Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

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Declaration

I, Salahuddin Ahmed, 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. I confirm that appropriate credit has been given in this thesis where references to the work of others have been mentioned.

Signature: Date: 12 August 2023

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List of Abbreviations

ACCORD	Academic and Clinical Central Office for Research & Development
ACCP-ATS	American College of Chest Physician – American Thoracic Society
AI	Artificial Intelligence
ALRI	Acute Lower Respiratory Infection
AMREC	ACCORD Medical Research Ethics Committee
ARI	Acute Respiratory Infection
ASM	Annual Scientific Meeting
BMC	BioMed Central
BMRC	Bangladesh Medical Research Council
CC	Community Clinic
CHCP	Community Health Care Provider
CHW	Community Health Worker
CLSA	Computerised Lung Sound Analysis
COPD	Chronic Obstructive Pulmonary Disease
EMPIC	Enhanced Management of Pneumonia in Community
ESPID	European Society for Paediatric Infectious Diseases
FGD	Focus Group Discussion
FRA	Field Research Assistant
HCW	Health Care Worker
Hib	*Haemophilus influenzae* type b
ICBHI	International Conference on Biomedical Health Informatics
iCCM	Integrated Community Case Management
ICMJE	International Committee of Medical Journal Editors
ILSA	International Lung Sounds Association
IMCI	Integrated Management of Childhood Illness

IPD	Invasive Pneumococcal Disease
ISPPD	International Symposium on Pneumococci and Pneumococcal Diseases
JHU	Johns Hopkins University
LMIC	Low- and Middle-Income Country
MOHFW	Ministry of Health and Family Welfare
MUAC	Mid-Upper Arm Circumference
NHS	National Health Service
NIHR	National Institute for Health Research
ODA	Official Development Assistance
PABAK	Prevalence-Adjusted Bias-Adjusted Kappa
PASS	Power Analysis and Sample Size
PCV	Pneumococcal Conjugate Vaccine
PERCH	Pneumonia Etiology Research for Child Health
PPIG	Patient Public Involvement Group
PRISMA-DTA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy
PRF	Projahnmo Research Foundation
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
RA	Research Associate
RESPIRE	The NIHR Global Health Research Unit on Respiratory Health
RSV	Respiratory Syncytial Virus
RVEG	Respiratory Viral Epidemiology Group
SDG	Sustainable Development Goals
SOP	Standard Operations Procedure
SpO_2	Peripheral Oxyhaemoglobin Saturation
STARD	Standards for Reporting of Diagnostic Accuracy Studies
TRC	Technical Review Committee

UHC	Upazila Health Complex
UNICEF	United Nations Children's Fund
URTI	Upper Respiratory Tract Infections
WHO	World Health Organization

Lay Summary

Pneumonia is a major cause of death in children under the age of five years worldwide, especially in developing countries. The World Health Organization developed a tool to manage common childhood illnesses called the Integrated Management of Childhood Illness (IMCI). This tool mainly uses manual counts of respiratory rates and observing for clinical signs of breathing difficulty to diagnose pneumonia in children. The main focus of the IMCI tool is to prioritize antibiotic access and therefore identify children who may have pneumonia rather than ruling out children who do not have pneumonia. In developing countries, health workers at the community level play an important role in the early identification and treatment of pneumonia cases by using the IMCI tool. This tool does not include listening to the lungs with a stethoscope as an approach to identify pneumonia. The reason for not using a conventional stethoscope is that it is difficult to standardise the interpretation of lung sounds between different people, and it is also difficult to train community health workers without any experience using stethoscopes for the proper use of it. Using a digital system to record and listen to lung sounds, potentially with the help of artificial intelligence (digital auscultation), could improve the diagnosis of pneumonia by community health workers in developing countries. If digital auscultation is included in the existing IMCI guideline, it could make it more accurate in detecting childhood pneumonia. The aim of my PhD was to improve the IMCI pneumonia diagnosis algorithm by adding digital auscultation to it.

First, I reviewed the published literature to assess the ability of digital auscultation or a computerised system for the assessment of lung sounds to identify abnormal lung sounds. I found that the accuracy of identifying abnormal lung sounds varied by study between moderate to almost perfect (66.3% to 100%). However, from the perspective of child pneumonia, the overall results were not as clear for identifying abnormal lung sounds.

Next, I conducted a prospective study to find out how well community health workers could record lung sounds in children younger than five years of age. I enrolled 990 children aged 2-59 months who had possible pneumonia (cough or breathing difficulty) and divided them into two groups using the current IMCI case definition: one with pneumonia and the other without pneumonia (thus, these children had only cough). The community health workers recorded lung sounds in four positions on the chest of participants. In parallel, a panel of children's doctors (paediatricians) were trained and certified to interpret lung sounds by digital auscultation. Two paediatricians then interpreted and classified the recorded lung sounds, and their classifications were compared. If there was a disagreement, a third paediatrician acted as a mediator to help decide the classification. The panel of paediatricians were able to interpret lung sound recordings in at least three chest positions in 87.6% of children. The percentage of interpretable lung sounds was almost equal in both the pneumonia and non-pneumonia groups. I found that healthcare worker experience using the digital stethoscope is important for achieving successful measurements. Specifically, if health workers enrolled more children, their success rate of recording lung sounds increased compared to those who enrolled fewer children. The overall timing of using the digital stethoscope appeared generally feasible, as in more than half of all children the lung sounds were recorded (at all four positions) within one minute.

I also wanted to understand the diagnostic performance of an automated computerised system developed to classify abnormal lung sounds when compared to a panel of paediatricians (reference standard). The same process for classifying lung sounds by paediatricians was followed as previously described. The automated computerised system had a moderate level of accuracy (sensitivity = 61.8%, specificity = 60.7%) in identifying normal or abnormal lung sounds when compared to paediatricians. Both automated findings of normal and abnormal were aligned to a reasonable extent (sensitivity = 61.8%, specificity = 60.7%) with the paediatricians but not perfectly.

Lastly, I wanted to understand the perceptions of the community and healthcare workers regarding the new digital stethoscope. For this, we had discussions with the children's mothers, fathers and the head of the community (community leader), and also with the community health workers. I found that mothers and female community leaders were more aware of the device as compared to male members. Usually, fathers did not visit the health centre for child health care, so fathers were less aware of the digital stethoscope. I also found that most of the community health workers gave positive feedback about the digital stethoscope.

In conclusion, the thesis demonstrated that community health workers working at rural and first-level health facilities could record quality lung sounds from young children using the digital stethoscope. This thesis also found computerised lung sound classification system could differentiate normal or abnormal sounds compared to paediatricians with a moderate level of accuracy. Community health workers welcomed this new technology and agreed to use it in their work. There were some limitations observed in the new digital device and the automatic computerised algorithm to classify lung sounds, and if these can be addressed, the performance of the device should improve further. After improving the digital stethoscope performance on computerised sound analysis and validating it in another study, it will be important to conduct a study in various clinical settings and contexts involving multiple countries for digital auscultation to impact at a policy level.

Abstract

Background

Pneumonia is a major cause of death in children younger than five years, especially in low- and middle-income countries (LMICs). The World Health Organization (WHO) Integrated Management of Childhood Illnesses (IMCI) tool primarily relies on manually counting the respiratory rate and observing for clinical signs of respiratory distress to diagnose childhood pneumonia. This tool intentionally prioritised sensitivity over specificity to ensure children with possible bacterial disease received antibiotics. Community-based health workers play a vital role in the early identification and treatment of pneumonia cases using the IMCI tool in LMICs. The IMCI tool does not include lung auscultation in the diagnostic algorithm for pneumonia because of its high interobserver variability and subjectivity and the related difficulty in training healthcare workers with limited auscultation experience to effectively use a conventional stethoscope. Digital auscultation augmented by an artificial intelligence algorithm for classification of lung sounds has the potential to be both a feasible and accurate diagnostic tool for use by healthcare workers in LMICs. Operationally, the inclusion of digital auscultation findings in the current IMCI guidelines could increase the specificity of the IMCI algorithm to diagnose childhood pneumonia and help to reduce unnecessary use of antibiotics in LMICs.

Aim and Objectives

My PhD aims to evaluate the feasibility of digital auscultation use by frontline health workers in Bangladesh within the context of IMCI among 2 – 59 months old children, as well as its accuracy compared to a reference panel of paediatricians. The specific objectives are:

1. To synthesise the evidence on the performance of digital auscultation compared to human listeners in identifying adventitious lung sounds among children with pneumonia.
2. To assess whether lung sounds from children recorded by community health care providers (CHCPs) at community-level health facilities using a prototype digital stethoscope meet pre-defined quality thresholds established by experts. (‘pre-defined quality threshold’ was defined over 50% of the patients would have ‘quality’ lung sound recordings, ‘quality’ was defined as having at least 75% interpretable lung sound segments per patient according to the human listening panel (i.e., ≥ 3 out of 4 chest positions)).
3. To determine the diagnostic accuracy of an automated lung sound classification algorithm for identifying adventitious lung sound, compared with a reference panel of paediatricians.
4. To explore the acceptability of a prototype digital stethoscope (Feelix Smartscope) among potential end-users (CHCPs, carers and community leaders).

Methods and Results

1. **Digital auscultation as a diagnostic aid to detect childhood pneumonia – systematic review**

I conducted a systematic review by searching eight bibliographic databases and citation indices (MEDLINE, Embase, CINAHL Plus, Web of Science, Global Health, IEEExplore database, Scopus, and ClinicalTrial.gov) and reference lists of included studies. Reported methodologies/approaches and performance metrics for classifying adventitious lung sounds varied widely across the included ten studies. All included studies except one reported the overall diagnostic performance of the digital auscultation/computerised lung sound analysis to distinguish adventitious lung sounds, irrespective of the disease condition or age of the participants. The reported accuracy for classifying adventitious lung sounds in the included studies varied from 66.3% to 100%. However, it remained unclear to what extent these results would be applicable for classifying adventitious lung sounds in children with pneumonia. This systematic review found very limited evidence on the diagnostic performance of digital auscultation to diagnose pneumonia in children.

2. **Ability of community health workers to record quality lung sounds from children younger than five years at first-level facilities – prospective observational research study**

A total of 990 children aged 2-59 months with possible pneumonia (cough or difficult breathing) were enrolled by nine CHCPs from selected nine community clinics in Zakiganj sub-district of Sylhet District, Bangladesh. Of them, 389 children were classified as having “any” pneumonia (pneumonia or pneumonia with respiratory danger signs), and 601 children had only cough or difficult breathing. Using a prototype digital stethoscope (Feelix Smartscope), CHCPs recorded lung sounds in four sequential chest positions – two posterior and two anterior positions – ~10 seconds in each position, allowing 3 to 4 complete breath cycles (inspiration and expiration) per recorded chest position. Each child's recorded lung sounds were then classified by two paediatricians trained to a standardized classification protocol and who were also blinded to the clinical findings. The paediatrician classifications were compared, and if not in agreement, a third trained paediatrician reader served as an arbitrator. A quality recording was defined as a child with at least three out of four chest positions assessed as interpretable by the listening panel. An interpretable chest position was classified by the listening panel as any of the following: no wheeze and no crackle, wheeze only, crackle only, or wheeze and crackles. Among all children, CHCPs recorded three or more chest positions in more than 98% of participants. The paediatrician listening panel classified 87.6% (95% CI: 85.4%, 89.6%) of all children, 88.2% (95% CI: 84.5%, 91.2%) of those with any pneumonia and 87.2% (95% CI: 84.3%, 89.8%) without pneumonia as interpretable in at least three chest positions. Among CHCPs, we observed a linear relationship between the number of children enrolled and the percentage of successfully recorded sound files from ≥3 chest positions. On average, the rate of success increased by 1% with every ten new enrolments by CHCPs. The proportion of children who were cooperative and quiet throughout the lung sound recordings was 81.6% (95% CI: 77.3%, 85.3%) among those with any pneumonia and 78.7% (95% CI: 75.1%, 81.9%) in children with no pneumonia. In the majority of children (56.6%) lung sounds were recorded in all four positions within one minute.

3. **Diagnostic accuracy of automated computerised lung sound analysis to identify adventitious lung sounds compared to the paediatrician listening panel – prospective observational research study**

Each child's lung sound recordings were randomly sent to two listening panel members, and if classifications did not agree, a third reader served as the arbitrator. The listening panel classified recorded lung sounds into normal (no wheeze and no crackles), crackles, wheeze, crackles and wheeze, or uninterpretable. An automated CLSA algorithm classified recorded sounds into the same categories, which were compared with the human panel classifications. Of 990 enrolled children, 867 had ≥3 chest positions interpretable by the listening panel. Compared to the consensus listening panel, the CLSA had a moderate sensitivity (61.8%; 95% CI: 55.7%, 67.6%) and a moderate specificity (60.7%; 95% CI: 56.6%, 64.6%) for classifying lung sounds as adventitious or normal. The agreement was low between panel classifications and CLSA classifications (Cohen's kappa = 0.20; 95% CI: 0.14, 0.26) of the recorded lung sounds.

4. **Acceptability of a prototype digital stethoscope (Feelix Smartscope) among potential end-users – qualitative study**

Four focus group discussions (FGDs) were conducted with beneficiaries (mother, father and community leaders) and service providers (CHCPs) who used the Feelix Smartscope prototype. Verbatim transcripts were prepared, and translations were completed. Coding was executed in Microsoft Excel, and relevant quotes were extracted to ascertain the emerging themes. Two researchers coded the dataset independently to ensure validity, and inconsistencies were resolved through discussion. Mothers were more aware of the digital stethoscope than fathers. CHCPs and the female community leaders were aware of the stethoscopes and accepted the stethoscope. Most CHCPs had positive perceptions of the digital stethoscope. They appreciated stethoscope training as they learned about new technology and diagnostic approaches. The users mentioned several technical shortcomings of the prototype device.

Conclusions

This thesis demonstrated that CHCPs at rural, first-level clinics in Bangladesh could feasibly record quality lung sounds using a novel digital stethoscope prototype (Feelix Smartscope) without a substantial increase in their workload. This study also showed an initial version of an automated algorithm could classify lung sounds as either adventitious or normal with moderate sensitivity and moderate specificity when using a paediatrician listening panel as the reference. The agreement was low between panel classifications and CLSA classifications (Cohen's kappa = 0.20) of the recorded lung sounds. CHCPs found the new technology generally acceptable. This thesis also highlights the potential for addressing current limitations that could be overcome by refining both device itself and the automated algorithms. After improving the stethoscope addressing the issues identified in this study and improving the automated sound classification algorithm, a validation study is required.

Chapter 1 Introduction

1.1 Epidemiology of childhood pneumonia

Despite a significant decline in the mortality of children younger than five years globally over the years, it remains a significant public health concern (1). There was a 59% decrease in the under-five mortality rate from 93 deaths per 1,000 live births in 1990 to 39 in 2018 (2). About 38.9 children per 1000 live births died before their fifth birthday in 2017 (3). There were 5.30 million deaths of under-five year old children in 2019 worldwide (4). Nigeria, India, Pakistan, the Democratic Republic of the Congo, Ethiopia, China, Indonesia, Tanzania, Bangladesh, and Angola reported the highest mortality tolls. These ten countries were responsible for about 3.15 million deaths, equivalent to 59.5% of all child deaths worldwide (4). The majority of these deaths are caused by preventable conditions such as pneumonia, diarrhoea, malaria, and malnutrition (2, 4).

There has been a decline in pneumonia incidence, morbidity, and mortality over the past several years (5). However, childhood pneumonia is one of the leading causes of death in children younger than five years globally (4). In low- and middle-income countries (LMICs), approximately 102 million child pneumonia episodes were estimated in 2015, with an incidence of 150 episodes per 1000 child-years (5). The World Health Organization (WHO) African Region and the South-East Asia Region contribute more than 75% of total deaths from pneumonia in children younger than five years (6). Pneumonia is also an important cause of hospital admission of children (7), and about 16.4 million children younger than five years in LMIC were admitted to hospital due to pneumonia in 2015 (6).

Bangladesh has significantly reduced child death rates in the last decade. In the period from 2011 to 2022, the child mortality rate decreased from 48 to 31 deaths per 1000 live births, according to the Bangladesh Demographic Health Survey (BDHS) 2022 (8). Even so, the death rate for children under five is among the highest in the world (2). In 2015, there were 4.2 million cases of pneumonia, with an incidence of 277 per 1000 children per year (6). A population-based study was conducted in about 5000 households in an urban slum in Dhaka, Bangladesh, with children younger than five years from 2004 to 2008. This study estimated that the annual incidence of pneumonia among children younger than five years was 360 episodes per 1000 child-years (9). Pneumonia is the primary infectious killer of children in Bangladesh, accounting for about 17% of all deaths (10). In 2015, pneumonia was responsible for more than 17,000 child deaths, with a mortality rate of 5.4 per 1,000 live births in Bangladesh (6). A prospective verbal autopsy study from 2008 to 2012 to identify pneumonia mortality in rural Bangladesh reported that the leading cause of mortality, accounting for 26.4% of all deaths, was pneumonia (11). Two population-based studies conducted between 2004 to 2009 reported a 2% to 4% case-fatality rate among children younger than five years due to pneumonia in Bangladesh. Pneumonia is a primary reason for hospitalisation for children younger than five years in Bangladesh. The most common diagnosis among the 156,847 admitted children found during surveillance conducted at seven hospitals in Bangladesh from May 2004 through April 2007 was pneumonia (32%) (12). A study conducted in an urban Dhaka slum in 2004-2008 reported that 7.3% of children with pneumonia were hospitalised (9).

1.2 Pathophysiology and aetiology of pneumonia

Pneumonia is a pathological change resulting in fluid-filled alveoli, and there are multiple aetiologies; most are infectious and mainly of bacterial or viral origin. It typically begins with an infection of the nasopharyngeal mucosa; the infection gradually spreads into the lower respiratory tract. Bacterial pneumonia has the potential to be transmitted through the bloodstream, leading to severe systematic infection. The symptoms and signs of pneumonia include cough, rhinorrhoea, dyspnoea, tachypnoea, crackles, wheeze, fever, headache, malaise/lethargy, and thoracic pain (13-20).

The most common causes of bacterial pneumonia in children are *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). The other common bacteria are non-typable *Haemophilus influenzae*, *Streptococcus aureus*, non-typhoid *Salmonella*, and *Mycobacterium tuberculosis*. The most frequent viral cause of pneumonia is the respiratory syncytial virus (RSV). Other viruses include rhino, adeno, influenza A and B, parainfluenza, corona, boca, human metapneumovirus and adenovirus (21-23). A systematic review to estimate the burden of childhood pneumonia for 192 countries in 2010-11 found that in around 29% of all episodes, RSV is the most prevalent pathogen in pneumonia cases (24). An estimate shows that globally 489 million lower respiratory infection (LRI) episodes occurred in 2019, leading to a total of 2·5 million deaths (25). Another systematic review to estimate the burden of LRTI due to RSV reported that globally 33.1 million episodes of RSV-related ALRI happened and about 59,600 in-hospital deaths among children younger than five years in 2015 (26). The majority of these estimates, however, were made before the pneumococcal conjugate vaccine (PCV) and Hib vaccine were made available in countries with a high prevalence of pneumonia. The introduction of PCV into national immunisation programmes led to a substantial decrease in the incidence and severity of pneumonia (27). As a result, the proportional contribution of RSV and other viruses in cases of childhood pneumonia has increased (28). A pilot study from the PERCH study site reported that a bacterial pathogen was identified in 23% of cases, while a viral pathogen was identified in 83% of cases (with 32% being RSV and 24% being rhinovirus) (29). The PERCH study on pneumonia aetiology in Bangladesh site reported most predominant cause of pneumonia was viral, about 77.7%, and RSV was the primarily responsible virus (31.2%). Among bacterial pathogens, *Mycobacterium tuberculosis* contributed 3.6%, *Enterobacteriaceae* 3.0%, and *Streptococcus pneumoniae* 1.8% (30).

1.3 Diagnosis of pneumonia – Integrated Management of Childhood Illness

Several studies were conducted during the 1980s to examine the sensitivity and specificity of the clinical features of pneumonia in developing countries to justify the use of antibiotics by minimally trained providers in resource-poor settings (31-34). In the mid-1990s, the WHO and UNICEF developed a tool called Integrated Management of Childhood Illness (IMCI) based on available evidence. This IMCI tool has been the foundation of pneumonia management in LMICs ever since (35, 36).

The IMCI tool is designed to address the major causes of childhood deaths and focuses on improving service provision and quality of care at first-level health facilities (35). The first-level health facilities are the first contact of community people, provide primary care, mainly maternal and child health, family planning, immunisation, and are staffed with minimally trained community health workers to registered nurses, which varies from country to country. The IMCI algorithm helps care providers take a child's history, do a clinical assessment, classify the child's illnesses, and provide treatment in a sequential way. As per the first version of the IMCI algorithm (published in 1995) (37), a child presenting with cough or difficulty breathing was to be assessed clinically for the presence of any danger signs. According to the algorithm, the child was classified into three treatment categories (Figure 1.1): (i) children with only cough or cold were treated with no antibiotics, (ii) children with pneumonia (age-specific fast breathing alone) were treated with oral antibiotics, and (iii) children with severe pneumonia (lower chest wall indrawing) or very severe disease (presence of danger signs) were referred to hospital (15).

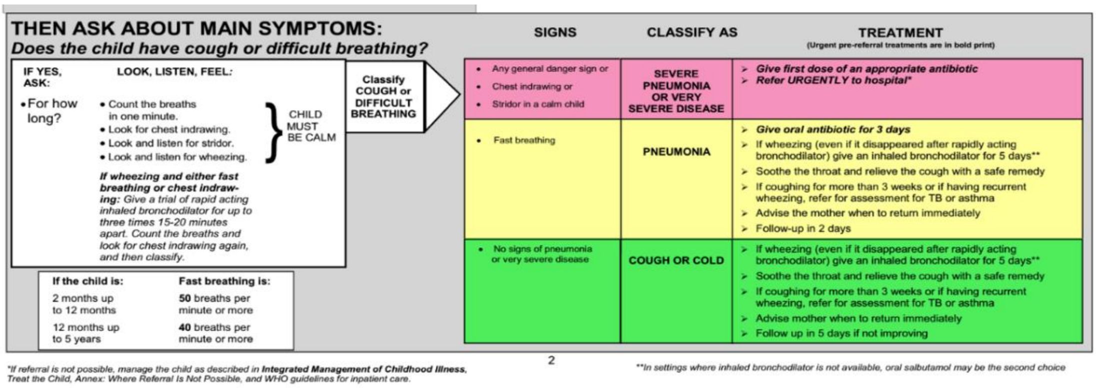

Figure 1.1 Clinical assessment and classification of children aged 2-59 months presenting with cough or difficult breathing as per the WHO IMCI chart booklet 1995 (37)

Two studies reported that the treatment failure rate among children with chest indrawing without any danger signs who were treated with oral antibiotics was non-inferior to parenteral antibiotics (38, 39). Based on these studies, other relevant evidence about the use of antibiotics in childhood pneumonia (40-43) and expert consultation, WHO revised the IMCI algorithm in 2014 (17). As per the modified IMCI algorithm, any child (2 months to 59 months) with age-specific fast breathing and/or chest indrawing without any danger signs is classified as pneumonia and treated with oral antibiotics (Figure 1.2).

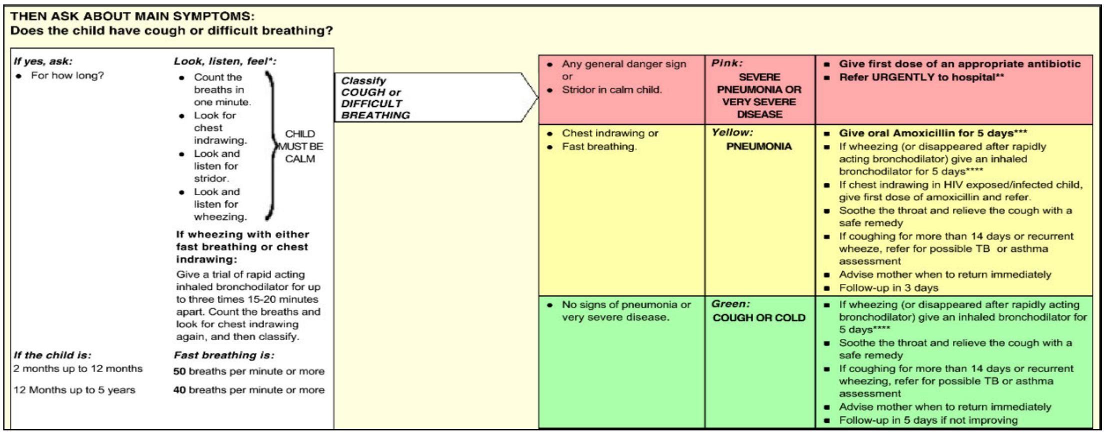

Figure 1.2 Clinical assessment and classification of children aged 2-59 months presenting with cough or difficult breathing as per the IMCI chart booklet 2014 (17)

An illustrative comparison of the 2008 and 2014 versions of IMCI algorithms is presented in Figure 1.3.

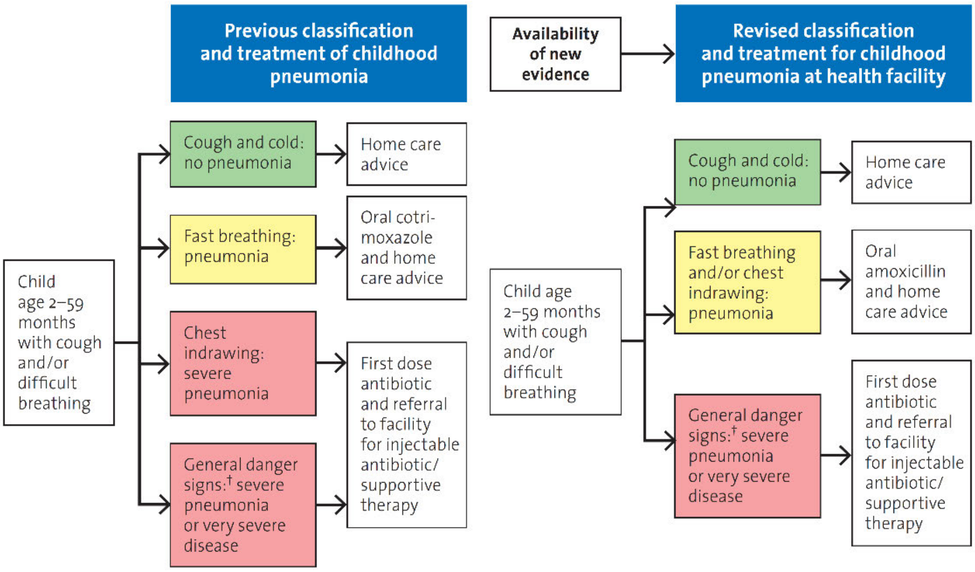

Figure 1.3 Difference in classification and treatment of children aged 2-59 months presenting with cough or difficult breathing as per IMCI guidelines 2008 (44) and 2014 (17)

Although the WHO has recommended considering chest in-drawing as one of the signs of pneumonia, a multisite pooled analysis on the treatment of pneumonia with chest in-drawing reported an average treatment failure rate of 8.5% on day-6, even in controlled environments in clinical trials (45). The treatment failure rates varied between as low as 6.4% in Ghana and as high as 22% in Pakistan among the different studies (45). This implies that some pneumonia cases with chest indrawing required inpatient care with special support in addition to oral antibiotics as recommended by WHO in 2014. Moreover, IMCI classifications of childhood illness greatly depend on the clinical assessment skills of service providers. Any variation in subjective assessment of clinical signs (danger signs, fast breathing, and chest indrawing) may lead to misclassification, which subsequently leads to inappropriate management of illness and potential treatment failure for locally managed pneumonia cases (46, 47). As IMCI is designed to use in resource-limited outpatient settings through minimally trained service providers, the risks of potential errors in clinical assessment and classification are substantial.

The IMCI tool has proven to be one of the most important childhood pneumonia interventions for low-resource settings to date, and reductions in childhood mortality in LMICs have been attributed to its implementation (48-52). A meta-analysis in 2003 by Sazawal and Black reported that the implementation of the community case management of pneumonia reduced pneumonia mortality by 36% among children younger than five years (52).

1.4 Issues in the current IMCI algorithm to diagnose pneumonia

Although the implementation of the IMCI algorithm in LMICs has significantly contributed to improving child survival (53), there remains room for improvement. Firstly, the IMCI algorithm is highly sensitive but has low specificity; the specificity needs to be improved to rationalise the use of antibiotics in children with possible pneumonia, (17, 35) particularly since in settings with PCV and Hib vaccines the underlying aetiology is most probably predominantly viral. The performance of the IMCI algorithm was evaluated in four studies in Kenya, (54) Gambia, (55) Uganda, (56) and Ethiopia (57). All those studies used paediatrician classification with radiography to confirm the diagnosis, apart from the study conducted in Ethiopia, which relied on paediatrician classification based on physical examination. The sensitivity of the pneumonia classification ranged from 76% to 97%, while specificity ranged from 49% for pneumonia without any danger sign to 89% for severe pneumonia (58). Mulholland et al. (34) reported high sensitivity for midwives identifying a binary yes/no classification of age-specific tachypnoea, but specificity was low (in Manila, Philippines: specificity was 39% for respiratory rate ≥ 40, 54% for respiratory rate ≥ 40 to 50, and 78% for respiratory rate ≥ 50; in Mbabane, Swaziland: 60%, 76%, and 89% respectively) compared to the paediatrician’s classification. Hazir et al. demonstrated that 82% of children with IMCI-defined pneumonia (age-specific tachypnoea) had normal chest radiographs (59). Thus, although the IMCI algorithm classifies many children as having pneumonia, these data suggest that not all of them require antibiotic treatment. Secondly, the IMCI algorithm does not include lung auscultation in the pneumonia classification for frontline healthcare workers (17). The exclusion of auscultation likely stems from its high inter-observer variability and subjectivity, regardless of healthcare providers training level (60-64). Miguel Palafox et al. measured the sensitivity and specificity of clinical signs of pneumonia using a chest radiograph as the gold standard (65). The sensitivity and specificity of age-specific tachypnoea were 74% and 67%, respectively; tachypnoea and chest indrawing combinedly slightly increased the specificity to 69%, but tachypnoea and alveolar crackles together further increased the specificity to 83% (65). Another study in India shows crackles only had sensitivity and specificity of 69.7% and 90.6% respectively to predict X-ray confirmed childhood pneumonia (66).

1.5 Nomenclature of respiratory sounds

Various nomenclatures are used to describe an adventitious respiratory sound (67). The American College of Chest Physicians – American Thoracic Society (ACCP-ATS) published a report in 1975 on pulmonary nomenclature to provide classification terminology used for adventitious respiratory sounds (68). At the 10th meeting of the International Lung Sounds Association (ILSA) in 1985, the terms wheeze, fine and coarse crackles, and rhonchi were agreed upon as the terminology to describe adventitious lung sounds (69). The ACCP-ATS committee recommended that discontinuous adventitious lung sounds are described as crackles, high-pitched continuous adventitious lung sounds are described as wheeze, and low-pitched continuous adventitious lung sounds are described as rhonchi. The committee also suggested that the term "rales" was considered undesirable because it had historically been used to describe both continuous and discontinuous adventitious lung sounds (70). The nomenclature committee recommended the terms "fine" and "coarse" be used to qualify crackles with a physiologic or acoustic basis (e.g., low-pitched, high-pitched, fine, coarse) rather than the traditional terms (e.g., dry, wet, sonorous, sibilant, etc.). The clinical characteristics of normal and adventitious lung sounds are summarised in Table 1.1 (71).

Table 1.1 The clinical characteristics of normal and adventitious lung sounds

(adopted from Bohadana et al. 2014 (71))

Respiratory Sound	**Clinical Characteristics**	**Clinical Correlation**
Normal tracheal sound	Hollow and non-musical, clearly heard in both phases of the respiratory cycle.	Transports intrapulmonary sounds, indicating upper-airway patency; can be disturbed (e.g., become more noisy or even musical) if upper-airway patency is altered; used to monitor sleep apnoea; serves as a good model of bronchial breathing
Normal lung sound	Soft, non-musical, heard only on inspiration and on early expiration	Is diminished by factors affecting sound generation (e.g., hypoventilation, airway narrowing) or sound transmission (e.g., lung destruction, pleural effusion, pneumothorax); assessed as an aggregate score with normal breath sound; rules out clinically significant airway obstruction
Bronchial breathing	Soft, non-musical, heard on both phases of the respiratory cycle (mimics tracheal sound)	Indicates patent airway surrounded by consolidated lung tissue (e.g., pneumonia) or fibrosis

Respiratory Sound	**Clinical Characteristics**	**Clinical Correlation**
Stridor	Musical, high-pitched, may be heard over the upper airways or at a distance without a stethoscope	Indicates upper-airway obstruction; associated with extra thoracic lesions (e.g., laryngomalacia, vocal-cord lesion, lesion after extubation) when heard on inspiration; associated with intrathoracic lesions (e.g., tracheomalacia, bronchomalacia, extrinsic compression) when heard on expiration; associated with fixed lesions (e.g., croup, paralysis of both vocal cords, laryngeal mass or web) when biphasic
Wheeze	Musical, high-pitched; heard on inspiration, expiration, or both	Suggests airway narrowing or blockage when localized (e.g., foreign body, tumour); associated with generalized airway narrowing and airflow limitation when widespread (e.g., in asthma, chronic obstructive lung disease); degree of airflow limitation proportional to number of airways generating wheezes; may be absent if airflow is too low (e.g., in severe asthma, destructive emphysema)

Respiratory Sound	**Clinical Characteristics**	**Clinical Correlation**
Rhonchus	Musical, low-pitched, similar to snoring; lower in pitch than wheeze; may be heard on inspiration, expiration, or both	Associated with rupture of fluid films and abnormal airway collapsibility; often clears with coughing, suggesting a role for secretions in larger airways; is non-specific; is common with airway narrowing caused by mucosal thickening or oedema or by bronchospasm (e.g., bronchitis and chronic obstructive pulmonary disease)
Fine crackle	Non-musical, short, explosive; heard on mid-to-late inspiration and occasionally on expiration; unaffected by cough, gravity-dependent, not transmitted to the mouth	Unrelated to secretions; associated with various diseases (e.g., interstitial lung fibrosis, congestive heart failure, pneumonia); can be the earliest sign of disease (e.g., idiopathic pulmonary fibrosis, asbestosis); may be present before detection of changes on radiology
Coarse crackle	Non-musical, short, explosive sounds; heard on early inspiration and throughout expiration; affected	Indicates intermittent airway opening, may be related to secretions (e.g., in chronic bronchitis)

Respiratory Sound	Clinical Characteristics	Clinical Correlation
	by cough; transmitted to the mouth	
Pleural friction rub	Non-musical, explosive, usually biphasic sounds; typically heard over basal regions	Associated with pleural inflammation or pleural tumours
Squawk	Mixed sound with short musical component (short wheeze) accompanied or preceded by crackles	Associated with conditions affecting distal airways; may suggest hypersensitivity pneumonia or other types of interstitial lung disease in patients who are not acutely ill; may indicate pneumonia in patients who are acutely ill

1.6 Evolution of stethoscope

Prior to the development of the stethoscope, doctors performed auscultation by placing their ear directly on the patient to listen to internal sounds. Rene Theophile Hyacinthe Laennec (1781–1826) invented the first version of a stethoscope in 1816 at the Necker-Enfants Malades Hospital in Paris (72). After the invention of Laennec's first version of the stethoscope, which was monoaural, the next major progress did not happen until the year 1851 when Arthur Leared, an Irish physician, invented the binaural version of the stethoscope (73). During the 1960s, Dr David Littmann re-engineered the stethoscope and for the first time introduced a two-sided chest piece (bell and diaphragm) capable of listening to both high-pitched sounds as well as low-pitched sounds (74). In 1998, the company 3M first introduced an electronic version of the stethoscope. After that, further improvements have occurred, and currently, digital stethoscopes can amplify sound up to 100 fold, filter background noises, record sounds and can transfer sounds to smartphones, tablets, and computers for additional post-processing (75).

1.7 Digital stethoscope and automated lung sound analysis

A digital stethoscope can convert an acoustic sound to electronic signals, which can be further amplified for optimal listening. These electronic signals can be further processed and digitalised to transmit to a computer (75). Automatic lung sound analysis, aiming to overcome the limitations of conventional auscultation, has been the recent focus of a significant amount of research, and some commercial systems are already in the market (76, 77). The National Institute for Health Research provided a list of already available commercial systems (78), such as the *Wheezometer* (79), the *Wholter (80),* the *VRI* (81), the *LSA-2000* (82), the *LEOSound (83)* and the multichannel *STG (84)* and STG for PC (85) or handheld STG (86). All the above-listed devices are typically large and complex, apart from Wheezometer; though it can provide a spot-check but cannot monitor lung sounds continuously. Ramanathan et al. recently conducted a review to identify available digital stethoscopes used in paediatric medicine and reported six digital stethoscopes (Table 1.2) currently used in paediatric medicine (87).

Table 1.2 Commercially available digital stethoscopes (adopted from Ramanathan et al.) (87)

Stethoscope name	Image	Technical properties
Littman Electronic Stethoscope Model 3200/400 (3M, Maplewood, MN, USA) (88)		Sound amplification: 24x acoustic Filters: Ambient noise reduction and frictional noise dampening (85% of ambient noise removal) Offers a remote TeleSteth system
Thinklabs One Digital Stethoscope (Thinklabs, Centennial, CO, USA) (89)		Sound amplification: 100x acoustic Filters: Multiple frequency filters Offers connection to a smartphone app
Clinicloud Digital Stethoscope (Clinicloud, Melbourne, VIC, Australia) (90)		Sound amplification: None Filters: None Records at 44.1 kHz, 16 bit
ViScope Visual Stethoscope (HD Medical, Silicon Calley, CA, USA) (91)		Sound amplification: 30x acoustic Filters: Tunable filters for heart sounds and murmurs

Stethoscope name	Image	Technical properties
		Offers real-time phonocardiograph display
EkoCore and EkoDuo Digital Stethoscope (Eko Devices, Berkeley, CA, USA) (92)		Sound amplification: 40x acoustic Filters: None Offers toggle on/off for electronic and acoustic auscultation
Welch Allyn Meditron/Meditron M30 Stethoscope (Meditron ASA, Oslo, Norway) (93)		Sound amplification: 30x acoustic Filter: Multiple frequency settings for focused auscultation

1.8 Advantages of the digital stethoscope

Acquisition of different skills is necessary to perform auscultation, and the digital stethoscope has advantages over conventional analogue stethoscopes in different stages of auscultation:

1. Positioning (identification of the auscultation area based on anatomical references): An analogue stethoscope requires the proper placing of the diaphragm or bell in the correct positions of the human body to listen to internal body sounds. More modern digital stethoscopes are more accommodating, as they can convert the acoustic wave into electric signals and replace the double-sided chest piece (diaphragm and bell)

with one interface that uses transducers to convert acoustic signals to electric signals. Moreover, the chest piece is packed with transducer arrays to achieve a uniform sensitivity over the entire active area; this design delivers a strong signal even when the chest piece is not placed in precisely the correct position (94). This advantage is essential for minimally trained healthcare providers.

2. Listening (the ability to hear a sound and understand that it is the correct sound): Conventional auscultation with an analogue stethoscope requires a quiet environment, ideally with the patient in a quiet position. This is difficult in hospitals, especially in LMICs where the number of patients is much higher than the capacity and outdoor services are provided in crowded conditions. As a result, the patient examination room could be filled with chattering people, ringing phones, and whirring fans; most importantly, the child being examined might be crying. Digital stethoscopes could improve listening capability through noise-cancelling technologies (10, 95). Limitations of the human auditory system range from 20 Hz to 20 kHz for young adults, and the range shrinks after middle age (96). This is also a drawback in conventional auscultation using an analogue stethoscope. Importantly, a digital stethoscope can amplify sounds up to 100 fold (89).
3. Interpreting (identifying and understanding the sounds by integrating the auscultation signs with the pathophysiology): A lot of experience is required to interpret body sounds, and inter-rater variability is high regardless of the healthcare provider's training level (63). Machine

learning techniques can be used in digital stethoscopes to auto-analysis of sounds (76) to make a diagnosis or treatment decision (86).

In sum, a digital stethoscope is easy to place on a patient's auscultation area, improves listening capacity by amplifying sounds and filtering ambient noises, and also allows the recording of sounds, replay, and computerised analysis.

1.9 The rationale of the study

The burden of childhood pneumonia is high in LMICs where the health system is either not properly functioning, or there is a lack of trained providers, or the quality of care is low, or there is a combination of these factors. The WHO IMCI is an approach in which Community Healthcare Workers (CHWs) deliver primary healthcare services in the community setting, including childhood pneumonia treatment (15). The IMCI tool is considered highly sensitive but relatively less specific in order to ensure that children with possible pneumonia receive antibiotic treatment (17). As a result, while this tool misses few children with pneumonia (high sensitivity), many children who do not have pneumonia incorrectly receive antibiotics (low specificity), resulting in antibiotic overuse. Innovations are needed to improve the specificity of the IMCI pneumonia criteria, especially considering ongoing concerns about rising antibiotic resistance (97). The IMCI tool did not include lung auscultation in the pneumonia algorithm for frontline healthcare workers (17). The exclusion of auscultation likely stems from its high inter-observer variability and subjectivity, regardless of the healthcare provider's training level (60-64). Traditional stethoscopes attenuate higher frequency sounds, like wheezing and crackles, yet transmit ambient noises and tubular resonance effects (62, 86). Automated real-time classification of lung sounds or digital auscultation by electronic stethoscopes may overcome these limitations (98). Digital auscultation has the potential to be a highly specific respiratory diagnostic tool that is feasible for use by community-based frontline healthcare workers in LMICs. Moreover, the inclusion of adventitious sound classifications in the current IMCI algorithm can potentially increase the specificity of pneumonia diagnosis (65) in LMICs to reduce the unwanted use of antibiotics. A digital stethoscope, Feelix Smartscope, was developed by Johns Hopkins University and Sonavi Labs, that can automatically distinguish healthy people from those with pneumonia with an accuracy of 87% (94), which has an automated interpretation algorithm of adventitious lung sounds of children. The Feelix Smartscope has been successfully validated against Thinklabs in the Pediatric Emergency Department at Johns Hopkins University Hospital and rural community clinics in Sylhet, Bangladesh and has demonstrated comparable results (99, 100).

Table 1.3 Average spectra and spectrotemporal feature values and statistics (data from noisy Community Clinics in Bangladesh) (100)

Feature	Feelix Mean	Thinklabs Mean	p-value
Peak frequency	122 Hz	132 Hz	0.030
Peak Max	3.65×10^3	6.78×10^3	<0.001
Peak Width	7.20 Hz	6.29 Hz	0.060
Spectral Slope	-0.152 dB/oct	-0.127 dB/oct	<0.001
Power Regression Line	1.29×10^3	2.26×10^3	<0.001
Power Ratio	-35.68	-23.25	<0.001
Bandwidth	1.36 c/o	1.42 c/o	<0.001
Dynamics (Positive)	8.39 Hz	8.25 Hz	<0.001
Dynamics (Negative)	5.64 Hz	5.81 Hz	<0.001

Table 1.4 Average spectra and spectrotemporal feature values and statistics (data from JHU Hospital) (100)

Feature	Feelix Mean	Thinklabs Mean	p-value
Peak frequency	121 Hz	95 Hz	<0.001
Peak Max	2.90×10^3	4.93×10^3	<0.001
Peak Width	7.31 Hz	6.49 Hz	0.176
Spectral Slope	-0.155 dB/oct	-0.153 dB/oct	0.590
Power Regression Line	1.20×10^3	1.18×10^3	0.779
Power Ratio	-66.41	-39.45	0.435
Bandwidth	1.36 c/o	1.36 c/o	0.708
Dynamics (Positive)	8.44 Hz	8.45 Hz	0.640
Dynamics (Negative)	5.61 Hz	5.63 Hz	0.876

The Feelix Smartscope was designed to be used in non-traditional clinical settings, such as rural or walk-in clinics, at home, or in low-resource areas, by trained or untrained personnel with the below advantages:

1. Feelix Smartscope has uniformly distributed highly sensitive five microphones array on the stethoscope head, enhancing signal sensitivity by uniformly distributing highly sensitive electret microphone arrays across the diaphragm. This microphone array provides a broad, flat frequency spectrum, which is key for identifying higher frequency sounds like wheeze and crackles. Figure 1.4 shows a comparison of Feelix Smartscope with other devices (ADC Adscope and Thinklabs one) that display signal power as a function of location on the stethoscope using a surface sensitivity heat map to show a more uniform surface than other devices (99). So, it does not require precise

placement on the body, allowing healthcare workers with minimal training to use the device effectively.

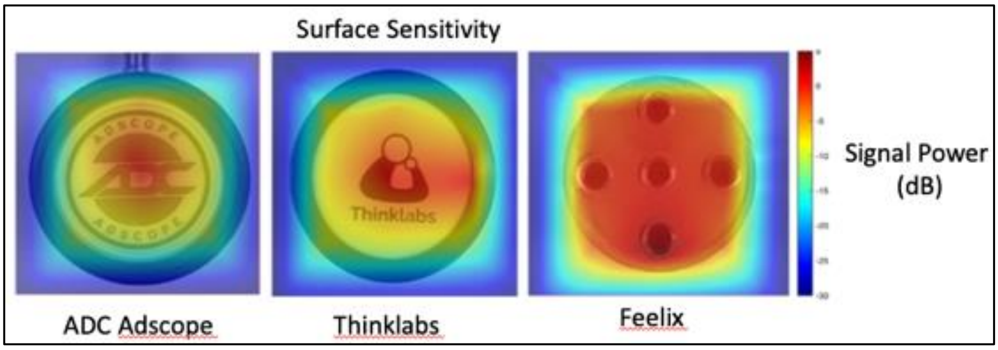

Figure 1.4 Sensitivity map of a traditional stethoscope head (left), sensitivity map of the Thinklabs One electronic stethoscope head (centre), and sensitivity map of the Feelix smart stethoscope (right) in decibels as compared to the power at the centre position(99)

2. It is the first digital stethoscope to offer an on-board implementation of an adaptive noise suppression algorithm to counter background noises without relying on an internet connection. An external facing microphone enables use of the patented noise filter to permit high-quality sound capture in loud environments with noises overlapping in time and frequency with lung sounds, which is important in non-traditional settings such as rural busy and crowded community clinics. In a laboratory evaluation of Feelix against Thinklabs One Digital Stethoscope and Littman Electronic Stethoscope, Feelix outperformed all devices across all simulated noise environment types. In 2020, the FDA awarded the Feelix device and its adaptive noise suppression algorithm with a 510(k) clearance (99).

3. Its 3.7 V and 250 amps/hour rechargeable battery can provide power >20 hours of use, which is important in rural communities with unreliable electricity.
4. The device mitigates movement artefacts and tubular resonance by using an ergonomic design to better secure the device on the child's chest. It also eliminates the rubber stethoscope tubing, a source of ambient noise and friction contamination. Notably, the device includes an integrated external facing microphone that captures simultaneous environmental noise to the lung sound recording and removes the unwanted ambient noises through an adaptive spectral subtraction schema.
5. The Feelix Smartscope also permits onboard data storage of up to 50 recordings with a micro SD card. That allows to transfer the recorded sound at convenience to a laptop or tablet.
6. Lung sound abnormality detection: A machine learning Computerised Lung Sound Analysis (CLSA) model was developed, called 'MixedNet' to find patterns and detect abnormal lung sounds. MixedNet is a lightweight, robust convolutional neural network using filters to identify spectrogram features (time-frequency sound representations) to model the relationships between the lung sound (input) and the sound classification (output). MixedNet uses shifting filters to search for learned signal features in any new data (i.e., lung sounds) presented to the network. Small convolutional filters were introduced to enhance computational efficiency. When applied to a dataset of ~1,000 young

children an early iteration of the algorithm achieved 87% accuracy distinguishing between normal and abnormal lung sounds compared to a paediatrician reference (98). MixedNet performed with 91% accuracy validation against a physician reference on ~10,000 recordings from 5 diverse datasets of patients (101, 102). MixedNet was designed for device deployment and does not require internet connection. Overall, Feelix is designed to run noise suppression and abnormality detection in real time, with <50ms delay for noise suppression and a classification decision in ~3 seconds.

This device has the potential to be used by frontline health workers in LMICs. I used this Feelix Smartscope in my PhD.

Chapter 2 Aim and objectives

2.1 Aim

To evaluate the feasibility of digital auscultation, use by frontline health workers in Bangladesh within the context of IMCI among 2 - 59 months old children, as well as the accuracy of an automated lung sound classification algorithm compared to a reference panel of paediatricians.

2.2 Objectives

1. To synthesise the evidence on the performance of digital auscultation, compared to human listeners, in identifying adventitious lung sounds among children with pneumonia.
2. To assess whether lung sounds from children recorded by community health care providers (CHCPs) at community-level health facilities using a prototype digital stethoscope meet pre-defined quality thresholds established by experts. (‘pre-defined quality threshold’ was defined over 50% of the patients would have ‘quality’ lung sound recordings, ‘quality’ was defined as having at least 75% interpretable lung sound segments per patient according to the human listening panel (i.e., $\geq$ 3 out of 4 chest positions)).
3. To determine the diagnostic accuracy of an automated lung sound classification algorithm for identifying adventitious lung sounds, compared with a reference panel of paediatricians.
4. To explore the acceptability of a prototype digital stethoscope (Feelix Smartscope) among potential end-users (CHCPs, carers and community leaders).

Chapter 3 Digital auscultation as a diagnostic aid to detect childhood pneumonia

One of the objectives of my thesis was to synthesise the evidence on detecting adventitious lung sounds by digital auscultation for childhood pneumonia diagnosis. The work presented in this chapter was published in the Journal of Global Health in 2022 (Ahmed S, Saima S, Khan AM, Islam MS, Habib GM, McLane IM, McCollum ED, Baqui AH, Cunningham S, Nair H. Digital auscultation as a diagnostic aid to detect childhood pneumonia: A systematic review. J Glob Health 2022;12:04033).

I conceptualised and led the systematic literature review with contributions from Saima Sultana (SS), Ahad Mahmud Khan (AMK), Mohammad Shahidul Islam (MSI), GM Monsur Habib (GMMH), Harish Nair (HN), Steve Cunningham (SC), Eric D McCollum (EDM). I developed the search strategies for all eight databases with support from Marshall Dozier, Academic Support Librarian at the University of Edinburgh, UK. I wrote the first draft with inputs from HN, SC, and EDM. All other named authors of this publication critically reviewed the initial manuscript. All authors read and approved the final manuscript. The full text of the publication is attached below. Some contents have been organised to comply with the format of this thesis.

URL: *https://jogh.org/2022/jogh-12-04033*

Digital auscultation as a diagnostic aid to detect childhood pneumonia: a systematic review

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3.1 Abstract

3.1.1 Background

Frontline healthcare workers use World Health Organization Integrated Management of Childhood Illnesses (IMCI) guidelines for child pneumonia care in low-resource settings. IMCI guideline pneumonia diagnostic criterion performs with low specificity, resulting in antibiotic overtreatment. Digital auscultation with automated lung sound analysis may improve the diagnostic performance of IMCI pneumonia guidelines. This systematic review aims to summarize the evidence on detecting adventitious lung sounds by digital auscultation with automated analysis compared to reference physician acoustic analysis for child pneumonia diagnosis.

3.1.2 Methods

In this review, articles were searched from MEDLINE, Embase, CINAHL Plus, Web of Science, Global Health, IEEExplore database, Scopus, and the ClinicalTrial.gov databases from the inception of each database to October 27,

2021, and reference lists of selected studies and relevant review articles were searched manually. Studies reporting diagnostic performance of digital auscultation and/or computerised lung sound analysis against physicians' acoustic analysis for pneumonia diagnosis in children under the age of 5 were eligible for this systematic review. Retrieved citations were screened and eligible studies were included for extraction. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. All these steps were independently performed by two authors and disagreements between the reviewers were resolved through discussion with an arbiter. Narrative data synthesis was performed.

3.1.3 Results

A total of 3801 citations were screened and 46 full-text articles were assessed. Ten studies met the inclusion criteria. Half of the studies used a publicly available respiratory sound database to evaluate their proposed work. Reported methodologies/approaches and performance metrics for classifying adventitious lung sounds varied widely across the included studies. All included studies except one reported overall diagnostic performance of the digital auscultation/computerised sound analysis to distinguish adventitious lung sounds, irrespective of the disease condition or age of the participants. The reported accuracies for classifying adventitious lung sounds in the included studies varied from 66.3% to 100%. However, it remained unclear to what extent these results would be applicable for classifying adventitious lung sounds in children with pneumonia.

3.1.4 Conclusions

This systematic review found very limited evidence on the diagnostic performance of digital auscultation to diagnose pneumonia in children. Well-designed studies and robust reporting are required to evaluate the accuracy of digital auscultation in the paediatric population.

3.2 Introduction

Pneumonia is the leading cause of mortality among infectious diseases in children under the age of five globally (103), accounting for an estimated 800,000 deaths per year, more than half of which occur in just five low- and middle-income countries (LMICs) (103, 104). In 2015, the estimated annual incidence of pneumonia in children under five years of age in developing countries was 231 episodes per 1000 children, resulting in about 138 million episodes of clinical pneumonia in this age group (6). Prompt recognition of illness and care-seeking is critical to reducing pneumonia-related child deaths (105).

Currently, health care providers in LMICs use practical, standardised case management guidelines called the Integrated Management of Childhood Illnesses (IMCI) guidelines developed by the World Health Organization (WHO) for childhood pneumonia care (16, 17). IMCI guidelines have proven to be one of the most important childhood pneumonia interventions for LMICs to date (48, 52).

IMCI guidelines prioritise sensitivity over specificity to ensure antibiotic treatment for children with an acute respiratory illness and suspected bacterial pneumonia (17). Where successfully implemented, this algorithm has shown a 30%–40% reduction in case mortality (52). Yet, IMCI has moderate sensitivity and a specificity largely contingent on disease severity. Specificity may range from 16% for children with an acute respiratory illness characterized by wheeze (106), to 49% for IMCI-defined non-severe pneumonia (i.e., disease lacking clinical danger signs), to 95% for IMCI-defined very severe pneumonia (i.e., disease with clinical danger signs) (58). Limitations of IMCI specificity are thought to be related to the attribution of milder disease to viral pathogens, an epidemiological pattern catalysed by the expanded exposure of children in LMICs to *Haemophilus influenzae* type B and access to pneumococcal conjugate vaccines (107-109). As a result, while the guidelines ensure few children with true bacterial pneumonia will be overlooked, most children, especially those with a milder illness, receive antibiotics inappropriately, resulting in antibiotic overuse.

Auscultation, the process of listening to the human body's internal sounds by using a stethoscope (110), has been an effective tool for diagnosing pulmonary diseases for more than two centuries. This requires a highly trained health professional, limiting its utility at first-level facilities in LMICs staffed by non-physician health workers. IMCI guidelines do not include lung auscultation in their pneumonia definition for frontline healthcare workers (17). The guidelines' exclusion of auscultation likely results from its high inter-observer variability and subjectivity, regardless of healthcare providers' training level (60-64). Furthermore, traditional stethoscopes are functionally limited since they attenuate higher frequency sounds, like wheezing and crackles, yet transmit ambient noises and tubular resonance effects (62, 86). Digital auscultation may overcome these limitations (98). Digital auscultation has the potential advantages of signal amplification and ambient noise reduction , reducing inter-observer reporting variation (111), and not requiring auscultation training for health care providers. Digital stethoscopes can record a patient's respiratory sounds for automated computerised lung sound analysis, which has been the recent focus of a significant amount of research, with some commercial systems already available (76, 77). These advantages may be important in LMICs that rely on varying cadres of non-physician clinicians, and as the burden of lower respiratory infections among children in LMICs is high.

To the best of our knowledge, there is currently no systematic review reporting the diagnostic accuracy of digital auscultation to detect adventitious lung sounds in childhood pneumonia. Therefore, we aimed to conduct a systematic review to summarize the current evidence on the diagnostic performance of digital auscultation to identify adventitious lung sounds compared to the physician's acoustic analysis to diagnose pneumonia in children.

3.3 Methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy (PRISMA-DTA) criteria (112). The review protocol was registered with the PROSPERO database (registration number CRD42020180821).

3.3.1 Information sources and search strategy

Search terms ("pneumonia", "lower respiratory infection", "auscultation", "respiratory sound", "lung sound", "digital", "electronic", "automatic", "computerized", "auscultation", "crackles", "wheeze", "child") were used to generate comprehensive search strategies for the following electronic databases: MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus, Web of Science, Global Health, IEEExplore database, Scopus and the ClinicalTrial.gov (*http://clinicaltrials.gov/*). Search strategies for all databases are shown in Supplementary table 13.1. The initial search was conducted in February 2019 and was updated on October 27, 2021, with no language restrictions. To avoid missing relevant studies, reference lists of identified studies and relevant reviews were also screened.

3.3.2 Eligibility criteria

Studies were selected based on the following inclusion criteria:

1. Participants: Children under five years of age.
2. Index test: Digital auscultation/computerised analysis of lung sounds.
3. Reference standards: Physicians' diagnosis of adventitious lung sounds (crackles and/or wheeze) by conventional auscultation/ acoustic analysis of recorded lung sounds.
4. Target condition: Pneumonia.
5. Outcome: Reported diagnostic accuracy measures of the digital/computerised analysis of adventitious lung sounds.
6. Types of studies: Observational and experimental studies.

Studies were excluded if 1) digital auscultation or computerised analysis of lung sounds were not used in the study, 2) reference standard was not a human classification of lung sounds, 3) the reports were reviews, conference proceedings, abstracts, case reports, editorials, and commentaries.

3.3.3 Screening and selection of studies

Search results were imported and merged into Endnote X9, and duplicates were removed. Two review authors (SA and MSI/SS/GMMH) independently screened the titles and abstracts of all included citations as per the predefined eligibility criteria, followed by a full-text review of all selected articles (SA and SS/AMK). Any discrepancies were resolved through discussion, or an arbiter (HN) was consulted where necessary. Reasons for the exclusion of studies were documented in Supplementary table 13.2.

3.3.4 Data extraction and quality assessment

Data extractions were independently carried out by two review authors (SA and AMK) using a standardized pretested data collection template (Supplementary table 13.3). Any discrepant judgments were evaluated by an arbiter (HN).

Two reviewers (SA and AMK) independently assessed the risk of bias and applicability of the included studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (113). Non-consensus between the reviewers were resolved through consultation with an arbiter (HN). This tool includes four domains to judge bias in the included study: patient selection, index test, reference standard, and flow and timing. A study would have an overall judgment of “low risk of bias” if it was judged as “low” on all domains. In contrast, it would be judged as a “high risk of bias” if it was judged “high” in one or more domains. The “unclear risk of bias” was categorised only when insufficient data were reported. To judge the concerns regarding the applicability of the included study to the review question, three domains (ie, patient selection, index test, and reference standard) were used.

3.3.5 Data synthesis

A descriptive synthesis was performed following the predefined review objectives and outcome measures. Meta-analyses could not be performed due to insufficient data and the heterogeneity in included studies in terms of methodology and outcome measures.

3.4 Results

3.4.1 Result of the search

The review process is summarised in Figure 3.1 using the PRISMA flow diagram (114). A total of 3798 citations were identified through the database search. After duplicates were removed, 3324 unique citations remained. In total, 3281 citations were excluded during the title and abstract screening, and 46 full-text articles (including three from citation searching) were reviewed. Of these, ten articles were eligible for inclusion (95, 98, 115-122).

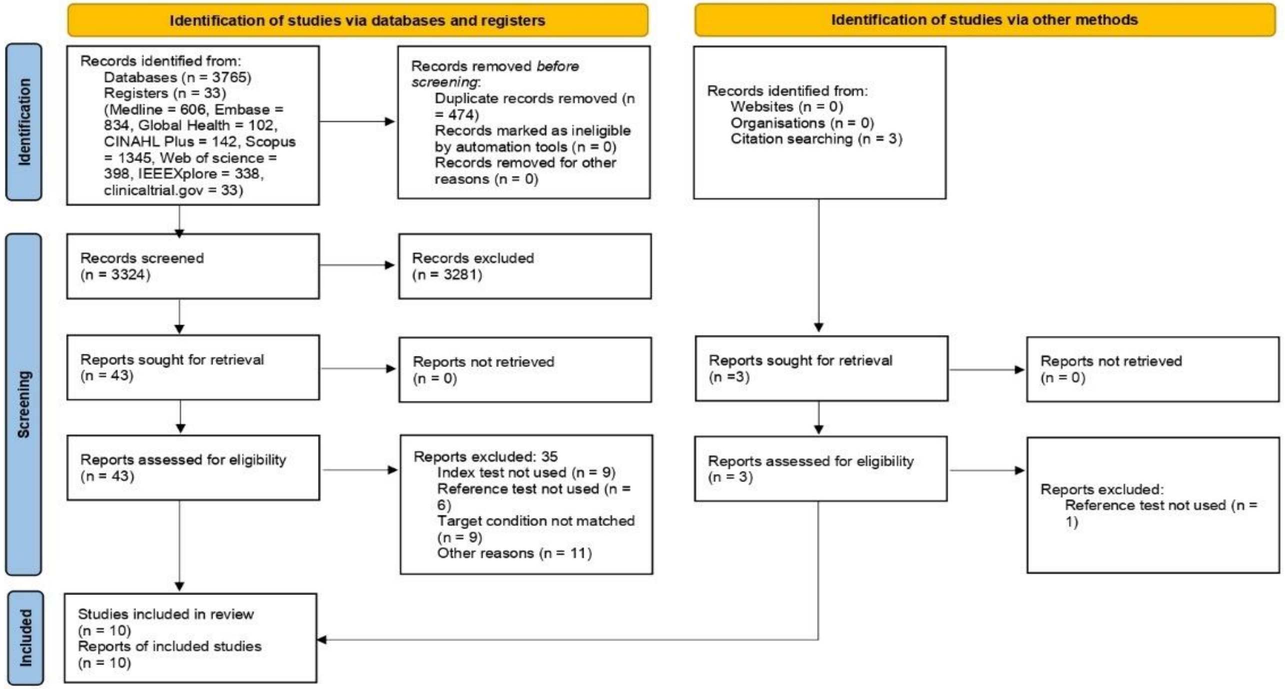

Figure 3.1 PRISMA flow diagram

3.4.2 Characteristics of the included studies

Table 3.1 Study Characteristics summarises the characteristics of the included studies. Of the selected articles, five studies evaluated lung sound recordings from primary studies, among which one study was conducted across multiple centres in Africa (The Gambia, Kenya, South Africa, Zambia) and Asia (Bangladesh, Thailand) (98), one in Australia (95), one in India (120), and the remaining two were from the same study conducted in Egypt (115, 119). These five studies recruited children from different age groups and varied from one another in the number of study subjects. For instance, one study enrolled 1157 children aged 1-59 months (98), one study enrolled 600 children aged 0-12 years (115, 119), while another study had only 20 children from 4.6-17.1 years (95). However, one study recruited 256 children but did not report any information on participants' age (120). Of these five studies, one study obtained lung sound recordings in outpatient and busy clinical settings (98), while another study recorded the lung sounds in a quiet room in the hospital (95). Three studies also recorded lung sounds in the hospital settings (115, 119, 120), but is unclear whether they were recorded in a controlled environment or a noisy clinical setting. The other five studies (116-118, 121, 122) evaluated their proposed work using the publicly available International Conference on Biomedical and Health Informatics (ICBHI) scientific challenge respiratory sound database containing 920 annotated lung sound recordings from 126 subjects (49 children and 77 adults) (101, 123).

We found only one study that specifically recruited children with IMCI-defined severe or very severe pneumonia and age-matched controls without clinical pneumonia (98), while seven studies included study subjects with a variety of respiratory diseases, including pneumonia (95, 116-118, 120-122). The other two studies did not report on the disease condition of the study subjects (115, 119, 120).

Table 3.1 Study Characteristics

Author, year	Country	Study type	Population	Number of subjects	Clinical condition of the subjects	Sound/ pathology analysed	Number of recordings studied	Lung sound recording device	Feature extraction method	Sound classification method	Outcome/Result
Fasseeh et al. 2015 (119)	Egypt	Case control	Infants and children (0-12 years)	Case: 500 Control: 100	Not reported	wheezes, stridor, rattle, normal	592	3M Littmann Electronic Stethoscope 3200	Short-time Fourier Transform (STFT)	Dynamic time warping (DTW) algorithm	Reported accuracy of validation for all wheezes was 81.93% (<12 months: 82.81% & ≥ 12 months: 89.15%) Reported accuracy of validation for all normal sounds was 89% (<12 months: 96.15% & ≥ 12 months: 90.54%).
Khan et al. 2017 (120)	India		Children	254	Not reported	Normal and pathological	254	Littmann 3200 electronic stethoscope	Short time Fourier transform (STFT)	k- Nearest Neighbour (k-NN); Support Vector Machine (SVM)	k-NN obtained sensitivity, specificity, and accuracy of 90.9%, 92.2% and 91.6% respectively. SVM obtained sensitivity, specificity, and accuracy of 92.2%.

Author, year	Country	Study type	Population	Number of subjects	Clinical condition of the subjects	Sound/ pathology analysed	Number of recordings studied	Lung sound recording device	Feature extraction method	Sound classification method	Outcome/Result
Kevat et al. 2017 (95)	Australia		Children (median age 6.7 years)	20	Cystic fibrosis, lower respiratory tract infection, asthma, preschool wheeze	Wheeze, crackles, normal	156	Littmann 3200 Electronic Stethoscope; Clinicloud DS	Not reported	Audio spectrographic analysis	Concordance between the Littman electronic stethoscope and standard auscultation was found to be moderate for wheeze (κ = 0.44) and almost perfect for crackles (κ = 1.0). Concordance between the Clinicloud DS and standard auscultation was found to be moderate for wheeze (κ = 0.55) and almost perfect for crackles (κ = 1.0).

Author, year	Country	Study type	Population	Number of subjects	Clinical condition of the subjects	Sound/ pathology analysed	Number of recordings studied	Lung sound recording device	Feature extraction method	Sound classification method	Outcome/Result
Abougabal et al. 2018 (115)	Egypt	Analysis of recorder lung sounds	Infants and Children (<13 years)	600	Not reported	stridor, rattle and wheeze, normal	592	3M Littmann Electronic Stethoscope 3200	Wavelet Transform (WT) coefficients	Dynamic time warping (DTW) algorithm	Reported recognition accuracy of 88.2% for wheeze and 86% for normal breath sounds.
Emmanouilidou et al. 2018 (98)	Gambia, Kenya, South Africa, Zambia, Bangladesh, Thailand	Case control	Children (median age 7 ± 11.4 month)	1157	Pneumonia, Normal	Normal, abnormal (wheeze and/or crackle)	1095	ThinkLabs ds32a	Rich spectro-temporal feature space	Support-Vector Machine (SVM) classifier	The classification system achieved an accuracy of 86.7%, sensitivity of 86.9%, and specificity of 86.6%
Chen et al. 2019 (118)		*Analysis of respiratory sound database	Not mentioned	Not mentioned	Not mentioned	wheeze, crackle, normal	489	3M Littmann 3200 Electronic Stethoscope; Welch Allyn Elite Meditron	Optimized-S-Transform (OST)	Deep Residual Networks (ResNets)	Classification accuracy of 98.79% with sensitivity of 96.27% and specificity of 100% was obtained to classify wheeze, crackle, and normal sounds.

Author, year	**Country**	**Study type**	**Population**	**Number of subjects**	**Clinical condition of the subjects**	**Sound/ pathology analysed**	**Number of recordings studied**	**Lung sound recording device**	**Feature extraction method**	**Sound classification method**	**Outcome/Result**
Perna et al. 2019 (121)		*Analysis of respiratory sound database	Children, adults	126	Pneumonia, Bronchiectasis, Bronchiolitis, COPD, Healthy, URTI	Normal, wheeze, crackle, both	920	AKG C417 L Microphone; 3 M Littmann Classic II SE Stethoscope; 3M Littmann 3200 Electronic Stethoscope; Welch Allyn Meditron Master Elite Electronic Stethoscope	Mel Frequency Cepstral Coefficients (MFCC)	Recurrent Neural Networks (RNN) models: Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU)	A sensitivity of 0.62 and specificity of 0.85 were reported for LSTM based model on four class anomaly driven prediction. (i.e., normal, presence of crackles, presence of wheezes, presence of both)
Acharya et al. 2020 (116)		*Analysis of respiratory sound database	Children, adults	126	Pneumonia, Bronchiectasis, Bronchiolitis, COPD, Healthy, URTI	Normal, wheeze, crackle, both	920	AKG C417 L Microphone; 3 M Littmann Classic II SE Stethoscope; 3M Littmann 3200 Electronic Stethoscope; Welch Allyn Meditron Master Elite	Mel-spectrograms	Hybrid CNN-RNN model	A score of 66.31% was obtained on four class respiratory cycle classification and a score of a71.81% was obtained for leave-one-out Validation.

Author, year	**Country**	**Study type**	**Population**	**Number of subjects**	**Clinical condition of the subjects**	**Sound/ pathology analysed**	**Number of recordings studied**	**Lung sound recording device**	**Feature extraction method**	**Sound classification method**	**Outcome/Result**
								Electronic Stethoscope			
Alva Alicia et al. 2021 (117)		*Analysis of respiratory sound database	Children, adults	126	Pneumonia, Bronchiectasis, Bronchiolitis, COPD, Healthy, URTI	Normal, abnormal	920	AKG C417L Microphone; 3M Littmann Classic II SE Stethoscope; Littmann 3200 Electronic Stethoscope; Welch Allyn Meditron Master Elite Electronic Stethoscope	Melspectogram; Short time Fourier transform (STFT); Mel Frequency Cepstral Coefficients (MFCC)	Convolutional Neural (CNN) Network Models	Accuracy values of 0.998 and 1 were obtained for normal sounds and abnormal sounds respectively. Accuracy values of 0.9959 and 0.9885 were reported for classification of pneumonia and other diseases.

Author, year	**Country**	**Study type**	**Population**	**Number of subjects**	**Clinical condition of the subjects**	**Sound/ pathology analysed**	**Number of recordings studied**	**Lung sound recording device**	**Feature extraction method**	**Sound classification method**	**Outcome/Result**
Shuvo et al. 2021 (122)		*Analysis of respiratory sound database	Children, adults	87	Pneumonia, Bronchiectasis, Bronchiolitis, COPD, Healthy, URTI	Chronic classification (healthy, chronic diseases, non-chronic diseases) Pathological classification (Healthy, Bronchiectasis, Bronchiolitis, COPD, Pneumonia, URTI)	917	AKG C417L Microphone; 3M Littmann Classic II SE Stethoscope; Littmann 3200 Electronic Stethoscope; Welch Allyn Meditron Master Elite Electronic Stethoscope	Hybrid scalogram using empirical mode decomposition (EMD) & continuous wavelet transform (CWT)	Lightweight Convolutional neural network (CNN) model	Weighted accuracy scores of 98.92% for three-class chronic classification and 98.70% for six-class pathological classification were obtained.

3.4.3 Stethoscopes used

For studies using the ICBHI data set, lung sounds were recorded using different devices (3M Littmann Classic II SE stethoscope, 3M Littmann 3200 electronic stethoscope, WelchAllyn Meditron Master Elite electronic stethoscope, and AKG C417 L Microphone) (116-118, 121, 122) from both clinical and home settings (123). In the other four studies, 3M Littmann 3200 electronic stethoscope was used (95, 115, 119, 120), while the Clinicloud DS was also used in one of the studies (95). The ThinkLabs ds32a digital stethoscope with a microphone (Sony- ICD-UX71-81) affixed to the stethoscope to record ambient noises was used in one study (98).

3.4.4 Lung sounds classification used

Variations were observed in classifying the lung sounds. For instance, three studies specifically performed the computerised analysis of lung sounds to classify normal and adventitious/ pathological sounds (98, 117, 120), two studies performed a four-class classification (normal, crackle, wheeze, both wheeze and crackle) (116, 121), one study performed a three-class classification (normal, crackle and wheeze) (118), one study classified wheeze and crackles (95) and another two analysed wheeze, rattle, stridor and normal lung sounds (115, 119). One study performed a three-class chronic classification (healthy, non-chronic diseases, chronic diseases) and six-class pathological classification (healthy, bronchiectasis, bronchiolitis, COPD, Pneumonia, URTI) based on the respiratory sound signal processing and computerised analysis (122).

3.4.5 Algorithm used to classify lung sounds

A substantial variation was observed in feature extraction methods (i.e., the process of identifying distinctive features of respiratory sound signals) and sound classification algorithms/models used in the included studies. For feature extraction, three studies employed Short-time Fourier Transform (STFT) (117, 119, 120), two studies employed Melspectrogram (116, 117), two used Mel Frequency Cepstral Coefficients (MFCC) (117, 121) while other four studies employed enhanced distinctive feature extraction methods- Wavelet Transform (WT) coefficients (115), rich spectro-temporal feature space (98), Optimized-S-Transform (OST) (118) and hybrid scalogram using empirical mode decomposition (EMD) and continuous wavelet transform (CWT) (122). Wide-ranging sound classification models/algorithms used across the studies are - Dynamic time warping (DTW) algorithm (115, 119), Support Vector Machine (SVM) (98, 120), k- Nearest Neighbour (k-NN) based classifier (120), audio spectrographic analysis (95), Deep Residual Networks (ResNets) (118), Recurrent Neural Networks (RNN) models with Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU) (121), hybrid CNN-RNN model (116), Convolutional Neural Network (CNN) models (117) and lightweight convolutional neural network (CNN) model (122).

3.4.6 Diagnostic performance of the used algorithms/models

Regarding diagnostic performance, diverse methodologies and diagnostic accuracy measures were used. Furthermore, in studies that included participants with different target conditions and age groups (ie, children and adults), the reported performance measures were only limited to overall accuracy on adventitious lung sounds classification (116-118, 121) or by pathological conditions classification (122). For these studies, reported accuracies varied from 66.3% to 100%. Of the five studies that recruited children (95, 98, 115, 119, 120), only one study (98) reported on the accuracy of the computerised sound classification system in children aged 1-59 months in pneumonia. In that study, the accuracy of the classification system was 86.7% (sensitivity 86.8%; specificity 86.6%) to differentiate between normal and adventitious lung sounds. Further, the researchers suggested that the system performance varied with the different window analyses of breath cycles ranging from shorter to longer duration. For example, the analysis window at 0.5s yielded an accuracy of 84.1% (sensitivity 87.2%; specificity 81%) while it was about 77% in longer time windows (>1s); thus, a short window size was recommended (98).

3.4.7 Assessment of risk of bias and applicability

The quality of the included studies according to the QUADAS-2 tool is summarized and displayed graphically in Figure 3.2 and Figure 3.3. In general, very few of the included studies met most of the quality criteria. Most of the studies were judged to be of unclear methodological quality because of insufficient reporting. For patient selection, four studies were evaluated as having a high risk of bias, and six were evaluated as having an unclear risk of bias due to inappropriate or poorly described sampling methods. For the index test, all 10 studies were judged as low risk of bias because there was no chance of non-blinding, as index tests were the machine classification. For the reference standard, all the studies were evaluated as having an unclear risk of bias due to poor reporting of target conditions and/or blinding status. In the flow and timing domain assessment, seven studies were deemed to have a low risk of bias as the recorded sounds were the second interpretation, and three were evaluated as an unclear risk because of underreporting. The overall concerns regarding applicability for this review were unclear, high, and low, for patient selection, index test, and reference standard, respectively.

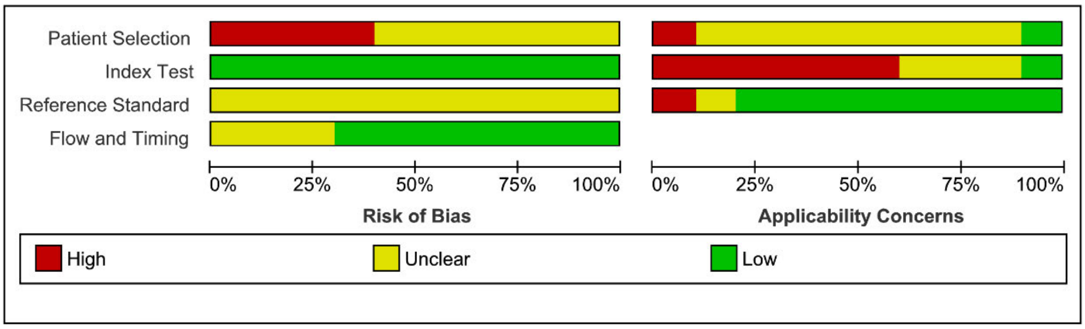

Figure 3.2 Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies

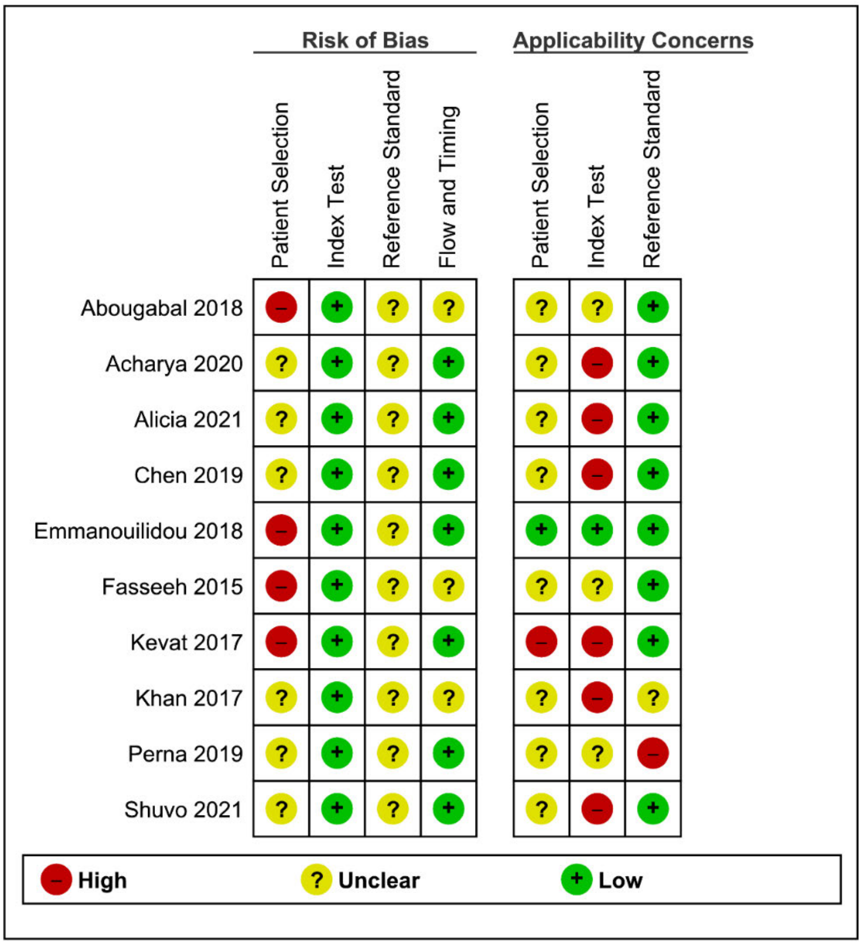

Figure 3.3 Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

3.5 Discussion

This systematic review included studies evaluating the diagnostic performance of digital auscultation/computerised analysis of adventitious lung sounds in pneumonia in children aged under 5 years. The literature search identified 10 articles that met the inclusion criteria. Of these included articles, five of them evaluated lung sound recordings from primary studies, while the remaining five utilised a publicly available respiratory sound database to evaluate their proposed lung sound classification system. Substantial variation was observed in the included studies in terms of study subjects, sample size, and use of feature extraction methods and sound classification models. For instance, seven types of feature extraction methods and nine types of sound classification models/algorithms were used across the studies. Hence, we could not draw any conclusion from this systematic review. However, the reported accuracies for classifying adventitious lung sounds ranged from 66.3% to 100%. This review identified only one study (98) that involved children aged under 5 years with pneumonia to evaluate an integrated computerised lung sound classification framework to detect adventitious lung sounds at an accuracy of 86.7% (sensitivity 86.5%; specificity 86. 6%). Although the rest of the studies demonstrated excellent accuracy, sensitivity, and specificity values, their results were primarily limited to overall diagnostic accuracy parameters in classifying lung sounds and did not provide disaggregated results by age and/by target condition/s. Therefore, the findings could not be directly applied to the paediatric population to diagnose childhood pneumonia. These shortfalls are important findings of this review and suggest a need for improved reporting of study findings. The authors should account for participants' contributing factors (such as age, disease/target condition) while analysing and reporting their data. Evidently, the methodological quality of the included studies was deemed to be unclear due to insufficient reporting in participant selection, sampling methods, and clinical/target conditions of the participants. The concerns regarding the applicability of the patient selection and index test domain were unclear and high, respectively.

To the best of our knowledge, this is the first systematic review assembling evidence on the discriminatory power of digital auscultation for the detection of adventitious lung sound/s against conventional auscultation or acoustic analysis of recorded lung sounds by physicians in childhood pneumonia diagnosis. Prior reviews focused on summarizing existing evidence on artificial intelligence and algorithms to classify adventitious lung sounds (76, 124). Another systematic review and meta-analysis by Gurung et al.(86) evaluated the performance of computerised lung sounds analysis to detect adventitious lung sounds in respiratory diseases against chest radiography or clinical diagnosis.

In line with our findings, this review emphasised methodological and analytical standardization, including completeness and transparency in reporting by following standardised guidelines, and the need for conducting more studies on the paediatric population. To date, the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 statement remains the most used tool for reporting of studies investigating diagnostic test accuracy and performance (125, 126). However, this tool has some shortcomings when reporting studies evaluating artificial intelligence (AI) driven interventions due to unclear methodological interpretation, lack of standardised nomenclature, use of unfamiliar outcome measures, and other issues, thereby limiting the comprehensive appraisal of these technologies (127). Thus, our study findings further reiterate the need for developing an AI-specific STARD guideline to ensure complete and robust reporting of the studies evaluating AI-driven technologies and interventions (127, 128).

The heterogeneous nature of the included studies and insufficient data prohibited us from performing meta-analyses and drawing conclusions on the diagnostic accuracy of digital auscultation and computerised analysis of lung sounds in childhood pneumonia diagnosis.

3.6 Conclusions

Given the paucity of available data in this area, there is a need for additional well-designed studies to generate evidence on accuracy, sensitivity, and specificity of digital auscultation and/or computerised analysis of lung sounds involving the paediatric population to diagnose pneumonia. Future investigations should also consider conducting the studies in real-life, noisy clinical settings rather than in a controlled laboratory or clinical environment to broaden the usability of the automated applications. This is a rapidly evolving field, and new and advanced applications with robust reporting of methods and findings within studies will enable meta-analysis in future reviews.

3.7 Acknowledgements

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3.9 Authorship contributions

SA, HN, EDM and SC conceptualised this systematic review. SA, MSI, SS, AMK, and GMMH obtained and apprised data with discrepancies resolved by HN. SA, SS and AMK prepared tables and figures presented in the manuscript. SA prepared the first draft. All co-authors reviewed the manuscript, provided intellectual inputs, and approved the final version.

3.10 Competing interests

The authors completed the ICMJE Unified Competing Interest form (available upon request from the corresponding author) and declared no conflicts of interest.

Chapter 4 Methodology

I conducted a cross-sectional study to evaluate digital auscultation as a novel diagnostic tool for childhood pneumonia in community-level health facilities in Bangladesh. After reviewing existing literature and consultation with experts on digital auscultation, I develop the research methodologies. Additionally, I consulted with the Bangladesh IMCI technical committee, the programme manager of IMCI, and district and sub-district level health managers of the Bangladesh Ministry of Health and Family Welfare to ensure local stakeholder inputs into the development of the implementation strategy. In this chapter, I have described the methodology of the study. The work presented in this chapter was published in BMJ Open in 2022. The full text of the publication is attached below. Some contents have been organised to comply with the format of this thesis. I added a detailed description of the Feelix Smartscope (page 334), user manual of the device (page 345), listening panel members' training manual (page 370) and brief description of the Machine Learning models (Computerised Lung Sounds Analysis) used for recorded lung sounds analysis (page 340) in this thesis as supplementary materials in appendix.

URL: *https://bmjopen.bmj.com/content/12/2/e059630*

Title: Digital auscultation as a novel childhood pneumonia diagnostic tool for community clinics in Sylhet, Bangladesh: protocol for a cross-sectional study

Authors: **Salahuddin Ahmed** (myself), Dipak Kumar Mitra, **Harish Nair** (supervisor), **Steven Cunningham** (co-supervisor), Ahad Mahmud Khan, ASMD Ashraful Islam, Ian Mitra McLane, Nabidul Haque Chowdhury, Nazma Begum, Mohammod Shahidullah, Muhammad Shariful Islam, John Norrie, Harry Campbell, Aziz Sheikh, **Abdullah H. Baqui** (co-supervisor), **Eric D. McCollum** (co-supervisor)

4.1 Abstract

4.1.1 Introduction

The WHO's Integrated Management of Childhood Illnesses (IMCI) algorithm for diagnosis of child pneumonia relies on counting respiratory rate and observing respiratory distress to diagnose childhood pneumonia. IMCI case definition for pneumonia performs with high sensitivity but low specificity, leading to overdiagnosis of child pneumonia and unnecessary antibiotic use. Including lung auscultation in IMCI could improve specificity of pneumonia diagnosis. Our objectives are: (1) assess lung sound recording quality by primary health care workers (HCWs) from under-5 children with the Feelix Smartscope and (2) determine the reliability and performance of recorded lung sound interpretations by an automated algorithm compared with reference paediatrician interpretations.

4.1.2 Methods and analysis

In a cross-sectional design, Community HCWs will record lung sounds of ~1,000 under-5-year-old children with suspected pneumonia at first-level facilities in Zakiganj sub-district, Sylhet, Bangladesh. Enrolled children will be evaluated for pneumonia, including oxygen saturation, and have their lung sounds recorded by the Feelix Smartscope at four sequential chest locations: two back and two front positions. A novel sound-filtering algorithm will be applied to recordings to address ambient noise and optimise recording quality. Recorded sounds will be assessed against a predefined quality threshold. A trained paediatric listening panel will classify recordings into one of the following categories: normal, crackles, wheeze, crackles and wheeze, or uninterpretable. All sound files will be classified into the same categories by the automated algorithm and compared with panel classifications. Sensitivity, specificity, and predictive values of the automated algorithm will be assessed considering the panel's final interpretation as reference standard.

4.1.3 Ethics and dissemination

The study protocol was approved by the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), Bangladesh (Registration Number: 09630012018) and Academic and Clinical Central Office for Research and Development Medical Research Ethics Committee, Edinburgh, UK (REC Reference: 18-HV-051). Dissemination will be through conference presentations, peer-reviewed journals and stakeholder engagement meetings in Bangladesh.

Trial registration number: NCT03959956

4.2 Introduction

Childhood pneumonia is one of the leading causes of death in children younger than five years globally (129) and accounts for an estimated 0.8 million deaths in children annually (103). The WHO estimates that the African and South-East Asian Regions contribute to more than 75% of total paediatric deaths from pneumonia (6). It is estimated that the annual incidence of childhood pneumonia in low- and middle-income countries (LMICs) is 231 episodes per 1,000 children (6). Pneumonia is also a significant cause of hospitalisation (130), and about 16.4 million children in LMICs were hospitalised due to pneumonia in 2015 (6). A population-based study in Bangladesh estimated that the annual incidence of pneumonia was 360 episodes per 1,000 child-years, of which 7.3% were hospitalised (9). The case-fatality rate of child pneumonia in Bangladesh is estimated to be 2% - 4% (131, 132).

The WHO and UNICEF Integrated Management of Childhood Illness (IMCI) guidelines have been the foundation of pneumonia management in LMICs since the mid-90s (35, 36). Per current IMCI guidelines, a child with fast breathing and/or chest indrawing without any danger signs is classified as non-severe pneumonia and treated at home with oral antibiotics (17). These guidelines have proven to be one of the most important childhood pneumonia interventions for LMICs to date, and up to 36% of the under-5-year-old mortality reductions in LMICs have been attributed to guideline implementation (48-52).

Despite its overall success, the IMCI algorithm for diagnosis of child pneumonia can still be improved. First, the guidelines were developed when access to vaccines was limited, and child pneumonia mortality was high, so the guidelines intentionally prioritised sensitivity over specificity to ensure children with possible bacterial disease received antibiotics (17, 35). Thus, the IMCI algorithm over-diagnoses many children with pneumonia who do not require antibiotics, and they may have different treatable diseases (133, 134). Second, the WHO guidelines do not include lung auscultation in their pneumonia definition for frontline healthcare workers despite lung auscultation serving as the cornerstone for pneumonia diagnosis in most ambulatory, well-resourced settings staffed by clinicians trained to perform lung auscultation (17) . The exclusion of auscultation findings in these guidelines likely stems from its high interobserver variability and subjectivity, regardless of the training level of healthcare providers, and the related difficulty in training healthcare workers to effectively use a conventional stethoscope (60-64). Traditional stethoscopes themselves are also limiting, attenuating higher frequency sounds, like wheezing and crackles, yet transmitting ambient noises and tubular resonance effects (62, 86, 135). Automated real-time classification of lung sounds or digital auscultation may overcome these limitations (98). Digital auscultation augmented by artificial intelligence algorithms has the potential to be a highly specific respiratory diagnostic tool feasible for use by front-line healthcare workers in LMICs. Operationally, the inclusion of adventitious sound classifications in current IMCI guidelines could help to reduce (65) unnecessary use of antibiotics in LMICs.

A digital stethoscope can convert an acoustic sound to electronic signals, which can be further amplified for optimal listening. These electronic signals can then be processed and digitalised to transmit to a personal computer or a laptop (75). Automatic lung sound analysis, aiming to overcome the limitations of conventional auscultation, has been the recent focus of a significant amount of research, and some commercial systems are already available in the market (76, 77).

The digital stethoscope has advantages over the analogue stethoscope in different stages of auscultation. An analogue stethoscope requires the proper placing of the diaphragm or bell in the correct positions of the human body to listen to internal body sounds. More modern digital stethoscopes do not necessarily require exact placement for two reasons. First, they convert the acoustic wave into electric signals and replace the double-sided chest piece (diaphragm and bell) with transducers to convert acoustic signals to electric signals. Second, the chest piece is packed with transducer arrays to achieve a uniform sensitivity over the entire active area. Together, this design delivers a strong signal even when the chest piece is not placed in precisely the right position (94, 136). This advantage is essential for minimally trained healthcare providers.

Conventional auscultation using an analogue stethoscope also requires a quiet environment, and ideally with the patient in a quiet, cooperative state, which is difficult in hospitals/clinics and especially hospitals/clinics in LMICs where the number of patients are typically usually higher than capacity. This often results in patient examination rooms filled with chattering people, ringing phones, and whirring fans; most importantly, the child being examined may then be agitated, uncooperative, and/or crying. Digital stethoscopes could improve listening capability through the use of noise-cancelling technologies (87, 95). Limitations of the human auditory system, which ranges from 20 Hz to 20 kHz for young adults and the range shrinks after middle age (96), are also a drawback in conventional auscultation using a conventional stethoscope. A digital stethoscope can amplify sounds up to 100 fold (89). Much experience is required to interpret breath sounds, and inter-rater variability is high regardless of healthcare providers' training level (63). Machine learning techniques can be used in digital auscultation to auto-analyse sounds (76) and produce a diagnosis or treatment decision (86).

Johns Hopkins University and Sonavi Labs developed a novel digital stethoscope named Feelix Smartscope (Figure 4.1) (94, 136), which improves lung signal strength by uniformly distributing highly sensitive microphones in an array pattern across the stethoscope diaphragm to increase the sensitivity and provide broader frequency response, a critical feature for identifying higher frequency pathologic lung sounds. Its 3.7 V and 250 amps/hour rechargeable battery can provide power >20 hours of use, which is important in rural communities with unreliable electricity. The device mitigates movement artefact and tubular resonance by using an ergonomic design to better secure the device on the child's chest. It also eliminates the rubber stethoscope tubing, a source of ambient noise and friction contamination. Notably, the device includes an integrated external facing microphone that captures simultaneous environmental noise to the lung sound recording and removes the unwanted ambient noises through an adaptive spectral subtraction schema (135, 137). The Feelix Smartscope also permits onboard data storage with a micro SD card. The device turns on when the user picks up the device or touches the top of the device. The device turns off automatically after 60 seconds when it does not sense any touch. The device has three touch buttons – button 1 to start recording, button 2 to start a new session to record a new child’s four chest points recording, and button 3 to establish a Bluetooth connection with a mobile phone or tablet. It also has a slider to control sound volume level. In each session, the device automatically records 10 seconds for each four chest points of a child. The Feelix Smartscope has been successfully validated in the laboratory against six other commercially available electronic stethoscopes – including the Littmann 3200 electronic stethoscope and Thinklabs – and has demonstrated comparable results (99, 100). Johns Hopkins and Sonavi Labs developed a machine learning algorithm that can provide an automated classification of adventitious lung sounds. This Feelix Smartscope and the machine learning algorithm will be used in this study.

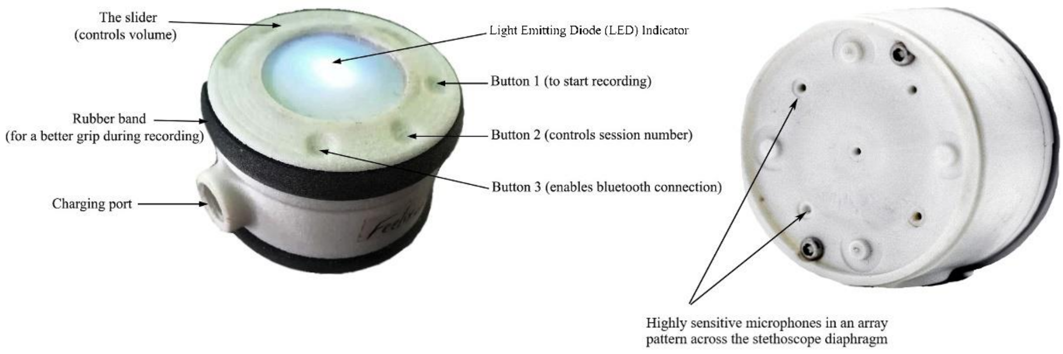

Figure 4.1 Feelix Smartscope

4.2.1 Objectives and hypotheses

The primary objectives of the study are:

1. To assess whether lung sounds from children recorded by community health care providers (CHCPs) at community-level health facilities using a prototype digital stethoscope meet pre-defined quality thresholds established by experts. ('pre-defined quality threshold' was defined over 50% of the patients would have 'quality' lung sound recordings, 'quality' was defined as having at least 75% interpretable lung sound segments per patient according to the human listening panel (i.e., ≥ 3 out of 4 chest positions)).
2. To determine the diagnostic accuracy of an automated lung sound classification algorithm for identifying adventitious lung sounds, compared with a reference panel of paediatricians.

The study hypotheses are:

1. More than 50% of patients will have ‘quality’ lung sound recordings (targeted goal), defined as at least 75% interpretable lung sound segments per patient (i.e., 3 out of 4 chest positions).
2. The agreement between automated computerised analysis (respiratory detector) and paediatric listening panel will be high (kappa >0.8).

4.3 Methods and analysis

4.3.1 Study setting

This study will be implemented in the Projahnmo field site, a site for maternal, new-born, and child health research, which was established in 2001 in Sylhet district of Bangladesh by a partnership of Johns Hopkins University, the Bangladesh Ministry of Health and Family Welfare (MOHFW), and several Bangladeshi institutions, including Non-Government Organisations and academia. A well-established routine community-based pregnancy, birth and under-5 child surveillance system are being maintained by trained female community health workers (CHWs) in this site. The CHWs identify sick children during routine household visits and refer the children to health facilities. They also educate carers of children about pneumonia signs and symptoms, so that the carers can visit nearby community clinic (CC) without delay.

Bangladesh has established about 13,000 CCs, one each for ~6,000 people (138). Each CC is staffed by a CHCP with at least 12th grade education and three months of preservice training, including the IMCI tool. Each CHCP is responsible for providing primary health care for the population, including its catchment area’s children. Nine CCs will be purposively selected from the Projahnmo surveillance area (Zakiganj sub-district of Sylhet district of

Bangladesh) (Figure 4.2). CHCP of respective CC will screen all under-5 children while providing primary healthcare.

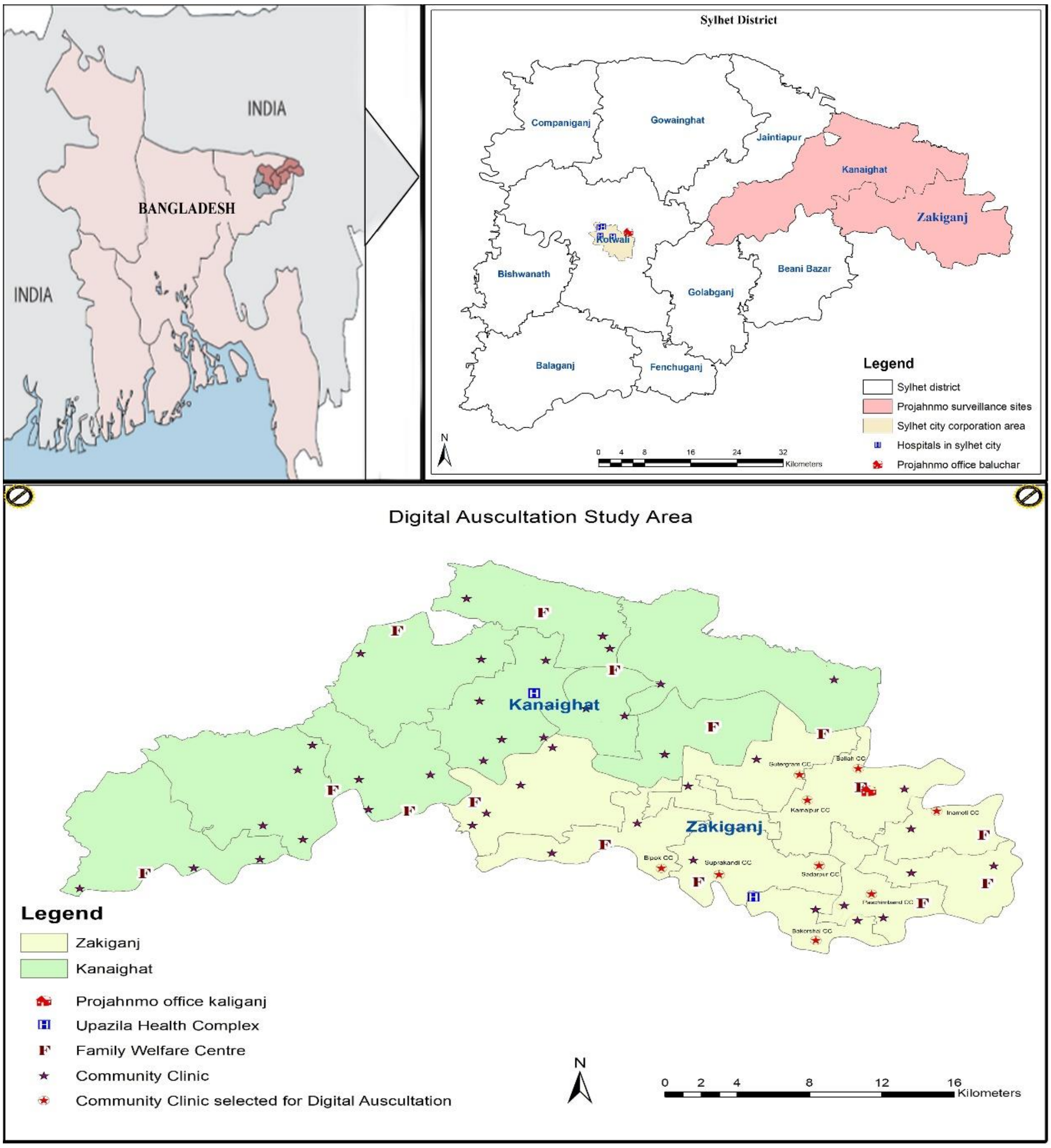

Figure 4.2 Study site

All CHWs and CHCPs will be trained and standardised to identify signs and symptoms of pneumonia according to WHO IMCI guidelines. CHWs and CHCP will be trained to identify nasal flaring, head nodding, tracheal tugging, grunting, intercostal retractions, and stridor when calm by a paediatrician using video documentation and clinical settings at hospitals. They will be equipped with a tablet and videos of those signs to watch regularly and a study physician will also conduct refresher training every two months to standardise them. A study physician will be recruited to provide training and supervision of CHCPs and CHWs in clinical assessments, measurement of peripheral oxyhaemoglobin saturation (SpO_2) and recording of lung sounds using the Smartscope. However, the study physician will not be directly involved in recording lung sounds from the study participants. CHCPs will pre-screen children using IMCI guidelines and refer severe pneumonia cases to higher-level hospitals. As respiratory danger signs are not part of IMCI guidelines, so, they will assess those signs (nasal flaring, head nodding, tracheal tugging, grunting, intercostal retractions) during assessment for research purposes. They will refer those cases to higher-level hospitals where oxygen support and injectable antibiotics are available.

4.3.2 Study design and procedure

Using a cross-sectional design, each CHCP will screen all children younger than five years consecutively visiting the CC. CHCP will obtain consent and record lung sounds of children who fulfilled the following criteria: history and/or observed cough, and/or history and/or observed difficult breathing in a permanent resident of the Projahnmo site and not enrolled in the study within the past 30 days. CHCP will record sounds from four chest locations – two from the back and two from the front (Figure 4.3). Each position will be recorded for approximately 10s, and the overall recording process will take about 1 minute. The recorded sound files will then be transferred to a password-protected server. The CHCP will also examine the child for fast breathing by manually counting respirations and observe for abnormal breathing patterns such as lower chest wall indrawing, nasal flaring, head nodding, tracheal tugging, grunting, intercostal retractions and stridor when calm.

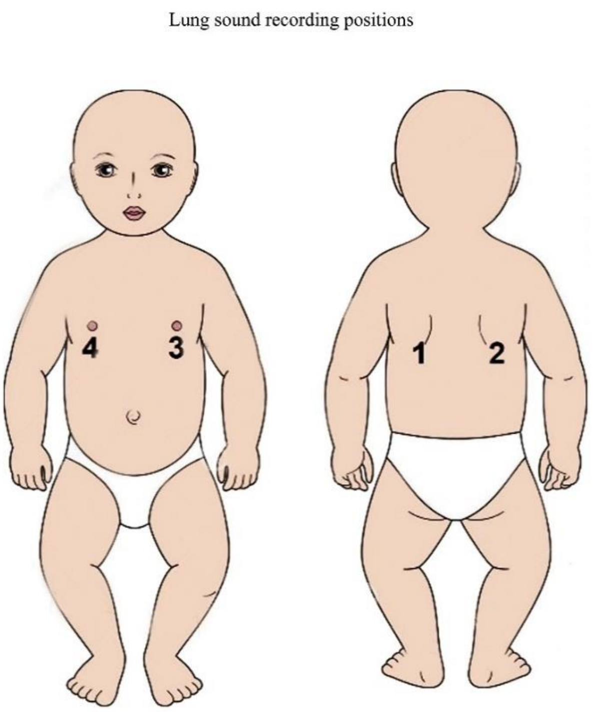

Figure 4.3 Lung sounds recording positions

CHCP will measure the SpO_2 using a Masimo Rad5 pulse oximeter, temperature using a digital thermometer, and anthropometry (weight, height and mid-arm circumference) using standard tools and techniques. The SpO_2 data will be used to classify pneumonia according to IMCI guidelines. If any child has a SpO_2 <90%, then referral to the sub-district health centre or Sylhet Osmani Medical College Hospital will be initiated. All enrolled children will be assessed after day-8 of enrolment by Projahnmo CHWs for treatment compliance and treatment outcome.

A total of 11 paediatricians will be trained in the methodology developed and validated during the Pneumonia Etiology Research for Child Health (PERCH) study (139). Only paediatricians successfully standardised to the methodology will serve as human listening panel members. Panellists will classify the recorded sound files of all four positions separately into five categories, for example (1) no wheeze and no crackles, (2) wheeze only (no crackles), (3) crackles only (no wheeze), (4) both wheeze and crackles or (5) uninterpretable. Two primary listeners will independently classify the recorded lung sounds, and any discrepancies will be arbitrated by the third listener (EDM). The panellists and EDM will be blinded to the clinical information of the children. Johns Hopkins and Sonavi Labs developed a machine learning algorithm; all sound files will also be classified into the same categories using this algorithm. This algorithm does not include the clinical information of the children, and this will be blinded to the panel classification. Finally, both classifications will be compared. Figure 4.4 depicts the study flow.

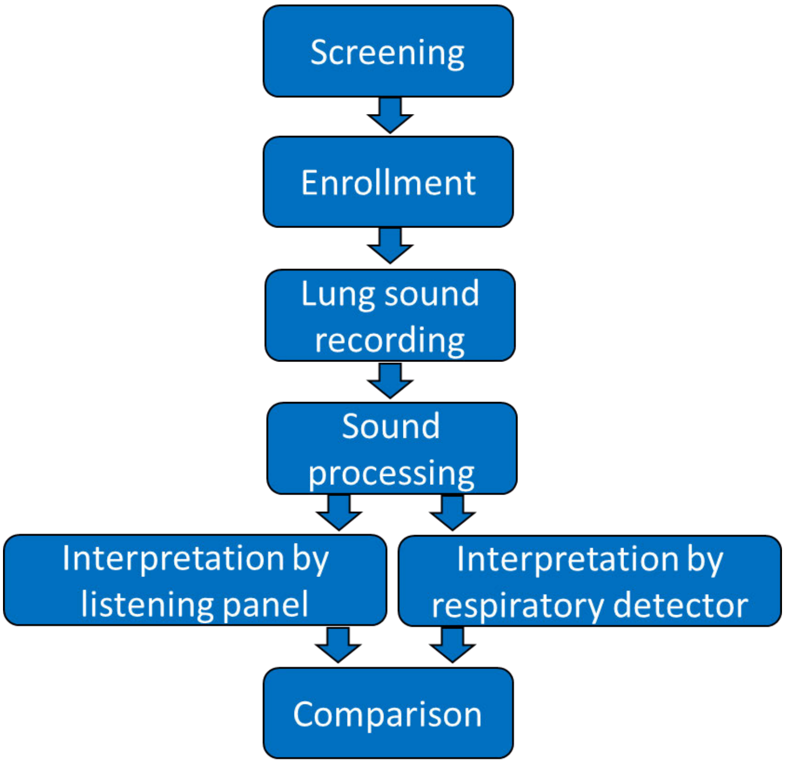

Figure 4.4 Study flow

4.3.3 Sample size calculation

Cohen's kappa will be used to assess inter-listener and computer-human agreement in this study. To detect a true kappa of 0.50 compared with a kappa of 0.40 under the null hypothesis and assuming two-sided type I error of 5%, power of 80% and two categories of frequencies equal to 70% and 30% normal and abnormal findings respectively, a sample size of 752 will be required (140). This sample size has been calculated in Power Analysis and Sample Size (PASS) software V.11.

We will include all quality recordings for this assessment. A quality recording is defined as a recording with >75% interpretable chest positions (i.e., three of the four chest positions recorded are interpretable). Assuming that 75% of all recordings will be of acceptable quality, we will need 1,003 subjects to be enrolled in this study to obtain our required sample size of 752.

4.3.4 Statistical analysis

A point estimate for the proportion of recordings along with a 95% CI that meets the definition of quality will be determined. The numerator will be the total number of recordings that were interpreted to meet quality criteria and the denominator will be the total number of recordings collected and interpreted. A raw agreement percentage will be determined between the interpretations of the two primary human listeners of the listening panel. The numerator will be the total number of recordings with an interpretation from the first and second human listener that agree, and the denominator will be the total number of recordings that have a final human interpretation from both primary listeners. Cohen's kappa, a metric that assesses the agreement beyond chance will be calculated, and a kappa adjusted for prevalence and bias will also be calculated. A kappa above 0.8 will be defined as perfect agreement, 0.61-0.8 as high agreement, 0.41-0.6 as moderate agreement, 0.21-0.4 as fair agreement, 0.01-0.2 as low agreement, and 0 as no agreement (141).

A raw agreement percentage between the overall human listening panel's final interpretation result and the computerised analysis algorithm's final interpretation result will be determined. The numerator will be the total number of recordings with an interpretation from the human listening panel and the computerised algorithm that agree, and the denominator will be the total number of recordings that have both a human and computerised interpretation.

Cohen’s kappa, a metric that assesses the agreement beyond chance will be calculated, and a kappa adjusted for prevalence and bias will also be calculated. The same kappa scale detailed previously will be used for interpretation.

The performance of the computerised interpretation algorithm will be evaluated when assuming the human listening panel’s final interpretation is the reference standard. Sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios will be assessed.

4.3.5 Patient and public involvement

We formed patient public involvement groups (PPIG) consisting of CHCPs, CHWs, Health Assistants, Physicians, community leaders, religious leaders, parents of under-5 children, teachers, local journalists and organised several meetings in the community for their insights, approval, and support to implement the study. They believe its feasible and acceptable to implement the study. We also consulted and engaged several district and national level stakeholders including public health program managers, policymakers, paediatricians, physicians, and civil society representatives during the development of the protocol and implementation strategy of the study. A technical review committee (TRC) consisting of policymakers and technical experts formed by the Bangladesh MOHFW reviewed and approved the protocol.

The study results will be reviewed by the PPIG and TRC before publishing in peer-reviewed journals, will be presented at international conferences and to health officials in Bangladesh. The findings also will be disseminated to stakeholders at Zakiganj subdistrict, Sylhet district and national level at Dhaka, Bangladesh.

4.3.6 Data collection and storage

Data will be collected using password-protected electronic devices (Samsung Galaxy Tab A V.7.0) in the Android platform. The data will be transferred to a server (SQL Server 2008 R2) located at Sylhet, Bangladesh in real-time using internet connectivity and will keep a backup copy daily in another server at the study Dhaka office. All the tablets and servers will be password protected. Recorded lung sounds will be transferred to the server. Paediatric listening panel members will fill up the lung sound interpretation on an online database which will also be stored on the server in real time. Data collection has been started on 07 November 2019 and this is planned to be completed by March 2022.

4.3.7 Ethics and dissemination

Ethical approval was obtained from the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), Bangladesh (Registration Number: 09630012018), and Academic and Clinical Central Office for Research and Development (ACCORD) Medical Research Ethics Committee (AMREC) NHS, Lothian, Edinburgh, UK (REC Reference: 18-HV-051). This study was registered with ClinicalTrails.gov (NCT03959956). Informed written consent will be obtained from the parent or guardian of each child. Access to collected data will be restricted to individuals from the research team treating the participants, representatives of the sponsor(s), and representatives of regulatory authorities. Dissemination will be through conference presentations, peer-reviewed journals and stakeholder engagement meetings in Bangladesh. Anonymised data files will also be stored securely in the DataStore repository at the University of Edinburgh, UK and will be shared after publication of main paper.

4.4 Discussion

This study aims to demonstrate the feasibility of collecting quality lung sounds by frontline health workers and to examine the performance of the machine learning algorithm against a panel of human listeners for identifying adventitial lung sounds. To our knowledge, this is the first study that will assess the recording of lung sounds of children younger than five years in first-level facilities by frontline workers in LMICs, where the burden of pneumonia and antibiotic use is high and diagnostic capacity is limited. The PERCH study enrolled children at a hospital setting and digital auscultation was performed by physicians, formally trained clinical assistants, or nurses (139), another study enrolled children at a tertiary level centre in Lima, Peru (142), and paediatricians recorded lung sounds in two tertiary level teaching hospitals in a study in Nepal (143). Recording lung sounds in a first-level facility poses unique challenges in that clinics are typically crowded, and the environment can be chaotic and noisy. Furthermore, ill children younger than five years of age can be especially uncooperative in uncomfortable ambulatory settings, leading to unique challenges like agitation, crying, vocalizations, and the associated auscultation artefacts these create. Healthcare providers in ambulatory settings may lack the necessary time to calm the child and address these issues due to pressures from a high patient volume. If frontline health workers can effectively use digital auscultation in their typical clinical setting, then many false-positive pneumonia cases may be spared from treatment with antibiotics, which may reduce the cost of treatment as well as reduce the chance of developing antimicrobial resistance. A systematic analysis of 132 national surveys from 73 countries reported that on average, 4 of 10 ill children below age 5 years in LMICs are treated with antibiotics (144). Recently, United Nations General Assembly announced that antimicrobial resistance is the most important and urgent threat globally (145).

One limitation of our study is that chest radiography will not be performed as it is not routinely available in first-level facilities in Bangladesh, and we will not compare radiographic imaging with lung sound classification. Instead, lung sound classifications will be compared with clinical findings among children meeting IMCI pneumonia to those who do not. Lack of a gold standard reference for pneumonia is well understood, and it is widely accepted that chest radiography itself lacks diagnostic accuracy for pneumonia (146). For example, it was found that many children with IMCI-defined clinical pneumonia (age-specific tachypnoea) had normal chest radiographs (59) and may have normal lung sounds and may not require antibiotics. In this study, we will utilise the paediatrician listening panel as our reference standard as previously described (139). We have shown that lung sound classifications of digital auscultation recordings generated using a listening panel approach have strong associations with radiographic findings and also mortality outcomes (147).

Future work ranges from additionally refining this device, based on lessons learned from the use of the device at the first-level facility during this study, as well as phase 1 and 2 clinical trials that prospectively integrate the digital auscultation into the WHO pneumonia management pathway to evaluate patient outcomes after digital auscultation-based decision-making. Eventually, if these preliminary studies are successful, a large multi-country clinical trial could be designed to evaluate the safety and efficacy of digital auscultation to improve pneumonia management.

4.5 Strengths and limitations of this study

- Evaluating the quality of lung sound recordings in a first-level facility where auscultation is usually unavailable and challenging to obtain due to a typically crowded and noisy environment and providers may not get enough time to calm the child due to time pressure from a high-volume patient.
- This study will assess the feasibility of recording lung sounds by frontline community health workers who do not usually use conventional stethoscopes during clinical care.
- Two standardised paediatricians masked to the child's clinical status will independently classify the recorded lung sounds, and a third masked and independent paediatrician will arbitrate any discrepancies.

- A machine learning algorithm developed by Johns Hopkins and Sonavi Labs will detect abnormal lung sounds and be compared with classifications by human listeners/paediatricians.
- The study will not have chest radiography findings of enrolled children, which is considered by many a gold standard for pneumonia diagnosis, as chest radiography is not available at this level of the health system in Bangladesh.

4.6 Conclusion

The methodology chapter details the approach taken to answer the research question and achieve the study's objectives. Some additional information, which were not available in the published paper, have been reported as supplementary materials on page 311 in Chapter 13. The results of the study, which are presented in Chapters 5 to 7, contribute to the existing body of knowledge on diagnosing childhood pneumonia and have implications for future research, policy, and practice.

4.7 Acknowledgements

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4.8 Contributors

SA, EDM, and AHB conceptualised and designed this study. AHB, EDM, HN, SC provided mentorship to SA. HC, AS and DKM critically review the study design. JN and DKM reviewed the sample size estimation and analysis plan. EDM will provide training to the human listening panel and IMM will analyse the recorded sound files using a machine learning algorithm. NHC and NB will be responsible for data management and AAI will manage the field implementation of this study. SA drafted the manuscripts and all authors critically reviewed and approved the final manuscript before submission.

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Chapter 5 Results: Socio-demographic and clinical characteristics

5.1 Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 flow

A total of 2,434 children aged 2-59 months were screened for enrolment in nine community clinics in Zakiganj sub-district of Sylhet District, north-east Bangladesh from 07 November 2019 to 19 December 2020 with an interruption from 23 March 2020 to 10 September 2020 due to COVID-19 lockdown. Of these, more than half (n=1,366) were ineligible due to not having cough or difficulty breathing. Among the 1,068 eligible children, 22 children were excluded due to severe illness requiring immediate referral during screening and 17 children were excluded as those children were enrolled previously within the past 30 days in this study, 56 children's carers refused to enrol, leaving a total of 990 children enrolled. Of the 990 children, 389 children were classified as having "any" pneumonia based on the IMCI case definition, and 601 children had no sign or symptom of pneumonia. Among 389 children with "any" pneumonia, lung sounds were recorded in 385 (99.0%) children, and from 601 children with no pneumonia, lung sounds were recorded in 595 (99.0%) children. Lung sounds were not recorded in a total of ten (four from any pneumonia and six from no pneumonia groups) children due to technical issues with the prototype Feelix Smartscope device (n=8), and the CHCP forgetting to record the participant (n=2). Lung sound files in 381 (97.9%, 381/389) children were successfully transferred from the Feelix Smartscope to a secure study laptop in the pneumonia group and 593 (98.7%, 593/601) in the no pneumonia group. Among the any pneumonia group, lung sounds were recorded in 378 (98.3%, 378/385) children in ≥3 chest positions and among the no pneumonia group in 588 (98.8%, 588/595) children. These recordings were then successfully transferred to the laptop for post-processing (Figure 5.1).

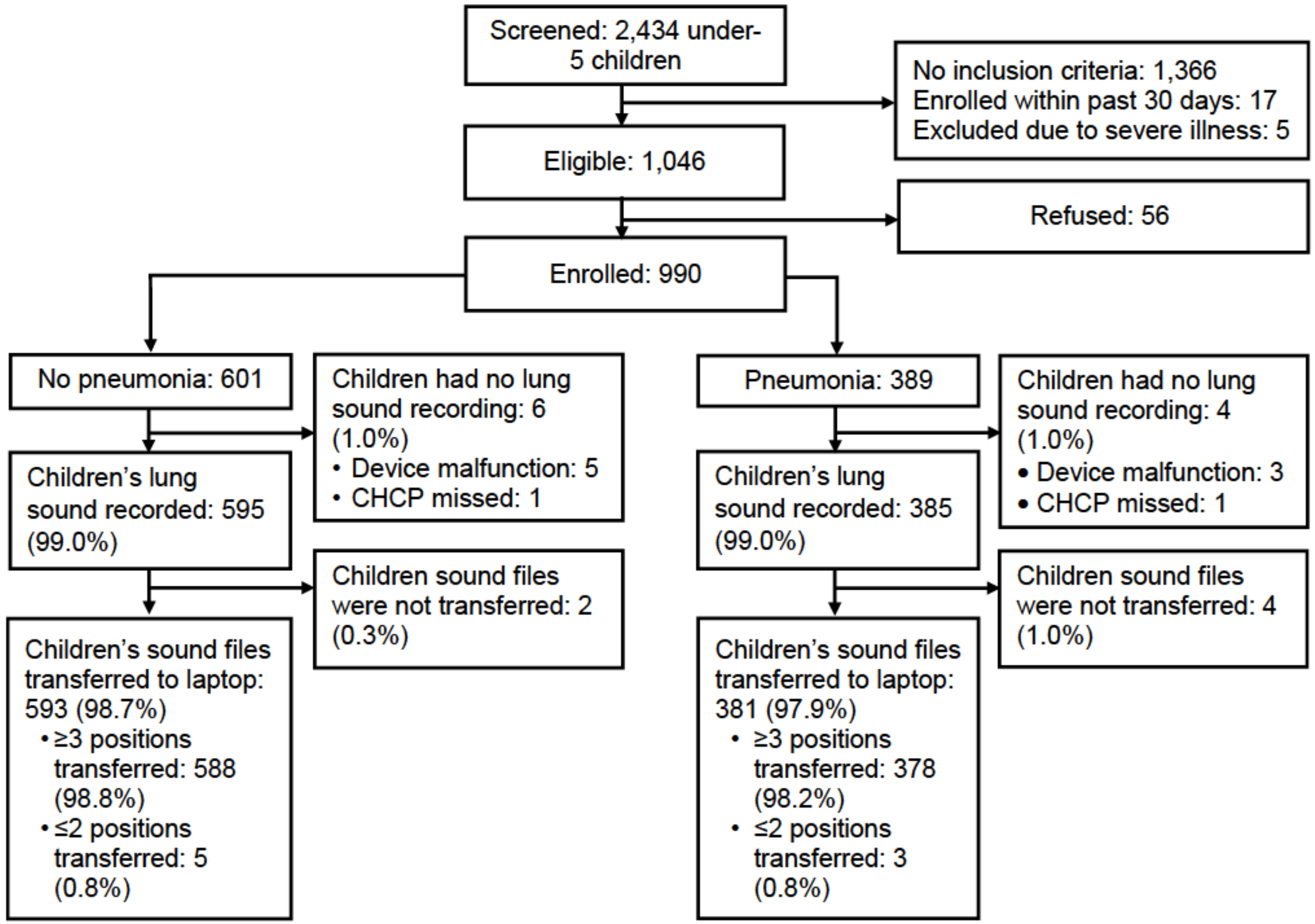

Figure 5.1 Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 flow diagram

5.2 Children's characteristics

Table 5.1 shows the selected characteristics of the enrolled children. The majority of children were 12 months or older (74.7%) and the proportion of this group was slightly higher in the any pneumonia group (76.6%) compared to the no pneumonia group (73.7%). The overall male-female ratio was 1:0.8. The proportion of males was higher in the 'any pneumonia' group (59.4%) than in the 'no pneumonia' group (53.4%). The prevalence of underweight, stunting and wasting was 36.8%, 46.3% and 17.0%, respectively. About 83.8% of children were breastfed for more than six months, but only 45.8% were exclusively breastfed for more than four months. About 17.3% of children had reported diarrhoea within the past two weeks during day-8 follow-up visits. The SpO_2 was 90-93% in 3.9% of children during enrolment. Notably, the proportion of children with SpO_2 in the 90% - 93% range was significantly higher in the 'any pneumonia' group than the 'no pneumonia' group (5.7% vs 2.8%, p=0.03). Fever was present in 7.7% of children; this proportion was significantly higher in the 'any pneumonia group' than the 'no pneumonia' group (10.8% vs 5.7%, p<0.01). The proportion of children fully immunised for age was 83.7% in both groups. About 86.2% of children were immunised for age with PCV vaccination; the proportion was almost equal in both groups.

Table 5.1 Selected child characteristics by IMCI pneumonia classification

Selected child characteristics	**Any Pneumonia**	**No pneumonia**	**Total**	**P-value**
	N (%)	N (%)	N (%)	
	389	601	990	
Age group				
2-11 months	92 (23.7)	158 (26.3)	250 (25.3)	0.35
12-59 months	297 (76.3)	443 (73.7)	740 (74.7)	
Sex				
Male	231 (59.4)	321 (53.4)	552 (55.8)	0.07
Female	158 (40.6)	280 (46.6)	438(44.2)	
Underweight (weight for age)				
Normal (Z Score ≥ -2)	249 (64.0)	377 (62.7)	626 (63.2)	0.66
Mild underweight (Z Score ≥ -3 to < -2)	93 (23.9)	158 (26.3)	251 (25.4)	
Severe underweight (Z Score < -3)	47 (12.1)	66 (11.0)	113 (11.4)	
Stunting (height for age)				
Normal (Z Score ≥ -2)	203 (52.2)	329 (54.7)	532 (53.7)	0.10
Mild stunting (Z Score ≥ -3 to < -2)	106 (27.2)	180 (30.0)	286 (28.9)	
Severe stunting (Z Score < -3)	80 (20.6)	92 (15.3)	172 (17.4)	
Wasting (weight for height)				
Normal (Z Score ≥ -2)	322 (82.8)	500 (83.2)	822 (83.0)	0.97
Mild wasting (Z Score ≥ -3 to < -2)	51 (13.1)	78 (13.0)	129 (13.1)	

Selected child characteristics	Any Pneumonia	No pneumonia	Total	P-value
	N (%)	N (%)	N (%)	
Severe wasting (Z Score < -3)	16 (4.1)	23 (3.8)	39 (3.9)	
Breastfeeding duration				
≤6 months	65 (16.7)	95 (15.8)	160 (16.2)	0.71
>6 months	324 (83.3)	506 (84.2)	830 (83.8)	
Exclusive breastfeeding duration				
≤4 months	217 (55.8)	320 (53.2)	537 (54.2)	0.43
>4 months	172 (44.2)	281 (46.8)	453 (45.8)	
Diarrhoea within last two weeks				
Yes	69 (17.7)	102 (17.0)	171 (17.3)	0.76
No	320 (82.3)	499 (83.0)	819 (82.7)	
Child received vitamin-A capsule in the past year				
Yes	248 (63.8)	393 (65.4)	641 (64.7)	0.60
No	141 (36.2)	208 (34.6)	349 (35.3)	
Child received Zinc supplementation within last two weeks				
Yes	35 (9.0)	58 (9.7)	93 (9.4)	0.73
No	354 (91.0)	543 (90.3)	897 (90.6)	

Selected child characteristics	**Any Pneumonia**	**No pneumonia**	**Total**	**P-value**
	N (%)	N (%)	N (%)	
Child received Iron syrup in the last six months				
Yes	16 (4.1)	23 (3.8)	39 (3.9)	0.82
No	373 (95.9)	578 (96.2)	951 (96.1)	
Child's clinical characteristics				
Oxygen saturation				
SpO_2 <90%	0 (0.0)	0 (0.0)	0 (0.0)	0.03
SpO_2 90% - 93%	22 (5.7)	17 (2.8)	39 (3.9)	
SpO_2 94% - 100%	367 (94.3)	584 (97.2)	951 (96.1)	
Fever (≥100.4°F)				
Yes	42 (10.8)	34 (5.7)	76 (7.7)	<0.01
No	347 (89.2)	567 (94.3)	914 (92.3)	
Immunisation status (all vaccines)				
Fully immunised for age	326 (83.8)	503 (83.7)	829 (83.7)	1.00
Partially immunised for age	56 (14.4)	87 (14.5)	143 (14.4)	
Unvaccinated	7 (1.8)	11 (1.8)	18 (1.8)	
PCV Vaccination status				
Fully immunised for age	334 (85.9)	519 (86.4)	853 (86.2)	0.81
Partially immunised for age	44 (11.3)	62 (10.3)	106 (10.7)	
Unvaccinated	11 (2.8)	20 (3.3)	31 (3.1)	

5.3 Parents' characteristics

Table 5.2 describes the selected characteristics of the parents. About 60.5% of mothers had completed secondary or higher educational levels, and the proportion was almost equal in the 'no pneumonia' group (61.3%) and 'any pneumonia' group (59.2%). About 98.1% of mothers were homemakers, and the majority of the mothers were aged 30 years or less (69.6%). About 52.4% of fathers had completed the primary level of education, and the proportion was almost equal in 'any pneumonia' group (53.4%) than the 'no pneumonia' group (51.7%). The majority of the fathers' occupation was related to physical work (70.6%), such as day labour or agriculture work. About 55.4% of fathers were in the 35 years or less age group.

Table 5.2 Selected parental characteristics of the children

Parental characteristics	Any Pneumonia	No pneumonia	Total	P-value
	N (%)	N (%)	N (%)	
	389	601	990	
Mother's characteristics				
Mother's educational status				
No schooling	34 (8.8)	51 (8.5)	85 (8.6)	0.81
Primary	124 (32.0)	181 (30.2)	305 (30.9)	
Secondary or higher	230 (59.2)	368 (61.3)	598 (60.5)	
Mother's occupation				
Housewife	382 (98.5)	587 (97.8)	969 (98.1)	0.49
Working	6 (1.5)	13 (2.2)	19 (1.9)	
Mother's age				
≤30 years	266 (68.6)	422 (70.3)	688 (69.6)	0.55
>30 years	122 (31.4)	178 (29.7)	300 (30.4)	
Father's educational status				
No schooling	63 (16.2)	103 (17.2)	166 (16.8)	0.88
Primary	207 (53.4)	311 (51.8)	518 (52.4)	
Secondary or higher	118 (30.4)	186 (31.0)	304 (30.8)	
Father's occupation				
Physical work	278 (71.6)	420 (70.0)	698 (70.6)	0.58
Non-physical work	110 (28.4)	180 (30.0)	290 (29.4)	
Father's age				
≤35 years	206 (53.1)	345 (57.5)	551 (55.8)	0.17
>35 years	182 (46.9)	255 (42.5)	437 (44.2)	

Note: One mother's and one father's data were missing.

5.4 Household characteristics

Table 5.3 illustrates the selected household characteristics and socioeconomic status (SES) of the participants. Sixty per cent of the participants' households had more than five members. The proportion of more than five household members was significantly higher in ‘any pneumonia’ group compared to the ‘no pneumonia’ group (64.3% vs 57.2%, p=0.03). Most households (89.6%) had one or two children younger than five years. About 72.0% of households had more than one bedroom, but three or more people slept per room in 40.4% of households. About 80.8% of households had at least one smoker who smoked inside the home; among them, the proportion in ‘any pneumonia’ group was 82.5%. About 97.6% of households used electricity for lighting, and 96.6% of households used wood/coal/animal dung for cooking as fuel where cooking and sleeping room were different (86.7%). Children went into the cooking area every day in about 71.4% of houses. Tube well/hand pump/borehole/public tap was the source of drinking water in about 78.8% of households and the majority of the houses had unhygienic toilets (66.8%). About 26.7% of households were lower class in terms of wealth quintiles, and this proportion of households that were lower class was higher in the ‘any pneumonia’ group than the ‘no pneumonia’ group (29.3% vs 25.0%, p=0.28), although the difference was not statistically significant.

Table 5.3 Selected household characteristics and socio-economic status

Selected household characteristics and SES	Any Pneumonia	No pneumonia	Total	P-value
	N (%)	N (%)	N (%)	
	389	601	990	
Number of household members				
≤5	139 (35.7)	257 (42.8)	396 (40.0)	0.03
>5	250 (64.3)	344 (57.2)	594 (60.0)	
Number of under-5 children in the household				
≤2	346 (88.9)	541 (90.0)	887 (89.6)	0.59
>2	43 (11.1)	60 (10.0)	103 (10.4)	
Number of bedrooms				
One	105 (27.0)	167 (27.8)	272 (27.5)	0.78
More than one	284 (73.0)	434 (72.2)	718 (72.5)	
Number of persons slept last night at home				
≤5	158 (40.6)	277 (46.1)	435 (43.9)	0.09
>5	231 (59.4)	324 (53.9)	555 (56.1)	
Number of persons slept per room				
≤3	228 (58.6)	362 (60.2)	590 (59.6)	0.61
>3	161 (41.4)	239 (39.8)	400 (40.4)	
Anyone smoked inside the house				
Yes	321 (82.5)	479 (79.7)	800 (80.8)	0.27
No	68 (17.5)	122 (20.3)	190 (19.2)	

Selected household characteristics and SES	Any Pneumonia	No pneumonia	Total	P-value
	N (%)	N (%)	N (%)	
Type of fuel used for cooking				
Electricity/gas	15 (3.9)	19 (3.2)	34 (3.4)	0.56
Wood/coal/animal dung	374 (96.1)	582 (96.8)	956 (96.6)	
Cooking and sleeping place				
Same room	54 (13.9)	78 (13.0)	132 (13.3)	0.68
Different room	335 (86.1)	523 (87.0)	858 (86.7)	
Child went into the cooking area				
Every day	271 (69.8)	434 (72.3)	705 (71.4)	0.40
Occasionally	117 (30.2)	166 (27.7)	263 (28.6)	
Type of fuel used for lighting				
Electricity	376 (96.7)	590 (98.2)	966 (97.6)	0.13
Kerosene/other	13 (3.3)	11 (1.8)	24 (2.4)	
Source of drinking water				
Tube well/hand pump/borehole/public tap	318 (81.7)	462 (76.9)	780 (78.8)	0.07
Surface water (river/dam/lake/pond)	71 (18.3)	139 (23.1)	210 (21.2)	
Type of toilet facility				
Flush/pour flush toilet	118 (30.3)	211 (35.1)	329 (33.2)	0.12
Unhygienic toilet	271 (69.7)	390 (64.9)	661 (66.8)	
Main material of the floor				

Selected household characteristics and SES	Any Pneumonia	No pneumonia	Total	P-value
	N (%)	N (%)	N (%)	
Natural or rudimentary floor	297 (76.3)	447 (74.4)	744 (75.2)	0.48
Finished floor	92 (23.7)	154 (25.6)	246 (24.8)	
Main material of the roof				
Tin/wood/ceramic tiles	382 (98.2)	580 (96.5)	962 (97.2)	0.12
Cement	7 (1.8)	21 (3.5)	28 (2.8)	
Main material of the exterior walls				
Natural or rudimentary walls	104 (26.7)	155 (25.8)	259 (26.2)	0.74
Finished walls	285 (73.3)	446 (74.2)	731 (73.8)	
Wealth quintiles				
Lowest	85 (21.9)	115 (19.1)	200 (20.2)	0.28
Lower	114 (29.3)	150 (25.0)	264 (26.7)	
Middle	48 (12.3)	82 (13.6)	130 (13.1)	
Higher	70 (18.0)	132 (22.0)	202 (20.4)	
Highest	72 (18.5)	122 (20.3)	194 (19.6)	

5.5 Children's clinical status during enrolment

Table 5.4 reveals the distribution of symptoms reported by carers during enrolment. The majority of them reported cough (99.3%) as the main symptom. Other reported symptoms were breathing difficulty (32.0%), which was significantly higher in 'any pneumonia' group in comparison to 'no pneumonia' group (50.6% vs 20.0%, p<0.01). Chest indrawing (1.7%) was less frequently reported as a symptom by the carers.

Table 5.4 Distribution of symptoms reported by carers during enrolment (multiple responses)

Symptoms reported by carers	**Any pneumonia N=389 n (%)**	**No pneumonia N=601 n (%)**	**Total N=990 n (%)**	**P-value**
Cough	383 (98.5)	600 (99.8)	983 (99.3)	0.01
Breathing difficulty	197 (50.6)	120 (20.0)	317 (32.0)	<0.01
Fever	87 (22.4)	154 (25.6)	241 (24.3)	0.24
Chest indrawing	17 (4.4)	0 (0.0)	17 (1.7)	<0.01

Table 5.5 shows the distribution of signs during enrolment identified by CHCPs among enrolled children. The CHCPs identified age-specific fast breathing in 37.6% of children. In the 'any pneumonia' group, CHCPs identified age-specific fast breathing in 95.6% of children and chest indrawing in 6.4% of children. The axillary temperature was ≥100.4°F in 10.8% of children in the 'any pneumonia' group and 5.7% children in the 'no pneumonia' group (p<0.01). None of the enrolled children had SpO_2 <90%. The SpO_2 was 90%-93% in 3.9% of children. The proportion of 90% - 93% SpO_2 was higher in the 'any pneumonia group' than the 'no pneumonia' group (5.7% vs 2.8%, p<0.03).

Table 5.5 Distribution of signs during enrolment identified by CHCP among enrolled children by IMCI classification (multiple responses)

Clinical signs	**Any pneumonia N=389 n (%)**	**No pneumonia N=601 n (%)**	**Total N=990 n (%)**	**P-value**
Runny nose	51 (13.1)	134 (22.3)	185 (18.7)	<0.01
Age-specific fast breathing	372 (95.6)	0 (0.0)	372 (37.6)	<0.01
Chest indrawing	25 (6.4)	0 (0.0)	25 (2.5)	<0.01
Head nodding	6 (1.5)	0 (0.0)	6 (0.6)	<0.01
Tracheal tugging	9 (2.3)	0 (0.0)	9 (0.9)	<0.01
Stridor when calm	32 (8.2)	0 (0.0)	32 (3.2)	<0.01
Nasal flaring	8 (2.1)	0 (0.0)	8 (0.8)	<0.01
Grunting	3 (0.8)	0 (0.0)	3 (0.3)	0.03
Intercostal retraction	12 (3.1)	0 (0.0)	12 (1.2)	<0.01
Any respiratory danger sign	47 (12.1)	0 (0.0)	47 (4.7)	<0.01
Axillary temperature ≥100.4°F	42 (10.8)	34 (5.7)	76 (7.7)	<0.01
SpO_2 <90%	0 (0.0)	0 (0.0)	0 (0.0)	<0.03
SpO_2 90% - 93%	22 (5.7)	17 (2.8)	39 (3.9)	
SpO_2 94% - 100%	367 (94.3)	584 (97.2)	951 (96.1)	

WHO defined pneumonia:

- Only fast breathing without any chest indrawing or danger signs;

- Chest indrawing (with or without fast breathing).

WHO defined severe pneumonia: - Pneumonia with respiratory danger signs (this could include children with or without fast breathing and/or chest indrawing).

Table 5.6 Distribution of children following WHO defined pneumonia categories

Categories	N	%
Only age-specific fast breathing	334	33.74
Only chest indrawing	2	0.20
Both age-specific fast breathing and chest indrawing	6	0.61
Any respiratory danger sign	47	4.75
Cough (no pneumonia)	601	60.71
Total	990	100.0
Pneumonia (age-specific fast breathing and/or chest indrawing)	342	34.54
Severe pneumonia (any respiratory danger sign with or without fast breathing and/or chest indrawing	47	4.74
Cough (no pneumonia)	601	60.71
Total	990	100.0

5.6 Quality control assessment of pneumonia identification by CHCP

A physician was masked to the CHCP assessment of pneumonia or no pneumonia, trained and standardised on respiratory rate counting and identifying chest indrawing, assessed randomly selected 118 children within 90 minutes of an assessment conducted by a CHCP. Table 5.7 shows the accuracy of the CHCP's classification of 'any pneumonia' and 'no pneumonia', considering the physician's classification as the reference standard. A total of 35.6% of children (42/118) were classified as having 'any pneumonia' by the CHCP compared to 30.5% (36/118) by the physician.

Table 5.7 CHCP classification of any pneumonia and no pneumonia compared to physician classification

	Physician classification		
CHCP classification	**Any pneumonia**	**No pneumonia**	**Total**
Any pneumonia	29	13	42
No pneumonia	7	69	76
Total	36	82	118
Raw % agreement	98/118 (83.0%)		
Sensitivity (95% CI)	80.6% (64.0 – 91.8)		
Specificity (95% CI)	84.2% (74.4 – 91.3)		
PPV (95% CI)	69.1% (52.9 – 82.4)		
NPV (95% CI)	90.8% (81.9 – 96.2)		
Kappa (95% CI)	0.62 (0.44 – 0.80)		

CI – Confidence interval, NPV – Negative predictive value, PPV – Positive predictive value

5.7 Association of characteristics of children with treatment compliance

All enrolled children were reassessed between days 8 to 14 after enrolment. During this visit, their treatment compliance data were collected. CHCPs provided or prescribed antibiotics if they were stocked out to all children who identified pneumonia. Children with respiratory danger signs were referred to higher-level hospitals. A total of 323 children used antibiotics, and 12 children's treatment compliance data were missing, so 311 children's data were analysed for treatment compliance analysis. As shown in Table 5.8, only child age was found to be associated with treatment compliance in children diagnosed with IMCI-defined pneumonia treated with antibiotics from the bivariate analysis. Treatment compliance with antibiotics was significantly lower among children aged 2-11 months compared to children aged 12-59 months (OR = 0.5, 95% CI: 0.3, 0.9; P = <0.05).

Table 5.8 Factors associated with treatment compliance in children diagnosed with IMCI-defined pneumonia treated with antibiotics

Characteristics	**Total (n)***	**Treatment compliance**		**Unadjusted OR (95%CI)**	**p-value**
		Yes, n (%)	**No, n (%)**		
Age of the child					
2-11 months	77	43 (55.8)	34 (44.2)	0.5 (0.3, 0.9)	<0.05
12-59 months	234	165 (70.5)	69 (29.5)	Ref	
Total	311	208 (66.9)	103 (33.1)		
Child's Sex					
Male	184	123 (66.8)	61 (33.2)	1.0 (0.6, 1.6)	0.99
Female	127	85 (66.9)	42 (33.1)	Ref	
Total	311	208 (66.9)	103 (33.1)		
Mother's educational status					
No schooling	22	14 (63.6)	8 (36.4)	Ref	
Primary	105	74 (70.5)	31 (29.5)	1.4 (0.5, 3.6)	0.53
Secondary or higher	183	119 (65.0)	64 (35.0)	1.1 (0.4, 2.7)	0.90
Total	310**	207 (66.8)	103 (33.2)		

Characteristics	Total (n)*	Treatment compliance		Unadjusted OR (95%CI)	p-value
		Yes, n (%)	No, n (%)		
Mother's occupation					
Housewife	306	204 (66.7)	102 (33.3)	Ref	
Working	4	3 (75.0)	1 (25.0)	1.5 (0.2, 14.7)	0.73
Total	310	207 (66.8)	103 (33.2)		
Mother's age					
≤30 years	216	142 (65.7)	74 (34.3)	Ref	
>30 years	94	65 (69.1)	29 (30.9)	1.2 (0.7, 2.0)	0.57
Total	310	207 (66.8)	103 (33.2)		
Father's educational status					
No schooling	50	34 (68.0)	16 (32.0)	Ref	
Primary	169	110 (65.1)	59 (34.9)	0.9 (0.4, 1.7)	0.71
Secondary or higher	92	64 (69.6)	28 (30.4)	1.1 (0.5, 2.2)	0.85
Total	311	208 (66.9)	103 (33.1)		
Father's occupation					

Characteristics	Total (n)*	Treatment compliance		Unadjusted OR (95%CI)	p-value
		Yes, n (%)	No, n (%)		
Physical work	221	147 (66.5)	74 (33.5)	Ref	
Non-physical work	90	61 (67.8)	29 (32.2)	1.1 (0.6, 1.8)	0.83
Total	311	208 (66.9)	103 (33.1)		
Father's age					
≤35 years	173	112 (64.7)	61 (35.3)	Ref	
36 and above	138	96 (69.6)	42 (30.4)	1.2 (0.8, 2.0)	0.36
Total	311	208 (66.9)	103 (33.1)		
Wealth quintiles					
Lowest	66	40 (60.6)	26 (39.4)	0.7 (0.4, 1.5)	0.39
Lower	92	61 (66.3)	31 (33.7)	0.9 (0.5, 1.9)	0.84
Middle	38	27 (71.1)	11 (28.9)	1.2 (0.5, 2.8)	0.74
Higher	59	42 (71.2)	17 (28.8)	1.2 (0.5, 2.6)	0.70
Highest	56	38 (67.9)	18 (32.1)	Ref	
Total	311	208 (66.9)	103 (33.1)		
Pneumonia category					

Characteristics	Total (n)*	Treatment compliance		Unadjusted OR (95%CI)	p-value
		Yes, n (%)	No, n (%)		
Pneumonia	277	183 (66.1)	94 (33.9)	Ref	
Pneumonia with respiratory danger signs	34	25 (73.5)	9 (26.5)	1.4 (0.6, 3.1)	0.38
Total	311	208 (66.9)	103 (33.1)		

*Among 323 children who used antibiotics, 12 children's treatment compliance data were missing.
**One mother's data were missing

5.8 Association of characteristics of children with treatment failure

Projahnmo Community Health Workers (CHWs) were trained on the IMCI tool and standardised on respiratory rate counting and chest indrawing assessment. They visited enrolled children at their homes between day 8 and 14. During that visit, CHWs assessed children following the IMCI tool. Treatment failure was defined as the continuation of signs recorded at enrolment or the appearance of new sign(s). Multivariate logistic regression shows the factors associated with treatment failure among children with IMCI-defined pneumonia (Table 5.9). We included all covariates in the multivariate logistic regression which were significant at univariate analysis at 20% level. I found the children fully vaccinated for age with PCV were less likely to have treatment failure compared to those unvaccinated with PCV (aOR = 0.1, 95% CI 0.0, 0.9).

Table 5.9 Factors associated with treatment failure among children with IMCI-defined pneumonia

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
Age of the child							
2-11 months	91	6 (6.6)	85 (93.4)	2.1 (0.7, 6.2)	0.16	1.0 (0.3, 3.3)	0.94
12-59 months	283	9 (3.2)	274 (96.8)	Ref		Ref	
Total	374	15 (4.0)	359 (96.0)				
Child's Sex							
Male	224	12 (5.4)	212 (94.6)	2.8 (0.8, 9.9)	0.12	2.5 (0.6, 9.5)	0.19
Female	150	3 (2.0)	147 (98.0)	Ref		Ref	
Total	374	15 (4.0)	359 (96.0)				
Mother's educational status							
No schooling	30	1 (3.3)	29 (96.7)	Ref			
Primary	122	8 (6.6)	114 (93.4)	2.0 (0.2, 17.1)	0.51		

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
Secondary or higher	221	6 (2.7)	215 (97.3)	0.8 (0.1, 7.0)	0.85		
Total	373**	15 (4.0)	358 (96.0)				
Mother's occupation							
Housewife	368	15 (4.1)	353 (95.9)				
Working	5	0 (0.0)	5 (100.0)				
Total	373**	15 (4.0)	358 (96.0)				
Mother's age							
≤30 years	256	10 (3.9)	246 (96.1)	Ref			
>30 years	117	5 (4.3)	112 (95.7)	1.1 (0.4, 3.3)	0.87		
Total	373**	15 (4.0)	358 (96.0)				
Father's educational status							

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
No schooling	60	3 (5.0)	57 (95.0)	Ref			
Primary	200	11 (5.5)	189 (94.5)	1.1 (0.3, 4.1)	0.88		
Secondary or higher	113	1 (0.9)	112 (99.1)	0.2 (0.0, 1.7)	0.13		
Total	373**	15 (4.0)	358 (96.0)				
Father's occupation							
Physical work	267	13 (4.9)	254 (95.1)	Ref			
Non-physical work	106	2 (1.9)	104 (98.1)	0.4 (0.1, 1.7)	0.20	0.4 (0.1, 1.9)	0.26
Total	373**	15 (4.0)	358 (96.0)				
Father's age							
≤35 years	201	7 (3.5)	194 (96.5)	Ref			
36 and above	172	8 (4.7)	164 (95.3)	1.4 (0.5, 3.8)	0.57		
Total	373**	15 (4.0)	358 (96.0)				

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
Wealth quintiles							
Lower	140	8 (5.7)	132 (94.3)	6.7 (0.8, 54.7)	0.07		
Middle	122	6 (4.9)	116 (95.1)	5.7 (0.7, 48.5)	0.11		
Higher	112	1 (0.9)	111 (99.1)	Ref			
Total	374	15 (4.0)	359 (96.0)				
Underweight (weight for age)							
Normal (Z Score ≥ -2)	238	9 (3.8)	229 (96.2)	Ref			
Mild underweight (Z Score ≥ -3 to < -2)	90	4 (4.4)	86 (95.6)	1.2 (0.4, 4.0)	0.79		
Severe underweight (Z Score < -3)	46	2 (4.3)	44 (95.7)	1.2 (0.2, 5.6)	0.86		

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
Total	374	15 (4.0)	359 (96.0)				
Stunting (height for age)							
Normal (Z Score ≥ -2)	194	10 (5.2)	184 (94.8)	Ref			
Mild stunting (Z Score ≥ -3 to < -2)	102	4 (3.9)	98 (96.1)	0.8 (0.2, 2.4)	0.63		
Severe stunting (Z Score < -3)	78	1 (1.3)	77 (98.7)	0.2 (0.0, 1.9)	0.18		
Total	374	15 (4.0)	359 (96.0)				
Wasting (weight for height)							
Normal (Z Score ≥ -2)	310	12 (3.9)	298 (96.1)	Ref			

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
Mild wasting (Z Score ≥ -3 to < -2)	48	2 (4.2)	46 (95.8)	1.1 (0.2, 5.1)	0.92		
Severe wasting (Z Score < -3)	16	1 (6.2)	15 (93.8)	1.7 (0.2, 13.7)	0.64		
Total	374	15 (4.0)	359 (96.0)				
Severity of pneumonia							
Pneumonia	327	10 (3.1)	317 (96.9)	Ref		Ref	
Pneumonia with respiratory danger signs	47	5 (10.6)	42 (89.4)	3.8 (1.3, 11.3)	0.02	2.7 (0.9, 8.2)	0.07
Total	374	15 (4.0)	359 (96.0)				
Treatment compliance							

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
when treated with antibiotic							
Yes	208	9 (4.3)	199 (95.7)	1.2 (0.4, 3.4)	0.73		
No	166	6 (3.6)	160 (96.4)	Ref			
Total	374	15 (4.0)	359 (96.0)				
PCV vaccination status							
Fully vaccinated for age	320	8 (2.5)	312 (97.5)	0.1 (0.0, 0.6)	0.01	0.1 (0.0, 0.6)	0.01
Partially vaccinated	43	5 (11.6)	38 (88.4)	0.6 (0.1, 3.7)	0.57	0.7 (0.1, 3.8)	0.68
Unvaccinated	11	2 (18.2)	9 (81.8)	Ref		Ref	
Total	374	15 (4.0)	359 (96.0)				
Adventitious lung sounds by							

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
paediatric listening panel							
Yes	127	6 (4.7)	121 (95.3)	1.3 (0.4, 3.7)	0.66		
No	239	9 (3.8)	230 (96.2)	Ref			
Total	366***	15 (4.1)	351 (95.9)				
Adventitious lung sounds by CLSA							
Yes	161	9 (5.6)	152 (94.4)	2.0 (0.7, 5.6)	0.20		
No	205	6 (2.9)	199 (97.1)	Ref			
Total	366***	15 (4.1)	351 (95.9)				
Wheeze (wheeze only or both wheeze and crackles) by							

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
paediatric listening panel							
Yes	94	6 (6.4)	88 (93.6)	2.0 (0.7, 5.7)	0.20		
No	272	9 (3.3)	263 (96.7)	Ref			
Total	366***	15 (4.1)	351 (95.9)				
Crackles (crackles only or both wheeze and crackles by paediatric listening panel							
Yes	73	2 (2.7)	71 (97.3)	0.6 (0.1, 2.7)	0.51		
No	293	13 (4.4)	280 (95.6)	Ref			
Total	366***	15 (4.1)	351 (95.9)				

Characteristics	Total*	Treatment failure		Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
		Yes n (%)	No n (%)				
IMCI pneumonia and normal lung sounds by both paediatric listening panel and CLSA							
Yes (No wheeze and no crackles)	148	4 (2.7)	144 (97.3)	0.5 (0.2, 1.7)	0.27		
No (wheeze/crackles/ both)	218	11 (5.0)	207 (95.0)	Ref			
Total	366***	15 (4.1)	351 (95.9)				

*15 children were excluded in this analysis as their follow up visit were conducted after 15 days of enrolment.
**1 mother and 1 father data were missing, so n=373.
***366 children had ≥3 chest positions lung sounds were interpretable and considered in this analysis and ≤2 chest position recordings were excluded.

Chapter 6 Results: Recording and interpretability of lung sounds

One of the objectives of my thesis was to evaluate whether CHCP can effectively record lung sounds from children younger than five years at government first-level community clinics. This chapter outlines the findings focusing on this objective.

6.1 Lung sound recording

Table 6.1 demonstrates that in more than 98% of children, lung sounds were recorded by CHCPs in ≥3 chest positions in both ‘any pneumonia’ and ‘no pneumonia’ groups. The proportions of children with ≥3 chest position recordings were not significantly different between the ‘any pneumonia’ group (98.5%) and ‘no pneumonia’ group (98.2%) (p=0.73).

Table 6.1 Recording lung sounds in ≥ 3 chest positions among under-5 children

	Any pneumonia N = 389 % (95% CI*) [n]	**No pneumonia N = 601 % (95% CI*) [n]**	**Total N = 990 % (95% CI*) [n]**	**p-value**
Children with ≥ 3 chest position recordings	98.5 (96.7, 99.4) [383]	98.2 (96.7, 99.1) [590]	98.3 (97.3, 99.0) [973]	0.73
Children with ≤ 2 chest positions recording	0.5 (0.1, 1.8) [2]	0.8 (0.3, 1.9) [5]	0.7 (0.3, 1.5) [7]	0.56
Children with no recording	1.0 (0.3, 2.6) [4]	1.0 (0.4, 2.2) [6]	1.0 (0.5, 1.8) [10]	0.96

* CI= Exact binomial confidence interval

Table 6.2 shows that lung sound recordings in 3 or more chest positions were classified as 'interpretable' by paediatric listening panel members in both 'any pneumonia' and 'no pneumonia' groups in about 88% of children. The proportion of children with interpretable lung sounds in 3 or more chest positions was not statistically different between the 'any pneumonia' group than in the 'no pneumonia' group (88.2% vs 87.2%, p=0.65).

Table 6.2 Children with interpretable lung sounds in ≥ 3 chest positions by IMCI classification

	Any pneumonia N = 389 % (95% CI*) [n]	**No pneumonia N = 601 % (95% CI*) [n]**	**Total N = 990 % (95% CI*) [n]**	**p-value**
Children with ≥ 3 interpretable chest positions	88.2 (84.5, 91.2) [343]	87.2 (84.3, 89.8) [524]	87.6 (85.4, 89.6) [867]	0.65
Children with ≤ 2 interpretable chest positions	5.9 (3.8, 8.7) [23]	6.8 (4.9, 9.1) [41]	6.5 (5.0, 8.2) [64]	0.57
Children with no recording or all four positions were uninterpretable	5.9 (3.8, 8.7) [23]	6.0 (4.2, 8.2) [36]	6.0 (4.6, 7.6) [59]	0.96

* CI= Exact binomial confidence interval

Table 6.3 shows the distribution of adventitious (i.e., abnormal) and normal lung sounds among children classified as having interpretable lung sound recordings in ≥ 3 vs ≤ 2 chest positions; there was no significant difference between the groups (p=0.62).

Table 6.3 Adventitious and normal lung sound distribution among children with interpretable lung sounds recorded in ≥ 3 vs ≤ 2 chest positions

	Interpretable lung sounds in ≤ 2 chest positions N = 64 % (95% CI*) [n]	**Interpretable lung sounds in ≥ 3 chest positions N = 867 % (95% CI*) [n]**	**Total N = 931 % (95% CI*) [n]**	**p-value**
Adventitious sounds	34.4 (22.9, 47.3) [22]	31.4 (28.3, 34.6) [272]	31.6 (28.6, 34.7) [294]	0.62
Normal sounds	65.6 (52.7, 77.1) [42]	68.6 (65.4, 71.7) [595]	68.4 (65.3, 71.4) [637]	

* CI= Exact binomial confidence interval

Table 6.4 shows the characteristics of children with interpretable lung sound recordings in 2 or less versus 3 or more chest positions. The proportion of the children with interpretable lung sound recordings in ≥ 3 chest positions was more common in children aged 12-59 months (94.0%) compared to children aged 2-11 months (90.3%), although this difference did not reach statistical significance (p=0.05). Interpretable lung sound recordings in three or more chest positions was less common in male (91.7%) than female children (95.0%), which was statistically significant (p <0.05), although the frequency was high among both sexes. Interpretable lung sound recordings in 3 or more chest positions was less common in children with SpO_2 90%-93% (87.5%) compared to those with SpO_2 94-100% (93.3%). However, this difference was again not statistically significant (p=0.20). From the perspective of the child's nutritional status, the proportion of children with interpretable lung sound recordings in ≥ 3 chest positions was also similar in the 'any pneumonia' group (93.7%) compared to 'no pneumonia group' (92.7%) (p=0.57). This proportion was lower in children with any respiratory danger sign (i.e., stridor when calm, nasal flaring, grunting, intercostal retractions, tracheal tugging, or head nodding) (88.6%) compared to those without any respiratory danger signs (93.3%), but was not statistically significant (p=0.23).

Table 6.4 Characteristics of children classified to have interpretable lung sound recordings in ≤ 2 vs ≥ 3 chest positions

	Total	**Children with interpretable recordings in ≤ 2 chest positions (n=64)**	**Children with interpretable recordings in ≥ 3 chest positions (n=867)**	**P-value**
Age group				
2-11 months	227	22 (9.7)	205 (90.3)	0.05
12-59 months	704	42 (6.0)	662 (94.0)	
Total	931	64 (6.9)	867 (93.1)	
Sex				
Male	515	43 (8.3)	472 (91.7)	<0.05
Female	416	21 (5.0)	395 (95.0)	
Total	931	64 (6.9)	867 (93.1)	
Oxygen saturation				
SpO_2 90% - 93%	32	4 (12.5)	28 (87.5)	0.20
SpO_2 94% - 100%	899	60 (6.7)	839 (93.3)	
Total	931	64 (6.9)	867 (93.1)	
Fever (≥100.4°F)				
Yes	74	5 (6.8)	69 (93.2)	0.97
No	857	59 (6.9)	798 (93.1)	
Total	931	64 (6.9)	867 (93.1)	
Underweight (weight for age)				
Normal (Z Score ≥ -2)	592	47 (7.9)	545 (92.1)	0.17
Mild underweight (Z Score ≥ -3 to < -2)	235	10 (4.3)	225 (95.7)	

	Total	Children with interpretable recordings in ≤ 2 chest positions (n=64)	Children with interpretable recordings in ≥ 3 chest positions (n=867)	P-value
Severe underweight (Z Score < -3)	104	7 (6.7)	97 (93.3)	
Total	931	64 (6.9)	867 (93.1)	
Stunting (height for age)				
Normal (Z Score ≥ -2)	499	39 (7.8)	460 (92.2)	0.33
Mild stunting (Z Score ≥ -3 to < -2)	274	18 (6.6)	256 (93.4)	
Severe stunting (Z Score < -3)	158	7 (4.4)	151 (95.6)	
Total	931	64 (6.9)	867 (93.1)	
Wasting (weight for height)				
Normal (Z Score ≥ -2)	774	51 (6.6)	723 (93.4)	0.27
Mild wasting (Z Score ≥ -3 to < -2)	122	12 (9.8)	110 (90.2)	
Severe wasting (Z Score < -3)	35	1 (2.9)	34 (97.1)	
Total	931	64 (6.9)	867 (93.1)	
Pneumonia status				
No pneumonia	565	41 (7.3)	524 (92.7)	0.57
Any pneumonia	366	23 (6.3)	343 (93.7)	

	Total	**Children with interpretable recordings in ≤ 2 chest positions (n=64)**	**Children with interpretable recordings in ≥ 3 chest positions (n=867)**	**P-value**
Total	931	64 (6.9)	867 (93.1)	
Any respiratory danger sign				
No	887	59 (6.7)	828 (93.3)	0.23
Yes	44	5 (11.4)	39 (88.6)	
Total	931	64 (6.9)	867 (93.1)	
Adventitious lung sound by paediatric listening panel				
No	637	42 (6.6)	595 (93.4)	0.62
Yes	294	22 (7.5)	272 (92.5)	
Total	931	64 (6.9)	867 (93.1)	

Table 6.5 shows the cooperation status of children during lung sound recordings. The proportion of cooperative and quiet children throughout the lung sound recordings was high in both 'any pneumonia' (81.6%) and 'no pneumonia' (78.7%) groups, and there was no significant difference in the child's cooperation status between the groups (p=0.3).

Table 6.5 Children's cooperation status during lung sounds recording by IMCI pneumonia classification

Children's cooperation status	**Any pneumonia**	**No pneumonia**	**Total**	**P-Value**
	%; (95% CI); [n]	**%; (95% CI); [n]**	**%; (95% CI); [n]**	
N	385	595	980	
Cooperative and quiet throughout	81.6 (77.3, 85.3) [314]	78.7 (75.1, 81.9) [468]	79.8 (77.1, 82.3) [782]	0.27
Cooperative but vocalized	2.3 (1.1, 4.4) [9]	2.9 (1.7, 4.5) [17]	2.7 (1.7, 3.9) [26]	0.62
Initially cooperative, became agitated but did not cry	3.9 (2.2, 6.3) [15]	3.2 (1.9, 4.9) [19]	3.5 (2.4, 4.8) [34]	0.56
Initially cooperative but agitated and cried	9.9 (7.1, 13.3) [38]	11.6 (9.1, 14.4) [69]	10.9 (9.0, 13.0) [107]	0.40
Did not cooperate	2.1 (0.9, 4.1) [8]	3.2 (1.9, 4.9) [19]	2.8 (1.8, 4.0) [27]	0.30

Children's cooperation status	**Any pneumonia**	**No pneumonia**	**Total**	**P-Value**
	%; (95% CI); [n]	**%; (95% CI); [n]**	**%; (95% CI); [n]**	
N	385	595	980	
throughout and cried				
Data missing	0.3 (0.0, 1.4) [1]	0.5 (0.1, 1.5) [3]	0.4 (0.1, 1.0) [4]	0.56

6.2 Interpretability of lung sounds recorded by CHCPs

Table 6.6 shows the distribution of children with different numbers of chest positions with lung sound recording by CHCPs. The proportion of children with interpretable lung sound recordings in ≥ 3 chest positions ranged from 73.1% to 94.7% by CHCP. Overall, lung sound recordings in ≥3 chest positions were interpretable in 87.6% (95% CI: 85.4%, 89.6%) children by the paediatrician listening panel.

Table 6.6 Distribution of children with ≥ 3 chest positions' sound recorded, transferred to laptop and interpretable

Code of the CHCP	**Children enrolled N**	**Any chest position lung sound recorded % [n]**	**≥ 3 positions lung sound transferred to laptop n (%)**	**≥ 3 chest positions were interpretable % (95% CI) [n]**
CHCP 1	38	97.4 [37]	97.4 [37]	76.3 (59.8, 88.6) [29]
CHCP 2	142	97.9 [139]	97.2 [138]	89.4 (83.2, 94.0) [127]
CHCP 3	130	97.7 [127]	97.7 [127]	82.3 (74.7, 88.4) [107]
CHCP 4	159	98.7 [157]	97.5 [155]	85.5 (79.1, 90.6) [136]
CHCP 5	86	95.3 [82]	94.2 [81]	80.2 (70.2, 88.0) [69]
CHCP 6	26	100.0 [26]	100.0 [26]	73.1 (52.2, 88.4) [19]
CHCP 7	179	98.3 [176]	97.2 [174]	92.7 (87.9, 96.1) [166]
CHCP 8	43	97.7 [42]	97.7 [42]	86.0 (72.1, 94.7) [37]

Code of the CHCP	Children enrolled N	Any chest position lung sound recorded % [n]	≥ 3 positions lung sound transferred to laptop n (%)	≥ 3 chest positions were interpretable % (95% CI) [n]
CHCP 9	187	100.0 [187]	99.5 [186]	94.7 (90.4, 97.4) [177]
Total	990	98.3 [973]	97.6 [966]	87.6 (85.4, 89.6) [867]

Among 990 children aged 2-59 months, 867 (87.6%) children had interpretable lung sound recordings at three or four positions (≥ 3 positions). Although the combined percentage (87.6%) of interpretable sound files ≥ 3 positions among enrolled children was high, percentages varied by CHCP and ranged from 73.1% to 94.7%. Figure 6.1 reveals that percentages of interpretable sound files ≥ 3 positions were low for CHCP 1 (76.3 %) and CHCP 6 (73.1%) compared to the overall estimate, although 95% confidence intervals were wide due to the limited number of recordings these CHCPs collected.

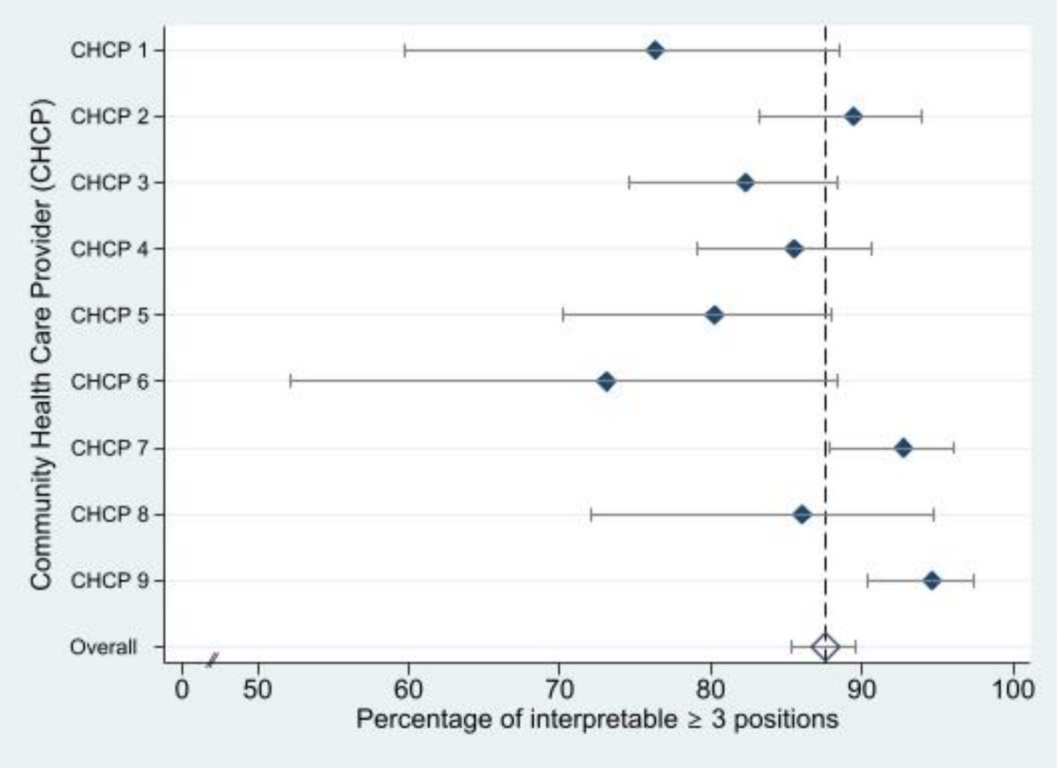

Figure 6.1 Percentage of children with interpretable lung sound recordings in ≥ 3 chest positions by CHCP

Figure 6.2 demonstrates a linear relationship between the number of enrolled children and the percentage of successfully recorded sound files in ≥3 chest positions (interpretable lung sounds in ≥ 3 chest positions for a child was defined as ‘successful’). The fitted linear regression model suggests the percentage of successful recordings by CHCPs increases with an increase in the enrolment number. On average, the percentage of successful recordings increased by 1% with every ten new enrolments.

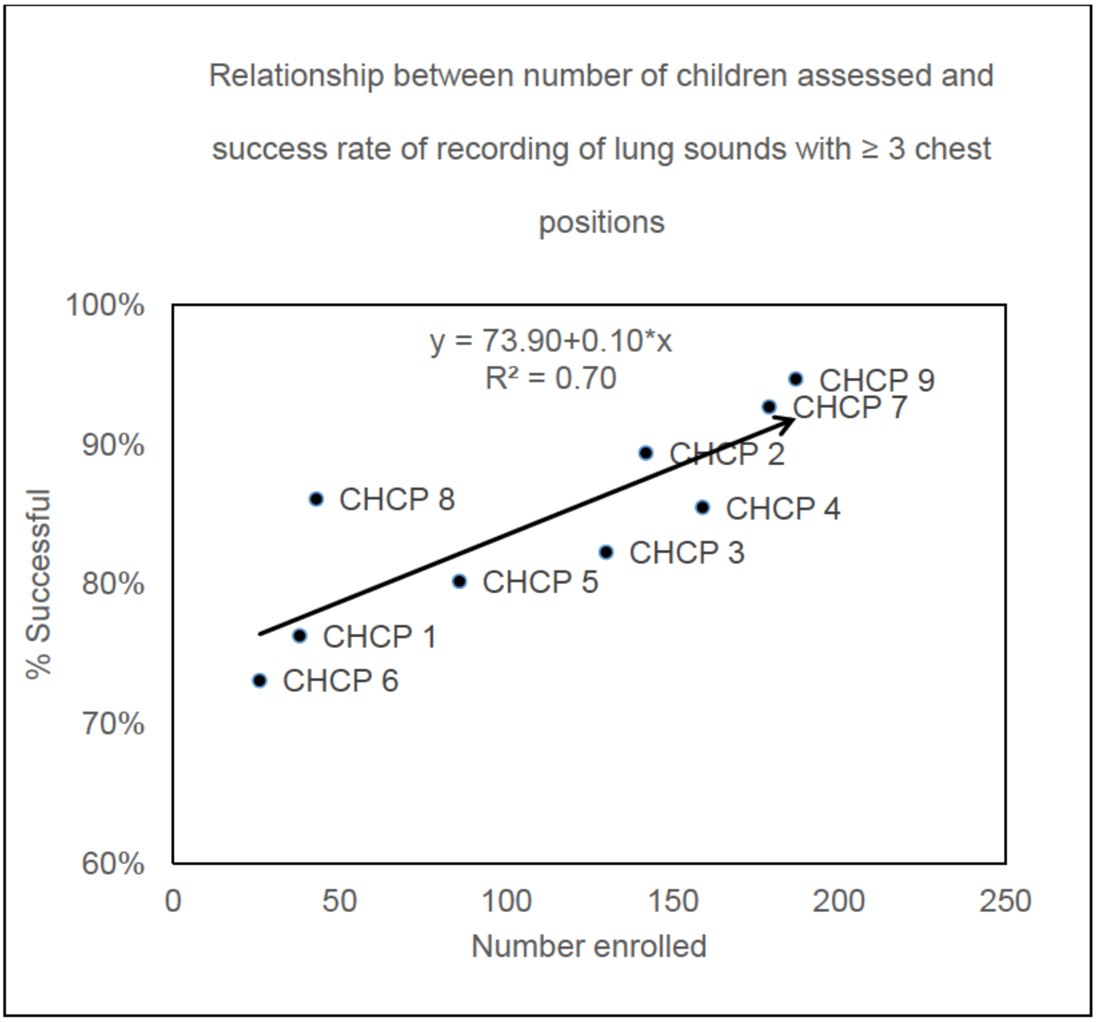

Figure 6.2 Distribution of number of enrolment and successfully recorded interpretable lung sounds in ≥ 3 chest positions

Table 6.7 shows the distribution of the number of children's sound files recorded, transferred from the prototype Feelix Smartscope to the study laptop, and then also deemed interpretable by the paediatric listening panel by chest position. We observed no variation in successfully recorded lung sounds according to chest position. CHCPs recorded interpretable sound files from more than 85% of back or front chest locations. As CHCPs recorded two back positions first, we observed that the success rate was significantly higher in back positions (positions 1 and 2) compared to front positions (positions 3 and 4) (92.0% vs 87.9%; $p<0.01$).

Table 6.7: Distribution of number of children's sound files recorded, transferred from the Smartscope to laptop, and interpretable by paediatric listening panel by chest position

Position	Number of children's sound files recorded	Number of sound files transferred from Smartscope to laptop	Percentage of sound files interpretable (among transferred)		Percentage of sound files interpretable *and* listeners were confident* (among transferred)	
			% (95% CI) [n]	p-value	% (95% CI) [n]	p-value
Position 1: (left back)	977	968	92.6 (90.7, 94.1) [896]		76.5 (73.8, 79.2) [741]	
Position 2: (right back)	978	970	91.3 (89.4, 93.0) [886]		74.9 (72.1, 77.6) [727]	
Position 3: (left front)	968	960	88.0 (85.8, 90.0) [845]		70.2 (67.2, 73.1) [674]	
Position 4: (right front)	971	963	87.7 (85.5, 89.8) [845]		72.6 (69.7, 75.4) [699]	
Back (left back and right back)	1955	1938	92.0 (90.6, 93.1) [1782]	<0.01	82.4 (80.5, 84.1) [1468]	0.39
Front (left front and right front)	1939	1923	87.9 (86.3, 89.3) [1690]		81.2 (79.3, 83.1) [1373]	

* Confidence was defined when the listener based their classification on at least one full, clear breath cycle in at least one chest position of a child

Table 6.8 reveals the time taken to record 3 or more interpretable lung sounds among all 4 chest positions. In the majority of children (56.6%) lung sounds were recorded in all four positions within one minute. The proportion of this group was significantly higher in the ‘no pneumonia’ compared to the ‘any pneumonia’ group (61.1% vs 49.7%, p<0.01). Only recording in 3.3% of children took 10 minutes or more, and this was attributed to technical issues with the prototype device.

Table 6.8 Time taken to record lung sounds classified as interpretable in ≥ 3 chest positions

Duration in minutes	**Any pneumonia n (%)**	**No pneumonia n (%)**	**Total N (%)**
1	167 (49.7)	316 (61.1)	483 (56.6)
2	26 (7.7)	23 (4.5)	49 (5.7)
3	53 (15.8)	71 (13.7)	124 (14.5)
4	31 (9.2)	47 (9.1)	78 (9.1)
5	20 (6.0)	12 (2.3)	32 (3.8)
6	12 (3.6)	11 (2.1)	23 (2.7)
7	9 (2.7)	8 (1.6)	17 (2.0)
8	6 (1.8)	7 (1.4)	13 (1.5)
9	3 (0.9)	3 (0.6)	6 (0.7)
10-18	9 (2.7)	19 (3.7)	28 (3.3)
Total	336 (100.0)	517 (100.0)	853 (100.0)

14 children were excluded in this analysis due to missing data

The time taken to record lung sounds and classified as interpretable by the listening panel in 3 or more chest positions is presented in Figure 6.3. The range of the time taken to record interpretable lung sounds in ≥3 chest positions was from a minimum of one minute to a maximum of 18 minutes. CHCPs recorded lung sounds in 56.6% of children within one minute and 89.7% of children within five minutes.

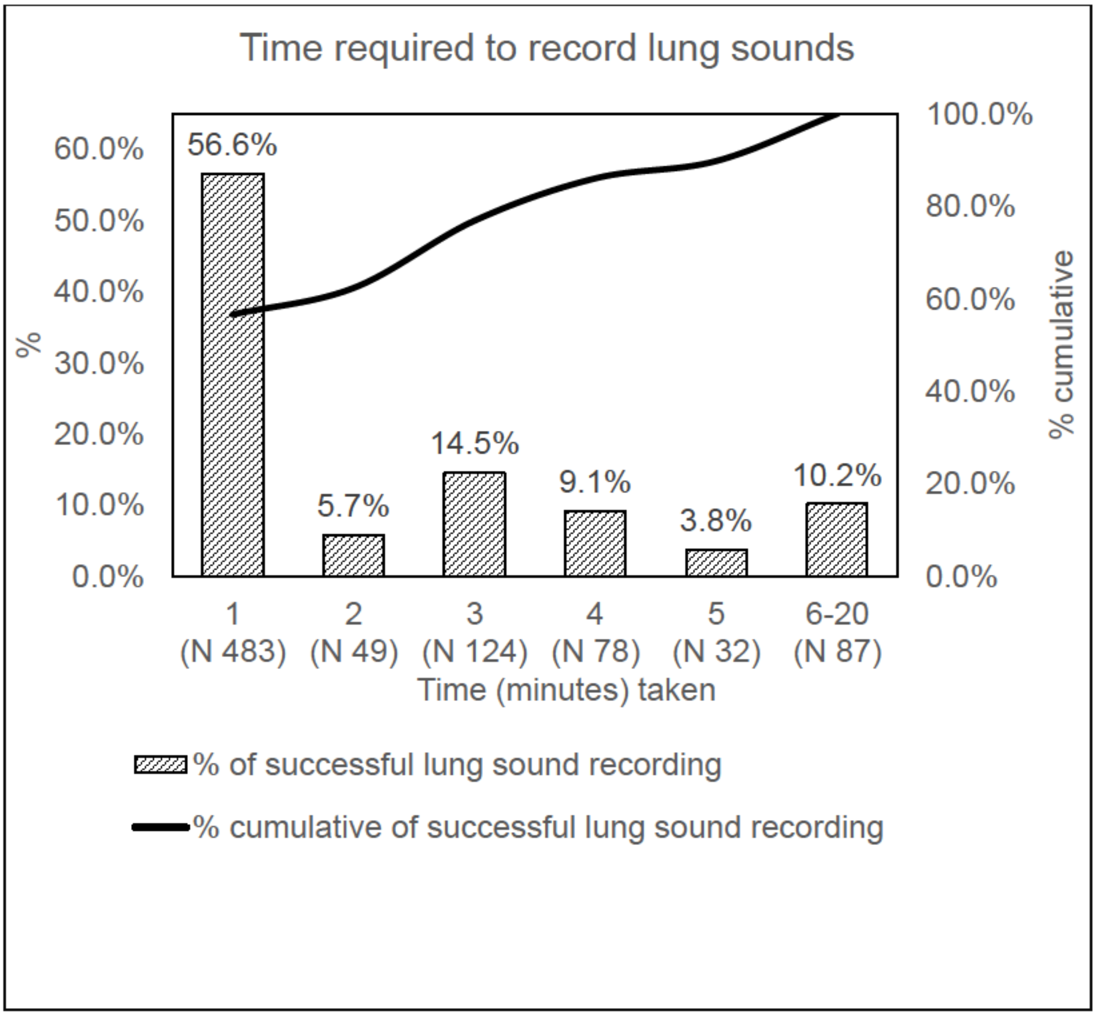

Figure 6.3 Time taken to record lung sounds classified as interpretable in ≥ 3 chest positions

Table 6.9 also shows the time taken to record interpretable lung sounds in ≥ 3 chest positions, but stratified by CHCP. The mean duration of recordings with ≥3 interpretable chest positions was 2.6 minutes with standard deviation (SD) of 2.6 minutes.

Table 6.9 Time taken to record lung sound classified as interpretable in ≥ 3 chest positions by CHCP

CHCP	Number of children enrolled	Minimum recording time	Maximum recording time	Mean	Standard deviation	First quartile	Median	Third quartile	Inter quartile range (IQR)
CHCP 1	29	1	7	1.8	1.4	1	1	3	2
CHCP 2	126	1	12	2.6	2.1	1	2	4	3
CHCP 3	107	1	17	2.3	2.5	1	1	3	2
CHCP 4	133	1	18	3.5	3.1	1	3	4	3
CHCP 5	66	1	11	2.2	2.0	1	1	3	2
CHCP 6	18	1	13	2.5	3.3	1	1	2	1
CHCP 7	162	1	16	3.5	3.0	1	3	5	4
CHCP 8	36	1	11	2.0	2.8	1	1	1	0
CHCP 9	176	1	16	1.5	1.6	1	1	1	0
Overall	**853**	**1**	**18**	**2.6**	**2.6**	**1**	**1**	**3**	**2**

A Kruskal-Wallis test showed that there was a statistically significant difference in recording time between CHCPs ($p < .01$)

Figure 6.4 shows the distribution of the time taken to record interpretable lung sounds in ≥ 3 chest positions according to each CHCP. CHCP #8 and CHCP #9 had almost no variability in the duration taken to record sound files, whereas CHCP #2 and CHCP #7 showed more variation than other CHCPs. It implies that the distribution of time taken to record interpretable lung sounds in ≥ 3 chest positions varied by CHCPs. A significant Kruskal-Wallis test ($p < 0.01$) also suggests unequal median recording duration and different time distributions among CHCPs.

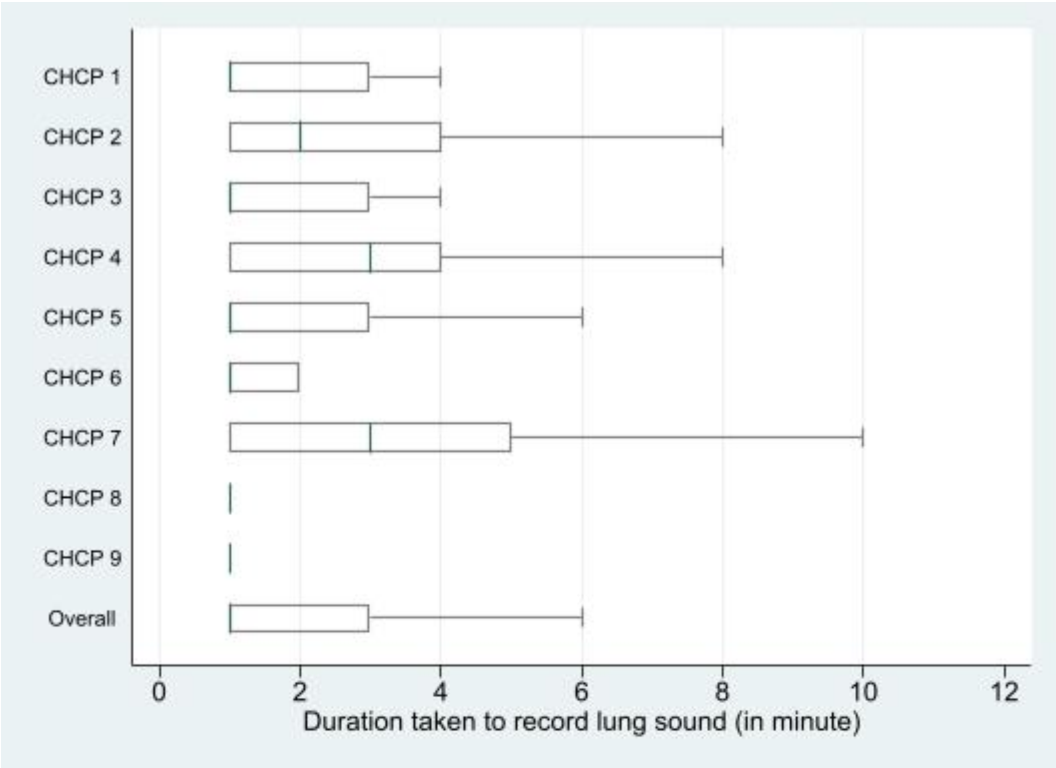

Figure 6.4 Time taken to record interpretable lung sounds in ≥ 3 chest positions by CHCP

From the scatterplot (Figure 6.5), no apparent trend was found between the number of children enrolled and the mean recording time. Linear regression suggests an upward trend in the mean recording time with an increase in the number of children enrolled. However, the trend was not statistically significant (slope β=0.004; p-value=0.39).

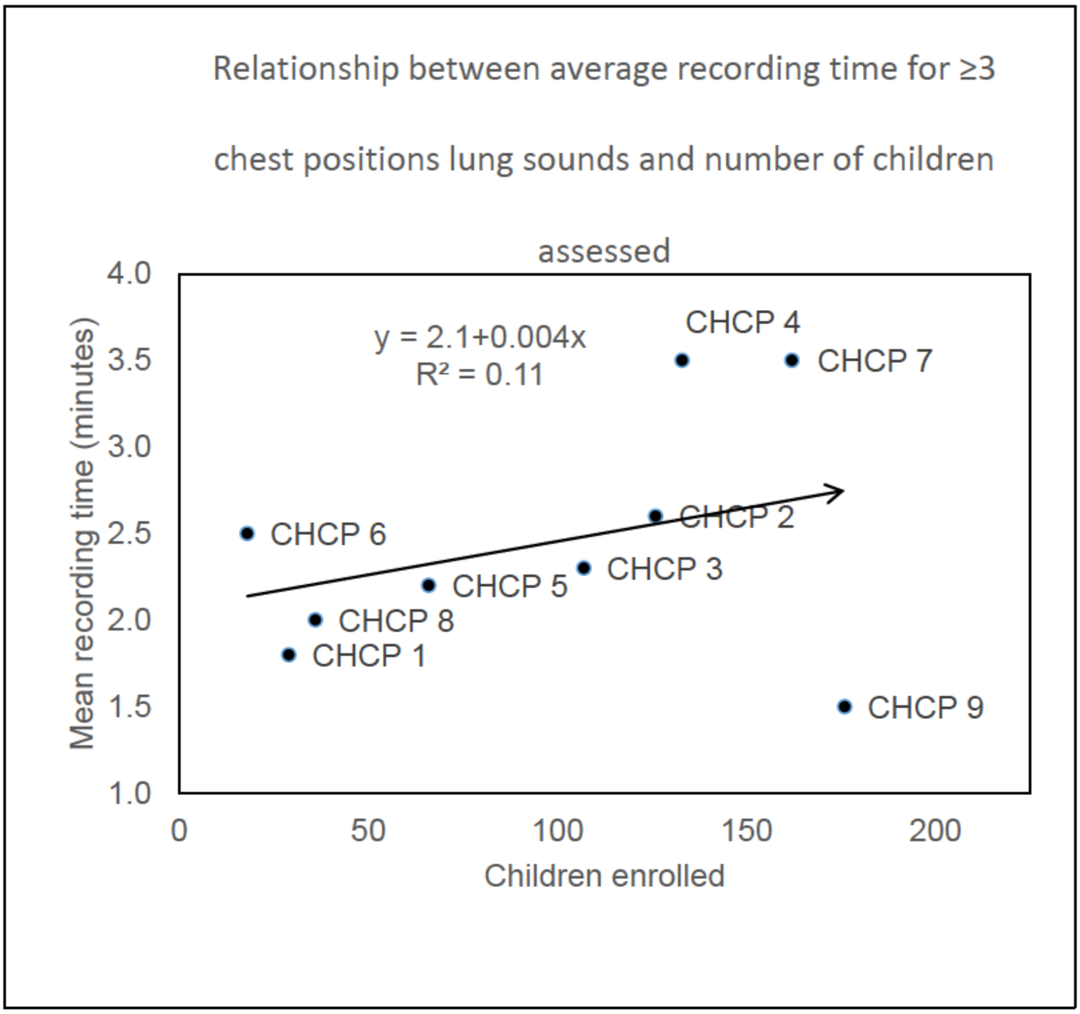

Figure 6.5 Number of children enrolled and time taken to record interpretable lung sounds in ≥ 3 chest positions by CHCP

Figure 6.6 shows the relationship between the average time to record lung sounds and the success rate of getting interpretable lung sounds in ≥3 chest positions by CHCP. Although linear regression showed an upward trend (slope β=1.30), the trend was not statistically significant (p-value=0.73).

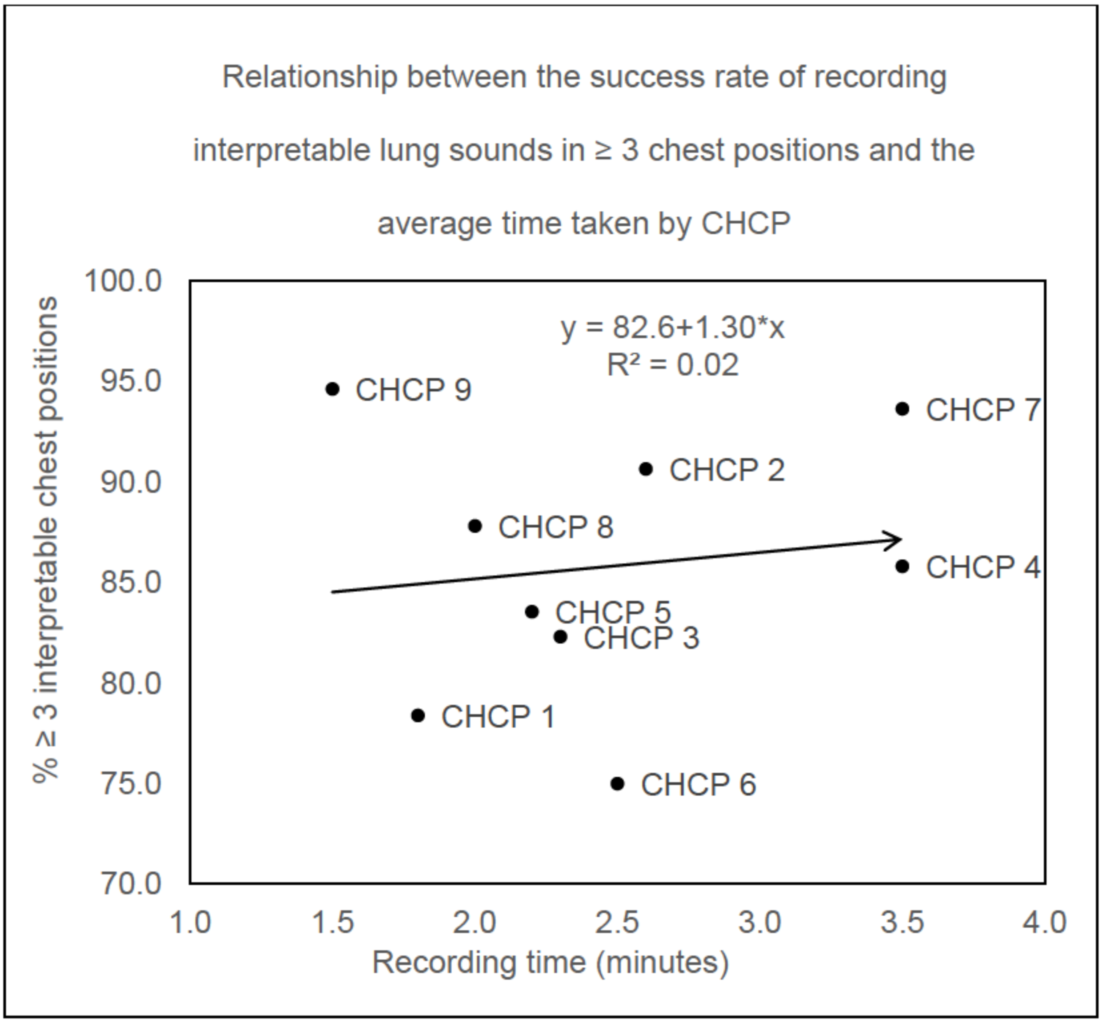

Figure 6.6 Relationship between success rate of recording interpretable lung sounds in ≥ 3 chest positions and time taken to record lung sounds by CHCP

Five CHCPs who enrolled more than 100 children were selected and the lung sounds recorded by them were divided into quartiles in ascending order by date of enrolment. Figure 6.7 shows the average recording time by each 25% of enrolment by selected five CHCPs. The last 25% of enrolment took less time in CHCP-#2, #3 and #9. However, CHCP #4 and #7 took more time to record lung sounds in the last 25% of enrolment compared to their first 75% enrolment. No decreasing trend was found in the average recording time with the increasing number of enrolments by CHCP.

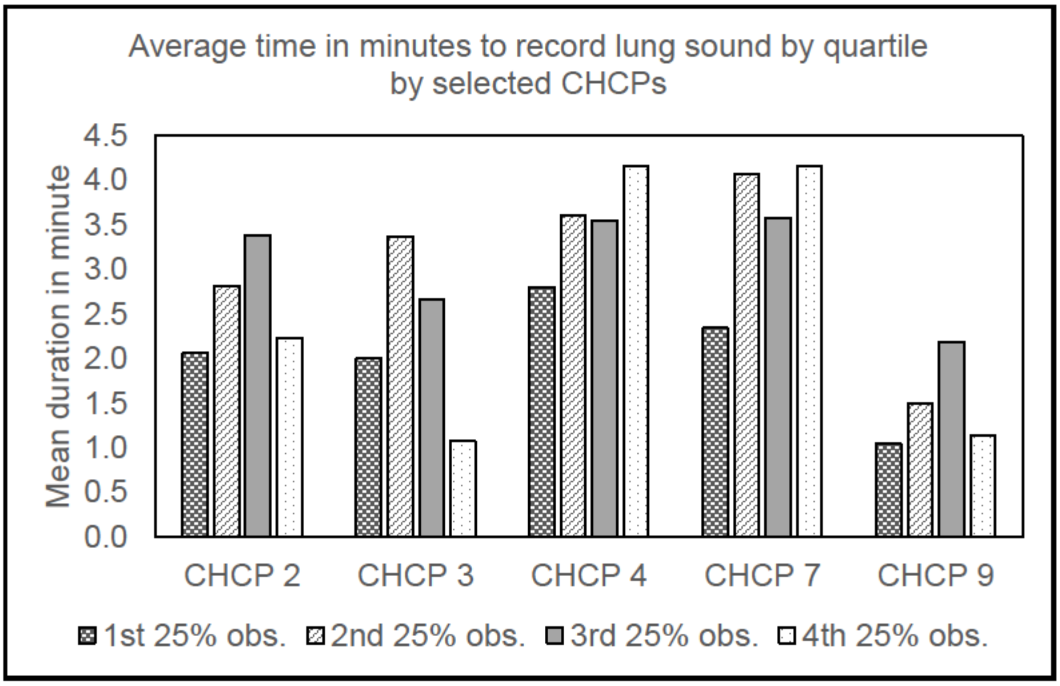

Figure 6.7 Selected* CHCP's average time to record lung sound by quartile of enrolment

* CHCPs who enrolled more than 100 children

Chapter 7 Results: Agreement between digital stethoscope-recorded lung sound classifications generated from computerised lung sound analysis and a paediatrician listening panel

One of the objectives of my thesis was to determine the diagnostic accuracy of digital stethoscope-recorded lung sound classifications generated from an automated computerised lung sound analysis (CLSA) compared with a reference panel of paediatricians. This chapter outlines the findings focusing on this objective.

Nine paediatricians received a two-day training following a standard operating procedure (SOP) adopted from the PERCH study (SOP is included on page 370). However, none of the nine paediatricians achieved satisfactory results on a post-training examination that required classification of lung sounds, and thus none qualified as a listening panel member after this initial training period. The training was focused on identifying wheezes and crackles and when to ignore portions of the recording as device artefact, vocalizations, and patient movement. Subsequently, two paediatricians among the initial trainees who performed better relative to their peers, received an additional five virtual (Zoom) training sessions in five weeks during the COVID-19 lockdown period. After more intensive training both paediatricians achieved satisfactory post-training examination results to allow them to serve as primary listening panel members. In parallel, refresher training and standardisation of two paediatricians who previously performed as listening panel members in the PERCH study enriched the listening panel to serve as primary listening panel members in this study. Ultimately, these four paediatricians (two from Bangladesh and two from PERCH) constituted the primary listening panel and classified recorded lung sounds. For recordings from one patient any of the two randomly allocated panel members independently listened to the recordings using a headset (Sennheiser HD 599 SE) while simultaneously viewing the sound spectrograms with open-source software (Audacity). Panellists entered their findings into an online electronic form. The panel members could listen to the recordings with the freedom to stop or repeat parts or the entire recording if necessary. They were blinded to all clinical information of the participants. Dr Eric D. McCollum, a paediatric pulmonologist at the Johns Hopkins School of Medicine, served as the panel arbiter, and listened to recordings in which the classification from the two panellists was discordant.

7.1 Agreement between two primary listening panel members

Table 7.1 shows the agreement in the interpretability of recorded lung sounds between the two primary listeners. Of the lung sounds recorded and successfully transferred to the study laptop from 974 children, 928 (95.3%) were interpretable by both primary listeners, whereas 13 (1.3%) were uninterpretable by both listeners. The agreement regarding interpretability between the two primary listeners was moderate (Cohen’s Kappa = 0.42, 95% CI: 0.36, 0.49).

Table 7.1 Agreement of interpretable and uninterpretable lung sounds by two primary listening panel members

		Listener 1		
		Interpretable	**Uninterpretable**	**Total**
Listener 2	**Interpretable**	928	15	943
	Uninterpretable	18	13	31
	Total	946	28	974

Cohen's kappa (95% CI): 0.42 (0.36, 0.49), raw agreement: 96.61%

Table 7.2 shows among the 864 children with lung sounds classified as interpretable in at least three chest positions, both primary listeners identified 163 (18.9%) children with adventitious lung sounds and 396 (45.8%) children with normal (no wheeze and no crackles) lung sounds. The agreement between the two primary listeners was fair (Cohen's Kappa = 0.24, 95% CI: 0.17, 0.31).

Table 7.2 Agreement between two primary paediatric listening panel members to detect adventitious and normal lung sounds among children with ≥3 chest positions were interpretable

		Listener 1		
		Adventitious	**Normal**	**Total**
Listener 2	**Adventitious**	163	150	313
	Normal	155	396	551
	Total	318	546	864

Cohen's kappa (95% CI): 0.24 (0.17, 0.31), raw agreement: 64.70%

Among the 342 children with IMCI-defined pneumonia classified as having interpretable lung sounds in at least three chest positions (Table 7.3), both primary listeners identified 74 (21.6%) children with adventitious lung sounds and 134 (39.2%) children with normal lung sounds. The agreement between the two primary listeners was low (Cohen's kappa = 0.20, 95% CI: 0.10, 0.30).

Table 7.3 Agreement between two primary paediatric listening panel members to detect adventitious and normal lung sounds among children with IMCI-defined pneumonia and having interpretable lung sounds in ≥3 chest positions

		Listener 1		
		Adventitious	**Normal**	**Total**
Listener 2	**Adventitious**	74	49	123
	Normal	85	134	219
	Total	159	183	342

Cohen's kappa (95% CI): 0.20 (0.10, 0.30); raw agreement: 60.82%

7.2 Distribution of recorded lung sounds classification by the paediatric listening panel

Table 7.4 illustrates the distribution of lung sound classifications by the paediatric listening panel when restricted to children with interpretable lung sounds recorded in 3 or more chest positions. The identification of 'wheeze only' was higher in children aged 2-11 months (14.6%) compared to children aged 12-59 months (12.4%) (p=0.04); in males (13.8%) compared to females (11.9%) (p=0.41); those with IMCI defined pneumonia (15.5%) compared to no pneumonia (11.3%) (p=0.07); and SpO_2 90-93% (28.6%) compared to SpO_2 ≥94% (12.4%) (p=0.01). The classification of 'crackles only' was higher but not statistically significant in children aged 12-59 months (9.2%) than 2-11 months (7.3%) (p=0.40); in males (8.9%) compared to females (8.6%) (p=0.88), 'any pneumonia' (9.9%) compared to 'no pneumonia' cases (8.0%) (p=0.33); and SpO_2 ≥94% (8.9%) compared to SpO_2 90-93% (3.6%) (p=0.32).

Identification of both ‘wheeze and crackle’ was more common in children aged 2-11 months (10.2%) than 12-59 months (9.5%) (p=0.75); males (10.2%) than females (9.1%) (p=0.60); ‘any pneumonia’ (11.4%) compared to ‘no pneumonia’ cases (8.6%) (p=0.18); and SpO_2 90-93% (28.6%) than SpO_2 ≥94% (9.1%) (p<0.01). The frequency of ‘any wheeze’ (i.e., wheeze with or without crackles) was higher in 2-11 month olds (24.9%) than 12-59 month olds (21.9%) (p=0.37); males (23.9%) compared to females (21.0%) (p=0.30); in children with ‘any pneumonia’ (26.8%) compared to ‘no pneumonia’ (19.8%) (p=0.02); and SpO_2 90-93% (57.1%) compared to SpO_2 ≥94% (21.5%) (p<0.01). The interpretation of ‘any crackles’ (i.e., crackles with or without wheeze) was higher in children aged 12-59 months (18.7%) compared to children aged 2-11 months (17.6%) (p=0.71); in males (19.1%) compared to females (17.7%) (p=0.61), in children with pneumonia (21.3%) compared to no pneumonia (16.6%) (p=0.08); and SpO_2 90-93% (32.1%) compared to SpO_2 ≥94% (18.0%) (p=0.06).

Table 7.4 Distribution of lung sounds classification by the consensus paediatrician listening panel

Characteristics of children	Total N	No wheeze and no crackle n (%)	Wheeze only n (%)	Crackle only n (%)	Wheeze and crackle n (%)	Any wheeze n (%)	Any crackles n (%)
Age group							
2-11 months	205	139 (67.8)	30 (14.6)	15 (7.3)	21 (10.2)	51 (24.9)	36 (17.6)
12-59 months	662	456 (68.9)	82 (12.4)	61 (9.2)	63 (9.5)	145 (21.9)	124 (18.7)
Total	867	595 (68.6)	112 (12.9)	76 (8.8)	84 (9.7)	196 (22.6)	160 (18.5)
Child's Sex							
Male	472	317 (67.2)	65 (13.8)	42 (8.9)	48 (10.2)	113 (23.9)	90 (19.1)
Female	395	278 (70.4)	47 (11.9)	34 (8.6)	36 (9.1)	83 (21.0)	70 (17.7)
Total	867	595 (68.6)	112 (12.9)	76 (8.8)	84 (9.7)	196 (22.6)	160 (18.5)
Pneumonia status							

Characteristics of children	**Total**	**No wheeze and no crackle**	**Wheeze only**	**Crackle only**	**Wheeze and crackle**	**Any wheeze**	**Any crackles**
No pneumonia	524	378 (72.1)	59 (11.3)	42 (8.0)	45 (8.6)	104 (19.8)	87 (16.6)
Pneumonia (fast breathing and/or chest indrawing)	304	202.(66.4)	42.(13.8)	29.(9.5)	31.(10.2)	73.(24.)	60.(19.7)
Severe pneumonia (Respiratory danger sign)	39	15.(38.5)	11.(28.2)	5.(12.8)	8.(20.5)	19.(48.7)	13.(33.3)
Total	867	595 (68.6)	112 (12.9)	76 (8.8)	84 (9.7)	196 (22.6)	160 (18.5)
Chest in drawing	21	8 (38.1)	3 (14.3)	2 (9.5)	8 (38.1)	11 (52.4)	10 (47.6)
Head nodding	6	2 (33.3)	2 (33.3)	1 (16.7)	1 (16.7)	3 (50.0)	2 (33.3)
Tracheal tugging	9	3 (33.3)	3 (33.3)	0 (0.0)	3 (33.3)	6 (66.7)	3 (33.3)
Stridor when calm	27	11 (40.7)	6 (22.2)	3 (11.1)	7 (25.9)	13 (48.1)	10 (37.0)
Nasal flaring	7	1 (14.3)	2 (28.6)	2 (28.6)	2 (28.6)	4 (57.1)	4 (57.1)
Grunting	3	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)

Characteristics of children	Total	No wheeze and no crackle	Wheeze only	Crackle only	Wheeze and crackle	Any wheeze	Any crackles
Intercostal retraction	8	1 (12.5)	3 (37.5)	1 (12.5)	3 (37.5)	6 (75.0)	4 (50.0)
Axillary temperature ≥100.4°F	69	55 (79.7)	5 (7.2)	7 (10.1)	2 (2.9)	7 (10.1)	9 (13.0)
Oxygen saturation							
SpO_2: 90% to 93%	28	11 (39.3)	8 (28.6)	1 (3.6)	8 (28.6)	16 (57.1)	9 (32.1)
SpO_2: 94% to 100%	839	584 (69.6)	104 (12.4)	75 (8.9)	76 (9.1)	180 (21.5)	151 (18.0)
Total	867	595 (68.6)	112 (12.9)	76 (8.8)	84 (9.7)	196 (22.6)	160 (18.5)

7.3 Comparison of four computerised lung sounds analysis (CLSA) models

All sound recordings were analysed using four different CLSA models developed by Sonavi Labs (details on page 340). Table 7.5 compares four CLSA models to detect adventitious lung sounds with the listening panel. When compared with the consensus listening panel's classification, among all the children, the sensitivity was highest in Model C (61.8%), the specificity was highest in Model B (77.6%), and the kappa value was maximum in Model C (0.20). Among children with IMCI-defined pneumonia, the maximum sensitivity was seen in Model C (63.5%), maximum specificity in Model B (81.6%) and maximum kappa in Model B (0.29). Among children with both IMCI-defined pneumonia and classifications designated as 'confident' by the listening panel during interpretation, Model C showed maximum sensitivity (69.8%), and Model B showed maximum specificity (81.6%). Model C had the highest sensitivity, capturing more adventitious sounds than the other models.

Table 7.5 Comparison of four computerised lung sounds analysis (CLSA) models to detect adventitious lung sounds with the consensus listening panel

	Model A	Model B	Model C	Model D
Among all children (N = 867)				
Sensitivity (95% CI)	52.2 (46.1, 58.3)	39.7 (33.8, 45.8)	61.8 (55.7, 67.6)	56.6 (50.5, 62.6)
Specificity (95% CI)	65.9 (61.9, 69.7)	77.6 (74.1, 80.9)	60.7 (56.6, 64.6)	62.2 (58.2, 66.1)
Positive predictive value (95% CI)	41.2 (35.9, 46.6)	44.8 (38.4, 51.3)	41.8 (36.9, 46.8)	40.6 (35.6, 45.8)
Negative predictive value (95% CI)	75.1 (71.2, 78.8)	73.8 (70.2, 77.2)	77.6 (73.6, 81.3)	75.8 (71.8, 79.6)
Prevalence (95%CI)	31.4 (28.3, 34.6)	31.4 (28.3, 34.6)	31.4 (28.3, 34.6)	31.4 (28.3, 34.6)
Kappa (95% CI)	0.17 (0.10, 0.23)	0.18 (0.11, 0.25)	0.20 (0.14, 0.26)	0.17 (0.11, 0.23)
Among children with IMCI defined pneumonia (N = 343)				
Sensitivity (95% CI)	50.8 (41.7, 59.8)	46.8 (37.9, 55.9)	63.5 (54.4, 71.9)	57.1 (48.0, 65.9)
Specificity (95% CI)	69.1 (62.5, 75.2)	81.6 (75.8, 86.5)	66.8 (60.1, 73.0)	66.8 (60.1, 73.0)

	Model A	Model B	Model C	Model D
Positive predictive value (95% CI)	48.9 (40.0, 57.7)	59.6 (49.3, 69.3)	52.6 (44.4, 60.8)	50.0 (41.6, 58.4)
Negative predictive value (95% CI)	70.8 (64.1, 76.8);	72.5 (66.5, 78.0)	75.9 (69.2, 81.8)	72.9 (66.1, 78.9)
Prevalence (95%CI)	36.7 (31.6, 42.1)	36.7 (31.6, 42.1)	36.7 (31.6, 42.1)	36.7 (31.6, 42.1)
Kappa (95% CI)	0.20 (0.09, 0.30)	0.30 (0.19, 0.40)	0.29 (0.19, 0.40)	0.23 (0.13, 0.34)
Among children with IMCI defined pneumonia and human were confident during interpretation (N = 303)				
Sensitivity (95% CI)	58.1 (47.0, 68.7)	55.8 (44.7, 66.5)	69.8 (58.9, 79.2)	67.4 (56.5, 77.2)
Specificity (95% CI)	69.1 (62.5, 75.2)	81.6 (75.8, 86.5)	66.8 (60.1, 73.0)	66.8 (60.1, 73.0)
Positive predictive value (95% CI)	42.7 (33.6, 52.2)	54.6 (43.6, 65.2)	45.5 (36.8, 54.3)	44.6 (35.9, 53.6)
Negative predictive value (95% CI)	80.6 (74.2, 86.1)	82.3 (76.6, 87.2)	84.8 (78.5, 89.8)	83.8 (77.5, 89.0)
Prevalence (95%CI)	28.4 (23.4, 33.8)	28.4 (23.4, 33.8)	28.4 (23.4, 33.8)	28.4 (23.4, 33.8)
Kappa (95% CI)	0.25 (0.14, 0.36)	0.37 (0.26, 0.48)	0.32 (0.21, 0.42)	0.30 (0.19, 0.40)

7.4 Agreement between automated CLSA and paediatrician listening panel to detect adventitious lung sounds

Model C showed the highest sensitivity among the four CLSA models, and was therefore compared to the paediatric listening panel to distinguish adventitious lung sounds from normal lung sounds in this thesis. According to this model, among all the enrolled children with cough or difficulty breathing, the sensitivity was 61.8%, specificity was 60.7%, and kappa value was 0.20. When we restricted the analysis to children with IMCI-defined pneumonia (age-specific fast breathing or chest indrawing), the sensitivity, specificity and kappa value were higher, increasing to 63.5%, 66.8% and 0.29, respectively. When we further restricted the analysis to children with IMCI-defined pneumonia and 'confident' classifications by the listening panel (confidence was defined when the listener based their classification on at least one full, clear breath cycle in at least one chest position of a child), these values were 69.8%, 66.8% and 0.32, respectively (Table 7.6). Figure 7.1 shows this automated CLSA model performed better in 'any pneumonia' cases compared to 'no pneumonia' cases.

Table 7.6 Evaluation of CLSA to detect adventitious (wheeze/crackles/both wheeze and crackles) and normal (no wheeze and no crackles) lung sounds compared to the consensus listening panel

	Among all children (N=867)	**Among children with IMCI-defined pneumonia (N=343)**	**Among children with IMCI-defined pneumonia and 'confident'* classification by listening panel members (N=303)**
Sensitivity (95% CI)	61.8 (55.7, 67.6)	63.5 (54.4, 71.9)	69.8 (58.9, 79.2)
Specificity (95% CI)	60.7 (56.6, 64.6)	66.8 (60.1, 73.0)	66.8 (60.1, 73.0)
PPV (95% CI)	41.8 (36.9, 46.8)	52.6 (44.4, 60.8)	45.5 (36.8, 54.3)
NPV (95% CI)	77.6 (73.6, 81.3)	75.9 (69.2, 81.8)	84.8 (78.5, 89.8)
Prevalence (95% CI)	31.4 (28.3, 34.6)	36.7 (31.6, 42.1)	28.4 (23.4, 33.8)
Raw percentage agreement (95% CI)	61.0 (57.7, 64.3)	65.6 (60.3, 70.6)	67.7 (62.1, 72.9)
Kappa (95% CI)	0.20 (0.14, 0.26)	0.29 (0.19, 0.40)	0.32 (0.21, 0.42)
Prevalence adjusted bias adjusted kappa (PABAK)	0.22 (0.15, 0.29)	0.31 (0.21, 0.41)	0.35 (0.24, 0.46)

*Confidence was defined when the listener based their classification on at least one full, clear breath cycle in at least one chest position of a child

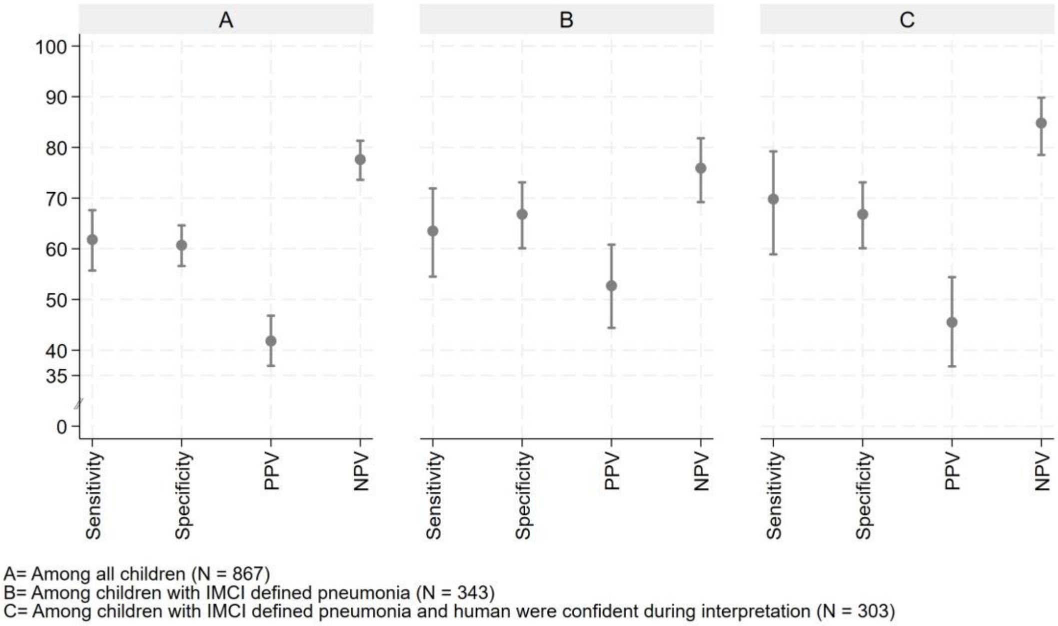

Figure 7.1 Accuracy of the CLSA to detect adventitious lung sounds compared to the listening panel

7.5 Agreement between CLSA and the paediatric listening panel to detect wheeze

Table 7.7 evaluates the accuracy of CLSA in classifying “any wheeze” (wheeze only or both wheeze and crackles) and non-wheeze (no wheeze and no crackles, or crackles only) compared to the listening panel. The sensitivity was 55.6% when all children were included in the analysis, but the sensitivity increased when the analysis was restricted to children with IMCI-defined pneumonia (59.8%), and it was highest when data were analysed for children with IMCI-defined pneumonia and ‘confident’ classifications by listening panel members (68.8%). The specificity was similar when the analysis was done with these three groups of children (71.2%, 72.1% and 73.2%, respectively). The kappa values for these groups were 0.23, 0.29, and 0.34, respectively, which was considered fair agreement.

Table 7.7 Evaluation of CLSA to detect any wheeze compared to the consensus listening panel

	Among all children (N= 867)	**Among children with IMCI-defined pneumonia (N=343)**	**Among children with IMCI-defined pneumonia and 'confident' classification by listening panel members (N=303)**
Sensitivity (95% CI)	55.6 (48.4, 62.7)	59.8 (49.0, 69.9)	68.8 (55.9, 79.8)
Specificity (95% CI)	71.2 (67.6, 74.6)	72.1 (66.1, 77.6)	73.2 (67.1, 78.7)
PPV (95% CI)	36.1 (30.7, 41.8)	44.0 (35.1, 53.2)	40.7 (31.4, 50.6)
NPV (95% CI)	84.6 (81.4, 87.5)	83.0 (77.4, 87.8)	89.7 (84.6, 93.6)
Prevalence (95% CI)	22.6 (19.9, 25.5)	26.8 (22.2, 31.8)	21.1 (16.7, 26.2)
Kappa (95% CI)	0.23 (0.16, 0.29)	0.29 (0.18, 0.39)	0.34 (0.23, 0.44)

7.6 Agreement between CLSA and the paediatric listening panel to detect crackles

Table 7.8 shows the accuracy of computerised lung sounds analysis (CLSA) in detecting 'any crackles' (crackles only or both wheeze and crackles) and non-crackles (no wheeze and no crackles, or wheeze only) compared to the consensus listening panel. The sensitivity of CLSA was 36.9% among all children; when restricting the analysis to IMCI-defined pneumonia, the sensitivity was 35.6%, and when further restricting the analysis to IMCI-defined pneumonia and 'confident' classifications by listening panel members, the sensitivity was 38.2%. Specificity, on the other hand, was 77.2% among all children, and it was higher among children with IMCI-defined pneumonia (82.6%) and among those with IMCI-defined pneumonia and 'confident' listening panel classification (82.7%). The kappa values among these three groups of children were 0.12, 0.18, and 0.20, respectively reflecting low agreement between the CLSA and listening panel for identifying 'any crackles'.

Table 7.8 Evaluation of CLSA to detect 'any crackles' compared to the consensus listening panel

	Among all children (N= 867)	**Among children with IMCI-defined pneumonia (N=343)**	**Among children with IMCI-defined pneumonia and 'confident' listening panel classification (N=303)**
Sensitivity (95% CI)	36.9 (29.4, 44.9)	35.6 (24.7, 47.7)	38.2 (25.4, 52.3)
Specificity (95% CI)	77.2 (74.0, 80.3)	82.6 (77.5, 86.9)	82.7 (77.4, 87.2)
PPV (95% CI)	26.8 (21.1, 33.2)	35.6 (24.7, 47.7)	32.8 (21.6, 45.7)
NPV (95% CI)	84.4 (81.4, 87.1)	82.6 (77.5, 86.9)	85.8 (80.7, 89.9)
Prevalence (95% CI)	18.5 (15.9, 21.2)	21.3 (17.1, 26.0)	18.2 (14.0, 23.0)
Kappa (95% CI)	0.12 (0.06, 0.19)	0.18 (0.08, 0.29)	0.20 (0.08, 0.31)

7.7 Agreement between CLSA and the paediatric listening panel to detect adventitious lung sounds stratified by chest positions

Table 7.9 shows the accuracy of computerised lung sounds analysis (CLSA) to detect ‘adventitious’ (wheeze only, or crackles only, or both wheeze and crackles) and ‘normal’ (no wheeze and no crackles) lung sounds by chest position, as compared to the consensus listening panel. Importantly, the adjudication of participant lung sound classification by the listening panel was considered at the patient level (i.e., all chest position classifications of the participant informed the participant’s overall classification rather than each individual chest position). CHCPs recorded lung sounds in four sequential chest locations – left back (position 1, reflecting the left lower lobe), right back (position 2, reflecting the right lower lobe), left front (position 3 (cardiac position, reflecting the left upper lobe)) and right front (position 4, reflecting the right upper lobe). Among all children, position 4 (right upper lobe) had the maximum sensitivity (46.6%) and position 2 (right lower lobe) had the maximum specificity (87.6%). Among IMCI-defined pneumonia, the maximum sensitivity (47.4%) and specificity (90.8%) for ‘adventitious’ lung sounds were noted in position 4 and position 2 as well. Among IMCI-defined pneumonia and ‘confident’ listening panel classification, the maximum sensitivity for ‘adventitial' lung sounds was in position 1 (left lower lobe) (52.1%), and the maximum specificity was in position 2 (right lower lobe) (90.8%). Compared to the listening panel, the identification of adventitious lung sounds by CLSA was moderately sensitive when considering all chest locations and all children, but notably the sensitivity increased when restricting the analysis to IMCI-defined pneumonia cases. The specificity of CLSA to detect adventitious lung sounds, compared to the listening panel, was high overall when taking into account all chest positions.

Table 7.9 Evaluation of CLSA to detect adventitious lung sounds compared to the consensus listening panel: according to chest position

	Position 1 (left back: left lower lobe)	Position 2 (right back: right lower lobe)	Position 3 (left front: left upper lobe)	Position 4 (right front: right upper lobe)
Among all children	**N = 896**	**N = 886**	**N = 845**	**N = 845**
Sensitivity (95% CI)	32.4 (25.0, 40.6)	30.4 (23.4, 38.2)	32.5 (25.3, 40.3)	46.6 (38.7, 54.6)
Specificity (95% CI)	86.9 (84.3, 89.2)	87.6 (85.0, 89.9)	84.7 (81.8, 87.3)	83.6 (80.6, 86.3)
PPV (95% CI)	32.9 (25.3, 41.1)	35.3 (27.3, 43.8)	33.1 (25.8, 41.1)	40.1 (33.0, 47.5)
NPV (95% CI)	86.7 (84.0, 89.0)	85.0 (82.2, 87.5)	84.3 (81.4, 86.9)	86.9 (84.1, 89.4)
Prevalence (95% CI)	16.5 (14.1, 19.1)	18.2 (15.7, 20.9)	18.9 (16.3, 21.7)	19.1 (16.5, 21.9)
Kappa (95% CI)	0.19 (0.13, 0.26)	0.19 (0.12, 0.26)	0.17 (0.11, 0.24)	0.28 (0.22, 0.35)
Among IMCI-defined pneumonia	**N = 352**	**N =349**	**N = 338**	**N = 333**
Sensitivity (95% CI)	43.1 (31.4, 55.3)	39.0 (28.0, 50.8)	34.7 (23.9, 46.9)	47.4 (35.8, 59.2)
Specificity (95% CI)	86.4 (81.9, 90.2)	90.8 (86.7, 94.0)	85.3 (80.5, 89.4)	86.8 (82.0, 90.7)
PPV (95% CI)	44.9 (32.9, 57.4)	54.5 (40.6, 68.0)	39.1 (27.1, 52.1)	51.4 (39.2, 63.6)
NPV (95% CI)	85.5 (80.9, 89.4)	84.0 (79.3, 88.0)	82.8 (77.9, 87.1)	84.8 (79.9, 88.9)
Prevalence (95% CI)	20.5 (16.4, 25.1)	22.1 (17.8, 26.8)	21.3 (17.1, 26.1)	22.8 (18.4, 27.7)
Kappa (95% CI)	0.30 (0.20, 0.40)	0.33 (0.23, 0.43)	0.21 (0.10, 0.32)	0.35 (0.24, 0.46)

	Position 1 (left back: left lower lobe)	Position 2 (right back: right lower lobe)	Position 3 (left front: left upper lobe)	Position 4 (right front: right upper lobe)
Among IMCI-defined pneumonia and listening panel members were confident during classification	**N = 328**	**N = 327**	**N = 306**	**N = 312**
Sensitivity (95% CI)	52.1 (37.2, 66.7)	44.6 (31.3, 58.5)	43.9 (28.5, 60.3)	51.8 (38.0, 65.3)
Specificity (95% CI)	86.4 (81.9, 90.2)	90.8 (86.7, 93.9)	85.3 (80.4, 89.3)	86.7 (81.9, 90.6)
PPV (95% CI)	39.7 (27.6, 52.8)	50.0 (35.5, 64.5)	31.6 (19.9, 45.2)	46.0 (33.4, 59.1)
NPV (95% CI)	91.3 (87.3, 94.4)	88.8 (84.5, 92.3)	90.8 (86.5, 94.1)	89.2 (84.6, 92.7)
Prevalence (95% CI)	14.6 (11.0, 18.9)	17.1 (13.2, 21.7)	13.4 (9.8, 17.7)	17.9 (13.9, 22.7)
Kappa (95% CI)	0.34 (0.23, 0.45)	0.37 (0.26, 0.48)	0.25 (0.14, 0.36)	0.37 (0.26, 0.48)

CI= normal approximate confidence interval was used for kappa. Exact binomial confidence intervals were used for all other statistics

7.8 Distribution of lung sounds classification by listening panel and CLSA

In patient level classification, among ‘any pneumonia’ group, the detection of ‘adventitious lung sounds’ was higher according to the CLSA (44.3%) than the listening panel (36.7%) ($p<0.05$). Similarly, among the children with ‘no pneumonia’, adventitious sound detection was also higher per the CLSA (47.7%) than the listening panel (27.9%) ($p<0.01$) (Table 7.10). In the ‘any pneumonia’ group, CLSA detected more children with ‘any wheeze’ compared to the listening panel (36.4% vs 26.8%, p=<0.01). Similarly, in ‘no pneumonia’ group, CLSA classified more children with ‘any wheeze’ than the listening panel (33.8% vs 19.8%, p=<0.01). CLSA also classified a higher frequency of children with ‘any crackles’, compared to the listening panel, in the ‘no pneumonia’ group (28.1% vs 16.6%, p= <0.01).

Table 7.10 Distribution of lung sounds classification by the listening panel and CLSA

Lung sound classification	**Any pneumonia Total = 343**			**No pneumonia Total=524**		
	Listening panel %, (95% CI); [n]	CLSA %, (95% CI); [n]	P-value	Listening panel %, (95% CI); [n]	CLSA %, (95% CI); [n]	P-value
No wheeze and no crackle	217 (63.3)	191 (55.7)	<0.05	378 (72.1)	274 (52.3)	<0.01
Wheeze only	53 (15.5)	79 (23.0)	<0.05	59 (11.3)	103 (19.7)	<0.01
Crackles only	34 (9.9)	27 (7.9)	0.35	42 (8.0)	73 (13.9)	<0.01
Both wheeze and crackles	39 (11.4)	46 (13.4)	0.42	45 (8.6)	74 (14.1)	<0.01
Any wheeze	92 (26.8)	125 (36.4)	<0.01	104 (19.8)	177 (33.8)	<0.01
Any crackles	73 (21.3)	73 (21.3)	1.0	87 (16.6)	147 (28.1)	<0.01
Adventitious sound	126 (36.7)	152 (44.3)	<0.05	146 (27.9)	250 (47.7)	<0.01
Normal	217 (63.3)	191 (55.7)	<0.05	378 (72.1)	274 (52.3)	<0.01

Figure 7.2 shows the detection of "wheeze only" among IMCI-defined children was higher in CLSA (23.0%) compared to the listening panel classification (15.4%) (p=<0.01), whereas detection of "crackles only" was higher by the listening panel (9.9%) than CLSA (7.9%) but this did not reach statistical significance (p=0.35).

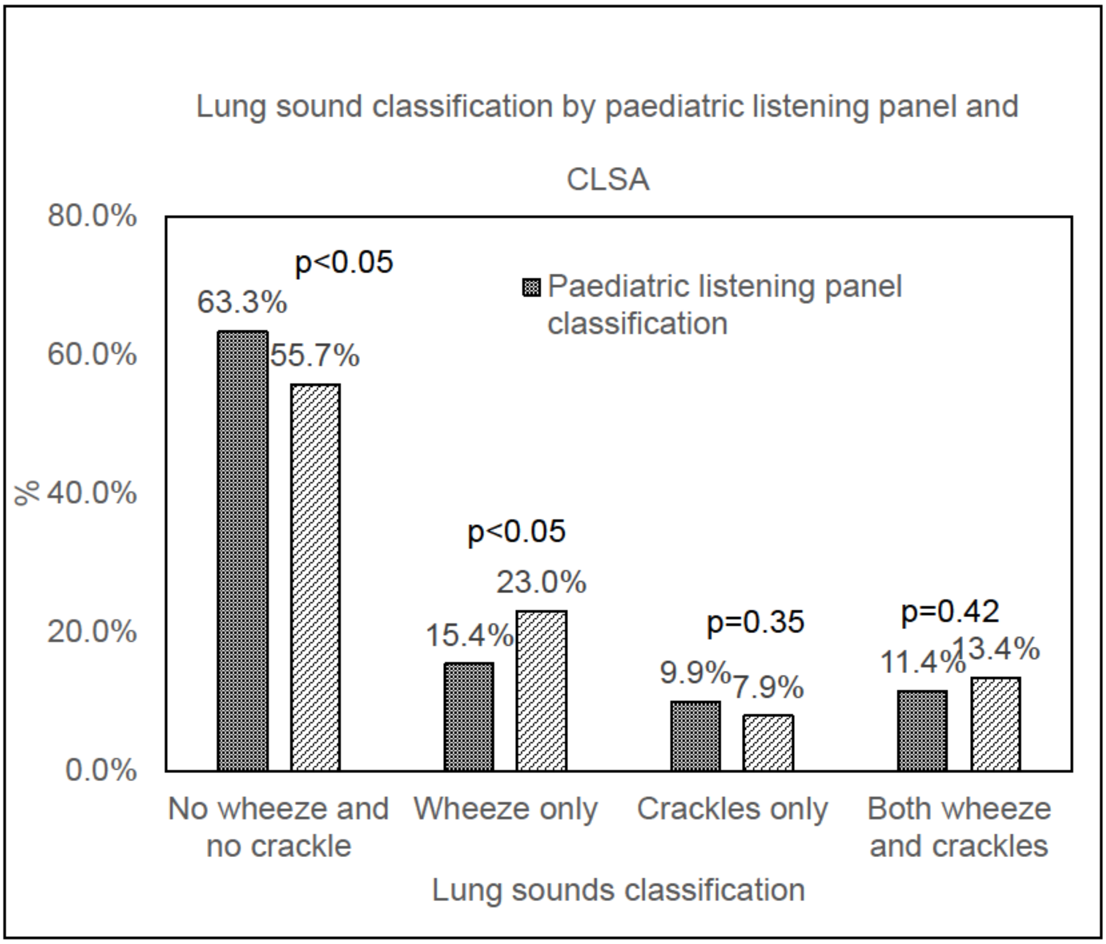

Figure 7.2 Distribution of lung sounds classification among IMCI defined pneumonia children by paediatric listening panel and CLSA

7.9 Association of selected characteristics of children with adventitious lung sounds classified by the listening panel

Table 7.11 presents the association of selected characteristics of children with adventitious lung sounds as classified by the consensus listening panel. From bivariate analysis, adventitious lung sounds were associated with pneumonia status ($p<0.01$), age-specific fast breathing ($p<0.05$), chest indrawing ($p<0.01$), any respiratory danger sign ($p<0.01$), axillary temperature ≥100.4°F ($p<0.05$), and SpO_2: 90% to 93% ($p<0.01$). Multivariable logistic regression reveals three variables that statistically contribute to the model ((1) presence of any respiratory danger sign, (2) axillary temperature ≥100.4°F, and (2) SpO_2: 90% to 93%). The classification of adventitious lung sounds was about 2.7 times more likely in the presence of any respiratory danger sign (aOR = 2.7, 95% CI: 1.1, 6.8). Compared to those without fever (axillary temperature <100.4°F), those with fever (axillary temperature ≥100.4°F**)** had a significantly lower probability of an adventitial lung sound classification (aOR = 0.5, 95% CI: 0.3, 0.9). Adventitious lung sounds were about 3.2 times more likely if SpO_2 was between 90% to 93% (aOR = 3.2, 95% CI: 1.4, 7.2).

Table 7.11 Association of selected characteristics of children classified as with adventitial lung sounds by the listening panel

Characteristics of children	**Total**	**Adventitious lung sounds n (%)**	**Normal lung sounds n (%)**	**Unadjusted OR 95%CI**	**p-value**	**Adjusted OR 95%CI**	**p-value**
Age group							
2-11 months	205	66 (32.2)	139 (67.8)	Ref			
12-59 months	662	206 (31.1)	456 (68.9)	1.0 (0.7, 1.3)	0.77		
Total	867	272 (31.4)	595 (68.6)				
Child's Sex							
Male	472	155 (32.8)	317 (67.2)	1.2 (0.9, 1.6)	0.32		
Female	395	117 (29.6)	278 (70.4)	Ref			
Total	867	272 (31.4)	595 (68.6)				
Pneumonia status							
No pneumonia	524	146 (27.9)	378 (72.1)	Ref		Ref	
Any pneumonia	343	126 (36.7)	217 (63.3)	1.5 (1.1, 2.0)	<0.01	1.1 (0.3, 4.5)	0.92
Total	867	272 (31.4)	595 (68.6)				

Characteristics of children	Total	Adventitious lung sounds n (%)	Normal lung sounds n (%)	Unadjusted OR 95%CI	p-value	Adjusted OR 95%CI	p-value
Fast Breathing							
Yes	328	118 (36.0)	210 (64.0)	1.4 (1.0, 1.9)	<0.05	1.2 (0.3, 4.8)	0.79
No	539	154 (28.6)	385 (71.4)	Ref		Ref	
Total	867	272 (31.4)	595 (68.6)				
Chest indrawing							
Yes	21	13 (61.9)	8 (38.1)	3.7 (1.5, 9.3)	<0.01	1.7 (0.5, 5.2)	0.37
No	846	259 (30.6)	587 (69.4)	Ref		Ref	
Total	867	272 (31.4)	595 (68.6)				
Any respiratory danger sign							
Yes	39	24 (61.5)	15 (38.5)	3.7 (1.9, 7.2)	<0.01	2.7 (1.1, 6.8)	<0.05
No	828	248 (30.0)	580 (70.0)	Ref		Ref	
Total	867	272 (31.4)	595 (68.6)				
Axillary temperature ≥100.4°F							
Yes	69	14 (20.3)	55 (79.7)	0.5 (0.3, 1.0)	<0.05	0.5 (0.3, 0.9)	<0.05

Characteristics of children	**Total**	**Adventitious lung sounds n (%)**	**Normal lung sounds n (%)**	**Unadjusted OR 95%CI**	**p-value**	**Adjusted OR 95%CI**	**p-value**
No	798	258 (32.3)	540 (67.7)	Ref		Ref	
Total	867	272 (31.4)	595 (68.6)				
Oxygen saturation							
SpO_2: 90% to 93%	28	17 (60.7)	11 (39.3)	3.5 (1.6, 7.8)	<0.01	3.2 (1.4, 7.2)	<0.01
SpO_2: 94% to 100%	839	255 (30.4)	584 (69.6)	Ref		Ref	
Total	867	272 (31.4)	595 (68.6)				

In contrast, Table 7.12 presents the association of selected characteristics of children with adventitious lung sounds as classified by the CLSA. From bivariate analysis, the classification of adventitial lung sounds was associated with the presence of any respiratory danger sign ($p<0.001$). Multivariable logistic regression did not identify any child characteristic as independently associated with the CLSA adventitial lung sound classification.

Table 7.12 Association of selected characteristics of children with the CLSA classification of adventitial lung sounds

Characteristics of children	Total	Adventitious lung sounds n (%)	Normal lung sounds n (%)	Unadjusted OR 95%CI	p-value	Adjusted OR 95%CI	p-value
Age group							
2-11 months	205	99 (48.3)	106 (51.7)	Ref			
12-59 months	662	303 (45.8)	359 (54.2)	0.9 (0.7, 1.2)	0.53		
Total	867	402 (46.4)	465 (53.6)				
Child's Sex							
Male	472	227 (48.1)	245 (51.9)	1.2 (0.9, 1.5)	0.27		
Female	395	175 (44.3)	220 (55.7)	Ref			
Total	867	402 (46.4)	465 (53.6)				
Pneumonia status							
No pneumonia	524	250 (47.7)	274 (52.3)	Ref			
Any pneumonia	343	152 (44.3)	191 (55.7)	0.9 (0.7, 1.1)	0.33		
Total	867	402 (46.4)	465 (53.6)				
Fast Breathing							
Yes	328	143 (43.6)	185 (56.4)	0.8 (0.6, 1.1)	0.20		

Characteristics of children	Total	Adventitious lung sounds	Normal lung sounds	Unadjusted OR 95%CI	p-value	Adjusted OR 95%CI	p-value
		n (%)	n (%)				
No	539	259 (48.1)	280 (51.9)	Ref			
Total	867	402 (46.4)	465 (53.6)				
Chest indrawing							
Yes	21	10 (47.6)	11 (52.4)	1.1 (0.4, 2.6)	0.91		
No	846	392 (46.3)	454 (53.7)	Ref			
Total	867	402 (46.4)	465 (53.6)				
Any respiratory danger sign							
Yes	39	24 (61.5)	15 (38.5)	1.9 (1.0, 3.8)	0.06	1.9 (0.9, 3.7)	0.07
No	828	378 (45.7)	450 (54.3)	Ref		Ref	
Total	867	402 (46.4)	465 (53.6)				
Axillary temperature ≥100.4°F							
Yes	69	28 (40.6)	41 (59.4)	0.8 (0.5, 1.3)	0.31		
No	798	374 (46.9)	424 (53.1)	Ref			
Total	867	402 (46.4)	465 (53.6)				
Oxygen saturation							

Characteristics of children	**Total**	**Adventitious lung sounds**	**Normal lung sounds**	**Unadjusted OR 95%CI**	**p-value**	**Adjusted OR 95%CI**	**p-value**
		n (%)	n (%)				
SpO_2: 90% to 93%	28	17 (60.7)	11 (39.3)	1.8 (0.8, 4.1)	0.15	1.8 (0.8, 4.0)	0.17
SpO_2: 94% to 100%	839	385 (45.9)	454 (54.1)	Ref		Ref	
Total	867	402 (46.4)	465 (53.6)				

7.10 ‘Normal’ lung sounds in IMCI-defined pneumonia children

Table 7.13 shows about 42% (145/343) of children diagnosed with IMCI-defined pneumonia by CHCPs were classified as having ‘normal’ lung sounds (no wheeze and no crackles) by both the human listening panel and the automated CLSA.

Table 7.13 Normal lung sounds classified by CLSA and listening panel in IMCI-defined pneumonia children

		Consensus listening panel		**Total**
		Normal	**Adventitious**	
CLSA	**Normal**	145	46	191
	Adventitious	72	80	152
	Total	217	126	343

Chapter 8 End-user acceptability of a prototype digital stethoscope

One of the objectives of my thesis was to explore the acceptability of a prototype digital stethoscope among potential end-users. We conducted four focus group discussions (FGDs) with mothers and fathers of under-5 year old children, influential community persons and CHCPs who used the Feelix Smartscope prototype. Mothers were more aware of the Feelix Smartscope than fathers. Most CHCPs had positive perceptions of Feelix Smartscope. The CHCPs also mentioned several technical shortcomings of the prototype device. The work presented in this chapter was submitted to BMC Digital Health on 10 February 2023, and published on 13 July 2023.

Taufique Joarder (TJ) and I drafted the manuscript with contributions from Samiun Nazrin Bente Kamal Tune (SNBKT), ASMD Ashraful Islam (ASMDAI), Arifa Islam (AI), Arunangshu Dutta Roy (ADR), Eric D. McCollum (EDM), Harish Nair (HN), Steven Cunningham (SC), Ian Mitra McLane (IMM), Mohammod Shahidullah (MS), Abdullah H. Baqui (AHB). The full text of the publication is attached below. Some contents have been organised to comply with the format of this thesis. The FGD guidelines are attached on pages 472, 473 and 475.

URL: https://bmcdigitalhealth.biomedcentral.com/articles/10.1186/s44247-023-00027-y

End-user acceptability of a prototype digital stethoscope to diagnose childhood pneumonia- A qualitative exploration from Sylhet, Bangladesh

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8.1 Abstract

8.1.1 Background

Considering the high frequency of respiratory infections among children in low- and middle-income countries (LMICs), the World Health Organization (WHO) developed a pragmatic guideline for managing pneumonia in low-resource settings. The guideline's low specificity leads to many false-positive pneumonia cases receiving antibiotic treatment. Integrating diagnostic technology to incorporate lung sounds into WHO guidelines could improve childhood pneumonia diagnosis and management. This qualitative study aimed to explore the acceptability of a prototype digital stethoscope device among potential end-users in Bangladesh.

8.1.2 Methods

We conducted four focus group discussions (FGDs) with beneficiaries and service providers who used a 2018 digital stethoscope prototype. The data collection was conducted in November 2020. The study was carried out at

Zakiganj Upazila (sub-district) of Sylhet district of Bangladesh. A total of 34 respondents, including parents of under-5 children, Community Health Care Providers (CHCPs), and community leaders were enrolled. Two researchers (TJ and a research assistant (not a co-author of this manuscript) conducted the FGDs. Verbatim transcripts were prepared, and translations were completed. Coding was executed in Microsoft Excel, and relevant quotes were extracted to ascertain the emerging themes. To ensure validity, two researchers coded the dataset independently and inconsistencies were resolved through discussion.

8.1.3 Findings

Mothers were more aware of the digital stethoscope than fathers. Except for the female community leaders, male leaders were unaware of the stethoscopes. Most CHCPs had positive perceptions of the digital stethoscope. They appreciated stethoscope training as they learned about new technology and diagnostic approaches. The users mentioned several technical shortcomings of the prototype device. A few stakeholders expressed dissatisfaction with the level of community involvement and information sharing from the study. The use of the device plummeted during the COVID-19 pandemic for fear of infection, to counteract which the CHCPs cleaned the device with chlorhexidine after every application as a precaution.

8.1.4 Conclusions

Overall, device use was supported by stakeholders despite perceptions that the prototype had some technological limitations, community engagement was suboptimal, and the COVID-19 pandemic caused disruptions. Stronger community engagement, addressing technological issues, and further research on its health systems application would improve the acceptability and effective use of the digital stethoscope.

8.2 Background

Respiratory tract infections, including pneumonia, are a major killer of children worldwide. Pneumonia is one of the leading causes of mortality in children aged below five years worldwide (129). While radiologic imaging is commonly used to diagnose pneumonia (148), It is estimated that approximately half of the world's population does not have access to imaging facilities (149). Availability, accessibility, and quality of care are important factors hindering care-seeking. More than 75% of pneumonia deaths occur in sub-Saharan Africa and South-East Asia (6). Care-seeking for children with acute respiratory infections (ARI) is one of the sustainable development goals (SDG) indicators (indicator 3.8.1) (150). This indicator has improved in Bangladesh over the last few years, but the rate is still low at 46.4% (151).

Given the high burden of respiratory infections among children in low- and middle-income countries (LMICs), the World Health Organization (WHO) developed a separate guideline for managing pneumonia in resource-limited settings. In these settings, the WHO guideline promotes antibiotic use for all children with cough and/or difficulty breathing, and with rapid breathing and/or lower chest wall indrawing (152). Due to a lack of diagnostic specificity of the guidelines, more than half of children incorrectly receive antibiotic treatment, which increases treatment costs, health system pressure, and also antimicrobial resistance.

The use of novel diagnostic technology, applicable in low-income settings, may be a solution to these challenges (139). A stethoscope for auscultating lung sounds could improve diagnosis, but this device has some limitations in low-resources settings like Bangladesh. First, using a conventional stethoscope requires advanced clinical skills, which is difficult to ensure in rural areas with few physicians. Second, its application demands a quiet environment, which may be difficult to find in crowded rural health centres such as Community Clinics (CCs) in Bangladesh. A technology that overcomes the limitations of standard conventional stethoscopes and, at the same time, is inexpensive and acceptable to end-users could be a transformative solution (153). We conducted a qualitative study in Bangladesh to explore the acceptance of a prototype digital stethoscope for children among potential end-users.

8.2.1 Description of prototype digital stethoscope

Engineers, physicians, and public health experts at Johns Hopkins University, Baltimore, USA collaborated to develop a prototype device that uses digital sensing technology for sound capture, active acoustics for noise cancellation, and artificial intelligence (AI) to assist health workers in diagnosing pneumonia (94). A detailed description of the device is available on page 334.

The prototype digital stethoscope was designed for non-traditional clinical settings, such as rural or walk-in clinics, homes, or low-resource areas, to be used by both trained and untrained personnel. It is equipped with advanced onboard and real-time algorithms that can detect adventitial lung sounds in recordings and improve the quality of the body sounds detected by the device through adaptive noise cancellation and the use of an externally facing microphone, mitigating any ambient noise typically present in non-traditional settings (153).

The device features multiple microphones and proprietary active noise suppression. One of the key advantages of the multiple microphone sensing array design is that the digital stethoscope does not require precise placement on the body, potentially permitting healthcare workers or carers with minimal training to also use the device. The adaptive noise suppression algorithm relies on comparing the signal from the sensor head to that obtained from an externally facing microphone. The algorithm operates through multiband spectral subtraction based on a classic, active signal denoising approach. As opposed to passive approaches such as low pass and high pass filtering found in current commercial products, this technique offers a real-time adaptation of the algorithm given the ambient environment. A classic spectral subtraction scheme has been extended into multiple frequency bands with weighted subtractions of each band that consider the signal-to-noise ratio of both the current frame and frequency component, which allows for more accurate adaptation to unseen environments and sounds.

An associated prototype mobile application has been designed, and this application takes recordings from the device via Bluetooth and associates the recording with a specific location and a nonidentifiable patient ID before transmitting it to a secure cloud database. This application can be applied to support clinical care and research projects involving the stethoscope. The application guides participants through the data collection process at four preset locations on the body -two from back and two from front chest (153). and subsequently asks participants questions regarding symptoms at the time of recording. The application can also push notifications and reminders daily to ensure that recordings are conducted. This application standardizes the study procedure across all the study participants when conducting studies at multiple sites.

8.2.2 Study objective

This is a qualitative study to explore the acceptability of the 2018 prototype digital stethoscope system among potential end-users. This study is a part of a larger study (153) aiming to compare automated lung sound classifications by digital auscultation based on trained paediatricians' reading, as part of a broader effort to improve the accuracy of childhood pneumonia diagnosis.

8.3 Methods

8.3.1 Study design, duration, and site

This qualitative study used a narrative research approach (154) and involved focus group discussions (FGDs) with beneficiaries and service providers using the 2018 digital stethoscope prototype. This study was conducted from a constructionism (155) point of view as it is primarily concerned with the individual's active role in constructing knowledge through their interactions with the environment, in our case, the application of the digital stethoscope in Zakiganj upazila (sub-district) of Sylhet district of Bangladesh in November

2020. The field data collection was carried out between 28 and 29 November 2020. The district map of the study site is shown in Figure 8.1

Figure 8.1 Study site in Zakiganj Upazila, Sylhet District, Bangladesh

Source: The map image is freely available for use from https://commons.wikimedia.org/wiki/File:BD_Sylhet_District_locator_map.svg

8.3.2 Study population

A total of 34 different respondents participated in four FGDs. Seventeen carers (Mothers, n=10; Fathers, n=7), eight Community Health Care Providers (CHCPs), and nine community leaders were included as FGD participants. The details of the methods followed are mentioned in Table 8.1.

Table 8.1 Total number of participants included in the FGDs

Method	Tool	Participants	Number
FGD	Topic guide for carers (Mothers and Fathers)	Mothers	10
		Fathers	7
	Topic guide for Community Health Care Providers (CHCPs)	CHCPs	8
	Topic guide for community leaders	Community leaders	9
Total number of respondents in 4 FGDs			34

Note: The purpose of using different topic guides for different types of respondents in FGDs was to explore varied perspectives on the acceptability of the prototype digital stethoscope used for the study among stakeholders.

8.3.3 Data collection and tool development

The first author (TJ) and a research assistant (not a co-author of this manuscript) conducted the FGDs. The selection of participants was done purposively. For carers, we generated a list (from the database) of enrolled children from which male and female carers were independently approached and were invited to participate in the discussion. Those who were interested in participating were selected and called for the FGD. Community leaders who were members of the CC support groups were approached and invited to participate in the discussion. Those who agreed were selected. All CHCPs who took part in the study activities at their CC were invited to participate in the discussion. The FGDs were held at the study office in Zakiganj, where the main trial on the effectiveness of the digital stethoscope was coordinated.

Considering the COVID-19 situation, we placed each participant in alternate chairs around a large conference table, maintaining at least a 1-meter distance. We also provided face masks during the FGD and kept the windows open to promote adequate ventilation. FGDs were conducted at the Projahnmo Research Foundation (PRF) Zakiganj office, but were held in a private room to ensure confidentiality and reduce social desirability bias (156). The data collectors identified themselves as external consultants with no affiliation with the project implementers.

Each of the four FGDs consisted of 7-10 participants, selected through a purposive sampling method. The FGDs had the following types of participants:

FGD 1: Mothers of the beneficiary children

FGD 2: Fathers of the beneficiary children

FGD 3: CHCPs who used the digital stethoscope prototype

FGD 4: Community leaders from the intervention area

The first author (TJ) of this paper facilitated the sessions while a Research Associate (RA) obtained written informed consent, which included permission for the audio recording of the FGD, and took written notes. Each FGD, lasting from 60 to 105 minutes, was conducted in Bengali, the native language of the respondents and the researchers. All participants received lunch (arranged at the PRF Zakiganj office) and transportation cost reimbursement. The summary of the open-ended questions in the FGD topic guides is given below:

1) Initial or ice-breaking questions, whether the participants were informed of the use of the digital stethoscope in the area.
2) General perception regarding the digital stethoscope, whether it is a good or a bad innovation.
3) Training on the use of the digital stethoscope (question for health workers and community leaders only)
4) Cooperation of beneficiaries with health workers to use the digital stethoscope (question for beneficiaries only)
5) Positive experiences using the digital stethoscope
6) Negative experiences using the digital stethoscope
7) Experience regarding troubleshooting support
8) Supervision of the digital stethoscope use (question for health workers and community leaders only)
9) Adaptation in work or the health centre for using the digital stethoscope (question for health workers only)
10) Improvement potential
11) Scaleup potential (question for health workers and community leaders only)
12) Comparison with the conventional acoustic stethoscope
13) Summary and recommendations

The tools are available on pages 472, 473 and 475 in Chapter 13.

8.3.4 Data analysis

The FGDs were immediately transcribed and translated by the RA. For analysis, we adopted the conventional content analysis method (157), which is appropriate in the scarcity of existing literature on a topic, as this method avoids using preconceived themes. We immersed ourselves in the data to allow new insights to emerge, then developed the inductive categories through the following steps: familiarizing ourselves with the data by listening to the records and reading the transcript, developing coding schema in Microsoft Excel based on the questions mentioned above, noting the first impressions followed by labelling the text segments by newly emerging codes, merging the similar-meaning codes, then sorting the codes into larger categories based on how different codes are related or linked. Appropriate quotations were extracted to substantiate the emerging themes. In order to increase validity, TJ and another qualitative researcher independently coded the dataset. We discussed and reached an agreement regarding the coding if any discrepancy was found. To increase the trustworthiness and credibility of the data, we used source triangulation (158) by conducting FGDs with various stakeholders, including mothers, fathers, CHCPs, and community leaders. This approach allowed us to compare and validate different perspectives on the prototype digital stethoscope.

8.4 Results

8.4.1 Background characteristics of the participants

A total of 34 respondents participated in four FGDs (Table *8.2*). The respondents' age ranged from 21 to 63 years; 16 were males, and 18 were females. Apart from the CHCPs, the other three groups of participants were heterogeneous in education and occupation. Female respondents other than the CHCPs were primarily housewives.

Table 8.2 Characteristics of the FGD participants

FGD	Age Range (Years)	Male/ Female	Education	Occupation
Mothers	21-40	0/10	Most completed 8th class or secondary school certificate (n=8), one completed 5th class, and one could only sign.	Most were housewives (n=9), and one tailor.
Fathers	29-52	7/0	Most completed 9th class or secondary school certificate (n=4), two could only sign, and one had a master’s degree.	Farmer (n=2), day labourer (n=2), one poultry farmer, one teacher, and one businessman.
CHCPs	29-36	3/5	Most held a bachelor’s degree (n=4), a master’s degree (n=3), and one had a higher-	All were full-time health workers.

			secondary school certificate.	
Community leaders	38-63	6/3	Most completed 10th class or higher-secondary school certificate (n=5), three completed between the 3rd and 5th class, and one completed bachelor's degree.	Most were businessmen (n=4), two farmers, two homemakers, and one day labourer.

8.4.2 General perception regarding the digital stethoscope prototype

All the mothers knew about the digital stethoscope, but the fathers did not. Fathers did not visit health centre for their children's health care, so, fathers were less aware of the device. Community leaders did not know much about the digital stethoscope, except for the female leaders, who learned about it from beneficiary mothers in their families. Mothers reported being slightly nervous initially, but they became familiar in subsequent uses, and the baby was calmer than the previous encounter. Expressing approval for the digital stethoscope, a mother said,

> "Baby always moves a lot. It is normal. As a mother, I knew the digital stethoscope is good for my baby. It helps him get cured of pneumonia. So, I cooperated with the health worker so that she could use the device well." [Mother, FGD 1]

Health workers knew how to select the beneficiaries and apply the digital stethoscope. They have been using it for the last one and a half years, and they apply it daily to two to three children on average. Most of them had a positive perception regarding the digital stethoscope. The reasons they cited were: first, digital equipment is generally good as they give more accurate results than non-digital ones, and second, it is a new technology, and anything new is usually better than the old.

8.4.3 Training

All participating CHCPs received a three-day training at the Zakiganj Upazila Health Complex (UHC) in April 2019. The local PRF staff and an overseas doctor provided the training. The training included using a pulse oximeter, detecting shortness of breath, measuring mid-upper arm circumference (MUAC), and use of the digital stethoscope on infants and children. They received two refresher training in July 2019 and January 2020.

The participants appreciated the training as they could learn about new technology and diagnostic approaches. The training was interactive (they could give feedback), detailed, and included practical demonstrations. They liked the training venue as it was a new place outside their workplace, getting to know new colleagues working in different CCs, good food, the presence of a ‘foreign’ trainer, and the amount of remuneration. They felt that another refresher training would be useful. The only negative aspect of the training was that there was not sufficient water at the training venue, and they wished the refresher training had been longer,

> “Practical demonstration was good, training was good, but I wish we received refresher training for two days instead of one.” [Male CHCP, FGD 3]

Community leaders needed to be sufficiently engaged in the training, and only one out of the nine participants knew about the training. However, they did not hear any complaints regarding the training, in general.

8.4.4 Support and supervision

The 14 CHCPs (later reduced to nine) received support from two Field Research Assistants (FRAs) and two physician supervisors. The FRAs provided technical assistance as requested by the CHCPs and replaced malfunctioning digital stethoscope prototypes when necessary. The two physician supervisors regularly visited the CHCPs to supervise patient enrolment and recordkeeping; and conducted quality control activities. Apart from the formal training at the Upazila Health Complex (UHC), the CHCPs received regular onsite training on-demand by the PRF staff. CHCPs said that the PRF staff tried to solve the problem immediately whenever they faced any technical glitches. However, sometimes it took a long time, and the mothers had to wait for two to three hours. A mother said,

> "There was no charge in the device. When the health worker called, another health worker [actually an FRA] came. It took around two to two and a half hours to solve the problem. Eventually, the new health worker [FRA] brought another device and conducted my baby's chest examination." [Mother, FGD 1]

The CHCPs were satisfied with the quality control activities and the supervisory support they received. According to the CHCPs, the actions of the PRF staff included: using standard devices to check if the measurements done by the CHCPs were correct, shadowing their activities to assess if there were problems in following the instructions provided by the project, waiting in the

CCs for the whole day if there was a long gap in patient enrolment. CHCPs appreciated the friendly behaviour of the PRF supervisors,

> "This is good that we never felt they [PRF staff] are checking on us. We feel good when they come to our CC. We get whatever we request them." [Female CHCP, FGD 3]

8.4.5 Positive experiences

According to mothers, health workers looked confident with the digital stethoscopes, and the babies were not afraid. They also felt that a digital instrument must be more accurate. A father said,

> "This is the digital era. Everything digital is good. It [the digital stethoscope] should be good too as scientists have put their brain into it." [Father, FGD 2]

Some health workers used a regular conventional stethoscope before but preferred the digital stethoscope prototype as they did not have to interpret the sounds. According to them, beneficiaries were happy too, so much so that some non-beneficiary mothers complained about why their baby was not examined by the digital stethoscope. Reflecting on its acceptability among the mothers, a CHCP said,

> "Usually, the extreme-poor mothers visit the Community Clinic. They become happy that they are getting something [examined by the digital stethoscope] that even the big hospitals cannot offer." [Male CHCP, FGD 3]

Some other benefits of using the digital stethoscope, as reported by the participants, are: easy to put the chest piece on the baby's chest (reported by eight mothers and three CHCPs), takes a short time to record the lung sound (reported by three mothers and three CHCPs, while several others complained of taking too long), does not require time or technical skills to clean it, and storage is easy and does not require much space.

8.4.6 Negative experiences

Some beneficiaries were unsure how the health worker would listen to the lung sound in the digital stethoscope, while the patients could clearly understand the mechanism in a regular stethoscope. They doubted the health workers' ability to correctly record and interpret the sound. Most mothers complained about the long time required to get enrolled and examined, especially on the first day. A mother expressed,

> “Examination took a long time initially, around 20 minutes, but later the time came down.” [Mother, FGD 1]

Health workers also accepted the complaints of taking a long time to enrolment. Other demand-side problems, as reported by the CHCPs, include: digital stethoscope patients’ crowded out other patients coming to the CC, patients become restless when the enrolment takes a long time and some suspect that the device might harm their child. A CHCP shared his experience,

> “When the red light of the pulse oximeter is lit, they thought we were sucking out blood from the baby. Since we check oxygen saturation,

> some patients became suspicious of the digital stethoscope too." [Female CHCP, FGD 3]

CHCPs reported some logistic or work-related challenges too. Reportedly, due to the additional time spent on digital stethoscope-related activities, some of their work, such as record keeping and reporting, were hampered. Other challenges include lack of electricity to charge the device, not getting troubleshooting support in time, concern about privacy as CHCP may initiate the digital stethoscope recording accidentally at times, anxiety about their children getting electrified while charging the digital stethoscope at home, and difficulty in carrying the extra load of the device regularly. A participant said,

> "Carrying these instruments is difficult as I travel by motorcycle. [Other CHCPs added] Previously, we kept our bag in the health centre; now we have to carry the extra load as we cannot leave such an expensive instrument there." [Male CHCP, supplemented by other participants, FGD 3]

CHCPs reported some technical problems with the digital stethoscope too. For example, the users need to record lung sounds from four locations, but the device sometimes stopped after recording the first sound. Sometimes the recording continues until someone from the PRF office provides technical support to stop it or change the device altogether. They also complained about the prototype's durability as the rubbers around the chest piece and other parts of the device eroded since the device was a 3-D printed prototype. Without a visual cue on the prototype device, users were often confused about whether the recording was done correctly. Sometimes the devices froze (becomes unresponsive), started auto-recording, drained their charge quickly, and did not record. A CHCP said,

> "In front of my Community Clinic, there is a garage. Passengers talk. Then their talking is recorded more than the lung sound." [Female CHCP, FGD 3]

8.4.7 Improvement potentials

The participants proposed several recommendations related to the technical aspects of the device itself, its functionality within the larger health system, or some demand-side requests for better application. The technical recommendations include solving the problem of the device freezing or becoming unresponsive, adding a display to show the reading, adding a holder to hold it easily in hand or hang it on the wall, increasing the battery life, using more durable, non 3-D printed materials for the chest piece and the surrounding rubber, adding indicator lights (green, yellow and red) to indicate the lung sound findings, and decreasing the number of chest positions for recording (currently there are four positions). A participant said,

> "Sometimes the baby starts crying after recording from three positions. Then we cannot complete the recording. So, it would be good to record from fewer positions." [Male CHCP, FGD 3]

In order to improve the functionality of the device within the health system, the participants recommended providing health workers with a back-up device so that they can replace it without having to keep the patients waiting, giving a good quality power bank to all health workers (currently, it is provided only in the CCs without electricity) so that they do not worry about the device turning off of the low battery, exempting health workers from any additional reporting related to the device use (since the prototype is currently being used as part of a study, currently, they have to take consent and fill out a register book). Community leaders emphasized informing the community people of the device for better acceptability,

> “Even being a community leader, I don't know this [the digital stethoscope] is available in my area. Now suddenly, you have come asking about this. This should not have happened. We must be informed first.” [Male community leader, FGD 4]

Beneficiaries demanded that the digital stethoscope should be made available in local private pharmacies as these serve as their first point of care,

> “Community Clinics are open only two or three days a week and only for a limited time. But the pharmacy is available even at 3 AM in the morning. If I walk just five minutes, I come across at least three or four pharmacies. So, it [the digital stethoscope] would be more useful in pharmacies. It would be more useful in the hand of informal providers.” [Father, FGD 2]

They also said that using the digital stethoscope should not be limited to pneumonia only; a device like this should be upgraded to detect other diseases, such as heart disease, tuberculosis, or even COVID-19. A participant mentioned,

> "If this device could detect more diseases, I would purchase one for myself to keep in my home. Just like we keep a thermometer in our home." [Father, FGD 2]

Albeit having shared their concerns and recommendations, the participants gave overall positive feedback regarding the digital stethoscope and emphasized its usefulness in the rural Bangladeshi context. They expressed their commitment to continue using the digital stethoscope should the device be made available and scaled up. A health worker expressed,

> "We commonly observe breathing difficulties, coughing, and pneumonia-related problems in children. If this [the digital stethoscope] remains available, then the people of the area will be benefited, plus the other people will also be benefited if the device is scaled up to other areas." [Male CHCP, FGD 3]

8.4.8 Impact of Covid-19

Concerns regarding COVID-19 were expressed in all FGDs. The fathers and the community leaders wished the digital stethoscope could detect COVID-19, as going to the district town to get tested for the disease was difficult for them. Mothers were afraid to go to the CCs for fear of contracting COVID-19. The CHCPs also supported the beneficiaries' remarks and confirmed that the use of the digital stethoscope was decreased due to the COVID-19 situation,

> "Previously, more children came on whom we used the digital stethoscope. During the COVID-19 lockdown, Community Clinics were

closed. Now that we have restarted, fewer children are coming." [Female CHCP, FGD 3]

In order to address the concerns, CHCPs proactively took some cautionary measures. They said they cleaned the device with cotton before and after applying it to every child. They explained how they use the readily available chlorhexidine solution to wipe the device after each use,

> "I clean it [the digital stethoscope] with hexisol [chlorhexidine]. I mix a little bit of water with the hexisol and clean the digital stethoscope, weight scale, pulse oximeter, and all the instruments that touch the baby. After completing one child's work, and before doing it for another child, we clean it with hexisol." [Male CHCP, FGD 3]

8.5 Discussion

Digital health technologies hold great potential to benefit LMICs, but many innovations fail to reach full scale due to the lack of acceptability of different stakeholders. By identifying the issues discouraging them from adopting innovation, technology developers and policymakers can produce better technology that is more context appropriate and make better decisions to allow the interventions to reach scale (159). The most important findings from this qualitative study are: i) The stakeholders, in general, approve of the digital stethoscope; ii) The users reported some technological limitations of the 2018 prototype device; iii) Some stakeholders complained about insufficient community engagement and information sharing regarding the device; iv) digital stethoscope study use during the COVID-19 pandemic faced challenges, against which health workers took proactive measures. These important points are discussed further below.

8.5.1 Approval of the digital stethoscope

The stakeholders we included in our study were the carers of the children who took their sick children to seek care from the CCs, the health workers who applied the digital stethoscope among the under-five children, and the community leaders residing in the catchment area of the CCs included in the study. All of them had something positive to say about the device. Carers were satisfied with modern technology that even the patients visiting large urban hospitals in Bangladesh cannot access. Providers were satisfied with PRF's training, support, and supervision activities. Community leaders did not hear complaints regarding the device from either of these two groups. To the best of our knowledge, this study was the first to evaluate how frontline workers in LMICs record the lung sounds of young children in primary-level facilities. Previously, lung auscultation with conventional stethoscopes were only available in tertiary-level healthcare facilities or by formal healthcare personnel in LMICs (139, 143).

8.5.2 End-user feedback on the prototype device and software application

One of the study's primary purposes was to identify users' technological, logistic, and social challenges in applying the prototype digital stethoscope in order to make iterative improvements in the technology. Our study identified some challenges with the prototype, such as difficulty in charging, needing to carry the device home daily because of security concerns with leaving the device in the clinic, and dealing with prototype software and device glitches. These include stopping of recording prematurely, not stopping the recording in due time, the durability of the 3-D printed prototype material, freezing during the application, draining the charge quickly, and picking up the ambient noise. These prototype challenges have been addressed in subsequent prototype iterations based on this end-user feedback.

8.5.3 Community engagement

Involving opinion leaders is crucial in diffusing innovations to the larger population (160). Although the study conducted community sensitization activities, there was a perception among community leaders that these activities did not sufficiently inform all community leaders and members. Reviewing this study’s community sensitization activities and addressing any shortcomings in future studies is likely to eliminate the likelihood of resistance and improve uptake. Our study found that the community leaders and the community's male members did not feel adequately informed of the prototype device study. It is possible that the community misunderstood that the device was a development prototype and healthcare workers were not using the device for medical decision-making.

8.5.4 Challenges of COVID-19

COVID-19 came as a challenge to all, as the beneficiaries were afraid to use the CCs, and the CHCPs were getting fewer patients. Consequently, we formed Patient Public Involvement Groups (PPIG) consisting of CHCPs, Community Health Workers, Health Assistants, Physicians, community leaders, religious leaders, parents of under-5 children, teachers, local journalists for their insights, approval, and support to implement the study. Despite the challenges, as per the PPIG's recommendations, the health workers carefully applied contact precautions to mitigate any disease transmission risk by an unclean digital stethoscope. They exploited an available cleansing solution (chlorhexidine, which they mixed with water) to sterilize the digital stethoscope and other instruments used. The fact that the prototype device was easy to clean facilitated its use during this time period.

8.5.5 Limitations of the study

The limitation of the study is that we could not achieve thematic saturation. We had to limit the number of FGDs due to time constraints and COVID-19 pandemic. Most male participants, except the CHCPs, also did not have information or familiarity regarding the digital stethoscope, which restricted their inputs.

8.5.6 Recommendations

Based on this qualitative study findings, we make the following three recommendations-

1. **Stronger community engagement is needed:**

   Stronger community engagement is necessary where the device is rolled out. Without the participation of the community and gathering their opinion regarding the device, the initiative will not be as effective. The community engagement activities for this study should be reviewed and revised to improve upon them for future studies.

2. **Technological issues with the prototype device should be addressed:**

   As the users mentioned, at times they faced some difficulties using the prototype device. Addressing their feedback will ensure future versions of the device are more effective and user-friendly. End-user feedback suggested to include a display showing the findings of the lung sound. A holder should be added to the device so that the recording is not turned on by inadvertent touch, and so that potentially the device could be hung on the wall. Since the prototype was 3-D printed the rubber and other materials were brittle. More durable materials should be used, especially in challenging settings like rural Bangladesh. There is a need to decrease the number of recording positions from four chest positions, as the healthcare workers indicated children had difficulty cooperating with all positions. Future research needs to address whether fewer chest positions would be adequate for diagnosis. Battery improvements can be made, as well as understanding whether the extreme environment in Bangladesh may impact battery performance. Future studies could provide users with a power bank and giving a back-up digital stethoscope could be considered if resources allow.

3. **Research exploring whether the device can be effectively used by private sector healthcare workers and improvement of the community clinic's security is crucial:**

Research exploring feasibility of implementing the device with informal providers serving in the local pharmacies should be considered as this could increase access to the device. Ensuring the health facilities' security is vital so the health workers do not need to carry around the device to their homes for charging, which can be challenging in rural Bangladesh.

8.6 Conclusions

The prototype device is an early version of a digital auscultation system for diagnosing childhood pneumonia in a resource-limited setting like Bangladesh. Both the carers and the service providers seem satisfied with the prototype device. Addressing the stakeholders' recommendations would further improve the acceptability of future versions of the device and contribute to the reduction of childhood respiratory infections.

8.7 Declarations

8.7.1 Ethics approval and consent to participate

The ethical approval for the study was obtained from the National Research Ethics Committee of Bangladesh Medical Research Council, Bangladesh (Registration number: 09630012018) and Academic and Clinical Central Office for Research and Development Medical Research Ethics Committee, Edinburgh, UK (REC Reference: 18-HV-051). A Research Associate (RA) obtained written informed consent, which included permission for the audio recording of the FGD, from all the study participants. All methods were performed in accordance with the ethical principles outlined in the Belmont Report.

8.7.2 Consent for publication

Not applicable

8.7.3 Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

8.7.4 Competing interests

The authors declare the existence of a financial competing interest. IMM owns equity in the commercial entity Sonavi Labs Inc. and serves as the company's Chief Technology Officer. EDM is a paid scientific consultant to Sonavi Labs Inc. Under a license agreement between Sonavi Labs Inc. and the Johns Hopkins University, the University is entitled to royalty distributions related to technology described in the study discussed in this publication. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies. The other authors declare that they have no competing interests.

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body did not play any roles in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

8.7.6 Authors' contributions

Conceptualization: TJ, SA. Data curation: TJ, SA. Formal analysis: TJ, SA. Funding acquisition: AHB, SA. Methodology: TJ, ADR, SA. Supervision: SA, ASMDAI. Literature Review: TJ, SNBKT, SA. Writing original draft: TJ. Writing – review & editing: SNBKT, ASDMAI, AI, ADR, EDM, HN, SC, IMM, MS, AHB, SA. All authors read and approved the final manuscript.

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Chapter 9 Discussion

In my PhD thesis, I mainly focused on two objectives: first, to evaluate the capability of CHCPs in recording lung sounds using a prototype digital stethoscope, and second, to determine the diagnostic accuracy of an automated CLSA for identifying adventitious lung sounds compared with a reference listening panel of paediatricians. This evaluation focused on children younger than five years who sought health care at government first-level community clinics in a rural area of Bangladesh. This thesis started with a systematic literature review that examined evidence on the detection of adventitious lung sounds through digital auscultation for diagnosing childhood pneumonia. I found minimal evidence regarding the diagnostic performance of digital auscultation in detecting pneumonia in children.

This chapter will critically analyse the study findings considering the literature reviewed in Chapter 1. First, the main findings of the thesis will be described. The findings will be interpreted, explained, and compared to previously published studies. Issues related to the methodology, analysis, strengths, and limitations will be explored. Finally, the implications of the research will be discussed, and future recommendations will be made.

9.1 Key findings

For this study, 990 children 2 to 59 months old and presenting to care with a respiratory illness characterised by cough and/or difficult breathing were enrolled; 389 (39.3%) children were identified as having ‘any pneumonia’ by CHCPs according to WHO IMCI clinical criteria, and the remaining 601 (60.7%) children did not meet WHO IMCI clinical pneumonia criteria (i.e., ‘no pneumonia). Lung sound recordings in ≥3 chest positions from 378 (97.2%) children with ‘any pneumonia’ and similar sound records from 588 (97.8%) children with ‘no pneumonia’, were transferred from the prototype digital stethoscope to a laptop for post-processing.

To assess CHCPs ability to record quality lung sounds, we hypothesized that over 50% of the patients would have ‘quality’ lung sound recordings, which was defined as having at least 75% interpretable lung sound segments per patient according to the human listening panel (i.e., ≥ 3 out of 4 chest positions). We found that CHCPs successfully recorded lung sounds from 966 (97.6%) children in three or more chest positions. Out of these, 867 (87.6%) children had recordings that met this *a priori* quality definition, indicating that three or more chest position recordings were classified as interpretable by the human listening panel members. Notably, CHCPs recorded 56.6% (483/853) of quality recordings within a one-minute timeframe.

To evaluate the agreement between lung sound classifications obtained from the prototype digital stethoscope-recorded data using a CLSA and the evaluations made by a panel of paediatricians trained and standardised in listening to lung sound recordings. In comparison to the consensus paediatric listening panel, the CLSA detected adventitious lung sounds (wheeze and/or crackles) among all enrolled children with 61.8% (95%CI: 55.7%, 67.6%)

sensitivity, 60.7% (56.6%, 64.6%) specificity, and 41.8% (36.9%, 46.8%) positive and 77.6% (73.6%, 81.3%) negative predictive values. Among children with ‘any pneumonia’, sensitivity was 63.5% (54.5%, 71.9%), specificity 66.8% (60.1%, 73.1%), positive predictive value 52.6% (44.4%, 60.8%), and negative predictive value 75.9% (69.2%, 81.8%). The Kappa statistic was 0.20 (95% CI: 0.14, 0.26) for all children together, and 0.29 (95% CI: 0.19, 0.40) when restricted to ‘any pneumonia’. When analysis was further restricted to ‘confident’ listening panel classifications the Kappa value increased to 0.32 (95% CI: 0.21, 0.42).

9.2 Interpretation of findings

9.2.1 Identification of IMCI-defined pneumonia at first-level facility by frontline health workers

A training manual following the IMCI tool was developed, and both theoretical training and on-the-job training were provided to CHCPs. CHCPs were standardised on respiratory rate counting and assessing chest indrawing every two months by a study physician who was also trained and standardised on respiratory assessment.

Among all children presenting to care at the community clinics with cough and/or difficulty breathing, CHCPs identified 39.3% with IMCI-defined pneumonia (i.e., ‘any pneumonia’). Most children with IMCI-defined pneumonia (95.6%) had age-specific fast breathing (respiratory rate: ≥ 50 breaths per minute for age 2 to 11 months and ≥ 40 breaths per minute for age

12 to 59 months). CHCPs identified chest indrawing in 6.4% of enrolled children. No children were identified with a peripheral oxygen saturation (SpO_2) below 90%.

The Enhanced community case management to increase access to pneumonia treatment study (EMPIC study) conducted in 2016-18 in Bangladesh, India, Ethiopia and Malawi with 2 to 59 month old children at first-level facilities demonstrated that frontline health workers (CHCPs in Bangladesh) identified 46.9% of children presenting to care with IMCI defined pneumonia, and among them only 7.2% children had chest indrawing (161); which is similar in frequency with what we observed. In another study conducted between 2003 and 2005 at first-level facilities in Bangladesh, 43% of children presenting to care were identified with IMCI-defined pneumonia (50).A study at the primary health centres in India between 2019 and 2020 identified 23% of children presenting to care with pneumonia (162). Physicians identified IMCI-defined pneumonia in 21.7% of children between 2014 to 2015 at the outpatient department of the sub-district level facility in Sylhet, Bangladesh (163).

In this study, a trained physician reassessed a subset of children within 90 minutes of the CHCP's assessment as part of study quality control. Using the trained physician as the reference standard, the sensitivity and specificity to diagnose IMCI-defined pneumonia by the CHCPs were 80.6% and 84.2%, respectively. The performance of health workers in identifying childhood pneumonia varies across studies. In a study conducted in Gambia by Weber et al., health workers achieved a sensitivity of 81% and a specificity of 89%, which was similar to my study (55). However, Hadi conducted a study in Bangladesh that demonstrated a low sensitivity of 68% and a high specificity of 95% (164). The high sensitivity and specificity of my study highlights competence of CHCPs in identifying pneumonia and this indicates that they might have misclassified a few cases.

9.2.2 Lung sound recordings

Digital auscultation is a new technology for frontline health workers like CHCPs as this cadre of health professionals in Bangladesh do not typically use conventional stethoscopes during routine clinical care activities. In this study, a SOP for recording lung sounds using a Feelix Smartscope prototype was developed, and CHCPs were trained to follow this SOP. To the best of my knowledge, this was the first study investigating the ability of frontline workers to record lung sounds at first-level facilities in LMICs. In the PERCH study, children were enrolled in hospital settings and digital auscultation was performed by nurses and physicians (147). In Peru, lung sounds were recorded at tertiary-level centre by study nurses and physicians (142). While in yet another study in Nepal, paediatricians recorded lung sounds at a tertiary-level hospital (143). While lung auscultation with conventional stethoscopes is usually unavailable at first-level facilities, it is also challenging due to the typically crowded and noisy environment of these facilities. Moreover, healthcare providers often do not get sufficient time to calm ill, sometimes scared, and agitated children due to the time pressures from a high-volume of patients. It is therefore crucial to understand whether obtaining quality lung sounds in a primary clinic environment by routine healthcare workers when using a digital stethoscope is feasible. In this study, CHCPs recorded lung sounds from four chest locations, starting with two on the back followed by another two on the front, which encompasses both the upper and lower lung lobe fields of each hemithorax. CHCPs successfully recorded lung sounds in 98% of children and there was no difference in the success rate between children with and without IMCI-defined clinical pneumonia. Importantly, CHCPs recorded lung sounds from only one or two chest positions in just seven children overall, and failed to record any lung sounds from any of the chest positions in only ten children. Either prototype device malfunction or an error in the software application used to transfer sound files from the device to the laptop were the main reasons for these failures. Thus, based on these data, we conclude that quality lung sounds from children younger than five years old can be feasibly recorded at first-level facilities by CHCPs capacitated with supportive tools and training.

9.2.3 Interpretability of lung sound recordings

My hypothesis was that if CHCPs can record lung sounds from at least three chest positions in a child and at least three chest position recordings were also classified as ‘interpretable’ by a paediatric listening panel, then the overall recording, transfer, and classification process will have met a minimum quality threshold. The rationale for establishing this quality threshold is that if these criteria are met, then lung sounds would be obtained from at least three of the five major lobes of the lung and from both hemithoraces. Typically, in children younger than five years, inflammation from pneumonia is present in multiple areas of the lung, and so these criteria would conceivably capture most pneumonia cases. In my study, the consensus listening panel was able to interpret 87.6% (867/990) of children's recordings from at least three chest positions, identifying the presence of wheeze, crackles, a combination of both, or no wheeze or crackles (considered normal). There was no difference in interpretability rate between the 'any pneumonia' and 'no pneumonia' groups. Building on the prior conclusion of feasibility, this finding further the notion that CHCPs with limited to no experience in conventional lung auscultation can be trained to use a digital stethoscope as a tool integrated within the WHO IMCI algorithm to diagnose and treat children with pneumonia. In the PERCH study, physicians conducted most of the recordings (using a commercially available digital stethoscope), and the interpretability rate was 89.5% in the pneumonia group and 92.4% in the no-pneumonia group, similar to this study (139). In our study we also observed that interpretability was modestly higher in children aged 12-59 months compared to children 2-11 months (94.0% vs 90.3%, p=0.05), as older children are likely to be more cooperative than younger children and the size of the diaphragm of the prototype stethoscope may not be ideally suited to the smaller chest size/shape of younger infants. We also observed a modestly higher interpretability rate among female children than in male children (95.0% vs 91.7%, p=0.05), which may reflect that female children were calmer than male children (165).

In this study, the proportion of children with three or more interpretable lung sound recordings by each CHCP ranged between 73.1% and 94.7%. The two CHCPs who enrolled the lowest number of children (26 and 38 children), also achieved the lowest level of success rates of 73.1% and 76.3%, respectively. In contrast, the success rate of CHCPs with the highest number of enrolled children (187 and 179 children) was 94.7% and 92.7%, respectively. Notably, the performance of CHCPs in recording interpretable lung sounds improved over time, and the percentage of successful recordings increased by 1% with every ten new enrolments. These findings suggest that experience using the prototype digital stethoscope improves the frequency of successfully using the device.

CHCPs followed a sequential order for recording lung sounds, starting with the patient's back on the left, then right, followed by the anterior left and then right. CHCPs were taught to start recording on the child’s back as this was felt to optimize cooperation since the child would be able to look away from the CHCP towards the carer or even hug the carer during this portion of the recordings. Interestingly, we found no statistically significant variation in the success rate of recording lung sounds between these four chest positions. However, we did discover a significant difference in interpretability between recordings obtained on the patient’s back and front (92.0% vs 87.9%; $p=<0.01$). As anticipated, the back positions are less intrusive than the anterior positions, and the back positions were also systematically collected before the two front positions. Three out of every four children were cooperative and quiet during the recording, while 9.9% of children were initially cooperative but became agitated and cried later in the recording examination.

The percentage of children having adventitious lung sounds was no different when one or two chest position recordings were interpretable (34.4%) compared to when three or four chest positions were classified as interpretable (31.4%; p=0.62) by the paediatric listening panel. This may have happened because inflammation from pneumonia is usually present in multiple areas of the lung. This finding is important for future studies to explore whether a fewer number of chest positions may be utilised to incorporate auscultation in the IMCI tool (e.g., one on the back and one on the front of the patient). In comparison, the PERCH and Peru studies recorded lung sounds in eight chest positions (142, 147), while the Nepal study in six positions (143) . Our findings suggest that the optimal number of positions for lung sound recordings in digital auscultation may be lower, which would further increase the feasibility of the implementation of this technology by shortening the time necessary for recording lung sounds by as much as 50%. This may be due to several reasons. First, the prototype stethoscope's chest piece is packed with transducer arrays to achieve a uniform sensitivity over the entire active area. This design advantage delivers a strong signal even when the chest piece is not placed in precisely the correct position and may also capture sounds transmitted from other areas of the lungs. Secondly, the use of noise cancelling technologies could also improve listening accuracy to allow a reduction in the number of chest position recordings needed. Lastly, the prototype digital stethoscope allows for sound amplification, which may also allow listeners to discern pathological sounds that otherwise would be missed with conventional stethoscopes.

9.2.4 Duration of lung sound recording

CHCPs recorded interpretable lung sounds in 89.7% of children with ≥3 chest positions in less than five minutes; the maximum time taken to record was 18 minutes. The Feelix Smartscope prototypes were auto programmed to record a duration of 10 seconds at each chest position. In about 50% of children classified with 'any pneumonia' and 61% with 'no pneumonia' CHCPs recorded interpretable lung sounds at ≥3 chest positions in an overall time of one minute or less. This finding suggests that incorporating digital auscultation into the IMCI tool is unlikely to significantly increase the already substantial workload of frontline health workers, which increases the potential of the technology being successfully implemented within a programmatic context. Interestingly, we found no relation between the number of children enrolled and the overall time taken to record the lung sounds by the CHCP. There were several challenges consistently identified when CHCPs took more than one minute to record lung sounds. Firstly, the device froze, which required the CHCP to either completely restart the Smartscope or drain the device battery charge over a 12-24 hour period (in this situation the device was then unusable). Secondly, children younger than five years of age are active, and although most children were initially cooperative, some became agitated during the recording period. When this happened CHCPs had to stop recording and take additional time to calm the child down before reattempting to record the lung sounds. Thirdly, sometimes there were ambient sounds from loudspeakers outside the community clinic or a call to prayer started after a recording was initiated. In this instance, the CHCP would stop recording until the end of the loudspeaker announcement or call to prayer. Finally, community clinics were usually busy at a certain time period during the day (such as 11 am to 1 pm). Many patients arrived simultaneously, which sometimes created an unfavourable environment to record sounds due to time constraints; instead, CHCPs prioritised treatment for another patient as recording lung sounds was considered a research activity, not routine care activity.

9.2.5 Inter-listener agreement

There is no reference standard for comparisons to automated CLSA lung sound classifications. As a result, we used the consensus listening panel's classification of lung sounds as the reference standard in this study. This study used a modified PERCH study (139) training manual and guidelines for lung sound classification to train and standardise four paediatricians – two from the aforementioned PERCH study panel and two new panellists from Bangladesh. Any of the two randomly allocated panel members independently listened to all the lung sound recordings with a headset and simultaneously viewed the sound spectrograms using Audacity (an open-source software). They entered their findings onto an online electronic form. The panel members could listen to the recordings with the freedom to stop or repeat parts or the entire recording if necessary. They were blinded to all clinical information of the participant, other than the knowledge that the child met the eligibility criteria of the study.

Four chest location sound files per patient were recorded and classified, but adjudication of any discordancy between classifications was made at the level of the patient rather than at the level of the chest position. Adjudicating discordances at the level of the patient was selected because one of the objectives of this study was to validate agreement between the classification of computerised lung sound analysis (CLSA) of children with the paediatric listening panel at the child level. In this child-based analysis, moderate agreement (k = 0.42) for interpretability and fair agreement (k = 0.24) for adventitious lung sounds were found between the two primary listening panel members (i.e., the first two members that listened to the recordings). However, primary listening members raw agreement was 96.6% for interpretability and 64.7% for adventitious lung sounds classification. Two of the four primary listeners were more experienced as they had participated as panellists in the PERCH study (139). The other two listeners were paediatricians with less than five years of experience and had not previously participated in a digital auscultation listening panel. This modest inter-listener agreement achieved by this study suggests that proper training can reduce inter-listener variability and attain a satisfactory degree of agreement for interpreting recorded lung sounds. Though recording lung sounds from children is harder than from adults, similar results were observed from an adult-based study in Norway between May 2015 and October 2016. In this Norwegian study 4033 participants were aged 40 and above, where k= 0.43 in inspiratory wheeze, k = 0.46 in inspiratory crackles and k = 0.20 in expiratory crackles (166). The PERCH study on children also found a similar moderate agreement (PABAK 0.50) between two listeners (139). Moderate agreement (k= 0.59) for identifying wheeze was found in another study where lung sounds were recorded from 120 sleeping infants using PulmoTrack (an automatic wheeze detection device) during lung function tests as part of routine follow-up after hospitalisation in intensive care (167). Fair inter-observer agreement (k = 0.30) on adventitious sounds was found in another study conducted between December 1989 and March 1990, where the patients (mean age was four months) were enrolled at the University of North Carolina Hospitals, the Elmwood Paediatric Group, and the paediatric outpatient department of Metro Health Medical Centre, Cleveland, Ohio and a second physician assessed patients sequentially not simultaneously (60).

9.2.6 Classification of lung sounds by the paediatrician listening panel

Typically, lung auscultation is performed by physicians during the clinical examination to diagnose and manage children who acutely present with respiratory signs such as cough, difficulty breathing or fast breathing. These children may suffer from a number of common acute illnesses, including pneumonia, asthma, bronchiolitis or upper respiratory infection. The detection of crackles through lung auscultation has been shown to be relatively specific but less sensitive to diagnosing pneumonia in children (33, 168, 169). However, when integrated with other clinical respiratory signs, such as tachypnoea and/or chest indrawing, specificity improved (65). In my study, the consensus listening panel of paediatricians found that among children with IMCI-defined pneumonia (i.e., ‘any pneumonia’), 63.3% exhibited normal lung sounds (no wheeze and no crackles), while 15.5%, 9.9% and 11.4% children had wheeze only, crackles only and both crackles and wheeze, respectively. In the PERCH study, 22.9%, 12.1% and 27.0% of acute respiratory illness cases had wheeze only, crackles only, and both crackles and wheeze, respectively, and 38.0% of children had normal lung sounds (139). Many children with fast breathing and/or chest indrawing and also either normal lung sounds, or wheeze could be ruled out as having pneumonia requiring antibiotic treatment, as both findings are suggestive of acute viral illnesses. A double-blind randomised placebo-controlled trial in Pakistan showed that treatment with three days of oral amoxicillin was equivalent to placebo among children with IMCI-defined non-severe pneumonia (170). A multicenter study in Pakistan showed children with auscultatory wheeze had better treatment outcomes when sent home without antibiotics and instead treated with a bronchodilator (171). In my thesis work, among the non-pneumonia group, 11.3%, 8.0% and 8.6% of children had wheeze only, crackles only, and both wheeze and crackles, respectively. In the PERCH study, among the control group (non-ARI cases), 9.2%, 2.5% and 3.5% of children had wheeze, crackles and both wheeze and crackles, respectively (139). Identification of adventitious lung sounds among the non-pneumonia group can be explained by several possibilities. Firstly, the digital stethoscope may capture sounds better than a conventional stethoscope because the chest piece of a digital stethoscope is packed with transducer arrays to achieve uniform sensitivity over the entire active area. This design delivers a strong signal even when the chest piece is not placed in precisely the proper position, so a digital stethoscope may capture more subclinical abnormalities. Subclinical adventitious lung sounds in children with only cough or difficulty breathing in LMICs may reflect ongoing small airway inflammation triggered by asthma or poor air quality (172). Non-pathological crackles occur during inspiration in healthy adults after deeply exhaling to the lung's residual volume, presumably due to the reopening of collapsed distal airways and gas exchange units (i.e., alveoli) (173). Secondly, the listening panel members were blinded to the clinical status of the children. In a clinical setting, during conventional auscultation, physicians visualize the child's clinical condition while auscultating, which may help to distinguish between wheezes, upper airway sounds such as cries, normal vocalisations, or transmitted nasal congestion, or crackles and movement artefact (139). As the listening panel members had not seen the children, clinical correlation was not possible and therefore the probability of misclassifications may have increased.

9.2.7 Agreement between automated CLSA and human paediatrician panel's lung sound classification

Among children presenting to care with cough or difficulty breathing, this study showed that an automated CLSA had moderate sensitivity (61.8%) and specificity (60.7%) for classifying lung sounds as adventitious or normal when compared to a reference human paediatrician listening panel. The sensitivity (63.5%) and specificity (66.8%) were modestly higher when analyses were restricted to children meeting IMCI-pneumonia criteria (n=343) and still further improved (sensitivity 69.8% and specificity 66.8%) when analysis was limited to sounds in which the listening panel classified their interpretation as confident (n=303). Confidence was defined as when the listener clearly identified at least one full breath sound as either normal or abnormal within one chest position segment of a child's total recordings. The concordance between automated CLSA and the listening panel was 0.20 in all children; it was 0.29 among IMCI-defined pneumonia. Among IMCI-defined pneumonia and when listeners were confident, the kappa value was 0.32. Cohen's kappa coefficient measures inter-rater reliability (agreement) between two observers (listeners). The kappa coefficient ranges between 0.2 to 0.4 are considered fair agreement between listeners (174). The raw percentage of agreement between listening panel and CLSA classification was 61.0%, 65.6% and 67.7% among all children, IMCI-defined pneumonia children and IMCI-defined pneumonia with 'confident' classified by listening panel, respectively. It is important to note that the kappa coefficient has limitations. A high percentage of observed agreement and low kappa value is known as the kappa paradox (175). Kappa can be influenced by prevalence and bias index. Thus, I also reported prevalence-adjusted bias-adjusted kappa (PABAK), which also showed fair agreement, indicated prevalence and bias issues were not large influences on the kappa statistic results in this study.

There are several potential reasons for the modest performance of the automated CLSA when compared to human reference classification. The crowded and noisy environment of first-level health facilities and uncooperative children might reduce the quality of the overall recording, even if the recording remained interpretable overall. Currently, the CLSA does not ignore portions of a recording that may be dominated by a crying, vocalising, or moving child.

The amplitude and frequency characteristics of sounds produced when crying, vocalising, or moving overlap with pathologic lung sounds like wheeze and crackles. This is not an uncommon scenario with children and is therefore an important source of continued disagreement between the human listener and the CLSA. Expert paediatricians understand these limitations to examine children clinically and are better able to ignore these portions of an otherwise interpretable recording. Improving the CLSA algorithm to similarly ignore such portions of a recording is likely to enhance agreement levels. This trend was observed when restricting the analysis to 'confident' classifications. In addition, the algorithm appears to perform better in identifying abnormal or normal lung sounds as compared to human listeners when the analysis is restricted to children meeting IMCI-pneumonia criteria than in all children with cough or difficulty breathing. A systematic review of studies done using computerised lung sound analysis in the detection of different abnormal lung sounds by Gurung et al. (86) showed an overall sensitivity and specificity of 80% and 85%, respectively. Most of the studies had a small sample size. In this review, one study had a sample size of 100 participants, and the remaining three had 60, 40 and 31. Another study enrolled 73 children, among them 33 were well and only 8 children had pneumonia, aged 5 months to 16 years and found sensitivity and specificity were 91% and 95% in detecting wheeze/crackles (176). A study used International Conference on Biomedical and Health Informatics (ICBHI) 2017 Respiratory Sound Database with 920 audio samples from 126 subjects and found automated neural model showed 47.37%

sensitivity and 82.46% specificity to classify adventitious lung sounds compared to physicians (177).

9.2.8 Comparisons of lung sound classification between the listening panel and CLSA

Among the children with IMCI-defined pneumonia, the consensus listening panel classified normal lung sounds (no wheeze and no crackles) in 63.3% of children while the automated CLSA approach found normal lung sounds in 55.7%, and this difference reached statistical significance ($p<0.05$). Among children without IMCI pneumonia, the consensus listening panel identified adventitious lung sounds (wheeze and/or crackles) in 27.9% of children while the CLSA found 47.7% to have adventitious lung sounds ($p<0.01$). Wheeze only was classified more frequently by the CLSA in both pneumonia (23.0% vs 15.4%, $p<0.05$) and the no-pneumonia groups (19.7% vs 11.3%, $p<0.01$) compared to human listeners. One potential explanation for these differences is the limitation of the CLSA approach to distinguish between recording artefact and adventitial lung sounds. This point is highlighted by the fact that the CLSA approach interpreted and classified 100% of the sound files but listening panel members interpreted 87.6% of children recordings as interpretable. It is conceivable that the system's limitation to filter crying, or other vocalisations led to these differences.

Among the IMCI pneumonia group, 42.3% (145/343) of children had normal lung sounds (no wheeze and no crackles) classified by both the human listening panel and the CLSA. Hazir et al. demonstrated that 82% of children with IMCI-defined pneumonia (age-specific tachypnoea) had normal chest radiographs (59), so they did not have pneumonia and may have normal lung sounds. Rhinitis and enlarged adenoids are common causes of nasal congestion in children and those are also causes of age-specific tachypnoea in many children. These children have normal lung sounds and were unlikely to need antibiotics.

In the children without pneumonia, the consensus listening panel identified 27.9% to have adventitious lung sounds, while the CLSA identified 47.7% with adventitial lung sounds ($p<0.01$). The presence of adventitial lung sounds in the ‘no pneumonia’ group suggests the potential for asymptomatic children may reflect ongoing small airway inflammation triggered by asthma or poor air quality (172). There may also be another disease in which adventitious lung sounds may be found as the enrolled children had cough or difficult breathing. Other than fast breathing or chest indrawing pneumonia, there are numerous conditions where adventitious lung sound may be identified, such as asthma, bronchitis, bronchiectasis, allergy or anaphylaxis, foreign body or any obstruction in lung or airway, heart failure, etc. The CLSA identified statistically significant more adventitious lung sounds among no pneumonia group, probably, CLSA forcefully classified lung sounds, particularly those with any artefact, to wheeze or crackles or both.

9.2.9 Misuse of antibiotics for pneumonia

In LMICs like Bangladesh, a large proportion of pneumonia cases are managed by non-doctors, including quacks and village doctors (178).

Unfortunately, these practitioners often use unnecessary antibiotics and sometimes even employ higher-generation antibiotics irrationally to make money (179). Adhering to the IMCI strategy could mitigate this issue, but its practical implementation poses challenges. Senn et al.'s 2014 study in Papua New Guinea reported concerning findings: 11% of children did not receive antibiotictic when warranted, while 29% received antibiotic unnecessarily (180). In my research, CHCPs administered antibiotics to all identified pneumonia cases if available, with referrals to higher-level facilities for those showing any danger signs. Ensuring adherence to the IMCI strategy and strengthening healthcare systems are essential to combat inappropriate antibiotic use and improve pneumonia management in LMICs.

9.2.10 Ability of CHCPs in diagnosing pneumonia

Community-level health workers play a vital role in identifying pneumonia in children. In my study involving a subsample of 118 cases for quality control purposes, I compared the performance of CHCPs to physicians and found that CHCPs identified pneumonia with a sensitivity of 80.6% and a specificity of 84.2%. CHCPs missed 7 out of 36 cases of pneumonia but incorrectly classified 13 out of 82 children as having pneumonia. Discrepancies in performance were evident across studies; for instance, in Ethiopia, health workers exhibited a sensitivity of 59% and specificity of 94% (181), while in Bangladesh, community health workers showed a sensitivity of 67.7% and specificity of 95.2% (182). Previous studies relied on clinical signs like fast breathing and chest indrawing for diagnosis, yet pneumonia can manifest without these symptoms. In my study, 16.6% of non-pneumonia cases exhibited crackles, and 63.3% of pneumonia cases had normal lung sounds, suggesting the potential utility of incorporating lung auscultation in pneumonia diagnosis.

9.3 Limitations

This study had a number of limitations.

9.3.1 Pneumonia seasonality

Data collection for this study started on November 2019, but all activities were suspended on March 23, 2020, due to the COVID-19 pandemic. Before the COVID-19 pandemic lockdown, 73.0% (723/990) children enrolled. Enrolment was resumed on September 10, 2020, and completed remaining 27.0% (267/990) enrolment on December 26, 2020. Pneumonia is seasonal and this study did not enrol participants from an entire calendar year. However, this study was unlikely to miss many cases during the pneumonia season, as several studies have shown that the pneumonia season in Bangladesh and India typically occurs from July to January (132, 183-186). This study was not aimed to measure pneumonia incidence rate or seasonality patterns, so the study findings were not influenced due to not having a complete year enrolment data.

9.3.2 Study site

Participants in the study were selected from Zakiganj sub-district of Sylhet district of Bangladesh, which has the highest rates of child morbidity and mortality in Bangladesh (187). This area lags behind in terms of care-seeking behaviour, and child healthcare access (188). This area also has diverse terrain and patchy healthcare access during the rainy and monsoon seasonal periods. Therefore, some of the study findings might not reflect the complete epidemiologic respiratory patterns and distribution of child pneumonia in this area of Bangladesh due to these data gaps.

9.3.3 Purposive selection of CHCPs and unequal number of children enrolled by CHCP

A varying number of children were enrolled by CHCPs in this study. Three CHCPs enrolled fewer than 50 children, while three CHCPs enrolled more than 150 children. Only nine CHCPs enrolled and recorded lung sounds in this study. I purposively selected nine CCs out of 24 CCs in Zakiganj sub-district after reviewing the number of children younger than five years and the number of pneumonia cases that received care during a calendar year prior to the study. For these reasons the performance of CHCPs recording lung sounds in this study may not be generalisable.

9.3.4 Lack of severe pneumonia cases

This study did not enrol severe pneumonia cases because of the unavailability of treatment required for severe pneumonia cases at CCs. Severe pneumonia cases would be expected to have a higher frequency of wheeze and crackles, which in turn can be expected to be identified more easily by paediatric panel members and the CLSA. The agreement between the panel and CLSA therefore could have been higher if this study enrolled severe pneumonia cases. Non-severe disease was targeted in this study as children with severe disease get antibiotics and hospitalisation regardless of their lung sounds. The 'use case' of the digital stethoscope in severe cases is not as straightforward as it is with non-severe cases, many of whom do not have bacterial disease and do not need antibiotics.

9.3.5 Lack of chest radiography

While radiologic imaging is commonly used to diagnose pneumonia (148), children enrolled in this study did not have a chest radiograph obtained. Chest radiography is not routinely available in first-level facilities (e.g., CC) in LMICs, including Bangladesh. Establishing radiography has many challenges besides cost, such as trained human resources and uninterrupted electricity supply. The lack of a gold standard reference for pneumonia is well understood, and it is widely accepted that chest radiography itself is imperfect, lacking overall diagnostic accuracy for pneumonia (146). For example, it has been previously reported that many children with IMCI-defined pneumonia have normal chest radiographs (59) and also normal lung sounds (189). A standardised paediatrician listening panel for lung sound classification served as a reference standard for CLSA in this study. McCollum et al. have shown that lung sound classifications of digital auscultation recordings generated using a listening panel approach strongly correlate with radiographic findings and mortality outcomes (147).

9.3.6 Gold standard for lung sounds classification

Inter-listener reliability was tested, but intra-listener reliability was not tested in this study. Agreement between listeners is important; however, if they cannot interpret the sounds accurately, the device cannot be validated. There is no established reference standard by which to determine the true accuracy of listeners. However, before interpreting any lung sound recordings in this study, all listeners were trained to a standardised set of lung sound recordings similar to the WHO chest X-ray training methodology (190). In the standardisation process, a reference set of sound files classified by a paediatric pulmonologist from Johns Hopkins School of Medicine (Dr Eric McCollum, co-supervisor) served as the reference standard. Listeners were required to classify this set of reference lung sounds to a minimum standard of at least 75% correct before proceeding to interpret study recordings. However, some degree of subjective interpretation may still exist due to the inherent bias that each paediatrician has developed over years of experience in listening to lung sounds. Though the paediatrician's training sound files were recorded in various clinical conditions, the set of recorded sounds used in the standardised process was recorded in a controlled environment and without any background noise. However, the test sound files were recorded in a crowded and noisy environment, so the panel members might be unable to confirm wheeze and crackles in certain recordings.

9.3.7 Technical issues with the prototype digital stethoscope

In this study CHCPs failed to record only eight children's lung sound due to device malfunction. However, this study identified several technical issues with the Feelix Smartscope prototype. These issues included the following: recordings stopping prematurely, recordings failing to stop, inadequate durability of the 3-D printed prototype device material, freezing of the device software during the recording process, and battery charge sometime drained too quickly. Addressing these issues will ensure future versions of the device are more effective and user-friendly. The fact that the digital stethoscope requires charging is a limitation for its use in first-level facilities in some areas in LMICs where the power supply is interrupted, or there is no power supply at all. Providing solar panels and a mobile power bank to charge the stethoscope may solve this issue.

9.4 Implications for future research

The overarching objective of this thesis work was to improve the diagnosis of childhood pneumonia in two main ways: (a) recording lung sounds using the Feelix Smartscope prototype at the first-level facility by frontline workers and (b) evaluating lung sound classification by the CLSA compared to a paediatrician listening panel's classification. This study created several new possible research areas.

The Feelix Smartscope prototype used in this study has several technical limitations we identified and detailed earlier in this thesis. Refining this prototype to address these limitations, based on lessons learned from its use at the first-level facility during this study, should be considered.

In this study, CHCPs demonstrated that they could feasibly record quality lung sounds without substantially increasing their workload. However, these findings were based on a purposively selected cohort of nine CHCPs in nine CCs within one sub-district in all of Bangladesh. A larger study involving a higher number of CCs in different geographic locations with differing patient volumes and CC environments, potentially including different countries in various outpatient clinical settings and contexts, is an important next step in assessing broader feasibility of the device. Our findings suggest also that performance of the CLSA algorithm could be improved by applying stricter interpretability criteria to the recording process, with the likely downside of reducing the usability of the device by CHCPs. Improving the device for better quality recordings, and further improvement of CLSA algorithm, the usability of digital auscultation would benefit from further study.

As noted, the CLSA algorithm achieved moderate sensitivity (61.8%) and specificity (60.7%) in classifying adventitious lung sounds compared to the reference paediatric listening panel. This study is the first to validate automated CLSA in an outpatient setting at a first-level facility by government frontline health workers. This study has laid the foundation for digital auscultation with automatic lung sound classification, which could be enhanced by further research to develop a CLSA model to classify lung sounds more accurately. The current CLSA model developed using the PERCH study data set as training, the CLSA model can be improved by using this study annotated sound files as a training data set.

Given that the IMCI pneumonia criteria relies on a child having fast breathing, if future generations of the digital stethoscope incorporate an automated respiratory rate into the lung sound interpretation algorithm this may also improve the overall performance of diagnosis of childhood pneumonia in

LMICs. This study's findings showed automated CLSA perform better when restricting the analysis of sensitivity and specificity of lung sound classification to IMCI-defined pneumonia cases. Adding automated respiratory rate count technology within the device has the potential to improve the performance of the automated CLSA.

After improving the stethoscope by addressing the issues identified in this study and improving the CLSA algorithm, a validation study is required to conduct. After that, a multi-country clinical trial needs to be conducted to provide evidence for integrating digital auscultation into the IMCI pneumonia management pathway to evaluate patient outcomes after digital stethoscope-based decision-making. An observer-blinded clinical trial could be conducted on children with non-severe disease treated with and without antibiotics based on their lung sounds to assess safety and efficacy of the lung sound system.

Finally, if clinical trial proves adding auscultation findings in IMCI guidelines beneficial, implementation research should be conducted, to evaluate usability, acceptability and cost-effectiveness before planning to scale up this technology at the field level.

9.5 Implications for practice and policy

In LMICs, frontline health workers play a significant role in the primary diagnosis and management of pneumonia. The use of digital technology by frontline health workers in the initial assessment of any illness may help improve early diagnosis in settings lacking diagnostic tools. In different primary healthcare facilities in LMICs, health workers use several digital devices like pulse oximeters and digital blood pressure machines. (191-193). The findings from my study suggest that frontline health workers working at first-level health facilities are capable of feasibly recording quality lung sounds from children using a digital stethoscope. The study results further indicate that the use of antibiotics by frontline health workers may be substantially reduced if a digital stethoscope with an automated interpretation algorithm were implemented as a point-of-care device within the IMCI algorithm, as 42.3% (145/343) of children diagnosed with IMCI pneumonia by the CHCPs had normal lung sounds (no wheeze and no crackles) according to both human listeners and the automated CLSA.

This study generated 3,861 segments of lung sound recordings from 974 children younger than five years in real clinical settings. These sound files have been annotated by the paediatric listening panel and could be used to further refine CLSA model to improve the performance of CLSA to detect adventitious lung sounds, especially given the algorithm has not been trained on lung sound recordings from CHCPs at this level of the health system.

Digital auscultation has the potential to be a respiratory diagnostic tool that is feasible for use in first level facilities in LMICs. This study evaluated the potential impact of digital auscultation at first-level facilities in rural Bangladesh and has the potential to contribute to better childhood pneumonia diagnosis in LMICs. This betterment of childhood pneumonia diagnosis has a linkage with SDG 3.2, which aims to end preventable deaths of newborns and children under five years of age by 2030, with all countries aiming to reduce neonatal mortality to 12 per 1000 live births and under-5 mortality to 25 per 1000 live births (194). After further refining the CLSA model, I recommend, as a next step to conduct either a multi-county clinical trial or several trials in various clinical settings and contexts, which will help advance digital auscultation towards adoption as policy.

Successful use of digital auscultation to record lung sounds at first-level facilities by frontline workers in LMICs will provide researchers with the capability and capacity to conduct more studies on other respiratory issues in resource-poor settings.

Chapter 10 Conclusions

In this thesis, I presented a comprehensive synthesis of evidence through a systematic review, highlighting the detection of adventitious lung sounds using digital auscultation for childhood pneumonia diagnosis. Additionally, I assessed the ability of community health workers (CHCPs) to record interpretable lung sounds using a prototype digital stethoscope from under-five children at first-level community health facilities in Bangladesh. Moreover, I validated an automated computerised lung sound analysis (CLSA) algorithm with reference lung sound classifications produced by a consensus listening panel. I also explored the acceptability of the prototype digital stethoscope among CHCPs and carers of children.

In the systematic review, I found limited evidence of the discriminatory power of digital auscultation for detecting adventitious lung sounds against either reference standard conventional auscultation or acoustic analysis of recorded lung sounds among children with confirmed or suspected pneumonia, including in LMICs. I observed substantial variation in the included studies in terms of study subjects, sample size, and sound classification. The results were primarily limited to overall diagnostic accuracy parameters in classifying lung sounds; disaggregated results by age and target conditions were not provided. This is potentially important as lung sounds are likely to vary according to lower respiratory infection aetiology and age. There were also variations in the framework and terminology used for lung sound classifications, e.g., adventitious vs normal, wheeze vs crackles vs normal, wheeze vs crackles vs both vs normal etc. These evidence gaps and limitations were important findings of this review, highlighting the need for standardised reporting of study findings. Therefore, I recommend that future studies in digital auscultation and CLSA should follow a minimum set of reporting guidelines that should include disaggregated reporting estimates by standard age bands (0-1 months, 2-11 months, 12-59 months), sex, pneumonia classification (e.g., radiographic pneumonia, severe pneumonia, fast breathing pneumonia, chest in-drawing pneumonia), anatomical site of recording, specification of the digital stethoscope, facility type (hospital, health centre), settings (inpatient, emergency, outpatient and community), provider type (doctors, nurses, paramedics, community health workers), etc. Future investigations should also consider conducting the studies in more generalisable, noisy clinical settings typical of LMICs rather than in a controlled laboratory or clinical environments to broaden the usability of the automated applications.

One of the key areas of focus for this thesis was to evaluate the ability of CHCPs to record quality lung sounds from children at first-level facilities in Bangladesh. I developed an SOP for CHCPs to record lung sounds using a prototype digital stethoscope (Feelix Smartscope), considering the challenges of recording lung sounds at the first-level facilities, e.g., the providers are not trained in auscultation, children younger than five years are active, sometimes agitated, and not necessarily cooperative, and the environment at the facilities may be noisy due to the crying of children, ringing of phones, chattering of people, whirring of fans and loudspeaker sounds from outside the clinics.

Despite these challenges, my analysis demonstrated that CHCPs recorded quality lung sounds from children without increasing their workload. However, the purposive selection of high-volume CCs with well-trained CHCPs by a non-random sampling technique potentially limits the generalisability of the results.

Another focus of this thesis was to assess the diagnostic accuracy of an automated CLSA to identify adventitious lung sounds compared to reference classifications produced by a paediatrician listening panel. The study results suggest that the automated CLSA had moderate sensitivity (61.8%; 95% CI: 55.7%, 67.6%) and moderate specificity (60.7%; 95% CI: 56.6%, 64.6%) for classifying lung sounds as adventitious or normal compared to the consensus listening panel. The agreement between panel classifications and CLSA was low. The automated CLSA performed better in identifying adventitious or normal lung sounds when the analysis was restricted to children meeting IMCI-defined pneumonia criteria than in all children with cough or difficulty breathing. The thesis results also showed that two out of five children who were identified as IMCI-defined pneumonia by CHCPs had normal lung sounds by both the automated CLSA and paediatrician listening panel, suggesting that these children did not have pneumonia and were unlikely to need antibiotic treatment.

The thesis demonstrates that while quality lung sound recordings can be achieved by frontline health workers in busy primary care clinics, there is a need for further refinement of the automated CLSA as well as the recording procedure itself to further optimise interpretability and sound recording quality.

The lung sound recordings generated from this study can be used in further research to improve the automated CLSA. The current CLSA model can be improved if the algorithm can be refined to further identify and exclude contaminating artefacts. After enhancing the performance of automated CLSA, a clinical trial in various settings and contexts is required.

Chapter 11 References

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Chapter 12 Scientific contributions and outputs

12.1 Publications

I published 62 papers in international peer-reviewed journals during the course of my PhD (Table 12.1). Three of them were based on my PhD thesis, and I was the first author of two articles and the senior author of one article. In addition, I published two papers as a first author and 57 papers as a co-author on different topics not directly related to PhD thesis during this period.

Table 12.1 Published articles in peer review journals during the PhD period

PhD thesis		
First author	1.	**Ahmed S**, Sultana S, Khan AM, Islam MS, Habib GM, McLane IM, **McCollum ED**, **Baqui AH**, **Cunningham S**, **Nair H**. Digital auscultation as a diagnostic aid to detect childhood pneumonia: A systematic review. J Glob Health. 2022 Apr 23;12:04033. doi: 10.7189/jogh.12.04033. PMID: 35493777; PMCID: PMC9024283. URL: https://jogh.org/2022/jogh-12-04033
	2.	**Ahmed S**, Mitra DK, **Nair H**, **Cunningham S**, Khan AM, Islam AA, McLane IM, Chowdhury NH, Begum N, Shahidullah M, Islam MS, Norrie J, Campbell H, Sheikh A,

		Baqui AH, **McCollum ED**. Digital auscultation as a novel childhood pneumonia diagnostic tool for community clinics in Sylhet, Bangladesh: protocol for a cross-sectional study. BMJ Open. 2022 Feb 9;12(2):e059630. doi: 10.1136/bmjopen-2021-059630. PMID: 35140164; PMCID: PMC8830242. URL: *https://bmjopen.bmj.com/content/12/2/e059630.abstract*
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12.2 Meeting and conference

I attended the 12th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD-12) in Toronto, Canada, in June 2022 and made an oral presentation on “Evaluation of machine learning to detect adventitious lung sounds using digital auscultation to aid childhood pneumonia diagnosis”. I got the Young Investigator Award in this symposium.

I virtually presented "Evaluating whether community health workers can successfully record lung sounds from children in Bangladesh using a digital stethoscope" in the 40th Annual Meeting of the European Society for Paediatric Infectious Diseases in Athens, Greece, in May 2022.

In the RESPIRE Annual Scientific Meeting (ASM) in November 2020 and September 2019, I made oral presentation on "Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh".

I attended the 38th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID) from October 26th to 29th 2020 and the sixth Global Symposium on Health Systems Research in November 2020, where I presented the study methods and preliminary study findings of "Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh".

I attended the Health System Global Workshop in Delhi, India in October 2019, and presented the study methods and preliminary study findings on "Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh."

Additionally, I submitted two abstracts and were accepted for oral presentation. However, I could not attend the conferences due to the Covid-19 situation:

- 38th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Rotterdam, the Netherlands, 26-29 October 2020.

ERS International Congress 2020: I have submitted one abstract and accepted for a poster presentation.

- 6th Global Symposium on Health System Research, Dubai: I submitted one abstract.

I made an oral presentation of my PhD study protocol at Respiratory Viral Epidemiology Group (RVEG) meeting on 27 September 2018 and a poster presentation at the Global Health Symposium in UoE (03 September 2018) and at the Edinburgh World Pneumonia Day Symposium in12 November 2018.

Chapter 13 Annexures

13.1 Supplementary materials

13.1.1 Chapter 3

Supplementary table 13.1 Search strategies for databases

A. Name of the database: Ovid MEDLINE(R) 1946 to October Week 5 2021 Search date: 27 October 2021		
1	exp pneumonia/ or exp respiratory tract infections/	487441
2	(pneumon* or bronchpneumon* or pleuropneumon*).tw.	185517
3	(lower respiratory tract infection* or lower respiratory infection* or lrti).tw.	7651
4	("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter$ or pneumonitis or "pulmonary inflammation" or "lung inflammation").ti,ab.	109801
5	Or/1-4	672032
6	Respiratory Sounds/ or pulmonary sound*.mp. or respiratory sound*.mp.	9663
7	(analy* or detect* or auscultation).mp.	8821403
8	Auscultation/ or computer* auscultation.mp. or exp Signal Processing, Computer Assisted/ or exp Diagnosis, Computer-Assisted/ or Sound Spectrography/	155871
9	6 and (7 or 8)	3775
10	((digital* or electronic* or automat* or computer*) adj3 auscultation).tw.	138
11	((lung or respiratory or breath or pulmonary) adj3 sound* adj3 (analy* or detect* or auscultation)).mp.	446
12	Or/9-11	3988
13	((crackle* or wheez*) adj3 (detect* or analy* or auscultation)).tw.	459

14	(5 and 12) or 13	1211
15	limit 14 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)")	606
B. Name of the database: Embase 1974 to 2021 Week 05 Search date: 27 October 2021		
1	exp pneumonia/	336217
2	respiratory tract infections.mp. or exp respiratory tract infection/	427829
3	(pneumon* or bronchpneumon* or pleuropneumon*).tw.	284528
4	(lower respiratory tract infection* or lower respiratory infection* or lrti).tw.	12413
5	("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter$ or pneumonitis or "pulmonary inflammation" or "lung inflammation").ti,ab.	157595
6	Or/1-5	825633
7	exp abnormal respiratory sound/ or exp wheezing/ or pulmonary sound.mp.	66116
8	auscultation.mp. or auscultation/ or exp lung auscultation/	17687
9	7 and 8	4092
10	((digital* or electronic* or automat* or computer*) adj3 auscultation).tw.	193
11	((lung or respiratory or breath or pulmonary) adj3 sound* adj3 (analy*or detect* or auscultation)).mp.	817
12	or/9-11	4722
13	((crackle* or wheez*) adj3 (detect* or analy* or auscultation)).tw.	1087
14	(6 and 12) or 13	2538
15	exp Child/ or Child*.tw.	3130174
16	exp Infant/ or Infant*.tw.	1135822

17	(paediatric* or pediatric* or toddler* or preschool*).tw.	641319
18	(infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).tw.	1048785
19	Or/15-18	3616232
20	14 and 19	834
C. Name of database: Global Health 1973 to 2021 Week 05 Search date: 27 October 2021		
1	pneumonia.mp. or exp pneumonia/	33494
2	exp lower respiratory tract infections/	10421
3	respiratory tract infections.mp.	9965
4	(pneumon* or bronchpneumon* or pleuropneumon*).tw.	58307
5	(lower respiratory tract infection* or lower respiratory infection* or lrti).tw.	5491
6	("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter$ or pneumonitis or "pulmonary inflammation" or "lung inflammation").ti,ab.	40785
7	or/1-6	100801
8	clinical examination/ or exp auscultation/	1624
9	((digital* or electronic* or automat* or computer*) adj3 auscultation).tw.	10
10	((lung or respiratory or breath or pulmonary) adj3 sound* adj3 analy*).mp.	16
11	or/8-10	1643
12	((crackle* or wheez*) adj3 (detect* or analy* or auscultation)).tw.	109
13	(7 and 11) or 12	188
14	child*.tw.	311973
15	Infant*.tw	100996
16	(paediatric* or pediatric* or toddler* or preschool*).tw.	62596

17	(infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).tw.	139379
18	or/14-17	394714
19	13 and 18	102
D. Name of database: CINAHL Plus **Search date: 27 October 2021**		
S1	(MH "Respiratory Tract Infections+")	89808
S2	(MH "Respiratory Syncytial Virus Infections")	2062
S3	TX LRTI	402
S4	S1 OR S2 OR S3	91122
S5	(MH "Signs and Symptoms, Respiratory+") OR (MH "Respiratory Sounds+")	32730
S6	TX respiratory sound	3995
S7	TX respiratory sound* OR TX pulmonary sound* OR TX lung sound* OR TX breath sound*	5258
S8	S5 OR S6 OR S7	34952
S9	(MH "Sound Spectrography")	794
S10	TX (analy* or detect* or auscultation)	2042380
S11	S9 OR S10	2042670
S12	S8 AND S11	10691
S13	TX auscultation N15 (digital* or electronic* or automat* or computer*)	127
S14	TX sound* N15 (analy* or detect* or auscultation) N15 (lung or respiratory or breath or pulmonary)	205
S15	S12 OR S13 OR S14	10786
S16	S4 AND S15	921
S17	TX (detect* or analy* or auscultation) N15 ((crackle* or wheez*)	479
S18	S16 OR S17	1332
S19	(MH "Child, Preschool") OR "children"	487369
S20	(MH "Infant+") OR "infant"	301860

S21	(MH "Infant, Newborn+") OR "neonate"	151306
S22	TX (paediatric* or pediatric* or toddler* or preschool*)	659202
S23	TX (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*)	588491
S24	S19 OR S20 OR S21 OR S22 OR S23	1048783
S25	S18 AND S24	142
E. Name of database: Scopus **Search date: 27 October 2021**		
1	(((ALL(respiratory tract infection)) OR (ALL(lower respiratory infection)) OR (ALL(lrti)) OR (ALL(pneumon* OR bronchpneumon* OR pleuropneumon*)) OR (TITLE-ABS-KEY("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter$ or pneumonitis or "pulmonary inflammation" or "lung inflammation"))) AND ((ALL(auscultation W/15 digital* OR electronic* OR automat* OR computer*)) OR (ALL(analy* W/15 "respiratory sound" OR "pulmonary sound" OR "lung sound" OR "breath sound")))) OR (ALL((detect* OR analy* OR auscultation) W/3 (crackle* OR wheez*)))) AND ((TITLE-ABS-KEY(paediatric* OR pediatric* OR toddler* OR preschool*)) OR (TITLE-ABS-KEY(child* OR infant*)) OR (TITLE-ABS-KEY(infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*)))	1345
F. Name of database: Web of science **<u>Web of Science Core Collection</u>** (1900-present): (Science Citation Index Expanded: 1900-present; Scocial Science Citation Index: 1900-present; Emerging Sources Citation Index: 2015-present) **Search date: 27 October 2021**		
1	TOPIC: (lower respiratory infection)	33453
2	TOPIC: (respiratory tract infection)	43076

3	TOPIC: (pneumon* OR bronchpneumon* OR pleuropneumon*)	246000
4	TOPIC: ("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter$ or pneumonitis or "pulmonary inflammation" or "lung inflammation")	141884
5	#4 OR #3 OR #2 OR #1	393725
6	TOPIC: ((lung or respiratory or breath or pulmonary) sound*)	6160
7	TOPIC: (analy* OR detect* OR auscultation)	16,924,176
8	#7 AND #6	3235
9	TOPIC: ((digital* or electronic* or automat* or computer*) NEAR/3 auscultation)	274
10	#9 OR #8	3415
11	#10 AND #5	338
12	TOPIC: ((crackle* OR wheez*) NEAR/3 (detect* OR analy* OR auscultation))	652
13	#12 OR #11	957
14	TOPIC: (child* OR infant*)	2383,798
15	TOPIC: (paediatric* or pediatric* or toddler* or preschool*)	532166
16	TOPIC: (newborn* OR baby* OR babies OR neonat* OR preterm* OR prematur*)	665218
17	#16 OR #15 OR #14	2993355
18	#17 AND #13	398
G. Name of database: IEEEXplore **Search date: 27 October 2021**		
1	((crackle* OR wheez* OR lung sound OR respiratory sound OR breath sound OR pulmonary sound) NEAR/3	338

	(detect* OR analy* OR auscultation OR digital OR electronic OR automated OR computer*))	
H. Name of database: Clinicaltrial.gov **Search date: 27 October 2021**		
1	(lung sound OR respiratory sound OR pulmonary sound OR breath sound OR crackle OR wheeze) AND (detect OR analysis OR diagnose OR auscultation OR digital OR electronic OR automated OR computer)	33

Supplementary table 13.2 Excluded studies with reasons for exclusion

Sl	Author, Year	Title	Reason for exclusion
1	Scrafford et al., 2016	Evaluation of digital auscultation to diagnose pneumonia in children 2 to 35 months of age in a clinical setting in Kathmandu, Nepal: a prospective case-control study	Reference test not used
2	Abeyratne, Swarnkar, Triasih, & Setyati, 2013	Cough sound analysis - a new tool for diagnosing pneumonia	Index test not used
3	Ellington et al., 2012	Computerised lung sound analysis to improve the specificity of paediatric pneumonia diagnosis in resource-poor settings: protocol and methods for an observational study	Study protocol
4	Elphick et al., 2004	Validity and reliability of acoustic analysis of respiratory sounds in infants	Results could not be stratified by disease condition
5	Fischer et al., 2016	Relationship Between Computerised Wheeze Detection and Lung Function Parameters in Young Infants	Index test not used
6	Furman, Malinin, Furman, &	Computer-Assisted Assay of respiratory sounds of Children suffering from Bronchial Asthma	Target condition not matched

Sl	Author, Year	Title	Reason for exclusion
	Sokolovsky, 2014		
7	Gross et al., 2007	Mobile nocturnal long-term monitoring of wheezing and cough	Results could not be stratified by disease condition
8	Guntupalli, Alapat, Bandi, & Kushnir, 2008	Validation of Automatic Wheeze Detection in Patients with Obstructed Airways and in Healthy Subjects	Study population and target condition not matched
9	Haider, Joseph, & Periyasamy, 2017	An investigation on the statistical significance of spectral signatures of lung sounds	Reference test not used
10	Lozano, Fiz, & Jané, 2016	Automatic Differentiation of Normal and Continuous Adventitious Respiratory Sounds Using Ensemble Empirical Mode Decomposition and Instantaneous Frequency	Reference test not used
11	Kang, Karpate, Almulla, Teach, & Shekhar, 2016	Automatic Identification of Wheezing in Auscultated Lung Sounds	Conference abstract
12	Kosasih, Abeyratne, Swarnkar, & Triasih, 2015	Wavelet Augmented Cough Analysis for Rapid Childhood Pneumonia Diagnosis	Index test not used

Sl	Author, Year	Title	Reason for exclusion
13	Julian et al., 2017	Automatic crackle detection in children with pneumonia	Conference abstract
14	Lovrenski, 2016	Stethoscope vs. ultrasound probe - which is more reliable in children with suspected pneumonia?	Index test not used
15	McCollum et al., 2017	Listening panel agreement and characteristics of lung sounds digitally recorded from children aged 1–59 months enrolled in the Pneumonia Etiology Research for Child Health(PERCH) case–control study	Index test not used
16	Emmanouilidou et al., 2017	Digitally Recorded Lung Sounds And Mortality Among Children 1-59 Months Old With Pneumonia In The Pneumonia Etiology Research For Child Health Study	Index test not used
17	Oletic & Bilas, 2018	Asthmatic Wheeze Detection From Compressively Sensed Respiratory Sound Spectra	Target condition not matched
18	Pasterkamp, Wiebicke, & Fenton, 1987	Subjective assessment vs computer analysis of wheezing in asthma	Target condition not matched
19	Pingale & Patil, 2017	Analysis of Cough Sound for Pneumonia Detection Using Wavelet Transform and Statistical Parameters	Lung sounds were not used

Sl	**Author, Year**	**Title**	**Reason for exclusion**
20	Prodhan et al., 2008	Wheeze Detection in the Pediatric Intensive Care Unit: Comparison Among Physician, Nurses, Respiratory Therapists, and a Computerised Respiratory Sound Monitor	Results could not be stratified by disease condition
21	Puder et al., 2014	Validation of computerised wheeze detection in young infants during the first months of life	Target condition not matched
22	(Puder, Wilitzki, Bührer, Fischer, & Schmalisch, 2016)	Computerised wheeze detection in young infants: comparison of signals from tracheal and chest wall sensors	Target condition not matched
23	Qiu, Whittaker, Lucas, & Anderson, 2005	Automatic wheeze detection based on auditory modelling	Unclear subjects' age and target condition
24	Song, 2015	Diagnosis of Pneumonia From Sounds Collected Using Low Cost Cell Phones	Reference test not used
25	Ahmed, McCollum, Nair, Cunningham, & Baqui, 2020	Community use of digital auscultation to improve diagnosis of childhood pneumonia in low resource setting	Conference abstract
26	Dramburg, Dellbrügger, van Aalderen, & Matricardi, 2021	The impact of a digital wheeze detector on parental disease management of pre-school children suffering from wheezing—a pilot study	Target condition not matched

Sl	Author, Year	Title	Reason for exclusion
27	Rennoll, McLane, Emmanouilidou, West, & Elhilali, 2021	Electronic Stethoscope Filtering Mimics the Perceived Sound Characteristics of Acoustic Stethoscope	Index test not used
28	Ferreira-Cardoso et al., 2021	Lung auscultation using the smartphone—feasibility study in real-world clinical practice	Index test not used
29	Bertrand, Segall, Sánchez, & Bertrand, 2020	Lung auscultation in the 21th century	Review article
30	Habukawa et al., 2021	Wheeze recognition algorithm for remote medical care device in children: Validation study	Target condition not matched
31	Khan, Badashah, & Mudda, 2019	Preliminary detection of lung diseases in pediatric population using soft computing	Reference test not used; unclear subject's disease condition
32	Kotb et al., 2020	The machine learned stethoscope provides accurate operator independent diagnosis of chest disease	Reference test not used
33	Ramanathan et al., 2019	Digital stethoscopes in paediatric medicine	Review article
34	Rocha et al., 2019	An open access database for the evaluation of respiratory sound classification algorithms	Index test not used

Sl	Author, Year	Title	Reason for exclusion
35	Khan, Jawarkar, & Ahmed, 2012	Cell phone based Remote Early Detection of Respiratory Disorders for Rural Children using Modified Stethoscope	Target condition not matched
36	Murphy et al., 2004	Automated lung sound analysis in patients with pneumonia	Reference test was not used

Supplementary table 13.3 Data extraction form

Reviewer		
Date form completed		
A. Study details		
Study ID		
Title		
Author		
Year Published		
Journal		
Location (country/city)		
B. Study design/method		
Type of study	Randomised controlled trial……………☐ Cross-sectional study……………………☐ Other …………………………………	
Study Setting	Hospital:…..……………………………..☐ Community:…………….………………☐ Other: ……………………………………..	
Study period		
Sampling method		
Sample size		
C. Population characteristics		
Target condition	Pneumonia:…………………………...……☐ ALRI:...……………………………………..☐ Asthma………………………….……….☐ Other: ……………………………………	
Enrolment Eligibility A. inclusion Criteria		

B. Exclusion Criteria		
Case definition		
Total number enrolled		
Age range (mean/median age)		
Gender (% female)		
Total number included in the analysis		
Notes		
D. Index test/s		
Recording device		
Brand of stethoscope		
Detail description of the index test/s		
Sound analysis software/technology used		
Lung sound classified (crackles, wheezes, pleural rub etc.)		
Notes		
E. Reference test		
Type of acoustic analysis	Conventional auscultation ………….◻ Analysis of recorded lung sounds…..◻	
Brand of stethoscope/recording device		
Detail description of reference test		

Lung sound classified (crackles, wheezes, pleural rub etc.)		
Notes		
F. Study findings		
True positive		
False positive		
False negative		
True negative		
Sensitivity (95% CI)		
Specificity (95% CI)		
Positive predictive value (95% CI)		
Negative predictive value (95% CI)		
Accuracy (95% CI)		
Kappa value		
Notes		

13.1.2 Chapter 4

13.1.2.1 Operational definition of any pneumonia

No pneumonia	***Pneumonia***	***Severe pneumonia***
Cough and/or difficulty breathing ***AND***	Cough and/or difficulty breathing ***AND***	Cough and/or difficulty breathing ***AND***
Respiratory Rate < 50 breaths / minutes (2 – 11 months) Respiratory Rate < 40 breaths / minutes (12 – 59 months) ***AND***	Respiratory Rate ≥ 50 breaths / minutes (2 – 11 months) Respiratory Rate ≥ 40 breaths / minutes (12 – 59 months) ***AND / OR***	Respiratory Rate ≥ 50 breaths / minutes (2 – 11 months) Respiratory Rate ≥ 40 breaths / minutes (12 – 59 months) ***AND / OR***
No chest indrawing ***AND***	Chest indrawing ***AND***	Chest indrawing ***AND***
No danger sign ***AND***	No danger sign ***AND / OR***	Any respiratory destress sign (Stridor OR Grunting OR Head nodding OR Tracheal tugging OR Nasal flaring OR Intercostal retractions)

In this thesis, “any pneumonia” is defined if a child had either “pneumonia” or “severe pneumonia”.

13.1.3 Chapter 6

Supplementary table 13.4 Characteristics of children with interpretable lung sound recordings in ≤ 2 vs ≥ 3 chest positions

Characteristics	**Interpretable recordings in ≤ 2 chest positions (n=64)**	**Interpretable recordings in ≥ 3 chest positions (n=867)**	**P-value**	**OR (95% CI)**	**P-value**	**AOR (95% CI)**	**P-value**
Age group							
2-11 months	22 (34.4)	205 (23.6)	0.05	Ref		Ref	
12-59 months	42 (65.6)	662 (76.4)		1.7 (1.0 - 2.9)	0.06	1.6 (0.9-2.9)	0.12
Sex							
Male	43 (67.2)	472 (54.4)	<0.05	0.6 (0.3 - 1.0)	<0.06	0.6 (0.3-1.0)	0.06
Female	21 (32.8)	395 (45.6)		Ref		Ref	
Oxygen saturation							
SpO_2 90% - 93%	4 (6.3)	28 (3.2)	0.20	0.5 (0.2 - 1.5)	0.21		
SpO_2 94% - 100%	60 (93.8)	839 (96.8)		Ref			
Fever (≥100.4°F)							
Yes	5 (7.8)	69 (8.0)	0.97	Ref			
No	59 (92.2)	798 (92.0)		1.0 (0.4 - 2.5)	0.97		

Characteristics	Interpretable recordings in ≤ 2 chest positions (n=64)	Interpretable recordings in ≥ 3 chest positions (n=867)	P-value	OR (95% CI)	P-value	AOR (95% CI)	P-value
Underweight (weight for age)							
Normal (Z Score≥-2)	47 (73.4)	545 (62.9)	0.17	Ref		Ref	
Mild underweight (-3≤ Z Score <-2)	10 (15.6)	225 (26.0)		1.9 (0.9 – 4.2)	0.10		
Severe underweight (Z Score<-3)	7 (10.9)	97 (11.2)		1.2 (0.5 – 2.72)	0.60		
Stunting (height for age)							
Normal (Z Score≥-2)	39 (60.9)	460 (53.1)	0.33	Ref		Ref	
Mild stunting (-3≤ Z Score <-2)	18 (28.1)	256 (29.5)		1.2 (0.7 - 2.2)	0.53	1.7 (0.8-3.8)	0.19
Severe stunting (Z Score<-3)	7 (10.9)	151 (17.4)		1.8 (0.8 - 4.2)	0.16	1.0 (0.4-2.5)	0.92

Characteristics	Interpretable recordings in ≤ 2 chest positions (n=64)	Interpretable recordings in ≥ 3 chest positions (n=867)	P-value	OR (95% CI)	P-value	AOR (95% CI)	P-value
Wasting (weight for height)							
Normal (Z Score≥-2)	51 (79.7)	723 (83.4)	0.27	Ref			
Mild wasting (-3≤ Z Score <-2)	12 (18.8)	110 (12.7)		0.7 (0.3 - 1.3)	0.21		
Severe wasting (Z Score<-3)	1 (1.6)	34 (3.9)		2.4 (0.3 – 18.1)	0.40		
Pneumonia category							
No pneumonia	41 (64.1)	524 (60.4)	0.57	0.9 (0.5 - 1.4)	0.56		
Pneumonia	23 (35.9)	343 (39.6)		Ref			
Any respiratory danger sign							
No	59 (92.2)	828 (95.5)	0.23	1.8 (0.7 - 4.7)	0.23		
Yes	5 (7.8)	39 (4.5)		Ref			

Characteristics	Interpretable recordings in ≤ 2 chest positions (n=64)	Interpretable recordings in ≥ 3 chest positions (n=867)	P-value	OR (95% CI)	P-value	AOR (95% CI)	P-value
Abnormal lung sound by paediatrician							
No	42 (65.6)	595 (68.6)	0.62	Ref			
Yes	22 (34.4)	272 (31.4)		0.9 (0.5 - 1.5)	0.61		

Supplementary table 13.5 Distribution of children's at least one chest position's sound recorded, transferred to laptop and interpretable

Code of the CHCP	Children enrolled N	≥ 1 chest position's lung sound recorded % [n]	≥ 1 chest position's lung sound transferred to laptop % [n]	≥ 1 chest position was interpretable by paediatric listening panel % [n]
CHCP 1	38	97.4 [37]	97.4 [37]	92.1 [35]
CHCP 2	142	98.6 [140]	97.9 [139]	95.8 [136]
CHCP 3	130	100.0 [130]	100.0 [130]	95.4 [124]
CHCP 4	159	100.0 [159]	99.4 [158]	92.5 [147]
CHCP 5	86	95.3 [82]	94.2 [81]	86.0 [74]
CHCP 6	26	100.0 [26]	100.0 [26]	92.3 [24]
CHCP 7	179	98.9 [177]	97.8 [175]	95.0 [170]
CHCP 8	43	97.7 [42]	97.7 [42]	95.3 [41]
CHCP 9	187	100.0 [187]	99.5 [186]	96.3 [180]
Total	**990**	**99.0 [980]**	**98.4 [974]**	**94.1 [931]**

13.1.4 Chapter 7

13.1.4.1 Comparison of four CLSA models among all children

Supplementary table 13.6 Evaluation of model A of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel

		Consensus listening panel		Total
		Adventitious	**Normal**	
Model A	**Adventitious**	142	203	345
	Normal	130	392	522
	Total	272	595	867

Supplementary table 13.7 Evaluation of model B of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel

		Consensus listening panel		Total
		Adventitious	**Normal**	
Model B	**Adventitious**	108	133	241
	Normal	164	462	626
	Total	272	595	867

Supplementary table 13.8 Evaluation of model C of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel

		Consensus listening panel		Total
		Adventitious	**Normal**	
Model C	**Adventitious**	168	234	402
	Normal	104	361	465
	Total	272	595	867

Supplementary table 13.9 Evaluation of model D of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel

		Consensus listening panel		Total
		Adventitious	**Normal**	
Model D	**Adventitious**	154	225	379
	Normal	118	370	488
	Total	272	595	867

13.1.4.2 Comparison of four CLSA models among IMCI-defined pneumonia children:

Supplementary table 13.10 Evaluation of model A of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model A	**Adventitious**	64	67	131
	Normal	62	150	212
	Total	126	217	343

Supplementary table 13.11 Evaluation of model B of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model B	**Adventitious**	59	40	99
	Normal	67	177	244
	Total	126	217	343

Supplementary table 13.12 Evaluation of model C of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model C	**Adventitious**	80	72	152
	Normal	46	145	191
	Total	126	217	343

Supplementary table 13.13 Evaluation of model D of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model D	**Adventitious**	72	72	144
	Normal	54	145	199
	Total	126	217	343

13.1.4.3 Comparison of four CLSA models among IMCI-defined pneumonia children and paediatric listening panel members were confident:

Supplementary table 13.14 Evaluation of model A of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia and paediatrician was confident during classification

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model A	**Adventitious**	50	67	117
	Normal	36	150	186
	Total	86	217	303

Supplementary table 13.15 Evaluation of model B of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia and paediatrician was confident during classification

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model B	**Adventitious**	48	40	88
	Normal	38	177	215
	Total	86	217	303

Supplementary table 13.16 Evaluation of model C of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia and paediatrician was confident during classification

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model C	**Adventitious**	60	72	132
	Normal	26	145	171
	Total	86	217	303

Supplementary table 13.17 Evaluation of model D of CLSA to detect adventitious and normal lung sounds compared to the consensus listening panel among under-5 children with IMCI-defined pneumonia and paediatrician was confident during classification

		Consensus listening panel		**Total**
		Adventitious	**Normal**	
Model D	**Adventitious**	58	72	130
	Normal	28	145	173
	Total	86	217	303

13.1.4.4 Evaluation of CLSA to detect wheeze compared to the listening panel

Supplementary table 13.18 Distribution of the number of wheeze (wheeze/both wheeze and crackles) and non-wheeze lung sounds diagnosed by the CLSA and the consensus listening panel among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Wheeze	**Non-wheeze**	**Total**
Computerised lung sounds analysis	**Wheeze**	109	193	302
	Non-wheeze	87	478	565
	Total	196	671	867

Supplementary table 13.19 Distribution of the number of wheeze (wheeze/both wheeze and crackles) and non-wheeze lung sounds diagnosed by the CLSA and the consensus listening panel among under-5 children with IMCI-defined pneumonia

		The consensus listening panel (Gold standard)		
		Wheeze	**Non-wheeze**	**Total**
Computerised lung sounds analysis	**Wheeze**	55	70	125
	Non-wheeze	37	181	218
	Total	92	251	343

Supplementary table 13.20 Distribution of the number of wheeze (wheeze/both wheeze and crackles) and non-wheeze lung sounds diagnosed by the CLSA and the consensus listening panel among under-5 children with IMCI-defined pneumonia and listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Wheeze	**Non-wheeze**	**Total**
Computerised lung sounds analysis	**Wheeze**	44	64	108
	Non-wheeze	20	175	195
	Total	64	239	303

13.1.4.5 Evaluation of CLSA to detect crackles compared to the listening panel

Supplementary table 13.21 Distribution of the number of crackles (crackles only/both wheeze and crackles) and non-crackles diagnosed by the CLSA and the consensus listening panel among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Crackles	**Non-crackles**	**Total**
Computerised lung sounds analysis	**Crackles**	59	161	220
	Non-crackles	101	546	647
	Total	160	707	867

Supplementary table 13.22 Distribution of the number of crackles (crackles only /both wheeze and crackles) and Non-crackles diagnosed by the CLSA and the consensus listening panel among under-5 children with IMCI-defined pneumonia

		The consensus listening panel (Gold standard)		
		Crackles	**Non-crackles**	**Total**
Computerised lung sounds analysis	**Crackles**	26	47	73
	Non-crackles	47	223	270
	Total	73	270	343

Supplementary table 13.23 Distribution of the number of crackles (crackles only/both wheeze and crackles) and Non-crackles diagnosed by the CLSA and the consensus listening panel among under-5 children with IMCI-defined pneumonia and listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Crackles	**Non-crackles**	**Total**
Computerised lung sounds analysis	**Crackles**	21	43	64
	Non-crackles	34	205	239
	Total	55	248	303

13.1.4.6 Evaluation of CLSA to detect adventitious lung sounds by chest position compared to listening panel among all children with interpretable lung sound recording in ≥ 3 chest positions

Supplementary table 13.24 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-1 (left back) among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	48	98	146
	Normal sounds	100	650	750
	Total	148	748	896

Supplementary table 13.25 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-2 (right back) among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	49	90	139
	Normal sounds	112	635	747
	Total	161	725	886

Supplementary table 13.26 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-3 (left front) among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	52	105	157
	Normal sounds	108	580	688
	Total	160	685	845

Supplementary table 13.27 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-4 (right front) among all enrolled under-5 children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	75	112	187
	Normal sounds	86	572	658
	Total	161	684	845

13.1.4.7 Evaluation of CLSA to detect adventitious lung sounds by chest position compared to the listening panel among children with IMCI defined pneumonia and having ≥ 3 interpretable chest positions

Supplementary table 13.28 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-1 (left back) among IMCI-defined pneumonia children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	31	38	69
	Normal sounds	41	242	283
	Total	72	280	352

Supplementary table 13.29 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-2 (right back) among IMCI-defined pneumonia children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	30	25	55
	Normal sounds	47	247	294
	Total	77	272	349

Supplementary table 13.30 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-3 (left front) among IMCI-defined pneumonia children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	25	39	64
	Normal sounds	47	227	274
	Total	72	266	338

Supplementary table 13.31 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-4 (right front) among IMCI-defined pneumonia children

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	36	34	70
	Normal sounds	40	223	263
	Total	76	257	333

13.1.4.8 Evaluation of CLSA to detect adventitious lung sounds by chest position compared to the listening panel among children with IMCI-defined pneumonia and listening panel members were confident during classification with interpretable lung sound recordings in ≥ 3 chest positions

Supplementary table 13.32 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-1 (left back) among IMCI-defined pneumonia children and the listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	25	38	63
	Normal sounds	23	242	265
	Total	48	280	328

Supplementary table 13.33 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-2 (right back) among IMCI-defined pneumonia children and the listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	25	25	50
	Normal sounds	31	246	277
	Total	56	271	327

Supplementary table 13.34 Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-3 (left front) among IMCI-defined pneumonia children and the listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	18	39	57
	Normal sounds	23	226	249
	Total	41	265	306

Supplementary table 13.35: Distribution of adventitious and normal sound classification by CLSA and the consensus listening panel members in chest position-4 (right front) among IMCI-defined pneumonia children and the listening panel members were confident during classification

		The consensus listening panel (Gold standard)		
		Adventitious sounds	**Normal sounds**	**Total**
Computerised lung sounds analysis	**Adventitious sounds**	29	34	63
	Normal sounds	27	222	249
	Total	56	256	312

13.1.4.9 Distribution of lung sounds classification by the listening panel and CLSA among IMCI-defined pneumonia children

Supplementary table 13.36: Distribution of lung sounds classification by the listening panel and CLSA among IMCI-defined pneumonia children

Classification of sound files	Listening panel's classification			Computerised lung sound classification (CLSA)		
	Any pneumonia %, (95% CI); [n]	**No pneumonia %, (95% CI); [n]**	**P- value**	**Any pneumonia %, (95% CI); [n]**	**No pneumonia %, (95% CI); [n]**	**P-value**
No wheeze and no crackle	217 (63.3)	378 (72.1)	<0.05	191 (55.7)	274 (52.3)	0.33
Wheeze only	53 (15.4)	59 (11.3)	0.07	79 (23.0)	103 (19.7)	0.23
Crackles only	34 (9.9)	42 (8.0)	0.33	27 (7.9)	73 (13.9)	<0.05
Both wheeze and crackles	39 (11.4)	45 (8.6)	0.18	46 (13.4)	74 (14.1)	0.77
Any wheeze	92 (26.8)	104 (19.8)	<0.05	125 (36.4)	177 (33.8)	0.42
Any crackles	73 (21.3)	87 (16.6)	0.08	73 (21.3)	147 (28.1)	<0.05
Adventitious sound	126 (36.7)	146 (27.9)	<0.05	152 (44.3)	250 (47.7)	0.33
Normal	217 (63.3)	378 (72.1)	<0.05	191 (55.7)	274 (52.3)	0.33

13.2 Overview of the prototype Feelix Smartscope

The prototype Feelix Smartscope is a first-of-its-kind digital stethoscope developed at Johns Hopkins University and Sonavi Labs, which detects abnormal lung sounds to more accurately diagnose respiratory conditions in young children. It was designed to be used in non-traditional clinical settings, such as rural or walk-in clinics, at home, or in low-resource areas, by trained or untrained personnel. Feelix Smartscope prototype is equipped with advanced onboard and real-time algorithms that (a) are able to correctly detect crackles and wheezes in lung sound recordings with an accuracy of 87% when compared to pulmonary specialists and (b) improve the quality of the body sounds picked up by the device through adaptive noise cancellation and the use of an externally facing microphone, mitigating any ambient noise typically present in non-traditional settings (Supplementary figure 13.1).

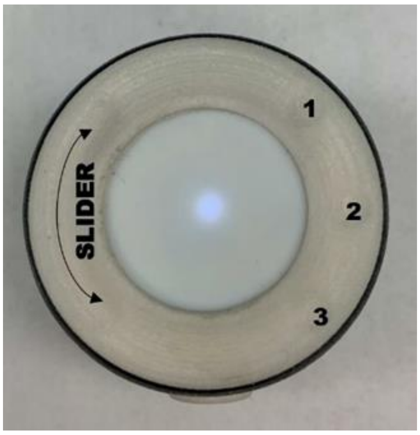
Supplementary figure 13.1 Feelix Smartscope prototype

The device features multiple microphones and proprietary active noise suppression. One of the key advantages of the numerous microphone sensing array design is that the Feelix Smartscope prototype does not require precise placement on the body, allowing healthcare workers or caregivers with minimal training to use the device effectively. The acoustic stethoscope is maximally sensitive at the centre of the stethoscope head, directly under the opening leading to the tubing, and its sensitivity decreases dramatically towards the edge. In contrast, the increased number of pickup positions across Feelix Smartscope's head provides a more uniform surface to capture body sounds.

The adaptive noise suppression algorithm relies on comparing the signal from the sensor head to that obtained from an externally facing microphone. The algorithm developed operates through multiband spectral subtraction, which is based on a classic, active signal denoising approach. As opposed to passive approaches such as low pass and high pass filtering found in current commercial products, this technique offers a real-time adaptation of the algorithm given the ambient environment. A classic spectral subtraction scheme has been extended into multiple frequency bands with weighted subtractions of each band that consider the signal-to-noise ratio of both the current frame and frequency component, which allows for more accurate adaptation to unseen environments and sounds.

Buttons

The device has three touch buttons and one slider, as shown in Supplementary figure 13.2



Supplementary figure 13.2 Buttons on top of the prototype digital stethoscope

Button 1 starts a recording preprogrammed to be a 10-second recording. When a new recording is initiated, the white light pulsates while it is taking the recording. Once the recording is complete, the green light blinks, and then the light returns to a solid white light.

Button 2 controls the session numbers. When a new patient is enrolled, a new session can be initiated. Then, all the recordings from that patient or session are labelled with the same session number.

Button 3 enables Bluetooth connection if it is not already on. One needs to touch the button until a green light appears, which indicates that Bluetooth is on and ready to be connected to the mobile/laptop application. Once connected, a solid blue light will show up.

The slider controls the volume level of the device. One needs to slide the finger clockwise to increase volume and counterclockwise to decrease it. In other terms, when oriented, as shown in Supplementary figure 13.2, sliding up increases, and sliding down decreases the volume.

LED indicator guide

A static white light means the device is on and ready to take recordings (Supplementary figure 13.3)

The Orange in the corner means that a new session was started.

A pulsating white light means that the device is currently recording.

A green flash at the end of the recording means that the recording was properly stored away.

A blue light means that Bluetooth is on and ready to connect.

Yellow in the corner means the device is connected to the phone or tablet or laptop.

Yellow flashing means that the device is transferring recordings to the phone or tablet or laptop.

Red means that the device is charging.

Supplementary figure 13.3 On the left, when the device is OFF; on the right, when the device is ON

Battery and charging

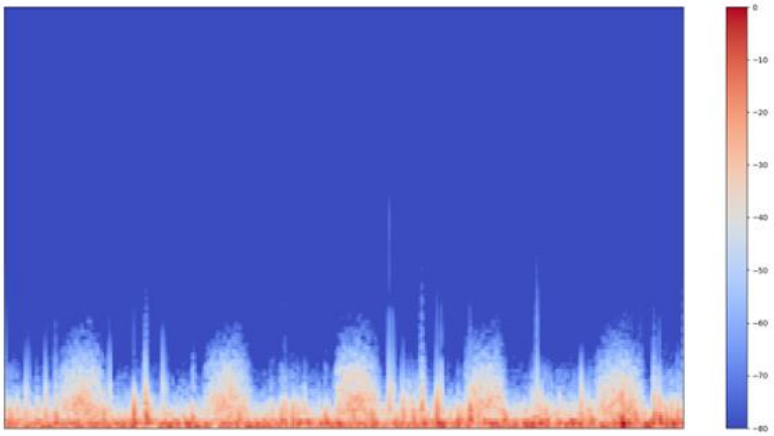
The battery is designed to last a full day of normal usage. It is recommended to charge the device nightly to avoid any issues during the day while collecting data. One needs to charge the battery by plugging in the cable that is provided with the device. When the device is charging, a red light on the outer rim of the device turns on (Supplementary figure 13.4). It takes about 60 minutes for the device to charge fully. Once fully charged, it lasts about three hours of continuous use, so actual usage is more prolonged, given that the device is not typically used continuously.

Supplementary figure 13.4 Charging the device

13.3 Description of machine learning computerised lung sounds analysis models

Four deep learning models (Models A, B, C, D) were developed by Sonavi Labs. These four models are formed on the same fundamental building block of a convolutional neural network (CNN), with differences in the depth of their network structure. Research has demonstrated that convolutional architectures have excellent performance in speech recognition and natural language processing. The studies have shown some achievements by extracting two-dimensional frequency domain features from one-dimensional audio data. The CNN specifically looks at each sound file and learns convolutional filters that highlight features in the two-dimensional representation that are characteristic of lung sound abnormalities to yield a classification. Generalized features may include the short, broad-spectrum nature of crackles and the presence of musical-like sounds of wheezes. Once a CNN learns the features associated with the lung sound classification decision, as new data is presented to the CNN, it uses shifting convolutional filters to search for these features in the signal.

The input to the model is a spectrogram image, which represents audio signals as a two-dimensional time-frequency image, with time on the x-axis, frequency on the y-axis, and intensity represented by the colour. In this representation, the sounds undergo a biomimetic non-linear transformation of the frequency scale, called the Mel Scale, such that the sounds more closely represent how a human listener may perceive the audio. This technique has been shown to improve audio signal classification tasks in many applications including speech, music, and bioacoustics. The two-dimension graphical representation, shown in the figure below, then becomes the input layer to the CNN.



Several CNN architectures were used to extract local features of normal and abnormal (crackle and wheeze) lung sounds. Two deep learning models (Model A/B and Model C/D) were introduced, which differ in the depth of the layers included in the network architecture. Both models leverage inception blocks to reduce the complexity of the models but maintain state-of-the-art accuracy. Two results are presented from each model type (Model A/B and C/D), which correspond to a different number of Mel scale bands (pitches) used at the input of the deep learning model. For Models A and C, 129 pitches are used to generate the Mel Spectrogram. For Models B and D, 64 pitches are used. Fewer pitches result in a smaller network architecture, with a tradeoff of a slight decrease in classification accuracy.

Model A and Model B

The convolutional architecture for Models A and B follows the following structure:

- Inception Block
- Average Pooling & Batch Normalization
- 2 Inverted Residual Blocks
- Global Average Pooling Layer
- Fully Connected Layer

The inception block used at the input of Model A and Model B is a powerful sparse layer that concatenates outputs from 16 separate filters of various sizes on the input spectrogram. It allows the model to select which filter size is the most relevant to the end-decision while capturing a wealth of information that subsequent layers can utilize.

The remainder of the model relies on two inverted residual layers with a kernel size of 6x6, an average pooling layer, a batch normalization layer, and a dropout layer. It is applied five times to create 32, 64, 128, 256 and 512 channels. The use of the residual layer that performs spatial filtering leads to much smaller filters and a reduced number of parameters, allowing for a lightweight model that learns and reduces the likelihood of overfitting.

Model C and Model D

The convolutional architecture for Models C and D follows the following structure:

- 6 Inception Blocks

- Global Average Pooling Layer
- Fully Connected Layer

Models C and D are more straightforward than Models A and B, as it applies the inception block described above sequentially six times, generating outgoing channels of value 8, 16, 32, 64, 128 and 256, respectively. It uses the same global average pooling and fully connected layer described above. Models C and D can be harder to optimize but provide flexibility to the model since different filter sizes can be optimised at different steps.

Model Training

The classification algorithm was trained on digital auscultation recordings acquired from children, ages 1 to 59 months in outpatient or busy clinical settings in Africa and Asia in the PERCH study. In total, 1157 children were enrolled into the study and were classified into one of the two categories: cases having IMCI-defined severe or very severe pneumonia or age-matched community controls without clinical pneumonia. The auscultation protocol called for recordings over 8 body locations: four across the child's back, two in the axilla and two on the chest area.

Nine expert reviewers (paediatricians or paediatric-experienced physicians) were enrolled for the annotation process. For each patient recording, two distinct primary reviewers annotated the 8 sites (per site or site annotation) as being Normal, Crackle, or Wheeze, with an accompanying descriptor label. If no full breath sounds could be distinguished (due to poor sound quality, technical errors, or unrecognizable contamination), a "non-interpretable" label descriptor was assigned. The above process ensured that every site recording was assigned an annotation explaining breath sound findings (per-site label), along with a confidence indicator for each finding. In case of disagreement between the two primary reviewers, more reviewers listened to the recording to resolve ambiguities, and provided additional labelling as needed. In total, 62 patients were excluded due to missing annotations, along with 29% of remaining site recordings, due to “noninterpretable” labels, missing audio, recording malfunctions in one of the two microphones, or high disagreement among reviewer labels. The final included data set consisted of more than 250 hours of recorded lung sounds.

All interpretable recordings were included in the training of the model, and final arbitrated per-site labels were used. Training was done on randomly shuffled recordings over 100 training epochs.

13.4 Standard operating procedure of lung sound recording and management

Background

- In the digital auscultation study, one of the major activities is the recording of lung sounds of eligible children at community clinics (CC) by Community Health Care Providers (CHCPs).
- CHCPs will perform lung sound recording for under-5 children who come to the community clinic for care seeking and are eligible for enrolment (i.e., presenting with cough and cold or difficulty breathing) and consented to enrol in this study at CC.
- The Standard Operating Procedure (SOP) is necessary to ensure that lung sound collection is carried out in a standard and reproducible way, and procedure for transfer and renaming each sound file by study staff.

Scope/Applicability

- This SOP will be utilized by CHCPs who have been trained in the digital auscultation procedure and their supervisors, including study physicians.
- Lung sound recording will be performed after the respiratory assessment at CC by CHCP.
- In addition to lung sound recording, this SOP will act as a guideline for Study Physician and Field Research Assistant/Field Research Officer on management of lung sounds, including transfer of the sound files from Feelix Smartscope to the tab (via Bluetooth connectivity) by using an application, renaming them and uploading in the server.

Roles/Responsibilities

- CHCPs will be trained on this procedure. They will be responsible for collecting basic clinical data from the participant's caregiver, recording lung sounds using the Smartscope, completing all the clinical assessments of the child and documenting all information in an electronic case report form (eCRF) using a Tab.
- CHCPs and their supervisors will be trained to record lung sounds using the digital Smartscope and will be responsible for reading the product manual, monitoring the safety and function of the equipment, and strictly adhering to the standard operating procedures as described in this manual.
- Study Physician (SP)/ Medical Officer (MO)/ Field Research Assistant (FRA)/ Field Research Officer (FRO) will be responsible for:

- ✓ Transferring the lung sounds from the Smartscope to a tab.
- ✓ Renaming of all recorded sound positions on each Study ID through a study encrypted online application.

- Study delegated Physician/ medical officer will be responsible for:
  - ✓ Transferring all sound files from Tab to site`s designated laptop for quality check, renaming each sound file.
  - ✓ Uploading and securely maintaining the data on the site's designated encrypted server, creating a backup data file and store in an encrypted and password-protected external hard drive.
  - ✓ Performing local quality control procedures.
  - ✓ Communicating with the PI regarding issues or challenges that arise regarding this activity.

Prerequisites/Supplies needed

- **Prerequisites**
  - ✓ This procedure needs to be undertaken in patient care setting as appropriate and practical.
  - ✓ The procedure should only be carried out by trained CHCPs.
  - ✓ Parental information sheet will be administered and obtained consent before enrolling a child.
  - ✓ The child should be calm and cooperative, as necessary for routine chest auscultation.

- ✓ According to the manufacturer, when in patient contact, the stethoscope should not be connected to any equipment that is "mains-powered". In other words, the stethoscope must be on battery power, and the stethoscope should not be used on a patient if it is connected to a charging iPod or a laptop connected to a LAN, AC power supply, or AC-powered peripheral.

Equipment needed

All equipment should be kept in a secure location when not in use. The supervisor must monitor where the equipment is located. Instruction manuals and accessories should be kept accessible. It is strongly recommended to keep the USB connection cable together with the Smartscope in a small bag/box. All the equipment must be handled with care at all times.

Name of equipment	Description
Digital stethoscope (Feelix Smartscope)	One Feelix Smartscope will be provided in each CC
Tab with SIM	One tab with active SIM will be provided to each designated CHCP/SP/MO/FRA/FRO. These tabs will be used for transferring lung sounds from device to the tab and renaming. CHCP also record data in the tab.
USB cable	Connects Smartscope to an external power source (adaptor or power bank) for charging the device.
Computer/laptop	It is preferable to save files to one designated desktop computer/ Laptop located in a secured room.

	All devices are compatible with PC (Windows 7 or 10) systems.

Data Collection Overview

a. **Pick up the device to turn it on.**

b. **Start a new session** by double tapping button 2. Device will flash an orange light and then this light will be solid, this indicates that a new session has been initiated.

c. **Take a recording** at location 1 by pressing button 1 once. Device will pulsate white light while taking the recording and then a green light will flash (after 10 seconds), indicating that the recording is completed and saved on the device.

d. Repeat step **c** for each recording location.

e. Once recording is completed, either put the device aside or initiate a Bluetooth connection.

f. Once ready to pull the recordings off, **initiate a Bluetooth connection by pressing button 3** to turn Bluetooth on. Or, if the device is off, turn on the device. A blue light should be on for the first 30 seconds.

g. Connect to the app to **download the recordings from the device to the tablet**. Yellow light will begin flashing as recordings are being pulled off.

h. If using an Android device, **plug in the mobile phone or tablet to a computer**. Navigate to the data folder and download all recordings and associated metadata files.

Power on and off

- **The device is OFF** when there are no lights on; it is in standby mode waiting to be used.
- **To turn the device ON simply pick of the device** or touch the top of the device and lights should turn on. It is equipped with a proximity sensor that senses when it has been picked up.
- **The device is ON and ready when there is a static white light**. You will be able to take recordings, start sessions and connect to Bluetooth. **A blue light will also be on for 30 seconds** to indicate that Bluetooth is on and ready for a connection.
- **The device will turn OFF automatically after 60 seconds** when it does not sense any touch. Simply put it down and walk away.

Session number in Smartscope

a. **Start a session**

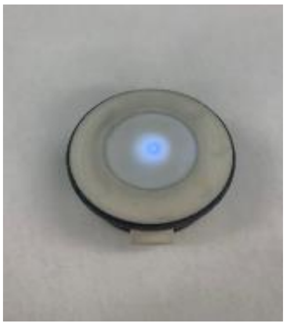
   - Sessions help keep track of which recordings are for which patient.
   - Sessions group all the recordings from one patient; all recordings taken in a session will have the same session number in the file name, S###, where ### is the unique session number.
   - To start a new session, double tap button 2. After a slight delay, an orange light will flash to indicate that a new session has been initiated.
   - Please note that a minimum of 5 recordings is required for a session to change (by default).

b. Take recordings

- To take a recording, **press button 1 once**. All recordings are preprogrammed to be exactly 10 second recordings (Supplementary figure 13.5).

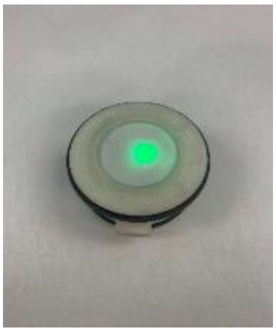
Supplementary figure 13.5 Recording started

- When a new recording is initiated, the white light will pulsate while it is taking the recording. To stop a recording, **press button 1 again** during those 10 seconds (Supplementary figure 13.6).



Supplementary figure 13.6 Device ready to record

- Once the recording is complete, a green light will flash after a few seconds and then the light will return to a solid white light. For each child, there will be 5 positions recorded. 1 is for study ID, and 4 for lung positions (Supplementary figure 13.7).



Supplementary figure 13.7 Recording saved

Order of auscultation

Order of auscultation:(1) back left; (2) back right; (3), left front (cardiac); (4) right front

Position 1 (back left)

Position 2 (back right)

Position 3 (left front, cardiac)

Position 4 (right front)

Sonavi app

A. Setting up the app- Sonavi

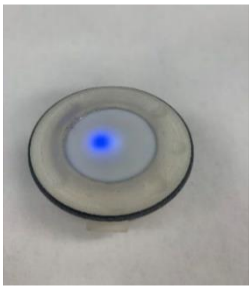
Install the app (sonavi_field-debug.apk) onto your device (Supplementary figure 13.8).

Supplementary figure 13.8 Home screen of Tab with Sonavi app

Bluetooth and connecting device to the app:

Bluetooth needs to be enabled on the device, and then a connection with a mobile phone or tablet needs to be initiated. Bluetooth is required to pair the device with phone or tablet. Once the device is paired, the Smartscope can be paired directly from the sonavi app.

When the blue light is on, it indicates that Bluetooth is enabled on the stethoscope and ready for a connection (Supplementary figure 13.9). If no connection to a phone or tablet is made, it will turn off in 30 seconds. The device will still remain on. **When the blue light is on, all other functions of the device still operate normally.**



Supplementary figure 13.9 Bluetooth ON

B. Enable Bluetooth on the device

There are two ways to enable Bluetooth on the device.

1. **Bluetooth automatically turns on when the device powers up.**
2. **Press button 3 to enable Bluetooth** if the device is already on and the blue light is not on.

The Bluetooth will remain enabled for 30 seconds and the blue light on. If no connection is made, it is disabled again.

C. Connect the device to phone or tablet

To connect the device to a secondary device like a mobile phone or tablet, enable Bluetooth, as shown above. Once it is enabled, connect to your phone or tablet by pairing with the device and connecting:

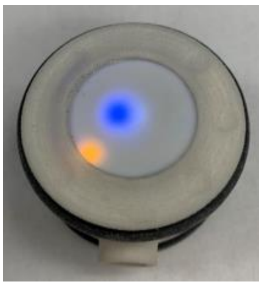
If this is the first time connecting to the device, **go to “Settings” on the mobile device and navigate to Bluetooth connections to pair the device.** It should show up under available as “Feelix_09XXXX” where XXXX represent the last four of the device’s unique identifier (Supplementary figure 13.10).

NOTE: You only need to pair once. Once you have paired, you can skip step 1 every time.

Supplementary figure 13.10 Device bluetooth options

Once you have paired the device to the mobile phone or tablet, navigate directly to the app

- Select the device you are trying to connect to from the list. This list is the list of paired devices to your mobile device.
- If the connection is successful, you should see "Connected to Feelix_09XXXX".
- Once the device is successfully connected, you should see a stable orange light, as shown below (Supplementary figure 13.11).



Supplementary figure 13.11 Device connected with the Tab

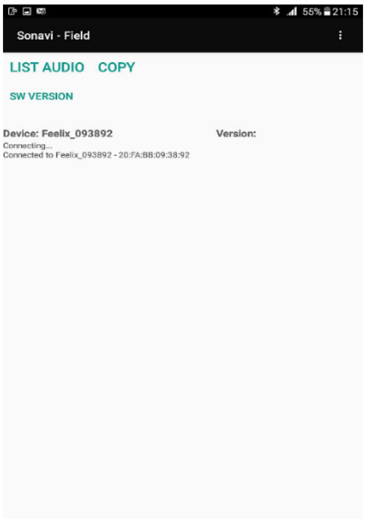
NOTE: While the mobile phone or tablet is connected, the blue light stays on. **The device will stay on as long as the Bluetooth connection stays on**. If you want the device to turn off, make sure to disconnect from the Bluetooth.

D. Receiving sound recordings from Smartscope and transferring them into tab.

1. Download recordings to the app

Once the device is successfully connected to the app, you can pull the recordings off the device. To do so:

- ♦ Once ‘connected’ is shown in the screen (i.e., the device is connected with the tab through Sonavi app), select the ‘List Audio’ (top left of the screen) (Supplementary figure 13.12 and Supplementary figure 13.13)
- ♦ Now all the sound files from the device will be listed in the screen.

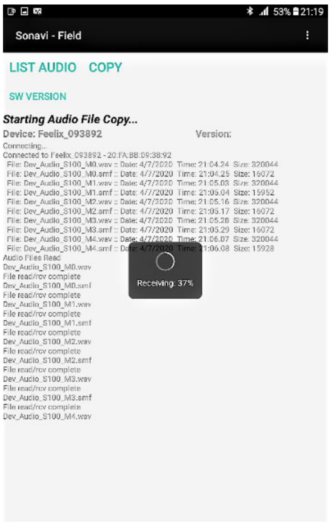


Supplementary figure 13.12 Device connected in the App

Supplementary figure 13.13 List of all the sound files from the device is showing in app

- Check that for each sound file there is a ‘wav’ and ‘smf’ files showing on the screen (Supplementary figure 13.14).
- Now select ‘copy’ (top right of the screen)
- All sounds will be transferred one by one from the device to the tablet (Supplementary figure 13.15). Do not close the screen during the sound transfer, which may lose the connection between device and app and will require again for reconnection.

Supplementary figure 13.14 Audio files (.wav and .smf)



Supplementary figure 13.15 Audio files copy in progress

- After all the sound files are transferred (Supplementary figure 13.16), the sounds are saved in Tablet, location: Myfiles/devicestorage/Android/data/sonavi.field

Supplementary figure 13.16 Audio files copy Done

Note: Please delete the sound files from the device after successful transfer from the device to the tab, otherwise, the device might get hanged due to shortage of storage.

- For deletion of sound files from the device, click on the '3 dots' situated on the upper right part of the screen. Select 'delete' button. Now each sound will be deleted one by one (Supplementary figure 13.17 and Supplementary figure 13.18).
- For confirmation, please click on the 'List Audio' again, now the screen will show that 'No audio file on device' (Supplementary figure 13.19).

Supplementary figure 13.17 Select Delete button

Supplementary figure 13.18 Audio files deletion in progress

Supplementary figure 13.19 Audio files deletion complete

2. **Transfer recordings from the app to your personal computer**
   You can transfer all the recordings from the mobile device to a computer by connecting the mobile device via a wired cable. Only phones or tablets running on Android OS will be able to do this.

   - Plug in the mobile phone or tablet to the computer.
   - **Navigate to My files/device storage/Android/data/sonavi.field.** The files should have timestamps in their name. All *.wav and *.smf files will be present in that folder and can be moved to a computer.

Stepwise Procedure of lung sound management by study staff

- The following stepwise procedure of Lung sound Transfer and renaming them in app will be done by Study Physician/ Medical Officer/FRA/FRM).

- This procedure should be performed on a daily basis, ie when collecting all the sound files from the selected community clinics, renaming them and uploading into the server.
- In addition, only Study physician/Medical Officer will perform further management, including main sound files rename, quality check, backup and its upload to a designated server.
- There are two steps in sound file rename:

  i) The first step involves auto rename of sound files using DA3b app in tab. This can only be done after all the sound files are transferred to the tab.

  ii) The second step involves renaming of the original sound files (in .wav format) by SP/MO after transferring them into a designated laptop.

Steps

1. Turn on bluetooth in the device (Smartscope) by pressing the button 3. Blue light will flash
2. Turn on the Bluetooth of the tablet
3. Go to the apps and select Sonavi-field
4. Now select the device name from the list.
5. The device will automatically pair with the Sonavi app connection will be established.
6. Once ‘connected’ is shown on the screen, select the ‘List Audio’ (top left of the screen).

7. Now all the sound files from the device will be listed on the screen.
8. Check that for each sound file, there is a 'wav' and 'smf' files showing on the screen.
9. Now select 'copy' (top right of the screen).
10. All sounds will be transferred one by one from the device to the tablet.
11. Do not close the screen during the sound transfer, which may lose the connection between device and app and will again need to reconnect.
12. After all the sound files are transferred, the sounds are saved in Tablet, location: My files/device storage/Android/data/sonavi.field
13. Listen to the sounds and confirm that all the sounds are being transferred.
14. Now go to the Sonavi-field app again and select 'List Audio'
15. Repeat steps 1-5 if a connection is lost.
16. Now to delete the sounds from the device, select the 3 dots on the upper right corner of the screen.
17. Now select delete. (NOTE: before selecting this option, you must ensure that all sounds have been successfully transferred from the device to the tablet. This procedure cannot be reversed)
18. All sounds will be deleted one by one.

19. After all the sounds are deleted, select the 'List Audio' again to check if any sound file is remaining on the device.

20. In any case, if sound files are seen on the list, first transfer the sound file to the tab (repeat step 9-10). Then delete the sound files following step 16-18.

21. The sound files transferred to the tab are named as such: Device code_MM-DD-YYYY-Hour-Min-Sec-Session ### _Position ## e.g.: 093827_01-14-2020-00-08-00-S11_M31

22. Once the sounds are in tab, the study staff opens the DA3b app and select an enrolled study ID

23. Study staff will listen to the sound files and confirm them for that specific ID, and completes the DA3b form (in app).

24. The System will automatically add study ID at the end of each sound files, e.g.: 093827_01-14-2020-00-08-00-S11_M31_901146

25. After completion of the renaming for all the positions for respective ID, study staff will save the ID and click on data backup for synchronization with the main server.

26. SP/MO will transfer all the sound files from the tab to the designated laptop/desktop.

27. The original sound files (files in .wav format) will be cross-checked with the respective study ID.

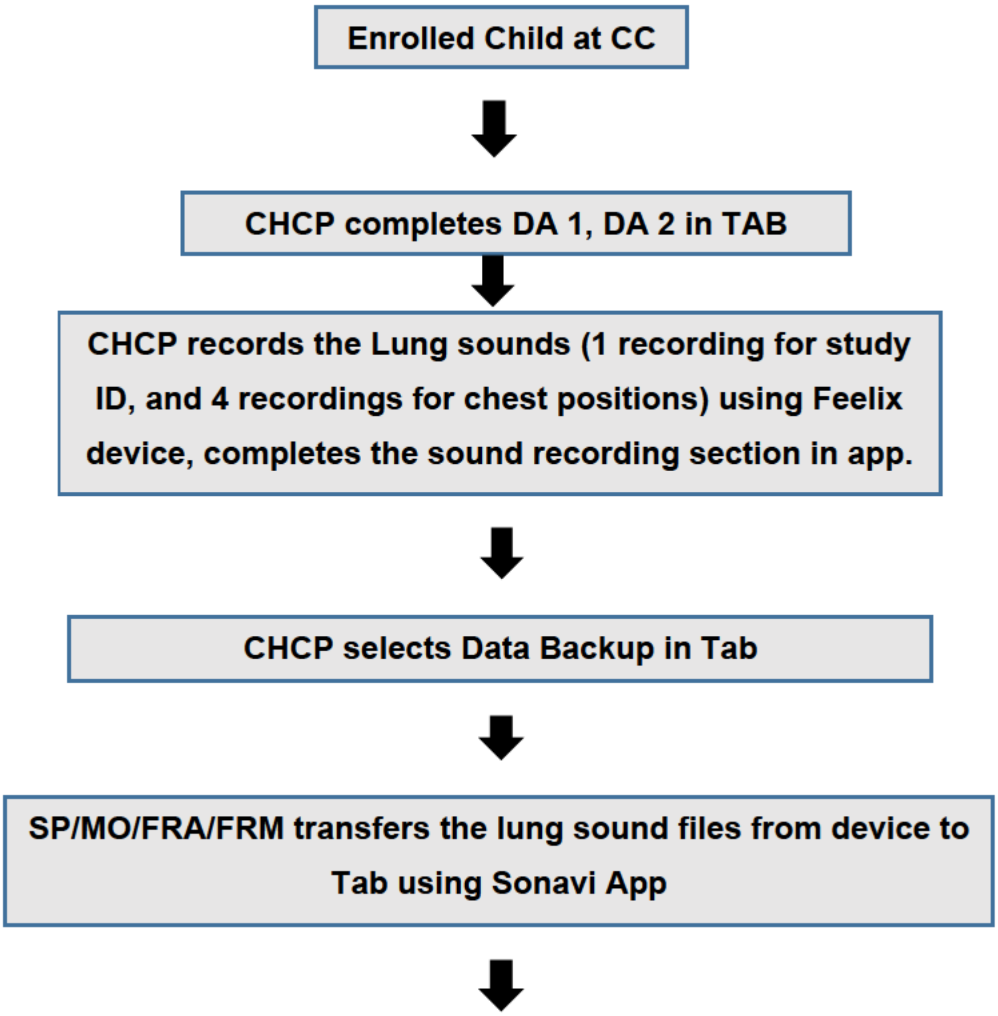
28. For each ID, there will be 5 recordings. 1st recording will be the Study ID, then 4 recordings are the four lung sound positions.

29. SP/MO will listen to the first sound file of the respective ID and confirm the sounds for that specific child.

30. S/he will then carefully listen all the positions and rename the sound file by adding the study ID at end of each file name. (e.g.: 093827_01-14-2020-00-08-00-S11_M31_901146).

31. Now that all the sound files have been renamed, SP/MO will securely upload the files to server and keep a backup in a password-protected hard drive.

Flow chart of lung sound collection and rename



Once the sound file transfers to the Tab, the file name appears as: 09382D_11-22-2019-03-49-05-S16_M6.wav

⬇

SP/MO/FRA/FRM Listens to all the transferred sound files and check them whether all are transferred successfully into the designated folder

⬇

Opens the sound file rename app (DA3b), generates the enrolled child list from database.

⬇

Selects the respective Study ID from the list

⬇

For linking the sound files with the respective ID, SP/MO/FRA/FRM selects the folder where the sound files originally kept and adds all the 4 position file names after confirming each sound files.

⬇

Saves the data and then selects backup, the sound files will be renamed as 09382D_11-22-2019-03-49-05-S16_M6.wav_9501108

Troubleshoot

1. **Device unresponsive to touch:** Common issue with the Smartscope is that the device may get hanged or become unresponsive to touch. This may happen during charging, recording a sound or even during sound transfer to the tab.

   Probable solution: In case the device is unresponsive, it needs to drain the charge. Unfortunately, there is no physical button to do so, we have to wait until the charge is drained and power turned off, then recharge the device and it will work again.

2. **Unwanted sound files in device:** Sometimes few sound files of unexpected name/size (file name may show as ???, large file size, 0 file size) can be found along with regular sound files after transferring them from device to Tab. These unusual files can't be transferred with Sonavi app and are not required.

   Probable solution: In these cases, we connect the device with previous version of app (Canoga) and then can manually delete the unwanted files from the device.

3. **Date and Time stamp issue:** The date and time of the device may not be synchronised, which may show an irregular date and time of recording.

   Probable solution: Though this issue will be resolved after the next app update, currently the date and time can be updated by clicking "Set Time" button on the 'option section' of the Sonavi app.

4. **Failure to transfer the sound file from the device:** Sometimes, the wav file of a sound may not be transferred from the device to the tab. Similar situation may also be with smf files.

   Probable solution: Retry again to transfer the sound files from the device by repeating the steps described earlier.

5. **Some sound files may be seen after deleting all the files from the device:**

   At times, even after deleting all sound files from the device (i.e., after copying them to Tab), the deleted files may again be seen in the audio file list.

   Probable solution: In such cases, these sound files need to be deleted again, but please confirm that you have copied them to the tab before delete again.

6. **Device may automatically record numerous files and get loaded and flash red/pink light in pressing button 1:** This may happen because the device is touch sensitive and may automatically record unwanted sound files.

   Probable solution: In such cases, please confirm that these sound files are not required, then delete the recorded files to empty the device storage. If this issue repeats/persists, connect the device with old version of the Canoga app after disconnecting with Sonavi app. In Canoga app, type “/” into LIST DIR. A list of the directories should be displayed. If “file_xfer” is not in that list, press the MKFS button to reformat the storage. And then, press DEFAULT DIRS to rebuild the folders. Turn off Bluetooth on the phone/tablet to disconnect Bluetooth and allow the device to turn off after 60 seconds. The device should be good to go now.

7. **Greenlight issue:** The device sometimes does not show green light after 10 seconds of recording and continues flashing white light even after 10 seconds.

   Probable solution: as this version of the device do not have the physical button to reset, please keep the device aside and allow it to drain. After charging, it should be ok. If not, please reset using the old Canoga app by connecting the device with the app and clicking on the reset button on the bottom right.

Maintenance

1. The digital stethoscope is very sensitive to touch; hence needs to handle carefully.
2. Rough handling of the device is discouraged; please use it carefully while recording so that it does not slip off hand and fall off. Always keep the device and cable in the box when not in use.
3. The device is NOT waterproof, so it may get damaged if in contact with water.
4. Charge the device regularly to get optimum battery performance.
5. Read and follow the instructions in this manual properly to avoid unwanted troubleshoots.

13.5 Standard operating procedure of listening panel training

Definitions: Specific to this SOP

- **Full breath sound** is when ***both*** the inspiration and expiration on one (1) breath cycle can be distinguished by the listener.
- **Partial breath sound** is when only part of inspiration or expiration can be distinguished by the listener.
- **Confident** is one or more (≥1) full breath sounds that can be classified with certainty (clearly).
- **Not confident** one or more (≥1) full breath sounds that can be classified with less certainty.
- **Lung sound classifications** are per the below table.

Lung Sound Classifications

Lung sound	Description	Respiration cycle	
Primary Sounds		Inspiration	Expiration
Normal	Soft, not musical; and sometimes found rough sound in both inspiration and expiration, commonly mistake with crackles (also called rough normal)	Throughout	Early only

Lung sound	Description	Respiration cycle	
Primary Sounds		**Inspiration**	**Expiration**
Crackle	Short, explosive, not musical, popping; repetitive (*sometimes*)	Primarily (but can be variable)	Possible but less common and not usually without inspiratory crackles
Wheeze	Musical, long duration; can be high *or* low pitch	Possible	Primarily, prolonged
Both Wheeze and Crackle	File has both the lung sounds as mentioned in the above sectioned	Same as before	Same as before
Uninterpretable	Uninterpretable can be due to persistent cry or agitation/ movement/ poor recording issue. If crying/ vocalization is present throughout the sound file, it is due to crying/ agitation. If there is no crying sound and vocalization heard but still no breath sound can be detected, it is due to poor quality/recording issue. Persistent crying or poor quality such that zero full breath sounds are heard.	Not applicable	
"Abnormal, other" Sounds			

Lung sound	Description	Respiration cycle	
Primary Sounds		**Inspiration**	**Expiration**
Upper airway sounds, not stridor	Generally louder at cheek position, may mimic a low pitch wheeze or have a "*snorting*" quality that may mimic a crackle, can also be a vocalization other than a cry	Possible	Possible
Upper airway sounds, primarily stridor	Generally louder at cheek, may mimic a high pitch wheeze although stridor is primarily inspiratory whereas wheeze is primarily expiratory	Primarily	Possible but less common
Crying, non-persistent	Crying or screaming with full breath sound(s) between crying episodes; inspiratory crackles can be present with expiratory cries	Possible	Primarily
Prolonged expiratory phase	A longer than normal expiratory phase, often associated with expiratory wheezes	Possible	Possible
Starter	Mechanical sound which is generated during placement of the stethoscope in the chest and found at the initiation of sound files.	Not applicable	
Audible wheeze	Musical, long duration and more prominent than normal wheeze	Possible	Primarily, prolonged

Lung sound	Description	Respiration cycle	
Primary Sounds		Inspiration	Expiration
Other, specify	Sound not previously described	Per listener	Per listener

Purpose / Background

The purpose of this SOP is to describe the listening panel procedures required to listen to, interpret and annotate lung sound files; and submit it in the online DA-L system (online data entry system of lung sounds classification by chest position).

Scope/Applicability

This SOP is intended for the expert listening panel participants responsible for classifying the digitally recorded lung sound files.

Prerequisites / Supplies Needed

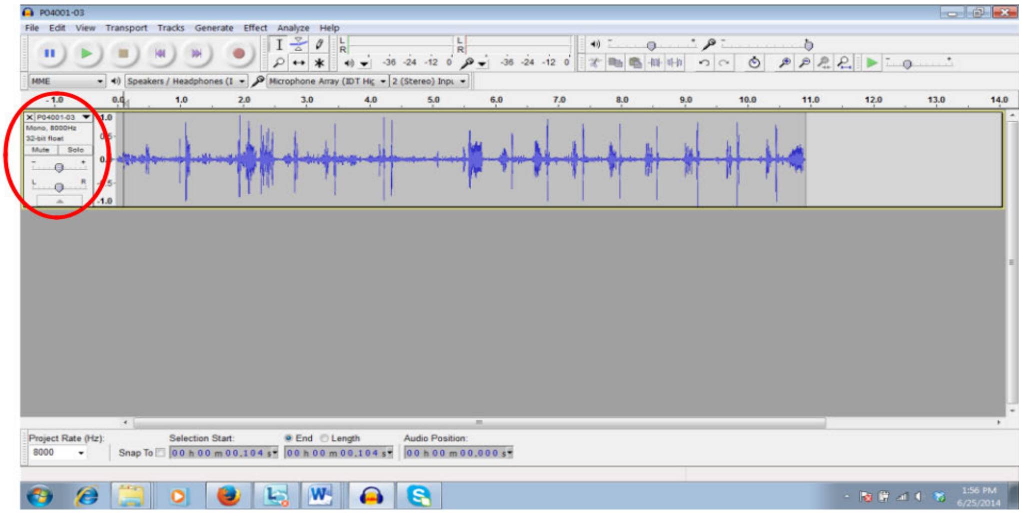
1. Audacity sound editing software (To download: http://audacity.sourceforge.net/download/)
2. Sound files (available in the DA-L system)

Roles / Responsibilities

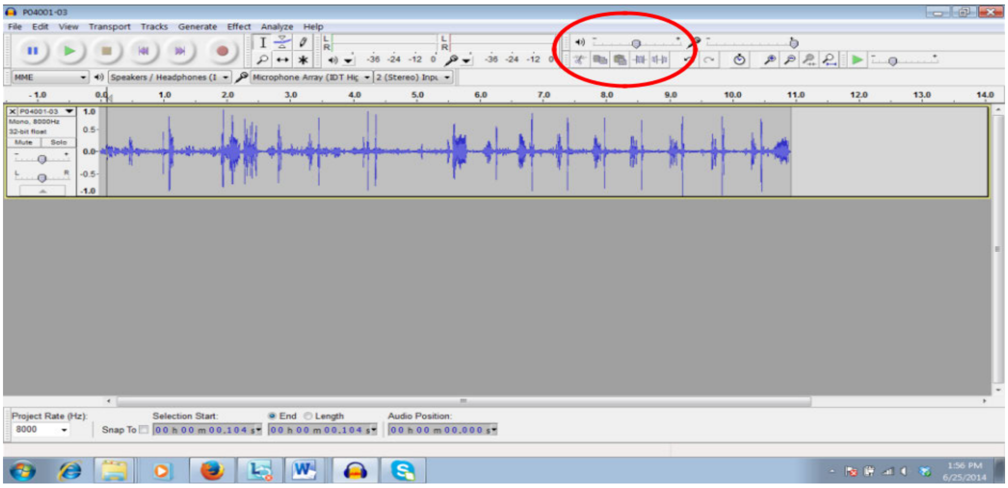
Each expert listening panel participant is responsible for listening to, classifying, and annotating the provided lung sound files and submitting them in the online DA-L system. They will save all labelled sound files adding their code at the end of each sound file and periodically provides those to the PRF contract person.

Notables for Audacity

1. We **do not** recommend altering any of the specifications directly to the left of the sound wave panel as circled below. We also do not recommend using any of the effects offered in Audacity other than amplify**.**



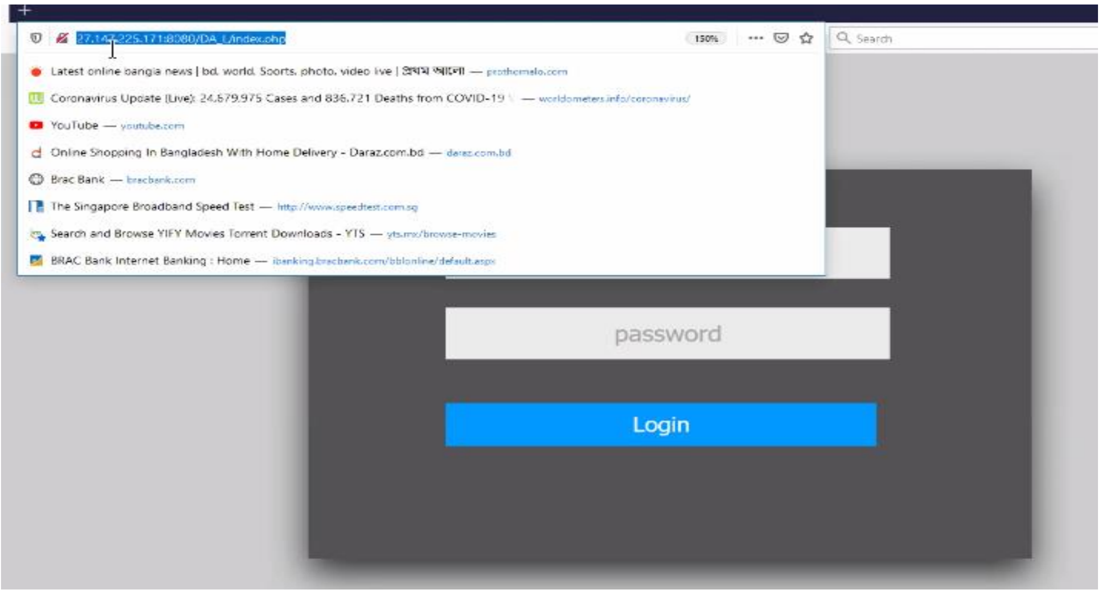
2. Output volume (same as computer volume) can be adjusted within Audacity as depicted below or on your computer per normal procedures.



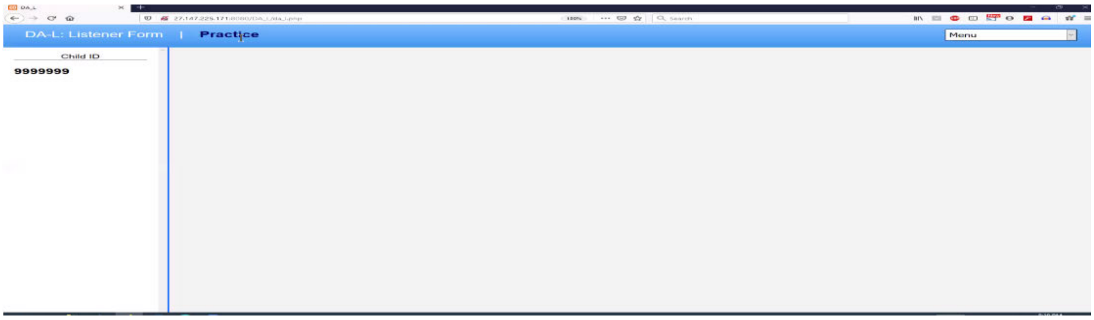
Procedural Steps

Identifying and accessing a patient's sound files: Each expert listening panel member has their own profile in the DA-L system. They can access their profile by logging in with their ID and password. Files are shared with the expert listening panel participants in their DA-L profile.

Step- 1: Access the DA-L site through Google Chrome or Firefox browser and log in to the participant profile

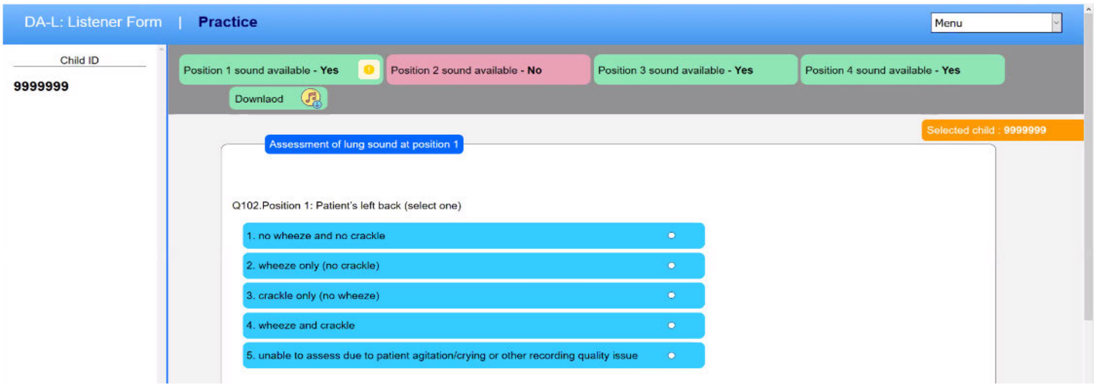


Step-2: After successfully logging in the participant profile, list of child ID (ex: 9999999) are visible in the left column under Child ID section



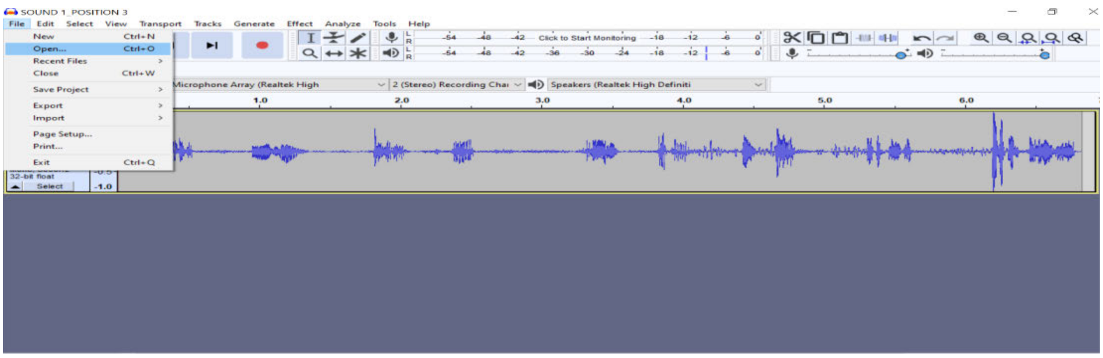
Step-3: After selecting a Child ID from the list, four chest position sound files are available in four different tabs. Pink coloured tab represents, sound file is not available in that chest position.

Step- 4: By clicking the radio button of position 1, the sound file for that chest position is visible for download. After downloading the sound file from that position, it needs to be opened by Audacity sound editing software for listening, classifying and annotating (steps are described below). Finally, listeners need to fill up the questions in the DA-L system as per their findings from their sound file. For the rest of the positions, the same procedure needs to be followed.



Step- 5: Double click with your mouse on the Audacity software program icon to open Audacity. 

. Click on the 'File' option, select 'Open' and select the downloaded sound file. Finally, it is ready for the user to listen, interpret and annotate by Audacity software.

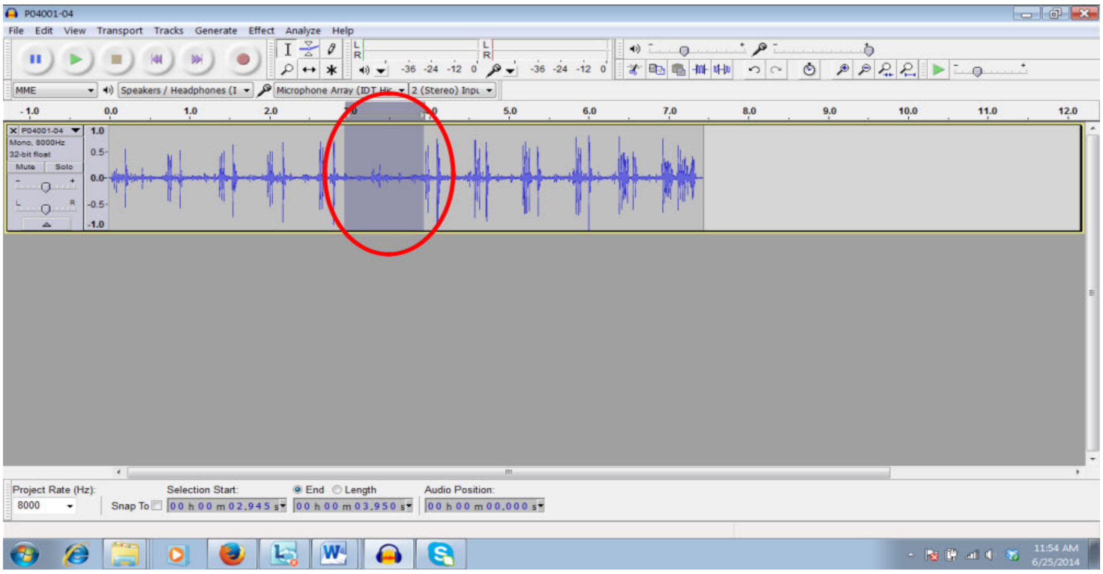


Step- 6:

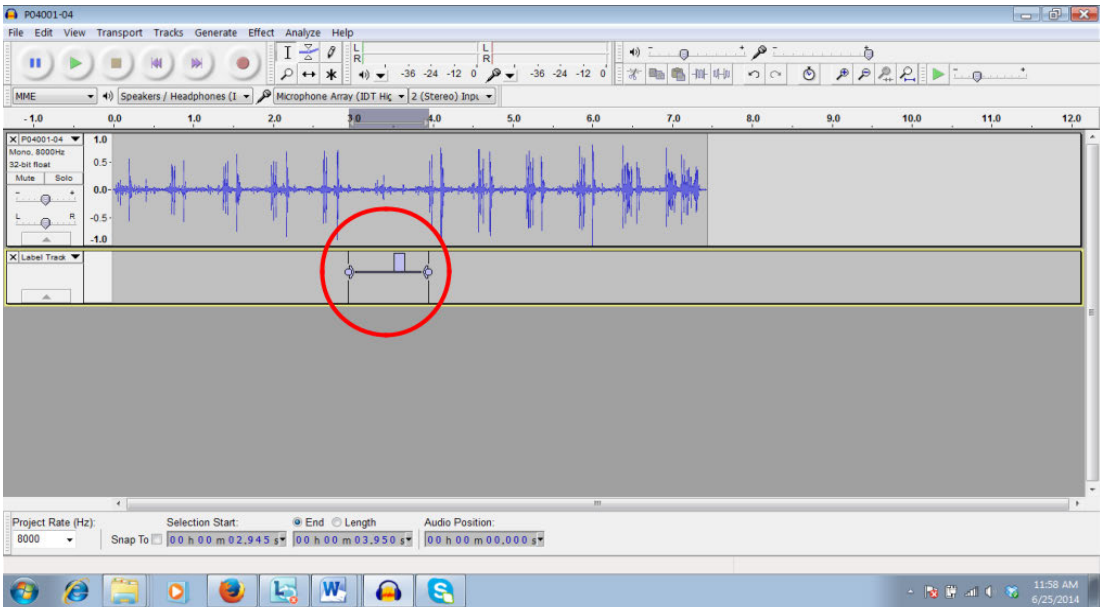
1) Initially focus on identifying the breath sounds within the file segment.
2) Then attempt to identify the inspiratory and expiratory phase
3) If breath sound is not clearly identified, listener can use sound amplification in Audacity (which is described in the next section)
4) Next listen "between" the breath sounds and to the sound segment "background" to discern the overall sound of the track and whether these sounds are potentially influencing the interpretation of the identified breath sounds.
5) Use the definitions presented in Section 1 'Definitions' to guide your classifications.

Step- 7: Annotation procedure

First position the cursor arrow within the sound file where the sound waves are present. Then 'left click' and hold while dragging the cursor arrow from left to right to highlight the breath sound intended to be annotated, as shown below. *Note no annotation is required if the sound segment meets "uninterpretable" criteria*.

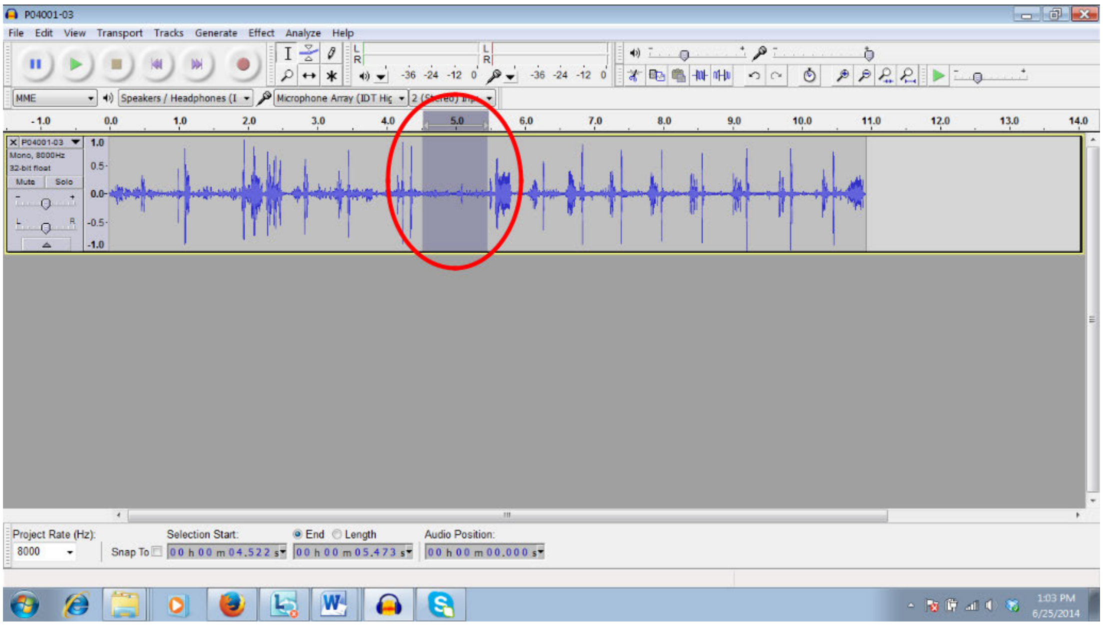


Next, press “Control” and “B” (Windows computer) or “Command” and “B” (Mac computer) to create a label with a text cursor as shown below and save the file after annotation accordingly.

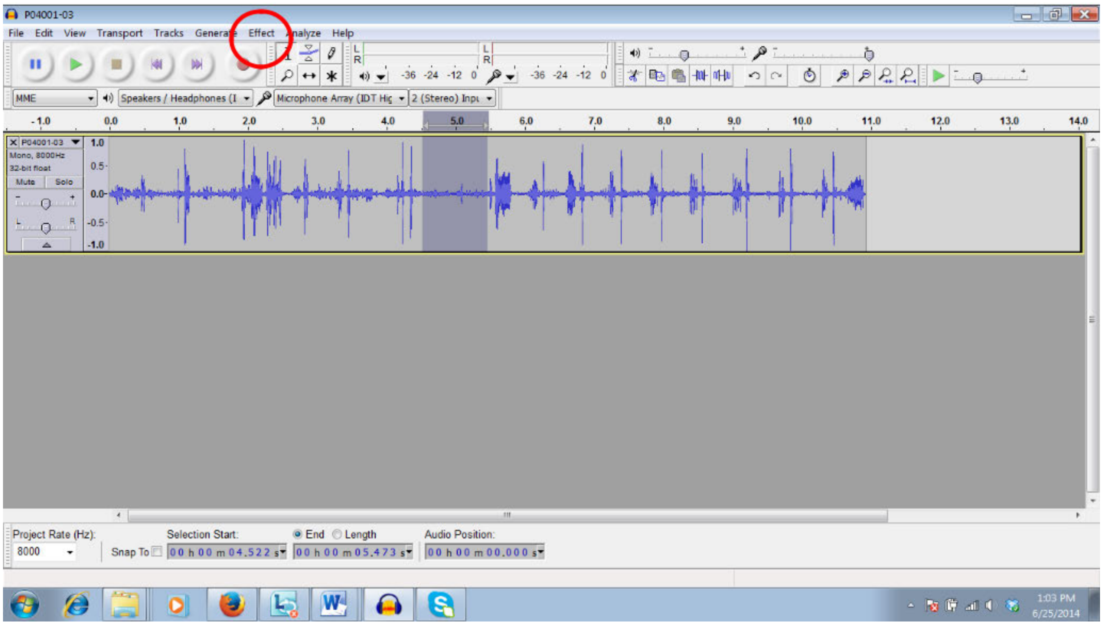


Sound amplification in Audacity: Sound amplification is permitted per the listener’s discretion. Sound clipping is never allowed as this can distort the sounds. It is recommended that only portions of the sound segment in need of more detailed listening are amplified *rather than the entire sound segment*. Sound amplification steps as follows:

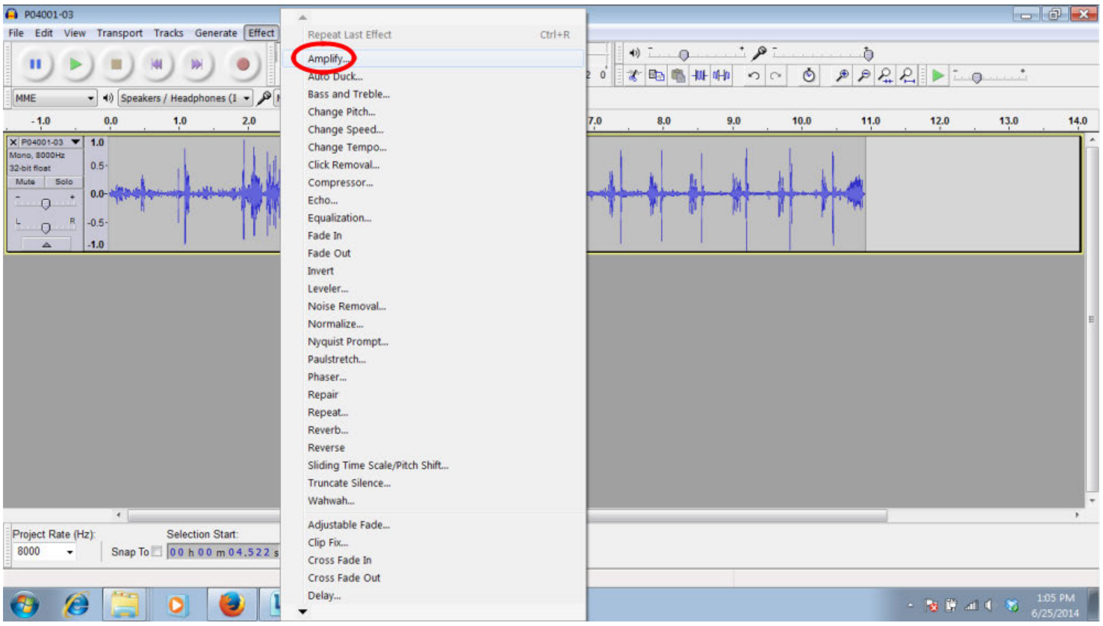
- Highlight the section in need of amplification as shown below by left clicking with the cursor/arrow and dragging from left to right to highlight the sound waves.



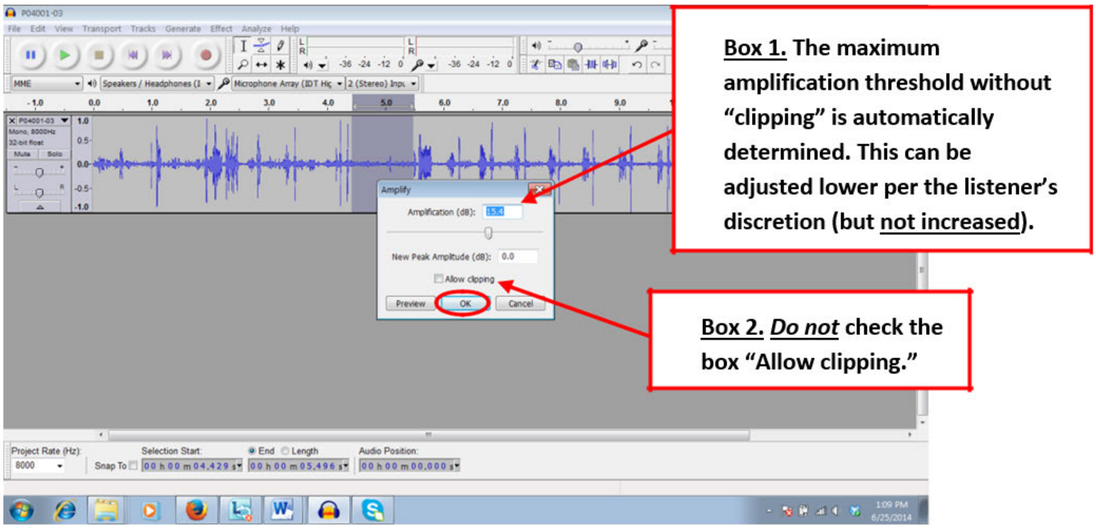
- Next select the “Effect” tab at the top of the Audacity program screen.



- Then select the “Amplify” option in the dropdown menu that appears after selecting the “Effect” tab.



The following screen prompt will then appear as shown below. It is critical to note that the maximum amplification is automatically determined by Audacity as shown below in Box 1. This level can be lowered per the listener's discretion but <u>not increased</u>. The box labelled as "Allow clipping" should never be selected () as clipping can distort the sounds and lead to false interpretations. Box 2 highlights this critical point. Once the desired amplification level is determined then "Ok" can be selected.



- Sometimes, recommended amplification is too much to assess the sound file, e.g., Audacity recommends 21 or so, but we as a listener can increase up to 12 or 15 to avoid maximum increase and vice versa. Sometimes amplification can be decreased to avoid too much sound in some of the selected files which can also be useful to assess the file.

13.6 Participant information sheet and consent form

13.6.1 Participant information sheet and consent form for screening

Participant Information Sheet for Screening

Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Pneumonia is a leading cause of death in under-five children worldwide including Bangladesh. The majority of child deaths from pneumonia are due

to either not seeking or delays in seeking medical attention. Trained frontline healthcare workers can play a key role to identify pneumonia.

The World Health Organization (WHO) guideline do not include listening to the chest in their algorithm for diagnosis by frontline healthcare workers because they have limited training using standard stethoscopes.

A new type of stethoscope can listen and interpret what is heard in the chest without a person having to listen and interpret the sounds. These are called digital stethoscopes. We wish to assess whether a low-cost digital stethoscope (the 'Smartscope') developed for use in children is able to be used by frontline healthcare workers to improve the diagnosis of pneumonia in children.

Our study will include 2,426 children under five years of age who have cough and/or difficult breathing at 12 community clinics in Zakiganj and Kanaighat sub-district of Sylhet district in Bangladesh. To enrol 2426 under five children, we will assess all consented under-five children who will visit the community clinic and we will invite to participate in the study.

Why have I been invited to take part?

You have been asked to take part as your child is visiting this community clinic and age of your child is below 5 years.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign or put thumbprint a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study at any time will not affect the healthcare that you and your child receive or your legal rights.

What will happen if I take part?

We will ask you about your child has a history of cough and/or breathing difficulty or we will observe your child is suffering from cough and/or breathing difficulty. If your child has cough or difficult breathing, then we will invite you for another consent to enrol the main study. However, if your child has been part of this study before (within the last 30 days), we will not include him/her again in this study.

I, the Community Health Care Provider (CHCP) of the Community Clinic (CC), will read out the consent form to you and explain the study procedures. If there are any questions, I will answer and ensure that you understand the research project. You will be given at least 10-15 minutes to decide whether or not to take part in the study; take longer if you wish. If you decide to take part, you will sign or put a thumbprint as proof of consent. In addition, in case of an illiterate carer, a person not involved in the study and present during the consent-taking procedure will be requested to sign the consent document as a witness.

If you give consent for your child's participation in the screening of this study, I will ask some questions, and we will examine your child and ask about his/her illness. If your child is eligible to enrol in the study then we will provide you with another information sheet and describe details of the study and ask for another consent before enrolling in the main study.

We will not offer any payment for your participation in the screening. There is no cost to you other than the time you will spend by joining this study.

The healthcare provided to the child will remain the same irrespective of your decision to enrol or not enrol in the screening procedure. During the study, we will tell you if we learn any new information on risks or benefits from participation in the study.

Is there anything I need to do or avoid?

No, there is no special precautions or requirements for you or your child to participate in this study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the diagnosis of pneumonia in children in the future. The results of this study may be used for the future commercial development of new diagnostics for childhood respiratory illness. Your participation in this study will not entitle you to benefit financially from the commercial development of the product.

What are the possible disadvantages of taking part?

Participation in the screening of this study will take approximately five to ten minutes. There is no cost to you other than the time you will spend by joining this study. We do not anticipate any risks from your child's participation in the screening of this study.

What if there are any problems?

If you have a concern about any aspect of this study please contact Dr Salahuddin Ahmed; he is Co-Investigator of this study, Director Research, Projahnmo Research Foundation and PhD student at the University of Edinburgh. If you feel that you have been treated unfairly or have been hurt by joining the study, you may call Dr Salahuddin Ahmed at +88-02-55035439 (extn-102). You can also contact the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

What will happen if I don't want to carry on with the study

Your child's participation in this study is completely voluntary and you can decide not to participate in the study. Once you decide to take part in the study, you will be able to withdraw your or your child's participation at any time during the study. Declining to take part or leaving study early will involve no consequence and you and your child will continue to receive the same health care from the community clinic. However, we will not destroy the data collected up to that point.

What happens when the study is finished?

Data will be preserved without limit of time in electronic format. All study documentation will be kept for a minimum of 3 years and maximum 5 years after completion of the study. Data will be stored on the PRF-secured server at Sylhet and Dhaka in Bangladesh, on DataStore of the University of Edinburgh, UK and US direct-attached high-capacity storage server in USA. After publishing main paper and accepting of PhD thesis, sharing of data will be made available to external researchers where they can demonstrate adequate training and expertise, have provided a research protocol and they have the required ethical and privacy permissions in place and sign data sharing agreement with the University of Edinburgh and PRF. Information collected from your child and you may be used in future in designing interventions to identify and treat pneumonia cases in Bangladesh or other countries.

Will my taking part be kept confidential?

All the information we collect during the course of the screening will be kept confidential and there are strict laws which safeguard your privacy at every stage. Study researchers may ask your permission to access your medical records to carry out this research project. Hard copies of the screening form will be stored in a locked cabinet in a locked room in Projahnmo Research Foundation (PRF) office at Sylhet, Bangladesh under the supervision of the principal investigators. Only approved study personnel will have access to this information. The data collected in this screening might be used in future studies. However, your child's and your identity will remain confidential. In order to monitor and audit the study, we will ask your consent for responsible representatives from the sponsor and Projahnmo monitoring team to access your data collected during the screening, where it is relevant to you taking part in this research. As the data will be collected in Bangladesh so identifiable information will be kept in a locked cabinet in a locked room in the Projahnmo Research Foundation office in Sylhet, Bangladesh.

What will happen to the results of the study?

This study will be written up as conference presentations and publications. However, you will not be identifiable in any published results. The results of the study will be made available to study participants by arranging community meetings with parents of the children and community leaders.

Who is organising and funding the research?

This study has been organised by Projahnmo Research Foundation and sponsored by The NIHR Global Health Research Unit on Respiratory Health (RESPIRE) at the University of Edinburgh. The study is being funded by RESPIRE.

Who has reviewed the study?

The study proposal has been reviewed by National Research Ethics Committee of Bangladesh Medical Research Council, Bangladesh Ministry of Health and Family Welfare and Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board.

Patients and the public have not been involved in the development of this study. But later, they were involved and provided opinions to identify sick children and referral strategies; the study team incorporated those in the protocol.

Researcher Contact Details

If you have any further questions about the study, please contact Dr. Salahuddin Ahmed on +88-02-55035439 (extn-102). or email on:

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact

Dr. Iqbal Kabir, President, Projahnmo Research Foundation, Flat: 5D, House: 37, Road; 27, Block: A, Banani, Dhaka-1213, Bangladesh; Phone: +88-01730-095515; email:

Complaints

If you wish to make a complaint about the study, please contact:

National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

Privacy Notice

The University of Edinburgh is the sponsor for this study. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations, we must inform you of how we will use and store your personal data.

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your and your child data in the ways needed to conduct and analyse the research study.

We will use information from you and your child and/or your medical records in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your and your child information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about your child that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

CONSENT FORM FOR SCREENING

Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh

Please **initial/thumb impression** box

1. I confirm that I have read and understand the information sheet (11 Dec 2018 and Version Number 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that my child participation is voluntary and that I am free to withdraw at any time without giving any reason and without my child medical care and/or legal rights being affected. ☐
3. I give permission for the research team to access my child medical records for the purposes of this research study ☐
4. I understand that relevant sections of my child medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from the Projahnmo monitoring team or from Bangladesh Medical Research Council or other regulatory authorities where it is relevant to my child taking part in this research. I give permission for these individuals to have access to my child data and/or medical records. ☐
5. I give permission to assess my child to identify s/he is eligible for the study or not eligible for the study. ☐

Name of Person Giving Consent	Date	Signature/ Left Thumb Impression
Name of Witness if provide thumb impression	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

13.6.2 Participant information sheet and consent form for enrolment

Participant Information Sheet for Enrolment

Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Pneumonia is a leading cause of death in under-five children worldwide including Bangladesh. The majority of child deaths from pneumonia are due to either not seeking or delays in seeking medical attention. Trained frontline healthcare workers can play a key role to identify pneumonia.

The World Health Organization (WHO) guidelines, do not include listening to the chest in their algorithm for diagnosis of by frontline healthcare workers because they have limited training using standard stethoscopes.

A new type of stethoscope can listen and interpret what is heard in the chest without a person having to listen and interpret the sounds. These are called digital stethoscopes. We wish to assess whether a low-cost digital stethoscope (the 'Smartscope') developed for use in children is able to be used by frontline healthcare workers to improve the diagnosis of pneumonia in children.

Our study will include 2,426 children under five years of age who have cough and/or difficult breathing at 12 community clinics in Zakiganj and Kanaighat sub-district of Sylhet district in Bangladesh.

Why have I been invited to take part?

You have been asked to take part as your child have cough and/or difficult breathing and age of your child is below 5 years.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign or put thumbprint a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study at any time will not affect the healthcare that you and your child receive or your legal rights.

What will happen if I take part?

We screen all under-five children who attend our selected community clinics for health care. As you said, your child has a history of cough and/or breathing difficulty or we have observed that child is suffering from cough and/or breathing difficulty, so we have invited you to take part in this study.

However, if your child has been part of this study before (within the last 30 days), we will not include him/her again in this study.

I, the Community Health Care Provider (CHCP) of the Community Clinic (CC), will read out the consent form to you and explain the study procedures. If there are any questions, I will answer and ensure that you understand the research project. You will be given at least 10-15 minutes to decide whether or not to take part in the study; take longer if you wish. If you decide to take part, you will sign or put a thumbprint as proof of consent. In addition, in case of an illiterate carer, a person not involved in the study and present during the consent taking procedure will be requested to sign the consent document as a witness.

If you give consent for your child's participation in this study, I will ask some questions, and we will examine your child and ask about their symptoms. We will measure oxygen levels in the body using a pulse oximeter and record lung sounds using Smartscope. The study will last for approximately 30 minutes. Pulse oximetry measures the oxygen levels in the body using a light shone through the skin. The pulse oximeter light sensor is placed on a finger or earlobe, or in the case of an infant, across a foot. The test takes about one minute to read the oxygen levels in the blood. Lung sound recordings using Smartscope look and feel just like when a doctor uses a regular stethoscope to listen to the chest – except the Smartscope does not have tubes going into the ears of the person using the stethoscope. When the Smartscope is placed on the child's chest it can record the sounds of breathing. We will place the stethoscope on four different positions – two in front and two in back on the child's chest for a total of about 1 or 2 minutes. All the procedures will take place in the community clinic. One of our community healthcare workers will visit your home within the next fifteen days and collect a few more information about you and your child's feeding and immunization history and measure your child's weight, height/length, mid-upper arm circumference and assess the child which will take around 30 minutes.

We will not offer any payment for your participation in the study. There is no cost to you other than the time you will spend by joining this study.

The healthcare provided to the child will remain the same irrespective of your decision to enrol or not enrol in the study. Recording lung sound using Smartscope and measuring oxygen saturation using pulse oximetry will be carried out for research purposes only and that information will not be used for treatment decision-making for the child. If we find your child's oxygen level below 90% and/or any clinical signs of severe illness, then we will refer your child to Sub-district hospital or Sylhet Osmani Medical College Hospital for further assessment. In that case, we will write your child's oxygen level in medical record which will be seen by referral centre's provider. During the study, we will tell you if we learn any new information on risks or benefits from participation in the study.

Is there anything I need to do or avoid?

No, there is no special precautions or requirements for you or your child to participate in this study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the diagnosis of pneumonia in children in the future. The results of this study may be used for the future commercial development of new diagnostics for childhood respiratory illness. Your participation in this study will not entitle you to benefit financially from the commercial development of the product.

What are the possible disadvantages of taking part?

Participation in this study will take approximately one hour in total of your time including home visit by a community health worker. There is no cost to you other than the time you will spend by joining this study. These tests are safe and do not cause any harm or pain. We do not anticipate any risks from your child's participation in this study. However, if there are any incidental findings such as low oxygen level or your child develops any complications, we will arrange referral to Sub-district hospital or Sylhet Osmani Medical College Hospital and treatment free of charge.

What if there are any problems?

If you have a concern about any aspect of this study please contact Dr Salahuddin Ahmed; he is Co-Investigator of this study, Director Research, Projahnmo Research Foundation and PhD student at the University of Edinburgh. If you feel that you have been treated unfairly or have been hurt by joining the study, you may call Dr Salahuddin Ahmed at +88-02-55035439 (extn-102).

You can also contact the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

What will happen if I don't want to carry on with the study

Your child's and your participation in this study is completely voluntary and you can decide not to participate in the study. Once you decide to take part in the study, you would be able to withdraw your or your child's participation at any time during the study. Declining to take part or leaving study early will involve no consequence and you and your child will continue to receive the same health care from the community clinic. However, we will not destroy the data collected up to that point.

What happens when the study is finished?

Data will be preserved without limit of time in electronic format. All study documentation will be kept for a minimum of 3 years and maximum 5 years after completion of the study. Data will be stored on the PRF-secured server at Sylhet and Dhaka in Bangladesh, on DataStore of the University of Edinburgh, UK and US direct-attached high capacity storage server in USA. After publishing the main paper and accepting of PhD thesis, sharing of data will be made available to external researchers where they can demonstrate adequate training and expertise, have provided a research protocol and they have the required ethical and privacy permissions in place and sign a data sharing agreement with the University of Edinburgh and PRF. Information collected from your child and you may be used in future in designing interventions to identify and treat pneumonia cases in Bangladesh or other countries.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. Study researchers may ask your permission to access your medical records to carry out this research project. Hard copies of the study-related forms will be stored in a locked cabinet in a locked room in Projahnmo Research Foundation (PRF) office at Sylhet, Bangladesh under the supervision of the principal investigators. Only approved study personnel will have access to this information. The data collected in this study might be used in future studies. However, your child's and your identity will remain confidential. In order to monitor and audit the study, we will ask your consent for responsible representatives from the sponsor and Projahnmo monitoring team to access your medical records and data collected during the study, where it is relevant to you taking part in this research. As the data will be collected in Bangladesh so identifiable information will be kept in a locked cabinet in a locked room in the Projahnmo Research Foundation office in Sylhet, Bangladesh.

What will happen to the results of the study?

This study will be written up as conference presentations and publications. However, you will not be identifiable in any published results. The results of the study will be made available to study participants by arranging community meetings with parents of the children and community leaders.

Who is organising and funding the research?

This study has been organised by Projahnmo Research Foundation and sponsored by The NIHR Global Health Research Unit on Respiratory Health (RESPIRE) at the University of Edinburgh. The study is being funded by RESPIRE.

Who has reviewed the study?

The study proposal has been reviewed by National Research Ethics Committee of Bangladesh Medical Research Council, Bangladesh Ministry of Health and Family Welfare and Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board.

Patients and the public have not been involved in the development of this study. But later, they were involved and provided opinions to identify sick children and referral strategies; the study team incorporated those in the protocol.

Researcher Contact Details

If you have any further questions about the study, please contact Dr. Salahuddin Ahmed on +88-02-55035439 (extn-102). or email on:

Independent Contact Details

If you would like to discuss this study with someone independent of the study, please contact Dr Iqbal Kabir, President, Projahnmo Research Foundation, Flat: 5B, House: 37, Road; 27, Block: A, Banani, Dhaka-1213, Bangladesh; Phone: +88-01730-095515; email:

Complaints

If you wish to make a complaint about the study please contact:

National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

Privacy Notice

The University of Edinburgh is the sponsor for this study based in Bangladesh. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations we must inform you of how we will use and store your personal data.

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your and your child's data in the ways needed to conduct and analyse the research study.

We will use information from you and your child and/or your medical records in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after you and your child's information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you and your child that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

CONSENT FORM FOR ENROLMENT

Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh

Please **initial/thumb impression** box

1. I confirm that I have read and understand the information sheet (30 January 2019 and Version Number 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that my or my child participation is voluntary and that I am free to withdraw at any time without giving any reason and without my/my child medical care and/or legal rights being affected. ☐
3. I give permission for the research team to access my child medical records for the purposes of this research study ☐
4. I understand that relevant sections of my child medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from the Projahnmo monitoring team or from Bangladesh Medical Research Council or other regulatory authorities where it is relevant to my child taking part in this research. I give permission for these individuals to have access to my child data and/or medical records. ☐
5. I give permission for collecting data from my home about me and my child including my child's weight, length/height and mid-upper arm circumference. . ☐
6. I agree to my identifiable data being used for future ethically approved studies ☐
7. I agree to my anonymised data being used in future studies ☐
8. I understand that the results of this study may be used for future commercial development of products/tests/treatments and I will not benefit financially from this ☐
9. I agree to take part in the above study ☐

Name of Person Giving Consent	Date	Signature/ Left Thumb Impression
Name of Witness if provide thumb impression	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

13.6.3 Participant information sheet and consent form for FGD with carers

Participant Information Sheet for FGD with carers

Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Pneumonia is a leading cause of death in under-five children worldwide including Bangladesh. The majority of child deaths from pneumonia are due

to either not seeking or delays in seeking medical attention. Trained frontline healthcare workers can play a key role to identify pneumonia.

The World Health Organization (WHO) guidelines, do not include listening to the chest in their algorithm for diagnosis by frontline healthcare workers because they have limited training using standard stethoscopes.

A new type of stethoscope can listen and interpret what is heard in the chest without a person having to listen and interpret the sounds. These are called digital stethoscopes. We wish to assess whether a low-cost digital stethoscope (the 'Smartscope') developed for use in children is able to be used by frontline healthcare workers to improve the diagnosis of pneumonia in children.

Our study will include 2426 children under five years of age who have cough and/or difficult breathing at 12 community clinics in Zakiganj and Kanaighat sub-district of Sylhet district in Bangladesh.

Why have I been invited to take part?

You have been asked to take part in this focus group discussion as your child participated in the study, and your child's lung sounds were recorded using the Smartscope at the community clinic.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign or put thumbprint a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study at any time will not affect the healthcare that you and your child receive or your legal rights.

What will happen if I take part?

I am a research staff of Projahnmo which is a partnership of Projahnmo Research Foundation, Shimantik, icddrb, Johns Hopkins University of USA and University of Edinburgh, UK. Projahnmo has been working in this community since 2001 to improve maternal and child health. I will read out the consent form to you and explain the study procedures. If there are any questions, I will answer them and ensure that you understand the research project. You will be given at least 10-15 minutes to decide whether or not to take part in the study; take longer if you wish. If you decide to take part, you will sign or put a thumbprint as proof of consent.

If you give consent for your participation in this study, I will ask you to share your opinions about what you think about the Smartscope technology and how you would feel about the Smartscope being used to diagnose pneumonia in your child. A tape recorder will be used to record the discussion for proper transcription of the discussion. All the procedures will take place in the Projahnmo offices or a suitable place in the government office. The focus group discussion will take approximately 1 hour 15 minutes of your time.

There is no cost to you other than the time you will spend by joining this study. The healthcare provided to you and your child will remain the same irrespective of your decision to take part or not to take part in the study. This focus group discussion will be carried out for research purposes only and that information will not be used for treatment decision-making for the child. During the study, we will tell you if we learn any new information on risks or benefits from participation in the study.

Is there anything I need to do or avoid?

No, there is no special precautions or requirements for you or your child to participate in this study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the diagnosis of pneumonia in children in future. The results of this study may be used for the future commercial development of new diagnostics for childhood respiratory illness. Your participation in this study will not entitle you to benefit financially from the commercial development of the product.

What are the possible disadvantages of taking part?

Participation in this study will take approximately 1 hour and 15 minutes in total of your time. There is no cost to you other than the time you will spend by joining this group discussion. We will pay for your travel costs for your participation.

What if there are any problems?

If you have a concern about any aspect of this study, please contact Dr Salahuddin Ahmed; he is Co-Investigator of this study, Director Research, Projahnmo Research Foundation and PhD student in the University of Edinburgh. If you feel that you have been treated unfairly or have been hurt by joining the study, you may call Dr Salahuddin Ahmed at +88-02-55035439 (extn-102). You can also contact the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

What will happen if I don't want to carry on with the study

Your participation in this study is completely voluntary and you can decide not to participate in the study. Once you decide to take part in the study, you will be able to withdraw your participation at any time during the study. Declining to take part or leaving the study early will involve no consequence and you and your child will continue to receive the same health care from the community clinic. However, we will not destroy the data collected up to that point.

What happens when the study is finished?

Data will be preserved without limit of time in electronic format. All study documentation will be kept for a minimum of 3 years and maximum 5 years after completion of the study. Data will be stored on the PRF secured server at Sylhet and Dhaka in Bangladesh, on DataStore of the University of Edinburgh, UK and US direct-attached high capacity storage server in the USA. After publishing the main paper and accepting of PhD thesis, sharing of data will be made available to external researchers where they can demonstrate adequate training and expertise, have provided a research protocol and they have the required ethical and privacy permissions in place and sign a data sharing agreement with the University of Edinburgh and PRF. Information collected from you may be used in future in designing interventions to identify and treat pneumonia cases in Bangladesh or other countries.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. Hard copies of the discussion notes will be stored in a locked cabinet in a locked room in Projahnmo Research Foundation (PRF) office at Sylhet, Bangladesh under the supervision of the principal investigators. Only approved study personnel will have access to this information. The data collected in this study might be used in future studies. However, your identity will remain confidential. In order to monitor and audit the study, we will ask your consent for responsible representatives from the sponsor and Projahnmo monitoring team to access the data collected during the study, where it is relevant to you taking part in this research. As the data will be collected in Bangladesh so identifiable information will be kept in a locked cabinet in a locked room in the Projahnmo Research Foundation office in Sylhet, Bangladesh.

What will happen to the results of the study?

This study will be written up as conference presentations and publications. However, you will not be identifiable in any published results. The results of the study will be made available to study participants by arranging community meetings with parents of the children and community leaders.

Who is organising and funding the research?

This study has been organised by Projahnmo Research Foundation and sponsored by The NIHR Global Health Research Unit on Respiratory Health (RESPIRE) at the University of Edinburgh. The study is being funded by RESPIRE.

Who has reviewed the study?

The study proposal has been reviewed by National Research Ethics Committee of Bangladesh Medical Research Council, Bangladesh Ministry of Health and Family Welfare and Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board.

Patients and the public have not been involved in the development of this study. But later, they were involved and provided opinions to identify sick children and referral strategies; the study team incorporated those in the protocol.

Researcher Contact Details

If you have any further questions about the study, please contact Dr. Salahuddin Ahmed on +88-02-55035439 (extn-102). or email on:

Independent Contact Details

If you would like to discuss this study with someone independent of the study, please contact

Dr. Iqbal Kabir, President, Projahnmo Research Foundation, Flat: 5D, House: 37, Road; 27, Block: A, Banani, Dhaka-1213, Bangladesh; Phone: +88-01730-095515; email:

Complaints

If you wish to make a complaint about the study, please contact:

National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

Privacy Notice

The University of Edinburgh is the sponsor for this study based in Bangladesh. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations, we must inform you of how we will use and store your personal data.

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your and your child's data in the ways needed to conduct and analyse the research study.

We will use information from you in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible

CONSENT FORM FOR FGD OF CARERS

Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh

Please **initial/thumb impression** box

1. I confirm that I have read and understand the information sheet (11 Dec 2018 and Version Number 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my/my child medical care and/or legal rights being affected.
3. I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from the Projahnmo monitoring team or from Bangladesh Medical Research Council or other regulatory authorities where it is relevant in this research. I give permission for these individuals to have access to the data collected from me.
4. I agree to my interview being audio recorded
5. I agree to my anonymised data being used in future studies
6. I understand that the results of this study may be used for future commercial development of products/tests/treatments and I will not benefit financially from this
7. I agree to take part in the above study

Name of Person Giving Consent	Date	Signature/ Left Thumb Impression
Name of Witness if provide thumb impression	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

13.6.4 Participant information sheet and consent form for FGD with healthcare providers

Participant Information Sheet for FGD with

Healthcare providers

Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Pneumonia is a leading cause of death in under-five children worldwide including Bangladesh. The majority of child deaths from pneumonia are due

to either not seeking or delays in seeking medical attention. Trained frontline healthcare workers can play a key role to identify pneumonia.

The World Health Organization (WHO) guidelines, do not include listening to the chest in their algorithm for diagnosis by frontline healthcare workers because they have limited training using standard stethoscopes.

A new type of stethoscope can listen and interpret what is heard in the chest without a person having to listen and interpret the sounds. These are called digital stethoscopes. We wish to assess whether a low-cost digital stethoscope (the 'Smartscope') developed for use in children is able to be used by frontline healthcare workers to improve the diagnosis of pneumonia in children.

Our study will include 2426 children under five years of age who have cough and/or difficult breathing at 12 community clinics in Zakiganj and Kanaighat sub-district of Sylhet district in Bangladesh.

Why have I been invited to take part?

You have been asked to take part in this focus group discussion as you are using the Smartscope to record lung sound in under-five children.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study at any time will not have any consequence on you, and your current job, or your legal rights.

What will happen if I take part?

I am a research staff of Projahnmo which is a partnership of Projahnmo Research Foundation, Shimantik, icddrb, Johns Hopkins University of USA and University of Edinburgh, UK. Projahnmo has been working in this community since 2001 to improve maternal and child health. I will read out the consent form to you and explain the study procedures. If there are any questions, I will answer and ensure that you understand the research project. You will be given at least 10-15 minutes to decide whether or not to take part in the study; take longer if you wish. If you decide to take part, you will sign as proof of consent.

If you give consent for your participation in this study, I will ask you to share your opinions about what you think about the Smartscope technology and how you would feel about the Smartscope being used to diagnose pneumonia in a child. A tape recorder will be used to record the discussion for proper transcription of the discussion. All the procedures will take place in the Projahnmo offices or a suitable place in a government office or a community clinic. The focus group discussion will take approximately 1 hour 15 minutes of your time.

We will not offer any payment for your participation in the study. There is no cost to you other than the time you will spend by joining this study.

This focus group discussion will be carried out for research purposes. During the study, we will tell you if we learn any new information on risks or benefits from participation in the study.

Is there anything I need to do or avoid?

No, there is no special precautions or requirements for you to participate in this study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the diagnosis of pneumonia in children in the future. The results of this study may be used for the future commercial development of new diagnostics for childhood respiratory illness. Your participation in this study will not entitle you to benefit financially from the commercial development of the product.

What are the possible disadvantages of taking part?

Participation in this study will take approximately 1 hour and 15 minutes in total of your time. There is no cost to you other than the time you will spend by joining this group discussion. We will pay your travel costs for your participation.

What if there are any problems?

If you have a concern about any aspect of this study please contact Dr Salahuddin Ahmed; he is Co-Investigator of this study, Director Research, Projahnmo Research Foundation and PhD student in the University of Edinburgh. If you feel that you have been treated unfairly or have been hurt by joining the study, you may call Dr Salahuddin Ahmed at +88-02-55035439 (extn-102). You can also contact the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

What will happen if I don’t want to carry on with the study

Your participation in this study is completely voluntary and you can decide not to participate in the study. Once you decide to take part in the study, you would be able to withdraw your participation at any time during the study. Declining to take part or leaving study early will involve no consequence on your job. However, we will not destroy the data collected up to that point.

What happens when the study is finished?

Data will be preserved without limit of time in electronic format. All study documentation will be kept for a minimum of 3 years and maximum 5 years after completion of the study. Data will be stored on the PRF secured server at Sylhet and Dhaka in Bangladesh, on DataStore of the University of

Edinburgh, UK and US direct-attached high capacity storage server in USA. After publishing the main paper and accepting of PhD thesis, sharing of data will be made available to external researchers where they can demonstrate adequate training and expertise, have provided a research protocol and they have the required ethical and privacy permissions in place and sign a data sharing agreement with the University of Edinburgh and PRF. Information collected from you may be used in future in designing interventions to identify and treat pneumonia cases in Bangladesh or other countries.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. Hard copies of the discussion notes will be stored in a locked cabinet in a locked room in Projahnmo Research Foundation (PRF) office at Sylhet, Bangladesh under the supervision of the principal investigators. Only approved study personnel will have access to this information. The data collected in this study might be used in future studies. However, your identity will remain confidential. In order to monitor and audit the study, we will ask your consent for responsible representatives from the sponsor and Projahnmo monitoring team to access data collected during the study, where it is relevant to you taking part in this research. As the data will be collected in Bangladesh so identifiable information will be kept in a locked cabinet in a locked room in the Projahnmo Research Foundation office in Sylhet, Bangladesh.

What will happen to the results of the study?

This study will be written up as conference presentations and publications. However, you will not be identifiable in any published results. The results of the study will be made available to study participants by arranging community meetings with parents of the children and community leaders.

Who is organising and funding the research?

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Who has reviewed the study?

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Patients and the public have not been involved in the development of this study. But later, they were involved and provided opinions to identify sick children and referral strategies; the study team incorporated those in the protocol.

Researcher Contact Details

If you have any further questions about the study, please contact Dr. Salahuddin Ahmed on +88-02-55035439 (extn-102). or email on:

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact

Dr. Iqbal Kabir, President, Projahnmo Research Foundation, Flat: 5D, House: 37, Road; 27, Block: A, Banani, Dhaka-1213, Bangladesh; Phone: +88-01730-095515; email:

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National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

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As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your and your child's data in the ways needed to conduct and analyse the research study.

We will use information from you in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

CONSENT FORM FOR FGD OF CHCPS

Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh

Please **initial box**

1. I confirm that I have read and understand the information sheet (11 Dec 2018 and Version Number 1.1)) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my current job and/or legal rights being affected. ☐
3. I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from the Projahnmo monitoring team or from Bangladesh Medical Research Council or other regulatory authorities where it is relevant in this research. I give permission for these individuals to have access to the data collected from me. ☐
4. I agree to my interview being audio recorded ☐
5. I agree to my anonymised data being used in future studies ☐
6. I understand that the results of this study may be used for future commercial development of products/tests/treatments and I will not benefit financially from this ☐
7. I agree to take part in the above study ☐

Name of Person Giving Consent	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

13.6.5 Participant information sheet and consent form for FGD with community leaders

Participant Information Sheet for FGD with community leaders

Community use of digital auscultation to improve diagnosis of childhood pneumonia in Sylhet, Bangladesh

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Pneumonia is a leading cause of death in under-five children worldwide including Bangladesh. The majority of child deaths from pneumonia are due to either not seeking or delays in seeking medical attention. Trained frontline healthcare workers can play a key role to identify pneumonia.

The World Health Organization (WHO) guidelines, do not include listening to the chest in their algorithm for diagnosis by frontline healthcare workers because they have limited training using standard stethoscopes.

A new type of stethoscope can listen and interpret what is heard in the chest without a person having to listen and interpret the sounds. These are called digital stethoscopes. We wish to assess whether a low-cost digital stethoscope (the 'Smartscope') developed for use in children is able to be used by frontline healthcare workers to improve the diagnosis of pneumonia in children.

Our study will include 2426 children under five years of age who have cough and/or difficult breathing at 12 community clinics in Zakiganj and Kanaighat sub-district of Sylhet district in Bangladesh.

Why have I been invited to take part?

You have been asked to take part in this focus group discussion as you are respected community leader in this area or respected member of the community clinic management group.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign or put thumbprint a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study at any time will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?

I am a research staff of Projahnmo which is a partnership of Projahnmo Research Foundation, Shimantik, icddrb, Johns Hopkins University of USA and University of Edinburgh, UK. Projahnmo has been working in this community since 2001 to improve maternal and child health. I will read out the consent form to you and explain the study procedures. If there are any questions, I will answer them and ensure that you understand the research project. You will be given at least 10-15 minutes to decide whether or not to take part in the study; take longer if you wish. If you decide to take part, you will sign or put a thumbprint as proof of consent.

You may know that CHCPs of community clinics are using a digital stethoscope named ‘Smartscope’ to record lung sound of the under-five children who has cough or difficulty breathing. If you give consent for your participation in this study, I will ask you to share your opinions about what you think about the Smartscope technology and how you would feel about the Smartscope being used to diagnose pneumonia in a child. A tape recorder will be used to record the discussion for proper transcription of the discussion. All the procedures will take place in the Projahnmo offices or a suitable place in a government office or community clinic. The group discussion will take approximately 1 hour 15 minutes of your time.

We will not offer any payment for your participation in the study. There is no cost to you other than the time you will spend by joining this study.

The healthcare provided to children will remain the same irrespective of your decision to take part or not to take part in the study. This group discussion will be carried out for research purposes only and that information will not be used for treatment decision making for children. During the study, we will tell you if we learn any new information on risks or benefits from participation in the study.

Is there anything I need to do or avoid?

No, there is no special precautions or requirements for you to participate in this study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the diagnosis of pneumonia in children in the future. The results of this study may be used for the future commercial development of new diagnostics for childhood respiratory illness. Your participation in this study will not entitle you to benefit financially from the commercial development of the product.

What are the possible disadvantages of taking part?

Participation in this study will take approximately 1 hour and 15 minutes in total of your time. There is no cost to you other than the time you will spend by joining this group discussion. We will pay your travel costs to participate this group discussion.

What if there are any problems?

If you have a concern about any aspect of this study please contact Dr Salahuddin Ahmed; he is Co-Investigator of this study, Director Research, Projahnmo Research Foundation and PhD student in the University of Edinburgh. If you feel that you have been treated unfairly or have been hurt by joining the study, you may call Dr Salahuddin Ahmed at +88-02-55035439 (extn-102). You can also contact the National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

What will happen if I don't want to carry on with the study

Your participation in this study is completely voluntary and you can decide not to participate in the study. Once you decide to take part in the study, you would be able to withdraw your participation at any time during the study. Declining to take part or leaving study early will involve no consequence and you and your child will continue to receive the same health care from the community clinic. However, we will not destroy the data collected up to that point.

What happens when the study is finished?

Data will be preserved without limit of time in electronic format. All study documentation will be kept for a minimum of 3 years and maximum 5 years after completion of the study. Data will be stored on the PRF secured server at Sylhet and Dhaka in Bangladesh, on DataStore of the University of Edinburgh, UK and US direct-attached high capacity storage server in USA. After publishing the main paper and accepting of PhD thesis, sharing of data will be made available to external researchers where they can demonstrate adequate training and expertise, have provided a research protocol and they have the required ethical and privacy permissions in place and sign a data sharing agreement with the University of Edinburgh and PRF. Information collected from you may be used in future in designing interventions to identify and treat pneumonia cases in Bangladesh or other countries.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. Hard copies of the discussion note will be stored in a locked cabinet in a locked room in Projahnmo Research Foundation (PRF) office at Sylhet, Bangladesh under the supervision of the principal investigators. Only approved study personnel will have access to this information. The data collected in this study might be used in future studies. However, your identity will remain confidential. In order to monitor and audit the study we will ask your consent for responsible representatives from the sponsor) and

Projahnmo monitoring team to access your data collected during the study, where it is relevant to you taking part in this research. As the data will be collected in Bangladesh so identifiable information will be kept in locked cabinet in a locked room in the Projahnmo Research Foundation office in Sylhet, Bangladesh.

What will happen to the results of the study?

This study will be written up as conference presentations and publications. However, you will not be identifiable in any published results. The results of the study will be made available to study participants by arranging community meetings with parents of the children and community leaders.

Who is organising and funding the research?

This study has been organised by Projahnmo Research Foundation and sponsored by The NIHR Global Health Research Unit on Respiratory Health (RESPIRE) at the University of Edinburgh. The study is being funded by RESPIRE.

Who has reviewed the study?

The study proposal has been reviewed by National Research Ethics Committee of Bangladesh Medical Research Council, Bangladesh Ministry of Health and Family Welfare and Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board.

Patients and the public have not involved in the development of this study. But later they involved and provided opinion to identify sick children and referral strategy; the study team incorporated those in the protocol.

Researcher Contact Details

If you have any further questions about the study, please contact Dr. Salahuddin Ahmed on +88-02-55035439 (extn-102). or email on:

Independent Contact Details

If you would like to discuss this study with someone independent of the study, please contact Dr Iqbal Kabir, President, Projahnmo Research Foundation, Flat: 5B, House: 37, Road; 27, Block: A, Banani, Dhaka-1213, Bangladesh; Phone: +88-01730-095515; email:

Complaints

If you wish to make a complaint about the study please contact:

National Research Ethics Committee of Bangladesh Medical Research Council (BMRC), BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh, Telephone: +880-2-9848396, Fax: +880-2-9848820; Email: info@bmrc.org

Privacy Notice

The University of Edinburgh is the sponsor for this study based in Bangladesh. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations, we must inform you of how we will use and store your personal data.

As a university, we use personally identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to participate in research. This means that when you agree to take part in a research study, we will use your and your child's data in the ways needed to conduct and analyse the research study.

We will use information from you in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your and your child's information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

CONSENT FORM FOR FGD OF COMMUNITY LEADERS

Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh

Please **initial/thumb impression** box

1. I confirm that I have read and understand the information sheet (11 Oct 2018 and Version Number 1.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care and/or legal rights being affected. ☐
3. I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from the Projahnmo monitoring team or from Bangladesh Medical Research Council or other regulatory authorities where it is relevant in this research. I give permission for these individuals to have access to the data collected from me. ☐
4. I agree to my interview being audio recorded ☐
5. I agree to my anonymised data being used in future studies ☐
6. I understand that the results of this study may be used for future commercial development of products/tests/treatments and I will not benefit financially from this ☐
7. I agree to take part in the above study ☐

Name of Person Giving Consent	Date	Signature/ Left Thumb Impression
Name of Witness if provide thumb impression	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

13.7 Data collection tools

13.7.1 Screening form

This form is to be completed for all under-5 children in the community clinic by CHCP					
1. Address and identification information					
1.01	Community clinic name and code				
1.02	Child's name				
1.03	Mother's name				
1.04	Child's date of birth		|__|__|/|__|__|/ |__|__|__|__| dd mm yyyyy		
1.05	Child age (if DOB is not known)		|__|__| months		
1.06	Child's sex		Male.................................. 1 Female..........................2		
1.07	CHCP's Name & Code				
1.08	Date and Time of screening		|__|__|/|__|__|/ |__|__|__|__| dd mm yyyyy	|__|__|: |__|__| hh mm	

2. Screening			
	Inclusion criteria		
2.01	Is the child's age between 2 to 59 months?	Yes...................................... 1 No 2	
2.02	Does the child have history of cough?	Yes...................................... 1 No.......................................2	
2.03	Does the child have observed cough?	Yes...................................... 1 No.......................................2	

2.04	Does the child have history of difficult breathing?	Yes.................................... 1 No................................2	
2.05	Does the child have observed difficult breathing?	Yes.................................... 1 No................................2	
2.06	Does the child fulfill the inclusion criteria for digital auscultation study? *[If 2.01=1 AND (2.02=1 OR 2.03=1 OR 2.04=1 OR 2.05=1)]*	Yes.................................... 1 No................................2	**If No → 2.09 (No)**
	Exclusion criteria		
2.07	Is the child severely ill and needs immediate referral?	Yes.................................... 1 No................................2	**If Yes → 2.09 (No)**
	Instruction: Please show the Digital stethoscope device (Smartscope) and ask the carer whether the child has been examined with this device within last 30 days.		
2.08	Has the child enrolled in digital auscultation study within last 30 days?	Yes.................................... 1 No................................2	**If Yes → 2.9 (No)**
2.09	Is the child eligible for enrolment in digital auscultation study? *[If 2.06=1 AND 2.07=2 AND 2.08=2]*	Yes.................................... 1 No................................2	→ 3.00 end interview but assess and provide treatment according to

			national guideline
	Instruction: Please provide and explain the patient information sheet and consent form and record the question below.		
2.10	Has the caregiver provided consent in digital auscultation study?	Yes...................................... 1	→ record 3.00 and Go to Form DA2
		No 2	→ record 3.00 and stop for the study but assess and provide treatment according to national guideline

3.00	End time of screening	|___|___|: |___|___| hh mm

13.7.2 Assessment and lung sound recording form

This form is to be completed for children age 2-59 months who will be eligible and consented for digital auscultation study in the community clinic by CHCP.

1. Address and identification information—from child card														
1.01	Upazila name and code													
1.02	Union name and code													
1.03	Village name and code													
1.04	Bari name and code													
1.05	Household name													
1.06	Community clinic name and code													
1.07	Child's PID													
1.08	Child's name													
1.09	Mother's name													
1.10	Mother's Current ID						-				-		-	
1.11	Mother's Permanent ID						-				-		-	

1.12	Father's name								
1.13	Phone number *(if mother does not have then father, if father does not have then any household member's)*		|___|___|___|-|___|___|___|___|___|___|___|___|						
1.14	Child's date of birth		|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy						
1.15	Child age (if date of birth is not known)		|___|___| months						
1.16	Child's sex		Male……………………1 Female......................2						
1.17	CHCP's Name & Code								
1.18	Date and starting time		|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy		|___|___|:|___|___| hh mm				

No	Questions	Responses	Skip
1.19	Respondent	Mother of the child……………………..1 Grandmother of the child……………..2 Aunt of the child……………………….3 Sister of the child……………………..4 Father of the child……………………..5 Grandfather of the child……………....6 Uncle of the child……………………..7 Brother of the child…………………….8 Other(specify)_________________...9	
1.20	Visit Outcome (please record/circle after completion of the assessment)	Completed……………………………..1 Incomplete……………………………..2 Refused………………………………..6 Other (specify)_________________...7	 →9.00 →9.00

2. Child morbidity history			
2.01	What are the signs of illness your child suffering from? *Instruction: Please write the signs and code illness from below list. Please record the duration of each mentioned signs/symptoms in the last column.*		
	Illness history	**Code**	**Duration (Days)**
	a. ________________________________	: |___|___|	|___|___|
	b. ________________________________	: |___|___|	|___|___|
	c. ________________________________	: |___|___|	|___|___|
	d. ________________________________	: |___|___|	|___|___|
	e. ________________________________	: |___|___|	|___|___|

Code list for illness of child (2.01): Cough—01, Fever – 02, Breathing difficulty – 03, Chest indrawing – 04, Body was cold to touch – 05, Ear pain – 06, Ear discharge – 07, Less movement - 08, Inability to drink – 09, Bulge fontanelle – 10, Stiff neck – 11, Convulsions – 12, Unconscious – 13, Vomits everything-14, Runny nose – 15, Others– 77					
	Instruction: Now ask carer whether the child has currently any of the following symptoms, circle 1 for yes, 2 for no and 9 for DK; write the duration of the "Yes" symptoms in days in last column. If mother already mentioned "cough or breathing difficulty", copy the duration from 2.01				
	Illness history	**Y**	**N**	**DK**	**Duration (Days)**
2.02	Cough	1	2	9	|____|___|
2.03	Chest indrawing (inward pulling below ribs during inspiration)	1	2	9	|____|___|
2.04	Breathing difficulty (i.e., anything abnormal with breathing including abnormal noises)	1	2	9	|____|____|

2.05. History of medication (ask the carer)			**Skip**
2.05.1	Over the last seven days has the child been given medicine?	Yes……………………...1 No ………………………2 Don't know…………....3	 →3.01 →3.01
2.05.2	Over the last seven days has the child been given antibiotics for this illness?	Yes……………………..1 No……………………...2 Don't know…………….3	 →3.01 →3.01

2.05.3	If Yes, please complete the following for each antibiotic given. Write 'Don't know' and code 999 if respondent cannot tell the antibiotic name.			
	Name and code	Route	Duration (days)	
a.	|__|__|__|	Oral……….1 Injection…...2	|__|__|	
b.	|__|__|__|	Oral……….1 Injection…...2	|__|__|	
c.	|__|__|__|	Oral……….1 Injection…...2	|__|__|	

No	Questions	Responses	Skip
3. Child assessment ***Instruction: Now conduct an assessment of the child and record the findings below***			
3.01	Did you (CHCP) examine the child?	Yes…………………………1 No…………………………..2	→4.01
3.02	If no, what is the reason?	Too sick to examine……..1 Uncooperative……………2 Refused……………………3 Other cause (Specify)_____________.7	→9.00 →9.00 →9.00 →9.00

4. Fast breathing, chest indrawing and observed cough		
	Assessment	**Findings**

4.01	Child's age group (from Q1.14/ 1.15)	2-<12month…Group-1 ≥12month……Group-2		
4.02	a. Count respiratory rate for 1 complete minute and record in the box b. If fast breathing for age group (Q 4.01), count again* *Fast breathing Criteria: ≥50 breaths/min for age Group 1 (2-<12 mo) ≥40 breaths/min for age Group 2 (≥12 mo)	|___|___| br/min |___|___| br/min	FAST BREATHING *must be fast breathing on BOTH respiratory rate counts	Yes..1 No…2 If No, skip to 4.04
4.03	*If the child has fast breathing then mention:* Does the child awake at rest or awake and agitated or asleep?		Awake at rest……….1 Awake and agitated..2 Asleep………………3	

4.04	Chest indrawing (inward pulling below ribs during inspiration)	Yes.......................1 No............................2	
4.05	Observed cough	Yes.......................1 No.........................2	

5. Respiratory danger signs			
	Assessment	**Findings**	
5.01	Stridor (high-pitched noise during inspiration)	Yes......................1 No.......................2	If any of the danger sign is present, refer the child to Sub-district Hospital or Sylhet Osmani Medical College Hospital
5.02	Grunting ('uh' sound during end expiration)	Yes......................1 No.......................2	
5.03	Head nodding (head moving up and down with respiration)	Yes.....................1 No.......................2	
5.04	Tracheal tugging (inward pulling of tissue of neck during inspiration)	Yes.....................1 No.......................2	
5.05	Nasal flaring (consistent and clear outward movement of nares during inspiration)	Yes.....................1 No.......................2	
5.06	Intercostal retractions (inward pulling of tissue between ribs during inspiration)	Yes......................1 No.......................2	

2	**Sound recording using digital stethoscope (Please see picture about sequence of sound recording)**			
2.01	Start time of sound recording			|___|___|: |___|___| hh mm
2.02	Did you record lung sound?	**Yes**	**No**	
a.	Position 1: child's left back	1	2	
b.	Position 2: child's right back	1	2	
c.	Position 3: child's left front (over the heart)	1	2	
d.	Position 4: child's right front	1	2	
2.03	End time of sound recording			|___|___|: |___|___| hh mm
2.04	If you could not record sound in all the four positions, please indicate why (for entry program: if NO in any of 2.02 a-d; if	Child uncooperative ………………………..1 Caregiver withdrew consent…………….2 Stethoscope malfunctioned……………..3 CHCP missed/CHCP's error …………....5 Other (please indicate)…………………..7		

<table>
<tr><td></td><td>all YES then skip this question)</td><td></td></tr>
<tr><td></td><td colspan="2">If QDA3_2.02 a-d=2 AND 2.04=3, then skip to QDA3_2.07</td></tr>
<tr><td>2.05</td><td>Patient's overall status during recording of lung sound

(for data entry system: if any one yes in 2.02 a-d then this question will be applicable)</td><td>Cooperative and quiet throughout 1
Cooperative but vocalizing 2
Initially cooperative but became uncooperative (agitated but NO crying).....................3
Initially cooperative but became uncooperative(crying)........................4
agitated but not crying........................5
Not cooperative throughout (crying)......6</td></tr>
<tr><td>2.07</td><td>Smartscope device code</td><td>|___|___|___||___|___|___|</td></tr>
</table>

3.	**Oxygen saturation assessment**		
3.01	Were you able to measure oxygen saturation of the child?	Yes..........................1 No............................2	→ **6.00**
3.02	Indicate patient site of the recorded measurement	Finger ....1 Thumb.......................2 Toe...........................3	
3.03	Record Oxygen saturation in room air	_____ I _____ I _____ %	
If Oxygen saturation is <90%, referral the children to the Upazila Health Complex.			

6. Temperature and weight

	Assessment		Findings	
6.01	Temperature (axillary - right)	|___|___|___|.|___| °F	Temperature ≥99.5^0F	Yes…1 No….2
6.02	Temperature (axillary - left)	|___|___|___|.|___| °F		
6.03a	Child weight		|___|___| . |___| kg	
	Instruction: Skip to Q6.04 if you can take child weight only. If you cannot, first take child weight with the carer and then take weight of the carer and write below			
6.03b	Child weight with carer		|___|___|___| . |___| kg	
6.03c	Weight of the carer		|___|___|___| . |___| kg	
6.04	MUAC of the child		|___|___| . |___| cm	
6.05	Length/ height of the child		|___|___|___| . |___| cm	

7. Treatment given by the CHCP			
7.01	Did you (CHCP) refer the child or provide home treatment?	Refer……………………………….1 Provide home treatment……….2	→8.01
7.02	Did you (CHCP) prescribe any medicine?	Yes……………………………….1 No………………………………..2	→8.01
7.03	Did you prescribe antibiotic? (If yes, then provide details below)	Yes……………………………….1 No………………………………..2	→8.01

7.04	**Drug Name**	**Given**	**Times/day**	**Duration (Days)**
a.	Amoxicillin	Yes......................1 No...................... 2	|__|	|__|__|
b.	Co-trimoxazole	Yes......................1 No...................... 2	|__|	|__|__|
c.	Azithromycin	Yes......................1 No...................... 2	|__|	|__|__|
d.	Cefixime	Yes......................1 No...................... 2	|__|	|__|__|
e.	Other (Please specify):________	Yes......................1 No...................... 2	|__|	|__|__|
f.	Other (Please specify):________	Yes......................1 No...................... 2	|__|	|__|__|

8.01	Is the child suffering from any congenital anomaly?	Yes..........................1 No..........................2	

9.00	End time of assessment/Interview	|___|___| hh |___|___| mm

13.7.3 Sound file transfer information form

This form is to be completed by FRA/FRO/FRM/Study Physician for lung sound file transfer information of enrolled children in digital auscultation study				
1. Address and identification information				
1.01	Child's PID			
1.02	Child's name			
1.03	Mother's name			
1.04	Mother's Permanent ID		- - -	
1.05	Date and starting time of lung sound recording		|__|__|/|__|__|/ dd mm |__|__|__|__| yyyy	|__|__|: |__|__| hh mm
1.06	Name and code of FRA/FRO/FRM/ SP/MO			Staff Code:
1.07	Date and time of lung sound transfer		|__|__|/|__|__|/ dd mm |__|__|__|__| yyyy	|__|__|: |__|__| hh mm

2. Sound file transfer information				
2.01	a.	Position 1: Sound recorded?	Yes ....1 No 2	→ 2.02

	b.	Position 1: Sound transferred?	Yes …………………1 No ………..……….2	→ 2.02
	c.	Sound file name of Position 1		
2.02	a.	Position 2: Sound recorded?	Yes …………………1 No ………..……….2	→ 2.03
	b.	Position 2: Sound transferred?	Yes …………………1 No ………..……….2	→ 2.03
	c.	Sound file name of Position 2		
2.03	a.	Position 3: Sound recorded?	Yes …………………1 No ………..……….2	→ 2.04
	b.	Position 3: Sound transferred?	Yes …………………1 No ………..……….2	→ 2.04
	c.	Sound file name of Position 3		
2.04	a.	Position 4: Sound recorded?	Yes …………………1 No ………..……….2	→ 3.00
	b.	Position 4: Sound transferred?	Yes …………………1 No ………..……….2	→ 3.00
	c.	Sound file name of Position 4		

3.00	End time	|___|___|: |___|___| hh mm

13.7.4 Listening panel sound classification form

Part A: This form (DA-L) will be filled up by listening panel member

1	**Identification information**	
11	Child ID	|___|___|-|___|___|___|___|___|___|
	Child ID	|___|___|-|___|___|___|___|___|___|
12	Listener's Code (this will autogenerate from login system)	|___|___|
13	Listener level	1st listener 2nd listener 3rd listener
14	Date of assessment (this will autogenerate from server by login date)	|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy
15	Time of entry (this will autogenerate from server by login date)	|___|___| 24 hours

2	**Assessment of lung sound at four positions**	
101	Is position 1 sound record available? (the sound file will add here from DA3b data file)	Yes=1 No=2 >>> **SKIP TO 201**
102	Position 1: Patient's left back (select one)	1. no wheeze and no crackle 2. wheeze only (no crackle) 3. crackle only (no wheeze) 4. wheeze and crackle

		5. unable to assess due to patient agitation/crying or other recording quality issue: **SKIP TO 105**	
103	Any transmitted upper respiratory sounds at patient's left back position	a. Sturter b. stridor c. vocalizations d. audible wheeze	YES=1 NO=2 YES=1 NO=2 YES=1 NO=2 YES=1 NO=2
104	Confidence of position 1 assessment	Confident Not confident	1 2
	In 102 if response is any of 1 or 2 or 3 or 4 then skip to 201		
105	Please check why position 1 recording were not interpretable	a. due to patient movement b. due to patient agitation/crying/ vocalizations c. due to a recording issue with the device	Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9
201	Is position 2 sound record available? (the sound file will add here from DA3b data file)	Yes=1 No=2 >>> **SKIP TO 301**	
202	Position 2: Patient's right back (select one)	1. no wheeze and no crackle 2. wheeze only (no crackle) 3. crackle only (no wheeze) 4. wheeze and crackle 5. unable to assess due to patient agitation/crying or other recording quality issue : **SKIP TO 205**	
203	Any transmitted upper respiratory sounds at	a. Sturter b. stridor	YES=1 NO=2 YES=1 NO=2

	patient's right back position	c. vocalizations d. audible wheeze	YES=1 NO=2 YES=1 NO=2
204	Confidence of position 2 assessment	Not confident Confident	1 2
	In 202 if response is any of 1 or 2 or 3 or 4 then skip to 301		
205	Please check why position 2 recording were not interpretable	a. due to patient movement b. due to patient agitation/crying/ vocalizations c. due to a recording issue with the device	Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9
301	Is position 3 sound record available? (the sound file will add here from DA3b data file)	Yes=1 No=2 >>> **SKIP TO 401**	
302	Position 3: Patient's left front (select one)	1. no wheeze and no crackle 2. wheeze only (no crackle) 3. crackle only (no wheeze) 4. wheeze and crackle 5. unable to assess due to patient agitation/crying or other recording quality issue : **SKIP TO 305**	
303	Any transmitted upper respiratory sounds at patient's left front position	a. Sturter b. stridor c. vocalizations d. audible wheeze	YES=1 NO=2 YES=1 NO=2 YES=1 NO=2 YES=1 NO=2
304	Confidence of position 3 assessment	Not confident Confident	1 2
	In 302 if response is any of 1 or 2 or 3 or 4 then skip to 401		

305	Please check why position 3 recording were not interpretable	a. due to patient movement b. due to patient agitation/crying/ vocalizations c. due to a recording issue with the device	Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9
401	Is position 4 (right front) sound record available? (the sound file will add here from DA3b data file)	Yes=1 No=2 >>> **SKIP TO 501**	
402	Position 4: Patient's right front (select one)	1. no wheeze and no crackle 2. wheeze only (no crackle) 3. crackle only (no wheeze) 4. wheeze and crackle 5. unable to assess due to patient agitation/crying or other recording quality issue : **SKIP TO 405**	
403	Any transmitted upper respiratory sounds at patient's right front position	a. Sturter b. stridor c. vocalizations d. audible wheeze	YES=1 NO=2 YES=1 NO=2 YES=1 NO=2 YES=1 NO=2
404	Confidence of position 4 assessment	Not confident Confident	1 2
	In 402 if response is any of 1 or 2 or 3 or 4 then skip to 501		
405	Please check why position 4 recording were not interpretable	a. due to patient movement b. due to patient agitation/crying/ vocalizations	Yes=1 No=2 Unsure=9 Yes=1 No=2 Unsure=9 Yes=1 No=2

		c. due to a recording issue with the device	Unsure=9
501	End time		

6	Final assessment of lung sound	
601	Final assessment: CONFIRM (select one) Auto generate using algorithm	1. no wheeze and no crackle 2. wheeze only (no crackle) 3. crackle only (no wheeze) 4. wheeze and crackle 5. unable to assess due to patient agitation/crying or other recording quality issue

After completion of **Part A** by two paediatricians, Q601 will be compared and if not match then will be send to 3rd reader and then **Part B** will be fill up by data system.

Part B: This part will be automatically filled-in after the listeners complete their assessment.

4	Listening panel final conclusion	
4.1	Final listening panel conclusion	◯ no wheeze and no crackle ◯ wheeze only (no crackle) ◯ crackle only (no wheeze) ◯ wheeze and crackle ◯ unable to assess due to patient agitation/crying or other recording quality issue
4.2	Final listening panel conclusion: agreement	◯ determined by primary listeners (i.e., first 2 listeners)

		◯ determined by any primary listener and arbiter (3rd reader) ◯ determined by arbiter (3rd reader)

Algorithm for 401:

Applicable if at least one sound file available**.**

1. **Not interpretable:**
   a. 102=5/NULL and 202=5/NULL and 302=5/NULL and 402=5/NULL
2. **No wheeze No crackles:**
   a. 102=1/NULL and 202=1/NULL and 302=1/NULL and 402=1/NULL
3. **Wheeze and crackle**

a. 102=4 or 202=4 or 302=4 or 402=4 or

b. 102=2 and (202=3 or 302=3 or 402=3) or

c. 102=3 and (202=2 or 302=2 or 402=2) or

d. 202=2 and (102=3 or 302=3 or 402=3) or

e. 202=3 and (102=2 or 302=2 or 402=2) or

f. 302=2 and (202=3 or 102=3 or 402=3) or

g. 302=3 and (202=2 or 102=2 or 402=2) or

h. 402=2 and (202=3 or 302=3 or 102=3) or

i. 402=3 and (202=2 or 302=2 or 102=2) or

4. Wheeze only:

A. 102=2 and (202=1 or 2 or 302=1 or 2 or 402=1 or 2) or

B. 202=2 and (102=1 or 2 or 302=1 or 2 or 402=1 or 2) or

C. 302=2 and (202=1 or 2 or 102=1 or 2 or 402=1 or 2) or

D. 402=2 and (202=1 or 2 or 302=1 or 2 or 102=1 or 2)

5. Crackles only:

A. 102=3 and (202=1 or 3 or 302=1 or 3 or 402=1 or 3) or

B. 202=3 and (102=1 or 3 or 302=1 or 3 or 402=1 or 3) or

C. 302=3 and (202=1 or 3 or 102=1 or 3 or 402=1 or 3) or

D. 402=3 and (202=1 or 3 or 302=1 or 3 or 102=1 or 3)

13.7.5 Socioeconomic status, confounders and treatment outcome form

This form is to be completed by CHW between 8 and 14 days of enrolment at child home.															
1. Address and identification information—from Projahnmo child register															
1.01	Upazila name and code														
1.02	Union name and code														
1.03	Village name and code														
1.04	Bari name and code														
1.05	Household name and code														
1.06	Child's PID														
1.07	Child's name														
1.08	Mother's name														
1.09	Mother's Current ID						-				-		-		
1.10	Mother's Permanent ID						-				-		-		
1.11	Child's date of birth		|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy												
1.12	Child's sex		Male................................ 1												

			Female............................ 2	
1.13	CHW's Name & Code			| | | | |
1.14	Date and starting time		|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy	|___|___|:|___|___| hh mm

No	Questions	Responses	Skip
1.15	Respondent	Mother of the child (PREFERRED)...........1 Grandmother of the child........................2 Aunt of the child...................................3 Sister of the child..................................4 Father of the child..................................5 Grandfather of the child...........................6 Uncle of the child...................................7 Brother of the child.................................8 Other (specify)___________________.......9	
1.16	Visit Outcome (record this after end of interview)	Completed...1 Incomplete..2 No respondent present.............................3 Migrated out..4 The child died..5 Refused...6 Not visited, specify the cause..................7 ________________________________	 →13.00 →13.00 →13.00 →13.00 →13.00

No	Questions	Responses	Skip

2. Demographic information

2.01a	What is date of birth of the child's mother? (Write down from register)	|___|___|/|___|___|/ dd mm |___|___|___|___| yyyy	
2.01b	If the date of birth is not available then ask: How old is the mother of the child?	I _____ I _____ I years	
2.02	Has the mother of the child ever attended school/madrasha?	Yes, School…………...1 Yes, Madrasha……….2 Yes, both……………...3 Neither………………...4	→2.04
2.03	What is the highest class the mother of the child completed?	Class I _____ I _____ I	
2.04	What is the working status of the mother?	Housewife……………..1 Working mother………2 Other (specify)………..7	→2.06

2.05	What is the occupation of the mother?	**Physical work:** Unskilled laborer……..11 Skilled worker………...12 **Non-physical work:** Business/trade……….13 Service holder………..14 Professional…………..15 Other (specify)………..77	
2.06	How old is the father of the child?	I _____ I _____ I years	
2.07	Has the father of the child ever attended school/ madrasha?	Yes, School……………1 Yes, Madrasha………..2 Yes, both………………3 Neither…………………4	→2.09
2.08	What is the highest class the father of the child completed?	Class I _____ I _____ I	

2.09	What is the occupation of the father?	**Physical work:** Unskilled laborer.......11 Skilled worker...........12 **Non-physical work:** Business/trade..........13 Service holder...........14 Professional.............15 Work abroad (Skilled /unskilled)................16 Religious leader........17 Other (specify)..........77	
2.10	How many rooms in this household are used for sleeping?	Room number I _____ I _____ I	
2.11	How many members live in your household?	Number I _____ I _____ I	
2.12	How many under-five children live in your household?	Number I _____ I _____ I	
2.13	How many people do live in your household last night?	Number I _____ I _____ I	

3. Socioeconomic information

3.01	Main material of the floor -Record observation	**Natural floor** Earth/Sand………………………..11 **Rudimentary Floor** Wood Planks/Bamboo…………..21 **Finished Floor** Ceramic Tiles/ Mosaic…………..33 Cement……………………………34 **Other (specify)**…………………77	
3.02	Main material of the roof - Record observation	**Natural roofing** Thatch/palm leaf…………………...2 **Rudimentary roofing** Palm/bamboo……………………..22 Wood planks………………………23 **Finished roofing** Tin…………………………………31 Wood………………………………32 Ceramic Tiles……………………..34 Cement…………………………....35 **Other (specify)**…………………..77	

3.03	Main material of the exterior walls - Record observation	**Natural Walls** Cane/Palm/Trunks………………...12 Dirt…………………………………..13 **Rudimentary walls** Bamboo with mud………………...21 Stone with mud…………………...22 Cardboard…………………………25 **Finished walls** Tin…………………………………...31 Cement……………………………..32 Stone with lime/Cement…………..33 Bricks………………………………34 Wood Planks/Shingles…………....36 **Other (specify)**…………………....77	
3.04	What kind of toilet facility do members of your household usually use?	**Flush or Pour Flush Toilet** Flush to piped sewer system…….11 Flush to septic tank………………12 Flush to pit latrine…………………13 Flush to somewhere else………...14 Flush, don't know where…………15 **Pit Latrine** Ventilated improved pit latrine……21 Pit latrine with slab………………...22 Pit latrine without slab/open pit…..23 **Composting toilet………………..**31 **Hanging toilet/hanging latrine…**51 **No facility/bush/field…………….**61 **Other (specify)……………………**77	

3.05	What is the main source of drinking water for members of your household?	**Piped water** Piped into dwelling………………...11 Piped to yard/plot………………….12 Public tap/standpipe………………13 **Tube well/ Hand pump or borehole**…………………………...21 Dug Well…………………………….31 Water from spring…………………41 Rain water………………………….51 Tanker truck………………………..61 Cart with small tank………………71 Surface water (river/ dam/lake/pond/ stream/canal/ irrigation channel)...81 Bottled water……………………….91 **Other (specify)**……………………77	

3.06	Does your household have? *Please ask one by one.*			**Yes**	**No**	
		a	Electricity	1	2	
		b	Solar Electricity	1	2	
		c	Radio	1	2	
		d	Television	1	2	
		e	Mobile telephone	1	2	
		f	Land phone	1	2	
		g	Refrigerator	1	2	
		h	Almirah/Wardrobe	1	2	
		i	Electric fan	1	2	
		j	CD/DVD/VCD player	1	2	
		k	Water pump	1	2	
		l	IPS/generator	1	2	

		m	Air conditioner	1	2	
		n	Computer/Laptop	1	2	
		o	Washing machine	1	2	
		p	Camera	1	2	
		q	Watch/clock	1	2	
		r	Pressure cooker	1	2	
		s	Bed/Cot	1	2	
		t	Sofa	1	2	
		u	Rickshaw/Van	1	2	
		v	Bicycle	1	2	
		w	Motorcycle or Motor scooter	1	2	

4. Feeding and illness history			
4.01	Was this child ever breastfed?	Yes……………………………….1 No……………………………….…2	 →4.05
4.02	Is this child still breastfeeding?	Yes……………………………….1 No……………………………….…2	→4.04
4.03	How many months of age did the child breastfeed?	|_____ I _____ I months	
4.04	Until how many months of age was this child exclusively breastfed (Received nothing other than breast milk and medicine; not even a drop of water)?	|_____ I _____ I months If the child was still exclusively breastfeeding…………………..77	

4.05	Did the child suffer from diarrhoea within last two weeks?	Yes……………………………….1 No………………………………..2	→4.07
4.06	If yes, how long was the child suffering from diarrhoea?	|____|____| days	
4.07	Has the child received a Vitamin-A capsule in the past year? *[Please show the sample of Vitamin A formulation to the caregiver]*	Yes…………………………….1 No………………………………2 Don't know……………………3	
4.08	Has zinc supplementation been given to the child within last two weeks? *[Please show the sample of zinc formulation to the caregiver]*	Yes…………………………….1 No………………………………2 Don't know……………………3	
4.09	Has the child received any Iron syrup or micronutrient supplementation in last six months? *[Please show the sample of Iron syrup and micronutrient packet to the caregiver]*	Yes…………………………….1 No………………………………2 Don't know……………………3	

5. Indoor air pollution exposure

5.01	Do you or anyone else smoke cigarettes, bidis or hookah inside your house, or inside a house where the child frequently goes?	Yes ....1 No...2	 →5.03
5.02	On a typical day over the last month, how long do you think the child was exposed to someone while they were smoking, either indoors or outdoors?	Every day, for at least 30 minute……………………………..1 Every day, but only briefly………2 Some days, for at least 30 minutes......................................3 Only occasionally........................4 Not at all ....5 Don't Know 7	
5.03	What type of fuel does your household mainly use for cooking?	Electricity ....01 LPG ....02 Natural gas ....03 Biogas......................................04 Kerosene ....05 Coal, lignite...............................06 Charcoal ....07 Wood ....08 Straw/shrubs/grass...................09 Agricultural crop........................10 Animal dung.............................11 No food cooked in household ...12 Other (specify) 77	 →5.06

5.04	Is the cooking usually done in the house, in a separate building, or outdoors? *READ THE ANSWERS*	In the same room of the house ... 1 In a separate room of the same building .... 2 In a separate building .... 3 Outdoors 4	
5.05	How often does the child go into the cooking area while food is being cooked?	Every day .... 1 More than once per week .... 2 At least once per week .... 3 Occasionally .... 4 Never 5	
5.06	What type of fuel does your household mainly use for lighting?	Electricity .... 1 Solar Electricity .... 2 Kerosene .... 3 Biogas .... 4 No light used in household .... 5 Other (specify) 7	

6. Vaccination information			
6.1	Vaccination card available during this visit?	Yes .... 1 No 2	→6.4
6.2	Does this child ever been vaccinated?	Yes .... 1 No 2	→7.01 →7.01

6.4	**If any date of vaccination written in the EPI card then first circle "Y" in the box and record the date. If no date is recorded in EPI card circle "N"**					
	[1st visit]	**[2nd visit]**	**[3rd visit]**	**[4th visit]**	**[5th visit]**	**[6th visit]**
BCG	6.41. Y / N					

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7. Care seeking history						
7.01	Did you seek treatment from any other facility or provider after visiting community clinic for this episode of illness?	Yes……………………………………1 No……………………………………..2				→7.05
7.02	Where did you go for treatment of your child other than community clinic?			Yes	No	
		a.	Sylhet Osmani Medical College Hospital	1	2	
		b.	Upazila Health Complex	1	2	
		c.	Other government facility (MCWC/UH&FWC)	1	2	
		d.	Private hospital/Clinic	1	2	
		e.	MBBS Doctor's chamber	1	2	
		f.	Unqualified doctor's chamber	1	2	
		g.	Pharmacy/drug seller	1	2	
		h.	Others	1	2	

7.03	Did the provider prescribe any medicine?	Yes…………………………………….1 No……………………………………...2			
7.04	What medicines were received by the child? (Ask carer and check prescription/Strip of drug/ Bottle. If carer does not know the name of medicine, then write 'Don't know and code 999)		**Name of Medicine & Code**	**Times/ Day**	**Duration (Days)**
		a.	________________________ |__|__|__|	|___|	|__|__|
		b.	________________________ |__|__|__|	|___|	|__|__|
		c.	________________________ |__|__|__|	|___|	|__|__|
		d.	________________________ |__|__|__|	|___|	|__|__|
		e.	________________________ |__|__|__|	|___|	|__|__|

7.05	The treatment provided at Community Clinic or at referral centre or other places, did the child take medicine(s) as per recommendation with – (1) full dose and duration, (2) partial dose or not full duration or (3) did not take medicine at all?	Yes, full dose completed……………………………1 No, partial dose completed……………………………2 No, the child did not receive medication…………………………...3	

8.	**Child current morbidity history**				
	Instruction: Now ask carer whether the child has currently any of the following symptoms, circle 1 for yes, 2 for no and 9 for DK; write the duration of the "Yes" symptoms in days in last column.				
	Illness history	**Y**	**N**	**DK**	**Duration (Days)**
8.01	Cough	1	2	9	|____|___|
8.02	Chest indrawing (inward pulling below ribs during inspiration)	1	2	9	|____|___|

8.03	Breathing difficulty (i.e., anything abnormal with breathing including abnormal noises)	1	2	9	|____|____|

9. Child assessment ***Instruction: Now conduct an assessment of the child and record the findings below***			
9.01	Did you (CHW) examine the child?	Yes....................................1 No 2	→10.01
9.02	If no, what is the reason?	Too sick to examine ....1 Uncooperative..................2 Refused...........................3 Absent.............................4 Child admitted in hospital .5 Other cause (Specify)______________.7	→13.00

10. Fast breathing, chest indrawing and observed cough					
	Assessment			**Findings**	
10.01	Child's age group (from Q1.11)	2-<12 month...............Group-1 ≥12 month.................Group-2			
10.02	a. Count respiratory rate for 1 complete minute and record in the box b. If fast breathing for age group (Q 10.01), count again*		|___|__| br/min	FAST BREATHING *must be fast breathing on BOTH respiratory rate counts	Yes..........1 No.............2 If 'No', skip to 10.04

	|___|__| br/min *Fast breathing Criteria: Group-1 ≥50 breaths/min for age Group 1 (2-<12 mo) Group-2 ≥40 breaths/min for age Group 2 (≥12 mo)		
10.03	*If the child has fast breathing then mention:* Does the child awake at rest or awake and agitated or asleep?	Awake at rest............1 Awake and agitated ....2 Asleep.........3	
10.04	Chest indrawing (inward pulling below ribs during inspiration)	Yes............1 No..............2	
10.05	Observed cough	Yes............1 No..............2	

11. Respiratory danger signs			
	Assessment	**Findings**	
11.01	Stridor (high-pitched noise during inspiration)	Yes ....1 No............................2	If anyone is yes, refer the child to Sub-district Hospital or Sylhet Osmani Medical
11.02	Grunting ('uh' sound during end expiration)	Yes ....1 No............................2	
11.03	Head nodding (head moving up and down with respiration)	Yes ....1 No............................2	

11.04	Tracheal tugging (inward pulling of tissue of neck during inspiration)	Yes .... 1 No 2	College Hospital
11.05	Nasal flaring (consistent and clear outward movement of nares during inspiration)	Yes .... 1 No 2	
11.06	Intercostal retractions (inward pulling of tissue between ribs during inspiration)	Yes .... 1 No 2	

12. Anthropometric measurements: Please measure weight, MUAC and height/length following SOP, and three times each and record below:					
Measurements			**1st measurement**	**2nd measurement**	**3rd measurement**
12.01a	Weight		|___|___| . |___| kg	|___|___| . |___| kg	|___|___| . |___| kg
	Instruction: Skip to Q12.02 if you can take child weight only. If you cannot, first take child weight with the carer and then take weight of the carer and write below:				
12.01b	Child weight with carer		|___|___|___| . |___| kg	|___|___|___| . |___| kg	|___|___|___| . |___| kg
12.02c	Weight of the carer		|___|___|___| . |___| kg	|___|___|___| . |___| kg	|___|___|___| . |___| kg

12.02	MUAC		|___|___|___| mm	|___|___|___| mm	|___|___|___| mm
12.03	Length/ height		|___|___|___| . |___| cm	|___|___|___| . |___| cm	|___|___|___| . |___| cm

13.00	End time of Interview	|___|___|:|___|___| hh mm

13.7.6 FGD topic guide

13.7.6.1 FGD topic guide for carers (mothers and fathers)

Topic Guides	
1	When you took your child to Community Clinic recently, the health worker used a digital stethoscope that looks like this (show the device). Do you know that is it different than the regular stethoscope?
2	Which one do you think is better for diagnosing your child's pneumonia? The regular stethoscope of the digital one? Why?
3	Can you tell based on your experience how did you help the health worker when she was examining your child with the prototype digital stethoscope?
4	How is your experience regarding the prototype digital stethoscope being used on the child? Probe positive experiences: Which issues did you like?
5	Probe negative experiences: Which issues did you not like?
6	[If any problem in using prototype digital stethoscope is reported] Did the health worker try to solve the problems? If yes, how did she do this? Did she face any difficulty in receiving help?
7	What additional changes to the prototype digital stethoscope, in your opinion, would improve the device further? Probe: What else would make the prototype digital stethoscope more user-friendly?
8	We want to know your opinion on different aspects of the prototype digital stethoscope comparing it with the regular stethoscope: (ask this question to each respondent separately)

	• Ease of putting and keeping the device on the child's chest • Time taken for recording lung sound
9	Finally, do you want to add anything else regarding the use of the prototype digital stethoscope in diagnosing childhood pneumonia? Any suggestions?

13.7.6.2 FGD topic guide for community health care providers

Topic Guides	
1	Primary question: How long have you been using prototype digital stethoscope? Do you use it on all children or only on certain children as per the directives? Approximately, on how many children do you use it daily?
2	Training: Have you received any training to use the prototype digital stethoscope? How long was the training? Where was the training held? Who were the trainers? How was the training? (Probe: Which aspects of the training were good? Which aspects could be improved? Do you need further training on this?)
3	How is your experience of using the prototype digital stethoscope on children? Probe positive experiences: Which issues did you like while using the prototype digital stethoscope on children?
4	Probe negative experiences: Which issues did you not like while using the prototype digital stethoscope?
5	[If they report any problem in using the prototype digital stethoscope]

	Did you try to solve the problems? If yes, how did you do this? Who helped you? Did you face any difficulty in receiving help?
6	Was there any arrangement to supervise whether you are using the prototype digital stethoscope correctly? What was the arrangement? How effective was the arrangement? Were there any gaps in the supervision? Please share your experience in this regard.
7	Did the use of the prototype digital stethoscope bring any change in your work? What are the changes? Probe: Changes in the storage location, cleaning facility, etc. Did you face any difficulty due to the changes?
8	What additional changes to the prototype digital stethoscope, in your opinion, would improve the device further? Probe: What else would make the prototype digital stethoscope more user-friendly?
9	Please share based on your experience, what additional considerations (for example, change in the device, training, or anything else) are needed if we want to scale-up digital auscultation to other Community Clinics?
10	We want to know your opinion on different aspects of prototype digital stethoscope comparing it with the regular stethoscope: (ask this question to each respondent separately) • Ease of putting and keeping the device on the child’s chest • Ease of recording lung sound • Durability • Battery life and charging

	• Time taken for recording lung sound • Ease of keeping it clean • Ease of storage
11	Finally, do you want to add anything else regarding the use of the prototype digital stethoscope in diagnosing childhood pneumonia? Any suggestions?

13.7.6.3 FGD topic guide for community leaders

Topic Guides	
1	Primary question: For how long has the prototype digital stethoscope been used? Is it being used on all children or the directive is to use it only on certain children?
2	Which one do you think is better for diagnosing the child's pneumonia? The regular stethoscope of the digital one? Why?
3	Training: Have health workers received any training to use prototype digital stethoscopes? How long was the training? Where was the training held? Who were the trainers? How was the training? Did you receive any complaints regarding the training?
4	How, do you think, is mothers' experience regarding the use of prototype digital stethoscopes on their children? Probe positive experiences: Which issues did they like?
5	Probe negative experiences of mothers: Which issues did they not like?
6	[If any problem in using prototype digital stethoscope is reported]

	Did you play any role to solve the problems? If yes, how did you do this? Who helped you? Did you face any difficulty in receiving help?
7	Was there any arrangement to supervise whether you are using the prototype digital stethoscope correctly? What was the arrangement? How effective was the arrangement? Were there any gaps in the supervision? Please share your experience in this regard.
8	What additional changes to the prototype digital stethoscope, in your opinion, would improve the device further? Probe: What else would make the prototype digital stethoscope more user-friendly?
9	Please share based on your experience, what additional considerations (for example, change in the device, training, or anything else) are needed if we want to scale up digital auscultation to other Community Clinics?
10	Finally, do you want to add anything else regarding the use of the prototype digital stethoscope in diagnosing childhood pneumonia? Any suggestions?

13.8 Ethics approval

13.8.1 Ethics approval from ACCORD Medical Research Ethics Committee (AMREC)

accord

Academic and Clinical Central Office for Research and Development

NHS Lothian

ACCORD Medical Research Ethics Committee (AMREC)

Waverley Gate
2 - 4 Waterloo Place
Edinburgh
EH1 3EG

Telephone: 0131 465 5473/5679

22 November 2018

Professor Aziz Sheikh
University of Edinburgh
Usher Institute of Population Health Sciences and Informatics
Old Medical School, Teviot Place
Edinburgh
EH8 9AG

Dear Professor Sheikh

Study title: **Improving paediatric pneumonia diagnosis using digital auscultation**
REC reference: **18-HV-051**
IRAS project ID:

Thank you for submitting documents for review by several emails for the application title above. I can confirm the REC has received the documents listed below.

Confirmation of review

On behalf of the Committee, I am pleased to confirm that the Committee raised no material ethical concerns in the context of what the Committee have had an opportunity to review and consider, albeit the Committee cannot provide an opinion on matters that are the proper remit of authorities in Bangladesh.

Documents reviewed

The final list of documents reviewed by the Committee is as follows:

Document	*Version*	*Date*
REC Application Form		16 July 2018
Research protocol or project proposal	Version 1.2	02 February 2018
Ethics Approval Letter - Bangladesh Medical Research Council		12 June 2018
Clinical Engineering Device Approval Digital Stethoscope Letter		21 April 2017
Participant information sheet (PIS) and Consent Form - Enrolment	Version 1	11 October 2018
Participant information sheet (PIS) and Consent Form - Surveillance	Version 1	11 October 2018
Participant information sheet (PIS) and Consent Form, Focus Group Discussion - Carers	Version 1	11 October 2018
Participant information sheet (PIS) and Consent Form - Focus Group Discussion – Community Leaders	Version 1	11 October 2018
Participant information sheet (PIS) and Consent Form - Focus Group Discussion – Service Providers	Version 1	11 October 2018
Data collection form – Digital Auscultation DA1 screening	Version 1	11 October 2018
Data collection form – Digital Auscultation DA2 clinical assessment	Version 1	11 October 2018
Data collection form – Digital Auscultation DA3 lung sound recording information	Version 1	11 October 2018
Data collection form – Digital Auscultation DA4 SES confounders	Version 1	11 October 2018
Data collection form – Digital Auscultation DA-L Listener	Version 1	11 October 2018
Data collection form – Digital Auscultation DA-S Surveillance	Version 1	11 October 2018
Data collection form – Digital Auscultation FGD Topic Guides	Version 1	11 October 2018
University of Edinburgh - Clinical Trial Liability Insurance		31 July 2018
University of Edinburgh - Public Liability		24 July 2018
University of Edinburgh - Professional Indemnity Insurance		31 July 2018
Summary CV for Chief Investigator (CI) - Professor Aziz Sheikh		
Summary CV for student - Dr Salahuddin Ahmed		
Summary CV for Academic supervisor - Prof Harish Nair		
Summary CV for Academic supervisor - Professor Steve Cunningham		

With the Committee's best wishes for the success of this project.

18-HV-051 Please quote this number on all correspondence

Yours sincerely,

Lindsay Murray
Chair

ACCORD Medical Research Ethics Committee (AMREC)

Email: sandra.wyllie@nhslothian.scot.nhs.uk

13.8.2 Ethics approval from the National Research Ethics Committee of Bangladesh Medical Research Council

বাংলাদেশ চিকিৎসা গবেষণা পরিষদ
Bangladesh Medical Research Council
BMRC

Ref: BMRC/NREC/2016-2019/690

Date: 12/06/2018

National Research Ethics Committee

Registration Number: 096 30 01 2018.

Principal Investigator:
Dr. Dipak Kumar Mitra
Research Scientist
Projahnmo Research Foundation
Apt: 5D, House # 37, Road # 27
Banani, Block-A, Dhaka-1213.

Title of the Project:
"Community use of digital auscultation to improve diagnosis of paediatric pneumonia in Sylhet, Bangladesh"

Duration of Project: 2 Years

Budget: BDT- 86,80,989/-
In words: Eighty Six Lac Eighty Thousand Nine Hundred Eighty Nine Taka Only.

Subject: Ethical Clearance

With reference to your application on the above subject, this is to inform you that above mentioned Research Title has been registered and approved by the National Research Ethics Committee (NREC).

(Dr. Mahmood-uz-jahan)
Director

N.B: You are requested to follow the guidelines as mentioned at page two.

BMRC Bhaban, Mohakhali, Dhaka-1212, Bangladesh.
Phone: +88 02 9848396, PABX : +88 02 9849311, Fax : +88 02 9848820, E-mail: info@bmrcbd.org. Web: www.bmrcbd.org

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THE ETHICAL GUIDELINES TO BE FOLLOWED BY THE PRINCIPAL / CO-INVESTIGATORS

- ❒ The rights and welfare of individual volunteers are adequately protected.
- ❒ The methods to secure informed consent are fully appropriate and adequately safeguard the rights of the subjects (in the case of minors, consent is obtained from parents or guardians).
- ❒ The Investigator(s) assume the responsibility of notifying the National Research Ethics Committee (NREC) if there is any change in the methodology of the protocol involving a risk to the individual volunteers.
- ❒ To report immediately to the NREC if any evidence of unexpected or adverse reaction is noted in the subjects under study.
- ❒ Principal Investigator will facilitate supervision of the project by the BMRC authority time to time.
- ❒ This approval is subject to Principal Investigator's reading and accepting the BMRC ethical principles and guidelines currently in operation.
- ❒ You are requested to submit a report to the BMRC half yearly and after completion of the research work.

Checked by: