IMPLEMENTATION OF IMPROVED OXYGEN SYSTEMS IN HOSPITALS: A HEALTH SYSTEMS RESEARCH PERSPECTIVE

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Introduction: Hypoxemia is a life-threatening condition and is commonly seen in children with severe pneumonia. A government-led, NGO-supported, multi-faceted oxygen improvement program was implemented to increase access to oxygen therapy in 29 hospitals in Kaduna, Kano, and Niger states. The program installed pulse oximeters and oxygen concentrators, trained healthcare workers and biomedical engineers, and provided regular feedback to healthcare staff through quality improvement teams.

Objective: The aim of this study is to evaluate whether the program increased screening for hypoxemia with pulse oximetry and prescription of oxygen for patients with hypoxemia.

Methodology: The study is an uncontrolled before-after interventional study implemented at the hospital level. Medical charts of patients under-five admitted for pneumonia between January 2017 and August 2018 were reviewed and information on patient care was extracted using a standardized form. The pre-intervention period of the study was defined as January 1 to October 31, 2017 and the post-intervention period as February 1 to August 31, 2018. The primary outcomes of the study were whether blood oxygen saturation measurements (SpO_2) were documented and whether children with hypoxemia were prescribed oxygen.

Result: A total of 3,418 patient charts were reviewed (1,601 during the pre-intervention period and 1,817 during the post-intervention period). There was a significant increase in the proportion

of patients with SpO_2 measurements after the interventions were conducted (aOR 5.0; 4.3-5.7, p<0.001). Prior to the interventions, only 13.7% (95% CI: 12.2-15.3) of patients had SpO_2 measurements and after the interventions 82.4% (95% CI: 80.7-84.1) had SpO_2 measurements. Oxygen administration for patients with clinical signs of hypoxemia also increased significantly (aOR 5.0; 4.2-5.9, p<0.001) – from 22.8% (95% CI: 18.8-27.2) to 77.9% (95% CI: 73.9-81.5).

Conclusion: Increasing pulse oximetry and oxygen therapy access and utilization in a low-resourced environment is achievable through a multi-faceted program focused on strengthening government-owned systems.

INTRODUCTION

Background

Hypoxemia, or low levels of oxygen in the blood, is a life-threatening complication of severe childhood illnesses such as pneumonia.[1] In children with pneumonia, the prevalence of hypoxemia has been found to be as high as 43% and this increases the risk of death.[2-11] The World Health Organization (WHO) recommends supplemental oxygen therapy for management of hypoxemia and pulse oximetry, a non-invasive method for measuring blood oxygen saturation, for detecting hypoxemia and monitoring oxygen administration.[1] Several studies have shown that strengthened oxygen systems, including provision of pulse oximeters, in low and middle-income countries (LMICs) can reduce pneumonia mortality by as much as 70%.[12-15]

However, though oxygen has been used in medicine for almost 100 years, functioning oxygen systems are often unavailable at facilities in LMICs.[5,16-18] A study across 12 countries in Africa found that only 44% of facilities had access to uninterrupted oxygen.[19] Even when oxygen is seemingly available (i.e. equipment is present), the equipment may not be operating optimally. A study in Southwest Nigeria found that only 5% of oxygen concentrators were emitting sufficiently

concentrated oxygen (i.e. 85% concentration).[20] Forty-two percent of concentrators emitted room air. Oxygen systems must fit the local context and require ongoing maintenance and repairs or will otherwise become non-functional in a few short months.[14,21] Thus, the challenges to improving hypoxemia management go beyond making oxygen available at facilities, and include developing clear policies and guidelines, drastically reducing costs of oxygen treatment to patients and facilities, improving access to and use of pulse oximeters for accurate screening of hypoxemia, and training healthcare workers and allied health professionals such as biomedical engineers.

Recently, there have been global efforts to prioritize hypoxemia management in LMICs and to increase access to pulse oximetry and oxygen.[22-25] In support of these efforts, the Clinton Health Access Initiative (CHAI) worked with the Federal Ministry of Health (FMoH) of Nigeria and State Ministries of Health (SMoH) in Kaduna, Kano, and Niger to implement a government-led, NGO-supported, multi-faceted oxygen improvement program to sustainably increase access to and appropriate use of oxygen therapy in the three states.

Study Objective

The aim of this study is to evaluate if the program increased routine use of pulse oximetry and prescription of oxygen for pediatric patients admitted to program facilities with pneumonia and hypoxemia.

METHODS

Study design

The study design is an uncontrolled before-after interventional study implemented at the hospital level. The pre-intervention period is January to August 2017 and is defined as the time prior to installing oxygen equipment in the facilities and training facility staff on the use and maintenance of the equipment and management of hypoxemia. The post-intervention period is February to

August 2018 and is defined as the time after installing oxygen equipment and providing training on hypoxemia management and the use and maintenance of the equipment. Installation of oxygen equipment and training of facility staff were conducted from November 2017 to January 2018.

Trained data collectors retrospectively extracted data from the patient chart files of children admitted to the hospital for pneumonia. The primary outcomes were the proportion of under-five pneumonia admissions with peripheral capillary oxygen saturation (SpO_2) measurements, and the proportion of under-five pneumonia admissions with hypoxemia prescribed oxygen. We defined patients as having hypoxemia if the patient had SpO_2<90% at any time during the admission, or, where SpO_2 measurements were not documented, if the patient had any of the following symptoms: central cyanosis, grunting, nasal flaring, crackles, respiratory distress, or inability to feed, drink, or breastfeed.

Setting

In Nigeria, pneumonia is the leading cause of mortality in children under-five. An estimated 134,000 Nigerian children under-five died of pneumonia in 2015.[26] Northern Nigeria, where Kaduna, Kano, and Niger states are located, often have worse maternal and child health indicators compared to the rest of the country.[27] Nationally, under-five morality is estimated at 132 deaths per 1,000 live births. In Kaduna, Kano, and Niger, under-five mortality are 187, 164, and 98 deaths per 1,000 live births, respectively.[28]

The program and study were conducted in 29 secondary and tertiary hospitals in Kano, Kaduna, and Niger. Thirty hospitals were initially chosen (ten in each state) based on the volume of pediatric patients served by the facility and recommendations from the Hospital Management Board (HMB) and the State Ministries of Health (SMoH). However, one of the hospitals in Niger required reconstruction during the middle of the program so data collection and interventions were

stopped at the facility. As shown in Table 1, the selected facilities varied greatly in their infrastructure and pre-program availability of oxygen equipment and pulse oximeters. All facilities provided inpatient care and had separate adult and pediatric inpatient units. The average number of beds across the facilities is 140 and ranged from 32 to 570 beds. All facilities were connected to the central electricity supply, but all facilities also experienced some interruption in electricity service. The average number of hours electricity was available at the facilities was 10 hours and ranged from 2 to 23 hours. Twenty-seven of the facilities had a back-up source of electricity. While 23 facilities were providing oxygen therapy services in at least one service area in the facility before the program began, only 13 had oxygen available in the pediatric inpatient unit. Additionally, only 1 pediatric inpatient unit had a pulse oximeter and only 6 had tubing available to deliver oxygen to patients.

Program implementation

The program launched in 2016 and was a government-led, NGO-supported, multi-faceted oxygen improvement program. The program activities focused on four key domains: developing policies and guidelines for oxygen provision at healthcare facilities, procuring and installing oxygen equipment (including pulse oximeters), training healthcare workers and biomedical engineers, and monitoring changes in patient care.

Domain 1: Developing policies and guidelines

Though the program worked intensively in Kaduna, Kano, and Niger states, the first set of activities beginning in 2016 focused on working with the Federal Ministry of Health to facilitate access to oxygen in health facilities throughout the country. The program first aimed to develop national policies and guidelines that would provide a legal and strategic framework for strengthening oxygen systems. These documents were the *National Policy on Medical Oxygen in*

Health Facilities and the *National Strategy for the Scale-up of Medical Oxygen in Health Facilities*. In partnership with the Department of Hospital Services and the Department of Family Health, the program conducted a desk review on medical oxygen and interviewed various key informants about the topic, including government officials, healthcare workers, biomedical engineers, and international experts. Results of the desk review and interviews were used to draft the documents, and the drafts were presented at review meetings which consisted of stakeholders from across the country. A dedicated core technical team finalized the documents which were published in October 2017. Together, these documents outline the government's key priority areas regarding oxygen access and use and provide a framework for implementing activities to support the government's goals.

Additionally, the program worked with the Federal Ministry of Health to update the National Standard Treatment Guidelines to include oxygen therapy for pneumonia case management and ensured that oxygen equipment, such as cylinders, concentrators, pulse oximeters, nasal cannulas, humidifier bottles, and other relevant accessories, were part of the national and state essential equipment lists. The inclusion of oxygen and oxygen accessories in these documents serve to guide state governments to prioritize oxygen equipment when budgeting for and procuring medical equipment.

Once these supportive policies were in place, the program worked closely with the State Ministries of Health in Kaduna, Kano, and Niger to implement the policies.

Domain 2: Strengthening procurement system

The program supported the planning, procurement, and installation of oxygen equipment in the pediatric wards of 29 hospitals. Between March and April 2017, the program conducted pre-installation assessments in the pediatric outpatient units and inpatient wards of the facilities to

evaluate whether the departments had existing equipment (e.g. functional pulse oximeters and oxygen concentrators) and the condition of the department's infrastructure, such as bed capacity and number of electrical outlets. Based on the pre-installation assessments, the program estimated the number of oxygen concentrators, pulse oximeters, and accessories required to fully equip the departments. Next, Tender Evaluation Committees (TECs), consisting of SMOH officials and CHAI technical staff, identified product specifications for oxygen concentrators and pulse oximeters that would meet Nigeria's context and produced public tenders for competitive bidding. The TECs also developed evaluation tools to assess the bids. The assessment considered after-sales support such as maintenance and warranty contracts in addition to cost. Many in-country suppliers were unfamiliar with this tendering process, particularly the rigorous specifications for devices being sought, so the program actively engaged suppliers to help them understand the tender requirements and the requested information. Between two and eight suppliers submitted bids for each state, and one supplier was selected for each state based on the bid assessments. The state governments, through domestic financial resources, and CHAI, through a grant from the Bill and Melinda Gates Foundation, co-funded the purchase of the equipment. In total, the program spent US$ 518,000 on equipment procurement and installation. A complete list of equipment purchased is included in Supplementary Table 1 and dates of installation are shown in Supplementary Table 2.

Domain 3: Training healthcare workers and biomedical engineers

Between November and December 2017, the program trained 1,206 healthcare workers, including doctors, nurses, pharmacists, and community health extension workers, in each facility on hypoxemia management. The training curriculum used was adapted from a program being implemented in Southwest Nigeria.[29] The curriculum covered use of pulse oximeters, delivery of

oxygen using cylinders and concentrators, and basic equipment maintenance. The program partnered with three pediatricians involved in the design of the Southwest Nigerian program's curriculum. The pediatricians trained 21 health professionals (three chief matrons and 18 doctors) over a 5-day period. The 28 health professionals were from the 3 program states and were nominated by the health facilities. The program then coordinated and supported these 21 health professionals to conduct 2-day trainings in their respective states. Separate trainings were conducted for different healthcare staff cadres. Doctors and pharmacists were trained together while nurses and community heath extension workers were trained together. Healthcare staff from multiple facilities were also brought together for the trainings. All doctors, nurses, pharmacists, and community health extension workers who worked in the pediatric inpatient and neonatal units were recruited for the trainings. In addition, pre-service and in-service curricula for healthcare providers were updated to include hypoxemia management for children, including screening using pulse oximetry and the safe, rational application of oxygen therapy when indicated.

The program also trained 15 biomedical engineers and technicians on the maintenance and repair of oxygen equipment. The program partnered with Lagos University Teaching Hospital and Engineering World Health to conduct a hands-on, 5-day training that covered basic principles of physics related to oxygen and pulse oximetry, oxygen hazards and safety, detailed description on the components of oxygen concentrators and pulse oximeters, planned preventative maintenance, and inventory management. Oxygen analyzers were included in the equipment procurement so that biomedical engineers could routinely monitor the functionality of the oxygen concentrators.

Domain 4: Ongoing monitoring and support

Lastly, the program worked closely with existing hospital committees to initiate quality improvement activities in support of pulse oximetry adoption and oxygen use. The program

identified indicators for measuring progress on pneumonia and hypoxemia management and developed a monthly summary form to collect data on the indicators (Supplemental Document 1 and 2). The indicators included percent of under-five pneumonia admissions screened for hypoxemia with pulse oximetry and percent of under-five pneumonia admissions with hypoxemia treated with oxygen. In November 2017, the program trained 95 medical records officers from program facilities on collecting the indicators. Beginning in February 2018, the program worked with the trained medical records officers to leverage existing monthly committee meetings to present the indictors and summary forms. In Kaduna, the program used monthly maternal and perinatal disease meetings; in Kano, the program used health management committee meetings; and in Niger, the program worked within quality improvement teams established by the Health Systems Development Foundation (HSDF), an initiative in Nigeria aimed at strengthening primary healthcare. Finally, the program worked with each state's HMB to set up a quality improvement desk at the HMB office to help the HMB provide greater leadership and accountability over performances of the facilities. The quality improvement desk collated the data from each facility and shared the results at regular HMB meetings.

Participants

Study participants included all patients under five years of age that were admitted by the pediatric inpatient unit, neonatal unit, or emergency unit of the study hospitals due to pneumonia. The pediatric inpatient units of the hospitals primarily cared for children up to age 12 years. Four of the facilities had separate neonatal units. In the other 25 facilities, sick neonates were often referred to tertiary health facilities though sometimes admitted to the pediatric ward along with older infants. Eight hospitals had emergency pediatric units that would sometimes admit severe cases until transferring to the pediatric inpatient unit. Study nurses retrospectively reviewed the unit

registers each month to identify under-five patients admitted with pneumonia. Registers in Nigeria are intended to catalogue every patient seen by the unit, though many are not well kept and may miss patients (See Limitations). Registers often include the patient's name, age, condition for which the patient is being admitted, date of admission, and outcome (e.g. discharge, death, or referred). All patients under-five with an admission diagnosis denoting pneumonia, regardless of severity (e.g. bronchopneumonia, community acquired pneumonia, lobar pneumonia, aspiration pneumonia, lower respiratory tract infection, etc.) were included in the study.

Data collection methods

Nurses from the study facilities were recruited to lead the data collection as they are familiar with the medical record keeping practices at their respective facility. A 3-day training was provided to nurse data collectors at the beginning of the study and a refresher training was conducted every six months. The trainings covered the sampling procedure and data capturing and uploading using the electronic software. Study nurses retrieved the medical charts of under-five patients admitted with pneumonia, extracted data on the patient's care at the facility, including the patient's presenting symptoms, diagnostic exams performed and their results, treatments administered, and outcomes, and directly entered the data onto an Android tablet programmed with the data entry application SurveyCTO (Dobility Inc, Boston MA USA).

Data analysis

We first created a binary variable to segment patients admitted between January to October 2017 ("pre-intervention period") from patients admitted between February to August 2018 ("post-intervention period"). Patients admitted between November 2017 and January 2018 were excluded from the analysis since trainings and equipment installation occurred during this period. Descriptive analysis was conducted to compare characteristics of the patient population during the

pre- and post-intervention periods. The outcome variables were whether the patient chart had a written blood oxygen saturation measurement (SpO_2) and, among patients with hypoxemia, whether they were prescribed oxygen. We assumed that if SpO_2 or oxygen therapy were not documented in the medical chart, then the patient did not receive pulse oximetry or oxygen treatment. We defined hypoxemia according to clinical signs as few children had documented SpO_2 in the pre-intervention period. The symptom list used to define hypoxemia was drawn from the WHO's guidelines on oxygen administration in children in low-resource settings and included the following: central cyanosis, grunting, nasal flaring, crackles, signs of respiratory distress, or inability to feed, drink, or breastfeed. Patient charts with at least one of the symptoms listed were coded as having hypoxemia. As above, we assumed that if these symptoms were not written in the patient medical chart, then the patient did not have the symptoms. As a secondary outcome, we also report on the proportion of patients that received oxygen among patients with confirmed hypoxemia using the WHO-recommended threshold of $SpO_2<90\%$. We used multilevel multivariate logistic regression models with random intercepts for state and facility to test whether the program period was significantly associated with increased measurement of SpO_2 and, among patients with hypoxemia, increased prescription of oxygen. Logistic regression models were adjusted for the child's age, sex, duration of admission, symptoms, and outcome. Data analysis was conducted using Stata 14 (StataCorp, College Station TX, USA).

Research ethics

The study was approved by Chesapeake IRB (Protocol number Pro00021493) in the United States and by the Research Ethics Committees of Kaduna (MOH/ADM/744/VOL.1/529), Kano (MOH/OFF/797/T.1/333), and Niger (MOH/STA/95/1/V-1). Informed written consent to review facility records were requested from the head of medical records at each facility.

RESULT

Sampling results

Figure 1 presents the participant flow diagram showing the number of identified pneumonia cases in the pre-intervention period (January to October 2017) and post-intervention period (February to August 2018). During the pre-intervention periods, 1,890 under-five pneumonia cases were identified from the pediatric inpatient register, of which 1,642 (91%) patient medical charts were located for review and data extraction. Upon review, we removed 41 (2%) patient medical charts since the diagnoses in the patient medical chart did not fit the inclusion criteria.

In the post-intervention, 2,813 under-five pneumonia cases were identified and 1,826 (65%) patient medical charts were reviewed for data extraction. We removed 9 (0.5%) patients from the dataset as the diagnoses in the patient medical chart did not fit the inclusion criteria.

The final dataset contained 3,418 patients with 1,601 patient medical charts included in the pre-intervention period and 1,817 patient medical charts included in the post-intervention period.

Participant characteristics

Table 2 presents characteristics of the patients by intervention period. In the post-intervention period, a greater proportion of the study population was from hospitals in Kaduna state (16.1% from the pre-intervention period vs. 30.0% from the post-intervention period) while a lower proportion was from Kano (55.3% vs. 46.1%) and Niger state (28.7% vs. 23.9%). The proportion of patients who were female did not significantly change between pre-intervention and post-intervention periods (45.0% vs. 44.8% female; $p=0.945$). The mean age of patients in the post-intervention period was slightly younger (1.33 years vs. 1.17 years; $p<0.001$). Patients in the post-intervention period also had shorter lengths of admissions (7.07 days vs. 3.95 days; $p<0.001$). Prevalence of documented symptoms differed between intervention periods with 13 out of 26

symptoms being significantly different between periods ($p<0.05$). Prevalence of nine out of the 13 symptoms were lower in the post-intervention period than the pre-intervention period, including convulsions, crackles or crepitations, diarrhea, malnourishment, and respiratory distress. Prevalence of four symptoms were higher in the post-intervention period: fast breathing/tachypnea, lower-chest indrawing, nasal flaring, and unable to unable to drink normally. Cough, fever, and difficulty breathing were the most common symptoms in both periods. Malaria was a common secondary diagnosis in both periods – whether laboratory confirmed or clinically diagnosed. In the pre-intervention period, 23.9% of patients had malaria and in the post-intervention period, 24.1% had malaria. There was no significant difference between the two periods ($p=0.904$). There was no difference between periods in the proportion of patients who died at the facility (5.6% vs. 6.2%; $p=0.514$).

Pulse Oximetry

Use of pulse oximetry increased rapidly after program interventions were implemented (Table 3). Between January and October 2017, the percent of patients with pneumonia assessed with pulse oximetry ranged between 2.4% and 26.0%. In February and March 2018, the first two months after oxygen equipment were installed and healthcare workers were trained, the percent of pneumonia patients receiving pulse oximetry was 56.5% and 81.7%, respectively. By August 2018, 94.5% of pneumonia patients had pulse oximetry done.

Table 4 shows the proportion of patients with SpO_2 measurements before and after program interventions. Use of pulse oximetry increased from 13.6% (95% confidence interval (CI): 12.2%, 15.2%) to 82.4% (95% CI: 80.7%, 84.1%). After adjusting for patient characteristics in multilevel multivariate regression, we found that the odds of a patient being screened for hypoxemia with pulse oximetry was 5.0 (95% CI: 4.3, 5.7; $p<0.001$) times greater in the post-intervention period

than the pre-intervention period. The odds of screening for hypoxemia were 5.9 (95% CI: 4.5, 7.4; p<0.001) times greater in the post-intervention period in Kaduna, 4.4 (95% CI: 2.6, 6.2; p<0.001) times greater in Kano, and 6.7 (95% CI: 5.4, 8.0; p<0.001) times greater in Niger.

Oxygen Treatment

Table 5 presents oxygen use for patients with hypoxemia. The proportion of cases with documented clinical signs of hypoxemia that were treated with oxygen before interventions was 22.8% (95% CI=18.8%, 27.2%). After program interventions, the proportion increased to 77.9% (95% CI=73.9%, 81.5%). After adjusting for other patient characteristics, we found the post-intervention period was associated with an increased odds ratio of 5.0 (95% CI=4.2, 5.9; p<0.001).When limiting the analysis to only patients with a documented SpO_2<90%, we found only 97 patient medical charts fitting that criteria prior to the program interventions but 874 patients after the program interventions. Among these cases, 88.9% (95% CI=79.3%, 94.3%) received oxygen prior to program interventions and 97.4% (95% CI=96.1%, 98.3%) received oxygen after program interventions.

DISCUSSION

Oxygen is an essential therapy but access to oxygen therapy, including pulse oximetry, is highly limited in low resource countries like Nigeria. Through this implementation study, we sought to determine whether it is feasible to scale-up pulse oximetry and oxygen treatment in a low-resourced environment through strengthening existing government structures and processes. Technical assistance was provided to the government in designing, implementing, and monitoring the interventions, but the program avoided creating parallel systems for the sole purpose of the project. For example, the program worked with the state government's existing procurement office to improve their tendering process and technical evaluations of bids. The

program supported the state's procurement office to develop rigorous technical specifications for pulse oximeters and oxygen concentrators that would meet the local and environmental context and worked with the government to also forecast the number of accessories and spare parts required for ensuring the pulse oximeters and oxygen concentrators would remain functional for the next several years. The results of the study demonstrate that interventions delivered through this approach could rapidly improve access and coverage of pulse oximetry and oxygen therapy. The percent of pediatric patients with pneumonia receiving pulse oximetry and oxygen significantly increased within the first two of months after trainings and equipment installation. These practices continued to increase and sustain through the end of the study period. By evaluating a program under this context, the study provides evidence that results seen in smaller controlled trials can be replicated at a larger scale through national systems.

While this approach was effective at achieving high levels pulse oximetry and oxygen treatment access and utilization, the approach was time intensive and required frequent recalibration of project timelines. Aspects of the project that required greater time and effort were in coordinating development of policies and guidelines, supporting suppliers to submit bids that met the tender requirements, and supporting facilities to monitor ongoing performance. Challenges in these areas led to project delays, however, we believe this approach was important for building capacity within existing government structures. This approach has also catalyzed sustained efforts from the government to improve hypoxemia management. With minimal support from NGOs, the state government of Kano invested additional domestic resources to increase access to pulse oximeters and oxygen systems to an additional 12 facilities.

Although there are many unique aspects of the Nigerian socioeconomic and political context, and those of Kaduna, Kano, and Niger states, many LMICs face similar challenges: lack of clear

policies and guidelines pertaining to hypoxemia management, weak and inefficient systems for managing medical device procurement, need to build capacities of healthcare workers, biomedical engineers, and other allied health professionals, and poorly kept medical record data. Addressing these areas in other LMICs will likely be important for scaling up pulse oximetry and oxygen therapy.

Pulse oximetry coverage

Previous studies introducing pulse oximetry were also able to achieve high rates of adoption after study interventions. The study in Southwest Nigeria provided pulse oximeters and oxygen systems to 12 hospitals, trained healthcare workers on basic oximetry, conducted quarterly supervisory visits, and provided an on-site project nurse for practical support. Through these interventions, the study was able to increase the percent of child admissions receiving pulse oximetry from 3% to 95% by the end of the study.[30] All facilities in the study achieved >50% coverage within the first 2-3 months of the study and >90% coverage within 6-12 months. In Lao PDR, Gray et al provided pulse oximeters and oxygen concentrators to 10 hospitals and initial training. The study also supported repairs and replacement of non-functional equipment throughout the evaluation. The percent of admissions receiving pulse oximetry increased from ~1% to ~35% for all pneumonia cases and ~1% to ~55% for severe pneumonia cases.[14] High rates of adoption have also been demonstrated in outpatient units in LMICs. In Malawi, McCollum et al. found that 94% of children seen for outpatient services or by community health workers were checked with pulse oximetry after provision of pulse oximeters and training.[31] Pulse oximeters are relatively simple medical devices to use which may facilitate their rapid adoption initially. However, ingraining this practice will require continued leadership from the government and within the facilities. Graham et al. found that several factors may influence

pulse oximetry adoption beyond training and provision, including shifting attitudes (e.g. pulse oximetry can make a healthcare worker's job easier) and gaining positive experiences through pulse oximetry use (e.g. saving a person's life due to pulse oximetry use). This program aimed to ensure that adoption of pulse oximetry would be sustained by working through existing government systems.

Hypoxemia prevalence

One of the implications of the increased use of pulse oximeters is that substantially more patients were found to have hypoxemia. Prior to the study interventions, only 98 out of 1,601 (6%) children admitted with pneumonia were found to have hypoxemia by pulse oximetry but once pulse oximetry was introduced into the facilities, 874 out of 1,817 (48%) pneumonia admissions were found to have hypoxemia using pulse oximetry. The true underlying prevalence of hypoxemia is unlikely to have changed this dramatically. Rather, the difference in hypoxemia prevalence found between study periods is driven by use of pulse oximeters, and the lack of available pulse oximeters in facilities prior to the program likely led to many missed hypoxemia cases. Increased access to pulse oximeters should be a key priority in global health in order to improve detection and treatment of hypoxemia.

The prevalence of hypoxemia found once pulse oximetry was introduced is higher than what Subhi et al found in a systematic review in 2009. The study found the median prevalence of hypoxemia was 13% among hospitalized, WHO-defined severe and very severe pneumonia, and in Africa, the systematic review found less than 10% of pneumonia cases had hypoxemia.[7] However, more recent studies have found higher prevalence of hypoxemia among children with pneumonia. In Southwest Nigeria, Graham et al. found 28% of children <15 years old admitted with acute lower respiratory infection had hypoxemia, while other studies in Nigeria have

reported similarly high rates of hypoxemia in children admitted with pneumonia to our study (42-49%).[9,32,33] Other studies elsewhere in Africa have also reported higher prevalence of hypoxemia in children diagnosed with pneumonia: 28-57%.[34-37]

Oxygen therapy coverage

Our study also found that coverage of oxygen therapy for children with hypoxemia increased after program interventions. Among children with signs and symptoms suggestive of hypoxemia, coverage of oxygen therapy improved from 23% to 78%, with 97% of children with hypoxemia detected via pulse oximetry receiving oxygen in the post-intervention phase. Discussions with healthcare workers during the monthly committee meetings indicated that healthcare workers relied primarily on pulse oximetry to guide oxygen administration. The practice changes seen in our study are higher than changes observed in the study in Southwest Nigeria where coverage of oxygen increased from 19% to 33% among children with signs of hypoxemia and 74% to 82% among children with SpO_2<90%. Similarly, Gray et al found only modest increases in oxygen administration practices with minimal differences from control facilities. In addition to trainings and supporting monthly committee meetings to change oxygen administration practices, the program's work on changing medical chart forms to facilitate better documentation of oxygen administration may be a reason why this program found greater evidence of improved oxygen coverage. The program helped revise medical administration forms used in these facilities to include oxygen.

Oxygen systems availability and functionality

Similar to previous studies in LMICs on oxygen availability[5,18-21], we found baseline availability of functional oxygen systems were low. Although nearly all the study facilities provided oxygen therapy services, a deeper investigation to assess the availability of oxygen equipment in the

pediatric inpatient units found that only 13/29 of the pediatric inpatient units had an oxygen source and only 6 of those had tubing to deliver the oxygen to patients. Interviews at the facilities found that if the facility did have oxygen equipment, it was prioritized to operating theatres. We also found many non-functioning oxygen concentrators during the initial assessment. Biomedical engineers did not have the parts to fix them and there also were concentrators across a wide range of manufacturers. The program aimed to ensure sustainability of the equipment procured by working through the state governments to develop technical specifications that met the local context and consolidate procurement. Procurement tenders also included spare parts for repairs and after-sales servicing agreements with the suppliers. Further studies are required to assess whether these interventions lead to greater durability of the oxygen systems.

Mortality impact of oxygen systems strengthening

Unlike other studies evaluating the impact of improved oxygen systems in hospital settings, we were unable to detect a significant difference in mortality after the introduction of improved oxygen systems.[12-15] There may be several reasons that we did not find a mortality change. First, constructing reliable, facility-based case fatality estimates is complicated by the program's influence on diagnosis and documentation practices. We found 923 more pneumonia admission cases in the patient registers during the post-intervention period (2,813) than the pre-intervention period (1,890) despite the post-intervention period being 3 months shorter. At least some of this increase is likely attributable to documentation improvements during the program. However, such a large increase is not likely the result of documentation improvements alone and may reflect frequent misdiagnosis of pneumonia in the pre-intervention period. Program interventions to strengthen pneumonia diagnosis and hypoxemia screening may have led to an increase in pneumonia cases identified and admitted in the post-intervention period, implying a larger

proportion of severely ill patients at a higher risk of death in the post-intervention period. As shown in Table 2, significantly more children admitted in the post-intervention period had documented symptoms of severe illness, such as lower chest-indrawing (11.2% vs 4.5%, $p<0.001$) and nasal flaring (6% vs 2.3%, $p<0.001$), than in the pre-intervention period. While this may reflect improved documentation practices, it is also consistent with an increase in admission of severely ill children. Unfortunately, rigorous analysis of differences in patient characteristics and outcomes (e.g. time to mortality, severity of illness on admission) was not possible as the program reviewed *in situ* facility medical records which did not reliably contain uniform information on these variables.

Other factors may have limited the program's impact on mortality despite large improvements in hypoxemia diagnosis and oxygen administration. The quality of oxygen administration may have affected the effectiveness of oxygen therapy provided to patients in the post-intervention study. As previously noted, other studies have demonstrated that concentrators in low-resource settings frequently produce low-quality oxygen or were not operating optimally.[14,20,21] As part of the program's efforts to ensure equipment functionality, BMEs routinely monitored the quality of oxygen produced. No significant or systemic quality issues were uncovered by this monitoring during the program. Likewise, sub-standard clinical practices related to oxygen administration could have negated the impact of increased hypoxemia diagnosis and oxygen administration on patient outcomes. While the program provided comprehensive training on hypoxemia management to facility staff, oxygen administration is complex and potentially dangerous—especially for younger, smaller children. However, it is more likely that the quality of hypoxemia management and oxygen administration was better in the post-intervention phase. Evidence from the patient chart reviews found that 63% of patients who were given oxygen in the post-

intervention phase also had documentation of a prescribed flow rate, target SpO_2 value, and monitoring plan for stopping oxygen administration and checking whether the patient experiences desaturation under room air. Only 20% of patients who received oxygen in the pre-intervention phase had such documentation. While we do not see evidence that oxygen was administered inappropriately, quality of care is a highly important consideration when increasing access to oxygen. Overall, we caution readers when interpreting the study's results regarding mortality as the study was not designed to evaluate the program's impact on mortality.

Limitations

The study methodology used retrospective reviews of patient medical charts to evaluate changes in case-note-recorded clinical practices. One of the limitations of this method is that in Nigeria, patient medical records are not well kept and preserved in the facility, thus introducing selection bias. As mentioned above, this is reflected in the large increase in pneumonia cases that were identified in the registers – 1,890 in the pre-intervention phase vs 2,813 in the post-intervention phase – and the large difference in the proportion of medical charts located for review – 87% (1642/1890) versus 65% (1826/2813). While the increase in pneumonia cases identified between phases could be explained by improved diagnoses due to program interventions, some of the increase may also be explained by better record maintenance as well. The low proportion of medical charts located for review in the post-intervention phase was a result of lack of funding for printing medical chart forms and space for storing those charts, particularly at high-volume facilities in Kaduna and Kano. Instead, documentation of patient care were written in books purchased by the patient and taken home after their discharge. Selection bias may change the effect estimates, but it is unlikely to negate the substantial observed changes in pulse oximetry and oxygen administration practices.

A second study limitation is that we were only able to evaluate the outcome of oxygen prescription among patients with documented symptoms associated with hypoxemia rather than based on SpO_2 values. However, symptoms are a poor predictor of hypoxemia. In addition, there is no standardized method for symptom assessment and documentation in Nigeria. Symptoms are documented in the patient's admissions note as unstructured texts and can vary by the healthcare worker doing the patient assessment and notes. Thus, there may also be selection bias in the sub-population used for analyzing oxygen treatment practices. Many patients who may have displayed symptoms associated with hypoxemia may have been missed, particularly in the pre-intervention phase. The program trained healthcare workers on recognizing symptoms associated with hypoxemia, and as shown in Table 2, there was an increase in the proportion of patients with documented symptoms associated with hypoxemia, such as nasal flaring. While healthcare workers were better trained to recognize symptoms of hypoxemia, the increase in hypoxemia cases found between periods is most likely due to pulse oximeters being available and used at the facilities. Overall, we believe that the selection bias due to differences in hypoxemia symptom recognition is more likely to overestimate oxygen provision in the pre-intervention phase than it is to underestimate the outcome. We assume that patients with documented signs associated with hypoxemia are more likely to receive oxygen than those whose symptoms were missed.

As mentioned above, there were likely differences in pneumonia case identification between pre-intervention and post-intervention phases due to trainings implemented by the program. During the trainings, diagnosis of pneumonia was a key feature of the training content, and we observed increased recognition of key symptoms such as lower chest in-drawing and nasal flaring in the post-intervention period. This likely resulted in more numbers of pneumonia cases being identified in the post-intervention phase and affects comparability of patient populations before

and after program interventions. Due to improved pneumonia case identification, changes in the patient population characteristics between pre-intervention and post-intervention period should be interpreted cautiously, including differences in the distribution by state, age, gender, duration of admission, and outcome. However, the study's findings on pulse oximetry screening and oxygen administration practices are unlikely to be affected by improved pneumonia case classification in the post-intervention period. While there may have been missed pneumonia cases in the pre-intervention period, pulse oximetry screening and oxygen administration would still have remained low since the facilities did not have pulse oximeters and reliable oxygen systems prior to the program interventions. Even with a much greater number of pneumonia cases being admitted to the facilities in the post-intervention period, the high coverage of both pulse oximetry and oxygen treatment suggests that these interventions were feasible to introduce in high-burden, low-resourced settings.

Lastly, the study design did not include a control group to account for potential effects over time, such as economic changes over the program period or other initiatives by the government or other partners that may have influenced these results. To the best of our knowledge, there were no other initiatives that could feasibly have improved pulse oximetry screening and oxygen administration in the facilities. There were some external factors, such as an economic downturn and healthcare worker strikes, that did occur in the program areas and facilities that may have affected healthcare seeking patterns and healthcare services. These factors would have likely led to worse healthcare services over the program period rather than explain the improved hypoxemia management practices observed.

CONCLUSION

Increasing pulse oximetry and oxygen therapy access and utilization in a low-resourced environment is achievable through a multi-faceted program focused on strengthening government-owned systems.

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AUTHOR CONTRIBUTIONS

CF, TM, TO, MG, SG, FL, AO, MM, AA, TO, AJ, KS, AB, JH, OW, and FL were involved in the study design and oversaw data collection. CF, TM, and FL contributed to the data analysis and manuscript preparation. All authors reviewed and provided feedback on the manuscript.

AUTHORSHIP DECLARATION OF CONFLICTS OF INTEREST

Members of the authorship team were employed by the Clinton Health Access Initiative and received funding to design, implement, and evaluate the program described. The authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no other conflicts of interest.

REFERENCES

1. World Health Organization. *Oxygen therapy for children: a manual for health workers.* 2016.
2. Onyango FE, Steinhoff MC, Wafula EM, Wariua S, Musia J, Kitonyi J. Hypoxaemia in young Kenyan children with acute lower respiratory infection. *BMJ.* 1993;306(6878):612-615.
3. Usen S, Weber M, Mulholland K, Jaffar S, Oparaugo A, Omosigho C, Adegbola R, Greenwood B. Clinical predictors of hypoxaemia in Gambian children with acute lower respiratory tract infection: prospective cohort study. *BMJ.* 1999;318(7176):86-91.
4. Lozano JM. Epidemiology of hypoxaemia in children with acute lower respiratory infection. *Int J Tuberc Lung Dis.* 2001;5(6):496-504.
5. Wandi F, Peel D, Duke T. Hypoxaemia among children in rural hospitals in Papua New Guinea: epidemiology and resource availability--a study to support a national oxygen programme. *Ann Trop Paediatr.* 2006;26(4):277-284.
6. Mwaniki MK, Nokes DJ, Ignas J, Munywoki P, Ngama M, Newton CR, Maitland K, Berkley JA. Emergency triage assessment for hypoxaemia in neonates and young children in a Kenyan hospital: an observational study. *Bull World Health Organ.* 2009;87(4):263-270.
7. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T, Hypoxaemia in Developing Countries Study G. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. *Lancet Infect Dis.* 2009;9(4):219-227.

8. Foran M, Ahn R, Novik J, Tyer-Viola L, Chilufya K, Katamba K, Burke T. Prevalence of undiagnosed hypoxemia in adults and children in an under-resourced district hospital in Zambia. *Int J Emerg Med.* 2010;3(4):351-356.

9. Orimadegun AE, Ogunbosi BO, Carson SS. Prevalence and predictors of hypoxaemia in respiratory and non-respiratory primary diagnoses among emergently ill children at a tertiary hospital in south western Nigeria. *Trans R Soc Trop Med Hyg.* 2013;107(11):699-705.

10. Lazzerini M, Sonego M, Pellegrin MC. Hypoxaemia as a Mortality Risk Factor in Acute Lower Respiratory Infections in Children in Low and Middle-Income Countries: Systematic Review and Meta-Analysis. *PLoS One.* 2015;10(9):e0136166.

11. Morgan MC, Maina B, Waiyego M, Mutinda C, Aluvaala J, Maina M, English M. Pulse oximetry values of neonates admitted for care and receiving routine oxygen therapy at a resource-limited hospital in Kenya. *Journal of paediatrics and child health.* 2017.

12. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, Subhi R, Peel D. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. *The Lancet.* 2008;372(9646):1328-1333.

13. Enarson PM, Gie RP, Mwansambo CC, Maganga ER, Lombard CJ, Enarson DA, Graham SM. Reducing deaths from severe pneumonia in children in Malawi by improving delivery of pneumonia case management. *PLoS One.* 2014;9(7):e102955.

14. Gray AZ, Morpeth M, Duke T, Peel D, Winter C, Satvady M, Sisouk K, Prasithideth B, Detleuxay K. Improved oxygen systems in district hospitals in Lao PDR: a prospective field trial of the impact on outcomes for childhood pneumonia and equipment sustainability. *BMJ Paediatr Open.* 2017;1(1):e000083.

15. Graham HR, Bakare AA, Ayede AI, Gray AZ, McPake B, Peel D, Olatinwo O, Oyewole OB, Neal EF, Nguyen CD, et al. Oxygen systems to improve clinical care and outcomes for children and neonates: a stepped-wedge cluster-randomised trial in Nigeria. *PLoS Medicine.* 2019 in press.

16. English M, Gathara D, Mwinga S, Ayieko P, Opondo C, Aluvaala J, Kihuba E, Mwaniki P, Were F, Irimu G, et al. Adoption of recommended practices and basic technologies in a low-income setting. *Arch Dis Child.* 2014;99(5):452-456.

17. Graham HR, Ayede AI, Bakare AA, Oyewole OB, Peel D, Falade AG, Duke T. Oxygen for children and newborns in non-tertiary hospitals in South-west Nigeria: A needs assessment. *Afr J Med Med Sci.* 2016;45(1):31-49.

18. Nabwire J, Namasopo S, Hawkes M. Oxygen Availability and Nursing Capacity for Oxygen Therapy in Ugandan Paediatric Wards. *Journal of Tropical Pediatrics.* 2018;64(2):97-103.

19. Belle J, Cohen H, Shindo N, Lim M, Velazquez-Berumen A, Ndihokubwayo JB, Cherian M. Influenza preparedness in low-resource settings: a look at oxygen delivery in 12 African countries. *J Infect Dev Ctries.* 2010;4(7):419-424.

20. Bakare AA, Graham H, Ayede AI, Peel D, Olatinwo O, Oyewole OB, Fowobaje KR, Qazi S, Izadnegahdar R, Duke T, et al. Providing oxygen to children and newborns: a multi-faceted technical and clinical assessment of oxygen access and oxygen use in secondary-level hospitals in southwest Nigeria. *Int Health.* 2019.

21. La Vincente SF, Peel D, Carai S, Weber MW, Enarson P, Maganga E, Soyolgerel G, Duke T. The functioning of oxygen concentrators in resource-limited settings: a situation assessment in two countries. *Int J Tuberc Lung Dis.* 2011;15(5):693-699.

22. Duke T, Subhi R, Peel D, Frey B. Pulse oximetry: technology to reduce child mortality in developing countries. *Annals of tropical paediatrics.* 2009;29(3):165-175.

23. Duke T, Graham SM, Cherian MN, Ginsburg AS, English M, Howie S, Peel D, Enarson PM, Wilson IH, Were W, et al. Oxygen is an essential medicine: a call for international action. *Int J Tuberc Lung Dis.* 2010;14(11):1362-1368.

24. Ginsburg AS, Izadnegahdar R, Klugman KP. World Pneumonia Day 2016: pulse oximetry and oxygen. *Lancet Glob Health.* 2016;4(12):e893-e894.

25. McCollum ED, King C, Colbourn T, Graham H, Bernstein M, Wilson IH, Checkley W. Pulse oximetry in paediatric primary care in low-income and middle-income countries. *Lancet Respir Med.* 2019.

26. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, Lawn JE, Cousens S, Mathers C, Black RE. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet.* 2016;388(10063):3027-3035.

27. Wollum A, Burstein R, Fullman N, Dwyer-Lindgren L, Gakidou E. Benchmarking health system performance across states in Nigeria: a systematic analysis of levels and trends in key maternal and child health interventions and outcomes, 2000-2013. *BMC Med.* 2015;13:208.

28. National Population Commission (NPC) [Nigeria] and ICF. *Nigeria Demographic and Health Survey 2018.* Abuja, Nigeria, and Rockville, Maryland, USA: NPC and ICF;2019.

29. Graham HR, Ayede AI, Bakare AA, Oyewole OB, Peel D, Gray A, McPake B, Neal E, Qazi S, Izadnegahdar R, et al. Improving oxygen therapy for children and neonates in

secondary hospitals in Nigeria: study protocol for a stepped-wedge cluster randomised trial. *Trials.* 2017;18(1):502.

30. Graham HR, Bakare AA, Gray A, Ayede AI, Qazi S, McPake B, Izadnegahdar R, Duke T, Falade AG. Adoption of paediatric and neonatal pulse oximetry by 12 hospitals in Nigeria: a mixed-methods realist evaluation. *BMJ Global Health.* 2018;3(e000812).
31. McCollum ED, King C, Deula R, Zadutsa B, Mankhambo L, Nambiar B, Makwenda C, Masache G, Lufesi N, Mwansambo C, et al. Pulse oximetry for children with pneumonia treated as outpatients in rural Malawi. *Bull World Health Organ.* 2016;94(12):893-902.
32. Ibraheem RM, Johnson WB, Abdulkarim AA. Hypoxaemia in hospitalised under-five Nigerian children with pneumonia. *West Afr J Med.* 2014;33(1):37-43.
33. Graham H, Bakare AA, Ayede AI, Oyewole OB, Gray A, Peel D, McPake B, Neal E, Qazi SA, Izadnegahdar R, et al. Hypoxaemia in hospitalised children and neonates: A prospective cohort study in Nigerian secondary-level hospitals. *EClinicalMedicine.* 2019;16:51-63.
34. Bassat Q, Lanaspa M, Machevo S, O'Callaghan-Gordo C, Madrid L, Nhampossa T, Acacio S, Roca A, Alonso PL. Hypoxaemia in Mozambican children <5 years of age admitted to hospital with clinical severe pneumonia: clinical features and performance of predictor models. *Trop Med Int Health.* 2016;21(9):1147-1156.
35. Wandeler G, Pauchard JY, Zangger E, Diawara H, Gehri M. Which clinical signs predict hypoxaemia in young Senegalese children with acute lower respiratory tract disease? *Paediatrics and International Child Health.* 2015;35(1):65-68.

36. Salah ET, Algasim SH, Mhamoud AS, Husian NEOSA. Prevalence of hypoxemia in under-five children with pneumonia in an emergency pediatrics hospital in Sudan. *Indian Journal of Critical Care Medicine.* 2015;19(4):203-207.

37. Tolla HS, Letebo M, Asemere YA, Belete AB, Tumbule TC, Fekadu ZF, Woyessa DB, Ameha S, Feyisa YM, Lam F. Use of pulse oximetry during initial assessments of children under five with pneumonia: a retrospective cross-sectional study from 14 hospitals in Ethiopia. *J Glob Health Rep.* 2019;3(e2019016).