-precision (narrow confidence intervals) studies, which may lead to a misleading interpretation of publication bias through the funnel plots (21). Rücker et al. suggested using the arcsine test (including random effects models) when there is substantial heterogeneity (τ^2 >0.1) (22). Although I found a high level of heterogeneity in our review, I did not conduct the arcsine test as its interpretation is based on the less familiar arcsine transformation.

I found a high level of heterogeneity regarding the prevalence of hypoxaemia reported in different studies included in our analysis. I wanted to account for this heterogeneity while reporting the pooled prevalence estimate. The aetiology, patterns and severity of pneumonia vary by region and settings due to the variability of vaccine coverage (PCV, HiB) and environmental conditions. Moreover, the studies included in our analysis adopted different designs, methods, measurements, and analysis approaches. Based on such variability, I adopted the random-effects model

for meta-analysis instead of the fixed effects model, which assumes that there is one common effect of the outcome of interest (23). I also acknowledge that these are simplistic approaches to reporting pooled estimates in a meta-analysis. I did not adopt other advanced statistics, such as mixed-effects models, hierarchical models, and factorial models, which may be more pertinent to studies with a high-level of variability in designs and analysis approaches and have provisions for adjusting the effects of moderators and mediators (24). Future reviews can extract specific information regarding moderators and mediators and adopt these advanced statistics to report the pooled prevalence after adjusting for their effects. However, I have also reported the median prevalence of hypoxaemia, which was not significantly different from our random-effects pooled prevalence. Therefore, it gave me confidence regarding the reliability of our reported estimate.

In our review, I included all children under-5 years of age with WHO-defined pneumonia. WHO changed its pneumonia classification in 2014. In the pre-2014 classification, pneumonia was categorised as very severe pneumonia, severe pneumonia, and pneumonia and chest indrawing was included as a stand-alone sign of severe pneumonia. Whereas the 2014-classification categorised pneumonia as severe pneumonia and pneumonia and did not include chest indrawing as a sign of severe pneumonia. Our review included studies that were published between January 2008 and October 2021. Although I conducted sensitivity analysis and reported the hypoxaemia prevalence based on the 2014-classification and pre-2014 classification separately, there can be issues with possible misclassifications. For articles that did not explicitly mention the specific version of the WHO classifications,

I assigned the version based on the study period. If a study was conducted before 2014, I assigned them to the pre-2014 classification group. If a study was conducted in 2014 or later, I assigned them to the 2014-classification group. In our review, 48 out of 61 prevalence reporting used the pre-2014 classification. Therefore, the pooled estimate has an over-representation of the pre-2014 classification. I also reported the hypoxaemia prevalence by severity classifications. I found that the prevalence was much higher among children classified as severe pneumonia than non-severe pneumonia. I extracted the prevalence estimates based on the severity classification reported by individual studies. Therefore, the pooled prevalence of hypoxaemia among children with severe pneumonia has some issues with misclassification as it also includes studies using the pre-2014 classification, where chest indrawing was considered an independent sign of severe pneumonia. I could not extract enough information regarding individual clinical signs, such as chest indrawing, from the studies included in our review to reconstruct the severity classification based on the 2014-classification. However, the sensitivity analysis revealed that the pooled prevalence of hypoxaemia among children with severe pneumonia did not differ substantially between the pre-2014 classification and 2014-classification groups. It gives me confidence that the misclassification related to chest indrawing had a minimum effect on the pooled estimate for children with severe pneumonia. However, it also raises a critical concern regarding children with chest in-drawing pneumonia, who are currently not recommended for hospital admission. If the prevalence of hypoxaemia among chest in-drawing pneumonia is higher than in fast breathing pneumonia, the current recommendation of

outpatient-based management through oral antibiotics may not be enough for those with chest in-drawing pneumonia. I recommend that future reviews should specifically focus on estimating the prevalence of hypoxaemia among chest indrawing and fast breathing pneumonia separately.

The specifications of a pulse oximetry device as well as the design, material and positioning of the probe may influence SpO_2 measurements and adversely affect the validity and accuracy of hypoxaemia identification through pulse oximetry (25, 26). Moreover, the type of training that the assessors receive may have implications on the validity and reliability of the SpO_2 readings (27, 28). Unfortunately, many studies included in our review did not report the pulse oximetry device and probe types as well as assessor characteristics and types of training they received regarding pulse oximetry. Due to the lack of availability of data, I could not conduct a relevant sensitivity analysis. Hence, I recommend that studies presenting the burden of hypoxaemia using pulse oximetry should report a minimum set of variables related to the device, probe, and assessor characteristics for standardisation and comparability.

The burden of hypoxaemia among children with pneumonia is inversely related to the age of the child (29). In our review, I included studies reporting hypoxaemia prevalence among children under-5 years of age. I could not report the prevalence disaggregated by narrower age bands as most of the studies included in our review did not present the prevalence by standardised age categories. I acknowledge that I could not reach out to the corresponding authors of the studies included in our

review and request them to share the disaggregated estimates based on standardised/pre-defined age categories. In addition, I restricted our analysis to studies reporting hypoxaemia prevalence among children under-5 years of age. This is different from the approach adopted by Subhi and colleagues, who included children aged under 12 years of age (9). Lastly, the WHO pneumonia classification is only applicable for children aged 2-59 months. In our review, I could not exclude children aged 0-1 month due to the lack of disaggregated reporting (by age) in the relevant studies. Hence, the pooled prevalence reported in our review may overestimate the true prevalence among children (2-59 months) with pneumonia.

According to WHO, the threshold for identifying hypoxaemia among children is SpO_2<90% (30, 31). Although most of the studies included in our review used the WHO recommended cut-off, some studies reported the prevalence with thresholds higher than 90%. I included all studies reporting hypoxaemia prevalence irrespective of the specific cut-offs that were used. Hence the pooled prevalence based on our review may be an overestimation of the true burden. However, I conducted a sensitivity analysis and did not find a substantial difference between the pooled estimate of studies using the WHO-recommended cut-offs and those that did not. Moreover, several studies have also reported that children with SpO_2 90-92% are at an increased risk of death and other adverse outcomes compared to those with SpO_2>92% (32, 33). It signifies the importance of revisiting the WHO-recommended threshold for defining hypoxaemia and may justify our approach of also including the studies that used a higher threshold while reporting the prevalence of hypoxaemia.

The distribution of SpO_2 among healthy children in high-altitude settings (>2500 metres) is different from that of sea-level settings (34, 35). Therefore, the threshold of SpO_2 should be lower than 90% for defining hypoxaemia in high-altitude settings (34). Unfortunately, WHO does not recommend any specific cut-off for such settings. In our review, I included six studies from Nepal and Guatemala, which are high-altitude settings. The Nepal studies used a SpO_2 cut-off of <90% and <93%, while the Guatemala studies considered <90% and <87%. Since I could not adjust the prevalence of hypoxaemia based on a standardised and lower threshold, the pooled prevalence for high-altitude settings may have overestimated the burden. Future studies conducted in high-altitude settings should report the prevalence of hypoxaemia with a lower threshold. Moreover, future systematic reviews should communicate with the individual study teams to generate the pooled prevalence for high-altitude settings based on a standardised and lower threshold of SpO_2.

In our review, the prevalence of hypoxaemia varied slightly between the Asia and Africa regions. I cannot confidently explain the reasons for this observation due to the extensive heterogeneity between studies in the two regions. One possible explanation could be the difference in the severity classification of pneumonia as a higher proportion of Asian studies included in this review represented very severe or severe pneumonia than that of the African studies. The other possible explanation is the differing aetiological spectrum of pneumonia across different countries and regions, which might have influenced the severity of pneumonia and, consequently, the prevalence of hypoxaemia (36, 37). I recommend further studies to understand

the regional difference by assessing the prevalence of hypoxaemia by specific aetiology.

The pooled prevalence of hypoxaemia reported in our review was much higher than the prevalence reported by Subhi et al. in 2009. Although both the reviews had similar objectives and adopted similar search strategies, there were some differences in execution and implementation. The 2009-review included both published and unpublished studies, whereas I only focused on published studies. Although the 2009-review adopted a quality checking mechanism for including unpublished studies in the meta-analysis, the proportionately high (around half) contribution of unpublished studies may have biased the overall estimates. Our search strategy included 11 international and regional databases, whereas the previous review was limited to three international databases. In our review, the pooled prevalence of hypoxaemia was based on more than 100,000 observations, whereas the 2009-review reported the global prevalence based on around 18,000 observations. The hypoxaemia prevalence reported in our review is somewhat similar to the estimates reported in another systematic review published in 2001. According to the 2001-review, the prevalence of hypoxaemia was 31% among children presenting with acute respiratory infections in the emergency settings, 43% among children with clinical pneumonia and 47% among hospitalised children with pneumonia (38). In our review, the overall prevalence was 31%, which was 33% among hospitalised children and 47% among children presenting in the emergency department with signs of clinical pneumonia. In contrast, the 2009-review reported an overall prevalence of 13%, which was substantially lower than that of all relevant

estimates reported in the 2001-review and our review (9, 38). Moreover, the 2009-review reported a hypoxaemia prevalence of less than 10% among children with pneumonia in the African region, which was much lower than the prevalence estimates (28% to 57%) reported in most of the recent studies coming out of the same region, such as Ethiopia, Mozambique, Nigeria, Senegal and Sudan (39-45). Another reason for the relatively high prevalence of hypoxaemia reported in our review could be the proportional contribution of hospitalised and young children presenting in the emergency and inpatient departments in the overall sample (46). It is more likely that these cases will be more severe, and consequently have a higher prevalence of hypoxaemia. Lastly, the increasing availability and use of pulse oximetry in LMICs may explain the high prevalence of hypoxaemia reported in our review. A study found that the hypoxaemia prevalence among children hospitalised with pneumonia increased from 6% to 48% after the health system strengthening and promoting the use of pulse oximetry on all eligible children in 12 district hospitals in Nigeria (47). The programmatic advancement regarding the routine assessment of oxygen saturation and an overall emphasis on oxygen security may have led to a higher level of detection of hypoxaemia than before (48, 49). These variations could possibly explain the difference that was observed between the hypoxaemia estimates in the two reviews.

Rapid identification of hypoxaemia supplemented by oxygen therapy can substantially reduce the burden of pneumonia-related deaths and potentially facilitate the journey towards achieving the ambitious 2030 SDG target (50). In this systematic review, I reported a high prevalence of hypoxaemia among children with

pneumonia in the LMIC context. The prevalence was particularly high among hospitalised children and children with severe pneumonia. These findings highlight the importance of investing in the overall oxygen security by introducing pulse oximetry at all points of contact with the health system supported by continuous and adequate oxygen support even in low resource settings. It will require global leadership, regional ownership, and country stewardship to establish a cost-effective oxygen system and a culture for promoting oxygen security at all levels of the health system.

10.1.2 What is the burden of hypoxaemia among children with pneumonia in Bangladesh?

Health care providers in outpatient or inpatient settings in public health facilities in Bangladesh do not routinely conduct pulse oximetry assessments on children. Most of the evidence related to the burden of hypoxaemia in Bangladesh is from the controlled environment of clinical research settings (51). Moreover, these studies are often conducted with relatively a small sample size within a short duration. After successfully demonstrating the effectiveness of a locally made bubble CPAP, pulse oximetry was introduced as a part of the routine assessment in icddr,b Dhaka Hospital in 2014 (52). I conducted a secondary analysis using this data, which included 2,646 children aged 2-59 months admitted with WHO-defined severe pneumonia between 2014 and 2017. The overall prevalence of hypoxaemia was 40% (95% CI, 39 to 43) upon admission. Hypoxaemia was found as one of the strongest predictors of mortality, need for referral to a higher-level facility and longer duration of hospital stay in our analysis.

I reported the prevalence of hypoxaemia based on data extracted from a secondary level non-government hospital situated in Dhaka, the capital of Bangladesh. Dhaka is one of the most densely populated and polluted cities in the world (53). According to the Air Quality Index, Dhaka is ranked as one of the worst cities in the world (54). Since several environmental factors, such as congested living conditions and air pollution, are strongly associated with the high burden of pneumonia and related complications, the children admitted to icddr,b Dhaka Hospital with severe pneumonia may not be representative of the children with similar clinical classification from other districts in Bangladesh. The hospital provides treatment to approximately 200,000 patients annually, of which more than half are children under-5 years of age (55). Although diarrhoea is the primary entry point for admission to this hospital, it has a long history of providing respiratory care to children and maintains a reasonably high standard of care pertaining to pneumonia management and oxygen therapy. Therefore, icddr,b Dhaka Hospital can be functionally considered a specialised paediatric hospital. Although most of the patients seeking care from this hospital are from the lower-socioeconomic background, I acknowledge the limitation regarding the national representativeness of icddr,b Dhaka Hospital as its context, capacity and environment are different from that of public and private hospitals in other districts. The patients seeking care from public health centres and the first level referral hospitals, particularly in rural settings, are expected to be different from patients seeking care from icddr,b Dhaka Hospital. From this study, I also could not assess the level of hypoxaemia among non-hospitalised children. Future studies should assess the hypoxaemia burden among

hospitalised and non-hospitalised children in different public and private health facilities in other districts to report a more representative national estimate.

I conducted the secondary analysis with children aged 2-59 months who were admitted to the special care ward of the hospital. At icddr,b Dhaka Hospital, all admitted children are kept in the short stay ward for the first 24 hours. Most of them are discharged within the first 24 hours after initial management. The rest of them are transferred to the special care ward. Hence, the children included in our analysis are expected to be suffering from more severe pneumonia, which requires a longer duration of hospital stay. As I have previously discussed, most of the patients seeking care from icddr,b Dhaka Hospital are of lower socio-economic conditions. Although many children with cough and difficulty in breathing receive treatment from icddr,b Dhaka Hospital, a large proportion of the children included in our analysis had diarrhoea as comorbidity since it is a specialised hospital for diarrhoeal disease management. It is important to note that diarrhoea-associated pneumonia patients will have higher comorbidity than other pneumonia patients (56). Hence, these children may not be an accurate representation of the whole population of interest, which is children with pneumonia and severe pneumonia irrespective of their comorbidity status.

At icddr,b Dhaka Hospital, on-duty nurses conducted the pulse oximetry assessments as a part of routine clinical assessments. Since I conducted a secondary analysis, I had limited information regarding the attainment, retention, and standardisation of these nurse's pulse oximetry-related knowledge and skills. I also had limited

information regarding the steps followed by the on-duty nurses while conducting pulse oximetry assessments and the accuracy of interpreting the SpO_2 reading while identifying hypoxaemia. I acknowledge that these assessor-related factors can influence the SpO_2 reading through pulse oximetry assessments (57). However, pulse oximetry was introduced as a part of routine assessment after the successful demonstration and testing of a locally made bubble CPAP for managing severe pneumonia in icddr,b Dhaka Hospital (52). The nurses and the other hospital staff were well-trained and well-motivated regarding pulse oximetry assessments and oxygen therapy. All of them received the same training and on-site supervision from medical officers and consultants. Therefore, I do not anticipate a major concern regarding the validity and reliability of pulse oximetry assessments conducted by the on-duty nurses.

The on-duty nurses conducted the pulse oximetry assessments using paediatric probes with various models of handheld devices, such as OxiMax N-600; Nellcor, Boulder, CO, USA. The accuracy and reliability of SpO_2 reading through pulse oximetry assessments vary by device characteristics and specifications and the design and materials used for the pulse oximetry probes (25, 26). I did not have enough information to assess whether the prevalence of hypoxaemia differed by the pulse oximetry device models. However, in chapter 8, I showed that although there were some variations in performance time of conducting pulse oximetry assessments using different models of Food and Drug Administration (FDA) approved pulse oximetry devices, the agreement level for detecting hypoxaemia (SpO_2<90%) remained relatively consistent across trained assessors. This gave me

confidence in the accuracy of the measurements and hypoxaemia estimates generated through this analysis.

I extracted the data from the routine inpatient records of icddr,b Dhaka Hospital. I acknowledge that there can be issues with the accuracy of data extracted from routine records (58-60). However, icddr,b Dhaka Hospital hosts many clinical research studies and has a history of generating high-quality evidence through its research and routine services. There is a high level of data awareness and data culture among all clinical and administrative staff at icddr,b Dhaka Hospital. Hence, I feel reasonably confident regarding the accuracy of data extracted from the routine records.

I reported the prevalence of hypoxaemia based on the WHO recommended cut-off of SpO_2<90%. However, children with a SpO_2 status between 90% and 92% are also at increased risk of death and other adverse outcomes than those with a SpO_2>92% (32, 33). I could not report the prevalence using a higher cut-off, such as 92%, due to the unavailability of data. Moreover, hypoxaemia can be a transient phenomenon, and SpO_2 status can change after initial stabilisation (39). I reported the prevalence of hypoxaemia based on the SpO_2 status on admission, which may be corrected using rapid management and oxygen support (3). I could not assess the frequency of transient hypoxaemia incidences in our analysis.

I conducted multivariable logistic regression to assess the effect of hypoxaemia on death during hospital stay and the need for referral to a higher-level facility after adjusting for the effect of some of the confounders and covariates. Unfortunately, I

had data only for a small number of variables related to the children's background characteristics and clinical conditions. I could not control for the effect of several potential confounders identified through the literature review (38, 61, 62). Also, I did not perform any goodness of fit test, such as the Hosmer-Lemeshow test which is the widely used goodness of fit test for logistic regression, especially the risk prediction models (63). I identified the variables which significantly explained the effect of hypoxaemia on adverse outcomes. Therefore, the model is expected to show evidence of adequacy from the conventional goodness of fit tests. Moreover, around 6% of children left against medical advice, and we did not have any information regarding their outcome, i.e., death, referral out. Therefore, I treated them as missing values in the regression analyses. I compared the background characteristics and the clinical condition of these children (loss to follow up) with those included in the analysis and did not find any notable difference. Hence, I believe the loss to follow-up cases did not have any significant impact on the overall results and their interpretations.

I extracted data of all children admitted to icddr,b Dhaka Hospital with severe pneumonia between 2014 and 2017 in my analysis. I found that the prevalence of hypoxaemia increased over time during this period. I reported the average annual rate of growth using the exponential growth equation. I acknowledge the limitation of this approach as it does not address the issues with autocorrelation and stationarity. I conducted a post-hoc analysis adopting the time-series approach and observed a similar trend of increase (64). Future studies may include more advanced

models and time-series analysis (ARIMA, SARIMA, etc.) with more data points to report the trend in the prevalence of hypoxaemia with a more robust estimate.

This study reported a high burden of hypoxaemia among children hospitalised with severe pneumonia in a secondary level specialised non-government hospital in Dhaka, Bangladesh. The high prevalence emphasised the need for rapid identification and management of hypoxaemia through adequate supply and appropriate use of oxygen at the national level. Pulse oximetry should be introduced as a part of the routine assessment for providing paediatric inpatient care. A strengthened hypoxaemia management system with oxygen security may contribute in averting a significant proportion of pneumonia-related deaths in Bangladesh. However, it is also important to acknowledge that a large number of children with pneumonia arrive in the health facilities with advanced hypoxaemia and related complications, which would require additional support beyond antimicrobials and oxygen therapy to prevent fatality.

10.2 UNDERSTANDING THE CONTEXT OF MANAGING CHILDREN WITH PNEUMONIA, INCLUDING HYPOXAEMIA IN BANGLADESH

The policymakers and stakeholders in Bangladesh acknowledged the importance of having an in-depth understanding of the context of childhood pneumonia and its management in Bangladesh. It would help them formulate the best strategy for introducing and integrating pulse oximetry into routine practice. The first evidence gap that was identified was related to the contribution of pneumonia among all under-5 deaths, the timing of death and care-seeking practice leading to these deaths. The second evidence gap was regarding the current health systems readiness

for managing pneumonia through outpatient services, mainly focusing on the essential equipment and logistics, including pulse oximetry devices.

10.2.1What is the context of childhood pneumonia-related deaths in Bangladesh?

The last (before I updated the estimate) national estimate regarding the causes of under-5 deaths was based on the 2011 Bangladesh Demographic and Health Survey (BDHS) (2). In addition, there was a more recent estimate on pneumonia-related deaths, but it was based on a study conducted in one peri-urban sub-district (65). Hence, I used the most recent round of BDHS (2017-18) and performed a secondary analysis to address the evidence gap (66). In chapter 5, I reported that pneumonia was the "major killer" among children, as it accounted for 19% of all under-5 deaths (67). The cause-specific mortality rate due to pneumonia was 8.5 per 1,000 live births, causing approximately 24,268 (95% CI, 21,626 to 26,695) deaths each year in Bangladesh. I observed that, unlike other major causes such as prematurity, low birth weight and birth asphyxia, which are predominantly a concern during the neonatal periods, pneumonia is one of the major killers among all sub-groups, i.e., neonates, infants (1-11 months) and children (12-59 months). I also found that more than 90% of the children who died due to pneumonia came in contact with the health system at some time point before death.

The secondary analysis was based on BDHS 2017-18 survey, which adapted an internationally recognised survey design, sampling, and methodology (68). All the tools used in BDHS 2017-18 were validated, adapted to the local context, translated

into Bangla and pre-tested. Specially trained data collectors conducted verbal autopsy interviews through follow-up visits to the households of the deceased persons. The verbal autopsy questionnaire was adapted from the standardised and validated WHO 2016 and BDHS 2011 verbal autopsy instruments (66). A national advisory group constituted by verbal autopsy experts supervised the country adaptation, translation and pretesting of the questionnaire. Trained physicians reviewed the completed verbal autopsy forms and assigned the cause of death based on ICD-10 codes. Moreover, before BDHS 2017-18, Bangladesh conducted another seven rounds of BDHS in 1993-94, 1996-97, 1999-2000, 2004, 2007, 2011, and 2014. BDHS 2004 and 2011. Adaption of internally recognised and validated design, methods and tools, and collective experience of the team involved in multiple rounds of DHS in Bangladesh gives me confidence regarding the quality of data and national representativeness of the cause of death estimates generated through our analysis.

BDHS 2017-18 was conducted with a nationally representative sample which covered the entire population residing in non-institutional dwelling units of the country. The Bangladesh Bureau of Statistics has a list of enumeration areas based on the latest Population and Housing Census round conducted in 2011. BDHS 2017-18 considered each of the enumeration areas as a primary sampling unit. In the first stage of sampling, 675 enumeration areas were selected from all eight administrative divisions based on the probability proportional to size approach. Among these, 250 were in urban areas, and 425 were in rural areas. All households of the selected enumeration areas were independently listed. On average, each enumeration area had around 120 households. In the second stage of sampling, 30

households were selected from each enumeration area, adopting a systematic sampling approach. A total of 20,250 households were selected through this approach. All ever-married women aged 15-49 years were approached for interviews from the selected households. From the surveyed households, 20,376 eligible women were identified, of which 20,127 were successfully interviewed. These women reported giving birth to 8,709 babies in the last five years, of which 456 children had died before completing their fifth year of life. The mother or the primary caregiver of all deceased children were approached, and around 99% of them were successfully interviewed. Based on this rigorous sampling design, I feel confident that the cause-specific mortality fraction of pneumonia reported through our analysis was nationally representative. However, I acknowledge that BDHS 2017-18 did not include ever-married women aged 50 years and above who may be still active in their reproductive lives. Hence, there is a possibility that some of the under-5 deaths were missed through this sampling approach. However, women aged 50 years and above constitute a negligible proportion of the annual birth cohort of Bangladesh. It is highly unlikely that the exclusion of these women would bias the overall estimates regarding pneumonia-related mortality in Bangladesh. BDHS 2017-18 also did not include and refugee populations (such as the Rohingyas from Myanmar). However, the objective of BDHS 2017-18 was to generate a national estimate focusing on the Bangladeshi citizens only. Although the BDHS 2017-18 sampling strategy had a representation of urban slums, it is likely to have missed other types of floating populations. I acknowledge that the pneumonia-related mortality rate and mortality fraction are expected to be higher among these vulnerable populations. However,

most of the floating population in Bangladesh is concentrated in a few big urban cities and constitutes a very small proportion of the overall population. Hence, it is improbable that their exclusion would substantially impact the overall estimates.

According to our analysis, pneumonia accounted for 19% of all under-5 deaths in Bangladesh. I would require a minimum sample size of 236 to report such a prevalence with 5% sampling error margin and 95% CI. Therefore, the number of under-5 deaths identified in BDHS 2017-18 (n=456) was much larger than the required sample size to report the cause-specific mortality fraction of pneumonia with an acceptable error margin. In addition to the cause-specific mortality fraction, I also reported the pneumonia-specific mortality rate (deaths per 1,000 live births) based on 8,709 live births. Therefore, the estimate had a wide confidence interval and should be interpreted with caution, particularly the disaggregated estimates by socioeconomic characteristics. I also acknowledge that the timing of death and care-seeking practice related estimates were based on 86 pneumonia-related deaths identified through physician reviews and had wide margins of error and should be interpreted with caution.

In verbal autopsy interviews, information regarding the signs, symptoms and case-seeking practices leading to the death is collected from a respondent who knows the most about the deceased person. Therefore, it heavily relies on the recall capacity and interpretations of the respondent. BDHS 2017-18 accepted a maximum recall period of five years for verbal autopsy interviews. Due to this long recall period, it is possible that the accuracy of information related to the history and clinical details of

the deceased children might be affected by recall errors. The verbal autopsy interviews were primarily conducted with the mother or the primary caregiver of the deceased child, who is expected to be emotionally connected and attached to the incident. Hence, the information reported by them might be influenced by potential recall bias. Moreover, pneumonia deaths among newborns may be difficult to distinguish from sepsis, which could have resulted in some misclassifications. Hence, the pneumonia-related mortality rate and fractions reported through our analysis could be an underestimation of the true burden.

Some misclassification bias may have been introduced in our analysis assignment of cause of death based on physician review depends on the physician's knowledge, training, and subjective interpretation (69). Although some automated verbal autopsy methods, such as Tariff, Random Forest and Simplified Symptom Pattern, perform better than the physician review method for hospital-based deaths after necessary adaptation with a high-quality training dataset, the physician review method is more effective for non-hospital-based community deaths (70-72). In Bangladesh, the majority of the deaths happen outside health facilities, and there is a lack of good training data to improve the validity of automated and computer coded verbal autopsy methods. Hence, I opted for the physician reviewed verbal autopsy method for assigning the cause of death in our analysis. BDHS 2017-18 employed three physicians who received extensive training and standardisation on different aspects of the cause of death assignment process. Several measures were taken to standardise the knowledge of the physician and the cause of death assignment process. Each physician reviewed a minimum of 30 BDHS 2011 verbal

autopsy questionnaires and assigned the cause of death during the training phase. The final review process (BDHS 2017-18) started after the physicians achieved >80% agreement level through their practice. Two physicians independently reviewed each verbal autopsy questionnaire. The physicians assigned the cause of death based on the online-2016-version of the International Classification of Deaths (ICD-10), allocating an underlying cause, a direct cause, and a contributory cause, where applicable. When two physicians agreed on an underlying cause of a child, it was considered the final cause of death for that child. In the absence of an agreement, an additional review was conducted by a third physician. If two out of the three physicians agreed on an underlying cause, it was considered the final cause of death. If no agreement was reached after the third physician review, the death was recorded as "undetermined." In a few cases where two physicians assigned identical causes of death but disagreed on whether these were the direct or underlying causes, a supervised discussion was arranged to reconcile the differences. I presented the results in this paper is based on the underlying causes. In BDHS 2017-18, the causes of death could not be determined for only 7 (1.5%) of U5 deaths. It was almost 3% in BDHS 2011 and 2.3% in BDHS 2004. The relatively lower proportion of deaths left undetermined after the physician review in BDHS 2017-18 signifies the quality of training and the standardisation process. Thus, I am reasonably confident regarding the validity and reliability of the physician determined causes of death and pneumonia-related estimates reported through our analysis.

I primarily used descriptive statistics in this analysis, as they were appropriate and adequate to answer our research questions. I could not test any hypothesis to

identify determinants or risk factors related to pneumonia-specific deaths as the sample size was insufficient for this. I projected the number of deaths due to pneumonia using the projected population size in 2015 based on the national census in 2011, crude birth rate from the 2015 Sample Vital Registration System (SVRS) report and the pneumonia-specific mortality rates reported in our paper (73, 74). I acknowledge that this estimate is based on some broad assumptions and approximates the true number of deaths with a wide uncertainty margin. Unfortunately, I could not conduct advanced modelling to generate a more robust and precise estimate due to time constraints and limited knowledge and skills regarding econometric modelling. In addition to pneumonia-related deaths, I reported the cause of death estimates for all major causes of death. It helped us present the burden of pneumonia-related deaths compared with other major causes.

Although BDHS 2017-18 used a five-year recall period for generating mortality-related estimates. Therefore, 2015 should be considered as the anchor year for the pneumonia-related mortality estimates reported by us. In Bangladesh, around 50% of under-5 deaths happen in health facilities, and the rate is increasing fast (2). Future studies can assess the coverage and validity of the medical certification of the causes of death for hospital-based deaths in Bangladesh and explore the feasibility of integrating the medical certification for hospital-based deaths and the verbal autopsy methods for non-hospitalised deaths for generating a more comprehensive, robust and accurate cause of death estimate (70). Lastly, estimates related to the

causes of death should be updated regularly, and up-to-date estimates should be used to reshape the policy, programme, and practice.

10.2.2What is the status of facility readiness regarding the availability of pulse oximetry for managing childhood pneumonia in Bangladesh?

The second evidence gap regarding the context of pneumonia management identified through the stakeholder consultation was related to the current status of service availability and readiness of health facilities providing IMCI services in Bangladesh. This information is important for understanding the health systems needs and taking course corrective measures to improve the provision and quality of pneumonia management in health facilities. To address this gap, I conducted a secondary analysis using the publicly available Bangladesh Health Facility Survey (BHFS) 2017-18 data (75). Our analyses suggested substantial gaps in the readiness related to IMCI-based pneumonia management in public health facilities in Bangladesh. Pulse oximetry was available in only around one-third of the district hospitals, one-fifth of the sub-district hospitals and none of the union level facilities. I also reported that only one-fifth of facilities had a high-readiness score based on a list of equipment, drugs, and logistics essential for managing pneumonia.

BHFS 2017-18 was conducted with a nationally representative sample of health facilities in Bangladesh. The survey adopted a stratified sampling approach, ensuring representation of all eight divisions (administration regions) and different types of registered health facilities. The six types of public health facilities included in this survey were district hospitals (DHs), mother and child welfare centres (MCWCs),

upazila (sub-district) health complexes (UHCs), union health and family welfare centres (UHFWCs), and community clinics (CCs). Additionally, some NGO clinics and private hospitals with 20 or more inpatient beds were also included in the sample. From each stratum, the facilities were selected randomly using a master list of facilities collected from MoHFW as a sampling frame. BHFS 2017-18 surveyed all DHs (62) and MCWCs (91), 141 of 421 UHCs , 713 out of 4,637 UHFWCs, 331 out of 13,211 CCs, 123 out of 826 NGO clinics and 106 out of 563 private hospitals. In this survey, the data collection teams approached 1,600 facilities and successfully collected data from 1,524 of them. The non-response rate was less than 5%, which reduced the risk of selection bias in the overall estimate. Although the overall sampling approach adopted in BHFS 2017-18 was reasonably robust, there were some issues regarding the comprehensiveness of the sampling frame for NGO clinics and private hospitals. The list of public facilities was exhaustive, and I only focused on public facilities in our analysis while reporting the pneumonia-management related readiness. The survey used weighting to minimise sampling error while reporting the national estimates. The number of facilities selected for each type is weighted or adjusted so that each types of contribution to the overall estimate is proportionate to the actual distribution of such type of health facilities in Bangladesh. All of the approaches and measures mentioned above have made me confident that our findings are nationally and regionally (division) representative of all types of public health facilities in Bangladesh.

I restricted our analysis to the facilities which are mandated to provide outpatient based IMCI services. According to the national IMCI programme, all DHs, MCWCs,

UHCs and UH&FWCs are responsible for providing facility-based IMCI services (76, 77). Although CCs are often the first point of contact for rural communities and provide selective outpatient-based child curative care, they are not mandated to provide formal IMCI services. Hence, I did not include CCs in our analysis. I acknowledge that many children with severe and non-severe pneumonia may initially seek care from CCs and could benefit from the introduction of pulse oximetry there. Future research should focus on exploration of the needs and potential benefits of introducing pulse oximetry in CCs and revisit programme planning and responses accordingly.

BHFS 2017-18 provides a cross-sectional picture of the surveyed facilities as it explored the availability and functionality of the required items on the day of the visit. The readiness may change over time. Therefore, the level of readiness reported through our analysis may not represent the overall status of IMCI services for a longer period of time. As information regarding the availability is self-reported by the facility representative, this may have introduced some information bias in our analysis. However, the data collectors physically verified the availability of required and essential items and assessed their functionality where applicable to minimise the information bias and reporting errors.

The survey was implemented by the National Institute of Population Research and Training (NIPORT) with technical assistance from ICF International (USA) and icddr,b. All these organisations possess relevant capacity, expertise and experience for conducting nationwide household- and health facility assessment surveys, which

ensured the quality of the information obtained from this survey (2, 66, 75, 78-84). BHFS-2017 also used an internationally validated tool developed by The Demographic and Health Survey (DHS) Program (85). The tool was adapted to the context of Bangladesh in consultation with technical specialists and experts from the MOHFW, Directorate General of Health Services (DGHS), Directorate General of Family Planning Services (DGFP), and other key stakeholders knowledgeable about the health services and health sector programme priorities. This tool was pre-tested, and field tested before data collection. Furthermore, the data collectors used a specially developed data capture application, which minimised data capturing and entry related errors. BHFS 2017-18 employed 80 enumerators with medical background for data collection. Of them, 40 interviewers were medical doctors (as team leads) and 40 were paramedics. They received extensive training for three weeks, which included classroom lectures and discussions, practical demonstrations, mock interviews, role plays, and field practice. A central team was responsible for monitoring the quality of data collection through on-site visits and refreshers training. I believe that these steps played an important role in improving the validity and reliability of data used in our analysis.

In this paper, I identified 17 items as 'required', which were categorised into four domains: A. staff, B. equipment, C. medicines and D. logistics & job aids. These items were identified through consultative workshops with the National IMCI Programme and IMCI experts of Bangladesh. Out of these 17 items, 14 were available, and three were absent in the BHFS 2017-18 tool. I identified proxy items (disposable syringe instead of insulin syringe or 5 cc syringe; monthly reporting form instead of IMCI

reporting form) in the tool for two of the absent items. However, the availability of the IMCI referral form remained unexplored in our paper using this tool. The National IMCI Programme and IMCI experts also identified 10 items from the list of 17 required items as essential for managing pneumonia based on the IMCI guidelines. The National IMCI Programme has already endorsed the list of required and essential items and integrated them in the national checklist for monitoring IMCI services. This is a step towards influencing the national policy and programme through our research and sensitisation activities. However, I acknowledge that these items were not internally validated and may change based on the context and priorities of other countries. I recommend conducting future studies to validate these items in different settings. Furthermore, the availability of certain items was not specific to the IMCI corner due to the design of the BHFS 2017-18 questionnaire. Therefore, I acknowledge the possibility of some misclassification as certain items which were not available in the IMCI corner but available in general outdoor or other departments were considered as available in the IMCI corner in our analysis. We recommend updating the tool for assessing pneumonia management readiness specific to IMCI corners or consultation rooms.

In our analysis, I used the 10 essential items and categorised the facilities as 'poor readiness: score 0-4, 'moderate readiness: score 5-7 and 'high readiness: score 8-10. The scoring system was developed in consultation with National IMCI Programme and IMCI experts. I acknowledge that the scoring system was not validated and may not truly represent the overall quality of IMCI services in the selected facilities. I also reported the readiness of IMCI facilities regarding the oxygen delivery system in

addition to pulse oximetry. The other items that were reported for the oxygen delivery system readiness were the availability of an oxygen concentrator, oxygen cylinder with a flow meter, oxygen cylinder without a flow meter, and oxygen distribution system. Although these items are not enough to comprehensively assess the oxygen delivery system readiness, the findings revealed a critical gap regarding oxygen security in the surveyed facilities.

I used descriptive statistics for reporting the availability and readiness for each item, which were further stratified by facility type, location and administrative divisions. I did not conduct any inferential analysis as it was not required to address our research questions. Also, I could not assess the gaps considering all the building blocks of the health systems as identified by WHO. I understand that some of the gaps in facility readiness are linked to some of the other building blocks, such as health financing and governance. I did not have sufficient data to investigate these root causes. For future studies, I recommend conducting predictive analysis using the health systems building blocks, and other contextual and environmental factors to identify key predictors of facility readiness for managing pneumonia based on the IMCI guidelines. Furthermore, I acknowledge the importance of keeping track of changes in facility readiness over time. This would help identify the gaps, take course corrective measures and assess the outcome of the response. Unfortunately, I could not conduct the trend analysis using the previously available BHFS data, which I recommend for future studies.

10.3 ASSESSING THE FEASIBILITY OF INTRODUCING PULSE OXIMETRY IN ROUTINE IMCI SERVICES

Introducing pulse oximetry into the routine IMCI services in Bangladesh would require integrating the relevant recommendations, instructions, and provisions in the *National IMCI Implementation Package*. It will also require developing a district implementation model based on a health system strengthening approach and demonstrating its feasibility in real-life settings. Hence, the first evidence gap identified in this regard was related to documenting the process and synthesising the learnings of updating the national package and developing the district model of implementation. The second evidence gap was regarding the adequacy and appropriateness of the updated training package in imparting necessary skills to minimally trained assessors for efficiently conducting pulse oximetry assessments in a reasonably controlled setting. The third evidence gap was regarding the feasibility of introducing pulse oximetry in routine IMCI services using the updated implementation package and adopting the district implementation model in a real-life setting.

The above-mentioned evidence gaps were outlined by the national IMCI programme and IMCI experts of Bangladesh. Addressing these critical evidence gaps through rigorous designs and appropriate methods was expected to convince the policymakers to make informed decisions for the national scale-up and promote sustainability.

10.3.1What is the process of integrating pulse oximetry in the national IMCI implementation package?

I adopted a comprehensive approach for engaging stakeholders to integrate pulse oximetry into the *National IMCI Implementation Package of Bangladesh* and develop *a district implementation model* based on a health system strengthening approach. Here, I critically discuss some of the strengths and limitations of the stakeholder engagement process and focus on key learnings regarding what worked and what did not.

I conducted an implementation research study to assess different aspects of the feasibility of introducing pulse oximetry in routine IMCI services in Bangladesh. Instead of considering stakeholder engagement as a stand-alone process, I included it as an integral component of the overall design. This approach of embedding the stakeholder engagement process in the broader discussions helped us fine-tune the general objective and specific research questions of the implementation research study based on the perspectives, priorities, and reflections of IMCI stakeholders in Bangladesh. It also contributed to promoting acceptance and developing a sense of ownership by key IMCI stakeholders regarding the findings of the implementation research study and its key recommendations.

I developed a conceptual framework to guide the stakeholder engagement process, which included four steps: identity, sensitise, involve, and engage. The framework was adapted from a stakeholder engagement model jointly developed by WHO and World Economic Forum (WEF) in 2007 to prevent non-communicable diseases in the

workplace (86). However, there are some differences in the approach and implementation of the two frameworks. The WHO-WEF model considered all stakeholders as equal and promoted their equal engagement at all steps. On the other hand, I wanted to ensure country ownership, government leadership, and active participation of key stakeholders while integrating pulse oximetry into the *National IMCI Implementation Package of Bangladesh*. Therefore, I considered the government, particularly the National IMCI Programme of Bangladesh, as the most important stakeholder and emphasised their participation, leadership, guidance, and recommendations in all steps. Moreover, the WHO-WEF model proposes sensitising the champions and highly motivated representatives of stakeholders after the initial involvement. Our model aimed to sensitise as many stakeholders as possible in the sensitisation phase but involved a few stakeholders in the design and development phase, who were prioritised based on their power and interest levels. Lastly, the WHO-WEF model adopted an approach for repeated sensitisation of the selected stakeholders to retain their interest, knowledge and understanding. Unfortunately, I formally sensitised the stakeholders once, which is one of the limitations of our approach. However, I prioritised a few stakeholders and ensured their continuous participation in the involvement and engagement steps. I believe that this approach helped retain the interest, knowledge and understanding of these key stakeholders regarding the importance of pulse oximetry in pneumonia assessment and management. I also acknowledge that there are several other models of stakeholder engagement that I could not adopt or adapt (87-91). The experience and outcomes

of our stakeholder engagement process could have been different had I adapted a different model.

In the first step, I conducted a thorough desk review, interviewed key informants, and conducted focus group discussions to identify national-level and district-level stakeholders related to the IMCI implementation in Bangladesh. I also categorised them based on their power and interest levels. This exercise helped us understand the overall landscape and prioritise stakeholders for involvement in the subsequent steps, i.e., sensitise, involve and engage. The prioritisation was necessary to manage the process efficiently and ensure optimum use of minimum resources (92). I acknowledge that stakeholder's power and interest levels are not static, but I categorised them based on a cross-sectional assessment of their power and interest levels. Although the mapping exercise included all national level stakeholders, I only focused on Kushtia district for identifying district-level IMCI stakeholders. Therefore, the list of district-level stakeholders may not be generalisable to other districts of Bangladesh. Lastly, the National IMCI Programme scored the power and interest levels of stakeholders based on a ten-point Likert scale (93). Although I independently involved the Programme Manager and all Deputy Programme Managers of the IMCI Programme in the scoring process, I acknowledge the issues regarding potential misclassifications due to their subjective interpretation and reporting bias.

In the second step, I sensitised all stakeholders with high interest-low power, high power-low interest, and high power-high interest. I organised separate meetings at

national, district and facility levels. I also contextualised the contents of the sensitisation materials and their mode of delivery based on the roles and involvement of meeting participants in IMCI services. I believe that targeting the national, district and facility level stakeholders separately and contextualising the sensitisation materials helped us effectively communicate with the stakeholders and generate a higher level of acceptance regarding pulse oximetry. However, it is essential to note that continuous sensitisation is critical to ensuring the sustainability of an idea or an intervention (94). I could not adopt a repeated sensitisation approach for the high power-low interest and high interest-low power stakeholders due to time and resource constraints.

In the third step, I involved five national-level stakeholders with high power-high interest and six district-level stakeholders with high power-high interest in updating the *National IMCI Implementation Package of Bangladesh* and developing the district implementation model with an implementation plan. In the fourth step, I engaged them in implementing the updated package in a real-life setting. Our involvement and engagement approach promoted government leadership throughout the process. I also ensured the active participation of national-, district- and facility-level stakeholders in the design, development, and implementation of the district model. I also followed a top-down approach to outline the overall implementation plan and a bottom-up approach to finalise the details with feedback from frontline health care providers and their supervisors. These approaches of inclusiveness may have contributed to developing a sense of ownership regarding the use of pulse oximetry in pneumonia assessment and classification. Moreover,

the involvement and engagement of government managers and frontline health workers (IMCI service providers) ensured that the district model adopted a health system strengthening approach and the implementation of this model was feasible through the routine system and structures. In addition to these strengths, I want to acknowledge some of the limitations of this approach. I involved only the stakeholders with a high power-high interest in these steps. Since I did not involve or engage with the stakeholders with high interest-low power, I might have missed some important and relevant technical feedback from them. Similarly, since I did not involve or engage with the stakeholders with high power-low interest, they could have used their power to create obstacles and barriers in the update process and its subsequent implementation. For example, the Directorate General of Family Planning (DGFP) Services is a high-power stakeholder since they manage an extensive network of union-level health centres in Bangladesh. The majority of DGFP managed health centres also provide curative child-care. Unfortunately, DGFP programme managers and district managers showed minimum interest in improving IMCI services in Bangladesh. Therefore, I did not involve them in developing the district implementation model or engaged with them in implementing the model in Kushtia district. Although I did not receive any negative feedback or impediments from DGFP during the development and implementation of the model, their acceptance and participation would be crucial for the national scale-up of pulse oximetry.

I acknowledge that stakeholder engagement is a context-driven and iterative process. Hence it requires firm commitment from the donor and the facilitating

organisation regarding the investment of inputs, efforts, and resources. In chapter 7, I summarised the inputs and activities of our stakeholder engagement process. Fortunately, the donor of this study highlighted stakeholder engagement as a fundamental part of transitional research and allocated a ring-fenced budget for it. However, the budget was not enough to undertake all relevant activities. Hence, I had to share some of the direct implementation costs with stakeholder engagement related activities to accommodate the shortfall. It is important to learn for future studies envisioning engaging stakeholders for changing policy and programmes. It will require having a common vision and understanding between the donor and the implementing agency regarding the aim, timeline, and resource requirements. It will also require extensive planning and the flexibility to change the plan based on the context and stakeholder's preferences, requirements and guidance.

The role of the organisation in facilitating the stakeholder engagement process is critical for achieving the intended outcomes. In our study, icddr,b facilitated the entire process under the leadership of the National IMCI Programme of Bangladesh. icddr,b, an international health research organisation has a long history of working with the Government of Bangladesh in finding innovative, effective, and affordable solutions to some of the most pertinent public problems and issues nationally and globally. icddr,b has several experiences of integrating its innovations into policies and programmes and facilitating the process of national and geographical scale-up (95, 96). icddr,b and the Government of Bangladesh are also collaborating on multiple health systems strengthening initiatives, many of which are focusing on improving child survival and quality of care. Finally, icddr,b has unparalleled

experience and achievements regarding introducing and scaling up of IMCI services in Bangladesh. icddr,b was involved with the multi-country evaluation of IMCI in 1998 and spearheaded the study in Bangladesh (97). The findings of that study helped the Government of Bangladesh take evidence-based decisions regarding national introduction, routine service integration and scale-up. icddr,b continued its support by providing technical assistance throughout the scale-up phase. Additionally, the Principal Investigator (myself) and Co-Principal Investigator of this study are members of the National Technical Working Committee for Newborn Health and the National Technical Working Committee for IMCI in Bangladesh. These are the highest-level technical committees in Bangladesh, where the members are selected based on their expertise, experience, contribution and leadership in newborns and child health in Bangladesh. Our memberships allowed us to have a unique position and power to influence relevant policies and programmes. Therefore, the technical capacity, position, and power of icddr,b contributed substantially to gaining access, acceptance, and trust among key stakeholders regarding its advocacy to introduce pulse oximetry in routine IMCI services in Bangladesh. The experience of icddr,b has also helped organise and manage the stakeholder engagement process efficiently.

10.3.2 Can health care personnel successfully and efficiently conduct pulse oximetry assessments with minimum training?

The National IMCI Programme of Bangladesh decided to introduce pulse oximetry in routine IMCI services to identify hypoxaemia among children presenting with cough and difficulty breathing. A national committee was formed with IMCI experts to

integrate pulse oximetry in the *National IMCI Implementation Package*. The committee updated the Bangladesh adapted version of the IMCI Chart Booklet based on WHO's most recent recommendation (IMCI Chart Booklet 2014) and added a short (one-day) training module on pulse oximetry to the existing training package. The national programme and the national committee wanted to assess the adequacy of the newly developed pulse oximetry training module before finalising and training the IMCI service providers in routine settings.

I adopted an observational design where we recruited nurses and paramedics who received training based on the newly developed training module and conducted pulse oximetry assessments on children admitted to the paediatric inpatient ward of Kushtia District Hospital. Each of the children was assessed with both Masimo and Lifebox pulse oximetry devices. Pulse oximetry performance, i.e., success rate in obtaining a stable SpO_2 reading and performance time to obtain a stable SpO_2 reading, was measured by independent assessors through structured observations. Our study concluded that minimally trained heath care personnel could successfully conduct pulse oximetry assessments with a reasonably short performance time with some variations by various device-related, provider-related and patient-related factors. The evidence generated through this study guided the National IMCI Programme in finalising the training modules before assessing the feasibility of introducing pulse oximetry in routine IMCI services. It also helped set benchmarks for pulse oximetry performance (success rate, performance time) and appropriate choice of pulse oximetry devices in routine clinical settings.

The National IMCI Programme decided to train the IMCI service providers using a short training module on pulse oximetry. Hence, I had to conduct an observational study to assess its adequacy. I could not justify adopting a design with appropriate controls or comparators (with no training on pulse oximetry). I acknowledge the limitation of directly attributing the pulse oximetry performance (success rate, performance time) reported in our study to the training. Moreover, there were two parts of the training: theoretical and practical. I do not know the attributable contribution of different parts of the training on pulse oximetry performance. Future studies can specifically look at the attributable contribution of training on pulse oximetry performance and identify the optimum duration of training for achieving an acceptable success rate and performance time.

I conducted the study in Kushtia District Hospital. Kushtia District was pre-selected for implementing the district model and feasibility assessment (Chapter 8). Moreover, we also involved and engaged the key stakeholders of Kushtia in updating the national implementation package and developing the district implementation model (Chapter 8). Therefore, it required less time and investments to access the health facilities and sensitise the facility managers and healthcare providers to conduct this adequacy study. Kushtia District Hospital is a secondary level referral facility with 250 inpatient beds. The infrastructure, service availability, readiness and case mix of patients treated in Kushtia District Hospital are comparable to most other district hospitals in Bangladesh. I enrolled the children from the paediatric inpatient department, whereas IMCI is designed to be selectively delivered through outpatient services. I acknowledge that the case mix and severity of the children receiving

outpatient based IMCI services differ from those hospitalised for inpatient care. Our study required conducting two pulse oximetry assessments on each child by study recruited assessors, which was not feasible in the IMCI consultation room in the outpatient department due to space constraints. Also, the National IMCI Programme wanted to introduce pulse oximetry in routine IMCI services and assess its feasibility after finalising the training module based on the findings of this study. Hence, conducting the adequacy study in IMCI settings was not operationally justifiable. I acknowledge that I could not explore the influence of environmental factors, such as patient load and space constraints, on the pulse oximetry performance through this study, which was later explored through the feasibility study (Chapter 8).

Pulse oximetry assessments were conducted on children aged 2-59 months who were admitted to the paediatric inpatient department of Kushtia District Hospital. I excluded children with unconsciousness, active bleeding and drowning since they required urgent medical interventions, which were not directly dependent on SpO_2 measurements. Furthermore, I enrolled the children for pulse oximetry assessments immediately after admission and initial stabilisation when needed. Therefore, some of the children already received some medications for initial stabilisation before conducting the pulse oximetry assessments. This could have influenced the pulse oximetry performance of the study recruited assessors, which I could not control in our analysis.

In Bangladesh, IMCI services are provided by doctors, nurses and paramedics. I recruited nurses and paramedics to conduct pulse oximetry assessments since most

of the IMCI services are provided by them. Moreover, a doctor would likely have previous exposure to pulse oximetry during their internship in different departments, including anaesthesia and ICU. Although I recruited nurses and paramedics with the equivalent academic qualifications to government-appointed nurses and paramedics, the study recruited nurses and paramedics might have a higher level of enthusiasm, motivation, and accountability, which could have influenced their pulse oximetry performance positively. The study nurses and paramedics went through a competitive recruitment process, ensuring that they were academically more sound and professionally more experienced. This may have also worked in favour of them while conducting the pulse oximetry assessments and demonstrating their performance.

I extracted the data from routine hospital records to collect information regarding the children's background characteristics and clinical details. I acknowledge the limitations regarding the standardisation, completeness and validity of hospital records in Bangladesh and other LMICs (98). This could have introduced some misclassification errors in our analysis and interpretation. Moreover, the limited availability of personal and clinical information in the hospital records did not allow us to conduct disaggregated analysis by various comorbid conditions, such as specific diagnosis and spectrum of pathologies causing the disease, while reporting the pulse oximetry performance. I could have undertaken independent interviews and conducted clinical assessments to collect the required information. However, I did not do that as I did not want to interfere with the inpatient department's existing system and documentation practice.

I appointed independent observers to assess the pulse oximetry performance of the study and recruited nurses and paramedics. The observers received extensive training on pulse oximetry and structured observation, including theoretical and practical sessions. I also set the operational definitions of pulse oximetry performance before data collection. Success was defined as obtaining a stable SpO_2 reading (±1% SpO_2 reading for at least 10 seconds) with adequate signal strength (four or more out of five) through pulse oximetry assessments. An assessment was considered unsuccessful if the signal strength was inadequate and they could not establish a stable SpO_2 reading within three minutes. Performance time was defined as the time (measured in seconds) to obtain a stable SpO_2 reading with adequate signal strength through pulse oximetry assessments. The operational definitions were set in consultation with the National IMCI Programme of Bangladesh based on operational feasibility and programme relevance. I oriented the observers regarding these operational definitions. The operational definitions were also printed on the data collection tools as visual reminders to the observers. The supervisors organised weekly review sessions with the observers to discuss different aspects of data collection, including the operational definitions of pulse oximetry performance. All observations were done by either of the two observers, which further minimises the chance of having significant inter-observer variations. I believe that these measures have improved the quality of data collected by the independent observers. However, I acknowledge that the observers still could have a subjective bias in their interpretation of obtaining a stable reading and adequate signal strength. I could have employed two observers to independently assess the pulse oximetry

performance of each assessment and report the level of agreement. However, I could not adopt this approach due to limited resources.

The observers collected information regarding performance time using digital stopwatches, which may have introduced some measurement errors. I could have minimised this error by using a specially designed android-application for capturing multiple events with timestamps through structured observations (99). However, it takes a considerable amount of time to develop a customised application of this nature. The National IMCI Programme of Bangladesh requested us to complete the study in the shortest possible time since the finalisation of the pulse oximetry training module, and the national implementation package was dependent on it. Therefore, I could not do it due to time and budgetary constraints. I tried to overcome these limitations in the feasibility study (discussed in Chapter 8)

The National IMCI Programme and the committee formed to update the *National IMCI Implementation Package of Bangladesh* explored the availability of various pulse oximetry devices available in the national and global market. Finally, they shortlisted the Masimo and Lifebox devices based on their technical specifications and performance reported in various reports and journal articles. The assessors (nurses or paramedics) conducted two pulse oximetry assessments on each of the children. One of the assessments was conducted with the Masimo device, and the other assessment was conducted with the LifeBox device. I instructed the study recruited assessors to use the devices alternately while conducting pulse oximetry assessments. If an assessor used the Masimo device for the first (out of the two)

pulse oximetry assessment of a child, he/she would use the LifeBox device for the first pulse oximetry assessments of the subsequent child. Thus, I wanted to minimise the effect of selection bias originating from the subjective preference of the assessors towards a particular device.

I only assessed the success rate and performance time regarding the pulse oximetry performance. I acknowledge that there are other aspects of pulse oximetry performance, such as fidelity (adherence to Standard Operating Procedure) and accuracy (SpO_2 measurements and hypoxaemia status). However, I did not check those variables as the national committee suggested focusing on the success and timing of using pulse oximetry in this study and conducting a more expanded assessment of pulse oximetry performance in the feasibility study in routine settings (Chapter 8).

I also acknowledge that the structured interview tool for barriers and operational challenges of using pulse oximetry was developed based on a qualitative exploration, which could not be validated. In addition, the sample size was not adequate to have conclusive interpretations regarding obstacles and operational challenges.

The nature of the distribution of the data can be assessed through various graphical and numerical methods. The graphical methods include Stem-and-leaf plot, Box-plot, Histogram, P-P plot and Q-Q plot (100). The numerical methods include Shapiro-Wilk test, Shapiro-Francia test, Anderson-Darling test, Kolmogorov-Smirnov test, Lilliefors test and Skewness Kurtosis test (100). At first, I visually inspected the normality of the distribution of performance time through histograms. Then, I

checked the normality of the distribution using the Shapiro-Wilk test (101). I used the Shapiro-Wilk test as it has the highest power over other numerical tests and better fit the data, which was positively skewed with long tails (101). Since the performance time data was non-normally distributed, I presented the central tendency through the median with an interquartile range. I also reported the median performance time by device-related factors (type of pulse oximetry device), provider-related factors (age, sex and designation of assessor) and patient-related factors (age, sex, weight for age of the children, on-admission diagnosis/classification) through boxplots. I had two pulse oximetry assessments for each child, i.e., one by the Masimo device and the other by the LifeBox device. Therefore, I considered them as paired observations and performed the non-parametric Wilcoxon Signed Rank test to check whether the median performance time varied by device characteristics. I considered the rest of the provider-related and patient-related factors as non-paired observations. Therefore, I performed the non-parametric Wilcoxon Ranksum test (also known as the Mann-Whitney test) to assess whether the median performance time varied by these factors. I also performed the non-parametric Mood's Median test to test the equality of two medians and did not find any difference in the overall findings (102). I recruited 11 nurses and seven paramedics to conduct pulse oximetry assessments in this study. I acknowledge that the pulse oximetry performance may vary by assessors. Hence, I reported the median performance time taken by each assessor and presented them through radar plots. In addition, I used the Kruskal Wallis test to assess whether there were any differences in the median time taken by each assessor. The Kruskal

Wallis one-way ANOVA is a non-parametric method for comparing more than two independent samples. It is roughly equivalent to a parametric one way ANOVA with the data replaced by their ranks (103) I have also reported the heterogeneity statistics for reporting the variation of performance across the assessors.

I also reported the success rate of obtaining a stable SpO_2 reading by different time cut-offs, such as ≤20 seconds, ≤30 seconds, ≤40 seconds, ≤50 seconds, ≤60 seconds, ≤90 seconds and ≤120 seconds. According to the IMCI guideline, a health care provider should count the respiratory rate for a full one minute. The National IMCI Programme wanted to align the pulse oximetry related recommendations with counting the respiratory rate. Therefore, they selected ≤60 seconds as the cut-off with programmatic importance. I wanted to assess the influence of various device-related, provider-related, and patient-related factors on the success rate of obtaining a stable SpO_2 reading ≤60 seconds. Since I have two pulse oximetry assessments per child, the assessments were not independent of each other.

Moreover, each assessor conducted multiple pulse oximetry assessments in this study, which were internally correlated. Hence it violates the assumption of independent observations made by traditional regression procedures, such as a logistic regression model. Therefore, I used the Generalized Estimating Equation (GEE) regression model, which accounts for the possible correlations among observations (104, 105). Moreover, GEE yields regression estimates with lower standard errors than other conventional approaches (106). The unadjusted and adjusted odds ratios were presented with 95% confidence intervals (CI) in addition

to reporting the p-values. The model adequacy was assessed using the Wald Statistics. However, I acknowledge that very few patient-related factors were included in the model due to the lack of availability of relevant information in the hospital records.

I wanted to assess the level of agreement in reporting the hypoxaemia status by using the Masimo device and the LifeBox device. Generally, Kappa is used for determining the level of agreement based on a reference standard, but it has been criticised for being highly dependent on the prevalence of the condition. Therefore, the prevalence-adjusted and bias-adjusted kappa (PABAK) has been developed to overcome this limitation (107, 108). Since the prevalence of hypoxaemia (SpO_2<90%) was low among children included in our study, I presented the level of agreement with the prevalence-and bias-adjusted kappa (PABAK) values.

10.3.3Can IMCI service providers perform pulse oximetry in routine outpatient settings in rural Bangladesh?

After assessing the adequacy of the short pulse oximetry related training module among the study recruited nurses and paramedics, the National IMCI Programme of Bangladesh decided to demonstrate the updated *National IMCI Implementation Package of Bangladesh* in a real-life setting to inform evidence-based scale-up.

I conducted an implementation research study, where the IMCI programme was responsible for implementing the district model adopting a health system strengthening approach and icddr,b was responsible for providing implementation facilitation support. Moreover, icddr,b conducted two rounds of assessments based

on WHO's Implementation Research Framework and implementation outcome variables (109). The IMCI programme and icddr,b jointly conducted a series of workshops with the district- and sub-district managers to finalise the research questions and set a benchmark for successful demonstration for each outcome variable (110). The data collection procedures included structured observation of IMCI service providers conducting pulse oximetry assessments during routine consultations by study nurses, re-assessment (history taking, clinical assessment and pulse oximetry) of children (after IMCI consultation) by study nurses, exit-interviews of the caregivers by study paramedics, data-extraction from IMCI-registers by data collectors, and structured-interviews with IMCI service providers by study paramedics.

I observed that the IMCI service providers almost universally conducted pulse oximetry assessments on almost all eligible children and could successfully measure SpO_2 with minimum attempts, within a relatively short time and without major challenges. Their assessments were accurate, and their performance was sustained or generally improved over time. The caregivers showed a positive attitude towards introducing this technology for assessing their children. Therefore, the adoption, feasibility, fidelity, appropriateness, acceptability, and sustainability of pulse oximetry introduction in routine IMCI services in a resource-poor setting like Bangladesh were demonstrated through this implementation research. Here, I discuss some of the strengths and limitations related to the study design, sample size and sampling, measurements, and analysis (in addition to what was discussed in Chapter 9).

I adopted an implementation research approach and conceptualised this study based on the WHO framework and implementation outcome variables (109). To the best of our knowledge, this is the first study assessing and reporting most of WHO's implementation outcome variables related to the pulse oximetry use in routine settings. I included national and district level managers and IMCI service providers in the identification of the specific research questions. Afterwards, each of those questions was contextualised before finalisation. The novelty, comprehensiveness, inclusiveness, and contextualisation of the overall assessment approach are key strengths of this study. However, I want to acknowledge that I did not have a comparison or control arm, and I could not conclusively attribute the results (i.e., implementation outcomes) to the interventions or the overall approach. I adopted a district model of implementation based on health systems strengthening approach. Therefore, it was not possible to assign the health facilities of the demonstration district to a comparison and an intervention arm. Also, I had limited resources to demonstrate and assess the updated *IMCI Implementation Package* in only one district. Therefore, it was not feasible to include an adjacent district as a comparison. Although I did not have a valid comparison, I set a benchmark defining success or feasibility for each implementation outcome variable. The benchmarks were set a-priori (i.e., before implementation) and in consultation with the National IMCI Programme of Bangladesh. I compared the implementation outcomes with the *a priori* benchmarks to have a relatively objective and standardised interpretation of success or feasibility. I also acknowledge that the implementation outcomes of the demonstration could result from a synergistic effect of the comprehensive

stakeholder engagement process (described in Chapter 7) and the district implementation model. As I do not have a control district, where only the district model was implemented, I could not attribute the contribution of the stakeholder engagement process to the overall results. Moreover, the district implementation model had four major components: 1) sensitisation of district- and sub-district managers and IMCI service providers through workshops and involving them in planning and implementation; 2) capacity development of IMCI service providers, supervisors, data officers and district- and sub-district managers; 3) health system strengthening to improve IMCI service readiness and distribution of pulse oximetry devices through the routine distribution channel; and 4) follow-up support to IMCI service providers through routine monitoring, supportive supervision and performance appraisal workshops. I also could not attribute the contribution of these different components of the district model to the overall results due to the limitation of the design (without any control/comparison). Lastly, the nature of the implementation outcome variables did not allow us to adopt a before-after design.

Kushtia district was selected as the demonstration site by the National IMCI Programme of Bangladesh as its under-5 mortality rate was close to the national average. A previous initiative strengthened the routine IMCI services in Kushtia for managing possible bacterial infection through outpatient services where the referral was not feasible (111). Hence, IMCI services were reasonably functioning in most of the public health facilities of Kushtia district, which was one of the key rationales for selecting this district for assessing the feasibility of introducing pulse oximetry. I acknowledge that I did not randomly select the district, and the results of one district

may not be generalisable to the whole country of 64 districts. Moreover, geographical diversity and variations can greatly influence the access to health care as well as service availability and readiness of health facilities. Though Bangladesh is mainly a plain land, there are some hard-to-reach areas, such as hilly areas, coastal areas, and water-locked areas (char, beel and haor). The hard-to-reach areas spread over 257 sub-districts and 50 districts in Bangladesh, which is around 25% of the geographical area of Bangladesh. Approximately one-fifth of the population in Bangladesh live in these hard-to-reach areas (112). Kushtia is predominantly composed of plain land. Therefore, the experience and the findings of our study may not represent the contexts and realities of hard-to-reach areas. Future studies can focus on identifying the challenges of introducing pulse oximetry in hard-to-reach areas so that the government can adjust the implementation model according to the need of those places.

Apart from the geographical variations, the service availability, readiness and functionality of health facilities and access to and coverage of child health services vary by broader administrative units in Bangladesh, such as divisions and districts, due to the differences in leadership, management and cultural influence (113, 114). I demonstrated the feasibility of introducing pulse oximetry in Kushtia district, which is under Khulna division. Bangladesh has eight divisions and the majority of the districts under Khulna division are better performing than that of the Sylhet and Chittagong divisions. According to the most recent edition of the national household survey providing district-specific estimates, antenatal care coverage by medically trained providers was 83% in Khulna, which was 64% in Sylhet and 72% in Chittagong.

The coverage of delivery by skilled birth attendants was 64% in Khulna, which was 38% in Sylhet and 46% in Chittagong. According to the most recent edition of the Bangladesh Health Facility Survey, Kushtia was ranked the 5th (out of 64 districts) in terms of the service availability and readiness regarding pneumonia management in public health facilities mandated to provide IMCI services. Therefore, the experience, barriers, and challenges of demonstrating the feasibility in the reasonably well functioning Kushtia district may not be generalisable to the low performing districts in other divisions. Future studies can focus on exploring the implementation experience and challenges of introducing pulse oximetry in the relatively low performing districts and adapt the district model accordingly.

The IMCI programme, in consultation with the district manager and sub-district managers of Kushtia district, selected the district hospital (secondary-referral), all five sub-district hospitals (primary-referral) and six union-level health centres as demonstration facilities. Instead of randomly selecting the union-level health centres, they were purposively selected (one health centre from each sub-district). The sub-district managers selected the union-level health centres based on the availability and utilisation of IMCI services and access from the sub-district headquarters. I wanted to demonstrate the pulse oximetry related interventions in health facilities where IMCI services are reasonably functioning and can be accessed easily for conducting routine monitoring and the implementation research related data collection. I acknowledge that this may have introduced some selection bias in the sampling strategy.

I approached all (total 22) the health care workers providing IMCI services in the selected health facilities and successfully enrolled them all. I took administrative approval from the National IMCI Programme of Bangladesh to conduct the study in Kushtia district. I also obtained local approval from the district manager to conduct the study in the selected health facilities. Moreover, I organised district, sub-district and facility-level sensitisation and planning workshops prior to implementation and data collection. These measures may have contributed in achieving this high rate of enrolment. I was fortunate that all the IMCI service providers enrolled in our study participated in both rounds of data collection (i.e., no dropouts). I conducted the assessments during the COVID-19 pandemic when health care providers were rarely transferred from one facility to another. Moreover, our assessments were conducted from December 2020 to June 2021. It may have also contributed to the low dropout rate as the financial year starts in July when most of the transfers take place. I want to acknowledge that the sample size was based on the children receiving IMCI services. Although I reported the pulse oximetry performance by types of IMCI service providers (i.e., doctors, nurses and paramedics), the sample size was not calculated to report the stratified estimates with acceptable precision and the differences with adequate power. Future studies should aim to assess the pulse oximetry performance by types of IMCI service providers with adequate sample sizes. I calculated the sample size based on the WHO implementation outcome variables, considering the maximum variance. I did not consider detecting the changes in the implementation outcome variables from round 1 to round 2 while calculating the sample size. However, I reported the difference (effect size) between

the two rounds with the available sample size and did not find any notable difference.

According to the updated IMCI guidelines, all children aged 2-59 months presenting to the outpatient consultation room with cough and difficulty in breathing should be assessed for hypoxaemia using pulse oximetry. The minimum sample size required per IMCI service provider was 30 children meeting the abovementioned criteria. I applied the time quota sampling method and included all eligible children visiting the selected health facilities on the day of the assessment. I continued enrolment till the end of service hours on the day the minimum required sample size was reached. Since I did not have a sampling frame, I could not adopt a simple random sampling strategy. Alternately, I could have opted for a systematic sampling strategy, which could have eased some pressure from our data collection team. I conducted data collection during the COVID-19 pandemic, where the utilisation of IMCI services decreased in all types of health facilities, particularly in union level-facilities, and there was an urgency to complete data collection in the shortest possible time to minimise the potential exposure to SARS COV-2 to our data collection team and IMCI service providers. Adopting a systematic sampling approach would have substantially increased the length and cost of data collection, which I could not afford.

As mentioned above, I conducted the assessments during the COVID-19 pandemic, which may have changed the overall case-mix of children visiting the facilities for IMCI services. The care seeking practices changed during the COVID-19 pandemic,

especially for routine and essential services like IMCI. Moreover, the Government of Bangladesh established the COVID-19 screening and triage protocol in each health facility. As a result, children presenting with severe respiratory complaints and distress were navigated to the dedicated COVID-19 services instead of receiving IMCI consultations. I analysed the monthly IMCI reports of the selected demonstration facilities and noticed that the proportion of children aged 2-59 months (among all under-5 children) receiving IMCI services with cough and difficulty in breathing decreased from 57% in the pre-pandemic period (October 2019 to March 2020) to 42% during the data collection period (December 2020 to June 2021). Similarly, the proportion of children classified as severe pneumonia or pneumonia (among all under-5 children with cough and difficulty in breathing) decreased from 31% during the pre-pandemic period to 14% during the data collection period. I also found that number of younger children receiving IMCI services markedly reduced during our data collection period. Therefore, the results of this study related to the pulse oximetry performance by IMCI service providers and the feasibility of introducing it in routine outpatient settings may not be generalisable to the pre-pandemic era. The COVID-19 pandemic is abating in Bangladesh, and the health systems have become more adept at continuing the routine and essential services during a COVID-19 surge. The National IMCI Programme should continue synthesising the implementation experience throughout the scale-up phase and adapting the district model based on the ever-changing context of the COVID-19 pandemic.

I acknowledge that the data collection tools used in this study for structured observations, re-assessments, exit interviews and IMCI service provider interviews

were not validated. Since I was conducting a novel study based on the WHO recommended implementation outcome variables, we did not find any validated tools. I conducted extensive desk reviews and expert consultations to construct the data collection tools. I also conducted qualitative explorations to understand the major issues related to acceptance, barriers and challenges, which helped us prepare the exit interview and IMCI service provider interview tools. I pretested each data collection tool before finalisation. I believe that these measures have contributed in improving the content and construct validity of the data collection tools that were used in this study.

Our enrolment officers approached all children in the waiting rooms/areas of the selected health facilities. They screened them based on their clinical history, i.e., whether they were suffering from cough or difficulty in breathing but did not conduct any physical examination or clinical assessment. Therefore, there was a possibility that we may have missed enrolling a few eligible children who could be later classified as pneumonia/severe pneumonia by the IMCI service providers after routine consultations. Since the screening approach that I adopted was very sensitive (based on history), the probability of missing eligible cases was extremely low. I conducted a post-hoc analysis of the data extracted from the IMCI registers and found only one such case in two rounds of assessments.

The study recruited nurses who performed structured observations of IMCI service providers conducting pulse oximetry assessments on children presenting with cough and difficulty in breathing in the selected health facilities. I acknowledge that the

observers could have a bias in their interpretation of a successful pulse oximetry assessment and measurement of the performance time. I set the operational definitions of a successful assessment and performance time before data collection and organised extensive training for the observers. The operational definitions were set in consultation with the National IMCI Programme and were consistent across the adequacy and feasibility studies. Moreover, I appointed only two observers to minimise the interobserver variability. Each observer conducted at least 100 pulse oximetry assessments on hospitalised children before commencing data collection. I believe that these measures have contributed to reducing the effect of observation bias in relevant measurements. I also acknowledge the potential Hawthorne effect on the pulse oximetry performance of IMCI service providers (115). The influence of Hawthorne effect can be minimised by building rapport with the study participants and establishing sustained contacts (116). I organised a preparatory and planning workshop in each facility with respective IMCI service providers and the data collection team, which helped build rapport. Moreover, the observers observed each of the IMCI service providers for 3-7 days, allowing enough time for further rapport building and establishing sustained contacts. Another possible way to address the Hawthorne effect is to drop the observations of the first couple of days. However, I could not adopt this strategy since I was struggling to reach the minimum sample size due to the COVID-19 pandemic. Therefore, I conducted a sensitivity analysis by comparing the success rate and performance time of the first one-third of the observations of each IMCI service provider with the remaining two-thirds of the observations. I did not observe any notable difference. Therefore, I believe that the

overall Hawthorne effect was minimum on the pulse oximetry performance of service providers in our study. One of the strengths of our study is that the re-assessments were conducted in a separate room where the study nurses were blinded to the pulse oximetry assessment outcomes (SpO_2 reading or hypoxaemia status) of the IMCI service providers. Another strength of our study is that I used a specially designed and validated android-app for capturing multiple events with time stamps through structured observations, which, I believe, reduced measurement errors, especially in recording the performance time (99).

Although the IMCI service providers have extensive experience, there are issues regarding adhering to the IMCI guidelines, which may affect the accuracy of IMCI classification assigned by them (117). Therefore, I used the classification assigned by the study recruited nurses based on re-assessments rather than the ones recorded by the IMCI service providers based on routine consultations. I organised extensive training for the study recruited nurses based on the *National IMCI Implementation Package of Bangladesh*. Each of the study recruited nurses conducted at least 100 pulse oximetry assessments on hospitalised children before commencing data collection (re-assessment). Moreover, the study recruited nurses were more motivated and had limited tasks to perform (only assessment of cough and difficulty in breathing according to IMCI guidelines, height, weight and SpO_2 measurement) than the IMCI service providers. For which, I believe that the assessments conducted by our study nurses were more accurate than the assessments conducted by the IMCI service providers.

Both the IMCI service providers and the study recruited nurses who used the same model of handheld pulse oximetry devices for measuring the SpO_2 status of children. Since I did not have any GOLD standard measurement (blood gas analysis), I could not report any validity measures, i.e., sensitivity and specificity. Moreover, the study recruited nurses could not perform repeat pulse oximetry assessments during the re-assessment as it was not feasible to convince the caretakers of the children to allocate more time after the routine consultation with the IMCI service providers, re-assessment by the study recruited nurses and exit interview by the study recruited interviewers. However, the pulse oximetry assessments conducted by the study recruited nurses prior to data collection revealed a very high level of success rates and agreements in identifying hypoxaemia (Chapter 8). Their median performance time was around 30 seconds. These statistics are indicative of the skills and accuracy of SpO_2 measurements by the study recruited nurses.

The data collectors took snapshots of the routine IMCI registers after service hours on the day of assessment, and a dedicated team of expert data operators entered the data using a desktop-based application that was specially developed for this study. A data entry supervisor checked the data extraction process and conducted re-entry of 5% observations. In case of any disagreement, the source document (snapshot of the IMCI register) was conducted for necessary correction. I believe that these measures have contributed to improving the quality of data extracted from the routine IMCI registers. However, I also want to note here that the completeness and consistency of documentation in the IMCI registers by the IMCI service providers were less than optimal.

The exit interviews of the caregivers showed a high level of acceptance of using pulse oximetry on their children. It is possible that this could have been influenced by social desirability bias. However, the qualitative exploration among caregivers (a part of the broader implementation research study but not part of this thesis) did not contradict these quantitative findings. Another possible explanation is that the caregivers were already aware of the role of pulse oximetry in identifying hypoxaemia in the context of the mass community awareness campaign conducted during the early phase of the COVID-19 pandemic in Bangladesh.

Another strength of this study is the relatively low loss to follow-up rates. Among the enrolled children, I successfully conducted structured observations of all of them. Around 99.1% of the enrolled children were re-assessed, and caretakers of 98.6% of the enrolled children were interviewed. In addition, I organised a preparatory and planning workshop in each of the selected facilities where the data collection team discussed the data collection plan and approach with the IMCI service providers, their respective supervisors and facility managers before finalising. Moreover, the enrolment officer helped navigate the study participants from one station to another to minimise attrition. These measures helped us customise the data collection based on the context of the facility without compromising the integrity of the study design.

The following indicators were selected as primary outcomes of interest: adoption-use, feasibility-success, feasibility-usability by attempt, feasibility-usability by time, fidelity-SoP adherence, fidelity-agreement, appropriateness-experience, acceptability-usefulness, acceptability-importance, and acceptability-satisfaction.

The National IMCI Programme of Bangladesh set *a priori* benchmarks for successful demonstration for each of these implementation outcome variables. I compared the results of the demonstration with the pre-set benchmarks. Naturally, the benchmarks were context-specific and aspirational. In real life, they are expected to vary by the contexts and settings.

I aimed to assess the feasibility through several indicators, which focused on different aspects of the pulse oximetry performance of the IMCI service providers, such as the number of attempts required, or the amount of time taken to obtain a stable SpO_2 reading. As a result, I found that the pulse oximetry performance of the IMCI service providers exceeded the benchmarks for all feasibility-related indicators. Such consistency has helped me gain confidence regarding my interpretation related to feasibility.

I checked the normality of the distribution of performance time with histograms as a graphical method and the Shapiro-Wilk test as a numerical method (101). I have discussed the rationale for choosing these tests rather than alternatives earlier in this chapter (adequacy study). Since the performance time data were non-normally distributed, I presented the central tendency as the median with an interquartile range. I considered the provider-related, patient-related and facility-related factors and assessment rounds as non-paired observations, and performed the non-parametric Wilcoxon Ranksum test (also known as the Mann-Whitney test). (102) Although there were very little differences between the median estimates of some categories, they were showing statistical significance at $p<0.5$. Therefore, I

performed the non-parametric Mood's Median test to assess whether there was any difference in the distribution of the data. Finally, I presented the differences in the median estimates by the non-parametric Mood's Median test, since it was easier to explain and interpret. I strongly believe that these were the best statistical options based on the non-parametric distribution of our data.

I also assessed the effect of different patient-related, provider-related, and facility-related factors and assessment rounds on the pulse oximetry performance of the IMCI service providers, such as success rate, success in one attempt, success within one minute and adherence to SoP. Since I observed multiple pulse oximetry assessments by each IMCI provider, the observations were not independent of each other and internally correlated. Therefore, I assumed an exchangeable correlation structure and performed the Generalised Estimating Equation (GEE) model to report the odds ratios with 95% CI. I also reported the p values for easier interpretations. Other options for this correlation were independent, auto-regressive, stationary, non-stationary, unstructured and fixed. However, as I did not have any time-series data, assuming an exchangeable correlation seemed reasonable. Considering the outcome of interests related to the performance of conducting pulse oximetry assessments, I used the binomial family with logit link in the analysis. Maximum iteration for these models were 100, and all the models resulted in convergence. The type of standard errors reported in the analysis was selected to be conventional, which is derived from the asymptotic theory. I added various covariates in the models to assess their adjusted effects on the performance of conducting pulse oximetry assessments. The patient-related factors, such as age, sex, weight-for-

height and clinical features; provider-related factors such as age, sex, designation and facility-related factor such as the type of facilities, the round of the survey was included in the models as covariates. I believe that adopting the GEE model over the logistic regression model helped me report the effect of different factors on the pulse oximetry performance with more validity, precision, and rigour (104-106).

According to WHO, hypoxaemia is defined as SpO_2<90%. However, I did not identify many hypoxaemic cases based on this cut-off during the assessment period. It may be due to the change in the case-mix of children receiving IMCI services resulting from establishing special screening and triage during the COVID-19 pandemic. Therefore, in consultation with the National IMCI Programme and IMCI experts in Bangladesh, I revised the cut-off and considered SpO_2<94% as hypoxaemia for assessing the agreement between IMCI service providers and study recruited nurses. I used the prevalence adjusted and bias-adjusted kappa (PABAK) for reporting the agreement in identifying hypoxaemia since the prevalence was less than 10% (107, 108) I also checked the agreement with a cut-off of SpO_2<92% and the findings were consistent with that of SpO_2<94%.

I found that approximately 2% of children receiving IMCI services from the selected health facilities with pneumonia or severe pneumonia had hypoxaemia (during the assessment round 1 and round 2). This apparently low rate of hypoxaemia among children with pneumonia or severe pneumonia in outpatient-based IMCI settings may be primarily explained by the changes in care seeking practices and health systems response (screening and triage) during the COVID-19 pandemic in

Bangladesh (described before in this chapter). However, even if the prevalence of hypoxaemia prevalence is relatively on the lower side in the IMCI settings in Bangladesh during non-COVID periods, it can make a large difference to the overall pneumonia-related mortality, if left undetected and untreated. In Bangladesh, IMCI services are provided through outpatient settings in Medical College Hospitals (40), District Hospitals (64), Upazila health Complexes (424 and Maternal and Child Welfare Centres (74). In addition, IMCI services are also provided in all Union Health and Family Welfare Centres (~5300). I extracted data from the national MIS database (DHIS2) for 2019, 2020 and 2021, and found that on average more than half-a-million children with pneumonia or severe pneumonia come in contact with public facility-based IMCI services every year. (118) Although, Community Clinics (~12,500) do not provide IMCI services, they offer selective child curative care, including children with cough and difficulty in breathing, with a simplified algorithm. The Community Clinics do not report to the National MIS regarding IMCI services or number of children receiving pneumonia-related care or management. Therefore, I assumed that a Community Clinic would have one-fourth of the childhood pneumonia cases of a Union Health and Family Welfare Centre. Hence, I estimated that approximately 300,000 children will visit Community Clinics with signs of pneumonia/severe pneumonia every year. If we consider the most conservative estimate, i.e., a hypoxaemia prevalence of 2% among children with pneumonia or severe pneumonia receiving IMCI services (based on the feasibility study), there will more than 16,000 children visiting the outpatient services of public hospitals with hypoxaemic pneumonia every year. According to the most recent round of the Bangladesh Health

Facility Assessment Survey, very few of the public health facilities (Medical College Hospitals, District Hospitals, Upazila Health Complexes, Union Health and Family Welfare Centres and Community Clinics) in Bangladesh have pulse oximetry devices (Chapter 9) and almost none of them have the device in the IMCI consultation rooms (67). It is highly likely that most of the children with hypoxaemia will remain undetected without the availability of pulse oximetry devices. I also found that around 17% of the children with hypoxaemic pneumonia died in a secondary level hospital run by icddr,b in Dhaka, Bangladesh (Chapter 4). I also assumed that the case-fatality rate among the undetected hypoxaemic cases in out-patient based IMCI settings would not be less than the case-fatality rate in icddr,b Dhaka hospital, which is reasonably well equipped and experienced to manage hypoxaemia. Finally, I estimated that a minimum of 2,800 children with hypoxaemic pneumonia would die each year due to the unavailability of pulse oximetry devices in IMCI consultation rooms of public health facilities in Bangladesh. This is more than one-tenth of the estimated number pneumonia-related under-5 mortality in Bangladesh (67). I acknowledge that I used very broad assumptions and a simplistic approach to estimate the impact, which requires further fine-tuning and advanced econometric modelling for the generating a more robust and valid estimate. However, the estimated numbers are based on the most conservative assumptions and helps us understand the gravity of the problem and the prospect of the solution.

Our study showed that the integration of pulse oximetry in IMCI guidelines and the introduction of pulse oximetry in routine IMCI services are feasible in Bangladesh. Based on the results of this study, the Government of Bangladesh felt confident

about scaling up this intervention nationally. As a part of the broader scale-up initiative, the National IMCI Programme of Bangladesh has already trained more than two 1,000 IMCI service providers based on the updated training package, which included the recommendation and instructions related to the use of pulse oximetry in pneumonia assessment. In addition, the IMCI Programme collaborated with the Management Information System (MIS) department to include hypoxaemia among children with pneumonia as one of the national reporting variables in DHIS2. The IMCI Programme has already revised its current plan and decided to procure pulse oximetry devices for IMCI consultation rooms in approximately 200 sub-district hospitals. In the next phase, the IMCI Programme is planning to procure pulse oximetry devices for the remaining sub-district hospitals and union level health centres. Additionally, other development partners have committed to support the IMCI Programme by introducing pulse oximetry in some of their supported districts. For example, UNICEF will provide support in eight districts, icddr,b in two districts, and Save the Children in one district. WHO has supported the government by printing the updated IMCI registers for all facilities nationally. Working closely with a range of stakeholders has thus helped to harmonise and align resources from different sources and make progress in fulfilling the agenda for national scale-up collectively.

There is still scope for future research related to the integration of pulse oximetry in routine health systems of resource-limited countries. First, our district implementation model was heavy on inputs. Further research can focus on fine-tuning the model by identifying the least-contributory elements and dropping

relevant inputs to make it more cost-effective. Second, the link between pulse oximetry and the overall oxygen delivery system was not demonstrated and assessed in our study, which requires further exploration. Third, effectiveness and cost-effectiveness trials should be conducted focusing on outcomes (quality of pneumonia management) and the impact (mortality) of introducing pulse oximetry in routine health systems. Lastly, follow-up assessments need to be conducted to explore whether the findings of the implementation outcomes variables are sustained over time.

10.4 REFERENCES:

1. Floyd J, Wu L, Hay Burgess D, Izadnegahdar R, Mukanga D, Ghani AC. Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Nature. 2015;528(7580):S53-9.
2. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2011. Dhaka, Bangladesh and Calverton, Maryland, USA; 2013.
3. Rahman AE, Hossain AT, Nair H, Chisti MJ, Dockrell D, El Arifeen S, et al. Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Global Health. 2022;10(3):e348-e59.
4. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health. 2019;7(1):e47-e57.
5. Mao C, Li M. Language Bias Among Chinese-Sponsored Randomized Clinical Trials in Systematic Reviews and Meta-analyses—Can Anything Be Done? JAMA Network Open. 2020;3(5):e206370-e.
6. Jia Y, Huang D, Wen J, Wang Y, Rosman L, Chen Q, et al. Assessment of language and indexing biases among Chinese-sponsored randomized clinical trials. JAMA network open. 2020;3(5):e205894-e.
7. Adams D, Wu T, Yasui Y, Aung S, Vohra S. Systematic reviews of TCM trials: how does inclusion of Chinese trials affect outcome? Journal of Evidence-Based Medicine. 2012;5(2):89-97.
8. Cohen JF, Korevaar DA, Wang J, Spijker R, Bossuyt PM. Should we search Chinese biomedical databases when performing systematic reviews? Systematic reviews. 2015;4(1):1-5.
9. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. The Lancet infectious diseases. 2009;9(4):219-27.
10. McAuley L, Tugwell P, Moher D. Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? The Lancet. 2000;356(9237):1228-31.
11. Conn VS, Valentine JC, Cooper HM, Rantz MJ. Grey literature in meta-analyses. Nursing research. 2003;52(4):256-61.
12. Schmucker CM, Blümle A, Schell LK, Schwarzer G, Oeller P, Cabrera L, et al. Systematic review finds that study data not published in full text articles have unclear impact on meta-analyses results in medical research. PloS one. 2017;12(4):e0176210.
13. Hartling L, Featherstone R, Nuspl M, Shave K, Dryden DM, Vandermeer B. Grey literature in systematic reviews: a cross-sectional study of the contribution of non-English reports, unpublished studies and dissertations to the results of meta-

analyses in child-relevant reviews. BMC medical research methodology. 2017;17(1):1-11.

14. Ma L-L, Wang Y-Y, Yang Z-H, Huang D, Weng H, Zeng X-T. Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: what are they and which is better? Military Medical Research. 2020;7(1):1-11.

15. Guise J-M, Butler ME, Chang C, Viswanathan M, Pigott T, Tugwell P, et al. AHRQ series on complex intervention systematic reviews—paper 6: PRISMA-CI extension statement and checklist. Journal of clinical epidemiology. 2017;90:43-50.

16. Zeng X, Zhang Y, Kwong JS, Zhang C, Li S, Sun F, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. Journal of evidence-based medicine. 2015;8(1):2-10.

17. Porritt K, Gomersall J, Lockwood C. JBI's systematic reviews: study selection and critical appraisal. AJN The American Journal of Nursing. 2014;114(6):47-52.

18. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994:1088-101.

19. Doi SA. Rendering the Doi plot properly in meta-analysis. JBI Evidence Implementation. 2018;16(4):242-3.

20. Sterne JA, Egger M. Regression methods to detect publication and other bias in meta-analysis. Publication bias in meta-analysis: Prevention, assessment and adjustments. 2005;99:110.

21. Lau J, Ioannidis JP, Terrin N, Schmid CH, Olkin I. The case of the misleading funnel plot. Bmj. 2006;333(7568):597-600.

22. Ministry of Health and Family Welfare. Facility Registry 2022 [Available from: http://facilityregistry.dghs.gov.bd/report_org_list.php.

23. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Research synthesis methods. 2010;1(2):97-111.

24. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. International journal of evidence-based healthcare. 2015;13(3):196-207.

25. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. Respiratory medicine. 2013;107(6):789-99.

26. Seifi S, Khatony A, Moradi G, Abdi A, Najafi F. Accuracy of pulse oximetry in detection of oxygen saturation in patients admitted to the intensive care unit of heart surgery: comparison of finger, toe, forehead and earlobe probes. BMC nursing. 2018;17(1):1-7.

27. Rahman AE, Ameen S, Hossain AT, Jabeen S, Majid T, Afm AU, et al. Success and time implications of SpO2 measurement through pulse oximetry among hospitalised children in rural Bangladesh: Variability by various device-, provider- and patient-related factors. Journal of Global Health. 2022;12.

28. Emdin CA, Mir F, Sultana S, Kazi A, Zaidi AK, Dimitris MC, et al. Utility and feasibility of integrating pulse oximetry into the routine assessment of young infants at primary care clinics in Karachi, Pakistan: a cross-sectional study. BMC pediatrics. 2015;15(1):141.

29. Shi T, McAllister DA, O'Brien KL, Simoes EA, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. The Lancet. 2017;390(10098):946-58.

30. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses: World Health Organization; 2013.

31. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet: World Health Organization; 2014.

32. McCollum ED, King C, Ahmed S, Hanif AA, Roy AD, Islam AA, et al. Defining hypoxaemia from pulse oximeter measurements of oxygen saturation in well children at low altitude in Bangladesh: an observational study. BMJ open respiratory research. 2021;8(1):e001023.

33. McCollum ED, King C, Deula R, Zadutsa B, Mankhambo L, Nambiar B, et al. Pulse oximetry for children with pneumonia treated as outpatients in rural Malawi. Bulletin of the World Health Organization. 2016;94(12):893.

34. Subhi R, Smith K, Duke T. When should oxygen be given to children at high altitude? A systematic review to define altitude-specific hypoxaemia. Archives of disease in childhood. 2009;94(1):6-10.

35. Grocott M, Montgomery H, Vercueil A. High-altitude physiology and pathophysiology: implications and relevance for intensive care medicine. Critical Care. 2007;11(1):1-5.

36. Saha SK, Schrag SJ, El Arifeen S, Mullany LC, Islam MS, Shang N, et al. Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study. The Lancet. 2018;392(10142):145-59.

37. O'Brien KL, Baggett HC, Brooks WA, Feikin DR, Hammitt LL, Higdon MM, et al. Causes of severe pneumonia requiring hospital admission in children without HIV infection from Africa and Asia: the PERCH multi-country case-control study. The Lancet. 2019;394(10200):757-79.

38. Lozano J. Epidemiology of hypoxaemia in children with acute lower respiratory infection [oxygen therapy in children]. The international journal of tuberculosis and lung disease. 2001;5(6):496-504.

39. Orimadegun AE, Ogunbosi BO, Carson SS. Prevalence and predictors of hypoxaemia in respiratory and non-respiratory primary diagnoses among emergently ill children at a tertiary hospital in south western Nigeria. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2013;107(11):699-705.

40. Ibraheem R, Abdulkarim A. Hypoxaemia in hospitalized under-five Nigerian children with pneumonia. 2014.

41. Graham H, Bakare AA, Ayede AI, Oyewole OB, Gray A, Peel D, et al. Hypoxaemia in hospitalised children and neonates: a prospective cohort study in Nigerian secondary-level hospitals. EClinicalMedicine. 2019;16:51-63.

42. Bassat Q, Lanaspa M, Machevo S, O'Callaghan-Gordo C, Madrid L, Nhampossa T, et al. Hypoxaemia in Mozambican children <5 years of age admitted to hospital with clinical severe pneumonia: clinical features and performance of predictor models. Tropical Medicine & International Health. 2016;21(9):1147-56.

43. Tolla HS, Letebo M, Asemere YA, Belete AB, Tumbule TC, Feleke Z, et al. Use of pulse oximetry during initial assessments of children under-5 with pneumonia: a retrospective cross-sectional study from 14 hospitals in Ethiopia. J Glob Health Rep. 2019;3:e2019016.

44. Salah ET, Algasim SH, Mhamoud AS, Husian NEOSA. Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2015;19(4):203.

45. Wandeler G, Pauchard J, Zangger E, Diawara H, Gehri M. Which clinical signs predict hypoxaemia in young Senegalese children with acute lower respiratory tract disease? Paediatrics and international child health. 2015;35(1):65-8.

46. Zhang L, Mendoza-Sassi R, Santos J, Lau J. Accuracy of symptoms and signs in predicting hypoxaemia among young children with acute respiratory infection: a meta-analysis. The International journal of tuberculosis and lung disease. 2011;15(3):317-25.

47. Fashanu C, Mekonnen T, Amedu J, Onwundiwe N, Adebiyi A, Omokere O, et al. Improved oxygen systems at hospitals in three Nigerian states: An implementation research study. Pediatric Pulmonology. 2020;55:S65-S77.

48. Graham H, Tosif S, Gray A, Qazi S, Campbell H, Peel D, et al. Providing oxygen to children in hospitals: a realist review. Bull World Health Organ. 2017;95:288-302.

49. Bakare AA, Graham H, Ayede AI, Peel D, Olatinwo O, Oyewole OB, et al. Providing oxygen to children and newborns: a multi-faceted technical and clinical assessment of oxygen access and oxygen use in secondary-level hospitals in southwest Nigeria. International health. 2020;12(1):60-8.

50. Scott JAG, Brooks WA, Peiris JM, Holtzman D, Mulholland EK. Pneumonia research to reduce childhood mortality in the developing world. The Journal of clinical investigation. 2008;118(4):1291-300.

51. Ashraf H, Mahmud R, Alam NH, Jahan SA, Kamal SM, Haque F, et al. Randomized controlled trial of day care versus hospital care of severe pneumonia in Bangladesh. Pediatrics. 2010;126(4):e807-e15.

52. Chisti MJ, Salam MA, Smith JH, Ahmed T, Pietroni MA, Shahunja K, et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. The Lancet. 2015;386(9998):1057-65.

53. Hasan S, Mulamoottil G. Environmental problems of Dhaka City: a study of mismanagement. Cities. 1994;11(3):195-200.

54. Hossain I, Rahman MS, Sattar S, Haque M, Mullick AR, Siraj S, et al. Environmental Overview of Air Quality Index (AQI) in Bangladesh: Characteristics and Challenges in Present Era. International Journal of Research in Engineering, Science and Management. 2021;4(7):110-5.

55. icddrb. icddr,b Annual Report. 2020.

56. Mulatya DM, Mutuku FW. Assessing comorbidity of diarrhea and acute respiratory infections in children under-5 years: evidence from Kenya's Demographic Health Survey 2014. Journal of primary care & community health. 2020;11:2150132720925190.

57. Howell M. Pulse oximetry: an audit of nursing and medical staff understanding. British Journal of Nursing. 2002;11(3):191-7.

58. Rahman AE, Hossain AT, Zaman SB, Salim N, KC A, Day LT, et al. Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy and childbirth. 2021;21(1):1-17.

59. Day LT, Rahman QS-u, Rahman AE, Salim N, Ashish K, Ruysen H, et al. Assessment of the validity of the measurement of newborn and maternal health-care coverage in hospitals (EN-BIRTH): an observational study. The Lancet Global Health. 2021;9(3):e267-e79.

60. Ameen S, Siddique AB, Peven K, Rahman QS-u, Day LT, Shabani J, et al. Survey of women's report for 33 maternal and newborn indicators: EN-BIRTH multi-country validation study. BMC Pregnancy and Childbirth. 2021;21(1):1-17.

61. Chisti MJ, Duke T, Robertson CF, Ahmed T, Faruque AS, Ashraf H, et al. Clinical predictors and outcome of hypoxaemia among under-five diarrhoeal children with or without pneumonia in an urban hospital, Dhaka, Bangladesh. Tropical Medicine and International Health. 2011;17(1):106-11.

62. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a mortality risk factor in acute lower respiratory infections in children in low- and middle-income countries: systematic review and meta-analysis. PLoS One. 2015;10(9):e0136166.

63. Hosmer DW, Hosmer T, Le Cessie S, Lemeshow S. A comparison of goodness-of-fit tests for the logistic regression model. Statistics in medicine. 1997;16(9):965-80.

64. Wei WW. Time series analysis. The Oxford Handbook of Quantitative Methods in Psychology: Vol 22006.

65. Ferdous F, Ahmed S, Das SK, Chisti MJ, Nasrin D, Kotloff KL, et al. Pneumonia mortality and healthcare utilization in young children in rural Bangladesh: a prospective verbal autopsy study. Tropical medicine and health. 2018;46(1):1-10.

66. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2017-18. Dhaka, Bangladesh and Calverton, Maryland, USA; 2020.

67. Rahman AE, Hossain AT, Siddique AB, Jabeen S, Chisti MJ, Dockrell DH, et al. Child mortality in Bangladesh–why, when, where and how? A national survey-based analysis. Journal of global health. 2021;11.

68. The DHS Program, USAID. Demographic and Health Surveys (DHS) 2020 [Available from: https://dhsprogram.com/what-we-do/survey-Types/dHs.cfm.

69. Uneke CJ, Uro-Chukwu HC, Chukwu OE. Validation of verbal autopsy methods for assessment of child mortality in sub-Saharan Africa and the policy implication: a rapid review. The Pan African Medical Journal. 2019;33.

70. Tunga M, Lungo J, Chambua J, Kateule R. Verbal autopsy models in determining causes of death. Tropical Medicine & International Health. 2021;26(12):1560-7.

71. Murray CJ, Lopez AD, Black R, Ahuja R, Ali SM, Baqui A, et al. Population Health Metrics Research Consortium gold standard verbal autopsy validation study: design, implementation, and development of analysis datasets. Population health metrics. 2011;9(1):1-15.

72. Murray CJ, Lozano R, Flaxman AD, Serina P, Phillips D, Stewart A, et al. Using verbal autopsy to measure causes of death: the comparative performance of existing methods. BMC medicine. 2014;12(1):1-19.

73. Bangladesh Bureaur of Statistics. Bangladesh Population and Housing Census 2011. 2011.

74. Bangladesh Bureaur of Statistics. Sample Vital Registration System. 2015.

75. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2017. Dhaka, Bangladesh; 2019.

76. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Neonatal, Child, & Adolescent Health (MNC&AH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

77. Ministry of Health and Family Welfare (MOHFW)-Government of Bangladesh. 4th Health, Population and Nutrition Sector Programmme (4th HPNSP): Operational Plan for Maternal, Child, Reproductive, & Adolescent Health (MCRAH) (January 2017-June 2022). Dhaka: Government of Bangladesh; 2017.

78. Mitra S, Ali MN, Islam S, Cross AR, Saha T. Bangladesh Demographic and Health Survey 1993-1994. Calverton, Maryland; 1994.

79. Mitra S, Al-Sabir A, Saha T, Kumar S. Bangladesh Demographic and Health Survey 1999-2000. Dhaka, Bangladesh and Calverton, Maryland USA; 2001.

80. Mitra SN, Al-Sabir A, Cross RA, Zamil K. Bangladesh Demographic and Health Survey 1996-1997. Dhaka and Calverton, Maryland; 1997.

81. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2014. Dhaka, Bangladesh and Calverton, Maryland, USA; 2016.

82. National Institute of Population Research and Training (NIPORT), Mitra and Associates, International I. Bangladesh Demographic and Health Survey 2007. Dhaka, Bangladesh and Calverton, Maryland, USA; 2009.

83. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ORC Macro. Bangladesh Demographic and Health Survey 2004. Dhaka, Bangladesh and Calverton, Maryland, USA; 2005.

84. National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), ICF International. Bangladesh Health Facility Survey 2014. Dhaka, Bangladesh; 2016.

85. Measure Evaluation, ICF International. DHS program 2022 [Available from: https://dhsprogram.com/.

86. Griffiths J, Maggs H, George E. Stakeholder Involvement': Background paper prepared for the WHO/WEF joint event on Preventing Noncommunicable Diseases in the Workplace (Dalian/China, September 2007). WHO Report Geneva, Switzerland: World Health Organization. 2008.

87. Mitchell S-L, Clark M. Reconceptualising product life-cycle theory as stakeholder engagement with non-profit organisations. Journal of Marketing Management. 2019;35(1-2):13-39.

88. Murtagh MJ, Minion JT, Turner A, Wilson RC, Blell M, Ochieng C, et al. The ECOUTER methodology for stakeholder engagement in translational research. BMC medical ethics. 2017;18(1):1-12.

89. Deverka PA, Lavallee DC, Desai PJ, Esmail LC, Ramsey SD, Veenstra DL, et al. Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. J Comp Eff Res. 2012;1(2):181-94.

90. Stocker F, de Arruda MP, de Mascena KM, Boaventura JM. Stakeholder engagement in sustainability reporting: a classification model. Corporate Social Responsibility and Environmental Management. 2020;27(5):2071-80.

91. Sinclair M-L. Developing a Model for Effective Stakeholder Engagement Management. Asia Pacific Public Relations Journal. 2011;12(2).

92. Cammaerts B. Power dynamics in multi-stakeholder policy processes and intra-civil society networking. The handbook of global media and communication policy. 2011:129-46.

93. Joshi A, Kale S, Chandel S, Pal DK. Likert scale: Explored and explained. Current Journal of Applied Science and Technology. 2015;7(4):396.

94. Alabi O, Doctor HV, Afenyadu GY, Findley SE. Lessons learned from setting up the Nahuche Health and Demographic Surveillance System in the resource constrained context of northern Nigeria. Global health action. 2014;7(1):23368.

95. Arifeen SE, Hoque DE, Akter T, Rahman M, Hoque ME, Begum K, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. The Lancet. 2009;374(9687):393-403.

96. Larson CP, Saha UR, Nazrul H. Impact monitoring of the national scale up of zinc treatment for childhood diarrhea in Bangladesh: repeat ecologic surveys. PLoS medicine. 2009;6(11):e1000175.

97. El Arifeen S, Blum LS, Hoque DE, Chowdhury EK, Khan R, Black RE, et al. Integrated Management of Childhood Illness (IMCI) in Bangladesh: early findings from a cluster-randomised study. The Lancet. 2004;364(9445):1595-602.

98. Rahman AE, Hossain AT, Zaman SB, Salim N, Ashish K, Day LT, et al. Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy childbirth. 2021;21(1):1-17.

99. Ruysen H, Rahman AE, Gordeev VS, Hossain T, Basnet O, Shirima K, et al. Electronic data collection for multi-country, hospital-based, clinical observation of maternal and newborn care: EN-BIRTH study experiences. BMC pregnancy and childbirth. 2021;21(1):1-15.

100. Mishra P, Pandey CM, Singh U, Gupta A, Sahu C, Keshri A. Descriptive statistics and normality tests for statistical data. Annals of cardiac anaesthesia. 2019;22(1):67.

101. Razali NM, Wah YB. Power comparisons of shapiro-wilk, kolmogorov-smirnov, lilliefors and anderson-darling tests. Journal of statistical modeling and analytics. 2011;2(1):21-33.

102. Mood AM. On the asymptotic efficiency of certain nonparametric two-sample tests. The Annals of Mathematical Statistics. 1954:514-22.

103. Oja H, Randles RH. Multivariate nonparametric tests. Statistical Science. 2004;19(4):598-605.

104. Hubbard AE, Ahern J, Fleischer NL, Van der Laan M, Satariano SA, Jewell N, et al. To GEE or not to GEE: comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. Epidemiology. 2010:467-74.

105. Kleinbaum DG, Klein M. Logistic Regresion for Correlated Data: GEE. Logistic regression: A self-learning text. 2002:327-75.

106. Sheu C-f. Regression analysis of correlated binary outcomes. Behavior Research Methods, Instruments, & Computers. 2000;32(2):269-73.

107. Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. J Clin Epidemiol. 1993;46(5):423-9.

108. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Physical therapy. 2005;85(3):257-68.

109. Peters DH, Tran NT, Adam T. Implementation research in health: a practical guide. Geneva: World Health Organization; 2013.

110. Rahman AE, Jabeen S, Genevie F, Banik G, Islam J, Ameen S, et al. Introducing pulse oximetry in routine IMCI services in Bangladesh: a context-driven approach to influence policy and programme through stakeholder engagement. J Glob Health. 2021;in press.

111. Rahman AE, Herrera S, Rubayet S, Banik G, Hasan R, Ahsan Z, et al. Managing possible serious bacterial infection of young infants where referral is not possible: Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. PloS one. 2020;15(5):e0232675.

112. Ahmed R, Hassan S. Hard-to-Reach Areas : Providing Water Supply and Sanitation Services to All. Water and sanitation program guidance note;. World Bank, Washington, DC. © World Bank. . 2012.

113. Rahman AE, Mhajabin S, Dockrell D, Nair H, El Arifeen S, Campbell H. Managing pneumonia through facility-based integrated management of childhood

management (IMCI) services: an analysis of the service availability and readiness among public health facilities in Bangladesh. BMC Health Services Research. 2021;21(1):1-13.

114. National Institute of Population Research and Training (NIPORT), International Centre for Diarrhoeal Disease Research Bi, MEASURE Evaluation. Bangladesh District Level Socio-demographic and Health Care Utilization Indicators. Dhaka, Bangladesh, and Chapel Hill, NC, USA: NIPORT, icddr,b, and MEASURE Evaluation. 2019.

115. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. Journal of clinical epidemiology. 2014;67(3):267-77.

116. Paradis E, Sutkin G. Beyond a good story: from Hawthorne Effect to reactivity in health professions education research. Medical education. 2017;51(1):31-9.

117. Lange S, Mwisongo A, Mæstad O. Why don't clinicians adhere more consistently to guidelines for the Integrated Management of Childhood Illness (IMCI)? Social Science & Medicine. 2014;104:56-63.

118. Khan MAH, Azad AK, de Oliveira Cruz V. Bangladesh's digital health journey: reflections on a decade of quiet revolution. WHO South-East Asia Journal of Public Health. 2019;8(2):71-6.

Chapter 11: CONCLUSION

The overall prevalence of hypoxaemia among children with pneumonia was high in LMICs, including Bangladesh. It was notably higher among clinically severe and hospitalised children with pneumonia. Disaggregated measures offer a chance to understand the burden in greater detail and identify the vulnerable population and risk factors for prioritising prevention, protection and treatment. Unfortunately, due to the lack of standardisation in published reporting, I could not extract the necessary information for reporting the prevalence of hypoxaemia disaggregated by co-variates and potential risk factors. Therefore, I strongly recommend that all studies reporting the prevalence of hypoxaemia should follow a minimum set of reporting principles, which may include reporting estimates disaggregated by smaller and standardised age bands (0-1 months, 2-11 months, 12-59 months), sex, co-morbid conditions (malnutrition, congenital health disease, chronic obstructive pulmonary disease, etc.), and pneumonia classification (severe pneumonia, fast breathing pneumonia, chest in-drawing pneumonia) Studies reporting the prevalence of hypoxaemia should also explicitly mention the specification of pulse oximetry device, probe types, anatomical site of probe placement, facility type (hospital, health centre), settings (inpatient, emergency, outpatient and community), provider type (doctors, nurses, paramedics, community health workers) altitude (high, low), etc. I did not include unpublished data, which is one of the major limitations of my review. Future reviewers can collaborate with the existing community- and facility-based surveillance networks on respiratory health to access up-to-date and unpublished data related to hypoxaemia to improve the

robustness of the methods and increase the validity and granularity of the estimates of childhood pneumonia. An alternate approach could be to reach out to prominent and prolific researchers in the field of respiratory health, pneumonia, and oxygen security, primarily through their publication track records as well as those known to be active in this area and use them as snowballs to identify other ongoing studies and unpublished data sources on hypoxaemia. Future systematic reviews can also collaborate with scholars, academic institutes, and research organisations from China to include Chinese language databases and publications in the review, which was one of the limitations of my review.

The prevalence of hypoxaemia reported in my review was much higher than that of the previous review conducted by Subhi et al. in 2009. Although the scope and search strategy were similar, there were some differences between the two reviews in the type of data included and the methods used. While this may partially explain the significant difference observed in the estimated prevalence of hypoxaemia between the two reviews, this may also indicate an increasing trend in the burden in LMICs. One underlying factor or explanation that I could not explore in detail is the effect of pneumonia aetiology on hypoxaemia. The introduction and rapidly increasing coverage of PCV and HiB vaccine in LMICs could have substantially changed the aetiological spectrum causing childhood pneumonia. Moreover, the RSV vaccines are now in the pipeline for introduction into the routine immunisation system. Therefore, I recommend establishing or leveraging existing community- and facility-based surveillance networks to track pneumonia aetiology and its relationship with

the prevalence of hypoxaemia. The latter can be undertaken with minimum incremental costs.

Lastly, the high burden of hypoxaemia in LMICs, including Bangladesh, demands greater attention and concerted efforts from the global, regional and national policymakers and stakeholders. In this regard, a critical first step would be to invest in and strengthen the health information system so that minimum information regarding hypoxaemia and its management is routinely documented, recorded, and reported. Such information will help generate real time and context-specific estimates to understand the burden of hypoxaemia, management outcomes and its trend over time, and make informed decisions.

My analysis showed that Bangladesh has a high burden of childhood pneumonia, with approximately 24,000 under-5 deaths per year due to pneumonia. I found significant gaps in the availability of pulse oximetry devices, oxygen sources, and the oxygen delivery system in Bangladesh's public health facilities and hospitals. This high burden of pneumonia, including hypoxaemia, combined with inadequate readiness of the health facilities for managing hypoxaemia, clearly shows the risk children face in this country and reveals the evident disconnect between existing policy priorities and programme planning. Hypoxaemia is also common among several diseases and conditions other than pneumonia, such as chronic lung diseases, severe sepsis, meningitis, complications of prematurity, trauma, obstetric emergencies and peri-operative care. The COVID-19 pandemic has substantially added to the burden of hypoxaemia and revealed the critical gaps in the oxygen

systems preparedness of health facilities and hospitals in Bangladesh and many other LMICs. The Government of Bangladesh should consider oxygen security as a strategic priority and invest in ensuring rapid identification of hypoxaemia through point-of-care diagnostics, such as pulse oximetry devices, and immediate management by appropriate oxygen therapy with reliable oxygen sources a functioning oxygen distribution system. Bangladesh takes a sector-wide approach to health, and the current health sector programme will end in June 2023. The next five-year health sector program is currently being designed and developed. Policymakers and health managers should consider oxygen security as a priority agenda in the upcoming health sector program. As part of the preparation, I recommend conducting a comprehensive assessment of the oxygen needs and capacities of the public health system of Bangladesh to identify, refer and manage hypoxaemia with adequate and appropriate oxygen therapy. The assessment should also identify gaps in existing policies, programmes, and practices. The results can play a decisive role in developing a need-based, context driven, feasible and cost-effective action plan for ensuring oxygen security in the next health sector programme.

Bangladesh was one of the first countries to nationally introduce and scale up IMCI services in paediatric outpatient settings. The implementation research study demonstrated that the IMCI service providers are willing to accept pulse oximetry in their routine practice, can successfully conduct pulse oximetry assessments and obtain a stable SpO_2 reading with minimum attempts and in a relatively short amount of time. These findings illustrate the adequacy of the training package and

district implementation model developed and tested. They also indicate the feasibility of introducing pulse oximetry in routine IMCI services in paediatric outpatient settings through a health system strengthening approach. Policymakers can capitalise on these encouraging findings and scale up pulse oximetry nationally. In addition to the paediatric outpatient settings, I strongly recommend introducing pulse oximetry in emergency and inpatient settings. This holistic approach will improve the accuracy of diagnosis and continuum and quality of management of pneumonia and other diseases associated with hypoxaemia. It will also address the need for regular monitoring of SpO_2 levels to use oxygen correctly and efficiently.

The district implementation model requires context-specific adaptation to overcome local level barriers and challenges, such as readiness of health facilities, training arrangements, monitoring mechanisms, etc. I recommend conducting implementation research studies in diverse contexts to adapt and modify the district implementation model for achieving greater acceptability, usability, utility, and sustainability. The pulse oximetry performance, including success rate and performance time, may be influenced by device characteristics, probe size and design, provider workload and age of the children. Introducing pulse oximetry devices with advanced signal strengths in high-volume facilities can help overcome the challenges associated with motion artefacts, particularly among younger children. The health managers will need to emphasise adhering to SoPs in training and routine monitoring. Special emphasis can be given to identifying providers who would benefit from targeted monitoring and follow-up support. Specific attention

should be given to these barriers and enablers during policy decision making and programme planning.

Based on the encouraging results of the adequacy and feasibility studies coupled with a comprehensive stakeholder engagement approach, the Government of Bangladesh has decided to integrate pulse oximetry into the national IMCI guidelines and scale-up pulse oximetry in all IMCI consultation rooms in phases. This presents a unique opportunity to assess the effect/impact of introducing pulse oximetry on improving the quality of pneumonia management through IMCI services and its impact on pneumonia-related childhood mortality. Therefore, I recommend embedding an effectiveness study in the Government of Bangladesh's plan to scale pulse oximetry nationally. A step-wedged design may be most appropriate in the context of the health sector programme. Future studies should also collect additional information required for assessing cost-effectiveness in routine outpatient settings.

As I mentioned above, using a point-of-care diagnostic tool, such as a pulse oximetry device, can substantially improve the provision of hypoxaemia identification and the accuracy of pneumonia classification by the health service providers. It will require around USD 5 million to introduce pulse oximetry in all IMCI consultation rooms and other outpatient and inpatient settings in Bangladesh. Nevertheless, this investment has the potential to avert around 2,800 childhood pneumonia deaths annually, which is only 0.06% of the total value of the current health sector programme and should be affordable in the context of the rapidly growing economy of Bangladesh.

Chapter 12: SCIENTIFIC CONTRIBUTION AND OUTPUTS

During my PhD journey, I published 35 articles in international peer review journals. Out of which, seven are directly derived from my PhD thesis and I contributed to all of them as a first author. Additionally, I published three articles as a first author, one as a last author and four as a co-author which are related to child health or hypoxaemia. I also published eight articles as a first author, four as a last author, and eight as a co-author on various other topics related to global health priorities in LMICs.

Table 12.1: Scientific contributions and outputs during the PhD period

PhD thesis		
First author	1.	**Rahman AE,** Ameen S, Hossain AT, Perkins J, Jabeen S, Majid T, Uddin AA, Shaikh MZH, Islam MS, Islam MJ, Ashrafee S, Alam HMS, Saberin A, Ahmed A, Banik G, Kabir AE, Khan M, Ahmed A, Chisti MJ, Cunningham S, **Dockrell DH, Nair H, Arifeen SE, Campbell H**. Introducing pulse oximetry for outpatient management of childhood pneumonia: An implementation research adopting a district implementation model in selected rural facilities in Bangladesh. eClinicalMedicine. 2022. (accepted)
	2.	**Rahman AE**, Ameen S, Hossain AT, Jabeen S, Majid T, Afm AU, Tanwi TS, Banik G, Shaikh MZH, Islam MJ, Ashrafee S, Alam HMS, Saberin A, Kabir AE, Ahmed S, Khan M, Ahmed AU, Rahman QS, Chisti MJ, Cunningham S, Islam MS, **Dockrell DH, Nair H, Arifeen SE, Campbell H**: Success and time implications of SpO_2 measurement through pulse oximetry among hospitalised children in rural Bangladesh: Variability by various device-, provider-and patient-related factors. Journal of Global Health 2022, 12. URL: *https://jogh.org/2022/jogh-12-04036*
	3.	**Rahman AE**, Jabeen S, Fernandes G, Banik G, Islam J, Ameen S, Ashrafee S, Hossain AT, Alam HMS, Majid T, Saberin A, Ahmed A, Kabir ANME, Chisti MJ, Ahmed S, Khan M, Jaskcon T, **Dockrell DH, Nair H, Arifeen SE,** Islam MS, **Campbell H**: Introducing pulse oximetry in routine IMCI services in Bangladesh: A context-driven approach to influence policy and programme through stakeholder engagement. Journal of global health 2022, 12:06001-06001. URL: *https://jogh.org/2022/jogh-12-06001*
	4.	**Rahman AE**, Hossain AT, **Nair H,** Chisti MJ, **Dockrell D, Arifeen SE, Campbell H**: Prevalence of hypoxaemia in children with pneumonia in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Global Health 2022, 10:e348-e359. URL: *https://www.thelancet.com/action/showPdf?pii=S2214-109X%2821%2900586-6*

	5.	**Rahman AE**, Hossain AT, Chisti MJ, **Dockrell DH, Nair H, El Arifeen S, Campbell H**: Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh. Journal of global health 2021, 11. URL: *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8442579/*
	6.	**Rahman AE**, Hossain AT, Siddique AB, Jabeen S, Chisti MJ, **Dockrell DH, Nair H, Jamil K, Campbell H, El Arifeen S**: Child mortality in Bangladesh–why, when, where and how? A national survey-based analysis. Journal of global health 2021, 11. URL: *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8442576/*
	7.	**Rahman AE**, Mhajabin S, **Dockrell D, Nair H, El Arifeen S, Campbell H**: Managing pneumonia through facility-based integrated management of childhood management (IMCI) services: an analysis of the service availability and readiness among public health facilities in Bangladesh. BMC health services research 2021, 21:1-13. URL: *https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-021-06659-y*
Child health and hypoxaemia		
First Author	8.	**Rahman AE**, Hossain AT, Zaman SB, Salim N, KC A, Day LT, Ameen S, Ruysen H, Kija E, Peven K, Shamim Q, Arifeen SE: Antibiotic use for inpatient newborn care with suspected infection: EN-BIRTH multi-country validation study. BMC pregnancy and childbirth 2021, 21:1-17. URL: *https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-03424-7*
	9.	**Rahman AE**, Banik G, Mhajabin S, Tahsina T, Islam MJ, Ahmed FU, Islam MU, Mannan MA, Dey SK, Sharmin S, M Fida, K Mahbuba, A Anisuddin, S Ahmed, S Shahin, A Ziaul, R Sayed, G Joby, K Afsana, S Mohammod, AE Shams: Newborn signal functions in Bangladesh: identification through expert consultation and assessment of readiness among public health facilities—study protocol using Delphi technique. BMJ open 2020, 10:e037418. URL: *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7467517/*
	10.	**Rahman AE**, Herrera S, Rubayet S, Banik G, Hasan R, Ahsan Z, Siraj W, Ahmed A, Siddique AB, Rahman QS-u, V Lara, I Jahurul, H Altaf, M Shahidullah, O Mohiuddin, AE Shams: Managing possible serious bacterial infection of young infants where referral is not possible: Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. PloS one 2020, 15:e0232675. URL: *https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0232675*
Last author	11.	Hossain AT, Ameen S, Nahya Salim K, Ruysen H, Tahsina T, Ahmed A, Rahman MH, Mhajabin S, Jabeen S, Peven K, Kong S, Louise DT, Yasir BN, Evelyne A, Shamim Q, R Qazi, Arifeen SE, **Rahman AE**: Measuring coverage and quality of supportive care for inpatient neonatal infections: EN-BIRTH multi-country validation study. Journal of Global Health 2022, 12. URL: *https://jogh.org/2022/jogh-12-04029*
Co-author	12.	Ameen S, Siddique AB, Peven K, Rahman QS-u, Day LT, Shabani J, Kc A, Boggs D, Shamba D, Tahsina T, **Rahman AE**, Zaman SB, Hossain AT, Ahmed A, Basnet O, Malla H, Ruysen H, Blencowe H, Arnold F, Requejo J, Arifeen SE,

		Lawn JE, EN-BIRTH SG: Survey of women's report for 33 maternal and newborn indicators: EN-BIRTH multi-country validation study. BMC Pregnancy and Childbirth 2021, 21:1-17. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7995710/
	13.	Day LT, Gore-Langton GR, **Rahman AE**, Basnet O, Shabani J, Tahsina T, Poudel A, Shirima K, Ameen S, KC A, Nahya S, Sojib Z, Donat S, Hannah B, Harriet R, Arifeen SE, Dorothy B, Vladimir G, Qazi R, Tanvir H, Elisha J, Sabu T, Rajendra P, Durga P, Priyanka C, Rabina K, Bibek C, Namala M, Anna W, Alodear K, Marystella S, Christostomus C, Amina S, Cleopatra M, Victoria M, John B, Japhet K, Godfrey M, Joy EL: Labour and delivery ward register data availability, quality, and utility-Every Newborn-birth indicators research tracking in hospitals (EN-BIRTH) study baseline analysis in three countries. BMC health services research 2020, 20:1-14. URL: https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-5028-7
	14.	Day L, Rahman S-u, **Rahman AE**, Salim N, KC A, Ruysen H, Tahsina T, Masanja H, Basnet O, Gore-Langton GR, Bin ZS, Shabani J, Kumar JA, Gordeev V, Ameen S, Shamba D, Jha B, Boggs D, Hossain T, Shirima K, Bastola RC, Peven K, Siddique AB, Mbaruku G, Paudel R, Baschieri A, Hossain AT, Kong S, Paudel A, Ahmed A, Cousens S, Arifeen SE, Lawn JE: Every Newborn-BIRTH observational study to assess validity of newborn and maternal coverage measurement in hospitals. The Lancet Global Health 2020. URL: https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30504-0/fulltext
	15.	Day LT, Ruysen H, Gordeev VS, Gore-Langton GR, Boggs D, Cousens S, Moxon SG, Blencowe H, Baschieri A, **Rahman AE**, Tazeen T, Sojib BZ, Tanvir H, Qazi R, Shafiqul A, Arifeen SE, KC Ashish, Shree KS, Naresh KC, Dela S, Anjani KJ, Bijay J, Nisha R, Omkar B, Elisha J, Asmita P,… Lara V, Nabila Z, Joy EL: "Every Newborn-BIRTH" protocol: observational study validating indicators for coverage and quality of maternal and newborn health care in Bangladesh, Nepal and Tanzania. Journal of global health 2019, 9. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6406050/
Others		
First author	16.	**Rahman AE**, Perkins J, Hossain AT, Banik G, Jabeen S, Wall S, El Arifeen S: Unpacking Caesarean in Rural Bangladesh: Who, What, When and Where. 2021. URL: https://onlinelibrary.wiley.com/doi/full/10.1111/birt.12636
	17.	Ruysen H, **Rahman AE (co-first),** Gordeev VS, Hossain T, Basnet O, Shirima K, Rahman QS-u, Zaman SB, Rana N, Salim N, Tazeen T, Georgia G, A Shafiqul A, Dorothy B, Stefanie K, Louise DT, Arifeen SE, Joy EL: Electronic data collection for multi-country, hospital-based, **clinical** observation of maternal and newborn care: EN-BIRTH study experiences. BMC pregnancy and childbirth 2021, 21:1-15. URL: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-03426-5
	18.	**Rahman AE**, Janet Perkins, Shumona Sharmin Salam, Shema Mhajabin, Aniqa Tasnim Hossain, Tapas Mazumder, Shams EL Arifeen What do women want? An analysis of preferences of women, involvement of men, and

		decision-making in maternal and newborn health care in rural Bangladesh. 2020. URL: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-2854-x
	19.	Perkins J, **Rahman AE**, Mhajabin S, Siddique AB, Mazumder T, Haider MR, El Arifeen S: Humanised childbirth: the status of emotional support of women in rural Bangladesh. Sexual and reproductive health matters 2019, 27:228-247. URL: https://www.tandfonline.com/doi/full/10.1080/26410397.2019.1610277
	20.	Perkins JE, **Rahman AE**, Siddique AB, Mazumder T, Haider MR, El Arifeen S: Awareness and perceptions of women regarding human rights related to maternal health in rural Bangladesh. Journal of global health 2019, 9. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6571109/
	21.	**Rahman AE**, Perkins J, Mazumder T, Haider MR, Siddique AB, Capello C, Santarelli C, El Arifeen S: Capacities of women and men to improve maternal and newborn health: effect of a community-based intervention package in rural Bangladesh. Journal of global health 2019, 9. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6318832/
	22.	Perkins JE, **Rahman AE**, Siddique AB, Haider MR, Banik G, Tahsina T, Arifeen SE: Opting for home birth in rural Bangladesh: An assessment of the current status and reasons. Birth 2019, 46:362-370. URL: https://onlinelibrary.wiley.com/doi/full/10.1111/birt.12404
	23.	**Rahman AE**, Perkins J, Islam S, Siddique AB, Moinuddin M, Anwar MR, Mazumder T, Ansar A, Rahman MM, Raihana S, C Cecilia, S Carlo, Arifeen SE: Knowledge and involvement of husbands in maternal and newborn health in rural Bangladesh. BMC pregnancy and childbirth 2018, 18:1-12. URL: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-018-1882-2
Last Author	24.	Mhajabin S, Hossain AT, Nusrat N, Jabeen S, Ameen S, Banik G, Tahsina T, Gurley E, Bari S, Chowdhury A, Arifeen SE, Rajesh M, **Rahman AE**: Indirect effects of the lockdown measure due to the COVID-19 pandemic on the coverage of essential maternal and newborn health services in a rural sub-district in Bangladesh. 2021. URL: https://bmjopen.bmj.com/content/12/2/e056951
	25.	Rahman MH, Banik G, Ahmed A, Arifeen SE, Hossain AT, Hasan MA, **Rahman AE**: Anxiety and depressive symptoms among COVID-19 patients admitted to three isolation facilities in Bangladesh. Health Psychology Open 2021, 8:20551029211046106. URL: https://journals.sagepub.com/doi/full/10.1177/20551029211046106
	26.	Siddique AB, Perkins J, Mazumder T, Haider MR, Banik G, Tahsina T, Islam MJ, Arifeen SE, **Rahman AE**: Antenatal care in rural Bangladesh: gaps in adequate coverage and content. PloS one 2018, 13:e0205149. URL: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0205149
	27.	Islam S, Perkins J, Siddique MAB, Mazumder T, Haider MR, Rahman MM, Capello C, Emdadul Hoque DM, Santarelli C, Arifeen SE, **Rahman AE**: Birth

		preparedness and complication readiness among women and couples and its association with skilled birth attendance in rural Bangladesh. PloS one 2018, 13:e0197693. URL: *https://www.researchgate.net/publication/325630883_Birth_preparedness_and_complication_readiness_among_women_and_couples_and_its_association_with_skilled_birth_attendance_in_rural_Bangladesh*
Co-author	28.	Ahmed T, **Rahman AE**, Amole TG, Galadanci H, Matjila M, Soma-Pillay P, Gillespie BM, El Arifeen S, Anumba DO: The effect of COVID-19 on maternal newborn and child health (MNCH) services in Bangladesh, Nigeria and South Africa: call for a contextualised pandemic response in LMICs. International Journal for Equity in Health 2021, 20:1-6. URL: *https://equityhealthj.biomedcentral.com/articles/10.1186/s12939-021-01414-5*
	29.	Chowdhury MAK, **Rahman AE**, Morium S, Hasan MM, Bhuiyan A, Arifeen SE: Domestic violence against women in urban slums of Bangladesh: a cross-sectional survey. Journal of interpersonal violence 2021, 36:NP4728-NP4742. URL: *https://journals.sagepub.com/doi/abs/10.1177/0886260518791235*
	30.	Salim N, Shabani J, Peven K, Rahman QS-u, Kc A, Shamba D, Ruysen H, **Rahman AE**, Kc N, Mkopi N, Sojib ZS… Sarah GM, Agbessi A, Tedbabe DH, Louise TD, Joy EL, EN-BIRTH SG: Kangaroo mother care: EN-BIRTH multi-country validation study. BMC pregnancy and childbirth 2021, 21:1-16. URL: *https://www.researchgate.net/publication/350404691_Kangaroo_mother_care_EN-BIRTH_multi-country_validation_study*
	31.	Zaman SB, Siddique AB, Ruysen H, Kc A, Peven K, Ameen S, Thakur N, Rahman QS-u, Salim N, Gurung R, Tahsina T, **Rahman AE**, Coffey P, Rawlins B, Louise TD, Joy EL, Arifeen SE, EN-BIRTH SG: Chlorhexidine for facility-based umbilical cord care: EN-BIRTH multi-country validation study. BMC pregnancy and childbirth 2021, 21:1-16. URL: *https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-03338-4*
	32.	Tahsina T, Hossain AT, Ruysen H, **Rahman AE**, Day LT, Peven K, Rahman QS-u, Khan J, Shabani J, Kc A, Mazumder T, Zaman SB, Ameen S, Kong S, Amouzou A, Lincetto O, Arifeen SE, Lawn JE, EN-BIRTH SG: Immediate newborn care and breastfeeding: EN-BIRTH multi-country validation study. BMC Pregnancy and Childbirth 2021, 21:1-17. URL: *https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-03421-w*
	33.	Rahman MM, Haider MR, Moinuddin M, **Rahman AE**, Ahmed S, Khan MM: Determinants of caesarean section in Bangladesh: Cross-sectional analysis of Bangladesh Demographic and Health Survey 2014 Data. PloS one 2018, 13:e0202879. URL: *https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0202879*
	34.	Salam SS, Ali NB, **Rahman AE**, Tahsina T, Islam M, Iqbal A, Hoque DM, Saha SK, El Arifeen S: Study protocol of a 4-parallel arm, superiority, community based cluster randomized controlled trial comparing paper and e-platform

		based interventions to improve accuracy of recall of last menstrual period (LMP) dates in rural Bangladesh. BMC public health 2018, 18:1-8. URL: *https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-018-6258-z*
	35.	Haider MR, Rahman MM, Moinuddin M, **Rahman AE**, Ahmed S, Khan MM: Ever-increasing Caesarean section and its economic burden in Bangladesh. PloS one 2018, 13:e0208623. URL: *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6287834/*

Chapter 13: ANNEXURES

Annex 13.1: DETAILED SEARCH LANGUAGE WITH KEYWORDS AND THEIR SYNONYMS FOR CHAPTER 3: BURDEN OF HYPOXAEMIA AMONG CHILDREN WITH PNEUMONIA IN LMICS

Search summary-1

Name of the database: MEDLINE (via Ovid)
Date of search: 08 October 2021
Timeline: November 2008 to October 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia.mp. or exp Hypoxia/	91820
2		exp Hypoxia/ or hypoxaemia.mp.	84800
3		anoxia.mp. or exp Hypoxia/	87644
4		hypoxia.mp. or exp Hypoxia/	155924
5		oximetry.mp. or exp Oximetry/	19678
6		exp Oximetry/ or oximeter.mp.	16924
7		exp Oximetry/ or oximetre.mp.	15892
8		exp Oximetry/ or oxymetry.mp.	16149
9		exp Oximetry/ or oxymeter.mp.	15980
10		exp Oximetry/ or oxymeter.mp.	15980
11		blood oxygen saturation.mp.	1426
12		arterial oxygen saturation.mp.	4055
13		exp Blood Gas Monitoring, Transcutaneous/ or blood gas monitoring.mp. or exp Blood Gas Analysis/	37305
14		blood gas analysis.mp. or exp Blood Gas Analysis/	40194
15		analysis blood gas.mp. or exp Blood Gas Analysis/	37226
16		SpO2.mp.	4886
17		SPO2.mp.	4886
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	211488
19	Pneumonia	exp Pneumonia, Bacterial/ or exp Pneumonia/ or exp Pneumonia, Viral/ or pneumonia.mp.	258674
20		exp Pneumonia, Bacterial/ or exp Pneumonia/ or severe pneumonia.mp. or exp Pneumonia, Viral/	205112
21		severe disease.mp.	18122
22		very severe disease.mp.	199
23		exp Bronchiolitis Obliterans/ or bronchiolitis.mp. or exp Bronchiolitis/ or exp Bronchiolitis, Viral/	13139

24		exp Respiratory Tract Infections/ or acute respiratory infection.mp. or exp Respiratory Syncytial Virus Infections/ ()	482032
25		exp Respiratory Tract Infections/ or ARI.mp. ()	478927
26		exp Respiratory Tract Infections/ or acute respiratory infections.mp. or exp Respiratory Syncytial Virus Infections/	482231
27		exp Respiratory Tract Infections/ or acute respiratory tract infection.mp.	476982
28		exp Respiratory Tract Infections/ or ARTI.mp.	478414
29		exp Respiratory Tract Infections/ or acute respiratory tract infections.mp.	477025
30		exp Respiratory Tract Infections/ or respiratory illness.mp. or exp Respiratory Tract Diseases/	1511022
31		exp Respiratory Tract Infections/ or respiratory illnesses.mp. or exp Respiratory Tract Diseases/	1510299
32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	1565662
33	Children under-5 years of age	Child.mp. or exp Child Health Services/ or exp Child Care/ or exp Child, Hospitalized/ or exp Child/ or exp Child Health/	2175248
34		Children.mp. or exp Child/	2200753
35		Infant.mp. or exp Infant Care/ or exp Infant Health/ or exp Infant/	1230190
36		Infants.mp. or exp Infant/	1226015
37		Pediatric.mp. or exp Pediatrics/	320962
38		Pediatrics.mp. or exp Pediatrics/	82943
39		exp Child/ or exp Child, Preschool/ or Paediatric.mp.	2022745
40		exp Child/ or exp Child, Preschool/ or Paediatrics.mp.	2012017
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40	2914291
42		18 and 32 and 41	7758
43	Low- and Middle-Income country	exp Developing Countries/ or developing countr*.mp.	122287
44		exp Developing Countries/ or low-and middle income country.mp.	78317
45		exp Developing Countries/ or low-and middle income countries.mp.	86721
46		exp Developing Countries/ or LMIC*.mp.	80240
47		exp Developing Countries/ or low income country.mp.	78344
48		exp Developing Countries/ or middle income country.mp.	79281

49		exp Developing Countries/ or low income countries.mp.	81795
50		exp Developing Countries/ or middle income countries.mp.	88815
51		exp Developing Countries/ or lower middle income country.mp.	77958
52		exp Developing Countries/ or lower middle income countries.mp.	78135
53		exp Developing Countries/ or upper middle income countries.mp.	77998
54		exp Developing Countries/ or upper middle income country.mp.	77880
55		Afghanistan.mp. or exp Afghanistan/	6592
56		Albania.mp. or exp Albania/	1248
57		Albania.mp. or exp Albania/	1248
58		American Samoa.mp. or exp American Samoa/	376
59		Angola.mp. or exp Angola/ ()	1583
60		Armenia.mp. or exp Armenia/	1842
61		Azerbaijan.mp. or exp Azerbaijan/	1762
62		Bangladesh.mp. or exp Bangladesh/	15112
63		Belarus.mp. or exp "Republic of Belarus"/	2679
64		Belize.mp. or exp Belize/	886
65		Benin.mp. or exp Benin/	3688
66		Bhutan.mp. or exp Bhutan/	809
67		Bolivia.mp. or exp Bolivia/	3888
68		(Bosnia and Herzegovina).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2655
69		Botswana.mp. or exp Botswana/	2537
70		Brazil.mp. or exp Brazil/	123075
71		Bulgaria.mp. or exp Bulgaria/	7816
72		Burkina Faso.mp. or exp Burkina Faso/	4440
73		Burundi.mp. or exp Burundi/	956
74		Cabo Verde.mp. or exp Cabo Verde/ ()	285
75		Cambodia.mp. or exp Cambodia/ ()	4644
76		Cameroon.mp. or exp Cameroon/ ()	7506
77		Central African Republic.mp. or exp Central African Republic/	1169
78		Chad.mp. or exp Chad/	1276
79		China.mp. or exp China/	276588
80		Colombia.mp. or exp Colombia/	14863

81		Comoros.mp. or exp Comoros/	508
82		exp "Democratic Republic of the Congo"/ or DRC.mp.	5714
83		Congo.mp. or exp Congo/ or exp "Democratic Republic of the Congo"/	14858
84		Costa Rica.mp. or exp Costa Rica/	5210
85		Ivory Coast.mp. or exp Cote d'Ivoire/	3830
86		Cuba.mp. or exp Cuba/	6536
87		Djibouti.mp. or exp Djibouti/	425
88		Dominica.mp. or exp Dominica/	445
89		Dominican Republic.mp. or exp Dominican Republic/	2294
90		Ecuador.mp. or exp Ecuador/	5474
91		exp Egypt/ or Egypt.mp.	20542
92		El Salvador.mp. or exp El Salvador/	1403
93		Equatorial Guinea.mp. or exp Equatorial Guinea/	476
94		Eritrea.mp. or exp Eritrea/	610
95		Ethiopia.mp. or exp Ethiopia/	16915
96		Fiji.mp. or exp Fiji/	1833
97		Gabon.mp. or exp Gabon/	2075
98		Gambia.mp. or exp Gambia/	3147
99		exp "Georgia (Republic)"/ or Georgia.mp.	16712
100		Ghana.mp. or exp Ghana/	11187
101		Grenada.mp. or exp Grenada/	325
102		Guatemala.mp. or exp Guatemala/	4218
103		Guinea.mp. or exp Guinea/	160323
104		Guinea-Bissau.mp. or exp Guinea-Bissau/	1223
105		Guyana.mp. or exp Guyana/	1181
106		Haiti.mp. or exp Haiti/	4001
107		Honduras.mp. or exp Honduras/	1895
108		India.mp. or exp India/	131814
109		Indonesia.mp. or exp Indonesia/	15431
110		Iran.mp. or exp Iran/	36150
111		exp Iraq/ or Iraq.mp.	9595
112		Jamaica.mp. or exp Jamaica/	4338
113		Jordan.mp. or exp Jordan/	6664
114		Kazakhstan.mp. or exp Kazakhstan/ (	3461
115		Kenya.mp. or exp Kenya/	21100
116		Kiribati.mp. or exp Micronesia/	2160
117		exp Korea/ or Korea.mp. or exp "Democratic People's Republic of Korea"/ or exp "Republic of Korea"/	64323
118		Kosovo.mp. or exp Kosovo/	840
119		exp Kyrgyzstan/ or Kyrgyz.mp.	1397
120		Lao.mp. or exp Laos/	3050
121		Lebanon.mp. or exp Lebanon/	5871

122		Lesotho.mp. or exp Lesotho/ ()	720
123		Liberia.mp. or exp Liberia/ ()	1809
124		Libya.mp. or exp Libya/	1526
125		exp "Macedonia (Republic)"/ or Macedonia.mp. ()	1212
126		Madagascar.mp. or exp Madagascar/	5100
127		Malawi.mp. or exp Malawi/	7388
128		Malaysia.mp. or exp Malaysia/	20092
129		Maldives.mp. or exp Indian Ocean Islands/	12867
130		Mali.mp. or exp Mali/	3870
131		Marshall Islands.mp. or exp Micronesia/	2167
132		Mauritania.mp. or exp Mauritania/	699
133		Mauritius.mp. or exp Mauritius/	985
134		exp Mexico/ or Mexico.mp.	57909
135		Micronesia.mp. or exp Micronesia/	2419
136		Moldova.mp. or exp Moldova/	1012
137		Mongolia.mp. or exp Mongolia/	4370
138		Montenegro.mp. or exp Montenegro/	799
139		Morocco.mp. or exp Morocco/	7636
140		Mozambique.mp. or exp Mozambique/	3784
141		Myanmar.mp. or exp Myanmar/	4020
142		Namibia.mp. or exp Namibia/	1713
143		Nauru.mp. or exp Micronesia/	2141
144		Nepal.mp. or exp Nepal/	11131
145		Nicaragua.mp. or exp Nicaragua/	2083
146		exp Niger/ or Niger.mp.	12614
147		exp Niger/ or Niger.mp.	12614
148		Nigeria.mp. or exp Nigeria/	34325
149		Pakistan.mp. or exp Pakistan/	23756
150		Papua New Guinea.mp. or exp Papua New Guinea/	5174
151		Paraguay.mp. or exp Paraguay/	1603
152		Peru.mp. or exp Peru/	12821
153		Philippines.mp. or exp Philippines/	11581
154		Romania.mp. or exp Romania/	12371
155		exp Russia/ or Russia.mp.	65165
156		Rwanda.mp. or exp Rwanda/	3437
157		exp Samoa/ or Samoa.mp. or exp "Independent State of Samoa"/	1107
158		Timor.mp.	662
159		Senegal.mp. or exp Senegal/	7527
160		Serbia.mp. or exp Serbia/ ()	5193
161		Sierra Leone.mp. or exp Sierra Leone/ ()	2347
162		Solomon Islands.mp. or exp Melanesia/ ()	6994
163		Somalia.mp. or exp Somalia/	2259

164		South Africa.mp. or exp South Africa/	52109
165		exp Sudan/ or exp South Sudan/ or Sudan.mp.	8651
166		Sri Lanka.mp. or exp Sri Lanka/	8063
167		Saint Lucia.mp. or exp Saint Lucia/	121
168		(Vincent and the Grenadines).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	8651
169		exp Sudan/ or Sudan.mp.	1168
170		Suriname.mp. or exp Suriname/	921
171		Swaziland.mp. or exp Swaziland/	2927
172		Syria.mp. or exp Syria/	999
173		Tajikistan.mp. or exp Tajikistan/	14642
174		Tanzania.mp. or exp Tanzania/	35246
175		Thailand.mp. or exp Thailand/	399
176		Timor-Leste.mp. or exp Timor-Leste/	1678
177		Togo.mp. or exp Togo/	451
178		Tonga.mp. or exp Tonga/	90
179		Tunisia.mp. or Tunisia/	10240
180		exp Turkey/ or Turkey.mp. ()	52290
181		Turkmenistan.mp. or exp Turkmenistan/ ()	747
182		Tuvalu.mp. ()	65
183		Uganda.mp. or exp Uganda/	16034
184		Ukraine.mp. or exp Ukraine/ ()	17586
185		Uzbekistan.mp. or exp Uzbekistan/ ()	2255
186		Vanuatu.mp. or exp Vanuatu/ ()	672
187		Venezuela.mp. or exp Venezuela/	6794
188		exp Vietnam/ or Vietnam.mp.	17976
189		(West Bank and Gaza).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] ()	205
190		Yemen.mp. or exp Yemen/	2008
191		Zambia.mp. or exp Zambia/	6101
192		Zimbabwe.mp. or exp Zimbabwe/	7411
193		43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54	138004

194		55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176 or 177 or 178 or 179 or 180 or 181 or 182 or 183 or 184 or 185 or 186 or 187 or 188 or 189 or 190 or 191 or 192	1530131
195		193 or 194	1590932
196		18 and 32 and 41 and 195	425

Final search output: 425

Search Summary-2

Name of the database: EMBASE (via Ovid)
Date of search: 08 October 2021
Timeline: November 2008 to October 2021
Search Language: English

Line #	Theme	Search Language	Output #
1.	Hypoxaemia	hypoxemia.mp. or exp hypoxemia	185053
2.		hypoxaemia.mp. or exp hypoxemia	179756
3.		anoxia.mp. or exp anoxia	18565
4.		hypoxia.mp. or exp hypoxia	220645
5.		exp pulse oximetry/ or exp oximetry/ or oximetry.mp.	32644
6.		oximeter.mp. or exp pulse oximeter/ or exp oximeter	9570
7.		exp pulse oximeter/ or oximetre.mp.	4696
8.		oxymetry.mp. or exp oximetry	29785
9.		oxymeter.mp. or exp oximeter	7032
10.		oxymetre.mp.	10
11.		blood oxygen saturation.mp. or exp blood oxygen tension/ or exp oxygen blood level	13047
12.		arterial oxygen saturation.mp. or exp arterial oxygen saturation/ or exp arterial oxygen tension	23200
13.		exp arterial oxygen tension/ or exp arterial gas/ or exp blood gas analysis/ or exp blood gas/ or blood gas monitoring.mp	96898
14.		blood gas analysis.mp. or exp blood gas analysis	26011
15.		exp arterial gas/ or exp blood gas analysis/ or analysis blood gas.mp. or exp blood gas	96821
16.		exp arterial oxygen saturation/ or exp oxygen saturation/ or exp pulse oximetry/ or SpO2.mp. or exp oximetry	98190
17.		exp arterial oxygen saturation/ or exp oxygen saturation/ or exp pulse oximetry/ or SPO2.mp. or exp oximetry	98190
18.		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	419024
19.	Pneumonia	exp pneumonia/ or exp bacterial pneumonia/ or pneumonia.mp. or exp virus pneumonia	378952
20.		exp pneumonia/ or severe pneumonia.mp. or exp bacterial pneumonia	335707
21.		severe disease.mp.	32437
22.		very severe disease.mp.	386
23.		bronchiolitis.mp. or exp bronchiolitis/ or exp viral bronchiolitis/ or exp bronchiolitis obliterans organizing pneumonia	26335
24.		acute respiratory infection.mp. or exp respiratory tract infection	422221
25.		exp pneumonia/ or exp respiratory tract infection/ or ARI.mp.	623374
26.		acute respiratory infections.mp. or exp respiratory tract infection	422453
27.		acute respiratory tract infection.mp. or exp respiratory tract infection	421869
28.		exp respiratory tract infection/ or ARTI.mp	422904

29.		acute respiratory tract infections.mp. or exp respiratory tract infection	421932
30.		respiratory tract disease/ or exp acute respiratory tract disease/ or exp respiratory tract infection/ or exp upper respiratory tract congestion/ or respiratory illness.mp.	478690
31.		respiratory tract disease/ or exp acute respiratory tract disease/ or exp respiratory tract infection/ or exp upper respiratory tract congestion/ or respiratory illnesses.mp.	477203
32.		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	757123
33.	children under 5 years of age	exp hospitalized child/ or child*.mp. or exp child care/ or exp child hospitalization/ or exp child health/ or exp child health care	2749801
34.		exp hospitalized child/ or child*.mp. or exp child hospitalization/ or exp child health/ or exp child health care	2746933
35.		exp infant care/ or exp hospitalized infant/ or infant*.mp.	868324
36.		exp infant care/ or exp hospitalized infant/ or infant*.mp.	868324
37.		Pediatric.mp. or exp pediatrics	575529
38.		Pediatrics.mp. or exp pediatrics	154873
39.		Paediatric.mp. or exp pediatrics	208410
40.		Paediatrics.mp. or exp pediatrics	118440
41.		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40	3203997
42.	Low- and Middle-Income Country	exp developing country/ or developing countr*.mp.	140390
43.		low-and middle income countr*.mp.	22831
44.		exp middle income country/ or LMIC*.mp. or exp developing country	109400
45.		exp middle income country/ or exp low income country/ or low income countr*.mp. or exp developing country	114651
46.		low income country/ or exp middle income country/ or exp developing country/ or middle income countr*.mp.	124293
47.		exp developing country/ or exp low income country/ or lower middle income countr*.mp.	102519
48.		upper middle income countr*.mp.	661
49.		Afghanistan.mp. or exp Afghanistan	9229
50.		Albania.mp. or exp Albania	2326
51.		American Samoa.mp. or exp American Samoa	470
52.		Angola.mp. or exp Angola	1968
53.		Armenia.mp. or exp Armenia	2288
54.		Azerbaijan.mp. or exp Azerbaijan	2495
55.		Bangladesh.mp. or exp Bangladesh	22201
56.		Belarus.mp. or exp Belarus	3346
57.		Belize.mp. or exp Belize	1098
58.		Benin.mp. or exp Benin	5566
59.		Bhutan.mp. or exp Bhutan	1185
60.		Bolivia.mp. or exp Bolivia	4793
61.		(Bosnia and Herzegovina).mp. [mp=title, abstract, heading word, drug trade name, original title, device	3562

		manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	
62.		Botswana.mp. or exp Botswana	3454
63.		exp Brazil/ or Brazil.mp.	156620
64.		Bulgaria.mp. or exp Bulgaria	9681
65.		Burkina Faso.mp. or exp Burkina Faso	5913
66.		Burundi.mp. or exp Burundi	1173
67.		Cabo Verde.mp. or exp Cape Verde	479
68.		Cambodia.mp. or exp Cambodia	6483
69.		Cameroon.mp. or exp Cameroon	9641
70.		Central African Republic.mp. or exp Central African Republic	1349
71.		Chad.mp. or exp Chad	1734
72.		China.mp. or exp China	405192
73.		Colombia.mp. or exp Colombia	25591
74.		Comoros.mp. or exp Comoros	559
75.		exp Democratic Republic Congo/ or exp Congo/ or Congo.mp.	20650
76.		Costa Rica.mp. or exp Costa Rica	6278
77.		Ivory Coast.mp. or exp Cote d'Ivoire	3959
78.		Cuba.mp. or Cuba	8837
79.		Djibouti.mp. or exp Djibouti)	553
80.		Djibouti.mp. or exp Djibouti	553
81.		exp "Dominican (Dominica)"/ or Dominica.mp. or exp Dominica	764
82.		Dominican Republic.mp. or exp Dominican Republic	3271
83.		Ecuador.mp. or exp Ecuador	7640
84.		exp Egypt/ or Egypt.mp	30517
85.		exp Egypt/ or Egypt.mp	30517
86.		El Salvador.mp. or exp El Salvador	2423
87.		Equatorial Guinea.mp. or exp Equatorial Guinea	705
88.		Eritrea.mp. or exp Eritrea	840
89.		Ethiopia.mp. or exp Ethiopia	23227
90.		Fiji.mp. or exp Fiji	2666
91.		Gabon.mp. or exp Gabon	2465
92.		Gambia.mp. or exp Gambia	3471
93.		Georgia.mp. or exp "Georgia (republic)"/ or exp "South Georgia and the South Sandwich Islands"	12977
94.		Ghana.mp. or exp Ghana)	15280
95.		Grenada.mp. or exp Grenada)	458
96.		Guatemala.mp. or exp Guatemala	5258
97.		exp Guinea-Bissau/ or Guinea.mp. or exp Guinea	112538
98.		Guinea-Bissau.mp. or exp Guinea-Bissau	1377
99.		Guyana.mp. or exp Guyana	1447
100.		Haiti.mp. or exp Haiti	5084
101.		Honduras.mp. or exp Honduras	2574
102.		exp India/ or India.mp.	231518
103.		exp India/ or India.mp.	231518
104.		exp India/ or India.mp.	231518
105.		Indonesia.mp. or exp Indonesia	28042
106.		Iran.mp. or exp Iran	76031
107.		Iraq.mp. or exp Iraq	15085

108.		Jamaica.mp. or exp Jamaica	4562
109.		Jordan.mp. or exp Jordan	11118
110.		Kazakhstan.mp. or exp Kazakhstan	4775
111.		Kenya.mp. or exp Kenya	26424
112.		Kiribati.mp. or exp Kiribati	250
113.		exp North Korea/ or Korea.mp. or exp Korea/ or exp South Korea	103268
114.		Kosovo.mp. or exp Kosovo	1431
115.		Kyrgyz Republic.mp. or exp Kyrgyzstan	1302
116.		Laos/ or Lao PDR.mp.	2756
117.		Lebanon.mp. or exp Lebanon	7757
118.		Lesotho.mp. or exp Lesotho	1009
119.		Liberia.mp. or exp Liberia	2270
120.		Libya.mp. or exp Libyan Arab Jamahiriya	2177
121.		exp "Macedonia (republic)"/ or Macedonia.mp.	2357
122.		Madagascar.mp. or exp Madagascar	6097
123.		Malawi.mp. or exp Malawi	9928
124.		Malaysia.mp. or exp Malaysia	31159
125.		Maldives.mp. or exp Maldives	551
126.		Mali.mp. or exp Mali	5296
127.		exp Marshall Islands/ or Marshall Islands.mp.	372
128.		Mauritania.mp. or exp Mauritania	902
129.		Mauritius.mp. or exp Mauritius	1345
130.		exp Mexico/ or exp Mexico City/ or Mexico.mp.	69945
131.		Micronesia.mp. or exp "Federated States of Micronesia"	1261
132.		Micronesia.mp. or exp "Federated States of Micronesia"	1261
133.		Moldova.mp. or exp Moldova)	1441
134.		exp Mongolia/ or Mongolia.mp.	6282
135.		Montenegro.mp. or exp "Montenegro (republic)"	1461
136.		Morocco.mp. or exp Morocco	10176
137.		Mozambique.mp. or exp Mozambique	5141
138.		Myanmar.mp. or exp Myanmar	5561
139.		Namibia.mp. or exp Namibia	2342
140.		Nauru.mp. or exp Nauru	191
141.		Nepal.mp. or exp Nepal	15738
142.		Nicaragua.mp. or exp Nicaragua	2880
143.		exp Niger/ or Niger.mp.	22149
144.		Nigeria.mp. or exp Nigeria	46805
145.		Pakistan.mp. or exp Pakistan)	38546
146.		Papua New Guinea.mp. or exp Papua New Guinea	6455
147.		Paraguay.mp. or exp Paraguay	2289
148.		Peru.mp. or exp Peru	17534
149.		Philippines.mp. or exp Philippines	14269
150.		Romania.mp. or exp Romania	15655
151.		Russian Federation.mp. or exp Russian Federation	58634
152.		Rwanda.mp. or exp Rwanda	4780
153.		exp Samoa/ or Samoa.mp.	1258
154.		(Sao Tome and Principe).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	223
155.		exp Senegalia senegal/ or exp Senegal/ or Senegal.mp.	8356

156.		Serbia.mp. or exp Serbia	8866
157.		Sierra Leone.mp. or exp Sierra Leone	3277
158.		Solomon Islands.mp. or exp Solomon Islands	998
159.		Somalia.mp. or exp Somalia	2583
160.		South Africa.mp. or exp South Africa	63344
161.		South Sudan.mp. or exp Sudan/ or exp South Sudan/	6815
162.		Sri Lanka.mp. or exp Sri Lanka	10832
163.		Saint Lucia.mp. or exp Saint Lucia	154
164.		(Saint Vincent and the Grenadines).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	90
165.		exp Sudan/ or Sudan.mp. or exp South Sudan	10875
166.		Suriname.mp. or exp Suriname	1225
167.		Swaziland.mp. or exp Swaziland	1565
168.		Syrian Arab Republic.mp. or exp Syrian Arab Republic/	2965
169.		Tajikistan.mp. or exp Tajikistan	1116
170.		Tanzania.mp. or exp Tanzania	18529
171.		Thailand.mp. or exp Thailand	45080
172.		Timor-Leste.mp. or exp Timor-Leste	760
173.		Togo.mp. or exp Togo	2096
174.		exp Tonga/ or Tonga.mp.	598
175.		Tunisia.mp. or exp Tunisia	12789
176.		Turkey.mp.	75844
177.		Turkmenistan.mp. or exp Turkmenistan	599
178.		Tuvalu.mp. or exp Tuvalu	102
179.		Uganda.mp. or exp Uganda	21051
180.		Ukraine.mp. or exp Ukraine	15286
181.		Uzbekistan.mp. or exp Uzbekistan	2386
182.		Vanuatu.mp. or exp Vanuatu	822
183.		Venezuela.mp. or exp Venezuela	7906
184.		Vietnam.mp. or exp Viet Nam	22219
185.		exp Palestine/ or Gaza.mp. or exp Palestinian	3329
186.		Yemen.mp. or exp Yemen	2713
187.		Zambia.mp. or exp Zambia	7731
188.		Zimbabwe.mp. or exp Zimbabwe	8083
189.		42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176 or 177 or 178 or 179 or 180 or 181 or 182 or 183 or 184 or 185	2085410

		or 186 or 187 or 188	
190.		18 and 32 and 41 and 189	807

Final search output: 807

Search Summary-3

Name of the database: GLOBAL HEALTH (via Ovid)
Date of search: 05 February 2019
Timeline: November 2008 to February 2019
Search Language: English

Line #	Theme	Search Language	Output #
1.	Hypoxaemia	hypoxemia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	505
2.		hypoxaemia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	217
3.		anoxia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	393
4.		hypoxia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4325
5.		oximetry.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	350
6.		oximeter.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	97
7.		oximetre.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1
8.		oxymetry.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	12
9.		oxymeter.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6
10.		oxymetre.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
11.		blood oxygen saturation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	83
12.		arterial oxygen saturation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	111
13.		blood gas monitoring.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6
14.		blood gas analysis.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	291
15.		analysis blood gas.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
16.		SpO2.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	395
17.		SPO2.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	395
18.		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	6094
19.	Pneumonia	pneumonia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	23912
20.		severe pneumonia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1056
21.		severe disease.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3526
22.		very severe disease.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	46

23.		bronchiolitis.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1597
24.		acute respiratory infection.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	846
25.		ARI.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	846
26.		acute respiratory infections.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	985
27.		acute respiratory tract infections.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	368
28.		ARTI.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	149
29.		acute respiratory tract infections.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	368
30.		respiratory illness*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2031
31.		respiratory illnesses*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	577
32.		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	31692
33.	children under 5 years of age	child.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	55244
34.		children.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	209960
35.		infant.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	34055
36.		infants.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	65307
37.		pediatric.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	22238
38.		pediatrics.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4805
39.		paediatric.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	8904
40.		paediatrics.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3341
41.		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40	263930
42.	Low- and Middle-Income Country	Afghanistan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1515
43.		Albania.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	735
44.		Albania.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	735
45.		American Samoa.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	112
46.		Angola.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	672
47.		Armenia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	326
48.		Azerbaijan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	546

49.		Bangladesh.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	7717
50.		Belarus.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	568
51.		Belize.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	181
52.		Benin.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2179
53.		Bhutan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	417
54.		Bolivia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1276
55.		(Bosnia and Herzegovina).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	578
56.		Botswana.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1097
57.		Brazil.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	57836
58.		Bulgaria.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3181
59.		Burkina Faso.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2593
60.		Burundi.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	291
61.		Cabo Verde.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	17
62.		Cambodia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2188
63.		Cameroon.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3674
64.		Central African Republic.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	398
65.		Chad.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	501
66.		China.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	140022
67.		Colombia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6489
68.		Comoros.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	168
69.		(Democratic Republic of Congo or DR Congo or DRC or the Congo).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4453
70.		Congo.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4298
71.		Costa Rica.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1257
72.		Ivory Coast.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1864
73.		Cuba.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2711
74.		Djibouti.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	159

75.		Dominica.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	148
76.		Dominican Republic.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	598
77.		Ecuador.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1523
78.		Egypt.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	8075
79.		El Salvador.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	471
80.		Equatorial Guinea.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	201
81.		Eritrea.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	227
82.		Ethiopia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	7844
83.		Fiji.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	382
84.		Gabon.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	777
85.		Gambia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	948
86.		Georgia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3603
87.		Ghana.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	5846
88.		Grenada.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	134
89.		Guatemala.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1227
90.		(Guinea-Bissau or Guinea Bissau).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	414
91.		Guyana.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	281
92.		Haiti.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1216
93.		Honduras.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	518
94.		India.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	71629
95.		Indonesia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6099
96.		Iran.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	39859
97.		Iraq.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2448
98.		Jamaica.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	819
99.		Jordan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2043
100.		Kazakhstan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	806

101.		Kenya.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	8859
102.		Kiribati.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	70
103.		Korea.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	19978
104.		Kosovo.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	400
105.		Kyrgyz.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	47
106.		Lao.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1180
107.		Lebanon.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1592
108.		Lesotho.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	369
109.		Liberia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	694
110.		Libya.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	575
111.		Macedonia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	849
112.		Madagascar.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1400
113.		Malawi.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3882
114.		Malaysia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	8375
115.		Maldives.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	109
116.		Mali.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1738
117.		Marshall Islands.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	87
118.		Mauritania.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	231
119.		Mauritius.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	327
120.		Mexico.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	13948
121.		Micronesia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	469
122.		Moldova.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	349
123.		Mongolia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1699
124.		Montenegro.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	487
125.		Morocco.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4146
126.		Mozambique.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1877

127.		Myanmar.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2052
128.		Namibia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	601
129.		Nauru.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	44
130.		Nepal.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4514
131.		Nicaragua.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	732
132.		Niger.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	7584
133.		Pakistan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	11064
134.		Papua New Guinea.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1144
135.		Paraguay.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	621
136.		Peru.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4376
137.		Philippines.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2927
138.		Romania.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	5990
139.		Russia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	7296
140.		Rwanda.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1357
141.		Samoa.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	277
142.		(Timor-Liste or Timor Liste or Timor).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	286
143.		Senegal.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2443
144.		Serbia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3061
145.		Sierra Leone.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	999
146.		Solomon Islands.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	263
147.		Somalia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	644
148.		South Africa.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	17163
149.		South Sudan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	386
150.		Sri Lanka.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2841
151.		Saint Lucia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	65
152.		(Vincent and the Grenadines).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	44

153.		Sudan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3106
154.		Suriname.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	279
155.		Swaziland.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	501
156.		Syria.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	820
157.		Tajikistan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	278
158.		Tanzania.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6627
159.		Thailand.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	13856
160.		Timor-Leste.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	173
161.		Togo.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	707
162.		Tonga.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	132
163.		Tunisia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	3836
164.		Turkey.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	25147
165.		Turkmenistan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	90
166.		Tuvalu.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	29
167.		Uganda.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	7227
168.		Ukraine.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1415
169.		Uzbekistan.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	337
170.		Vanuatu.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	211
171.		Venezuela.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2273
172.		Vietnam.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	5464
173.		(West Bank and Gaza).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	101
174.		Yemen.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	916
175.		Zambia.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2634
176.		Zimbabwe.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2171
177.		42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94	569993

		or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176	
178.		developing countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	567746
179.		low-and middle income countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	5367
180.		LMIC*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1389
181.		low income countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2855
182.		middle income countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	6787
183.		lower middle income countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	285
184.		upper middle income countr*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	143
185.		178 or 179 or 180 or 181 or 182 or 183 or 184	570617
186.		177 or 185	623022
187.		18 and 32 and 41 and 186	130

Final search output
130

Search Summary-4

Name of the database: Cochrane (Advanced)
Date of search: 30 September, 2021
Timeline: January 2008 to September 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia	3,210
2		hypoxaemia	3,210
3		anoxia	264
4		hypoxia	7,110
5		oximetry	4,239
6		oximeter	1,611
7		oximetre	10
8		oxymetry	212
9		oxymeter	126
10		oxymetre	1
11		blood oxygen saturation	7,914
12		arterial oxygen saturation	5.098
13		blood gas monitoring	1,513
14		blood gas analysis	5,573
15		analysis blood gas	5,573
16		SpO2	4,599
17		SPO2	4,599
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR (blood oxygen saturation) OR (arterial oxygen saturation) OR (blood gas monitoring) OR (blood gas analysis) OR (analysis blood gas) OR SpO2 OR SPO2	27,530
19	Pneumonia	pneumonia	18,602
20		severe pneumonia	4,571
21		severe disease	49,561
22		very severe disease	8,482
23		bronchiolitis	1,648
24		acute respiratory infection	5,442
25		ARI	6,581
26		acute respiratory infections	4,112
27		acute respiratory tract infection	2,953
28		ARTI	116
29		acute respiratory tract infections	2,394
30		respiratory illness*	6,484
31		respiratory illnesses*	997
32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 pneumonia OR (severe pneumonia) OR (severe disease) OR (very severe disease) OR bronchiolitis OR (acute respiratory infection) OR ari OR (acute respiratory infections) OR (acute respiratory tract infection) OR arti OR (acute respiratory tract	77,649

		infections) OR (respiratory illness*) OR (respiratory illnesses*)	
33	children under 5 years of age	child	176,881
34		children	176,879
35		infant	53,917
36		infants	35,995
37		pediatric	55,900
38		pediatrics	28,695
39		paediatric	55,893
40		paediatrics	28,695
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 Child* OR children* OR infant* OR infants* OR pediatric* OR pediatrics* OR paediatric* OR paediatrics*	226,372
42	low- and middle-income countries	Albania OR Algeria OR Angola OR American Samoa OR Armenia OR Azerbaijan OR Bangladesh OR Benin OR Belarus OR Belize OR Bhutan OR Bolivia OR “Bosnia and Herzegovina” OR Botswana OR Brazil OR Bulgaria OR "Burkina Faso" OR Burundi OR Cambodia OR Cameroon OR "Cape Verde" OR “Central African Republic” OR Chad OR China OR Colombia OR Comoros OR ”Congo, Dem. Rep” OR “Congo, Rep.” OR "Costa Rica" OR "Cote d'Ivoire" OR Cuba OR Djibouti OR Dominica OR “Dominican Republic” OR “Ecuador” OR " Egypt, Arab Rep." OR "El Salvador" OR Eritrea OR Ethiopia OR Ethiopia OR Fiji OR Gabon OR “Gambia, The” OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guyana OR “Guinea-Bissau “ OR Haiti OR Honduras OR India OR Maldives OR Indonesia OR “Iran, Islamic Rep.” OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR “Korea, Dem. People's Rep.” OR Kosovo OR “Kyrgyz Republic” OR “Lao PDR” OR Lebanon OR Lesotho OR Liberia OR Libya OR “Macedonia, FYR” OR Madagascar OR Malaysia OR Malawi OR Mali OR “Marshall Islands” OR Mauritania OR Mauritius OR Mexico OR “Micronesia, Fed. Sts.” OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nauru OR Nicaragua OR Niger OR Nigeria OR Pakistan OR “Papua New Guinea” OR Paraguay OR Peru OR Philippines OR Romania OR “Russian Federation” OR Rwanda OR Samoa OR " São Tomé and Principe" OR Senegal OR Serbia OR " Sierra Leone" OR Somalia OR Grenadines OR “Samoan Islands” OR " South Africa" OR “St. Lucia” OR “St. Vincent and the Grenadines” OR Sudan OR Suriname OR Swaziland OR " Syrian Arab Republic" OR "Sri Lanka" OR Tajikistan OR Tanzania OR Thailand OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR “Timor-Leste” OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela, RB OR Vietnam OR “West Bank and Gaza” OR “Yemen, Rep.” OR Zambia OR Zimbabwe OR (developing countr*) OR (low-and	184,808

		middle income countr*) OR (LMIC*) OR (low income countr*) OR (middle income countr*) OR (lower middle income countr*) OR (upper middle income countr*)	
43		18 AND 32 AND 41 AND 42	153

Final search output: 153

Search Summary 5

Name of the database: Clinicaltrails.gov
Date of search: 30 September, 2021
Timeline: November 2008 to September 2021
Search Language: English

Line #	Theme	hypoxemia	Output #
1	Hypoxaemia	hypoxemia	884
2		hypoxaemia	884
3		anoxia	35
4		hypoxia	2383
5		oximetry	1978
6		oximeter	960
7		oximetre	0
8		oxymetry	1978
9		oxymeter	41
10		oxymetre	2
11		blood oxygen saturation	2514
12		arterial oxygen saturation	4182
13		blood gas monitoring	198
14		blood gas analysis	1433
15		analysis blood gas	1413
16		spo2	1883
17		spo2	1883
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR blood oxygen saturation OR arterial oxygen saturation OR blood gas monitoring OR blood gas analysis OR analysis blood gas OR spo2 OR spo2	9238
19	Pneumonia	pneumonia	10129
20		“severe pneumonia”	1707
21		“severe disease”	40422
22		“very severe disease”	6447
23		bronchiolitis	447
24		acute respiratory infection	2159
25		ari	406
26		acute respiratory infections	2159
27		acute respiratory tract infection	2335
28		arti	63
29		acute respiratory tract infections	2335
30		respiratory illness	1233
31		respiratory illnesses	1233
32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 pneumonia OR "severe pneumonia" OR "severe disease" OR "very severe disease" OR bronchiolitis OR acute respiratory infection OR ari OR acute respiratory infections OR acute respiratory tract infection OR arti OR acute respiratory tract infections OR respiratory illness OR respiratory illnesses	9,179

33	children under 5 years of age	child	85169
34		children	85169
35		infant	14246
36		infants	14246
37		pediatric	15308
38		pediatrics	6618
39		paediatric	6609
40		paediatrics	6618
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 child OR children OR infant OR infants OR pediatric OR pediatrics OR paediatric OR paediatrics	89244
42		developing country OR developing countries OR low-and middle income country OR low-and middle income countries OR LMIC OR LMICs OR low income country OR low income countries OR middle income country OR middle income countries OR lower middle income country OR lower middle income countries OR upper middle income country OR upper middle income countries OR Afghanistan OR Albania OR Albania OR American Samoa OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia and Herzegovina OR Botswana OR Brazil OR Bulgaria OR Burkina Faso OR Burundi OR Cabo Verde OR Cambodia OR Cameroon OR Central African Republic OR Chad OR China OR Colombia OR Comoros OR DRC OR Congo OR Costa Rica OR Ivory Coast OR Cuba OR Djibouti OR Dominica OR Dominican Republic OR Ecuador OR Egypt OR El Salvador OR Guinea OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guinea-Bissau OR Guyana OR Haiti OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Lao OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia, FYR OR Madagascar OR Malawi OR Malaysia OR Maldives OR Mali OR Marshall Islands OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nauru OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Romania OR Russia OR Rwanda OR Samoa OR Timor OR Timor-Liste OR Senegal OR Serbia OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR Sudan OR Sri Lanka OR Saint Lucia OR St. Vincent and the Grenadines OR Sudan OR Suriname OR Swaziland OR Syria OR Tajikistan OR Tanzania OR Thailand OR Timor-Leste OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR Gaza OR Yemen OR Zambia OR Zimbabwe	154,847

43		18 AND 32 AND 41 AND 42 (hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR blood oxygen saturation OR arterial oxygen saturation OR blood gas monitoring OR blood gas analysis OR analysis blood gas OR spo2 OR spo2) AND (pneumonia OR "severe pneumonia" OR "severe disease" OR "very severe disease" OR bronchiolitis OR acute respiratory infection OR ari OR acute respiratory infections OR acute respiratory tract infection OR arti OR acute respiratory tract infections OR respiratory illness OR respiratory illnesses) AND (child OR children OR infant OR infants OR pediatric OR pediatrics OR paediatric OR paediatrics) AND (developing country OR Developing countries OR low-and middle income country OR low-and middle income countries OR LMIC OR LMICs OR low income country OR low income countries OR middle income country OR middle income countries OR lower middle income country OR lower middle income countries OR upper middle income country OR upper middle income countries OR Afghanistan OR Albania OR Albania OR “American Samoa” OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia and Herzegovina OR Botswana OR Brazil OR Bulgaria OR Burkina Faso OR Burundi OR Cabo Verde OR Cambodia OR Cameroon OR Central African Republic OR Chad OR China OR Colombia OR Comoros OR DRC OR Congo OR Costa Rica OR Ivory Coast OR Cuba OR Djibouti OR Dominica OR Dominican Republic OR Ecuador OR Egypt OR El Salvador OR Guinea OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guinea-Bissau OR Guyana OR Haiti OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Lao OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia, FYR OR Madagascar OR Malawi OR Malaysia OR Maldives OR Mali OR Marshall Islands OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nauru OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Romania OR Russia OR Rwanda OR Samoa OR Timor OR Timor-Liste OR Senegal OR Serbia OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR Sudan OR Sri Lanka OR Saint Lucia OR St. Vincent and the Grenadines OR Sudan OR Suriname OR Swaziland OR Syria OR Tajikistan OR Tanzania OR Thailand OR	85

		Timor-Leste OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR Gaza OR Yemen OR Zambia OR Zimbabwe)	

Final search output: 85

Search Summary 6

Name of the database: SCOPUS (Advanced)
Date of search: 29 September, 2021
Timeline: November 2008 to September 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia	77,572
2		hypoxaemia	18,843
3		anoxia	126,145
4		hypoxia	703,759
5		oximetry	58,162
6		oximeter	15,210
7		oximetre	1
8		oxymetry	2,156
9		oxymeter	400
10		oxymetre	93
11		“blood oxygen saturation”	5,699
12		“arterial oxygen saturation”	16,179
13		“blood gas monitoring”	3,389
14		“blood gas analysis”	38,710
15		“analysis blood gas”	23
16		SpO2	9,072
17		SPO2	9,072
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (hypoxemia) OR (hypoxaemia) OR (anoxia) OR (hypoxia) OR (oximetry) OR (oximeter) OR (oximetre) OR (oxymetry) OR (oxymeter) OR (oxymetre) OR ("blood oxygen saturation") OR ("arterial oxygen saturation") OR ("blood gas monitoring") OR ("blood gas analysis") OR ("analysis blood gas") OR (spo2) OR (spo2)	910,266
19	Pneumonia	pneumonia	608,133
20		“severe pneumonia”	15,974
21		“severe disease”	43,407
22		“very severe disease”	302
23		bronchiolitis	51,454
24		“acute respiratory infection”	28,443
25		ARI	176,104
26		“acute respiratory infections”	28,443
27		“acute respiratory tract infection”	13,820
28		ARTI	30,077
29		“acute respiratory tract infections”	13,820
30		“respiratory illness*”	38,309
31		“respiratory illnesses*”	9,267
32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (pneumonia) OR ("severe pneumonia") OR ("severe disease") OR ("very severe	910,802

		disease") OR (bronchiolitis) OR ("acute respiratory infection") OR (ari) OR ("acute respiratory infections") OR ("acute respiratory infections") OR ("acute respiratory tract infection") OR (arti) OR ("acute respiratory tract infections") OR ("respiratory illness*") OR ("respiratory illnesses*")	
33	children under 5 years of age	Child*	7,610,183
34		Children*	5,027,116
35		Infant*	2,626,853
36		Infants*	1,074,853
37		Pediatric*	3,941,378
38		Pediatrics*	2,339,629
39		Paediatric*	985,834
40		Paediatrics*	437,141
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 (child*) OR (children*) OR (infant*) OR (infants*) OR (pediatric*) OR (pediatrics*) OR (paediatric*) OR (paediatrics*)	9,337,152
42	low- and middle-income countries	Albania OR Algeria OR Angola OR American Samoa OR Armenia OR Azerbaijan OR Bangladesh OR Benin OR Belarus OR Belize OR Bhutan OR Bolivia OR “Bosnia and Herzegovina” OR Botswana OR Brazil OR Bulgaria OR "Burkina Faso" OR Burundi OR Cambodia OR Cameroon OR "Cape Verde" OR “Central African Republic” OR Chad OR China OR Colombia OR Comoros OR ”Congo, Dem. Rep” OR “Congo, Rep.” OR "Costa Rica" OR "Cote d'Ivoire" OR Cuba OR Djibouti OR Dominica OR “Dominican Republic” OR “Ecuador” OR " Egypt, Arab Rep." OR "El Salvador" OR Eritrea OR Ethiopia OR Ethiopia OR Fiji OR Gabon OR “Gambia, The” OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guyana OR “Guinea-Bissau “ OR Haiti OR Honduras OR India OR Maldives OR Indonesia OR “Iran, Islamic Rep.” OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR “Korea, Dem. People's Rep.” OR Kosovo OR “Kyrgyz Republic” OR “Lao PDR” OR Lebanon OR Lesotho OR Liberia OR Libya OR “Macedonia, FYR” OR Madagascar OR Malaysia OR Malawi OR Mali OR “Marshall Islands” OR Mauritania OR Mauritius OR Mexico OR “Micronesia, Fed. Sts.” OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nauru OR Nicaragua OR Niger OR Nigeria OR Pakistan OR “Papua New Guinea” OR Paraguay OR Peru OR Philippines OR Romania OR “Russian Federation” OR Rwanda OR Samoa OR " São Tomé and Principe" OR Senegal OR Serbia OR " Sierra Leone" OR Somalia OR Grenadines OR “Samoan Islands”	758,189

		OR " South Africa" OR “St. Lucia” OR “St. Vincent and the Grenadines” OR Sudan OR Suriname OR Swaziland OR " Syrian Arab Republic" OR "Sri Lanka" OR Tajikistan OR Tanzania OR Thailand OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR “Timor-Leste” OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela, RB OR Vietnam OR “West Bank and Gaza” OR “Yemen, Rep.” OR Zambia OR Zimbabwe OR (developing countr*) OR (“low-and middle income countr*”) OR (LMIC*) OR (“low income countr*”) OR (“middle income countr*”) OR (“lower middle income countr*”) OR (“upper middle income countr*”)	
43		18 AND 32 AND 41 AND 42 (with filter NURSING, MEDICINE-Limit to HUMAN, HUMANS- Limit to JOURNAL- Limit to)	665

Final search output : 665

Search Summary 7

Name of the database: CINHAL
Date of search: 30 September, 2021
Timeline: November 2008 to September 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia	3,895
2		hypoxaemia	678
3		anoxia	7,135
4		hypoxia	14,894
5		oximetry	6,768
6		oximeter	3,134
7		oximetre	0
8		oxymetry	47
9		oxymeter	19
10		oxymetre	4
11		blood oxygen saturation	1,351
12		arterial oxygen saturation	990
13		blood gas monitoring	645
14		blood gas analysis	5,354
15		analysis blood gas	1,293
16		SpO2	1,718
17		SPO2	1,718
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR (blood oxygen saturation) OR (arterial oxygen saturation) OR (blood gas monitoring) OR (blood gas analysis) OR (analysis blood gas) OR SpO2 OR SPO2	33,731
19	Pneumonia	pneumonia	46,202
20		severe pneumonia	786
21		severe disease	3,915
22		very severe disease	45
23		bronchiolitis	3,219
24		acute respiratory infection	1,114
25		ARI	4,183
26		acute respiratory infections	1,114
27		acute respiratory tract infection	386
28		ARTI	6,416
29		acute respiratory tract infections	386
30		respiratory illness*	4,802
31		respiratory illnesses*	627
32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 pneumonia OR (severe pneumonia) OR (severe disease) OR (very severe disease) OR bronchiolitis OR (acute respiratory infection) OR ari OR (acute respiratory infections) OR (acute respiratory tract infection) OR arti OR (acute respiratory tract infections) OR (respiratory illness*) OR (respiratory illnesses*)	67,715

33	children under 5 years of age	Child*	848,219
34		Children*	401,406
35		Infant*	314,473
36		Infants*	76,280
37		Pediatric*	182,754
38		Pediatrics*	33,177
39		Paediatric*	27,335
40		Paediatrics*	12,813
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 Child* OR children* OR infant* OR infants* OR pediatric* OR pediatrics* OR paediatric* OR paediatrics*	998,872
42	low- and middle-income countries	Albania OR Algeria OR Angola OR American Samoa OR Armenia OR Azerbaijan OR Bangladesh OR Benin OR Belarus OR Belize OR Bhutan OR Bolivia OR “Bosnia and Herzegovina” OR Botswana OR Brazil OR Bulgaria OR "Burkina Faso" OR Burundi OR Cambodia OR Cameroon OR "Cape Verde" OR “Central African Republic” OR Chad OR China OR Colombia OR Comoros OR ”Congo, Dem. Rep” OR “Congo, Rep.” OR "Costa Rica" OR "Cote d'Ivoire" OR Cuba OR Djibouti OR Dominica OR “Dominican Republic” OR “Ecuador” OR " Egypt, Arab Rep." OR "El Salvador" OR Eritrea OR Ethiopia OR Ethiopia OR Fiji OR Gabon OR “Gambia, The” OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guyana OR “Guinea-Bissau “ OR Haiti OR Honduras OR India OR Maldives OR Indonesia OR “Iran, Islamic Rep.” OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR “Korea, Dem. People's Rep.” OR Kosovo OR “Kyrgyz Republic” OR “Lao PDR” OR Lebanon OR Lesotho OR Liberia OR Libya OR “Macedonia, FYR” OR Madagascar OR Malaysia OR Malawi OR Mali OR “Marshall Islands” OR Mauritania OR Mauritius OR Mexico OR “Micronesia, Fed. Sts.” OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nauru OR Nicaragua OR Niger OR Nigeria OR Pakistan OR “Papua New Guinea” OR Paraguay OR Peru OR Philippines OR Romania OR “Russian Federation” OR Rwanda OR Samoa OR " São Tomé and Principe" OR Senegal OR Serbia OR " Sierra Leone" OR Somalia OR Grenadines OR “Samoan Islands” OR " South Africa" OR “St. Lucia” OR “St. Vincent and the Grenadines” OR Sudan OR Suriname OR Swaziland OR " Syrian Arab Republic" OR "Sri Lanka" OR Tajikistan OR Tanzania OR Thailand OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR “Timor-Leste” OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela, RB OR Vietnam OR “West Bank and Gaza” OR “Yemen, Rep.” OR Zambia OR Zimbabwe OR (developing countr*) OR (low-and middle income countr*) OR (LMIC*) OR (low income	438,431

		countr*) OR (middle income countr*) OR (lower middle income countr*) OR (upper middle income countr*)	
43		18 AND 32 AND 41 AND 42	66

Final search output : 66

Search Summary 8

Name of the database: PubMed (Advanced)
Date of search: 29 September, 2021
Timeline: November 2008 to September 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia	181,951
2		hypoxaemia	181,951
3		anoxia	174,123
4		hypoxia	170,128
5		oximetry	20,991
6		oximeter	4,324
7		oximetre	0
8		oxymetry	21,276
9		oxymeter	157
10		oxymetre	11
11		blood oxygen saturation	37,918
12		arterial oxygen saturation	17,275
13		blood gas monitoring	13,164
14		blood gas analysis	60,188
15		analysis blood gas	60,188
16		SpO2	7,221
17		SPO2	7,221
18		Search ((((((((((((((hypoxemia) OR hypoxaemia) OR anoxia) OR hypoxia) OR oximetry) OR oximeter) OR oximetre) OR oxymetry) OR oxymeter) OR oxymetre) OR blood oxygen saturation) OR arterial oxygen saturation) OR blood gas monitoring) OR blood gas analysis) OR analysis blood gas) OR SpO2) OR SPO2	263,664
19	Pneumonia	pneumonia	335,840
20		severe pneumonia	64,569
21		severe disease	763,868
22		very severe disease	763,868
23		bronchiolitis	14,288
24		acute respiratory infection	86,480
25		ARI	7,231
26		acute respiratory infections	80,388
27		acute respiratory tract infection	73,381
28		ARTI	2,155
29		acute respiratory tract infections	71,954
30		respiratory illness*	47,137
31		respiratory illnesses*	6,388
32		Search ((((((((((pneumonia) OR severe pneumonia) OR severe disease) OR very severe disease) OR bronchiolitis) OR acute respiratory infection) OR ARI) OR acute respiratory infections) OR acute respiratory tract infection) OR ARTI) OR acute respiratory tract infections) OR respiratory illness*) OR respiratory illnesses*	1,122,148
33	children under 5 years of age	Child*	2,960,040
34		Children*	1,515,039
35		Infant*	1,351,126

36		Infants*	282,393
37		Pediatric*	988,382
38		Pediatrics*	524,507
39		Paediatric*	187,928
40		Paediatrics*	79,099
41		Search (((((((Child*) OR Children*) OR Infant*) OR Infants*) OR Pediatric*) OR Pediatrics*) OR Paediatric*) OR Paediatrics*	3,722,177
42	low- and middle-income countries	Search (Albania OR Algeria OR Angola OR American Samoa OR Armenia OR Azerbaijan OR Bangladesh OR Benin OR Belarus OR Belize OR Bhutan OR Bolivia OR “Bosnia and Herzegovina” OR Botswana OR Brazil OR Bulgaria OR "Burkina Faso" OR Burundi OR Cambodia OR Cameroon OR "Cape Verde" OR “Central African Republic” OR Chad OR China OR Colombia OR Comoros OR ”Congo, Dem. Rep” OR “Congo, Rep.” OR "Costa Rica" OR "Cote d'Ivoire" OR Cuba OR Djibouti OR Dominica OR “Dominican Republic” OR “Ecuador” OR " Egypt, Arab Rep." OR "El Salvador" OR Eritrea OR Ethiopia OR Ethiopia OR Fiji OR Gabon OR “Gambia, The” OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guyana OR “Guinea-Bissau “ OR Haiti OR Honduras OR India OR Maldives OR Indonesia OR “Iran, Islamic Rep.” OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR “Korea, Dem. People's Rep.” OR Kosovo OR “Kyrgyz Republic” OR “Lao PDR” OR Lebanon OR Lesotho OR Liberia OR Libya OR “Macedonia, FYR” OR Madagascar OR Malaysia OR Malawi OR Mali OR “Marshall Islands” OR Mauritania OR Mauritius OR Mexico OR “Micronesia, Fed. Sts.” OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nauru OR Nicaragua OR Niger OR Nigeria OR Pakistan OR “Papua New Guinea” OR Paraguay OR Peru OR Philippines OR Romania OR “Russian Federation” OR Rwanda OR Samoa OR " São Tomé and Principe" OR Senegal OR Serbia OR " Sierra Leone" OR Somalia OR Grenadines OR “Samoan Islands” OR " South Africa" OR “St. Lucia” OR “St. Vincent and the Grenadines” OR Sudan OR Suriname OR Swaziland OR " Syrian Arab Republic" OR "Sri Lanka" OR Tajikistan OR Tanzania OR Thailand OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR “Timor-Leste” OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela, RB OR Vietnam OR “West Bank and Gaza” OR “Yemen, Rep.” OR Zambia OR Zimbabwe OR (developing countr*) OR (low-and middle income countr*) OR (LMIC*) OR (low income countr*) OR (middle income countr*) OR (lower middle income countr*) OR (upper middle income countr*))	5,178,516
43		18 AND 32 AND 41 AND 42 ((((((((((((((((((((hypoxemia) OR hypoxaemia) OR anoxia) OR hypoxia) OR oximetry) OR oximeter) OR oximetry) OR oxymetry) OR oximeter) OR oxymetry) OR blood oxygen	907

		saturation) OR arterial oxygen saturation) OR blood gas monitoring) OR blood gas analysis) OR analysis blood gas) OR SpO2) OR SPO2)) AND ((((((((((((pneumonia) OR severe pneumonia) OR severe disease) OR very severe disease) OR bronchiolitis) OR acute respiratory infection) OR ARI) OR acute respiratory infections) OR acute respiratory tract infection) OR arti) OR acute respiratory tract infections) OR respiratory illness*) OR respiratory illnesses*)) AND (((((((Child*) OR Children*) OR Infant*) OR Infants*) OR Pediatric*) OR Pediatrics*) OR Paediatric*) OR Paediatrics*)) AND ((albania OR algeria OR angola OR american samoa OR armenia OR azerbaijan OR bangladesh OR benin OR belarus OR belize OR bhutan OR bolivia OR "Bosnia and Herzegovina" OR botswana OR brazil OR bulgaria OR "Burkina Faso" OR burundi OR cambodia OR cameroon OR "Cape Verde" OR "Central African Republic" OR chad OR china OR colombia OR comoros OR "Congo, Dem. Rep" OR "Congo, Rep." OR "Costa Rica" OR "Cote d'Ivoire" OR cuba OR djibouti OR dominica OR "Dominican Republic" OR "Ecuador" OR "Egypt, Arab Rep." OR "El Salvador" OR eritrea OR ethiopia OR ethiopia OR fiji OR gabon OR "Gambia, The" OR georgia OR ghana OR grenada OR guatemala OR guinea OR guyana OR "Guinea-Bissau " OR haiti OR honduras OR india OR maldives OR indonesia OR "Iran, Islamic Rep." OR iraq OR jamaica OR jordan OR kazakhstan OR kenya OR kiribati OR "Korea, Dem. People's Rep." OR kosovo OR "Kyrgyz Republic" OR "Lao PDR" OR lebanon OR lesotho OR liberia OR libya OR "Macedonia, FYR" OR madagascar OR malaysia OR malawi OR mali OR "Marshall Islands" OR mauritania OR mauritius OR mexico OR "Micronesia, Fed. Sts." OR moldova OR mongolia OR montenegro OR morocco OR mozambique OR myanmar OR namibia OR nepal OR nauru OR nicaragua OR niger OR nigeria OR pakistan OR "Papua New Guinea" OR paraguay OR peru OR philippines OR romania OR "Russian Federation" OR rwanda OR samoa OR "Sao Tome and Principe" OR senegal OR serbia OR "Sierra Leone" OR somalia OR grenadines OR "Samoan Islands" OR "South Africa" OR "St. Lucia" OR "St. Vincent and the Grenadines" OR sudan OR suriname OR swaziland OR "Syrian Arab Republic" OR "Sri Lanka" OR tajikistan OR tanzania OR thailand OR togo OR tonga OR tunisia OR turkey OR turkmenistan OR tuvalu OR "Timor-Leste" OR uganda OR ukraine OR uzbekistan OR vanuatu OR venezuela, rb OR vietnam OR "West Bank and Gaza" OR "Yemen, Rep." OR zambia OR zimbabwe OR (developing countr*) OR (low- and middle income countr*) OR (LMIC*) OR (low income countr*) OR (middle income countr*) OR (lower middle income countr*) OR (upper middle income countr*)))	

Final search output: 907

Search Summary 9

Name of the database:

- Global Index Medicus (WHO)
- African Index Medicus (AFRO)
- literature of Latin America and the Caribbean (AMRO/Pan American Health Organizaton)
- The Index Medicus for the Estern Mediterranean Region (IMEMR/ EMRO)
- The Index Medicus for South- East Asia Region (IMSEAR/ SEARO)
- Western Pacific Region Index Medicus (WPRIM/ WPRO)

Date of search: 30 September, 2021

Timeline: November 2008 to September 2021

Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	(tw:(hypoxemia)) AND (instance:"ghl")	3.987
2		tw:(hypoxaemia) AND (instance:"ghl")	101
3		tw:(anoxia) AND (instance:"ghl")	4,848
4		tw:(hypoxia) AND (instance:"ghl")	9.655
5		tw:(oximetry) AND (instance:"ghl")	1.034
6		tw:(oximeter) AND (instance:"ghl")	297
7		oximetre	0
8		tw:(oxymetry) AND (instance:"ghl")	83
9		tw:(oxymeter) AND (instance:"ghl")	37
10		oxymetre	0
11		tw:(blood oxygen saturation) AND (instance:"ghl")	2.152
12		tw:(arterial oxygen saturation) AND (instance:"ghl")	1.616
13		tw:(blood gas monitoring) AND (instance:"ghl")	620
14		tw:(blood gas analysis) AND (instance:"ghl")	3.715
15		tw:(analysis blood gas) AND (instance:"ghl")	3.715
16		tw:(spo2) AND (instance:"ghl")	1.095
17		tw:(spo2) AND (instance:"ghl")	1.095
18		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 tw:(hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR (blood oxygen saturation) OR (arterial oxygen saturation) OR (blood gas monitoring) OR (blood gas analysis) OR (analysis blood gas) OR spo2 OR spo2) AND (instance:"ghl")	18,269
19	Pneumonia	tw:(pneumonia) AND (instance:"ghl")	22.597
20		tw:(severe pneumonia) AND (instance:"ghl")	4.682
21		tw:(severe disease) AND (instance:"ghl")	41.648
22		tw:(very severe disease) AND (instance:"ghl")	2.533
23		tw:(bronchiolitis) AND (instance:"ghl")	1.540
24		tw:(acute respiratory infection) AND (instance:"ghl")	6.270
25		tw:(ari) AND (instance:"ghl")	703
26		tw:(acute respiratory infections) AND (instance:"ghl")	5.168
27		tw:(acute respiratory tract infection) AND (instance:"ghl")	2.266
28		tw:(arti) AND (instance:"ghl")	140
29		tw:(acute respiratory tract infections) AND (instance:"ghl")	2.084
30		tw:(respiratory illness*) AND (instance:"ghl")	3.477
31		tw:(respiratory illnesses*) AND (instance:"ghl")	1.398

32		19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 tw:(pneumonia OR (severe pneumonia) OR (severe disease) OR (very severe disease) OR bronchiolitis OR (acute respiratory infection) OR ari OR (acute respiratory infections) OR (acute respiratory tract infection) OR arti OR (acute respiratory tract infections) OR (respiratory illness*) OR (respiratory illnesses*)) AND (instance:"ghl")	68.111
33	children under 5 years of age	tw:(child*) AND (instance:"ghl")	253.850
34		tw:(children*) AND (instance:"ghl")	212.838
35		tw:(infant*) AND (instance:"ghl")	169.620
36		tw:(infants*) AND (instance:"ghl")	92.959
37		tw:(pediatric*) AND (instance:"ghl")	56.773
38		tw:(pediatrics*) AND (instance:"ghl")	13.240
39		tw:(paediatric*) AND (instance:"ghl")	4.003
40		tw:(paediatrics*) AND (instance:"ghl")	669
41		33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 tw:(child* OR children* OR infant* OR infants* OR pediatric* OR pediatrics* OR paediatric* OR paediatrics*) AND (instance:"ghl")	327.748
42		18 AND 32 AND 41	376

Final search output: 376

Search Summary 10

Name of the database: IndMed (Advanced)
Date of search: 29 January 2019
Timeline: November 2008 to January 2019
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	hypoxemia OR hypoxaemia OR anoxia OR hypoxia OR oximetry OR oximeter OR oximetre OR oxymetry OR oxymeter OR oxymetre OR blood oxygen saturation OR arterial oxygen saturation OR blood gas monitoring OR blood gas analysis OR analysis blood gas OR SpO2 OR SPO2	685
2	Pneumonia	pneumonia OR severe pneumonia OR severe disease OR very severe disease OR bronchiolitis OR acute respiratory infection OR ARI OR acute respiratory infections OR acute respiratory tract infection OR ARTI OR acute respiratory tract infections OR respiratory illness OR respiratory illnesses	3081
3	children under 5 years of age	child OR children OR infant OR infants OR pediatric OR pediatrics OR paediatric OR paediatrics	15800
4		1 AND 2 AND 3	33

Final search output :33

Search Summary 11

Name of the database: Web of Science (Advanced)
Date of search: 29 September, 2021
Timeline: November 2008 to September 2021
Search Language: English

Line #	Theme	Search Language	Output #
1	Hypoxaemia	TS=(Hypoxemia)	19,563
2		TS=(hypoxaemia)	2,790
3		TS=(anoxia)	14,241
4		TS=(hypoxia)	164,284
5		TS=(oximetry)	14,422
6		TS=(oximeter)	4,006
7		TS=(oximetre)	2
8		TS=(oxymetry)	502
9		TS=(oxymeter)	155
10		TS=(oxymetre)	0
11		TS=(blood oxygen saturation)	16,069
12		TS=(arterial oxygen saturation)	10,510
13		TS=(blood gas monitoring)	6,075
14		TS=(blood gas analysis)	15,105
15		TS=(analysis blood gas)	15,105
16		TS=(SpO2)	1,910
17		TS=(SPO2)	1,910
18		#17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	233,989
19	Pneumonia	TS= (Pneumonia)	144,419
20		TS=(severe pneumonia)	25,168
21		TS=(severe disease)	336,104
22		TS=(very severe disease)	21,394
23		TS=(bronchiolitis)	16,072
24		TS=(acute respiratory infection)	42,365
25		TS=(acute respiratory infections)	42,365
26		TS=(ARI)	4,984
27		TS=(acute respiratory tract infection)	11,598
28		TS=(acute respiratory tract infections)	11,598
29		TS=(ARTI)	705
30		TS=(respiratory illness*)	25,705
31		TS=(respiratory illnesses*)	5,564
32		#31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19	517,330
33	Children under 5 years of age	TS=(child*)	2,013,398
34		TS=(children*)	1,585,570
35		TS=(infant*)	474,019
36		TS=(infants*s)	7
37		TS=(pediatric*)	379,321
38		TS=(pediatrics*)	44,193
39		TS=(paediatric*)	75,210
40		TS=(paediatrics*)	8,380
41		#40 OR #39 OR #38 OR #37 OR #36 OR #35 OR #34 OR #33	2,472,694

42	Low- and Middle-Income Country	CU=(Afghanistan) OR CU=(Albania) OR CU=(Algeria) OR CU=(Angola) OR CU=(American Samoa) OR CU=(Armenia) OR CU=(Azerbaijan) OR CU=(Bangladesh) OR CU=(Benin) OR CU=(Belarus) OR CU=(Belize) OR CU=(Bhutan) OR CU=(Bolivia) OR CU=(Bosnia and Herzegovina) OR CU=(Botswana) OR CU=(Brazil) OR CU=(Bulgaria) OR CU=("Burkina Faso") OR CU=(Burundi) OR CU=(Cambodia) OR CU=(Cameroon) OR CU=("Cape Verde") OR CU=(Central African Republic) OR CU=(Chad) OR CU=(China) OR CU=(Colombia) OR CU=(Comoros) OR CU=(Congo, Dem. Rep) OR CU=(Congo, Rep.) OR CU=("Costa Rica") OR CU=("Cote d'Ivoire") OR CU=(Cuba) OR CU=(Djibouti) OR CU=(Dominica) OR CU=(Dominican Republic) OR CU=(Ecuador) OR CU=(Egypt) OR CU=("El Salvador") OR CU=(Eritrea) OR CU=(Ethiopia) OR CU=(Ethiopia) OR CU=(Fiji) OR CU=(Gabon) OR CU=(Gambia) OR CU=(Georgia) OR CU=(Ghana) OR CU=(Grenada) OR CU=(Guatemala) OR CU=(Guinea) OR CU=(Guyana) OR CU=(“Guinea-Bissau") OR CU=(Haiti) OR CU=(Honduras) OR CU=(India) OR CU=(Maldives) OR CU=(Indonesia) OR CU=(Iran) OR CU=(Iraq) OR CU=(Jamaica) OR CU=(Jordan) OR CU=(Kazakhstan) OR CU=(Kenya) OR CU=(Kiribati) OR CU=(Korea) OR CU=(Kosovo) OR CU=(Kyrgyz Republic) OR CU=(Lao PDR) OR CU=(Lebanon) OR CU=(Lesotho) OR CU=(Liberia) OR CU=(Libya) OR CU=(Macedonia, FYR) OR CU=(Madagascar) OR CU=(Malaysia) OR CU=(Malawi) OR CU=(Mali) OR TS=(Marshall Islands) OR CU=(Mauritania) OR CU=(Mauritius) OR CU=(Mexico) OR CU=(Micronesia) OR CU=(Moldova) OR CU=(Mongolia) OR CU=(Montenegro) OR CU=(Morocco) OR CU=(Mozambique) OR CU=(Myanmar) OR CU=(Namibia) OR CU=(Nepal) OR CU=(Nauru) OR CU=(Nicaragua) OR CU=(Niger) OR CU=(Nigeria) OR CU=(Pakistan) OR CU=(Papua New Guinea) OR CU=(Paraguay) OR CU=(Peru) OR CU=(Philippines) OR CU=(Romania) OR CU=(Russia) OR CU=(Rwanda) OR CU=(Samoa) OR CU=(Senegal) OR CU=(Serbia) OR CU=("Sierra Leone") OR CU=(Somalia) OR CU=(Grenadines) OR CU=(Samoan Islands) OR CU=("South Africa") OR CU=(St. Lucia) OR CU=(St. Vincent and the Grenadines) OR CU=(Sudan) OR CU=(Suriname) OR CU=(Swaziland) OR CU=(Syrian) OR CU=("Sri Lanka") OR CU=(Tajikistan) OR CU=(Tanzania) OR CU=(Thailand) OR CU=(Togo) OR CU=(Tonga) OR CU=(Tunisia) OR CU=(Turkey) OR CU=(Turkmenistan) OR CU=(Tuvalu) OR CU=(Timor-Leste) OR CU=(Uganda) OR CU=(Ukraine) OR CU=(Uzbekistan) OR CU=(Vanuatu) OR CU=(Venezuela) OR CU=(Vietnam) OR CU=(Gaza*) OR CU=(Yemen) OR CU=(Zambia) OR	17,062,517

		CU=(Zimbabwe) OR CU=(developing countr*) OR CU=(low-and middle income countr*) OR CU= (LMIC*) OR CU=(low income countr*) OR CU=(middle income countr*) OR CU=(lower middle income countr*) OR CU=(upper middle income countr*)	
43		#42 AND #41 AND #32 AND #18	628

Final search output : 628

Annex 13.2: List of articles dropped with reason for chapter 3: Burden of hypoxaemia among children with pneumonia in LMICs

ID	Title	Reason for exclusion
1	Nasal continuous positive airway pressure combined midazolam for micro pump infusion for severe pneumonia in infants	Full text not found
2	Accuracy of selected devices for the detection of pneumonia symptoms-results from laboratory testing and field evaluations of respiratory rate counters and pulse oximeters with frontline health workers in sub-Saharan Africa and Southeast Asia	Full text not found
3	Non-invasive positive pressure ventilation to reduce childhood mortality from acute respiratory failure in rural Ghana	Full text not found
4	Clinical predictors of hypxemia in children with acute respiratory tract infection admitted in pediatric department of Southe Valley university hospital	Full text not found
5	Cost illness of RSV infection in Colombia	Full text not found
6	Discrimination of pneumonia from other lower respiratory tract infections (LRTI) in children aged 0 to 5 years living at high altitude in Peru	Full text not found
7	Viral and bacterial causes of severe acute respiratory illness among children aged less than 5 years in a high malaria prevalence area of Western Kenya, 2007-2010	Full text not found
8	Pneumocystis jirovecii pneumonia among HIV-exposed, uninfected children in Botswana	Full text not found
9	Can we distinguish pneumonia from wheezy diseases in tachypnoeic children under low-resource conditions? A prospective observational study in four Indian hospitals	Full text not found
10	Impact of Human Immunodeficiency Virus Infection on the Etiology and Outcome of Severe Pneumonia in Malawian Children	Full text not found
11	The combination of CRP,myocardial enzymes measurement and blood gas analysis in neonatal pneumonia	Full text not found
12	Detection of myocardial enzymes, cardiac troponin T and hepatic and renal function in the diagnosis and treatment of severe pneumonia in children	Full text not found
13	Value of lung ultrasound on diagnosing transient tachypnea of newborn	Full text not found
14	Clinical characteristics of Mycoplasma pneumoniae pneumonia with different imaging changes in children	Full text not found
15	Effect of Tanreqing injection assisted Ganciclovir on children with respiratory syncytial virus pneumonia	Full text not found
16	[Nasal continuous positive airway pressure ventilation in children with community-acquired	Full text not found

	pneumonia under five years of age: a prospective, multi-center clinical study]	
17	Role of zinc in severe pneumonia	Full text not found
18	Performance of the world health organization diagnostic criteria for pneumonia in hospitalized Malawian infants with exposure to human immunodeficiency virus	Full text not found
19	Assessment of pneumonia in children in resource-limited settings	Full text not found
20	Stunting predicts poor outcome in children with severe pneumonia	Full text not found
21	Blood oxygen saturation levels associated with respiratory viruses in children hospitalized with pneumonia in Guatemala, 2008-2011	Full text not found
22	Clinical and radiologic features of pneumonia caused by staphylococcus aureus and streptococcus pneumoniae	Full text not found
23	Obstructive respiratory disease complicating pneumonia in children; possible role of viruses in a resource poor setting	Full text not found
24	An observational study of peripheral muscle oxygenation using nirs in a cohort of nourished and malnourished children with pneumonia	Full text not found
25	Predictors of treatment failure among infants with acute lower respiratory infection due to respiratory syncytial virus in Botswana	Full text not found
26	Lactate as a predictor of mortality in Malawian children with WHO-defined pneumonia	Full text not found
27	Predictors of prolonged length of hospital stay for infants with bronchiolitis	Full text not found
28	Efficacy of Bronchodilators in Wheeze Associated Respiratory Tract Infections	Full text not found
29	Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan	Full text not found
30	[Analysis of clinical manifestations of 159 hospitalized children infected with 2009 novel influenza A (H1N1) virus]. [Chinese]	Full text not found
31	Prevalence of human coronavirus infection in children with acute lower respiratory tract infection	Full text not found
32	Barriers to pediatric inpatient care guideline adherence: A mixed method assessment of eight hospitals in Asia and Africa	Full text not found
33	Human rhinovirus infections in hospitalized children: clinical, epidemiological and virological features	Full text not found
34	Viral and bacterial etiologies of community-acquired acute lower respiratory infections among hospitalized Cambodian patients	Full text not found
35	Efficacy of mechanical expectoration combined with oxygen inhalation treatment of infant bronchiolitis	Full text not found

36	Interventional bronchoscopy via laryngeal mask airway (LMA) under general anesthesia in children using adult flexible bronchoscope	Full text not found
37	Mortality and morbidity of acute hypoxemic respiratory failure and acute respiratory distress syndrome in infants and young children	Full text not found
38	Response to oxygen therapy using oxygen concentrators run off solar power in children with respiratory distress in remote primary health facilities in Papua New Guinea	Full text not found
39	Clinical Profile and Predictors of Outcome of Pediatric Acute Respiratory Distress Syndrome in a PICU: A Prospective Observational Study	Full text not found
40	Determinants of Outcome among Under-Five Children Hospitalized with Pneumonia at a Tertiary Health Facility in South-West Nigeria	Full text not found
41	Efficacy of high flow nasal oxygen therapy in children with acute respiratory failure	Full text not found
42	Clinical profile, severity pattern and socio-demographic risk factors of acute lower respiratory tract infection (Alrti) in children in Enugu, Nigeria	Full text not found
43	Hypoxemia predicts death from severe falciparum malaria among children under 5 years of age in Nigeria: The need for pulse oximetry in case management	Hypoxaemia prevalence/denominator could not be found
44	Density of upper respiratory colonization with Streptococcus pneumoniae and its role in the diagnosis of pneumococcal pneumonia among children aged <5 years in the PERCH study	Hypoxaemia prevalence/denominator could not be found
45	Nutritional rickets and vitamin D deficiency - Association with the outcomes of childhood very severe pneumonia: A prospective cohort study	Hypoxaemia prevalence/denominator could not be found
46	Zinc supplementation in severe acute lower respiratory tract infection in children: A triple-blind randomized placebo controlled trial	Hypoxaemia prevalence/denominator could not be found
47	High Mortality Risk in Hypoglycemic and Dysglycemic Children Admitted at a Referral Hospital in a Non Malaria Tropical Setting of a Low Income Country	Hypoxaemia prevalence/denominator could not be found
48	Oil instillation pneumonia - A social evil	Hypoxaemia prevalence/denominator could not be found
49	Child mortality after discharge from a health facility following suspected pneumonia, meningitis or septicaemia in rural Gambia: A cohort study	Hypoxaemia prevalence/denominator could not be found
50	Predictors of death in under-five children with diarrhoea admitted to a critical care ward in an urban hospital in Bangladesh	Hypoxaemia prevalence/denominator could not be found
51	Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial	Hypoxaemia prevalence/denominator could not be found

52	Incidence and characteristics of early childhood wheezing, Dhaka, Bangladesh, 2004-2010	Hypoxaemia prevalence/denominator could not be found
53	Safety of induced sputum collection in children hospitalized with severe or very severe pneumonia	Hypoxaemia prevalence/denominator could not be found
54	Humoral immune responses to Pneumocystis jirovecii antigens in HIV-infected and uninfected young children with Pneumocystis pneumonia	Hypoxaemia prevalence/denominator could not be found
55	Utility and feasibility of integrating pulse oximetry into the routine assessment of young infants at primary care clinics in Karachi, Pakistan: A cross-sectional study	Hypoxaemia prevalence/denominator could not be found
56	Early predictors of unresponsiveness to high-flow nasal cannula therapy in a pediatric emergency department	Hypoxaemia prevalence/denominator could not be found
57	Altered regulatory cytokine profiles in cases of pediatric respiratory syncytial virus infection	Hypoxaemia prevalence/denominator could not be found
58	Clinical predictors of chest radiographic abnormalities in young children hospitalized with bronchiolitis: a single center study	Hypoxaemia prevalence/denominator could not be found
59	Improved oxygen systems in district hospitals in Lao PDR: a prospective field trial of the impact on outcomes for childhood pneumonia and equipment sustainability	Hypoxaemia prevalence/denominator could not be found
60	Oral salbutamol for symptomatic relief in mild bronchiolitis a double blind randomized placebo controlled trial	Hypoxaemia prevalence/denominator could not be found
61	Hypoxaemia in hospitalised under-five Nigerian children with pneumonia	Hypoxaemia prevalence/denominator could not be found
62	Etiology of severe pneumonia in Ecuadorian children	Hypoxaemia prevalence/denominator could not be found
63	Pentraxin 3 as a clinical marker in children with lower respiratory tract infection	Hypoxaemia prevalence/denominator could not be found
64	Non-treatment of children with community health worker-diagnosed fast-breathing pneumonia in rural Malawi: Exploratory subanalysis of a prospective cohort study	Hypoxaemia prevalence/denominator could not be found
65	Can we predict oral antibiotic treatment failure in children with fast-breathing pneumonia managed at the community level? A prospective cohort study in Malawi	Hypoxaemia prevalence/denominator could not be found
66	Comparing the efficacy of 7%, 3% and 0.9% saline in moderate to severe bronchiolitis in infants	Hypoxaemia prevalence/denominator could not be found
67	Clinical predictors of hospital admission in acute lower respiratory tract infection in 2 months to 2-year-old children	Hypoxaemia prevalence/denominator could not be found

68	Pneumocystis pneumonia in South African children diagnosed by molecular methods	Hypoxaemia prevalence/denominator could not be found
69	Clinical outcomes of children with acute asthma and pneumonia in Mulago hospital, Uganda: a prospective study	Hypoxaemia prevalence/denominator could not be found
70	Respiratory tract cryptosporidiosis is common in HIV-seronegative children with intestinal cryptosporidium and cough	Hypoxaemia prevalence/denominator could not be found
71	Impaired gas exchange: accuracy of defining characteristics in children with acute respiratory infection. (Special Issue: Doctorate education and producing knowledge in nursing.)	Hypoxaemia prevalence/denominator could not be found
72	Phenotypical characterization of human rhinovirus infections in severely premature children	Hypoxaemia prevalence/denominator could not be found
73	Development and Internal Validation of a Predictive Model Including Pulse Oximetry for Hospitalization of Under-Five Children in Bangladesh	Hypoxaemia prevalence/denominator could not be found
74	Normal saline vs. hypertonic saline nebulization for acute bronchiolitis: a randomized clinical trial	Hypoxaemia prevalence/denominator could not be found
75	Sustainability in the AAP Bronchiolitis Quality Improvement Project	Hypoxaemia prevalence/denominator could not be found
76	Efficacy and safety of Laggera pterodonta in children 3-24 months with acute bronchiolitis: a randomized controlled trial	Hypoxaemia prevalence/denominator could not be found
77	Relation between pulse oximetry and clinical score in infants with acute bronchiolitis	Hypoxaemia prevalence/denominator could not be found
78	Safety and efficacy of phenylephrine nasal drops in bronchiolitis	Hypoxaemia prevalence/denominator could not be found
79	Clinical and epidemiological characteristics of pandemic influenza A/(H1N1) in hospitalized pediatric patients at a University Hospital, Istanbul, Turkey	Hypoxaemia prevalence/denominator could not be found
80	EV-D68 infection in children with asthma exacerbation and pneumonia in Mexico City during 2014 autumn	Hypoxaemia prevalence/denominator could not be found
81	Y Influenza in patients with hematological malignancies: Experience at two comprehensive cancer centers	Hypoxaemia prevalence/denominator could not be found
82	Providing oxygen to children and newborns: a multi-faceted technical and clinical assessment of oxygen access and oxygen use in secondary-level hospitals in southwest Nigeria	Hypoxaemia prevalence/denominator could not be found
83	Antenatal corticosteroids for women at risk of preterm delivery: the "Emperor's New Clothes" tale in medical practice	Hypoxaemia prevalence/denominator could not be found

84	Acute respiratory illness among a prospective cohort of pediatric patients using emergency medical services in India: Demographic and prehospital clinical predictors of mortality	Hypoxaemia prevalence/denominator could not be found
85	High-resolution Chest CT Features and Clinical Characteristics of Patients Infected with COVID-19 in Jiangsu, China	Hypoxaemia prevalence/denominator could not be found
86	Oxygen systems to improve clinical care and outcomes for children and neonates: A stepped-wedge cluster-randomised trial in Nigeria	Hypoxaemia prevalence/denominator could not be found
87	Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study	Hypoxaemia prevalence/denominator could not be found
88	Identify clinical factors related to Mycoplasma pneumoniae pneumonia with hypoxia in children	Hypoxaemia prevalence/denominator could not be found
89	Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants	Hypoxaemia prevalence/denominator could not be found
90	Respiratory compromise in children presenting to an urban emergency department of a tertiary hospital in Tanzania: a descriptive cohort study	Hypoxaemia prevalence/denominator could not be found
91	Treatment of respiratory distress syndrome in premature infants: A comparison of LISA and INSURE methods in the Vietnamese context	Hypoxaemia prevalence/denominator could not be found
92	Nebulised normal saline in moderate acute bronchiolitis and pneumonia in a low- to middle-income country: a randomised trial in Papua New Guinea	Hypoxaemia prevalence/denominator could not be found
93	Bubble CPAP and oxygen for child pneumonia care in Malawi: a CPAP IMPACT time motion study	Hypoxaemia prevalence/denominator could not be found
94	Usability and acceptability of a multimodal respiratory rate and pulse oximeter device in case management of children with symptoms of pneumonia: A cross-sectional study in Ethiopia	Hypoxaemia prevalence/denominator could not be found
95	Seizure in Children Under Five Presenting with Pneumonia in a Critical Care Ward in Bangladesh: Prevalence, Associated Factors, and Outcome	Hypoxaemia prevalence/denominator could not be found
96	Response to oxygen therapy using oxygen concentrators run off solar power in children with respiratory distress in remote primary health facilities in Papua New Guinea	Hypoxaemia prevalence/denominator could not be found
97	Randomised controlled trial of oxygen therapy and high-low nasal therapy in African children with pneumonia	Hypoxaemia prevalence/denominator could not be found
98	Performance of five pulse oximeters to detect hypoxaemia as an indicator of severe illness in children under five by frontline health workers in low resource settings A prospective, multicentre, single-blinded, trial in Cambodia, Ethiopia, South Sudan, and Uganda	Hypoxaemia prevalence/denominator could not be found

99	Oxygen systems and quality of care for children with pneumonia, malaria and diarrhoea: Analysis of a stepped-wedge trial in Nigeria	Hypoxaemia prevalence/denominator could not be found
100	Limitations to current methods to estimate cause of death: a validation study of a verbal autopsy model	Hypoxaemia prevalence/denominator could not be found
101	Human bocavirus-1 screening in infants with acute lower respiratory tract infection	Hypoxaemia prevalence/denominator could not be found
102	Etiology, clinical characteristics and coinfection status of bronchiolitis in Suzhou	Hypoxaemia prevalence/denominator could not be found
103	Near-Infrared Spectroscopy Monitoring of Cerebral Oxygenation and Influencing Factors in Neonates from High-Altitude Areas	Hypoxaemia prevalence/denominator could not be found
104	Estimated Cost-effectiveness of Solar-Powered Oxygen Delivery for Pneumonia in Young Children in Low-Resource Settings	Hypoxaemia prevalence/denominator could not be found
105	Employing learning health system principles to advance research on severe neonatal and paediatric illness in Kenya	Hypoxaemia prevalence/denominator could not be found
106	Effect of ten-valent pneumococcal conjugate vaccine introduction on pneumonia hospital admissions in Fiji: a time-series analysis	Hypoxaemia prevalence/denominator could not be found
107	Clinical characteristics of 967 children with pertussis: a single-center analysis over an 8-year period in Beijing, China	Hypoxaemia prevalence/denominator could not be found
108	Acute respiratory illness among a prospective cohort of pediatric patients using emergency medical services in India: Demographic and prehospital clinical predictors of mortality	Hypoxaemia prevalence/denominator could not be found
109	The impact of pulse oximetry and Integrated Management of Childhood Illness (IMCI) training on antibiotic prescribing practices in rural Malawi: A mixed-methods study	Hypoxaemia prevalence/denominator could not be found
110	Aerosol inhalation of ambroxol hydrochloride combined with terbutaline can promote recovery of children with severe pneumonia	Hypoxaemia prevalence/denominator could not be found
111	Clinico-virological profile, intensive care needs, and outcome of infants with acute viral bronchiolitis: A prospective observational study	Hypoxaemia prevalence/denominator could not be found
112	Risk factors for mortality from severe community-acquired pneumonia in hospitalized children transferred to the pediatric intensive care unit	Hypoxaemia prevalence/denominator could not be found
113	Comparison of 3% saline and 0.9% normal saline nebulization as diluent in children with bronchiolitis	Hypoxaemia prevalence/denominator could not be found
114	Morbidity pattern and outcome of children admitted to a paediatric intensive care unit of Eastern India	Hypoxaemia prevalence/denominator could not be found
115	Effect of cefoperazone sulbactam sodium combined with meropenem on the immune function in the treatment of neonatal pneumonia caused by multidrug-resistant bacteria	Hypoxaemia prevalence/denominator could not be found

116	A multicenter survey of pediatric flexible bronchoscopy in western China	Hypoxaemia prevalence/denominator could not be found
117	Epidemiology and genetic characterization of respiratory syncytial virus in children with acute respiratory infections: Findings from the influenza sentinel surveillance network in Central African Republic, 2015 to 2018	Hypoxaemia prevalence/denominator could not be found
118	Survival and predictors of mortality among severe acute malnourished under-five children admitted at Felege-Hiwot comprehensive specialized hospital, northwest, Ethiopia: a retrospective cohort study	Hypoxaemia prevalence/denominator could not be found
119	Severe recurrent pneumonia in children: Underlying causes and clinical profile in Vietnam	Hypoxaemia prevalence/denominator could not be found
120	Antibiotic-Resistant Bacteremia in Young Children Hospitalized with Pneumonia in Bangladesh Is Associated with a High Mortality Rate	Hypoxaemia prevalence/denominator could not be found
121	Saturation oxygenation pressure index: a non-invasive bedside measure for severity of respiratory disease in neonates on CPAP	Hypoxaemia prevalence/denominator could not be found
122	Optimal level of positive end-expiratory pressure during nasal continuous airway pressure for severe bronchiolitis: a prospective study	Hypoxaemia prevalence/denominator could not be found
123	Complications of pneumonia and its associated factors in a pediatric population in Osogbo, Nigeria	Hypoxaemia prevalence/denominator could not be found
124	A multicentered study on efficiency of noninvasive ventilation procedures (SAFE-NIV)	Hypoxaemia prevalence/denominator could not be found
125	Risk Factors for Pneumonia Mortality in Under-five Children in a Tertiary Care Hospital of Darjeeling District of West Bengal: A Prospective Case-Control Study	Hypoxaemia prevalence/denominator could not be found
126	Hypoglycaemia in children aged 1 month to 17 years admitted to the children's emergency room of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria	Hypoxaemia prevalence/denominator could not be found
127	The role of body temperature on respiratory rate in children with acute respiratory infections	Hypoxaemia prevalence/denominator could not be found
128	Venoarterial Extracorporeal Membrane Oxygenation for Severe Neonatal Acute Respiratory Distress Syndrome in a Developing Country	Hypoxaemia prevalence/denominator could not be found
129	Community-based amoxicillin treatment for fast breathing pneumonia in young infants 7-59 days old: a cluster randomised trial in rural Bangladesh, Ethiopia, India and Malawi	Hypoxaemia prevalence/denominator could not be found
130	A Self-criticism of Diagnostic and Therapeutic Decision Making in Children Admitted With Acute Lower Respiratory Infection at a Single Pediatric Emergency Department	Hypoxaemia prevalence/denominator could not be found

131	Oxigenoterapia inalatória em pacientes pediátricos internados em hospital universitário	Hypoxaemia prevalence/numerator could not be found
132	[Clinical features and treatment of macrolide-resistant Mycoplasma pneumoniae pneumonia in children]	Hypoxaemia prevalence/ numerator could not be found
133	Ventilação não invasiva na insuficiência respiratória aguda na bronquiolite por vírus sincicial respiratório	Hypoxaemia prevalence/ numerator could not be found
134	Methods of a double-blind randomized controlled clinical trial of three versus five days amoxicillin dispersible tablets for chest-indrawing pneumonia among children 2-59 months of age presenting to kamuzu central hospital in Lilongwe, Malawi	Protocol paper
135	Performance, Acceptability, and Usability of Respiratory Rate Timers and Pulse Oximeters When Used by Frontline Health Workers to Detect Symptoms of Pneumonia in Sub-Saharan Africa and Southeast Asia: Protocol for a Two-Phase, Multisite, Mixed-Methods Trial	Protocol paper
136	Improving oxygen therapy for children and neonates in secondary hospitals in Nigeria: study protocol for a stepped-wedge cluster randomised trial	Protocol paper
137	Children's Oxygen Administration Strategies Trial (COAST): A randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia	Protocol paper
138	CPAP Improving Mortality for Pneumonia in African Children Trial	Protocol paper
139	Effectiveness Trial of Day-care vs. Usual Care of Severe Pneumonia & Malnutrition in Children	Protocol paper
140	RCT of Efficacy of Amoxicillin Over Ampicillin on Severe Pneumonia	Protocol paper
141	Impact of Pulse Oximetry on Hospital Referral Acceptance in Children Under 5 With Severe Pneumonia	Protocol paper
142	Immunomodulation by Zinc Supplementation in Children With Pneumonia	Protocol paper
143	Solar-powered oxygen delivery: study protocol for a randomized controlled trial	Protocol paper
144	CPAP IMPACT: a protocol for a randomised trial of bubble continuous positive airway pressure versus standard care for high-risk children with severe pneumonia using adaptive design methods	Protocol paper
145	Automated Respiratory Rate Counter to Assess Children for Symptoms of Pneumonia: Protocol for Cross-Sectional Usability and Acceptability Studies in Ethiopia and Nepal	Protocol paper
146	Solar-powered oxygen delivery for the treatment of children with hypoxemia: protocol for a cluster-randomized stepped-wedge controlled trial in Uganda	Protocol paper

147	Smart triage: Triage and management of sepsis in children using the point-of-care Pediatric Rapid Sepsis Trigger (PRST) tool	Protocol paper
148	Design and conduct of facility-based surveillance for severe childhood pneumonia in the Household Air Pollution Intervention Network (HAPIN) trial	Protocol paper
149	Development of a Robust and Reliable Pulse Oximeter for Children With Pneumonia in Low-income Countries	Published before 2008
150	Use of Bubble Continuous Positive Airway Pressure Compared to Nasal Prong Oxygen or Humidified High Flow in Children Under Five With Severe Pneumonia and Hypoxaemia	Published before 2008
151	Assessing the Feasibility and Effectiveness of Introducing Pulse Oximetry in IMCI Services	Published before 2008
152	CPAP Improving Mortality for Pneumonia in African Children Trial	Published before 2008
153	Infant Pulse Oximetry in Pakistan Study	Published before 2008
154	Vitamin-D Supplementation: Impact on Severe Pneumonia Among Under-five Children	Published before 2008
155	Electronic Algorithms Based on Host Biomarkers to Manage Febrile Children	Published before 2008
156	Impact of Pulse Oximetry on Hospital Referral Acceptance in Children Under 5 With Severe Pneumonia	Published before 2008
157	Multimometer - Vital Signs Device for Diagnosis of Pneumonia	Published before 2008
158	Randomized Controlled Trial (RCT) in Children With Severe Pneumonia	Published before 2008
159	Innovative Treatments in Pneumonia (ITIP) 3	Published before 2008
160	Immunomodulation by Zinc Supplementation in Children With Pneumonia	Published before 2008
161	RCT of Efficacy of Amoxicillin Over Ampicillin on Severe Pneumonia	Published before 2008
162	The Efficacy of Zinc as Adjunct Therapy in the Treatment of Severe Pneumonia in Children	Published before 2008
163	High Flow Oxygen Therapy vs Standard Care in Infants With Viral Bronchiolitis	Published before 2008
164	Vitamin D Supplementation and Respiratory Index of Severity in Children (RISC) in Pneumonia	Published before 2008
165	Nebulized Hypertonic Saline (3%) Versus Nebulized Adrenaline for Treatment of Bronchiolitis	Published before 2008
166	Solar Powered Oxygen Delivery	Published before 2008
167	Advancement of Modified Bubble CPAP	Published before 2008
168	Montelukast for Acute Bronchiolitis and Postbronchiolitis Viral Induced Wheezing	Published before 2008
169	Ceftriaxone Versus Chloramphenicol for Treatment of Severe Pneumonia in Children	Published before 2008
170	A Study to Evaluate a Single IM Dose of Motavizumab Treatment of Children With RSV (Respiratory Syncytial Virus) Illness	Published before 2008
171	Salbutamol versus epinephrine in the treatment of acute bronchiolitis	Published before 2008

172	Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study	Published before 2008
173	Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial	Published before 2008
174	Respiratory syncytial virus and human metapneumovirus in children with acute respiratory infections in Yemen	Published before 2008
175	Epidemiology and clinical characteristics of respiratory syncytial virus infections in Jordan	Published before 2008
176	Oral amoxicillin is as effective as injected penicillin for severe pneumonia in young children	Published before 2008
177	Hypoxemia in children with pneumonia and its clinical predictors	Published before 2008
178	Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old	Published before 2008
179	Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial	Published before 2008
180	Pneumonia case-finding in the RESPIRE Guatemala indoor air pollution trial: standardizing methods for resource-poor settings	Published before 2008
181	Acquired pneumonia's behavior in a community in the pediatrics service at the Fundacion Cardio Infantil, Bogota, Colombia. [Spanish]	Published before 2008
182	Risk factors for hypoxemia and respiratory failure in respiratory syncytial virus bronchiolitis	Published before 2008
183	Case fatality proportions and predictive factors for mortality among children hospitalized with severe pneumonia in a rural developing country setting	Published before 2008
184	Treatment of respiratory syncytial virus infection with vitamin A: A randomized, placebo-controlled trial in Santiago, Chile	Published before 2008
185	Hypoxaemia in acute respiratory and non-respiratory illnesses in neonates and children in a developing country	Published before 2008
186	Hypoxaemia in children with severe pneumonia in Papua New Guinea	Published before 2008
187	Chloramphenicol versus benzylpenicillin and gentamicin for the treatment of severe pneumonia in children in Papua New Guinea: A randomised trial	Published before 2008
188	Predicting hypoxia in children with acute lower respiratory infection: A study in the highlands of Papua New Guinea	Published before 2008
189	PREDICTING HYPOXIA IN CHILDREN WITH ACUTE LOWER RESPIRATORY-INFECTION - A STUDY IN THE HIGHLANDS OF PAPUA-NEW-GUINEA	Published before 2008
190	Hypothetical performance of syndrome-based management of acute paediatric admissions of children aged more than 60 days in a Kenyan district hospital	Published before 2008

191	Causes and outcome of young infant admissions to a Kenyan district hospital	Published before 2008
192	Clinical overlap between malaria and severe pneumonia in African children in hospital	Published before 2008
193	Clinical indicators of Pneumocystis jiroveci pneumonia (PCP) in South African children infected with the human immunodeficiency virus	Published before 2008
194	Vitamin A supplementation and severity of pneumonia in children admitted to the hospital in Dar es Salaam, Tanzania	Published before 2008
195	Brief hospitalization and pulse oximetry for predicting amoxicillin treatment failure in children with severe pneumonia	Published before 2008
196	ORAL VERSUS NEBULIZED ALBUTEROL IN THE MANAGEMENT OF BRONCHIOLITIS IN EGYPT	Published before 2008
197	Caretaker recognition of respiratory signs in children: Correlation with physical examination findings, X-ray diagnosis and pulse oximetry	Published before 2008
198	Clinical presentation and outcome of Pneumocystis carinii pneumonia in Malawian children	Published before 2008
199	Relación entre signos clínicos e hipoxemia en niños menores de 5 años con enfermedad respiratoria aguda baja	Published before 2008
200	A study of some viral pathogens in infants and children with lowe respiratory tract infection and attending the intensive care unit	Published before 2008
201	MATERNAL REPORTING OF ACUTE RESPIRATORY-INFECTION IN EGYPT	Published before 2008
202	The spectrum of hypoxaemia in children admitted to hospital in The Gambia, West Africa	Published before 2008
203	Evaluation of clinical and radiological signs in diagnosis of pneumonia in the first five years of life	Published before 2008
204	Remark on the changes of blood gas in newborn babies with respiratory impairment due to pneumonia in the Department of Neonate at the National Institute of Pediatry -2001 - 2002 period	Published before 2008
205	High rates of Chlamydia trachomatis infections in young Papua New Guinean infants	Published before 2008
206	Can Clinical Symptoms or Signs Accurately Predict Hypoxemia in Children with Acute Lower Respiratory Tract Infections?	Published before 2008
207	Clinical predictors of acute radiological pneumonia and hypoxaemia at high altitude	Published before 2008
208	Central nervous system infection is an important cause of death in underfives hospitalised with World Health Organization (WHO) defined severe and very severe pneumonia	Published before 2008
209	The role of pulse oximetry: Its use as an indicator of severe respiratory disease in Peruvian children living at sea level	Published before 2008
210	Equivalency Of Oral Amoxicillin Vs Injectable Penicillin In Children With Severe Pneumonia	Published before 2008

211	Hypoxaemia in young Kenyan children with acute lower respiratory infection	Published before 2008
212	Analysis of Acid-Base Disturbance Caused by Severe Pneumonia in Newbern Infants	Published before 2008
213	Prevalence and prediction of hypoxemia in children with respiratory infections in the Peruvian Andes	Published before 2008
214	Respiratory Syncytial Virus (RSV) in infants hospitalized for acute lower respiratory tract disease: Incidence and associated risks	Published before 2008
215	Características clínicas e da saturação transcutânea de oxigênio em lactentes hospitalizados com bronquiolite viral aguda	Published before 2008
216	Clinical predictors of hypoxaemia in children with pneumonia	Published before 2008
217	Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: A randomized, double-blind, placebo-controlled trial	Published before 2008
218	Effectiveness of intramuscular penicillin versus oral amoxicillin in the early treatment of outpatient pediatric pneumonia	Published before 2008
219	Clinical predictors of hypoxaemia in Gambian children with acute lower respiratory tract infection: Prospective cohort study	Published before 2008
220	Hypoxaemia among children in rural hospitals in Papua New Guinea: Epidemiology and resource availability - A study to support a national oxygen programme	Published before 2008
221	Clinical Analysis of Complications of 115 Children with Serious Pneumonia with Ventilatory Support	Published before 2008
222	The clinical spectrum of respiratory syncytial virus disease in The Gambia	Published before 2008
223	An epidemiological study of RSV infection in the Gambia	Published before 2008
224	Long-term morbidity and mortality following hypoxaemic lower respiratory tract infection in Gambian children	Published before 2008
225	Observational follow-up study following two cohorts of children with severe pneumonia after discharge from day care clinic/hospital in Dhaka, Bangladesh	Same study reported prevalence
226	Co-morbidity: Exploring the clinical overlap between pneumonia and diarrhoea in a hospital in Dhaka, Bangladesh	Same study reported prevalence
227	Risk factors for mortality in childhood pneumonia in a rural West African region	Same study reported prevalence
228	Predictors of prolonged hospitalisation in childhood pneumonia in a rural health centre	Same study reported prevalence
229	Safety, Effectiveness and Feasibility of Outpatient Management of Children with Pneumonia with Chest Indrawing at Port Moresby General Hospital, Papua New Guinea	Same study reported prevalence

230	Impaired Gas Exchange: Prognostic Clinical Indicators of Short-Term Survival in Children with Acute Respiratory Infection	Same study reported prevalence

Annex 13.3: DATA COLLECTION TOOL FOR CHAPTER 8: MINIMALLY TRAINED HEALTH PERSONNEL PERFORMING PULSE OXIMETRY IN HOSPITAL SETTINGS

International Centre for Diarrhoeal Disease Research, Bangladesh

Assessing the feasibility and effectiveness of introducing pulse oximetry in IMCI services to manage acuterespiratoryinfectionatfirstlevelhealthfacilitiesof Bangladesh

Validation tools for pulse oximeter

Child name: _____ Hospital ID no- _____

Age: _____ Study ID no- _____

Sex: _____

Weight: _____kg

Height (≥2 years of age)/Length (<2yrs years of age): _____ (cm)

Name of the Control Pulse oximeter:

_____

General Symptoms			
	QUESTIONS	**10:00**	**14:00**
G01	Body temperature (in C/ F)		
G02	Pulse rate (per minute)		
G03	Respiratory rate (per minute)		
G04	RBS (mmol/L)		
G05	Blood Pressure (mm of Hg)		

10:00

	Question	CODING CATEGORIES	CODING CATEGORIES	SKIP
		Life box	**Control**	
P01	Placement of pulse oxymeter in first attempt?	On toe .....0 On index finger…….1 Other place ---------- (Specify)	On toe..... 0 On index finger… ..... 1 Other place ---------- (Specify)	
P02	Was the first attempt successful?	Yes.....1 No..... 0	Yes ..... 1 No 0	→**P06**
P03	How long did it take to get the reading in the first attempt?	---------- (completed) seconds	---------- (completed) seconds	
P04	SpO_2 reading in first successful placement	……%	……%	
P05	Pulse rate in first successful	…… / minute	…… / minute	

	placement			
P06	Placement of pulse oxymeter in second attempt?	On toe ..... 0 On index finger… ..... 1 Other place ---------- (Specify)	On toe..... 0 On index finger… ..... 1 Other place ---------- (Specify)	
P07	Was the second attempt successful?	Yes..... 1 No..... 0	Yes ..... 1 No 0	→**P12**
P08	How long did it take to get the reading in the second attempt?	---------- (completed) seconds	---------- (completed) seconds	
P09	SpO_2 reading in second successful placement	……%	……%	
P10	Pulse rate in second successful placement	…… / minute	…… / minute	
P11	If SpO_2 <90% in first attempt, was second reading attempted?	Yes..... 1 No..... 0	Yes..... 1 No..... 0	
P12	Was the baby diagnosed as hypoxemic?	Yes..... 1 No..... 0	Yes..... 1 No..... 0	

14:00

Comments (if any):

Annex 13.4: DATA COLLECTION FOR CHAPTER 9: IMCI SERVICE PROVIDERS PERFORMING PULSE OXIMETRY IN ROUTINE OUTPATIENT SETTINGS IN RURAL BANGLADESH

13.4.1 Observation tool

Registration			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
1	Registration Date	|___||___||___||___| / |___||___| / |___||___| **YYYY/MM/DD**	
2	Observation ID	_____	
3	Name of patient	_____	
4	Age of patient	|____|____| days |____|____| months	
5	Sex	Male ..... 1 Female ..... 2 Others 7	
6	Hospital ID	_____	
8	Name of the facility	_____	
7	Name of service provider	_____	
9	Informed written consent taken?	Yes ..... 1 No 2	→End

Pulse oximeter use timing			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
	Pulse oximeter turned on	_____	
	Prob placed	_____	
	Stable SpO2 reading obtained	_____	

Pulse oximeter use outcome			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
	Observation ID	_____	
1	What is the outcome of measuring SpO2 using pulse oximeter?	Successful ..... 1 Unsuccessful 2	→8

2	How many attemtps needed to obtain successful SpO2 reading?	One ..... 1 Two ..... 2 Three ..... 3 Four ..... 4 Five ..... 5 More than five 6	
3	Placement of pulse oximeter	On toe ..... 1 On index finger ..... 2 On ear lobule ..... 3 Others ..... 7 (Please Specify)	
4	SpO_2 status?	|____|____|____| %	
5	Steps of using pulse oximeter	Service provider ensured the baby was calm ..... 1 Service provider ensured that the area of attachment (finger/toe) is clean before using pulse oximeter ..... 2 Service provider placed the probe properly (not too loose or too tight ..... 3 Service provider cleaned the probe after using it 4	
6	Type of pulse oximeter used?	Masimo ..... 1 Lifebox ..... 2 Others ..... 7 (Please Specify)	
7	Check whether baby was calm	Calm ..... 1 Not Calm 2	→End →End
8	Reason for unsuccessful attempt for using pulse oximeter according to service provider?	Provider related ..... 1 Patient related ..... 2 Device related ..... 3 Environment related 4	
9	Please mention the specific reason	_____	
10	Reason for unsuccessful attempt for using pulse oximeter according to observer's judgement?	Provider related ..... 1 Patient related ..... 2 Device related ..... 3 Environment related 4	
11	Please mention the specific reason	_____	

13.4.2 Reassessment tool

Registration			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
1	Registration Date	|___||___||___||___| / |___||___| / |___||___| **YYYY/MM/DD**	
2	Re-assessment ID	_____	
3	Name of patient	_____	
4	Age of patient	|____|____| days |____|____| months	
5	Sex	Male ..... 1 Female ..... 2 Others 7	
6	Hospital ID	_____	
12	Name of the facility	_____	
14	Informed written consent taken?	Yes ..... 1 No 2	→End
15	Observation ID	_____	

Pulse oximeter use timing			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
1	Pulse oximeter turned on	_____	
2	Prob placed	_____	
3	Stable SpO2 reading obtained	_____	

Pulse oximeter use outcome			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
	Re-assessment ID	_____	

1	What is the outcome of measuring SpO2 using pulse oximeter?	Successful ..... 1 Unsuccessful 2	→12
2	How many attemtps needed to obtain successful SpO2 reading?	One ..... 1 Two ..... 2 Three ..... 3 Four ..... 4 Five ..... 5 More than five 6	
3	Placement of pulse oximeter	On toe ..... 1 On index finger ..... 2 On ear lobule ..... 3 Others ..... 7 (Please Specify)	
4	SpO_2 status?	|____|____|____| %	
6	Type of pulse oximeter used?	Masimo ..... 1 Lifebox ..... 2 Others ..... 7 (Please Specify)	
7	Check whether baby was calm	Calm ..... 1 Not Calm 2	→End →End
12	Reason for unsuccessful attempt for using pulse oximeter according to assessor?	Provider related ..... 1 Patient related ..... 2 Device related ..... 3 Environment related 4	
13	Please mention the specific reason	_____	

Other assessments			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
	Re-assessment ID	_____	
1	Age	0 to 59 days ..... 1 2 to 59 months 2	→2→4 →3

2	Assessment for children 0-59 days	Unconscious/drowsy ..... 01 Convulsion/history of convulsion ..... 02 Unable to feed ..... 03 Persistent vomiting ..... 04 Bulging fontanels ..... 05 Apnoea ..... 06 Central cyanosis ..... 07 Major bleeding ..... 08 Major congenital malformation ..... 09 Surgical condition required hospitalization ..... 10 Severe chest indrawing ..... 11 Move only when stimulated or no movement at all ..... 12 Difficulty in feeding ..... 13 Umbilicus is red or draining pus ..... 14 Skin pustules ..... 15 Restless, irritable ..... 16 Sunken eyes ..... 17 Skin pinch goes back slowly or very slowly 18	
3	Assessment for children 2-59 months	Not able to drink or breast feed ..... 01 Vomits everything ..... 02 Had convulsion or convulsing now ..... 03 Lethargic or unconscious ..... 04 Stridor in calm child ..... 05 Chest in-drawing ..... 06 No signs of pneumonia or very severe disease ..... 07 Diarrhoea for 14 days or more with dehydration present ..... 08 Diarrhoea for 14 days or more with no dehydration ..... 09 Blood in the stool ..... 10 Stiff neck ..... 11 RDT POSITIVE/ Other Malaria Test POSITIVE ..... 12 RDT NEGATIVE/ Other Malaria Test NEGATIVE ..... 13 Other cause of fever present 14	
4	Weight (Kg)	_____	
5	Height/Length (inch)	_____	
6	Temperature (F)	_____	
7	MUAC? (CM)	_____	
8	Respiratory rate? (Breaths per minute)	_____	
8a	Heart rate (Beats per minute)	_____	

9	IMCI classification for 0-59 days?	Possible Serious Bacterial Infection or Very Severe Disease - Critical Illness (VSD-CI) ..... 11 Possible Serious Bacterial Infection or Very Severe Disease - Clinical Severe Infection (VSD-CSI) ..... 12 Possible Serious Bacterial Infection or Very Severe Disease - Fast Breathing Pneumonia (0-6 days) ..... 13 Fast Breathing Pneumonia (7-59 days) ..... 14 Local Bacterial Infection ..... 15 Severe Dehydration ..... 16 Some Dehydration ..... 17 No Dehydration ..... 18 Others ..... 97 (Please Specify)	
10	IMCI classification for 2-59 months?	Severe pneumonia or very severe disease ..... 11 Pneumonia ..... 12 Cough or cold ..... 13 Severe Dehydration ..... 16 Some Dehydration ..... 17 No Dehydration ..... 18 Severe persistent diarhhoea ..... 19 Persistent diarhhoea ..... 20 Dysentery ..... 21 Very severe febrile disease ..... 22 Malaria ..... 23 Fever ..... 24 Others ..... 97 (Please Specify)	

13.4.3 Exit interview tool

Section A: Facility & exit interviewer information			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
A01	Date of exit interview	|____||____||____||____| / |____||____| / |____||____| **YYYY/MM/DD**	
A02	Name of exit interviewer		
A03	Code of exit interviewer	|____|____|	
A04	Name of facility		
A05	Type of facility	Medical College Hospital ..... 1 District Hospital ..... 2 MCWC ..... 3 Upazila Health Complex ..... 4 Union Health and Family Welfare Centre ..... 5 Community Clinic ..... 6 Others ..... 7 (Please Specify)	
A06	Code of the facility	|____|____|	

Section B: Patient information			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
B01	Name of the child		
B02	Observation ID		
B03	Hospital Registration Number		
B04	Age of the child	|___|____| days |___|____| months	
B05	Sex of the child	Male ..... 1 Female..... 2 Others 7	
B06	Informed written consent taken?	Yes..... 1 No..... 2	Sec E

Section C: Information of mother			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
C01	What is your age?	|___|____| completed years Don't know..... 9	
C02	How many years of formal education have you had?	|___|____| years Don't know..... 9	
C03	How many living children do you have?	|___|____| children Don't know..... 9	
C04	Do you have a mobile number?	Yes.....1 No .....2 Don't know 9	
C05	May I have your mobile number?	Yes (_____).....1 No .....2 Don't know 9	
C06	Does your husband or family member have a mobile number?	Yes .....1 No .....2 Don't know 9	
C07	Can I record that number?	Yes (_____).....1 No .....2 Don't know 9	

Section D: Assessment of the child					
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**			**SKIP**
D01	Do you have any concern regarding the oxygen test?	Yes ..... 1 No ..... 2 Don't know 9			 →D03 →D03
D02	What are the concerns?	Unprompted	Prompted	Not mentioned	
	Pain/discomfort	1	2	3	
	Heat/burning	1	2	3	
	Sensor was wrapped too tightly	1	2	3	
	Test was taking too long	1	2	3	
	Others 1 (Please mention)	1	2	3	
	Others 2 (Please mention)	1	2	3	
	Others 3 (Please mention)	1	2	3	
D03	Were you satisfied with the oxygen test?	Yes ..... 1 No ..... 2 Don't know 9			
D04	Would you permit the oxygen test to be performed on your baby again in the future?	Yes ..... 1 No ..... 2 Don't know 9			
D05	Do you believe the oxygen test was useful for the nurses/doctors to check your baby?	Yes ..... 1 No ..... 2 Don't know 9			

Section E: Final status			
NO.	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
E01	What is the status of exit interview for this patient?	Complete .....1 Incomplete.....2	→D03
E02	Reason for incomplete exit interview		
E03	Exit interview tool reviewed by supervisor?	Yes.....1 No 2	
E04	Name and Signature of supervisor		
E05	Date of review by supervisor	|____||____||____||____| / |____||____| / |____||____| **YYYY/MM/DD**	
E06	Data entry completed	Yes.....1 No 2	
E07	Name and Signature of data entry person		
E08	Date of data entry	|____||____||____||____| / |____||____| / |____||____| **YYYY/MM/DD**	