Evaluation of pulse oximetry as a tool to prevent childhood pneumonia related morbidity and mortality

Study Report

Regional Technical Resource Centre for Health Technology Assessment,
Achutha Menon Centre for Health Science Studies,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum - 695011

In Collaboration with

Health Technology Assessment in India (HTAIn),

Department of Health Research (DHR), Ministry of Health and Family Welfare (MoH&FW), Government of India

September 2019

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Suggested citation:

Moosan H, Stanley A, Raman Kutty V, Soman B, Abraham P. Evaluation of pulse oximetry as a tool to prevent childhood pneumonia related morbidity and mortality. Regional Technical Resource Centre for Health Technology Assessment, Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum and Department of Health Research, Ministry of Health and Family Welfare, Government of India. 2019

Acknowledgements

We would like to extend our sincere gratitude to the Secretaries of DHR, for selecting SCTIMST, Trivandrum as an HTA Resource Hub, assigning projects and building the team's capacity to carry out the work of HTAIn, DHR.

We are also deeply thankful to the Additional Secretary, Joint Secretary and Deputy Secretaries of the DHR for the continuous administrative support.

We gratefully acknowledge the work of our former Additional Chief Secretary, Sri Rajeev Sadanandan IAS, for his unwavering commitment to establish a centre for HTA in Kerala.

We would like to thank Dr. Rajan N. Khobragade, Principal Secretary, Health and Family Welfare, Government of Kerala for his unconditional motivation and support for the centre and its activities.

We would also like to thank Sri Keshvendra Kumar IAS, State Mission Director, National Health Mission, Kerala for his continued support and partnership with the Regional Technical Resource Centre.

We thank the members of the Technical Appraisal Committee, HTA In, for their constructive suggestions throughout this study.

We sincerely thank Dr. Santhosh Kumar, Professor and Head, Department of Paediatrics and Dr. Purushothaman K K, Paediatrician, Government Medical College, Thrissur, for their valuable inputs related to the protocol of diagnosing and management of childhood pneumonia.

We would also like to thank Dr. Nita Vijayan, State Programme Manager (RCH) for taking the time to discuss concerns on childhood pneumonia, current standards of prognostic tools available in India, and the issues around the treatment and length of stay for children with severe pneumonia.

We express our sincere thanks Dr. Sreehari M. State Nodal Officer, CH & RBSK for his inputs on the different types of oximetry devices used to treat and monitor different stages of pneumonia.

We would like to thank Dr Malkeet Singh, Junior Health Economist, Department of Health Research, for his technical support in developing the decision tree model for this study.

We thank Dr Mohammad Ameel, Senior Consultant, Healthcare Technologies (Medical Devices) at National Health Systems Resource Centre for his inputs on the pulse oximeter device specification.

We would like to express our heartfelt gratitude to Dr Kavitha Rajsekar, Scientist E, DHR & HTAIn Co-Ordinator, without whose feedback and constant encouragement this report could not have been completed. And finally we would like to express our sincere thanks and acknowledgement to the team at Department of Health Research (DHR) especially Dr. Oshima Sachin (Scientist D) and Ms. Jyotsna Naik (Scientist C), Government of India, for their unwavering support and guidance throughout the study.

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Executive Summary

Introduction:

Globally, pneumonia is the leading cause of death in children <5 years of age. Despite interventions being available, it is estimated that pneumonia is responsible for 15% of childhood deaths worldwide. In the absence of appropriate prognostic tools at the frontline, currently recommended World Health Organization (WHO) guidelines for integrated management of childhood illness (IMCI) often lead to an overuse of antibiotics and the under-referral of patients with severe pneumonia who require hospital care.

The present recommended strategy for diagnosis and prognosis of pneumonia is IMCI tool for professional health workers at health facilities and iCCM tool for community health workers. Currently, identification of these IMCI symptoms remains inconsistent and unreliable among health-care personnel. The use of pulse-oximetry devices (used to measure the oxygen level in the blood) in community health-care settings has been proposed as a method to identify hypoxic children at risk of treatment failure.

Objectives:

- To determine the effectiveness (i.e. sensitivity, specificity, positive and negative predictive values) and cost effectiveness of pulse oximetry devices in screening of childhood pneumonia by health workers in resource poor settings (LMICs).
- To identify whether children have lower mortality rates, lower morbidity, and shorter length of stay where pulse oximeters are used to inform diagnosis and treatment compared with where pulse oximeters are not used.

Methods:

A systematic literature review (SLR) was conducted with PICO as population consisting of patients aged 0-5 years with pneumonia in LMIC's, Intervention was IMCI +Pulse Oximetry and the comparator was IMCI alone. The outcomes was diagnostic accuracy of

pulse oximetry, cost per QALY gained, and incremental deaths averted with the introduction of pulse oximetry. The SLR was conducted using electronic databases such as Database of Cochrane, PubMed, Web of Science, ProQuest, Google Scholar and WHO Global Health Library, with no language restrictions. A decision tree model was developed for estimating the Incremental Cost Effectiveness Ratio (ICER). For populating the model we required data pertaining to disease progression, care-seeking, health-care, prognostic and cost parameters. In addition to data gathered from SLR, we did a scoping review wherever necessary to extract data for the decision model.

We extracted the costs of the IMCI implementation in Indian primary healthcare settings from previous studies. The average number of hospital visits (outpatient and inpatient) were calculated including the associated out of pocket health expenditure for each category. We indexed the amount to the current INR rate using inflation tools. Pulse oximeters which fit the predefined specifications were shortlisted and their net average cost was taken for costing purposes. The training cost is derived from consultation with the program implementers.

Results:

The evidence from the systematic review was overwhelmingly in favour of the use of pulse oximetry along with the existing guidelines. Out of the seven studies which were eventually shortlisted, 6 of them favoured the use of PO. When it came to costing, the cost of Pulse oximetry per patient per year is INR 0.36. We did a budget impact analysis, which showed that if we were to provide a pulse oximeter to all the PHC's in India, the cost of the roll-out of pulse oximeters would be INR 64,125,000. The cost of training frontline health workers to use PO is INR 26,334,000. The overall cost of roll-out of pulse oximeters in PHC's would amount to INR 90,459,000. In absolute terms, the introduction of pulse-oximetry devices to IMCI is estimated to result in annual reductions in pneumonia deaths in India. The deaths averted per year for PO2 within a cohort of 10000 pneumonia cases would be 367 if the sensitivity is 85% and 213 if the sensitivity is 70%. Owing to the large under-five populations (128 million) India could significantly reduce the mortality due to childhood pneumonia by the introduction of PO into the existing IMCI.

Recommendations:

- IMCI+PO is a cost saving prognostic tool as compared to IMCI alone provided there is supplementary oxygen availability.
- IMCI should be the basic prognostic tool for childhood pneumonia but PO is beneficial in the referral of cases.
- Pulse oximetry in general may be used to measure oxygen saturation in cases wherever required. Among outpatients with pneumonia, oxygen saturations <90% were associated with increased morbidity and mortality.
- A hospital admission threshold of <92% would be safer and clinically better justified.
- All severe cases, irrespective of availability of Pulse oximeter, should be referred to a tertiary care facility for expert management.

Evaluation of pulse oximetry as a tool to prevent childhood pneumonia related morbidity and mortality

1. Introduction

Pneumonia is an infection of the lower respiratory tract that involves the airways and parenchyma with consolidation of the alveolar spaces. Lobar pneumonia describes pneumonia localized to one or more lobes of the lung. Atypical pneumonia describes patterns typically more diffuse or interstitial than lobar pneumonia. Infectious agents that commonly cause community-acquired pneumonia vary by age1. Most common causes are respiratory syncytial virus (RSV) in infants, other respiratory viruses (parainfluenza viruses, influenza viruses, human meta-pneumovirus, adenoviruses) in children younger than 5 years old, and Mycoplasma pneumonia in children older than age 5 years. Streptococcus pneumonia is the most common bacterial cause of lobar pneumonia, and occurs in children of any age outside the neonatal period[1]. M. pneumoniae and Chlamydophila pneumoniae are principal causes of atypical pneumonia.

Globally, pneumonia is the leading cause of death in children <5 years of age[2]. Despite interventions being available, it is estimated that pneumonia is responsible for 15% of childhood deaths worldwide. Reductions in annual mortality remain modest, with nearly 950,000 under-5 year olds dying of pneumonia in 2013. Immunizations have brought down the incidence of pneumonia caused by Haemophilus influenza type b, and S. pneumoniae. But despite the unprecedented rate of Haemophilus influenzae type B (Hib) and pneumococcal vaccine (PCV) introduction, achieving high levels of coverage in developing countries is still challenging. Therefore, in regions where vaccine introduction and scale-up lags behind other countries, improved access to diagnosis and treatment is crucial.

A crucial component of improving pneumonia outcomes is the early identification of patients at risk of treatment failure and the timely provision of supportive care[3]. However, in the absence of appropriate prognostic tools at the frontline, currently recommended World Health Organization (WHO) guidelines for integrated management

of childhood illness (IMCI) often lead to an overuse of antibiotics and the under-referral of patients with severe pneumonia who require hospital care[4,5].

IMCI is a global strategy designed to strengthen health systems, implement clinical guidelines in health facilities, and implement community based interventions that might include care by community health workers (CHW). By using simple diagnostic algorithms based on a small number of clinical signs CHWs can detect and treat diseases like pneumonia to some extent. The most recent 2015 technical update of IMCI guidelines defines non-severe pneumonia as the presence of fast breathing or chest in-drawing or both, which is treatable with oral antibiotics. Severe pneumonia is defined as cough or difficulty breathing in the presence of danger signs, and requires referral to a hospital or health facility for injectable antibiotics or other supportive care such as oxygen therapy. Currently, identification of these IMCI symptoms remains inconsistent and unreliable among community health-care workers or carers without clinical training. Therefore, improved prognostic and diagnostic tools for case-management are necessary to substantially reduce pneumonia-associated morbidity and mortality[6]. Hypoxaemia and malnutrition are strong predictors of mortality in children who are hospitalized for pneumonia. This has led to increasing support for the use of oxygen therapy and monitoring oxygen saturation in the management of severe cases. It is estimated that 15% of children who are hospitalized for pneumonia have hypoxaemia[7] (oxygen saturation, or SpO2, of <90%) and that around 1.5 million children with severe pneumonia require oxygen treatment each year. Misclassification of a disease as pneumonia can also lead to the potential overuse of Amoxicillin thereby leading to antibiotic resistance.

The use of pulse-oximetry devices (used to measure the oxygen level in the blood) in community health-care settings has been proposed as a method to identify hypoxic children at risk of treatment failure. Unfortunately, current treatment coverage remains low, and, more importantly, most childhood pneumonia deaths result from a lack of, or delay in, accurate diagnosis. These devices may be particularly beneficial at the frontline given that they require little training and reduce the reliance on clinical symptoms. The current pulse-oximetry systems are also quick, non-invasive and require minimal infrastructure. As international organisations are investing in programmes to increase pulse oximeter use in low-income settings, more research is needed on the optimal use

of pulse oximeters (eg, appropriate oxygen saturation thresholds), and how pulse oximeter use affects referral and admission rates, length of stay, resource utilisation and health outcomes. We therefore reviewed the evidence on the effectiveness, and cost-effectiveness of pulse oximetry devices introduction alone and when combined with the existing IMNCI guidelines.

2. Methods:

a. Objectives

This study attempted to address the following questions:

c. "What is the effectiveness (i.e. sensitivity, specificity, positive and negative predictive values) and cost effectiveness of pulse oximetry devices in screening of childhood pneumonia by health workers in resource poor settings (LMICs)?"

d. "Do children have lower mortality rates, lower morbidity, and shorter length of stay where pulse oximeters are used to inform diagnosis and treatment compared with where pulse oximeters are not used?"

b. The PICO

Table 1. Details of PICO used for the study

Population • Patients aged 0-5 years with pneumonia
Intervention • IMCI + Pulse Oximetry
Comparator • IMCI
Outcome • Diagnostic Accuracy of Pulse Oximetry   ○ (Sensitivity, Specificity, Positive and Negative Predictive Values) • Referral and admission rates, length of stay, resource utilisation and health outcomes • Cost per QALY gained/ DALY averted • Incremental deaths averted with the introduction of pulse oximetry by community health workers in community settings

c. Types of studies considered

The types of studies considered for the review included the following:

For the effectiveness we considered randomized controlled trials, field/ community trials and quasi-randomized trials. The cost effectiveness data was extracted from full economic evaluations (studies in which both the costs and outcomes of the alternatives were examined and in which a comparison of two or more interventions or case alternative was undertaken) including trial-based, non-trial based (i.e. observational studies), simulation-based, decision model, trial-based model and partial economic evaluations such as cost analysis, costing of interventions with or without comparator.

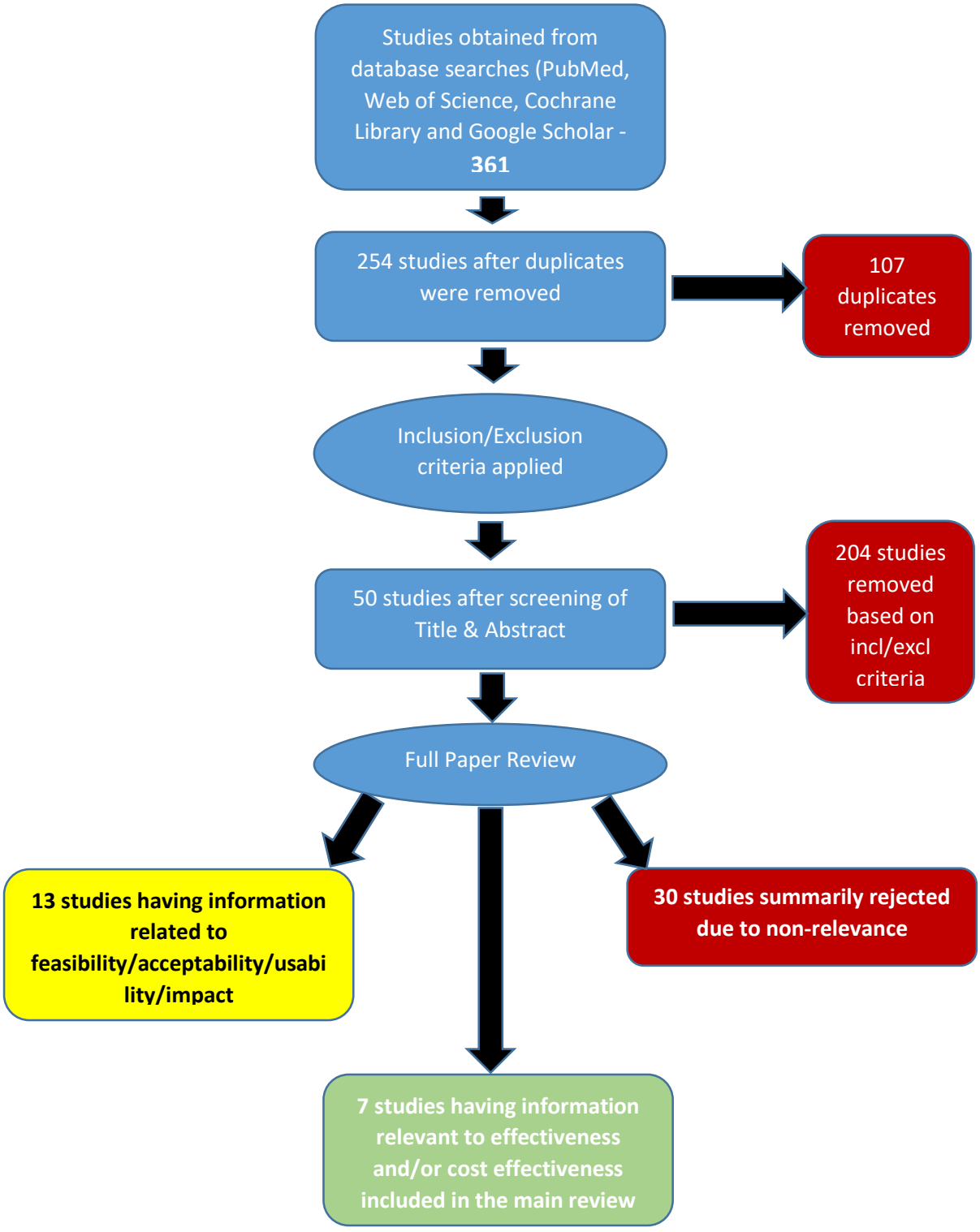
The population selected were patients aged 0-5 years with pneumonia in LMIC's. Intervention was the use of Pulse oximetry alone or in combination with the existing IMNCI guidelines. The comparators were IMCI alone or the existing local pneumonia management guideline. In other words, we included studies with at least one intervention group in which a pulse oximeter reading was taken and at least one control group in which pulse oximetry was not used.

The outcomes of interest included diagnostic accuracy of pulse oximetry, referral and admission rates, and length of stay, resource utilisation and health outcomes, cost per QALY gained/ DALY averted, incremental deaths averted, difference in mortality and morbidity, referral rates and length of stay in critical care where pulse oximeters are used to inform diagnosis and treatment compared with where pulse oximeters are not used.

We systematically searched the Database of Cochrane, PubMed, Web of Science, ProQuest, Google Scholar and WHO Global Health Library, with no language restrictions. Study references were checked. Websites of non-governmental organisations, health organisations and development organisations were searched for unpublished reports using the terms 'pulse oximeter' and 'pulse oximetry'. Topic experts were contacted for additional materials. Studies that were not relevant based on title/abstract were excluded. We read the remaining studies' full texts and excluded those not fulfilling the inclusion criteria. All full texts were read by a second person, and if inclusion was uncertain, a third. We extracted data using a tailored Cochrane data collection form and assessed risk of bias using the Cochrane ACROBAT tool[8]. We intended to calculate risk ratios, mean differences and CI's, and if possible pool data within subgroups and conduct

a meta-analysis. However, due to the small number of studies and the study design/outcome variability this was not possible. Instead we narratively describe the evidence using a structured approach while drawing insights where possible, a standard strategy in such situations.

Figure 1: PRISMA Chart



3. Results of the Systematic Review

a. Search Results

We found 361 reports initially, which underwent removal of duplicates and application of the inclusion and criteria, followed by screening of all titles and abstracts. The shortlisted potentially relevant studies amounted to 50. They were divided into three categories based on their relevance to the PICO. Studies with serious and critical level of risk of bias were not included in the final summary. Most of the studies fell into the moderate risk category. Seven studies, were closely aligned (see PRISMA flow diagram) to the PICO, and thirteen studies were relatively associated with the PICO. Finally 20 studies were considered for inclusion. We've added them to the analysis as supportive evidence (see Table 2).

b. Risk of Bias

Table 6 and 7 in the addendum of this document demonstrates the risk of bias for each study included.

c. Disease Progression

In 2013, Rudan et al.[9] estimated that in India alone, the number of new episodes (incidence) of community–acquired pneumonia in children 0–4 years of age is 127,960,004. The number of new severe episodes (according to WHO's definition) that required hospitalizations was 4,066,541. The estimates of the number of child deaths attributable to pneumonia was 388,144.

By 2015, Farooqui et al.[10] projected that there were 3.6 million (3.3–3.9 million) episodes of severe pneumonia and 0.35 million (0.31–0.40 million) all cause pneumonia deaths in children younger than 5 years in India. In addition, to the overall figure, state-wise breakup of data suggested that the states that merit special mention include Uttar Pradesh where 18.1% children reside but contribute 24% of pneumonia cases and 26% pneumonia deaths, Bihar (11.3% children, 16% cases, 22% deaths) Madhya Pradesh (6.6% children, 9% cases, 12% deaths), and Rajasthan (6.6% children, 8% cases, 11% deaths). In the latest Pneumonia and Diarrhoea Progress Report 2018, the number of Pneumonia deaths in children under 5 years has come down to 158,176.

The proportion of pneumonia severe on day 1 was 5% (2–10%) according to Pitt et al.[11] The mean duration of non-severe illness before recovery was 3 days (2–4 days)[12]. The mean duration of non-severe illness before progression to severe illness was 10 days (9–11 days)[12]. The mean duration of severe illness before recovery was 4 days (3–5 days)[13]. Mean duration of severe illness before death was 7 days (6–8 days)[14]. The proportion of bacterial versus viral infection was 15% bacterial (10-25%) and 85% viral (75–90%)[15].

d. Care-seeking and health-care parameters

The mean duration of illness before care seeking in the case of non-severe illness was 3 (2–4) days and 0.75 (0.5–1) days in the case of severe illness[14]. Foran M et al.[16] found that oximetry data changed clinical management in all observed cases of hypoxemia and several cases of normoxemia, leading to application of supplemental oxygen, initiation of further diagnostic testing, prolongation of inpatient stay, or expedited discharge home. According to McCollum et al., the availability of oximetry appeared to have increased the referral rate for severely hypoxaemic children without chest indrawing or danger signs from 0% to 27.2%. In the absence of oximetry, if the relevant World Health Organization (WHO) guidelines published in 2014 had been applied, 390/568 (68.7%) severely hypoxaemic children at study health centres and 52/84 (61.9%) severely hypoxaemic children seen by community health workers would have been considered ineligible for referral[17,18].

The Pneumonia & Diarrhea Progress Report 2018 states that in India, 73% of patients with pneumonia were taken to an appropriate healthcare provider. The probability of community-based treatment curing non-severe bacterial case was 0.925 (0.90–0.95)[19] and the probability of treatment with amoxicillin curing severe case if it adhered to the prescription (based on treatment failure rates of patients with hypoxia at baseline) was 0.65 (0.6–0.7). However the optimal dosing recommendation for amoxicillin remains unclear with limited pharmacological and clinical evidence[20].

e. Prognostic parameters

Clinical signs alone or in combination are not suitable to diagnose hypoxaemia[21]. According to Fu LY et al.[22] the inclusion of oximetry data improved the predictive ability at baseline, 12 hours, and 24 hours. The ability to predict failure after 12 hours of

observation with oximetry data was similar to the predictive ability after 24 hours without pulse oximetry data.

The sensitivity of IMCI was 0.55 (0.5–0.6)[23] whereas the sensitivity of pulse oximetry with IMCI was 0.85 (0.8–0.9)[24]. Pulse oximetry misclassified notably fewer well children than did the WHO algorithm (4% vs 35%)[24]. Pulse oximetry and the WHO algorithm together (SATWHO) detected 99% and 87% of pneumonic ALRI and radiologic pneumonias, respectively, and both methods detected 94% of all cases of pneumonic and non-pneumonic ALRI diagnosed clinically. No single clinical sign can perform as well as pulse oximetry for predicting hypoxia in children with severe pneumonia[25].

The adherence of community health workers to management guidelines especially the dosing and referral guidelines in non-severe prognosis (IMCI) is 0.55 (0.5–0.6)[26] and 0.65 (0.6–0.7) in case of severe prognosis (IMCI). The general perception is that a physical tool would increase the likelihood of adherence, hence for pulse oximetry use it is set at a range of 65% to 85%.

f. Sensitivities and specificities based on thresholds of hypoxaemia[27]

Hypoxaemia definitions varied from <92% to 95%. According to Majumdar et al., raising the admission threshold to 92% entails 1 additional hospitalization for every 14 patients discharged. Among outpatients with pneumonia, oxygen saturations<90% were associated with increased morbidity and mortality[28]. Their results indicated a hospital admission threshold of <92% to be safer and clinically better justified.

Table 2. Sensitivity, Specificity, Positive Predictive Value & Negative Predictive Value of Pulse oximetry to diagnose pneumonia

Saturation level	N	Died or Critical Care (%)	OR (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
SpO2 <88%	(n=69)	36.2	3.3 (1.9-5.7)	29.8	88.5	36.2	85.2

SpO2 ≤90%	(n=131)	29.8	2.7 (1.7-4.5)	46.4	76.0	29.8	86.6
SpO2 ≤92%	(n=187)	26.7	2.6 (1.6-4.3)	59.5	64.2	26.7	87.9
SpO2 <95%	(n=271)	22.5	2.2 (1.3-3.7)	72.6	45.2	22.5	88.3

** Adapted from Thomas Bewick et al. 2010

Table 3. Value of low oxygen saturations in predicting outcome[27]

	SpO2 >90% (n=336)	SpO2 ≤90% (n=131)
Inpatient death by 30 days (%)	6.8	19.1
Critical care admission (%)	7.4	15.3
Mechanical ventilation	1.8	5.3
Median LOS in days (IQR)	6.56 (8.54)	9.75 (10.33)

Among outpatients with pneumonia, oxygen saturations <90% were associated with increased morbidity and mortality. A hospital admission threshold of <92% would be safer and clinically better justified[7,28].

Comparison of Arterial Oxygen Saturation Measured Both by Pulse Oximeter and Arterial Blood Gas Analyzer in Hypoxemic and Non-hypoxemic Pulmonary Diseases[29]
In pulmonary diseases with SpO2 ≥ 80%, pulse oximetry has high accuracy in estimating SaO2 and may be used instead of arterial blood gases (ABG). In patients with SpO2 < 80%, however, the exact estimation of SaO2 and the evaluation of oxygenation by pulse oximeter is not a good substitution for ABG analyzer.

g. Cost parameters

The cost of Amoxicillin treatment per child is INR 47.77 as per Jan Aushadi rates (http://janaushadhi.gov.in/old-data/New_MRP_Oct15.pdf). The average hospital cost per episode is INR 207 if it's a primary healthcare facility, INR 293 when it is a secondary healthcare facility and INR 437 when the referral is to a tertiary healthcare facility (WHO CHOICE database). The cost of a USFDA approved Life Box Pulse oximeter is $250. [30] Each set of batteries can be used for approximately 840 readings. The lifetime of device is 2 years.[31] There are ISO certified finger pulse oximeters available in the GeM which cost anywhere between INR 1800 – 4000. The number of devices needed is 1 per 1,000 children under 5 (0.8–1.2). The DALY's lost due to pneumonia[32] in young children amount to 121·15 (105·92 to 138·3) * 10^5.

Floyd et al.,[33] evaluated the incremental cost-effectiveness of pulse oximetry in comparison to a baseline of using IMCI alone. The costing was undertaken from a public health provider perspective and hence no societal, economic or private sector costs were included. Since sufficient data were not available to inform the sensitivity of IMCI when combined with pulse oximetry, two scenarios were proposed: one in which the addition of pulse oximetry increases the sensitivity of IMCI to 70%, and one in which the sensitivity of the combination is increased to 85%, reflecting the potential of pulse oximetry to identify both people with hypoxic cases and cases with abnormal oxygen saturation (90–95%) who would benefit from referral. Estimated cost-effectiveness (US$ per disability adjusted life year (DALY)) of combined integrated management of childhood illness (IMCI) and pulse oximetry with 70% sensitivity and combined IMCI and pulse oximetry with 85% sensitivity compared with IMCI were US$14 and US$12 per disability-adjusted life year averted respectively.

h. Feasibility, Usability and Acceptability

Ginsburg AS et al., reported that healthcare professionals and caregivers viewed the pulse oximeter and breath counter favourably. Challenges included electricity requirements for charging and the time needed to complete the application. Some caregivers saw it as a sign of modernity, increasing their trust in the care received. Other caregivers were hesitant or confused about the new technology. Overall, this technology was valued by users and is a promising innovation for improving quality of care in frontline health

facilities[34]. In Spence et al., community health workers (CHW) and national stakeholders across the four countries perceived the acute respiratory infection (ARI) timer and fingertip pulse oximeter as highly scalable and easy for CHWs to use. CHWs placed greater priority on device acceptability to caregivers and children. Both groups felt that heavy reliance on electricity reduced potential scalability and usability in rural areas. Device simplicity, affordability and sustainability were universally valued[35].

4. Discussion (based on the systematic review)

In general, the states having a high prevalence of pneumonia risk factors and poor access to health services had a higher burden of pneumonia cases and deaths[10]. Although hypoxemia is common, the absence of routine pulse oximetry results in most hospitalized hypoxemic children not receiving available oxygen treatment. It is important to recognize that referral/ admission rates is dependent on the thresholds for oxygen therapy. Setting a uniform threshold for a country as geographically varied as India is complicated because pulse oximeter results may not be considered in isolation from clinical findings, SaO2 can naturally fluctuate over a day, and studies show that 'healthy' SaO2 differs by age and altitude.

Clinical signs alone are poor predictors of hypoxemia, and using pulse oximetry in resource-poor health facilities to target oxygen therapy is likely to save costs. The relative ease of implementation of a pulse oximetry-based intervention (even with the assumption of perfect availability) compared with the elimination of low birth weight or malnutrition makes it an important candidate for an intervention against pneumonia in resource-poor settings. Many of these studies considered have not taken into account the positive impact pneumococcal vaccine would have for infants. In Sinha et al.[13], it is seen that the vaccine has the potential to directly avert around 262,000 deaths in under-5s across 72 countries. Taking that vaccine into consideration might decrease the cost-effectiveness of pulse oximetry. Still it should compare favourably with the pneumococcal vaccine.

The breadth of different views on pneumonia diagnostic aids emerging from the research activities can be seen amongst the different participant groups. The fingertip pulse oximeter was deemed the most usable and scalable in most of the studies. There is evidence to indicate that pulse oximetry may lead to improved health outcomes, with

lower mortality rates (when combined with improved/adequate oxygen administration); pulse oximetry may change physicians' decisions regarding illness severity, and increase hospital admissions related to previously unrecognised hypoxaemia. Routine pulse oximetry may also influence diagnostic tests and treatments used. Pulse oximetry could facilitate swifter diagnosis, so effective treatment starts earlier and recovery likelihood increases, reducing future resource use. Oximetry can reduce resource waste by indicating when to end treatment, and by decreasing false positives. The emphasis should be to ensure all aids are accurate, affordable and acceptable to the communities where they will be used.

Table 4. Pulse Oximeter specifications as per the Technical Specifications of Medical Devices for Neonatal & Pediatric Care ICUs[36]

Weight (gram)	**Less than 300 g**
Noise Level (dB)	<40 dB
GMDN name and Code	Pulse oximeter CT 1446
Definition	A photoelectric device intended for the continuous transcutaneous measurement and display of haemoglobin oxygen saturation (SpO2). The signals, typically produced by light-emitting diodes (LEDs) and a receiving detector in a probe, or directly built-in, are used to make the measurements using the principle of spectrophotometry The oximeter displays the SpO2 values and may calculate / display other parameters, e.g., pulse rate, respiratory rate.
Technical characteristics (specific to this type of device)	a. SpO2 measurement range at least 40-70 and 70 to 99 %, minimum gradation 1% b. Accuracy of SpO2 better than +-1% for range 40-70 and better than +-3% for range 70-99 c. Accuracy of pulse rate better than ± 5 bpm

	d. Audio-visual alarms required: high and low SpO2 and pulse rate; operator variable settings; sensor disconnected, sensor failure, low battery e. Pulse rate range at least 30 to 240 bpm, minimum gradation 1 bpm
Power consumption	1.5 Watt
Power input and frequency	220 to 240V, 50 Hz
Display type	Color OLED
Heat Dissipation	Should maintain nominal temperature and prevent overheating of the probe
Mobility, portability	Protective splash-proof case for clean storage and safe transport
Operating condition	Capable of operating continuously in ambient temperature of 0 to 50 degree Celsius and relative humidity of 15 to 90% in ideal circumstances
Standards & Safety	Should be FDA / CE approved product / ISO 80601-2-61-2011: Medical Electrical equipment-part 2-61: Particular requirements for the basic safety and essential performance of pulse oximeter. Manufacturer/ supplier should have ISO 13485 certificate for quality standard. Electrical safety conforms to standards for electrical safety IEC-60601-1, shall meet IEC-60601-1-2 (General requirements for safety - electromagnetic compatibility)
Signal strength or quality to be visually displayed	Yes

Memory	Minimum 24 hour trend memory for SpO2 & PR
User's interface	Easily accessible touch button to operate the machine
Display must allow easy viewing in all ambient light levels	Yes
Warranty	1 year warranty with minimum 3 free servicing.
Accessories	Sell in standard: -A lithium battery -A user manual -A USB line -A New born oximeter probe -A power adapter Sell in addition: -Adult prone -Pediatric probe

5. Supply of oxygen in hospitals

The Public Health Standards of India which was published in 2012 detailed the minimum expected infrastructure and human resources needed to run the country's healthcare services, from sub-centres to district hospitals. These standards apply to government-run healthcare facilities. As per the document, oxygen is an essential commodity for any maternal birthing unit, including sub-centres, the most 'peripheral' of India's rural health facilities, and that all district hospitals should have piped oxygen to their sickest patients (intensive care units and casualty). It is important to make sure that the procurement is done by appropriately by fairly awarding contracts, payments without delay, and prevention of theft of procured stocks. The challenge is to create a system which makes these outcomes more likely and limits harm to patients from almost inevitable human and other error.

Oxygen therapy must be more widely available; in many remote settings, this can be achieved by use of oxygen concentrators, which can run on regular or alternative sources of power. Several conditions must be met for hypoxemic children to receive appropriate,

uninterrupted oxygen therapy for as long as is necessary to save their lives. A 2016 gap analysis of gas use in the Armed Forces Medical College Hospital in Pune found limited documentation from the oxygen supplier and major gaps in pipeline maintenance, particularly in the lack of alarm mechanisms to alert staff to shortages. Medical oxygen comes under the National List of Essential Medicines (NLEM) of India, one of the key instruments in a balanced healthcare delivery system. Medical oxygen is also on the World Health Organization's (WHO) list of essential medicines. No ICU or hospital for that matter can run without a smooth supply of oxygen as medical oxygen comes under essential medical list.

6. Costing of incorporation of Pulse-oximeter to IMCI guidelines in Indian primary healthcare

a. Methodology

We extracted the costs of the IMCI implementation in Indian Primary healthcare settings from previous studies[37]. The average number of hospital visits (outpatient and inpatient) were calculated including the associated out of pocket health expenditure for each category. We indexed the amount to the 2019 INR rate using inflation tools. Pulse oximeters which fit the predefined specifications were shortlisted and their net average cost was taken for costing purposes. The cost for the equipment (pulse oximeters) were derived from the Government e-Marketplace. The power consumption for the finger pulse oximeter was negligible. The training cost is derived from consultation with the program implementers. We assumed the life of a training to be two year (similar to the lifespan of the device) and therefore dealt with the training cost as capital in nature. The life of training was considered to be 2 years, based on a need for retraining health workers after an interval of 2 years. Since the PO's will be handled by the frontline health workers, no additional human resources will be required to implement this project.

b. Results

Per patient cost of treatment of non-severe pneumonia (home based) before recovery came to INR 1117 (Table 12). This figure was arrived at by assuming that the patient had to make at least 1 OPD Visit and the associated OOP. Per patient cost of treatment of non-severe pneumonia (home based) before progression to severe illness came to INR 2234 taking into account 2 OPD visits and OOP. Per patient cost of treatment for severe pneumonia (hospital based) is INR 10592. Per infant cost of general health system administration and program cost (IMCI) came to INR 161[37]. The average cost of a pulse oximeter in GeM portal with the required specification is INR 2500. The cost of training one frontline health worker is INR 513.33 (Table 13). This takes into account the cost of trainer honorarium, stationery, and reimbursements for trainee, infrastructure and logistics, and travelling costs. We want to train two frontline health worker per facility. Hence the cost per facility will be INR 1026.66. Summing up the common expenses for training two health workers per facility and the instrument cost, the total cost to install pulse oximeter in a PHC will be INR 3526.67. The expected life of the equipment is 2 years.

The annualization factor was taken 0.5226 and the discount rate was 3% (Table 11). Therefore, per year cost of PO will come to INR 1833.52 (3526*0.522). The number of patients in the 0-5 age group with acute respiratory infection visiting a PHC OPD (other than immunisation) in a day is around 10-15, which may increase up to 25 depending on the availability of the paediatrician. This indicator when extrapolated to a year comes to around 5040. The cost of Pulse oximetry per patient per year is INR 0.36

7. Budget Impact Analysis

Since the pulse oximeter devices are being planned to be rolled out at a national level in a phased manner, it is all the more prudent to look at the budget impact analysis along with the cost effectiveness analysis. In contrast to cost-effectiveness analysis, which measures both cost and clinical outcomes without regards to underlying disease prevalence, budget impact models focus exclusively on cost and adjust for the underlying prevalence of disease. Adjusting for disease prevalence is critical, because a medical technology that is 'cost-effective' might apply to a large subset of patients, and therefore have a prohibitive budget impact. It is important for the health ministry to be made aware of the overall budget needed for rolling out the pulse oximeter to all the 1.5 lakh Health and Wellness Centres in India. Depending on the overall budget, structured plans can be made as to whether the roll-out is made in a single phase or in multiple phases.

a. Methodology

The Ayushman Bharat targets operationalizing 1.5 lakh Health and Wellness Centres in India. Each centre is expected to have at least one functioning pulse oximeter and two trained staff. The cost of PO was gathered from the finger pulse oximeters available in the GeM portal. The net average cost of all the oximeters which had the recommended specifications were taken. This was multiplied by the number of proposed Health and Wellness Centres. One year warranty and three free servicing was included in the recommended terms and conditions. Training of frontline health workers formed another major part of the budget. The training was planned in a phased manner. Costs for central level, state level and district level training for trainers was budgeted. This was followed by training of frontline health workers at the CHC/ PHC levels. The common

expenses for the training included trainer honorarium, stationary items, trainee reimbursement (TA+DA), infrastructure and logistics.

The health system already has a functioning IMCI unit. The pulse oximetry is an add-on to the existing IMCI. Hence, no additional human resources will be required to implement it.

b. Results

The cost of roll-out of pulse oximeters for 1.5 lakh health and wellness centres

- Number of health and wellness centres: 150000
- Cost of PO: 2500
- Overall cost of PO: 150000*2500 = INR 375,000,000

But, as on 31st March 2017, there were only 25650 Primary Health Centres (PHCs) functioning in India[38]. If we were to provide a pulse oximeter to all the PHC's in India, the cost of the roll-out of pulse oximeters would be INR 64,125,000 (25650*2500). The cost of training frontline health workers to use PO is INR 26,334,000. The overall cost of roll-out of pulse oximeters in PHC's would amount to INR 90,459,000.

The number of functioning Community Health Centres (CHCs) in India was 5510 as on 31st March, 2016[39]. Each community health centre would require at least 4 finger-tip pulse oximeters which should ideally be placed in the casualty, OP and inpatient ward. If there are dedicated structured pulmonary rehabilitation programme like SWAAS[40] an additional pulse oximeter might be needed in the specific clinic as well. The cost of equipping all the CHC's with specified number of pulse oximeters amount to INR 55100000 (5510*2500*4).

8. Economic Evaluation

a. General Model Description

A decision tree was parameterized on MS-Excel spreadsheet to estimate the incremental cost effectiveness of implementing pulse oximetry + IMCI program over IMCI alone. (Supplementary Material).

A lifetime study horizon starting from base year of 2019 was considered appropriate to cover all costs and effects comprehensively. Pneumonia have a predominant risk within the first 5 years of life, with gradually declining risk till about 15 years.

We evaluated the costs and effects from both health system and societal perspective. Effect was measured in terms of illness episodes averted, child deaths prevented, life years gained and quality-adjusted life years (QALY) gained. Costs were discounted at 3% and an annualization factor of 0.52 was added for time preference of cost. We estimated the standardized unit cost from health system and societal perspective. We report our findings as incremental cost of implementing IMCI + PO for infants per QALY gained and per infant death averted as compared to IMCI alone.

The cost data for analysis was extracted from previous costing studies done with IMNCI and pulse oximetry[33,37]. The parameters used for the economic model are shown in the input parameter table. The sensitivity of 'IMCI' and the sensitivity of 'IMCI + PO' were taken from previous studies[23,24]. We started with an initial base cohort of pneumonia patients of same size for both interventions. Using the abovementioned sensitivity for IMCI and IMCI+PO respectively, we screened both groups of severe and non-severe pneumonia. Per patient cost of treatment of non-severe pneumonia (home based) before recovery, per patient cost of treatment of non-severe pneumonia (home based) before progression to severe illness, and per patient cost of treatment for severe pneumonia (hospital based) were calculated from previous studies conducted in India[37]. The mean duration of non-severe pneumonia before recovery, the mean duration of non-severe illness before progression to severe illness, the mean duration of severe illness before recovery and the mean duration of severe illness before death were computed from secondary data[12,14].

Table 5. Results of Cost effectiveness of IMCI + PO as compared to IMCI Alone

Intervention	Cost	LY	QALY	ICER
IMCI (0.55)	32247526	601736.1	601736.1	**-117.32**
IMCI+PO (0.85)	29503112	625127.9	625127.9	
Intervention	**Cost**	**LY**	**QALY**	**ICER**
IMCI (0.55)	32247526	601736.1	601736.1	**-18.7521**
IMCI+PO (0.7)	31993096.31	615304.17	615304.17	

Number given in brackets in the first column is the sensitivity of each intervention

In absolute terms, the introduction of pulse-oximetry devices to IMCI is estimated to result in annual reductions in pneumonia deaths in India. The deaths averted per year for PO2 within a cohort of 10000 pneumonia cases would be 367 if the sensitivity is 85% and 213 if the sensitivity is 70%. Owing to the large under-five populations (128 million) India could significantly reduce the mortality due to childhood pneumonia by the introduction of PO into the existing IMCI. The detailed decision tree model with probabilities and cost for IMCI and IMCI+PO is given as supplementary material. We found that the ICER is -117.32 and -18.75 when the sensitivity of the IMCI+PO is 85% and 70% respectively. This suggests that it is a cost-saving intervention from a societal perspective. The sizeable number of people with non-severe pneumonia who are undiagnosed develops severe pneumonia and require inpatient treatment in hospitals increasing the out of pocket health expenditure and the overall cost of treatment.

Figure 2: Decision Model – IMCI

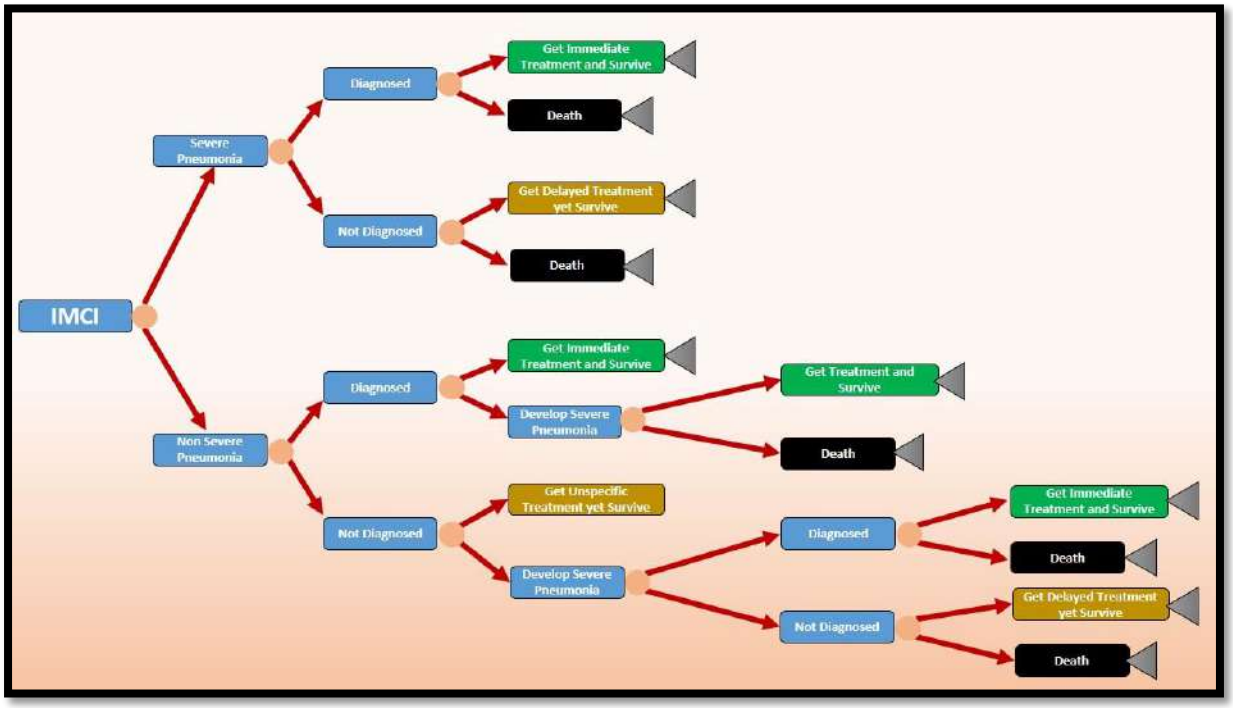
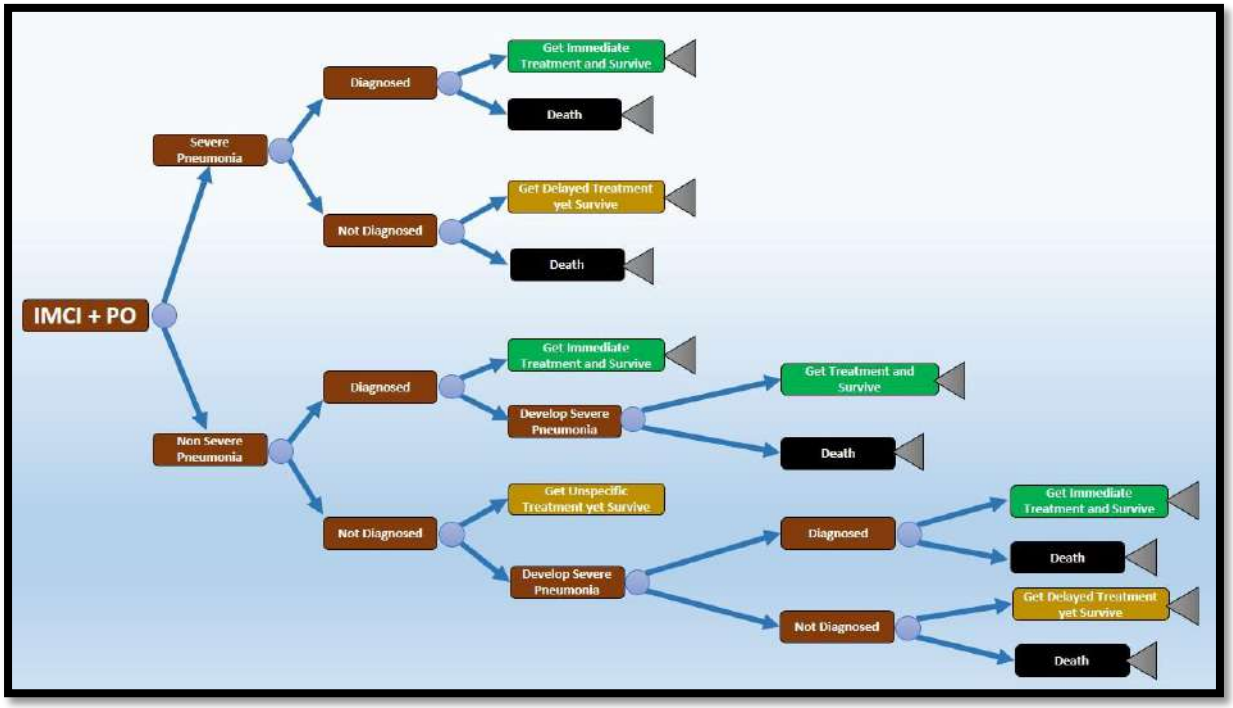


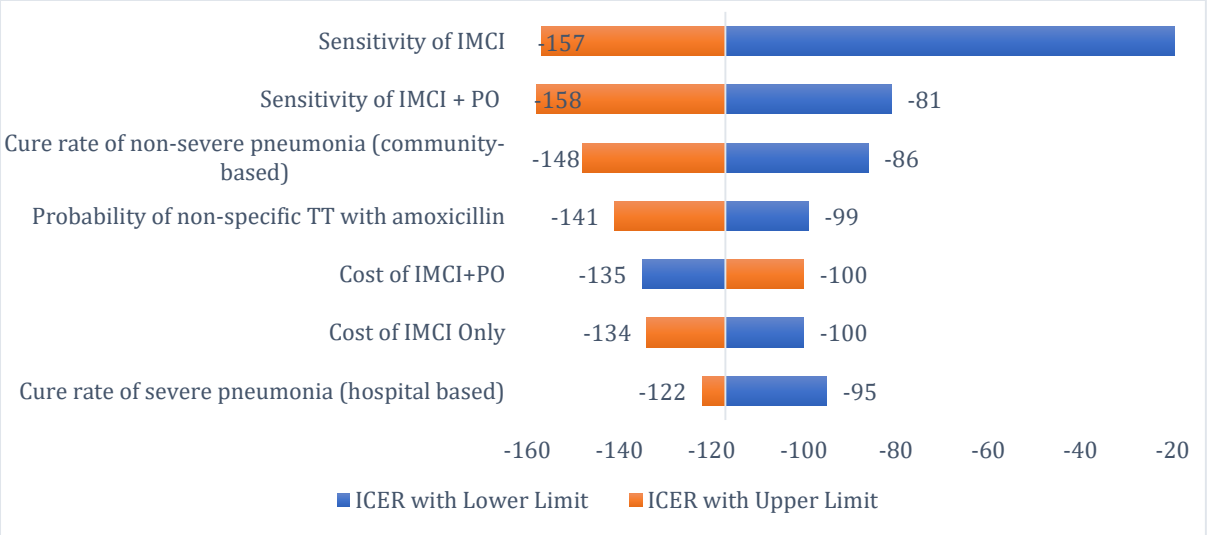
Figure 3: Decision Model – IMCI + PO



b. Sensitivity Analysis

We did one-way sensitivity analysis by varying costs of all input parameters from their lower limit to upper limit and ascertained their effect on ICER of intervention. We finally selected input parameters which had maximum impact on cost-effectiveness of introduction of Pulse-oximeter in IMCI guidelines. We plotted these parameters and variation in ICER attributed to them in tornado chart as given in Figure 4.

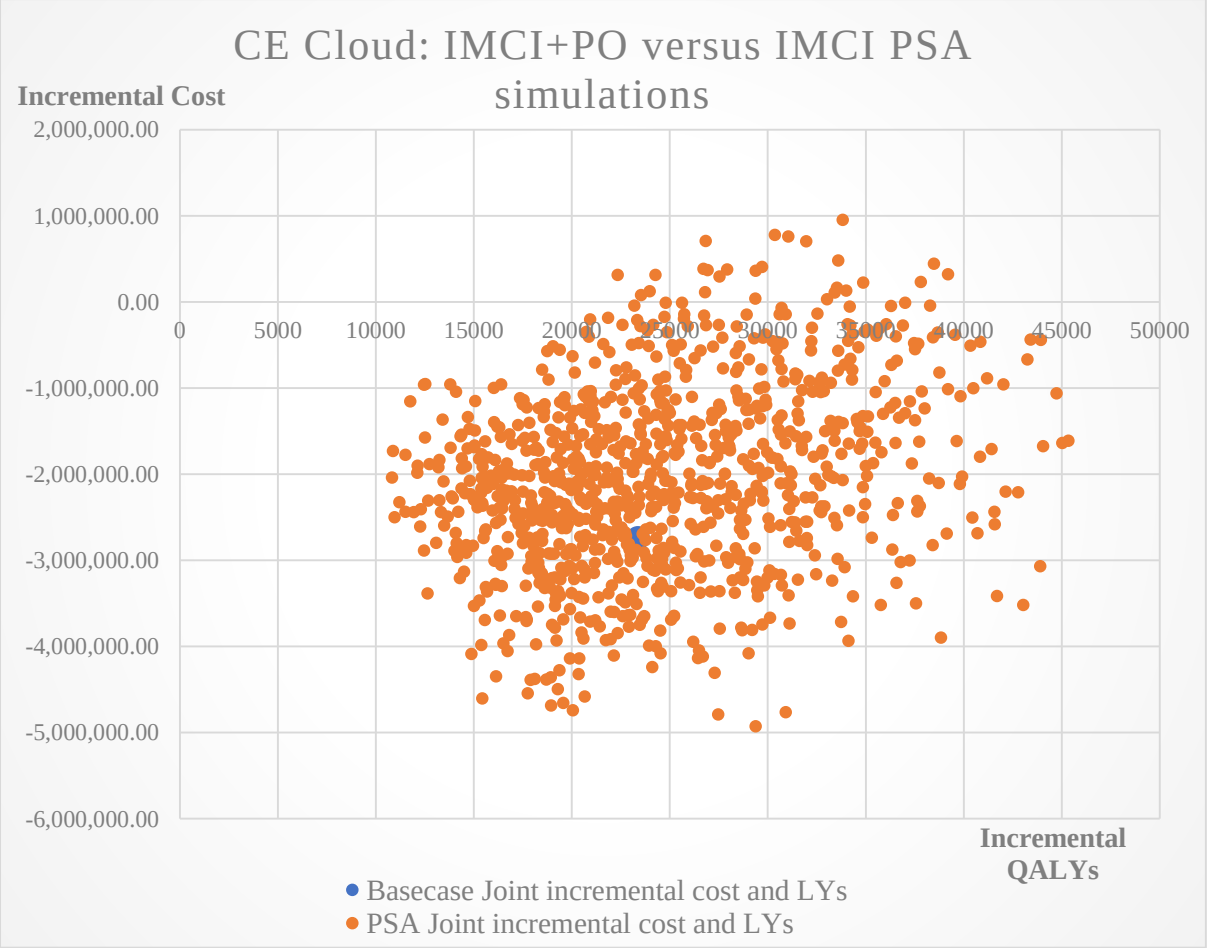
Figure 4. Tornado diagram for one-way sensitivity analysis



We also conducted a probabilistic sensitivity analysis to ascertain the variation in ICER which may arise from uncertainty in input parameters and all assumptions we took during the process of this evaluation. In Microsoft excel, we used Visual Basics to run PSA where ICER was calculated for 1000 times by randomly varying the values of input parameters, taking any random value from their lower to upper bound.

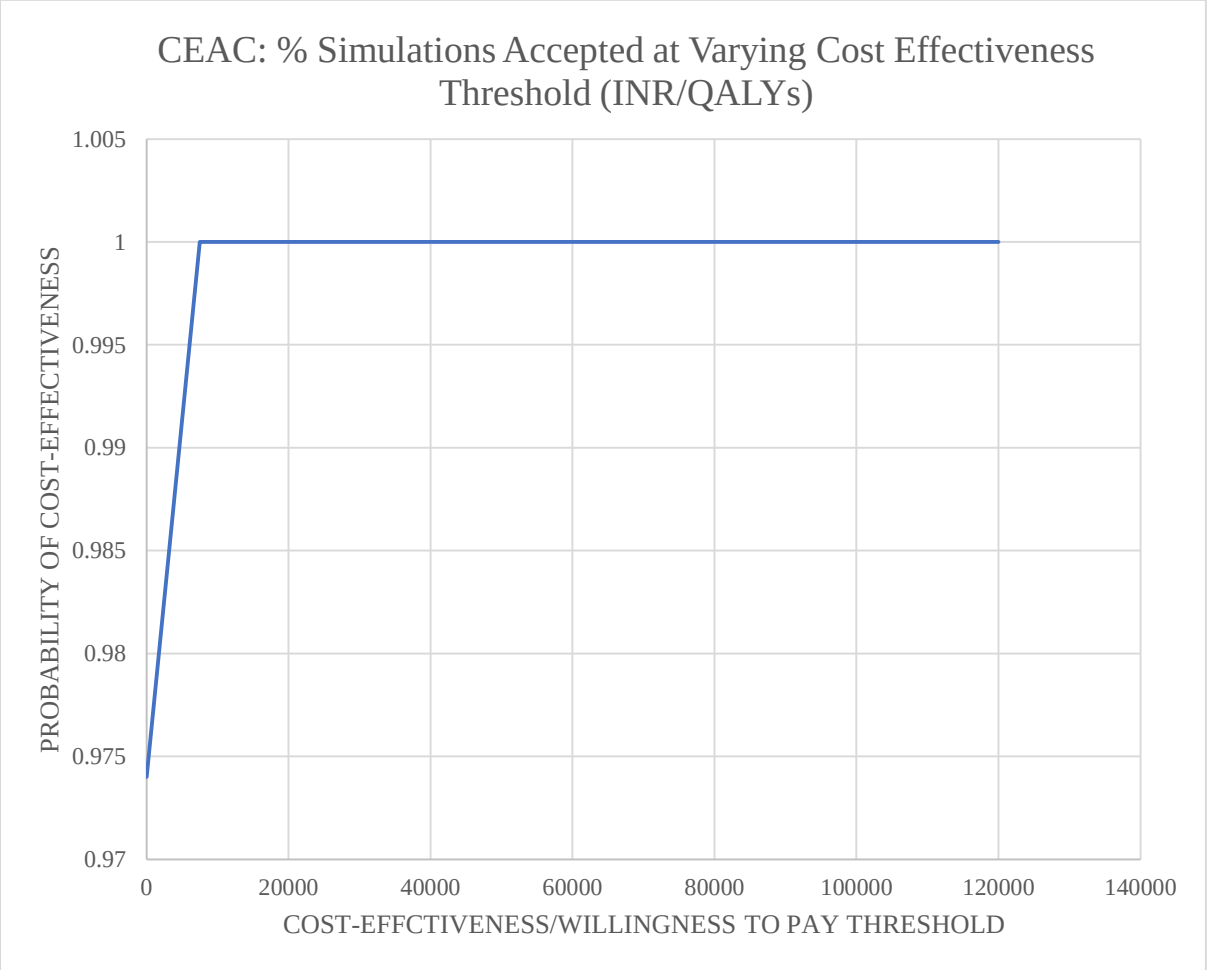
All these 1000 iterations were plotted against base case to present the variation and proportions of ICER falling in different quadrants. We can see, that all values fall in right upper and right lower quadrant; out of which majority (97.4) of values are in right lower quadrant, signifying ICER to be negative with gain in QALYs and less cost incurred in intervention scenario as presented in Figure 5.

Figure 5. Results of PSA plotted against Base-Case ICER



ICER was also compared to the willingness to pay threshold (which is considered to be one times per capita GDP of the country) and results of PSA were presented in the form of Cost-Effectiveness Acceptability Curve (CEAC) to compare ICER values with willingness to pay threshold as presented in Figure 6.

Figure 6: Cost Effectiveness Acceptability Curve



9. Discussion (based on decision model and budget impact analysis)

From the evidence brought forth by our systematic review, it seems that pulse oximetry, used in conjunction with clinical guidelines like the IMCI, is beneficial in screening and diagnosis of pneumonia in the community. It is important to note here that such diagnoses have to be coupled with prompt provision of oxygen therapy at the community level institutions, in order to reap the benefits of a more early and accurate diagnosis. The deaths averted due to childhood pneumonia when IMCI+PO is used instead of IMCI alone is 21 and 36 per 1000 patients when the sensitivity is 70% and 85%. When we take a lifetime horizon this results in a QALY gain of 1356 and 2339 years respectively.

The ICER for both sensitivities show a negative value suggesting that PO when added to the existing IMCI would become a cost saving intervention. The costing and budget impact analysis showed that the introduction of pulse oximeter along with existing IMNCI will increase the cost per patient per year by INR 0.36 only. The overall cost of roll-out of pulse oximeters in PHC's would amount to INR 90,459,000. The cost of equipping all the CHC's with specified number of pulse oximeters amount to INR 55,100,000. The overall domestic general government health expenditure per capita for India is US$61.40[41]. For a three trillion dollar economy which spends 1% of its GDP on healthcare, the implementation of the IMNCI+PO would cost only 0.003% of its annual budget.

It is important to know how to interpret the information received from oximetry. The inherent limitation of being a non-invasive technology makes it all the more important for proper training to be given to frontline health workers. The technical specifications of Finger Pulse Oximeter for use in Health and Wellness Centres (Table 4) should be maintained and updated at regular intervals. The relative ease of implementation of a pulse oximetry-based intervention (even with the assumption of perfect availability) compared with the elimination of low birth weight or malnutrition makes it an important candidate for an intervention against pneumonia in resource-poor settings. The decision tree was able to show that on top of the large reduction in deaths due to pneumonia, the addition of pulse oximetry to IMCI has the potential to increase the correct treatment of severe cases. Thus, pulse oximetry appears to be both an effective and cost-effective option for the government to contemplate implementation of the same in the primary healthcare institutions.

In the case of IMNCI+PO, the value of ICER was less than the GDP per capita in all simulations as part of the probabilistic sensitivity analysis. The sensitivity analysis also showed that majority of the values fell into the right lower quadrant, signifying ICER to be negative with gain in QALYs and less cost incurred in the intervention scenario. The implementation of IMNCI+PO imposes only a small increase in the overall budget. With an overall health system spending of US$61.40 per capita per year[41], this implies a 0.003% increase in budget which appears reasonable, considering the Government of India's strong commitment to raise resource allocation to health for achieving universal health care. Recommending a program or strategy for scale-up merely on grounds of cost-effectiveness may not be prudent.

10. Conclusions and Recommendations

1. IMNCI+PO is a cost saving prognostic tool as compared to IMNCI alone provided there is supplementary oxygen availability.
2. IMNCI should be the basic prognostic tool for childhood pneumonia but PO is beneficial in the referral of cases. Pulse oximetry in general may be used to measure oxygen saturation in cases wherever required.
3. Among outpatients with pneumonia, oxygen saturations <90% were associated with increased morbidity and mortality. A hospital admission threshold of <92% would be safer and clinically better justified. All severe cases irrespective of availability of Pulse oximeter will be referred to a tertiary care facility for expert management.
4. In tertiary care, when SpO2 ≥ 80%, pulse oximetry has high accuracy in estimating SaO2 and may be used instead of ABG; in patients with SpO2 < 80%, however, the exact estimation of SaO2 and the evaluation of oxygenation by pulse oximeter is not a good substitute for ABG analyzer.
5. Pulse oximeter specification may be as mentioned in Table 4.
6. In tertiary care hospitals, especially in ICU's Parameters multipara monitors which measures ECG, Respiration, Pulse Rate, Temperature, SPO2, NIBP suitable for adult and neonates should be used.

11. Limitations and assumptions

There were several limitations to our analysis. One major limitation of the study was a lack of data on the availability of oxygen support and how it is distributed throughout the health system. The IMNCI was functional (at least on paper) in most of the states in India. But the mortality rate of children in the age group 0-5 is different for different states. There is still no good quality evidence as to why there is a disparity in the death rates due to pneumonia despite most states opting to implement IMNCI. So, the question of whether it is the poor implementation of IMNCI or whether IMNCI as a tool is unsatisfactory is not conclusively proven. The assumptions made for the decision model and the economic evaluation is given in Table 14.

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13. Addendum

Summary of findings

Table 6: Evidence Summary

No.	Title/ Authors/ Journal/ Year/ Country	Type of study and number of participants	Overall outcome	Risk of bias rating - overall	Remarks
1	Evaluating the impact of pulse oximetry on childhood pneumonia mortality in resource-poor settings. Floyd J et al. Nature. 2015 Dec 3	Modelling study Continuous-time deterministic compartmental model.	The cost-effectiveness of implementing pulse oximetry in India with PO1 and PO2 are US$11.84 and US$9.56 per DALY, respectively.	Moderate	Favouring the use of pulse oximetry
2	The Role of Pulse Oximetry: Its Use as an Indicator of Severe Respiratory Disease in Peruvian Children Living at Sea Level Madico et al. Archives of Pediatrics and Adolescent Medicine 1995 Peru	Comparative study. 162 well children 269 children with ARI	Children with pneumonic and non-pneumonic ALRI (59%, 160/269) had a mean (+/- SD) arterial oxygen saturation significantly lower than well children (93.8% +/- 3.5% vs 98.7% +/- 1.51%; P < .01). Pulse oximetry misclassified notably fewer well children than did the WHO algorithm (4% vs 35%). Pulse oximetry and the WHO algorithm together (SATWHO) detected 99% and 87% of pneumonic ALRI and radiologic pneumonias, respectively, and both methods detected 94% of all cases of pneumonic and non-pneumonic ALRI diagnosed clinically.	Moderate	Favouring the use of pulse oximetry
3	Emergency triage assessment for hypoxaemia in neonates and young children in a Kenyan hospital: an observational study.	Validation study Hypoxemia was found in 977 of 15289 (6.4%) of all admissions	Hypoxemia was strongly associated with inpatient mortality (age-adjusted risk ratio: 4.5; 95% confidence interval, CI: 3.8-5.3). 5-15% of the children who had hypoxaemia on admission were missed, and 18% of the children were incorrectly identified as hypoxaemic.	Moderate	Favouring the use of pulse oximetry

	Mwaniki MK et al. Bull World Health Organ. 2009 Apr Kenya		Clinical signs are poor predictors of hypoxemia, and using pulse oximetry in resource-poor health facilities to target oxygen therapy is likely to save costs.		
4	Hypoxaemia in Mozambican children <5 years of age admitted to hospital with clinical severe pneumonia: clinical features and performance of predictor models. Bassat Q et al. Trop Med Int Health. 2016 Sep 21 Mozambique	Hospital-based survey 825 children	The prevalence of hypoxemia on admission was 27.9%, and 19.8% of these children died (OR compared with non-hypoxaemic children 3.22, 95% CI 1.98-5.21, P < 0.001). None of the models performed well when tested in different case scenarios of oxygen availability through mathematical modelling, with over 50% of hypoxaemic children not receiving oxygen even in favourable case scenarios. Clinical signs alone or in combination are not suitable to diagnose hypoxaemia. The use of pulse oximeters should be strongly encouraged.	Moderate	Favouring the use of pulse oximetry
5	Prevalence of undiagnosed hypoxemia in adults and children in an under-resourced district hospital in Zambia. Foran M et al. Int J Emerg Med. 2010 Nov 11 Zambia	Cross-sectional analysis 192 patients	Oximetry data changed clinical management in all observed cases of hypoxemia and several cases of normoxemia, leading to application of supplemental oxygen, initiation of further diagnostic testing, prolongation of inpatient stay, or expedited discharge home.	Moderate	Favouring the use of pulse oximetry
6	Pulse oximetry for children with pneumonia treated as outpatients in rural Malawi. McCollum ED et al. Organ. 2016 Dec 1 Malawi	Survey-based assessment N= 14092	The availability of oximetry appeared to have increased the referral rate for severely hypoxaemic children without chest indrawing or danger signs from 0% to 27.2% (P < 0.001). In the absence of oximetry, if the relevant World Health Organization (WHO) guidelines published in 2014 had been applied, 390/568 (68.7%) severely hypoxaemic children at study health centres and 52/84 (61.9%) severely hypoxaemic children seen by community health workers would have been considered ineligible for referral.	Moderate	Favouring the use of pulse oximetry

7	The Use of Pulse Oximetry to Exclude Pneumonia in Children The American Journal of Emergency Medicine 2002 Oct USA	Retrospective comparison study. In our study population of children under the age of 24 months, 803 chest radiographs were obtained and analyzed.	The median pulse oximetry reading of children with radiographic pneumonia was 97% (interquartile range 95th- 98th percentile) compared with 98% (interquartile range 96th-99th percentile) in the control group. Forty-five percent (35 of 78) of children with radiographic pneumonia showed oxygen saturations of 98% or higher with greater than 10% (8 of 78) displaying oxygen saturations of 100%. By using logistic regression, pulse oximetry was not found to be a statistically significant predictive variable for radiographic pneumonia. Pulse oximetry could not be used to rule out the presence of radiographic pneumonia in children less than 2 years of age who presented with respiratory complaints	Moderate	Do not favour the use of pulse oximetry

Table 7: Summary of studies with supportive evidence for pulse oximetry

No.	Title/ Authors/ Year/ Country	Type of study and number of participants	Overall outcome	Risk of Bias - Overall	Remarks
1.	Beyond Critical Congenital Heart Disease: Newborn Screening Using Pulse Oximetry for Neonatal Sepsis and Respiratory Diseases in a Middle-Income Country. Jawin V et al. PLoS One. 2015 Sep 11 Malaysia	Comparative cross-sectional study. N = 5247	The sensitivity and specificity of pulse oximetry screening for non-cardiac diseases were 42% and 99.9% respectively, and 100% and 99.7% for CCHD, respectively. Expanded use of pulse oximetry has immediate implications for low- and middle-income countries contemplating strategies to reduce neonatal mortality and morbidity.	Moderate	Favours expanded use of pulse oximetry.
2.	What is the role of pulse oximetry in the assessment of patients with community-acquired pneumonia in primary care? Bewick T et al. Prim Care Respir J. 2010 Dec UK	Prospective cohort study N = 467	$SpO_2 \leq 90\%$ has good specificity but low sensitivity for adverse outcomes in CAP.	Moderate	Pulse oximetry complements rather than replaces clinical severity scoring.
3.	Adoption of paediatric and neonatal pulse oximetry by 12 hospitals in Nigeria: a mixed-methods realist evaluation. Graham et al. BMJ Glob Health. 2018 Jun 26 Nigeria	Mixed-methods realist evaluation. Between January 2014 and April 2017, 38525 children (38% aged ≤28 days) were admitted to participating hospitals (23401	Prior to our intervention, 3.3% of children and 2.5% of neonates had oximetry documented on admission. In the 18 months of intervention period, all hospitals improved oximetry practices, typically achieving oximetry coverage on >50% of admitted children after 2-3 months and >90% after 6-12 months.	Moderate	Favouring the use of pulse oximetry

		pre-training; 15 124 post-training).	However, oximetry adoption varied in different contexts.		
4.	Brief hospitalization and pulse oximetry for predicting amoxicillin treatment failure in children with severe pneumonia. Fu LY et al. PEDIATRICS 2006 Dec 9 locations in 8 countries	Post-hoc cohort analysis was nested within a previously completed, randomized trial	The inclusion of oximetry data improved the predictive ability at baseline, 12 hours, and 24 hours. The ability to predict failure after 12 hours of observation with oximetry data was similar to the predictive ability after 24 hours without pulse oximetry data.	Moderate	Favouring the use of pulse oximetry
5.	Multi-center study of hypoxemia prevalence and quality of oxygen treatment for hospitalized Malawian children. McCollum ED et al. Trans R Soc Trop Med Hyg. 2013 May Malawi	Prospective, multicenter observational study. N= 761	No hospital used pulse oximetry routinely, and only 9 of 40 (22.5%) patients<15 years old with SpO2<90% were treated with oxygen by hospital staff. Study personnel using WHO criteria for children<5 years old achieved a higher sensitivity (40.0%) and lower specificity (82.7%) than Malawian clinicians (sensitivity 25.7%, specificity 94.1%). Although hypoxemia is common, the absence of routine pulse oximetry results in most hospitalized hypoxemic Malawian children not receiving available oxygen treatment.	Low	Favouring the use of pulse oximetry
6.	Can clinical signs predict hypoxaemia in Papua New Guinean children with moderate and severe pneumonia? Moses Laman et al. Annals of Tropical Paediatrics 2005 PNG	Comparative cross-sectional study N= 77	Clinical findings were correlated with different levels of hypoxaemia: <93%, <90% and <85%. Cyanosis, head nodding and drowsiness were good predictors of hypoxia but lacked sensitivity. Decisions to use oxygen based on these signs would therefore result in a	Moderate	Favouring the use of pulse oximetry

			significant number of children with hypoxia not receiving oxygen. Pulse oximetry is the best indicator of hypoxaemia in children with ALRI and, although relatively expensive, its use might be cost-effective in controlling oxygen requirements.		
7.	Tachypnea and Other Danger Signs vs Pulse Oximetry for Prediction of Hypoxia in Severe Pneumonia/Very Severe Disease. Alwadhi V et al Indian Pediatr. 2017 Sep 15 India	Cross-sectional study N= 112	Multiple logistic regression revealed that age-specific tachypnea (RR≥70/min for 2-12 mo, and RR ≥60/min for ≥12 mo), head nodding, and inability to drink/breastfeed were independent predictors for hypoxia with sensitivity of 70.2%, 50.9% and 75.4%, respectively; and specificity of 88.9%, 96.4%, and 90.9%, respectively. When all three predictors were used in conjunction, the sensitivity increased to 91.2% and specificity was 81.8%. No single clinical sign can perform as well as pulse oximetry for predicting hypoxia in children with severe pneumonia.	Moderate	Favouring the use of pulse oximetry
8.	mPneumonia, an Innovation for Diagnosing and Treating Childhood Pneumonia in Low-Resource Settings: A Feasibility, Usability and Acceptability Study in Ghana. Ginsburg AS et al. PLoS One. 2016 Oct 27 Ghana	Qualitative study based in ground theory methods	HCPs and caregivers viewed the pulse oximeter and breath counter favorably. Challenges included electricity requirements for charging and the time needed to complete the application. Some caregivers saw mPneumonia as a sign of modernity, increasing their trust in the care received. Other caregivers were hesitant or confused about the new technology. Overall, this technology was valued by users and is a promising innovation for improving quality of care in frontline health facilities.	Low	Favouring the use of pulse oximetry

9.	Childhood pneumonia diagnostics: community health workers' and national stakeholders' differing perspectives of new and existing aids. Spence H et al. Glob Health Action. 2017 Cambodia, Ethiopia, Uganda and South Sudan.	Qualitative methodology, combination of pile-sorting activities and focus group discussions (FGDs).	CHWs and national stakeholders across the four countries perceived the acute respiratory infection (ARI) timer and fingertip pulse oximeter as highly scalable and easy for CHWs to use. National stakeholders were less receptive to new technologies. CHWs placed greater priority on device acceptability to caregivers and children. Both groups felt that heavy reliance on electricity reduced potential scalability and usability in rural areas. Device simplicity, affordability and sustainability were universally valued.	Low	Favouring the use of fingertip pulse oximetry
10.	Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan. Salah ET et al. Indian J Crit Care Med. 2015 Apr Sudan	Cross-sectional study N = 150	Of the total number, 42.7% had hypoxemia (with pulse oximeter oxygen saturation <90%), out of them 36 (56.25%) were in the age group <2 months. Of the hypoxic patients, 30 (46.88%) had severe pneumonia, and 7 (10.94) had very severe pneumonia ($P < 0.001$). There was a significant association between the hypoxemia and small age group and very severe pneumonia. In limited resource settings pulse oximeter can be used to correctly identify hypoxemia in under five children particularly among those diagnosed clinically as very severe pneumonia.	Moderate	Favouring the use of pulse oximetry
11.	Prevalence and prediction of hypoxemia in children with respiratory infections in the Peruvian Andes. Reuland DS et al.	Comparative cross-sectional study N = 423	Compared with previous studies of children living at lower altitudes, the presence of tachypnea was relatively nonspecific as a predictor of radiographically determined pneumonia or of hypoxemia, especially in infants.	Moderate	Favouring the use of pulse oximetry

	J Pediatr. 1991 Dec Peru		Radiographic pneumonia was not a sensitive predictor of hypoxemia or clinically severe illness. In contrast, the presence of hypoxemia was a useful predictor of radiographic pneumonia, with both sensitivity and specificity of 75% in infants. We conclude that acute lower respiratory tract infection in children living at high altitude is frequently associated with hypoxemia, and that oxygen should be administered to children with a diagnosis of pneumonia in these regions. Case management algorithms developed in low-altitude regions may have to be modified for high-altitude settings. In this setting, pulse oximetry is a good predictor of pneumonia. Because pulse oximetry is more objective and cheaper than radiography, its role as a clinical and investigative tool merits further exploration.		
12.	Accuracy of symptoms and signs in predicting hypoxaemia among young children with acute respiratory infection: a meta-analysis. Zhang L et al. Int J Tuberc Lung Dis. 2011 Mar	Meta-analysis N = 11 diagnostic studies with 5787 patients	There was substantial variation in sensitivity and specificity between different symptoms and signs as well as across studies. Cyanosis, inability to feed, head nodding, respiratory rate > 70/min and unresponsiveness/impaired reusability had high specificity but low sensitivity. In contrast, reported rapid breathing and crepitations in lung auscultation had relatively high sensitivity but low specificity. Five models of a combination of symptoms and signs presented moderate sensitivity (range 0.60-0.84) and specificity (range 0.63-0.82).	Low	Favouring the use of pulse oximetry

			Both single nor combined symptoms and signs have satisfactory performance in predicting hypoxaemia among young children with ARI. Improved access to pulse oximetry is needed in developing countries.		
13.	Does pulse oximeter use impact health outcomes? A systematic review Enoch AJ et al. Arch Dis Child. AUG 2016	Systematic Review 5 studies included	The evidence is low quality and hypoxaemia definitions varied across studies, but the evidence suggests pulse oximeter use with children can reduce mortality rates (when combined with improved oxygen administration) and length of emergency department stay, increase admission of children with previously unrecognised hypoxaemia, and change physicians' decisions on illness severity, diagnosis and treatment. Pulse oximeter use generally increased resource utilisation.	Low	Favouring the use of pulse oximetry

Table 8 A: Parameters of Disease Progression

Parameter	Value (Range)	Sources
Incidence	3.6 million (3.3–3.9 million) episodes of severe pneumonia and 0.35 million (0.31–0.40 million) all cause pneumonia deaths occurred in children younger than 5 years in India. 0.075 per child per year 4066541 new severe episodes (severe morbidity)/ year 127,960,004 new episodes (incidence)/ year.	Habib Farooqui et al. Burden of Severe Pneumonia, Pneumococcal Pneumonia and Pneumonia Deaths in Indian States: Modelling Based Estimates Rudan, I. et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. J. Glob. Health 3, 010401 (2013).
Proportion severe on day 1	5% (2–10%)	Pitt, C., Roberts, B. & Checchi, F. Treating childhood pneumonia in hard-to-reach areas: a model-based comparison of mobile clinics and community-based care. BMC Health Serv. Res. 12, 9 (2012).
Mean duration of non-severe illness before recovery	3 days (2–4 days)	Hazir, T. et al. Comparison of oral amoxicillin with placebo for the treatment of world health organization-defined nonsevere pneumonia in children aged 2–59 months: a multicenter, double-blind, randomized, placebo-controlled trial in pakistan. Clin. Infect. Dis. 52, 293–300 (2011).
Mean duration of non-severe illness before progression to severe illness	10 days (9–11 days)	Hazir, T. et al. Comparison of oral amoxicillin with placebo for the treatment of world health organization-defined nonsevere pneumonia in children aged 2–59 months: a multicenter, double-blind, randomized, placebo-controlled trial in pakistan. Clin. Infect. Dis. 52, 293–300 (2011).
Mean duration of severe illness before recovery	4 days (3–5 days)	Sinha, A., Levine, O., Knoll, M. D., Muhib, F. & Lieu, T. A. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. Lancet 369, 389–396 (2007).
Mean duration of severe illness before death	7 days (6–8 days)	Källander, K. et al. Delayed care seeking for fatal pneumonia in children aged under five years in Uganda: a case-series study. Bull. World Health Organ. 86, 332–338 (2008).
Proportion bacterial versus viral (NSV)	85% viral (75–90%) 15% bacterial (10-25%)	Le Roux, D. M., Myer, L., Nicol, M. P. & Zar, H. J. Incidence and severity of childhood pneumonia in the first year of life in a South African birth cohort: the Drakenstein Child Health Study. Lancet. Glob. Heal. 3, e95–e103 (2015).

Table 8B: Care-seeking and health-care parameters

Mean duration of illness before care seeking	**NSV 3 (2–4) days** **SV 0.75 (0.5–1) days**	**Källander, K. et al.** **Delayed care seeking for fatal pneumonia in children aged under five years in Uganda: a case-series study. Bull. World Health Organ. 86, 332–338 (2008).**
Probability that timely hospital access	0.61 ± 10%	Walter, N. D. et al. Why first-level health workers fail to follow guidelines for managing severe disease in children in the Coast Region, the United Republic of Tanzania. Bull. World Health Organ. 87, 99–107 (2009).
Probability of community-based treatment curing non-severe bacterial case	0.925 (0.90–0.95)	Straus, W. L., Qazi, S. A., Kundi, Z., Nomani, N. K. & Schwartz, B. Antimicrobial resistance and clinical effectiveness of co-trimoxazole versus amoxycillin for pneumonia among children in Pakistan: randomised controlled trial. Pakistan Co-trimoxazole Study Group. Lancet 352, 270–274 (1998)
Probability of treatment with hospital care curing case	0.925 (0.80–0.95)	Assumed to be high if oxygen is available with lower values representing poorer standard of care
Probability of treatment with amoxicillin curing severe case if prescription adhered to	0.65 (0.6–0.7) (based on treatment failure rates of patients with hypoxia at baseline)	Fu, L. Y. et al. Brief hospitalization and pulse oximetry for predicting amoxicillin treatment failure in children with severe pneumonia. Pediatrics 118, e1822–e1830 (2006).

Table 9: Prognostic parameters

Probability of prognostic available	**1 (0.9–1)**	**Assumed to be high for the purpose of this analysis**
Sensitivity of IMCI	0.55 (0.5–0.6)	Kelly, J. M. et al. Community health worker performance in the management of multiple childhood illnesses: Siaya District, Kenya, 1997–2001. Am. J. Public Health 91, 1617–1624 (2001).
Sensitivity of PO+IMCI	0.85 (0.8–0.9)	Madico, G. The role of pulse oximetry. Arch. Pediatr. Adolesc. Med. 149, 1259 (1995).
Specificity of IMCI	0.85 (0.8–0.9)	Assumed to be high given low overall referral rates
Specificity of PO	0.85 (0.8–0.9)	Assumed to be similar to IMCI
Adherence to non-severe prognosis (IMCI)	0.55 (0.5–0.6)	Chinbuah, M. A. et al. Assessment of the adherence of community health workers to dosing and referral guidelines for the management of fever in children under 5 years: a study in Dangme West District, Ghana. Int. Health 5, 148–156 (2013). Acácio, S. et al. Under treatment of pneumonia among children under 5 years of age in a malaria-endemic area: population-based surveillance study conducted in Manhica district- rural, Mozambique. Int. J. Infect. Dis. 36, 39–45 (2015).
Adherence to severe prognosis (IMCI)	0.65 (0.6–0.7)	Chinbuah, M. A. et al. Assessment of the adherence of community health workers to dosing and referral guidelines for the management of fever in children under 5 years: a study in Dangme West District, Ghana. Int. Health 5, 148–156 (2013).
Adherence to non-severe prognosis	0.55 (0.5–0.6)	Assumed to be similar to IMCI
Adherence to severe prognosis	0.85 (0.8–0.9)	Assumed to be high for the purpose of this analysis

Table 10: Cost parameters

	Unit Cost	Source of information
Amoxicillin treatment per child	INR 47.77	http://janaushadhi.gov.in/old-data/New_MRP_Oct15.pdf Management Sciences for Health. International Drug Price Indicator Guide. http://erc.msh.org/dmpguide/pdf/DrugPriceGuide_2013_en.pdf (MSF, 2013).
Average hospital cost per episode	INR 82.36 (PHC) INR 116.81 (CHC) and INR 172.80 when the referral is to a tertiary healthcare facility	World Health Organization. Health Service Delivery Costs http://www.who.int/choice/cost-effectiveness/inputs/health_service/en/ (WHO, 2015).
Pulse oximeter	US$250	Lifebox Foundation. Lifebox: Saving Lives Through Safer Surgery http://www.lifebox.org/about-lifebox/our-product/ (Lifebox Foundation, 2015)
	INR 2500	Government e-Marketplace Portal
Batteries	$2 ($1.5–2.5)	Assumed
Uses per set of batteries	840	UNICEF. Supply Catalogue https://supply.unicef.org/ (UNICEF, 2015).
Lifetime of device	2 years	UNICEF. Supply Catalogue https://supply.unicef.org/ (UNICEF, 2015).
Number of devices needed	1 per 1,000 children under 5 (0.8–1.2)	Assumed

Table 11: Annualization formula

Expected life of equipment	***Discount Rate***	***Annual Factor***
2	***0.03***	***0.5226***

Table 12: Cost of treatment[37]

Per Patient cost of treatment		Indexed Figure for 2019
Non-severe pneumonia (home based) before recovery	**1 OPD Visit + OOP**	**1117**
Non-severe pneumonia (home based) before progression to severe illness	**2 (OPD visits + OOP)**	**2234**
Severe pneumonia (hospital based)	**(1 OPD visit + Per patient IPD Cost + OOP)**	**10592**

Table 13: Cost of training frontline health-worker[42]

Trainer Honorarium	1000	Per session of 30
Stationery	**1000**	**Per session of 30**
DA for Trainee	**7500**	**250/trainee/session**
*Infrastructure and logistics	**3000**	**100/trainee/session**
TA for trainee	**3000**	**100/trainee/session**
Cost of training one person	**513.3333**	

 # one session is expected to have 30 frontline health workers

**** TA/DA payable to ANM/ ASHA as per state government norms**

Table 14: Assumptions made for the decision tree in the study

Assumption
Once a patient is diagnosed with pneumonia, he/ she gets full treatment. Dropout/ poor compliance has not been factored.
Probability of treatment with hospital care curing severe pneumonia is assumed to be high since we expect oxygen to be available in most FRU's. **The sensitivity and specificity of diagnosing any severity of pneumonia is the same.**
Due to lack of availability of transition probabilities (for e.g.: percentage of patients going back into non-severe state and not complete cure from severe state after treatment) some of the intermediate states have been merged.
Proportion of patients with non-severe pneumonia who develop severe pneumonia, if not given proper treatment **Proportion of patients with non-severe pneumonia who get cured and survive, if not given proper treatment.**
The proportion of children reaching an appropriate health facility may vary significantly between various states and so having one single parameter for all the 28 states could result in inaccurate estimates

Search strings: Pulse oximetry for the diagnosis of pneumonia in children

Pubmed Search

- pulse oxime*[tiab] AND pneumon*[tiab] : **216**
- pulse oxime*[tiab] AND pneumon*[tiab] AND child*[tiab] : **89**
- (efficacy[ti] OR effectiveness[ti] OR success[ti] OR benefit[ti] OR "Diagnostic Test Accuracy"[ti]) AND pulse oximet*[ti] : **29**
- (sensitivity[ti] OR specificity[ti]) AND pulse oximet*[ti] :**14**
- ("positive predictive value"[tiab] OR "negative predictive value"[tiab]) AND pulse oximet*[ti] :**63**
- cost[ti] AND pulse oximet* : **35**
- (cost analysis[tiab] OR cost effective*[tiab] OR costing approach[tiab]) AND pulse oximet* : **96**
- (Child OR Children OR infant OR infants) AND (Health related quality of life[tiab]) AND pneumon* : **18**
- ((child*[ti] OR infant[ti] OR infants[ti]) NOT adult[ti]) AND pulse oxime* [ti] : **221**

Web of Science Search: 140

pulse oxime* AND pneumon* AND child

or

pulse oxime* AND pneumon* AND paedi*

or

pulse oxime* AND pneumon* AND infant